Myths and Misses in Medicine

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Conflict of Interest

- Family Doctor for >10 yrs
- Academic 7 years
- Pay from U of A and Alberta Health
- Research and Speaking Fees
  - Non-Profit Sources (ACFP, CEDAC, ENPCN, TI, TOP, etc)
  - No funding from Industry

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What's Up Doc?

- We are going to address random myths
  - No pain relief for acute abdo: wrong – 12 trials
  - Anti-oxidant A&E vitamins:↑ mortality NNH~250
- Topic areas
  - Pediatrics - DM
  - Women's Health - MSK
  - Dermatology - Miscellaneous
  - Cardiac - CRP
  - (Slides not covered: Recent TFP myths)

1. JAMA 2006;296:1764-74 2. Lancet 2003;361:2017-23. Ann Int Med. 2005;142:37-46.

Some Ped Myths

Fever Fever

A 5 year old has a nasty fever but otherwise is classic URTI. His mother wants some advise to treat this fever.

- You say: Well, if you want to treat it (don't have to), ibuprofen is probably best.
- True: RCT, 156 children 6mo-6yrs, Primary care, Paracetamol 15mg/kg or ibuprofen 10mg/kg or both
- 1° outcome time w/o fever 1st 4hr
  - Para + ibu > para diff = 55.3mins (p<0.001)
  - Para + ibu vs ibu diff = 16.2mins (p=0.2)
  - Time w/o fever in 24hrs (stat sign): para+ibu> para (4.4hr), para + ibu> ibu (2.5hr)
- Ibu shown previously to be superior to acetaminophen for relief of fever.[1] No evidence that reducing fever improves outcome or reduces comps – may prolong illness.[2,3] Overdosing of meds reported in 33 children in this study

BMJ 2008;337:a13021. Arch Pediatr Adolesc Med 2004;158:521-6. 2. Lancet 1997;350:704-9. 3. J Pediatr 1989;114:1045-8.

ENT: Pediatric Cough

- 2 children (age 3 & 5) are in with their mother. Mom is very concerned about their cough (and sleeping). She wants your suggestion about an OTC cough med
- You say: OTC medicines have no effect on reducing cough in pediatric patients?
- True
  - Meta-analysis: 6 studies, 438 kids, 1 stat sign, No clinical benefit

1. Arch Dis Child 2002; 86: 170-5.

ENT: Mild Croup

- A 3 year old child is in with his mother. He has a barking cough and mom reports a classic stridor episode early today. She is concerned and would like a medicine
- You say: Dexamethasone only benefits patients with moderate to severe croup
- False
  - RCT, 720pts, mild croup, oral 0.6mg/kg, 1 dose
  - Return med care: 15% vs 7% (NNT 13)

1. NEJM 2004; 351: 1306-13.

Sleepless in Seattle

- A young mother is frazzled by her sleepless 1 y.o. infant. She is considering Benadryl?
- You say: We don't know if it works
- False: We know it doesn't!
- RCT 44 kids 6-15 months
  - 3 (14%) placebo vs 1 (5%) in diphenhydramine got better night-time sleeping.
  - No diff in parental happiness

Arch Pediatr Adoles Med. 2006;160:707-712

Diagnosing AOM

- You are examining a 5 y.o. with sore ears and your NP students asks what is the best sign or symptom for making the Dx of AOM
- You say: Pneumatic Otoscopy is the most reliable method for Diagnosis of AOM
- False[1]
  - Meta-analysis (6 trials, 3900 pts)
  - Best Sym = Ear Pain LR 3-7.3 (ear pulling 3.3).
  - Signs= TM Bulging (LR 20-51), Cloudy (LR 11-34), Immobile (LR 8-31), Distinctly Red (LR 2.6-8.4)

1) JAMA 2003;290:1633–40

Women's Health

Gyne: PAP test I

- You are about to show the PAP test to a med student and she asks about cleaning-swabbing the cervix before the PAP test
- You say: Cleaning of the Cervix will enhance the Quality of the PAP test
- False[1]
  - RCT, 616 ♀, Family Practice
  - No difference

