29th Annual
Best Science Medicine Course

Formerly the Drug Therapy Decision Making Course – 25 years

May 4th and 5th, 2018

Fairmont Waterfront Hotel
Vancouver, B.C.

SATURDAY Syllabus

COURSE DIRECTORS
Drs. James McCormack, G. Michael Allan and Robert Rangno

COMMITTEE MEMBERS
Drs. Rita McCracken and Tracy Monk

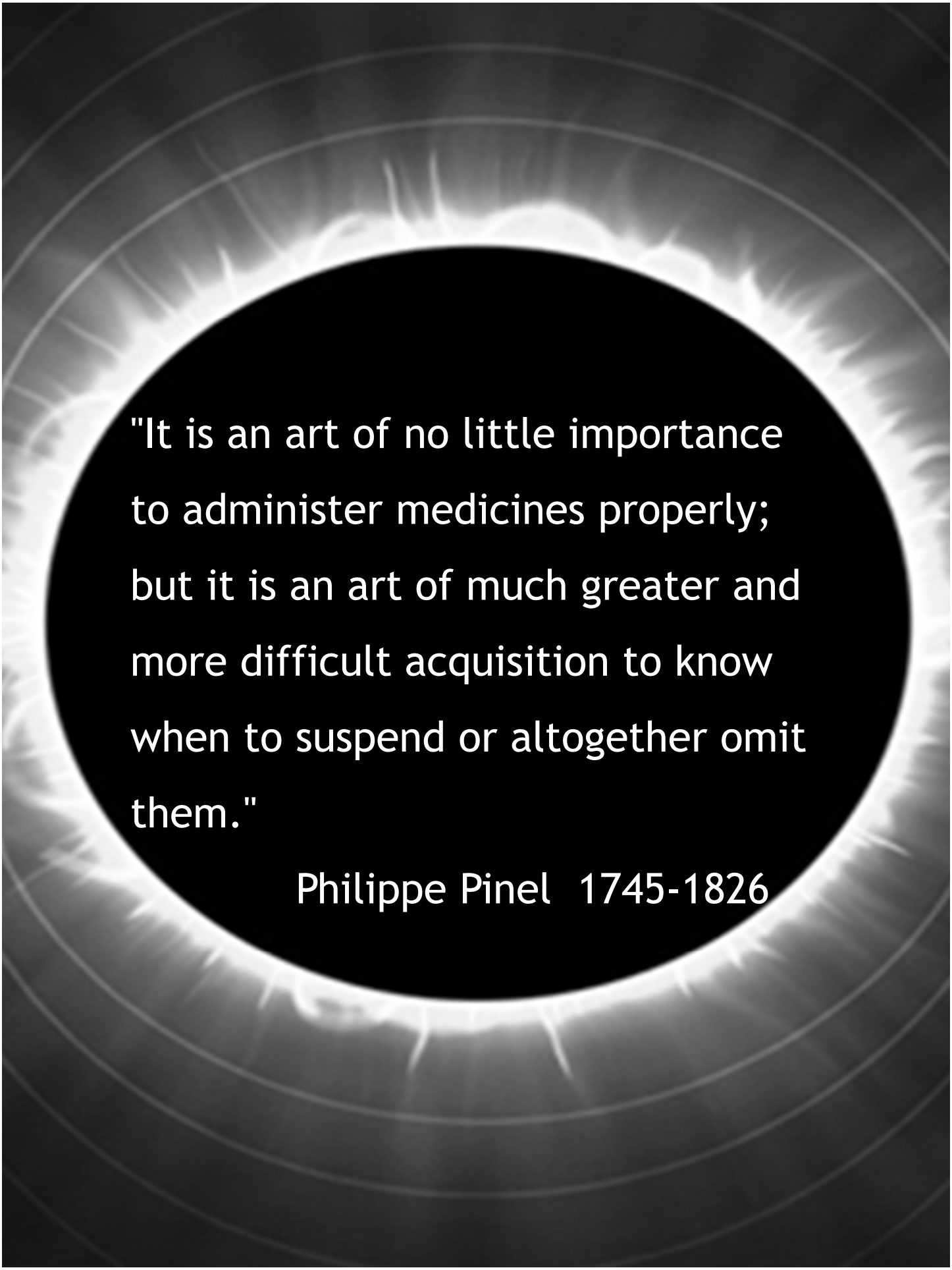
DEPARTMENT OF FAMILY MEDICINE | Leaders in primary care, champions of community health

Providence HEALTH CARE ST PAUL'S HOSPITAL

Evidence Based Therapeutics TEC

A long time ago on a planet far,

far away ….


