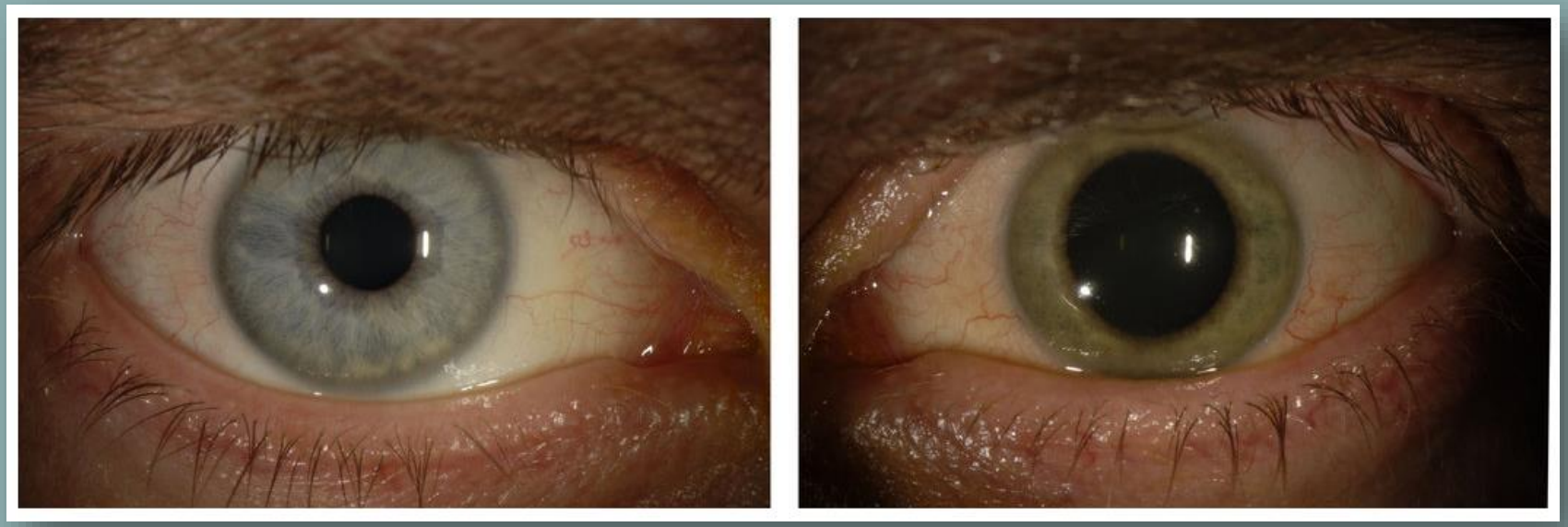
Key Articles & Clinical Developments of 2015 in Family Medicine

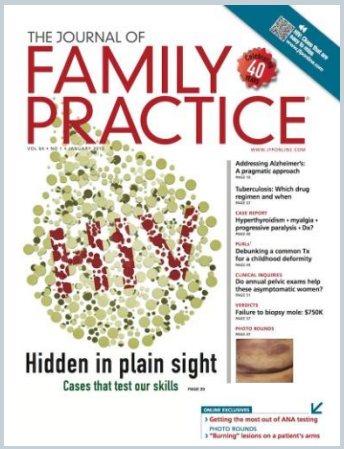
WHAT WAS IMPORTANT…

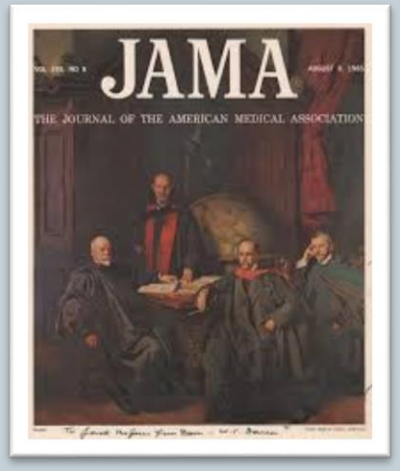
…AT LEAST TO SOME OF US

DAN WALDMAN, MD
UNM FAMILY AND COMMUNITY MEDICINE



What This Talk is About…





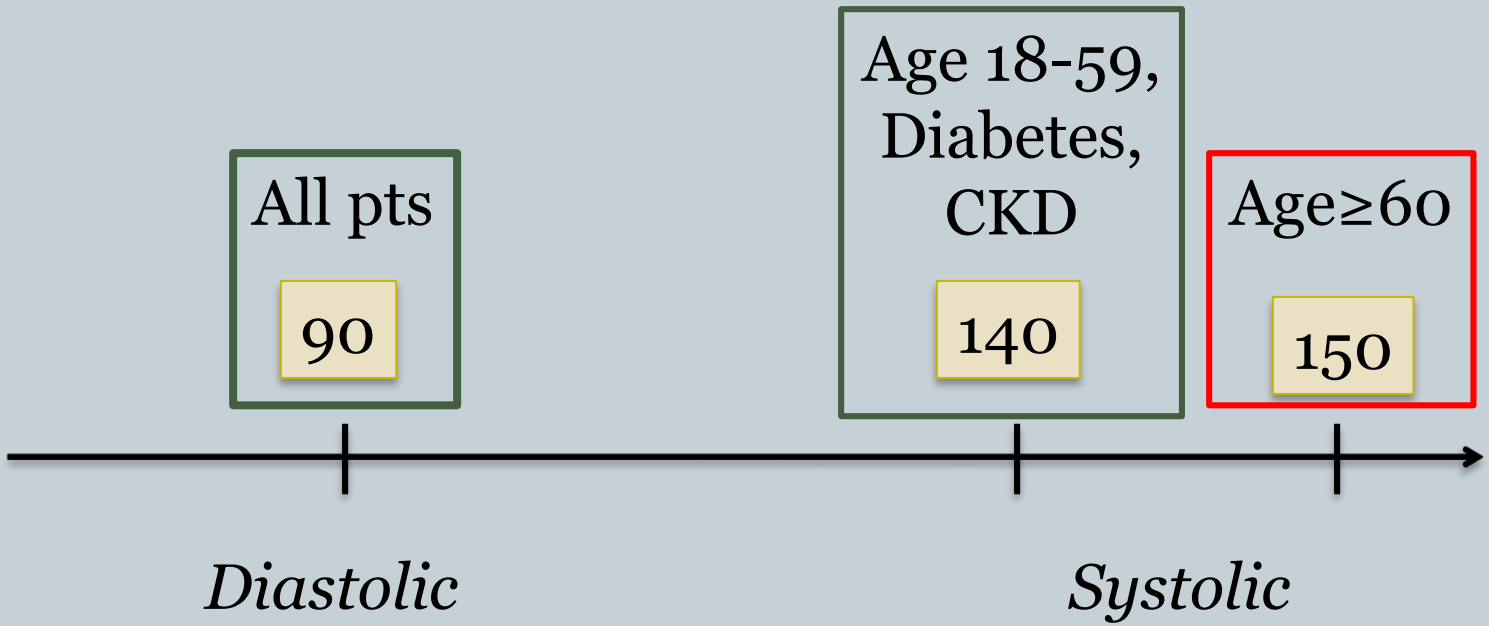
How Did I Choose What I Chose?