1. Can Fam Physician 2007;53:1328-1329.

Gyne: Pap Test II

- You preparing to do a PAP test on a 35 year old and she asks "Is that lubricant? My gynecologist says it wrecks the PAP test."
- You say: Lubricant on a Speculum will not impact the PAP test
- True
  - 2 RCTs, 182 & 2,900 ♀, 1 clinic &5 Public Health
  - No diff in quality

1. Obstet Gynecol 2002; 100: 889-92. & Obstet Gynecol 2002;100:887–8

Obs: PCOS infertility

- A 28 y.o. woman with Polycystic Ovarian Syndrome (PCOS) raises that she & her husband are interested in trying for kids but she has not had much luck (even after previously seeing Obs)
- You say: Women with infertility associated with PCOS require a referral to O&G
- Maybe but
  - Meta-analysis, 13 RCT (543 pts), Metformin 500mg TID
  - Alone: Ovulation rate ↑ 22% (NNT 5)
  - With Clomiphene ↑ 34% (NNT 3) & Preg ↑ 25% (NNT 4)

1 BMJ. 2003; 327: 951-6.

Dermatology

Derm: Psoriasis

- A 35 year old man is in for Psoriasis (elbows and buttocks). A clinic doctor gave him a Elidel sample and he would like to know your thoughts
- You say: Pimecrolimus is as effective as steroid or dovonex for psoriasis
- False (RCT 80pts)
  - Betamethasone>dovonex>Vehicle=pimecrolimus

1) Arch Dermatol 2006;142:1138-43.

Acne: What's on First?

- A 20 y.o. ♂ complains of facial acne, has moderate severity & wants oral Abx
- You say: Topical meds are just as effective
- True: RCT, 650 pts x18 wks, 5 arms
  - Oral: Tetracycline 500 BID; Minocycline 100 OD
  - Topical: 5% B.P. (BID); 5% B.P. with 3% Erythro (BID); 2% Erythro (am) and 5% B.P. (qhs)
- No Diff (except AE: oral was GI, Topical was skin)
  - Cost: Minocycline 8x Erythro + BP
  - Erythro + B.P. (63-66%) vs oral Abx (54-55%)

•Lancet 2004; 364: 2188-95.

Suturing: Gloves

- You are seeing a 20 year old male with 10 cm laceration on his shoulder. You realize you have no sterile gloves! You make plans to send him to ER
- You say: Sterile gloves are required for lower infection rates in laceration repair
- False[1]
  - RCT, 816 pts, ER Canada
  - Infection rate ns (6% sterile vs 4.3%)

1) Ann Emerg Med 2004; 43(3): 362-370.

Suturing: Water Cleansing

- Same patient. You decide to suture but realize you have no sterile water! Apart from screaming at your staff
- You say: Sit tight, we can use tap water, infection rates are the same as sterile water
- True
  - Sys Rev: 11 studies, Meta = 3 trials (1338 pts)
  - Infection rate 7% sterile vs 4.4% tap (sign), NNH 39

1) Cochrane 2008;(1):CD003861.

Diabetes

Intense Sugar Control: A bitter pill?

- A drug rep, promoting a new DM med, says "Don't you think it's important to give patients the health benefits of having a HgbA1C at national guideline levels (<7%)?"
- You say: No, I don't think there are many health benefits
- True: 3 Big RCT's (mean age 60s, 40% ♀*)
  - ACCORD (10K pts, x 3.5 yrs): 6.4 vs 7.5 HgbA1C
  - ADVANCE (11K pts, x 5 yrs): 6.5 vs 7.3 HcbA1C
  - VADT (1.8K ♂ pts, x 5.6 yrs): 6.9 vs 8.4 HgbA1C

NEJM 2008;358:2545-59. NEJM 2008;358: 2560-72. NEJM 2009;360: e-pub Dec 17, 08

Intense Sugar Control: A bitter pill

- No Diff: CVD events & CVD mortality
  - Except Mortality NNH 100[1]
- ↓ Microalbuminuria (1-2.5% reduction)[1-3]
- Increase Harms (some examples)
  - 3rd Party rescue Hypoglycemia (10.5% vs 3.5%)[1]
  - Hospitalization (45% vs 43%)[2]
  - Weight Gain >10kg (28% vs 14%)[1]
  - Doctors visits, phone calls, dose changes, drugs, etc.