"It is an art of no little importance to administer medicines properly; but it is an art of much greater and more difficult acquisition to know when to suspend or altogether omit them."
Philippe Pinel 1745-1826

The New Therapeutic Commandments

Thou shalt

1. Have no aim except to help patients according to their goals
2. Always seek knowledge of the benefits, harms, and costs of treatment
3. If all else fails consider watchful waiting
4. Honour balanced sources of knowledge
5. Treat according to level of risk and not to level of risk factor
6. Not bow down to treatment targets
7. Honour thy elderly patient
8. Not pile one treatment upon another
9. Diligently try to find the best treatment for the individual
10. Start with the lowest dose possible

Written by R Lehman, J McCormack, T Perry, A Tejani, J Yudkin

SATURDAY, MAY 5, 2018

07:30 Registration (Coffee & Muffins)
Chairs – Bob Rangno and James McCormack

"You think Yoda stops teaching, just because his student does not want to hear?" – Yoda

08:30	Stem cell therapies "Do not assume anything Obi-Wan. Clear your mind must be if you are to discover the real villains behind this plot."	Tim Caulfield
08:50	More top 5 new pediatric studies "Size matters not. Look at me. Judge me by my size, do you? Hmm? Hmm."	Tina Korownyk
09:10	Heart failure – increase drugs not dose?	Mustafa Toma
09:30	Questions	
09:50	Refreshment Break	

"The only true wisdom is knowing you know nothing" – Socrates = Greek for Yoda

10:10	Anxiety evidence – "Once you start down the dark path, forever will it dominate your destiny, consume you it will."	Adrienne Lindblad
10:30	A GI potpourri "I've got a bad feeling about this."	Mike Kolber
10:50	Questions	
11:10	Medical Marijuana "The Force is strong with this one."	Mike Allan
11:30	Questions	
11:50	Lunch	

"Ready are you? What know you of ready?" – Yoda

12:40	MRSA and what do we need to treat – how long ABX "I've got a bad feeling about this."	Natasha Press
13:10	10 silly studies that you may or may not need to know about.	R2-D2 and C-3PO
13:50	Now how to do all you've learned "Do. Or do not. There is no try."	The Gang plus the Audience
15:00	"I'm one with the Force. The Force is with me."	

BSMC

29th Annual

Best Science Medicine Course

Formerly The Drug Therapy Decision Making Course

"May The Fourth Be With You"

Best Science Medicine Course 2018

FACULTY

Course Committee

Co-Chairs:

Bob Rangno, Emeritus Prof., Medicine, Pharmacology, UBC & PHC
James McCormack, Prof., Pharmaceutical Sciences, UBC
G. Michael Allan, Prof., Family Medicine, University of Alberta
& Director, Evidence and CPD Program, Alberta College of Family Physicians

Committee:

Rita McCracken, Clin. Assist. Prof., Medicine and Associate Head, Family Medicine, PHC
Tracy Monk, Clin. Assist. Prof., Medicine, UBC

Guest Faculty

G. Michael Allan, Prof., Family Medicine, University of Alberta
& Director, Evidence and CPD Program, Alberta College of Family Physicians
Alan Cassels, Adj. Prof., Human and Social Development, University of Victoria
Timothy Caulfield, Prof., Faculty of Law, University of Alberta
Canada Research Chair in Health Law and Policy (Tier 1)
Mike Kolber, Assoc. Prof., Family Medicine, University of Alberta
Tina Korownyk, Assoc. Prof., Family Medicine, University of Alberta
Adrienne Lindblad, Assoc, Clin. Prof., Family Medicine, University of Alberta
& Knowledge Translation and Evidence Coordinator, Alberta College of Family Physicians