- Our Faculty
- Essential Evidence
- Journal Watch
- “Top of 2015” Lists

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

The Blood Pressure Saga Continues

Reminder: JNC8 BP Goals



(*JNC8 was based largely on RCT data*)

SPRINT Trial

- ACCORD (2010): treating pts with DM2 and hypertension to systolic goal of <120 wasn't better than <140 (4,733 patients enrolled)
- Now SPRINT: same <140 vs <120 systolic comparison
  - 9361 **"high risk"** non diabetic patients
  - Trial stopped after 3.3 years (early)
  - Nonfatal + fatal adverse CV events lower in <120 group
  - Some adverse events higher in <120 group
  - Mean # of BP meds: 1.8 in <140 systolic group, 2.8 in <120

Sprint Outcomes

- Reduction in all cause mortality
  - 3.3% vs 4.5%, NNT 83 over 3 years
- Reduction in CV mortality
  - 0.8% vs 1.4%, NNT 167 over 3.3 years
- Reduction in heart failure development
  - 1.3% vs 2.1%, NNT 125 over 3.3 years

The Sprint Research Group: N Engl J Med 2015; 373:2103-2116

The NEW ENGLAND JOURNAL of MEDICINE

Table 2. Primary and Secondary Outcomes and Renal Outcomes.*

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% per year*	*no. of patients (%)*	*% per year*		
All participants	**(N=4678)**		**(N=4683)**			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	**(N=1330)**		**(N=1316)**			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline‖	**(N=3332)**		**(N=3345)**			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m^2§	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
‖ No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.

Some thoughts…

- Was ACCORD underpowered?
- High risk group
- Less than ½ of the <120 systolic group met that target
- BP measurements were done carefully…they let people sit and equilibrate, 3 readings averaged
- Excluded:
  - resistant hypertension
  - Diabetes
  - Stroke history
  - Institutionalized Elderly
- Increased complications: syncope, electrolyte abnormalities, AKI

What now?

- Well…it's unclear
- very challenging to implement <120 goal
- A reasonable editorial suggested <130 systolic for those over 50 without DM or stroke
- Some felt the rush to make the data public felt "rushed"

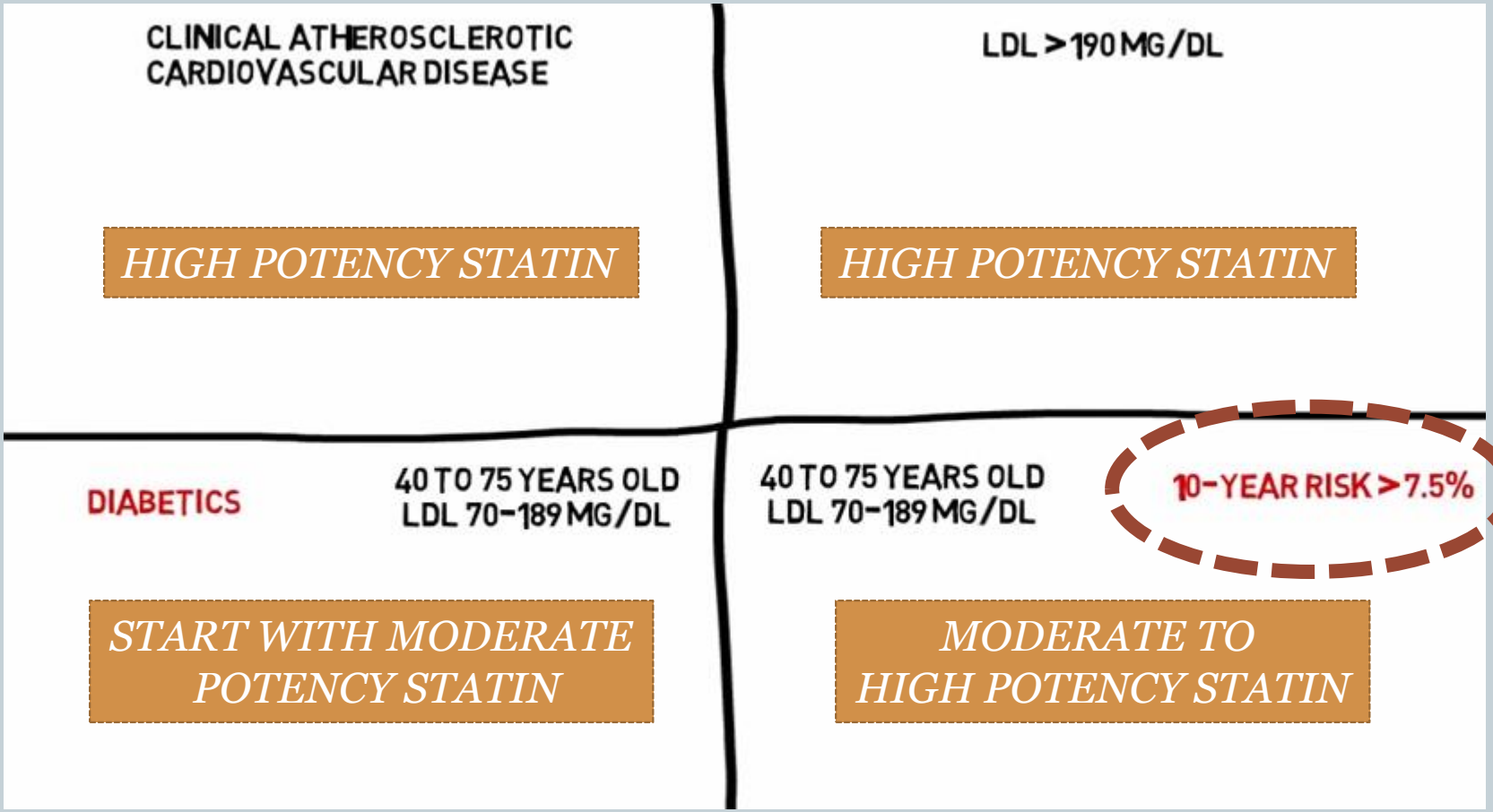
Spironolactone for Resistant Hypertension

- "Resistant Hypertension" = uncontrolled BP despite treatment with meds from 3 classes
- Interesting study design (rotated meds)
- Spironolactone lowered systolic~9mmHg, others ~4
- Don't use if GFR <45

Williams B et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): A randomised, double-blind, crossover trial. Lancet 2015 Sep 20; [e-pub]

The Cholesterol Story Also Continues

ACC/AHA Guidelines

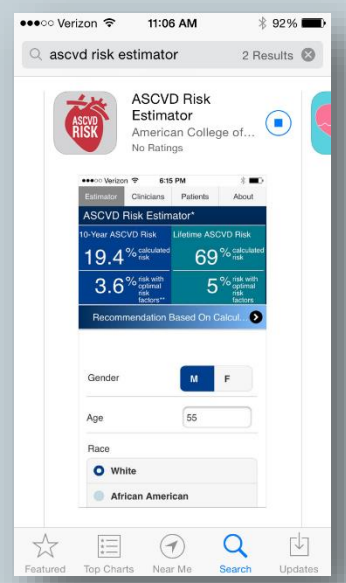


Issues with the ACC/AHA Risk Calculator?