NEJM 2008;358:2545-59. NEJM 2008;358: 2560-72. NEJM 2009;360: e-pub Dec 17, 08

Diabetes is Coronary Heart Disease Risk Equivalent!

- A 42 year old woman has come to discuss her confirmatory blood sugar (7.4, verifying DM)
- You say: Oh My God, you have Diabetes! Get your Affairs in Order!
- Hopefully not: DM is likely not a CVD risk equivalent
  - Although a few studies suggest DM maybe a CVD equivalent[1]
  - Multiple studies have show it is not a CVD risk equivalent[2]
  - To assess your patients CVD risk, consider
  - The UKPDS risk engine is generally recommended: http://www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/download.php
  - Also University of Edinburgh Cardiovascular Risk Calculator http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp

1. Arch Intern Med. 2003 Jul 28;163(14):1735-40 2. Diabet. Med 2009; 26: 142–148. Diabetes Care. 2006;29(2):391-7. Arch Intern Med. 2004;164(13) :1438-43

Screening Diabetics for CAD

- A 60 year old male Diabetic is in and heard all diabetics should have cardiac screening. He is asymptomatic
- You say: It is likely that will be any help to you
- True: RCT [DIAD][1]: 1123 pts with DM got myocardial perfusion imaging or normal care
  - No diff: MI/CAD death (2.7% screened vs 3% not) x 5yrs
  - No others significantly diff either
- Although some[2] have historically recommended routine CAD screening in DM, No evidence it helps

1 JAMA 2009;301:1547–55. 2 Diabetes Care 1998; 21:1551–9.

DM: More testing, Better Care?

- A 48 y.o. ♀ was diagnosed with DM 8 months ago. Her DM med is Metformin only. She is testing 2 x a day but finds it frustrating, expensive and painful
- You say: Testing is an important part of improved diabetes care
- False: 2 Meta-analysis (HgbA1C: -0.25%[1]-0.39%[2])
- RCT: No stat diff in HgbA1c, new drugs, wgt[3]
  - More hypoglycemic in self monitoring (NNH=6)
  - 1/3 mod intensity gave up, ½ high intensity
- RCT: No diff Hgb A1C, med use, hypoglycemia[4]
  - Higher depression scores (by 6%)

1) Diabet Med. 2000;17:755-61. 2) Cochrane. 2005;2:CD005060 3) BMJ 2007;335;132- 4) BMJ 2008 doi: 10.1136/bmj.39534.571644.

"Assessing Risk is Risky"

- A 46 year newly diagnosed diabetic is back from DM teaching. He is wondering about the dose of ASA (they recommended)
- You say: I doubt you need it all?
- True: 2 RCTs directly address
  - JPAD[1] and POPODAD[2]: no benefit for ASA in DM
    - Except maybe ≥65
- The PPP[3] study found their DM group didn't benefit while other 1º prevention pts with ≥1 risk factor did
- Guidelines[4] loosening but still people they list as candidates which did not benefit in these studies

1. JAMA. 2008;300(18):2134-2141. 2. BMJ. 2008 Oct 16;337:a1840. 3. Diabetes Care. 2003 Dec;26(12):3264-72. 4. Can J Diabet 2008; 32: S102-06.