Local Faculty

Tommy Gerschman, Clin. Instr., Pediatrics, UBC & FHA
Natasha Press, Clin. Assoc. Prof., Inf. Diseases, UBC & PHC
Kam Shojania, Clin. Prof., Medicine, Head, Rheumatology, UBC & PHC
Christy Sutherland, Clin. Asst. Prof., Family Medicine, UBC
Aaron M Tejani, Clin. Asst. Prof., Pharmaceutical Sciences, UBC
Mustafa Toma, Clin. Assoc. Prof., Cardiology, UBC & PHC

FHA – Fraser Health Authority
PHC – Providence Health Care
UBC – University of British Columbia
VCHA – Vancouver Coastal Health Authority
VGH – Vancouver General Hospital

Timothy Caulfield

Stem cell therapies

"Do not assume anything Obi-Wan. Clear your mind must be if you are to discover the real villains behind this plot."

Timothy Caulfield

Faculty/Presenter Disclosure

- **Faculty/Presenter:** Timothy Caulfield
- **Relationships with commercial interests:**
  - **Speakers' Spotlight**
  - **Producer and host, Peacock Alley Entertainment**
  - **Publisher: Penguin Random House Canada**

Disclosure of Commercial Support

- My talks are not associated with any financial support from a commercial entity. The research was supported by grants from entities like the Stem Cell Network, CIHR and Genome Canada.

Mitigating Potential Bias

- Speakers' Spotlight, my publisher and the TV production company have no say or involvement in the content of my presentations.

Learning Outcome Objective Slide

Talk: "Stem Cell Therapies"

Objectives: 1) Explain the current state of stem cell research and the growing problem associated with the marketing of therapies; and

2) Outline drivers of this trend and what can be done to moderate the problem.

Beware the hype on stem-cell breakthroughs

TIMOTHY CAULFIELD
SPECIAL TO THE GLOBE AND MAIL
PUBLISHED MARCH 20, 2017UPDATED MARCH 24, 2017

Health science gets a lot of attention in the popular press. People love hearing about breakthroughs, paradigm shifts and emerging cures. The problem is, these stories are almost always misleading.

While optimistic miscalculations of the state of biomedical research may seem as if it were a harmless distraction, there is a growing body of evidence that suggests it can be the source of real social harm. It can drive unrealistic expectations, affect the public utilization of health-care resources and even shape a less-than-ideal research agenda. It can also help to legitimize the marketing of unproven therapies.

This week, the New England Journal of Medicine (NEJM) reported on three individuals who went blind after receiving an unproven stem cell treatment at a Florida clinic. The patients paid thousands of dollars for what they thought was a clinical trial on the use of stem cells to treat macular degeneration.

The primary fault, both legally and morally, for the marketing and use of unproven stem-cell therapies lies with the providers who are involved with the practice. We need national regulators (e.g., Health Canada, the U.S. Food and Drug Administration) and the bodies that oversee the relevant health-care professionals (e.g., the colleges that regulate physicians) to take a more active role – a point noted by Dr. George Daley in an essay accompanying the NEJM case report.

Indeed, it is hard to blame patients for being drawn to providers that present optimistic portrayals of benefit. We live in confusing times. It is becoming increasingly difficult to tease out the real science from the bad and the "fake health news" from a genuinely exciting scientific advance. Not only is the science twisted by multiple systemic forces – publication pressures, overenthusiastic news releases, commercial interests and media spin – misinformation is being broadcast on a growing number of communication platforms. Social media, for example, have allowed for the rapid dissemination of false promises and creation of confirmation bubbles in which like-minded believers can trade anecdotes of success. And studies have shown clinics exploit platforms such as Twitter to create buzz about and demand for unproven therapies.

For the general public, here is a good rule of thumb: Doubt every claim that suggests a significant breakthrough. Doubt everything. This may sound a tad cynical, but if you adopt this approach you will be pleasantly surprised when something actually pans out. More important, this nothing-ever-works-as-promised strategy will be correct 99 per cent of the time.

For patients seeking a treatment, be cautious of any clinic offering a therapy that seems too good to be true, because virtually every time it will be too good to be true.

Consider stem-cell research. Think of all the hype, the headlines about near-future applications and the pronouncement about revolutionary regenerative therapies. This hand waving has been going on for almost two decades. So much so that the phrase "stem cells" has morphed into cultural marker for "cutting edge." But despite all this unrelenting, upbeat noise, there are very few stem-cell therapies that are currently ready for clinical application. Daley, who is a renowned stem-cell researcher and the current dean of Harvard Medical School, concludes there are just a handful: those used for the blood-related ailments and for the skin (epithelium) conditions. The International Society for Stem Cell Research agrees with Daley and notes "the list of diseases for which stem-cell treatments have been shown to be beneficial is still very short."