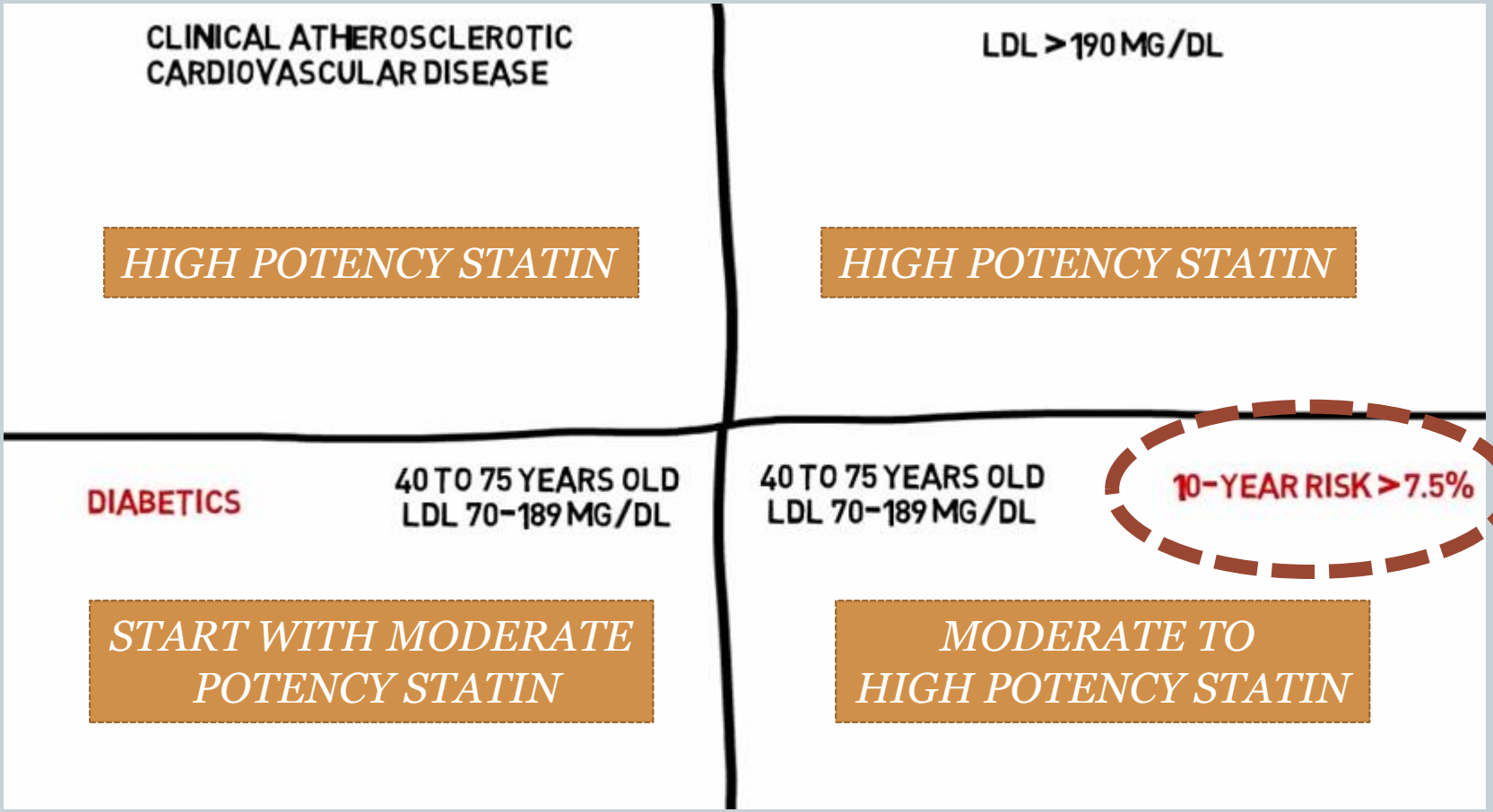
Challenge to risk calculator: ACC/AHA calculator may overestimate 10 year risk, causing more people to need statins

DeFilippis AP et al. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. Ann Intern Med 2015 Feb 17; 162:266

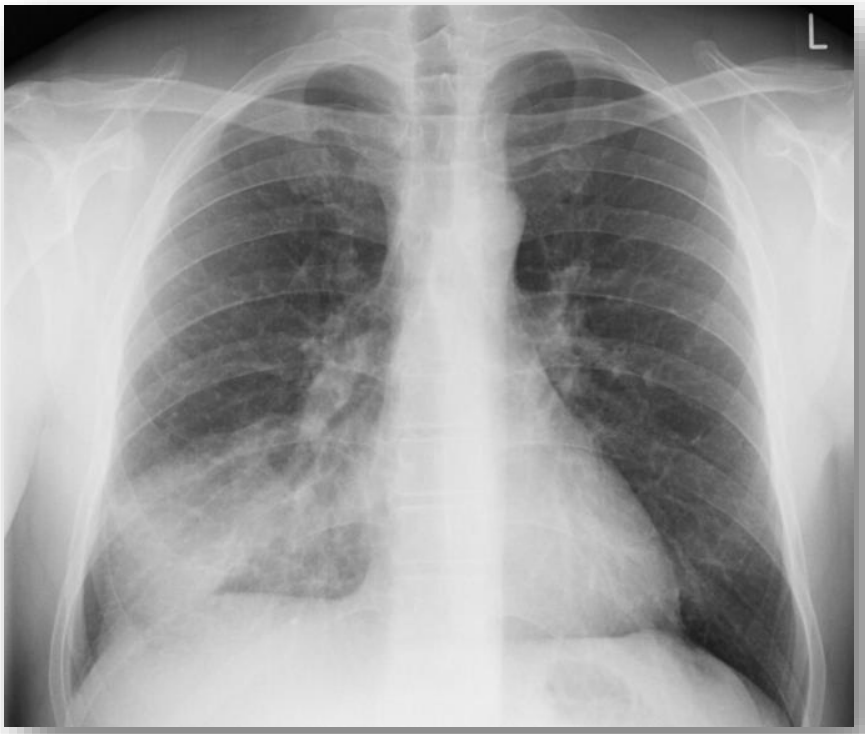
ACC/AHA 10 year risk	Observed in Data
7.5%-10%	3.0% in men 5.1% in women



ACC/AHA Guidelines



Steroids for Community-Acquired Pneumonia (CAP)



Background

- As many as 20% of patients with CAP worsen despite guideline-adherent antimicrobial therapy

- When a pathogen is identified (*only 38% of the time*), most commonly it's a virus (*about 60% of identified pathogens*)

Jain S, Self WH, Wunderink RG, et al, for the CDC EPIC Study Team. Community-acquired pneumonia requiring hospitalization among US adults. N Engl J Med 2015;373(5):1415-1427.

Small RCT

Spanish RCT: 120 patients with severe CAP

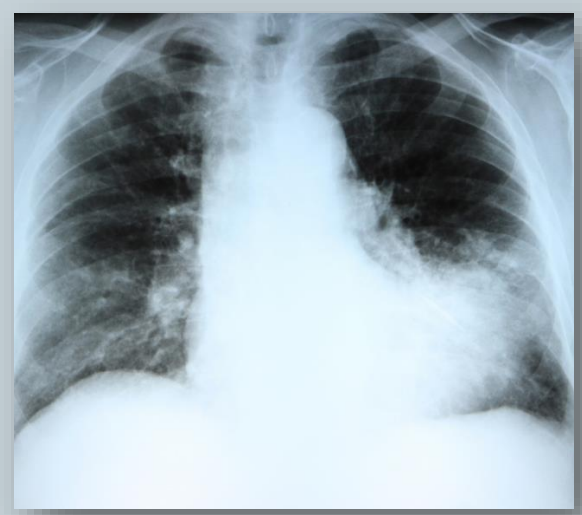
- Steroid group less likely to experience a multicomponent treatment-failure endpoint (3% vs 14%, P = 0.04)
  - Mechanical ventilation
  - Shock
  - Death
- Also less radiographic progression (13% vs. 31%)

Torres A, Sibila O, Ferrer M, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response. JAMA 2015;313(7):677-686.