Musculoskeletal

Rotator Cuff Injections: Horseshoes & Hand-grenades

- You are teaching a medical student to inject a sub-acromial bursa for rotator cuff but she is nervous
- You say: Don't worry, close is good enough
- True (likely). RCT, 106 pts, mean 51 yrs, 61% ♀, Rot cuff >3 months
  - RCT virtually no difference between radiologically guided bursa injection and buttock injection

BMJ 2009;338:a3112

OA: Topical NSAIDs

- A 50 year old male is with knee OA. He finds NSAIDs irritating to the stomach but doesn't get much help from Acetaminophen. He has heard that creams may work
- You say: Topical NSAIDs are less effective than oral NSAIDs in knee OA
- False
  - RCT 622pts, oral vs topical, No diff except AE
  - 2 Meta vs placebo, ES=0.40, NNT 5

J Rheumatolo 2004;31(10): 2002-12. BMJ 2004;329(7461):324. www.Bandolier.com March 05

Tennis Elbow: First do…

- J. McEnroe (42) has lateral epicondylitis & has tried NSAIDs (Topical & oral), splint & physio. He wonders about steroid injections
- He wonders what works

Tennis Elbow: First do…

- Steroid Injection[1]
  - RCT, 198 pts, 3 arms (injection/physio/usual)
  - Results: physio < pain meds
  - 6 weeks Injection = NNT 8
  - 52 wks Injection = NNH 4
  - Injections= ↑ recurrences & poor long term outcome

Improve	Steroid	Physio	Usual
6 wks	78%	65%	27%
52 wks	68%	94%	90%

Tennis Elbow: First do…

- Transdermal Nitro[2]
  - Placebo vs ¼ Nitro 5mg/24hr patch (95 elbows)
  - Nitro group: ↑ strength & ↓ pain/tenderness
  - Asymptomatic ADL (6 mon): AB =21% or NNT 5
  - Side-effects frequent (12% quit, NNH=8)

1. BMJ 2006;333:939
2. 2. Am J Sports Med 2003;31:915–20

Miscellaneous

All Plugged Up & No Way to Go

- A 42 y.o. female has chronic constipation. BM's are q4 days & she is uncomfortable 50% of the time. She wants to start Docusate
- You say: Docusate doesn't work
- True: Sys Review of >50 trials & 13 therapies
- Best Evidence for
  - Polyethylene Glycol (8 T - 743pts): 2-3bm/wk, NNT=2
  - Lactulose (10 T – 700 pts): 1-3 extra BM/wk, NNT=4
  - Psyllium (9 T – 997 pts): 1-3 extra BM/wk

Am J Gastroenterol 2005; 100: 936-71.

Iron: A Plug for Therapy

- 80 y.o. ♀ with fatigue has ongoing anemia (Hgb 101 + Ferritin 8). Unchanged x 4 yrs & scope then -ve. Iron causes her constipation
- You say: A low dose of iron works as well and doesn't cause constipation
- True: RCT, 90 elderly anemic x2m (150, 50, 15mg)
  - Hgb ↑ significantly (14 Hgb points), no diff between doses
  - AE ↑ significantly as dose ↑, Dropout 15mg vs 150mg NNH = 5
- 15mg elemental iron = 2.5 ml's of Fer-In-Sol

30mg of elemental iron = Ferrous sulphate 150mg

Am J Med 2005; 118: 1142-7

Gabapentin: Fix-all or Fixed

- A 50 year old woman with neuropathic pain is in today. Your resident asks, shouldn't we try gabapentin?
- You say: Yes, there is pretty good evidence for it
- False: Review of unpublished Gabapentin research[1]
  - Of 20 studies, only 60% published… of those
    - Only 33% used predefined Primary outcome
    - Only 32% of the secondary outcomes reported
    - 73% of primary outcomes +ve in published vs 29% from protocol
- Note: Pregabalin[2] evidence for pain pretty poor
  - CDR review (9 trials): Intermittently better than placebo
  - One trial active comparator: TCA >placebo, pregabalin not >placebo

1) N Engl J Med 2009;361:1963-71. 2) http://www.cadth.ca/media/cdr/complete/cdr_complete_Lyrica%20Resubmission_September_25-2009.pdf http://www.cadth.ca/media/cdr/complete/cdr_complete_Lyrica_Jan26-06.pdf

Sore throat be gone!