Don't get me wrong; I believe stem-cell research remains a fantastically promising area of science. But true medical breakthroughs are rare. Incredibly rare. In fact, if a study claims a large effect size, which is often the case in stories about breakthroughs, there is a good chance the results will be overturned by subsequent work. In a well-known 2003 analysis, it was found that out of 101 studies published between 1979 and 1983 in top science journals and framed as clinically promising interventions, only one was "used extensively for the licensed indications" (yes, about 99 per cent of the peer-reviewed predictions were wrong). The authors concluded that "even the most promising findings of basic research take a long time to translate into clinical experimentation, and adoption in clinical practice is rare."

Yes, we need regulators to crack down on the marketing of unproven stem-cell therapies. As demonstrated by these recent reports of treatment-induced blindness, these clinics can cause serious harm. But we also need to do our best to curb the science noise that helps to legitimize the false claims made by the purveyors of stem-cell products. Scientists, clinicians, policy makers and journalists should do their best to counter misinformation in all its forms.

More good science, less science-y noise.

Timothy Caulfield is Canada Research Chair in Health Law and Policy at the University of Alberta, a Trudeau Fellow and author of Is Gwyneth Paltrow Wrong About Everything?

This story first appeared in Healthy Debate, an online publication guided by health-care professionals and patients that covers health policy and evidence-based medicine in Canada.

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Tina Korownyk

Top 5 ish New Pediatric Studies

"Size matters not. Look at me. Judge me by my size, do you? Hmm? Hmm."

Tina Korownyk

Faculty/Presenter Disclosure

- **Faculty/Presenter: Tina Korownyk**
- **Where I get Personal $:** U of A, Alberta Health
- **Where I get Grant/ Program $:** Alberta College of Family Physicians, Other Colleges of Family Physicians, Toward Optimized Practice, Other non-profit organizer

- **Relationships with commercial interests:**
  - **Grants/Research Support:** Not applicable
  - **Speakers Bureau/Honoraria:** Not applicable
  - **Consulting Fees:** Not applicable
  - **Other:** None

Objectives

- Review and discuss recent studies involving little people
- 5 observational studies
- 5 randomized controlled trials

Observing Kids

- **Fruit Juice and BMI**, 8 studies, 34,470 children.[1]
  - 1-18 yrs: 1 additional 6-8 oz 100% fruit juice = 0.003 unit increase in BMI z score/year (not clinically significant)
- **E-cigarette use**, 9 studies, 17389 adolescents. [2]
  - Probability of cigarette smoking initiation
  - 30.4% for ever e-cigarette users
  - 7.9% for never e-cigarette users
- **Adverse Childhood Events,** 35 studies[3]
  - Associated with cognitive delay, asthma, infection, somatic complaints, sleep disruption & endocrine/immune changes.
  - Outcomes highly variable and may be acute or delayed

1) Pediatrics. 2017;139(4):e20162454 2) JAMA Pediatr. 2017;171(8):788. 3) BMC Pediatr. 2018; 18: 83.TX: 4) Acad Pediatr. 2015 ; 15(5): 480–492. 5) Clin Child Fam Psychol Rev. 2018; 21(2): 171–202 6) Acad Pediatr. 2012 Jul-Aug; 12(4): 259–268.

Tina Korownyk

Influenza Vaccine Effectiveness Against Pediatric Deaths: 2010–2014

Case-Control, 358 influenza associated deaths 2010-2014, children 6 mo – 17 yrs, US.

- Vaccination status known for 291
  - Cases: 26% vaccinated (≥ 14 days prior)
  - Comparison: 48% vaccinated
- 153/291 (53%) had ≥ 1 high risk medical conditions
  - No high risk medical condition 20% vaccinated
  - ≥ 1 high risk medical conditions 31% vaccinated
- Overall Vaccine effectiveness: 65% (CI 54%-74%)
- As per other studies, varies with year and strain (ie 29-87%)
- **Bottom Line:** Seems like a good bet

Pediatrics. 2017 May;139(5). pii: e20164244. Clin Infect Dis. 2016 Dec 15;63(12):1564-1573. Vaccine. 2017 May 9;35(20):2685-2693. Pediatrics. 2018 Apr;141(4). pii: e20172918.