Larger RCT

Swiss trial of 785 patients

- included patients with less-severe CAP
- results: steroids significantly shortened time to clinical stability from 4.4 days to 3.0 days



Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet 2015;385(9977):1511-1518

Larger RCT

Swiss Trial: Exclusion Criteria

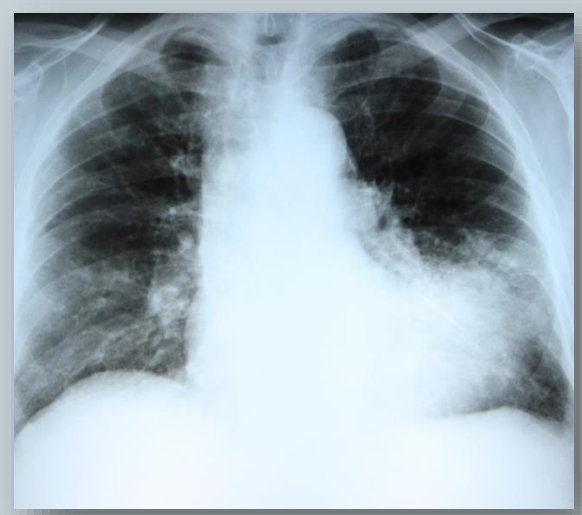
- permanent inability for informed consent
- active intravenous drug use
- acute burn injury
- gastrointestinal bleeding within the past 3 months
- known adrenal insufficiency
- a condition requiring more than 0·5mg/kg per day prednisone equivalent
- pregnancy or breastfeeding
- severe immunosuppression

Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet 2015;385(9977):1511-1518

Larger RCT

Swiss trial:

- LOS reduced by 1 day (7 to 6 days…)
- No significant increase in complications associated with community-acquired pneumonia

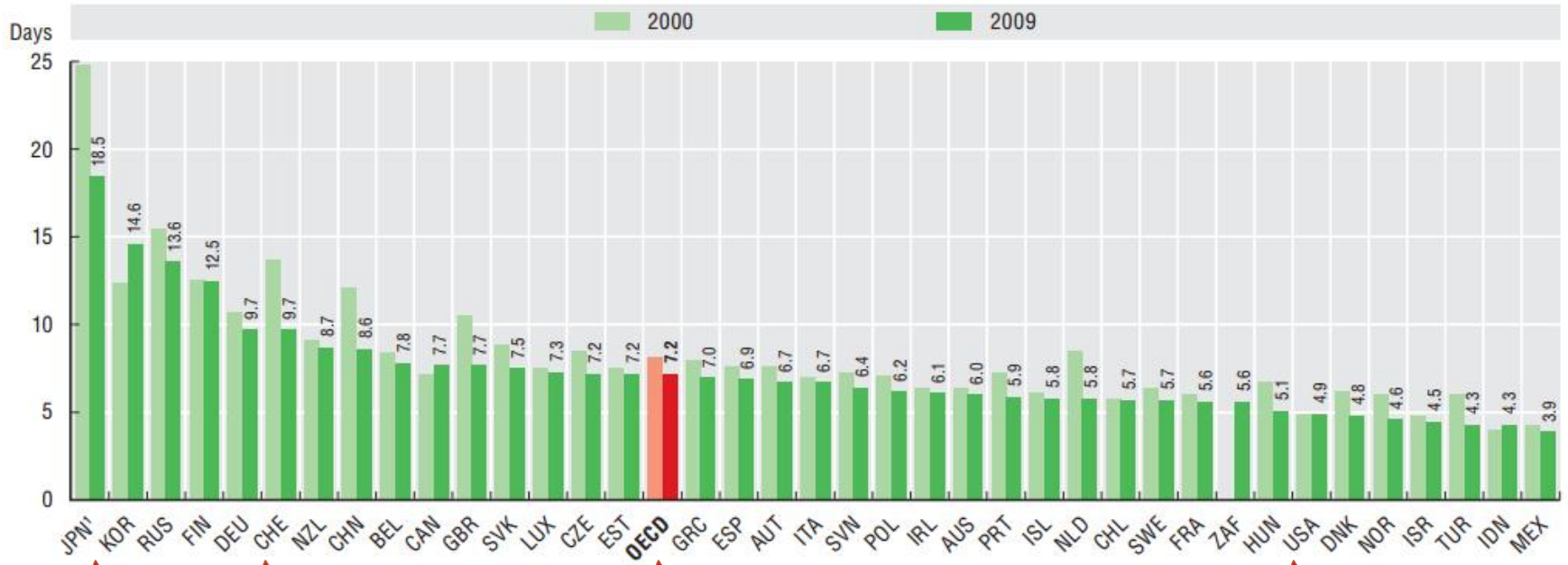


Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet 2015;385(9977):1511-1518

4. HEALTH CARE ACTIVITIES

4.5. Average length of stay in hospitals

4.5.1 Average length of stay in hospital for all causes, 2000 and 2009 (or nearest year)



1. The data for Japan refer to average length of stay for acute care (excluding long-term care beds in hospitals).

Source: OECD *Health Data* 2011; WHO-Europe for the Russian Federation and national sources for other non-OECD countries.

StatLink http://dx.doi.org/10.1787/888932524659

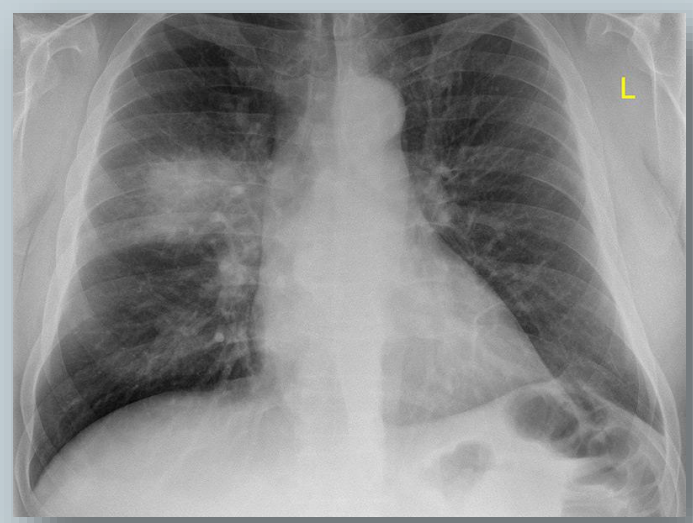
Meta-analysis

Meta-analysis: 13 RCT's (including the two 2015 trials)

- Results: moderate systemic corticosteroid doses (20–60 mg of prednisone or equivalent total daily dose) led to these differences:
  - ARDS (0.4% vs. 3.0%; number needed to treat, 38)
  - mechanical ventilation (3.1% vs. 5.7%; NNT, 38)
  - shortened hospital length of stay (by 2.9 days!)
  - Hyperglycemia requiring treatment: more common in corticosteroid group
  - other adverse events were similar in corticosteroid and placebo groups
- Mortality Rates
  - Lower all-cause mortality with steroids was of borderline statistical significance in the entire treatment population (5.3% vs. 7.9%; NNT, 38)
  - significant mortality benefit occurred in patients with severe pneumonia (7.4% vs. 22.0%; NNT, 7)

Conclusions?