- You see a 19 year old man with a very sore throat (4/4 for strep score). You give penicillin but he asks is there anything to get rid of the pain sooner
- You say: The only thing is pain meds like Ibuprofen
- False: A Sys Rev & Meta looked at Steroids in sore throat
  - 8 trials (369 peds & 374 adult pts), generally one oral dose
- Results: SS reduced time to pain relief, 6.3 less hrs
  - Pain resolved 24hours, 39% vs 12%, NNT 4
  - Pain resolved 48 hours, 76%-47%, NNT 4
- Bottom-line: Steroids (around ~50mg prednisone in adults) reduce pain but using them without Abx uncertain

•BMJ 2009;339:b2976.

"Butt-Out!"

- A 35 y.o. ♂ is considering quitting smoking. She would like a pill but is nervous about Varencline
- You say: The only other option is Buproprion
- False: Meta-analysis; Bupropion (16 studies, 5K pts), Nortriptyline (5 studies, 1K pts)
  - Nortrip 75-100mg = Bup 150/300mg (NNT = 11)
  - Drop-out: Nortrip (4-9%), Bup (7-12%)
  - 10 weeks: Nortrip $22 & Bup $175

Hughes JR, et al The Cochrane Library, 2004, Issue 3, Art. NO CD 000031.

Cardiac

↓BP = ↓CVD ?

- A 57 y.o. ♂ is in for med renewal. He is on HCTZ 12.5mg, Ramipril 5mg & Atenolol 50mg. His BP (125/75) is stable x3 years
- You say: All those meds are vital
- False for Atenolol
- Systematic review: 8 Trials (24K pts), 4.6 yr[1]
  - Placebo: No benefit
  - Med: Harm (NNH = All-mortality 110, CVS mortality 145, Stroke 79)
- Other Beta-blockers: Less clear[2]

1) Lancet 2004; 364: 1684-9. 2) Lancet. 2005; 366: 1545-53.

ACE plus ARB = ?

- A DM patient still has BP at 140 on HCTZ, Amlodipine & Ramipril. Your colleague says she heard ARB + ACE protects the kidney
- You say: I thought the evidence wasn't there
- True: RCT 26K pts; ACE, ARB vs ACE&ARB
  - No CVD diff in any! (BP similar)
  - Renal impairment 13.5% vs 10.2% undefined
  - Discontinuing due to adverse events, NNH 21-25 [1,2]
  - Hyperkalemia (K+≥5.5), Symptomatic Hypotension

N Engl J Med 2008;358:1547-59. Arch Intern Med. 2007;167:1930-6. Lancet 2008; 372: 547–53

Ezetimibe

– A 60 year old male with a one vessel PCI (following work-up for intermittent CP) has an LDL of 2.8 on 80mg Atorvastatin
- You say: You should really be on Ezetimibe too
- False. 3 RCT have provided some outcome data
- RCT[1], 720 pts, Ezetimibe 10mg or placebo (added to statin)
  - ↓ LDL 1.3 more (& ↓ CRP) but no change in carotid thickness
  - CVD events: 7 Statin alone vs 10 with Ezetimibe (not statistically different)

1. N Engl J Med 2008;358:1431-43. 2. N Engl J Med 2009;361:2113-22. 3. N Engl J Med 2008;359:1343-56. 4. N Engl J Med 2008;359:1357-66

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Ezetimibe

- RCT[2], 363 pts, Ezetimibe vs Niacin (added to statin)
  - Both predictable Lipid changes but Niacin improved Carotid thickness, not ezetimibe
  - CVD events (ss): 5% Ezetimibe vs 1% Niacin. NNT 24
- SEAS trial[3], 1873pts, Ezetimibe & statin vs placebo
  - No difference in combined CVD outcomes but CABG reduced (3.5%, NNT 29).
  - However, Sign more Cancers death, 1.6%, NNT 63 (& not completely dismissed[4])
- Nothing at present supports this drug being better than placebo, it appears worse than other drugs and it may be harmful

1. N Engl J Med 2008;358:1431-43. 2. N Engl J Med 2009;361:2113-22. 3. N Engl J Med 2008;359:1343-56. 4. N Engl J Med 2008;359:1357-66

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Weak hearts ticking longer?