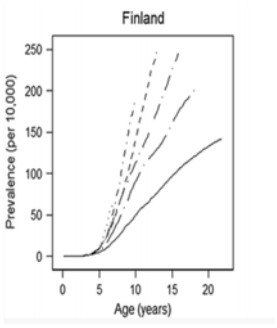
Diet & ADHD

- Case control
  - 60 children with ADHD, 60 controls
  - Energy, dietary intake and adherence to mediterranean diet
- **Results**: Low adherence to mediterranean diet associated with ADHD diagnosis (RR 2.80)
  - Significantly associated with:
  - Lower frequency of consuming fruits, vegetables, pasta, rice
  - Higher frequency of skipping breakfast, eating fast food
  - Higher frequency of sugar, candy, cola and non-cola beverages
  - Low consumption of fatty fish
  - (No diff olive oil, nuts, other carbs)
- **Bottom Line**: Mediterranean diet always good, at minimum for CV outcomes.

The mediterranean diet and adhd in children and adolescents. Pediatrics 2017. rios-hernandez

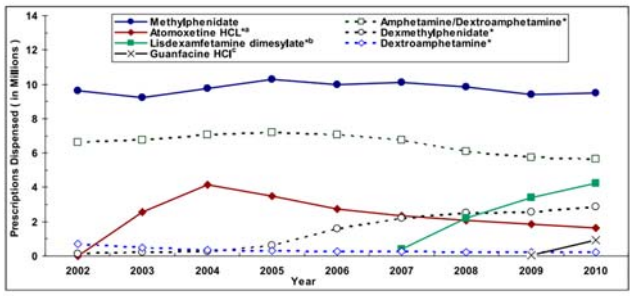
Increasing Prevalence of ADHD

- United States:[1,2]
  - 1.4% in 1976
  - 7.8% in 2003
  - 9.5% in 2007
  - 11.0% in 2011
- Israel: ↑ from 7% to 14% (2005-2014)[3]
- UK: 2x ↑in children on meds (2003-2008) [4]
- Significant ↑in other European Countries (1990-2007)[5]
- ~70% receive medication for ADHD[6]
- Methylphenidate top rx for adolescents in US 2010
  - All ADHD meds ↑ 46% since 2002[7]



1) Pediatrics. 2000 Jun;105(6):1313-21 2) https://www.cdc.gov/ncbddd/adhd/data.html 3) BMC Pediatr. 2017 Dec 29;17(1):218 4) BMC Pediatr. 2012 Jun 19;12:78. 5) Eur Child Adolesc Psychiatry. 2015 Feb;24(2):173-83. 6) J Pediatr. 2018 Jan;192:240-246.e1. 7) Pediatrics. 2012 Jul;130(1):23-31.

Prescriptions for ADHD Medications Kids age 0-17 years



Pediatrics. 2012 Jul;130(1):23-31.

Tina Korownyk

ADHD

- Recent AHRQ REVIEW 2018
- Omega 3/6 supplements – moderate evidence of no benefit
- Moderate evidence of benefit for CBT, child or parental training to improve ADHD symptoms, but not academic performance
- No evidence to inform monitoring once treatment initiated
- Bottom Line: Mediterranean diet always good, at minimum for CV outcomes.

Kemper AR, Maslow GR, Hill S, et al. Attention deficit hyperactivity disorder: diagnosis and treatment in children and adolescents. Comparative Effectiveness Review No. 203. AHRQ Publication No. 18-EHC005-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2018. (Review)

Cabbage, Not Just for Casseroles

RCT, 227 breastfeeding moms; cabbage leaves, gel packs or usual care:
- Versus routine care, cabbage decreased:
  - Pain: 30 minutes, 1 & 2 hours by ~0.4-1 (10-point scale).
  - Breast hardness: 0.2-0.4 (6-point scale).
- Versus gel packs, cabbage decreased:
  - Pain: 2 hours by 0.5
  - Hardness at 2 hours by 0.4
- Satisfaction: cabbage 99%, routine care 70%, gel packs 81% NNT=4-6