- More research ongoing
- Notably in a Spanish H1N1 study pts did worse
- Consider 5-7 days of 20-60mg daily prednisone (40mg?) for hospitalized pts with CAP



Siemieniuk RAC, Meade MO, Alonso-Coello P, et al. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia. Ann Intern Med 2015;163(7):519-528.

HIV Pre-Exposure Prophylaxis

Background: HIV Pre-Exposure Prophylaxis

- New HIV infections continue. Example: 1 new HIV infection per day in the city of San Francisco
- Tenofovir/emtricitabine (*Truvada*): FDA Approved in 2012 for HIV Pre-exposure prophylaxis
- Cochrane review 2012
  - TDF-FTC versus placebo showed a reduction in the risk of acquiring HIV infection (RR 0.49; 95% CI 0.28 to 0.85; 8918 participants)

New Study this year: "On Demand" Truvada

RCT (government funded)

- 400 HIV negative men with unprotected anal intercourse with ≥ 2 men in previous 6 months
- Excluded: impaired renal function, hepatitis B/C
- Intervention:
  - 2 pills between 2 and 24 hours before intercourse
  - 3rd pill at 24 hrs afterward
  - 4th at 48 hrs after first 2 taken
- Followed for median 9.3 months

PrEP

- Intervention group less likely to develop HIV (14 vs 2 infections)
  - 6.6 vs 0.91 per 100 person-years of follow up
  - NNT = 17 per year

Molina JM, Capitant C, Spire B, et al, for the ANRS IPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015;373(23):2237-2246.

The Washington Post

Health & Science

With a little pill, could one city's AIDS epidemic be ending?

Matthew Sachs, 29, is a graduate student in San Francisco who is HIV-negative. He lists his PrEP status on social media. (Nick Otto for The Washington Post)

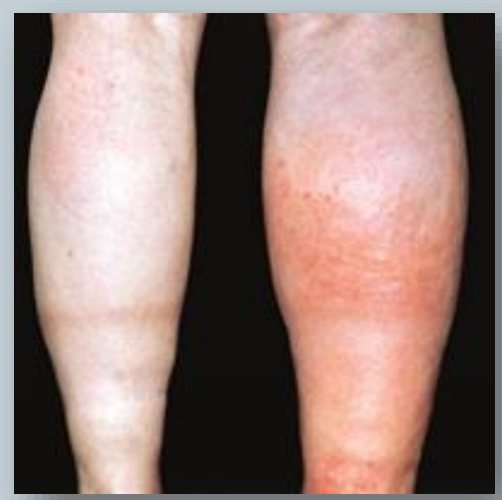
By Ariana Eunjung Cha January 26 Follow @arianaeunjung

SAN FRANCISCO — On online dating sites, Matthew Sachs identifies himself as a 5-foot-8, 130-pound grad student who likes hiking, performance art and community service. He says he's interested in meeting a broad range of guys, from jocks to geeks, and notes that — oh, by the way — he's "On PrEP."

Long Term ASA after VTE

Long term ASA for DVT (late 2014)

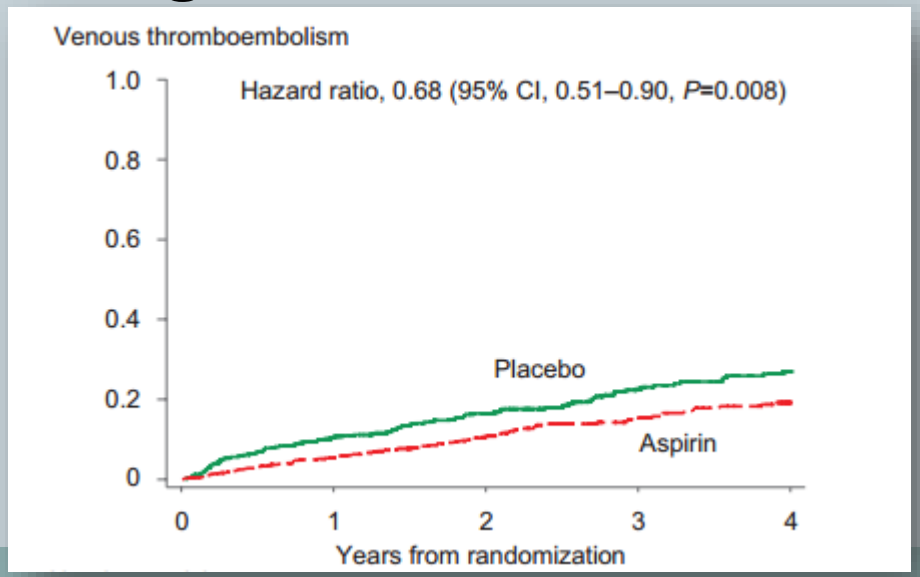
- Meta-analysis (of 2 trials total ~1200 patients)
- Nonpregnant adults with a **first unprovoked** DVT or PE
- aspirin 100mg QD vs matching placebo (after anticoagulation period ends)



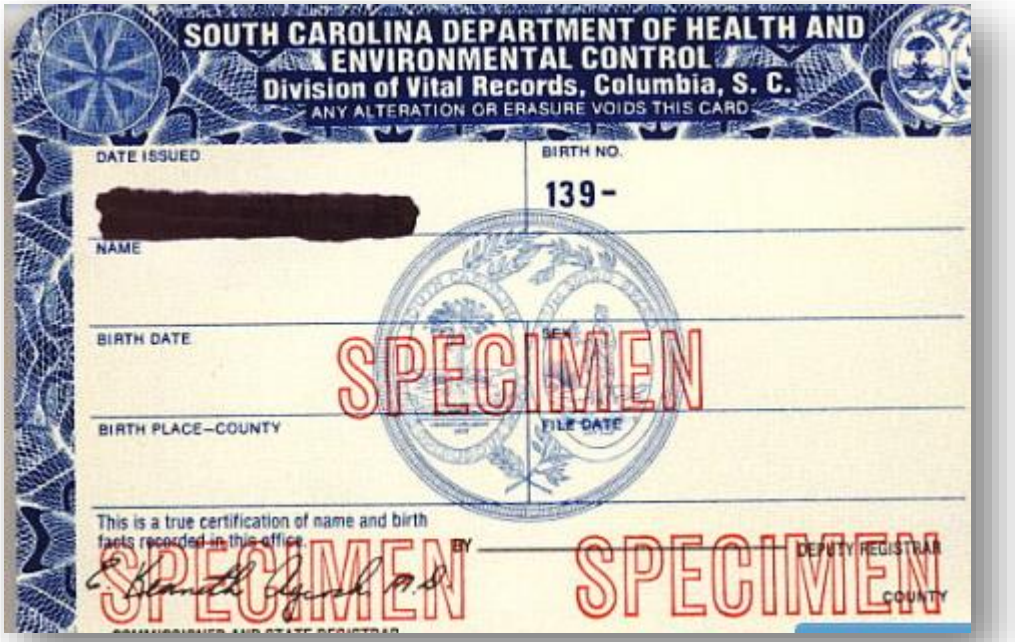
Simes J, Becattini C, Agnelli G, et al, for the INSPIRE Study Investigators (International Collaboration of Aspirin Trials for Recurrent Venous Thromboembolism). Aspirin for the prevention of recurrent venous thromboembolism: The INSPIRE collaboration. Circulation 2014;130(14):1062-1071.