- A 60 year old man is in 7 weeks post-MI. His recent echo shows EF of 35%. He is on Clopid, ACE, Beta-blocker, statin and ASA
- You say: I like to consider spironolactone
- True (likely). Meta-analysis of aldosterone antagonists in LV dysfunction post-MI or HF?
  - Overall Morality (15% vs 19%, NNT 27)
    - Post MI (EPHESUS): 16 mon, mortality, 14.4% vs 16.7%, NNT 44
    - HF (RALES): 24 mon, mortality, 34,5% vs 45.9%, NNT 9
    - Adverse Events: Serious Hyperkalemia (>6) 1-1.6% higher, Renal impairment 7% higher

1) European Heart Journal (2009) 30, 469–477.

Toward Optimized Practice

You gotta know when to hold 'em

- A sturdy 70 year old woman with A fib has an INR of 6 today
- You say: Let's hold a dose and recheck
- True: RCT comparing 1.25mg of Vitamin K vs placebo (waiting) for high INR (4.5-10)
  - No Stat Diff in bleed across any time (7, 30 or 90 days)
    - No diff in thromboembolism
    - Mean INR decrease 1 day: 2.8 Vit K vs 1.4 plac (ss)
    - Note: 67% of INRs between 4.5-6
- Likely best follow CPG: hold dose(s) for INR 5-9 or hold 1 dose & Vit K 1.25mg, esp if any bleeding risk
    - Higher INR suggest 2.5-5mg Vit K

1) Ann Intern Med. 2009;150:293-300. Chest 2008;133:160–98S.

Toward Optimized Practice

CRP

Comprehensive Risk Profile
or
Clinical Redundant Practice

Toward Optimized Practice

CRP: Comprehensive Risk Profile or Clinical Redundant Practice

1) What do biomarkers add to standard CVD risk models?
2) What might be the role of biomarkers like hsCRP?
3) What did the JUPITER trial add and what did not add?

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Studies of hsCRP & Biomarkers

- "C-reactive protein concentration (and the other inflammatory markers that were assessed) provided comparatively little additional predictive value over that provided by assessment of major established risk factors" (N Engl J Med 2004;350:1387-97)

Studies of hsCRP & Biomarkers

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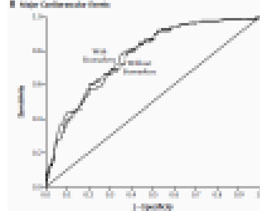
- Age, sex, and traditional risk factors provided 0.76 value in CVD predictive models compared to the 0.77 value when ten different biomarkers (including hsCRP) were added.[2]



N Engl J Med 2006; 355: 2631-2639

Studies of hsCRP & Biomarkers

Toward Optimized Practice

- 2 more studies assessing risk calculation
- Elevated hsCRP ~ increased risk of CHD (hazard rate ratio 1.19, $p < 0.001$) but similar to, or less than, many other markers including D-dimer (1.36), interleukin-6 (1.28), and lipoprotein-associated phospholipase A2 (1.17)[1]
- "hsCRP does not perform better than the Framingham risk equation for discrimination. The improvement in risk stratification or reclassification ...is small and inconsistent."[2]

1. Arch Intern Med 2006; 166: 1368-1373. 2. Int J Epidemiol 2009; 38: 217-231.

Some hs CRP Facts

Toward Optimized Practice

- Median hsCRP = 2.5 mg/l (♀) and 1.5 mg/l (♂).[1]
- Within-subject standard deviation is 1.2 mg/l.[2]
  - "to reduce the intra-individual variation sufficiently, each subject is likely to require blood samples collected on at least 10 occasions".[3]