- Other RCTs:
  - No difference chilled vs room temperature
  - No difference chilled gel packs vs chilled cabbage
    - 2/3 of women preferred cabbage (worked quicker)
    - 1/3 preferred gel (lasted longer)
- **Bottom Line: Women report high levels of satisfaction with cabbage leaves (NNT=4-6). Cabbage leaves reduce pain (by ~1 point out of 10) and breast hardness (by ~0.4 points out of 6).**

TFP 2018

Little Updates on Lactobacillus

- RCT (438): kids (age ~5) on Abx, Lactobacillus vs placebo
  - 15-28d: No difference in Loose BM 39% vs 45%; Abx Associated diarrhea 3% vs 4%, Abdominal pain, etc.
- RCT (184): High risk Infants, first 6 mo
- Lactobacillus vs control
  - 2 years: No difference in Eczema 31% vs 29%;
  - 5 years: No difference in Asthma 17% vs 10%

A Olek, J Pediatr 2017; epub. Pediatrics. 2017 Sep;140(3). pii: e20163000.

Inhaled Steroids in Asthma

- RCT, double blind, 254 children (5-11yrs), mild to moderate asthma on daily inhaled steroids
- Intervention group: increase steroids x5 when symptoms worsen (yellow zone)
- **Results:**
  - Exacerbations requiring steroids/year
    - Intervention group 0.48, control 0.37
  - Growth Rate
    - Intervention group 5.43cm, control 5.65 (diff = 0.22, p =0.06)
- **Bottom line: Increasing inhaled steroids at sign of worsening asthma does not significantly reduce exacerbations, and may affect height**.
- Cochrane 2010 - no benefit increased ICS in adults.

1) N Engl J Med 2018; 378:891-901 2) Cochrane Database of Systematic Reviews 2010, Issue 12.

Tina Korownyk

NOT - Acute Appendicitis

- **2 Meta-analysis**, 5 & 10 studies (1 RCT, 9 cohort), 404-766 kids, 5-18 yrs
- Non-operative treatment successful in 91% - 97%
- (Symptom free in 48 hrs, no recurrence at 1 mo)
  - 17 - 27% had recurrence / appendectomy within the year
  - No significant difference in complications

- **1 RCT,** 50 children, appendicitis, excluded if ruptured/ appendiceal mass
- Surgery vs IV meropenem & metronidazole x 48 hours (then oral)
  - Non operative tx successful for 92% (improving by 48hrs, no recurrence 3 mo)
  - By 1 year, 38% (9/24) non-operative group underwent surgery
  - Hospital stay longer with abx (~1/2 day), cost similar

Bottom Line: Challenges our current way of thinking. Not yet ready for prime time.

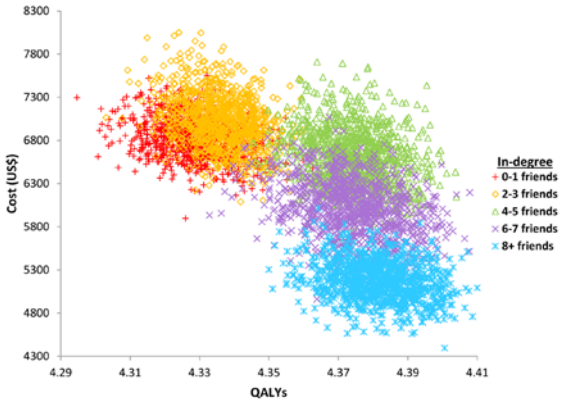
JAMA Pediatr. 2017 May 1;171(5):426-434. Pediatrics. 2017 Mar;139(3). pii: e20163003. Ann Surg. 2015 Jan;261(1):67-71.

Kindness Counts

- Nested RCT, 19 classrooms, 415 students, mean 11 yrs
- Randomized to perform 3 acts of kindness/week (for anyone) or visit 3 places (anywhere they wish) x 4 weeks
- **Results**: Those randomized to acts of kindness had significant change in:
  - Peer nominations 1.6 vs 0.7
    - "gained an average of 1.6 friends"
  - Positive affect scale (?clinical significance unknown)
  - No significant difference in happiness or life satisfaction
- **Bottom Line: Prompting prosocial behavior in preadolescents boosts peer acceptance and well-being**

Layous K, Nelson SK, Oberle E, Schonert-Reichl KA, Lyubomirsky S (2012). PLoS ONE 7(12): e51380. doi:10.1371/journal.pone.0051380

Are friends helpful?