Long term ASA for DVT

- Rate of recurrent VTE ~ 1/3 lower in the aspirin group (5.1% vs 7.5% per year; P = .008; NNT = 42 per year)
- Similar reduction for DVT or PE
- no difference in major bleeding



Out-of-Hospital Births in the U.S.

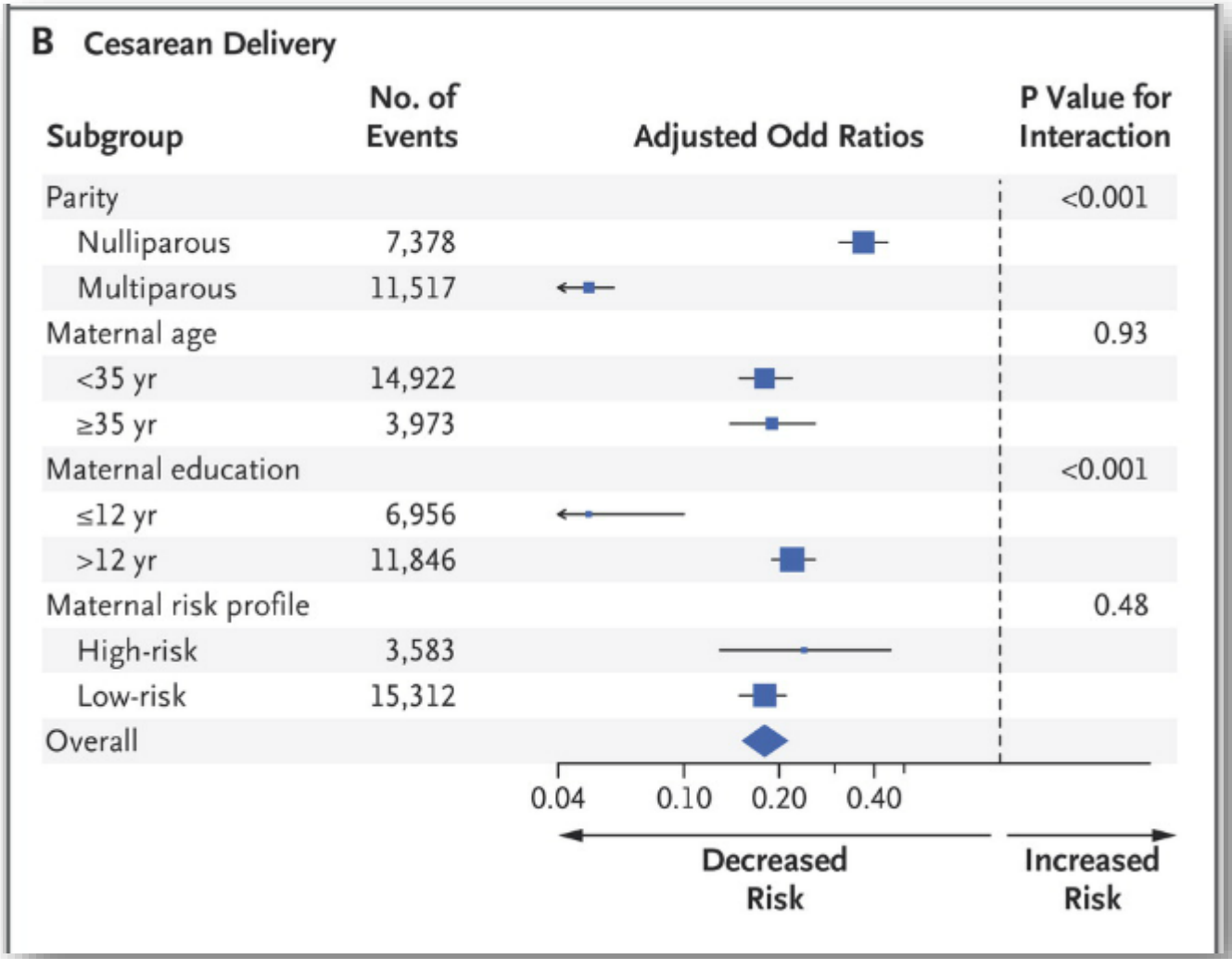


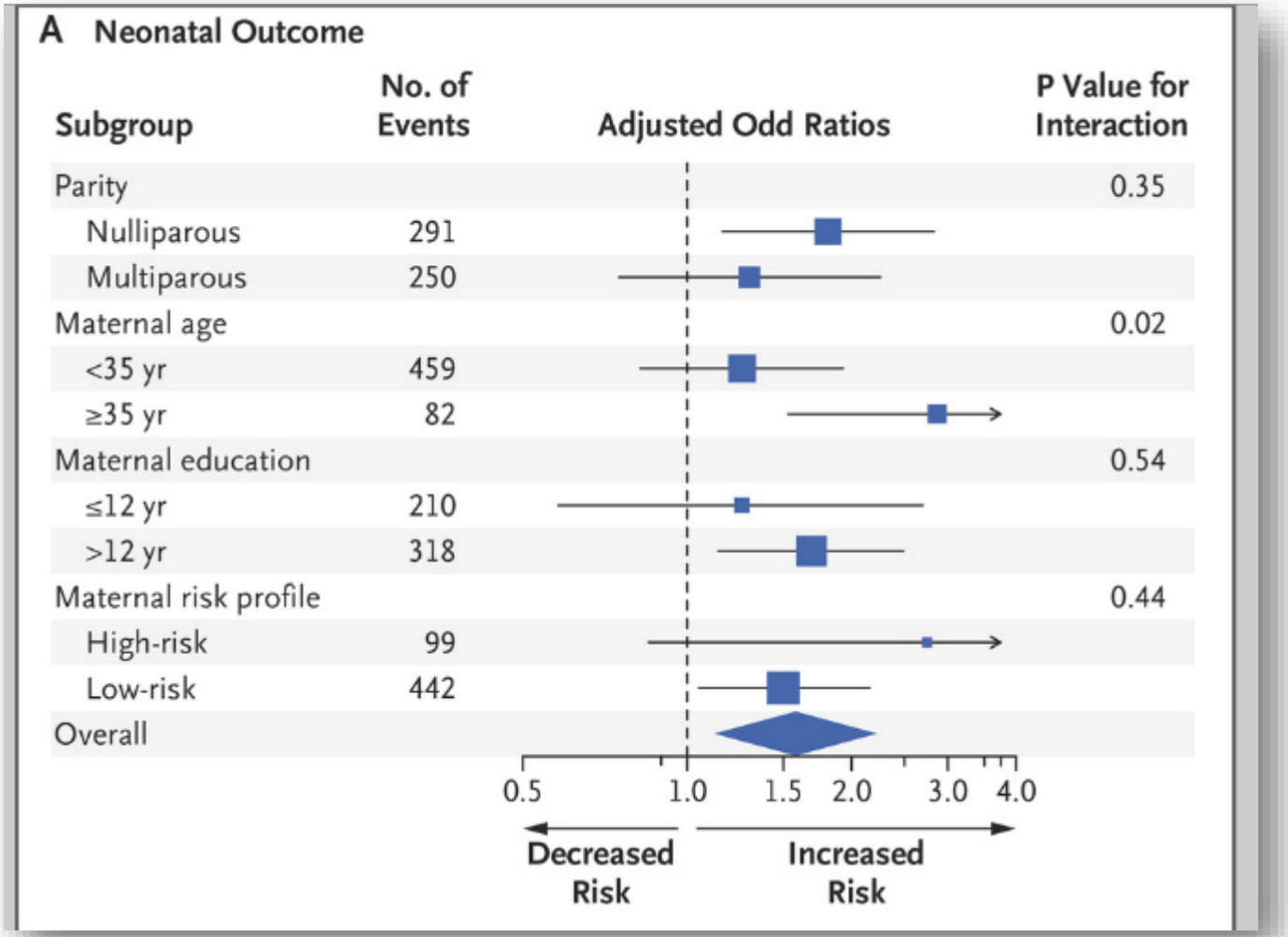
Out-of-Hospital Births in the U.S. Background