Med	Statin	Vit E	Rosiglitazone	Rofecoxib
CRP	↓ (15-50%)[4]	↓ (50-80%)[4]	↓ (40%)[4]	↓ (variable)[8]
CVD	↓ [5]	↑ (mortality)[6]	↑ [7]	↑ [9]

1. N Engl J Med 2005; 352: 1611-1613. 2. Clin Chem 2001; 47: 444-450. 3. Ann Clin Biochem 2002; 39: 85-88. 4. Cardiovasc Drug Rev 2006; 24: 33-50. 5. Lancet 2008; 371: 117-125. 6. JAMA. 2007;297:842-57. 7. JAMA 2007; 298: 1189-1195. 8. Circulation 2004; 110: 934-939. 9. CMAJ 2002; 166: 1649-1650

When might hsCRP help?

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- General screening no but reclassifying?
- 2 studies, reclassify ≤18% of people between arbitrary risk classes (high-mid-low)[1]
  - Numbers reclassified up & down similar
- Others suggest less (5.6%)[2]
- Even if true, important to understand absolute benefits of Tx with statin
  - At 19% risk, statin (25% RR) gives a 4.75% ARR
  - At 21% risk (with CRP), statin (25% RR) give 5.25% ARR
  - Difference CRP added was 0.5% ARR over 10 years

1. Circulation 2008; 118: 2243-51 & Ann Intern Med 2006; 145: 21-29. 2 Circ Cardiovasc Qual Outcomes 2008; 1: 92-97.

What if we go off World: JUPITER

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- JUPITER: RCT, screened almost 90,000 primary prevention patients to find 17,802 with a LDL<130mg/dL (3.4 mmol/L) & hsCRP≥ 2mg/L
- 20mg rosuvastatin OD or placebo
- Stopped early after a median 1.9 years due to benefit
  - Combined CVD outcome: 2.8% placebo vs 1.6% rosuvastatin (NNT 82)
  - Mortality: 2.8% to 2.2% rosuvastatin (NNT 182)
  - More new cases of diabetes in the rosuvastatin group (3% vs 2.4%)
- Overall a good design but potential biases include:
  - Industry funding, Previous research has shown that funding can influence clinical trial outcomes (CMAJ, 2004; **170**(4): 477-80) and conclusions (JAMA, 2003. **290**(7): 921-8), including statin research (PLoS Med, 2007. **4**(6): p. e184)
  - Run-in
  - Stopping early (JAMA 2005; 294: 2203-9)
  - Large number of excluded patients

Bringing JUPITER Down to Earth

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- We know primary prevention patients benefit from statin therapy
  - Combined cardiovascular outcomes (NNT 73 – 4 yrs)[2]
  - Mortality in males (NNT 228 - 3.3 yrs)[3]
- Some argue that CRP as enrolment criteria demonstrated utility, especially with a low LDL:
  1) CRP levels were not part of the randomization so cannot conclude causation
  2) Without CRP levels, most patients in Jupiter were intermediate risk (10%-20% risk over 10 years) & get more benefit from therapy
  3) Mean CRP in Jupiter would add only about 1-3% to the calculated risk[4] and would done little to the absolute benefit
  4) ASCOT trial already showed statins reduce CVD endpoints from 9.5% to 7.5% (NNT 50) over 3.3 yrs in intermediate risk patients with a low LDL[5]

1. NEJM 2008;359:2195-207. 2. Arch Intern Med. 2006;166:2307-2313. 3. Arch Intern Med. 2005;165 :725-30. 4. http://www.reynoldsriskscore.org/ 5. Lancet 2003; 361: 1149–58.

Biomarkers Bottom-line

- Recommendations to include biomarker testing based on conflicting evidence
  - And Jupiter misinterpreted/exaggerated
- If any use, perhaps in patients at the borderline of needing or not needing Tx, but
  - Cut-offs arbitrary
  - Absolute change small
- If not willing to take drug, testing unnecessary

Tools for Practice

Opioids always trump NSAIDs

- A 11 year old boy has a rolled ankle. It looks pretty bad but X-ray is negative. His mom asks about pain medications
- You say: Here's acetaminophen with codiene, it's the best
- False: Ibuprofen best. 3 trials of pediatric MSK injury
- 336 children; ibuprofen, acetaminophen or codiene[1]
  - Ibuprofen better than either (for pain score and attaining "adequate" pain relief
- 68 children; ibuprofen or aceta+codiene[2]
  - No difference in pain scores
- 336 children; ibuprofen vs acetaminophen+codeine[3]
  - No difference in mean pain scores
  - Ibuprofen less functional limitation & adverse events

1) Pediatrics 2007;119:460-7. 2) Acad Emerg Med 2009;16(8):711-716. 3) Ann Emerg Med 2009 Oct;54(4):553-60. Epub 2009 Aug 19.

For whom the bell tolls…

- A 43 year old male presents to your office with onset unilateral facial nerve paralysis over 24 hrs. You Dx Bell's Palsy
- You say: You should take acyclovir & steroids immediately
- False & True: RCT, double blind, 551 pts
  - Acyclovir: No benefit
- Prednisilone 25mg BID x 10 d
  - **3 mo**, 83% vs 63% (pred vs no pred) **NNT = 6**
  - **9 mo,** 94% vs 82% (pred vs no pred) **NNT = 8**

N Engl J Med 2007;357:1598-607

B12: Pill or Poke?

- A 50 year old woman comes in for her monthly B12 shot. You offer to switch her to oral B12. She thinks you're crazy
- You say: I am not crazy, it works!
- True(?): Systematic Rev[1] of 2 RCTs[2,3]
  - B12 levels and associated biochemical B12 markers (total homocysteine and serum methylmalonic acid)
  - Hematological and neurological responses
  - Other data also supports[4]
- A dose of 1000mcg (1mg) orally a day likely adequate & most commonly recommended

1) Cochrane Database Syst. Rev. 2005(3):004655. 2) Blood 1998; 92:1191-8. 3) Clinical Therapeutics. 2003; 25(12): 3124-34. 4) Postgrad Med J 2003; 79:218–220. Drug Therap Bull. DTB 2009; 47: 19-21.

"Sticks and Stones…?"

- A 34 y.o. ♂ was Dx with a stone 2 nights ago in ER. He's referred to urology but it will be 18 days. He is hoping for something to help
- You say: Sorry, but we only have pain relief
- False: Sys Rev, 9 Trials (693 pts)
  - Distal 1/3 of ureter and 4-8 mm stones
  - Stone pass: 47% vs 78%, NNT = 4 at 4wks
  - nifedipine 30mg, terazosin 5mg, doxazosin 4mg or tamusolin 0.4mg for 4 weeks

1) Lancet 2006; 368: 1171-9. 2) Ann Emerg Med 2007; 50:552-63

Fan of Fads: Vitamin D

- **A 55 year old woman wonders if she should take Vitamin D and does she need a test?**
- **<u>You say</u>: You don't need a test, just take it**
- **True: 3 Met-analysis show it helps (stat. sign)**
  - Fracture (19 trials)[1]: >400IU/day Vitamin D
    - Reduced Non-vertebral fractures 1.1%, NNT 93
  - Falls (5 trials)[2]: Reduced 7%, NNT 15
  - Mortality (18 trials)[3]: ↓ Mortality by ~ 0.4%, (NNT 147)
- **No studies enrolled patients based on tests. Most people are Vit D insufficient[4]**
- **Treat with 1000 IU daily and don't bother to test**

1) Arch Intern Med. 2009;169(6):551-561. 2) JAMA. 2004;291(16):1999-2006. 3) Arch Intern Med. 2007;167(16):1730-1737. 4) CMAJ 2002;166(12):1517-24. Am J Clin Nutr 2007;85:860–8. Arch Intern Med. 2009;169(6):626-632