- Rate of out-of-hospital birth in the U.S. increasing, data on safety/outcomes is evolving
- Rate of C-sections in hospitals is more than double 1970, yet no change in intrapartum fetal mortality
- Data problem: misclassification of transfers as “hospital births”
- Other national health systems more uniform
- Recent addition of field in the Oregon birth certificate: “intended delivery location”

New Study

- Data
  - 75,923 planned and completed hospital births in Oregon
  - 1968 completed home births
  - 1235 completed birth-center deliveries
  - Excluded unplanned home births
- No difference in statistics based on "*actual place of birth*"
- When births reclassified based on *intended site*: higher perinatal mortality out of hospital (3.9 vs 1.8 per 1000 births)
- Note: inability to distinguish between transfers from birth centers and transfers from home


B Cesarean Delivery
Subgroup
No. of Events
Adjusted Odd Ratios
P Value for Interaction
Parity
<0.001
Nulliparous
7,378
Multiparous
11,517
Maternal age
0.93
<35 yr
14,922
≥35 yr
3,973
Maternal education
<0.001
≤12 yr
6,956
>12 yr
11,846
Maternal risk profile
0.48
High-risk
3,583
Low-risk
15,312
Overall
0.04
0.10
0.20
0.40
Decreased Risk
Increased Risk



Composite neonatal outcome: fetal death, infant death, a 5-minute Apgar score of less than 4, or neonatal seizures

Positive Existing Data on Out-of-Hospital Births

- 2013: 15,574 women in 79 midwifery-led U.S. birth centers, in 33 states had good outcomes.

Rutledge et al. Outcomes of Care in Birth Centers: Demonstration of a Durable Model. Journal of Midwifery and Women's Health. Vol 58, Issue 1 Page 3-14. Jan/Feb 2013

- More data (and guidelines) out there…largely from other countries and Midwifery journals.

*De Jonge A, van der Goes BY, Ravelli ACJ, et al. Perinatal mortality and morbidity in a nationwide cohort of 529,688 low-risk planned home and hospital births. BJOG. 2009;**116**(9):1177-1184.*

*Janssen PA, Saxell L, Page LA, Klein MC, Liston RM, Lee SK. Outcomes of planned home birth with registered midwife versus planned hospital birth with midwife or physician. CMAJ. 2009;**181**(6–7):377-383.*

Cheyney et al. Outcomes of care for 16,924 planned home births in the United States: the Midwives Alliance of North America Statistics Project, 2004 to 2009. J Midwifery Womens Health. 2014 Jan-Feb;59(1):17-27. doi: 10.1111/jmwh.12172.

Torjesen I. Midwife led delivery is safer than a labour ward for low risk pregnancies, says NICE guidance. BMJ 2014;349:g7421.

Should all babies in the U.S. be born in a hospital?

- No
- Other national systems: integrated out-of-hospital delivery infrastructure, training regulation and transfer protocols
- Serious adverse events were rare **in all settings covered**. Even in this study, out of hospital births were associated with an "excess" of <1 fetal death/1000 deliveries
- Also: is Oregon a "worst case scenario?"

Considerations for Out-of-Hospital Birth

- How close is the hospital?
- Is there a relationship with an OB unit?
- Is the midwife skilled?
- Avoid high risk births out of hospital
- Ultimately it's a question of informed decision making

http://www.nytimes.com/2015/12/31/health/as-home-births-grow-in-us-a-new-study-examines-the-risks.html?_r=0

VBAC at Home?

- Maternal/neotnatal outcomes for planned VBAC at home
  - 12,092 women without prior cesarean
  - 1,052 women with a prior cesarean
  - Transfer rates 18% for women with prior cesarean, 7% for others
  - 4.75 neonatal deaths per 1000 in prior cesarean group vs 1.24/1000 in control group
  - Higher rates of some other complications
- Consider avoiding VBAC at home

Cox KJ, Bovbjerg ML, Cheyney M, Leeman LM. Planned Home VBAC in the United States, 2004-2009: Outcomes, Maternity Care Practices, and Implications for Shared Decision Making. Birth 2015 Dec;42(4):299-308. doi: 10.1111/birt.12188

Quicker Summaries

More Questions About A1C

- No reduction in CV or all-cause mortality at 10 years for T2DM in “intensive” glycemic control
- A1C 6.9% vs 8.4% in “usual care”
- VA study, largely in men (97%)
- Small improvement in the morbidity outcome (combo of MI, CVA or new/worsening HF)

Hayward RA, Reaven PD, Wiitala WL, et al, for the VADT Investigators. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2015;372(23):2197-2206.

Goodhart's Law

"When a measure becomes a target, it ceases to be a good measure."

Pediatrics: Get Rid of Your Dishwasher?

Swedish study: parents of 1,209 7-8 year olds were sent a survey

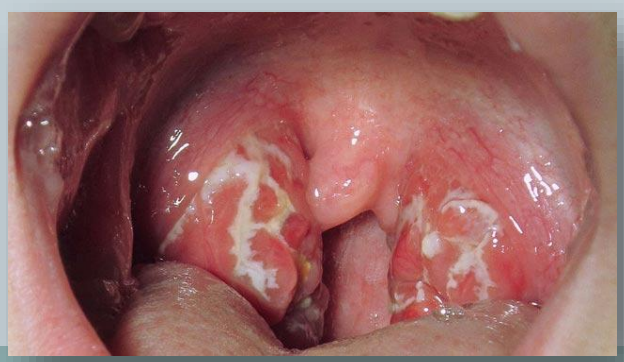
- Hand washing dishes: associated with lower rate of allergic disease development
- 12% hand-washed dishes
- Odds ratio 0.57 (0.37-0.85)

Hesselmar B, Hicke-Roberts A, Wennergren G. Allergy in children in hand versus machine dishwashing. Pediatrics 2015;135;e590

Pediatrics: Back up Strep Culture?

- Back up Cx not needed for Neg rapid strep in a country with low incidence of rheumatic fever (like the U.S.)

- Using confirmatory cultures to back up "RADT's" costs >$8 million per additional case of rheumatic heart disease prevented



Lean WL, Arnup S, Canchin M, Steer AC. Rapid diagnostic tests for group A streptococcal pharyngitis: a meta-analysis. Pediatrics 2014;134(4);771-781.

Behavioral Health

- Giving patients financial incentives helps them quit smoking

Halpern SD, French B, Small DS, et al. Randomized trial of four financial-incentive programs for smoking cessation. N Engl J Med 2015;372(22):2108-2117

- Drug therapy for PTSD works but doesn't work great (meta-analysis). Paxil may be slightly better than others

Hoskins M, Pearce J, Bethell A, et al. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. Br J Psychiatry 2015;206(2):93-100.

Musculoskeletal/Procedures

- Platelet-rich plasma injections aren't better than hyaluronic acid for knee DJD

Filardo G, Di Matteo B, Di Martino A, et al. Platelet-rich plasma intra-articular knee injections show no superiority versus viscosupplementation: a randomized controlled trial. Am J Sports Med 2015;43(7):1575-1582.

- Sterile gloves aren't needed for minor skin excisions

Heal C, Sriharan S, Buttner PG, Kimber D. Comparing non-sterile with sterile gloves for minor surgery: a prospective randomised controlled non-inferiority trial. Med J Aust 2015;202(1):27-32.

Adult Medicine: $$ Wasters

- USPSTF says there isn't evidence to support routine screening for thyroid disease

LeFevre ML, on behalf of the U.S. Preventive Services Task Force Screening for thyroid dysfunction: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2015;162(9):641-650.

- ACP releases a practice guideline that says don't screen low-risk adults for cardiac disease

Chou R, for the High Value Care Task Force of the American College of Physicians. Cardiac screening with electrocardiography, stress echocardiography, or myocardial perfusion imaging: advice for high-value care from the American College of Physicians. Ann Intern Med 2015;162(6):438-447.

Graduate Medical Education

- The latest duty hour reforms haven't had a measurable effect on mortality or hospital readmissions

Patel MS, Volpp KG, Small DS, et al. Association of the 2011 ACGME resident duty hour reforms with mortality and readmissions among hospitalized Medicare patients. JAMA 2014;312(22):2364-2373.

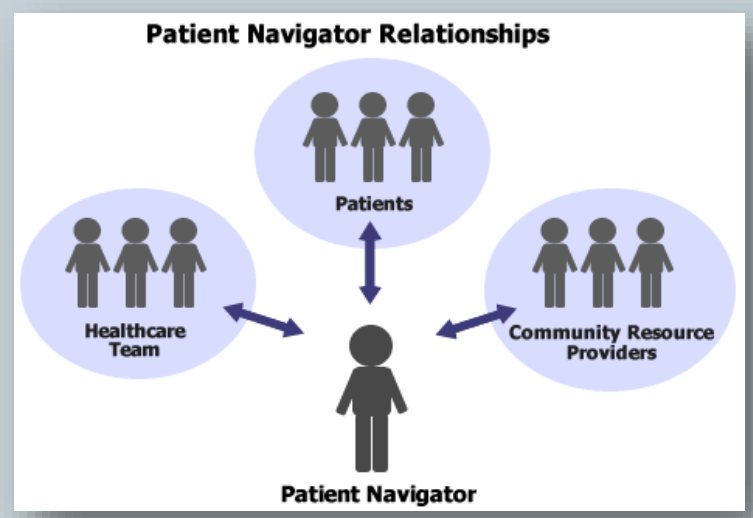
- Prevalence of depression and depressive symptoms among residents is…depressingly high (28.8%)

Mata D et al. Prevalence of Depression and Depressive Symptoms Among Resident PhysiciansA Systematic Review and Meta-analysis JAMA. 2015;314(22):2373-2383

Other Inpatient Medicine

- Patient navigators slightly decrease (4%) readmission rates for older patients, and increase (12%) readmissions in younger patients

Balaban RB, Galbraith AA, Burns ME, Vialle-Valentin CE, Larochelle MR, Ross-Degnan D. A patient navigator intervention to reduce hospital readmissions among high-risk safety-net patients: a randomized controlled trial. J Gen Intern Med 2015;30(7):907-915



Bridging Therapy

- Bridging therapy, more harm in both:
  - Atrial fibrillation

Steinberg BA, Peterson ED, Kim S, et al, for the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation Investigators and Patients. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Circulation 2015;131(5):488-494.

  - Low risk VTE patients who need warfarin interrupted for procedures

Clark NP, Witt DM, Davies LE, et al. Bleeding, recurrent venous thromboembolism and mortality risks during warfarin interruption for invasive procedures. JAMA Intern Med 2015;175(7):1163-1168.

Most Importantly…

Health Advice on TV Medical Talk Shows

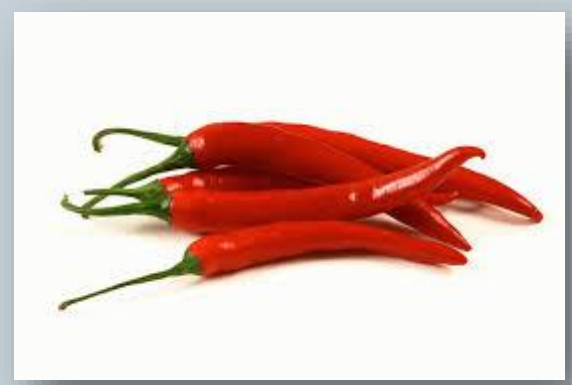
- TV docs: 54% of their recommendations had some evidence to support them
  - "The Doctors" 53%
  - Dr. Oz: 33%

Korownyk C, Kolber MR, McCormack J, et al. Televised medical talk shows--what they recommend and the evidence to support their recommendations: a prospective observational study. BMJ 2014;349:g7346.

Spicy Foods…

Chinese Population based prospective cohort study

- 199,293 men and 288,082 women aged 30 to 79
- Spicy food consumption: inverse associations with total mortality in both men & women (after adjustment for other risk factors)



Jun LV Consumption of spicy foods and total and cause specific mortality: population based cohort study. BMJ 2015;351:h3942

Spicy Food…

Table 2 Association of weekly spicy food consumption with total and cause specific mortality among 487 375 participants. Values are hazard ratios (95% CIs) unless stated otherwise

Cause of death	No of participants	Frequency of spicy food consumption			
		Less than once a week*	1 or 2 days	3-5 days	6 or 7 days
No of participants	487 375	278 491	31 740	28 549	148 595
No of person years	3 500 004	1 990 589	228 112	204 972	1 076 330
All causes:					
No of deaths†	20 224	12 145	1014	876	6189
Model 1		1.00	0.90 (0.84 to 0.96)	0.85 (0.79 to 0.91)	0.83 (0.79 to 0.86)
Model 2		1.00	0.89 (0.83 to 0.95)	0.84 (0.79 to 0.90)	0.82 (0.79 to 0.86)
Model 3		1.00	0.90 (0.84 to 0.96)	0.86 (0.80 to 0.92)	0.86 (0.82 to 0.90)

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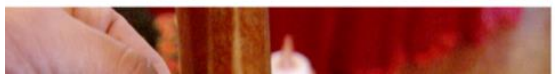

How to Stay Current?

- Journal Watch
- Essential Evidence
- Run your own clinic “journal club”

THANKS!