Appl Health Econ Health Policy. 2014 April ; 12(2): 191–201.

Can you Identify this rash?

1991 - 100 children (85% <5yrs) 0-5d febrile, unknown widespread rash[1]
- Throat, rectal swabs, urine and blood samples
- Identified cause (infectious agent) in 65%.
- Overall 47% (47/100) viral (17 viruses identified).
  - 13 due to bacteria, 3 mycoplasma pneumoniae, 2 had 2 or more
  - 9 rash patterns, multiple patterns observed with individual viruses

2012 - 108 children with atypical rash (excluded measles, rubella, varicella)[2]:
- Identified cause in 77%,
- 52% (56/108) viral
- Multiple outcomes, more likely viral if:
  - mucous membranes, buttocks, hands/ feet

- **Bottom Line**: Only find cause for ~70%. Half due to viruses we can identify. Clinical representation often unhelpful in defining the causative agent

1) Br J Dermatol. 1991 May;124(5):433-8. 2) J Am Acad Dermatol. 2012 Dec;67(6):1282-8.

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Providence HEALTH CARE
How you want to be treated.

Heart Failure – Increase Drugs *not* Dose?

BSMC 2018

Mustafa Toma, MD SM FRCPC ABIM
Clinical Associate Professor, UBC
May 5th, 2018

Disclosures

- Faculty: Mustafa Toma
- Relationships with Commercial Interests:
  - Research Support/Grants: Novartis, Servier
  - Speakers Bureau/Honoraria: Novartis, Servier
  - Advisory Board/Consulting: Novartis, Servier
  - Clinical Trials: Novartis, Servier, Merck

Mitigating Bias

- Most slides from CCS guidelines *or CCS* accredited CME slide decks
- EBM/Guidelines focus
- No industry funding for today's presentation

Objectives

- To be familiar with the 2017 CCS HF Guidelines
- To understand the role of triple therapy in HF management
- To be aware of new therapies available for the treatment of HFrEF in 2018

Mustafa Toma

HF: The Fastest Rising Cardiovascular Condition In Canada

- The prevalence of HF has increased over the past few decades[1]
  - More accurate diagnostic algorithms
  - Increasing numbers of elderly and patients with risk factors for HF
  - Improved survival rates of cardiac and other chronic conditions
- An estimated 600,000 Canadians are living with HF and 50,000 new patients are diagnosed each year[2]
  - 1.4 million hospital days per yea
- Up to 40% to 50% of people with congestive heart failure die within five years of diagnosis

1. Johansen H, *et al. Can J Cardiol.* 2003;19(4):430-435 / 2. Ross H, *et al. Can J Cardiol.* 2006;22(9):749-754.

Current Challenges Associated With HF Care In Canada

- HF cannot be "cured" by relieving symptoms
  - Often progresses without signs or symptoms
  - Clinical focus has been to control symptoms
- Risk/Mismatch for patient care is common
- Patients discharged are often unprepared and unsupported
  - Patients unable to self-manage – information overload
  - Frequent returns to emergency
  - 30-day readmission rates are high

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Practical Tips in HF Diagnosis

- HF can be diagnosed without a history or current evidence of volume overload. Thus, the term 'heart failure' is generally preferred over 'congestive heart failure'
- A normal LVEF does not exclude HF as a diagnosis
  - (e.g., HF with preserved systolic function – HFpEF)

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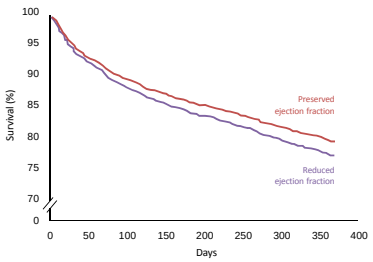
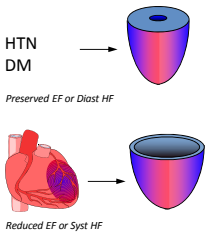
Arnold JMO, Liu P et al. *Can J Cardiol* 2006;22(1):23-45.

HFrEF vs. HFpEF: Different Diseases With The Same Prognosis?

Adjusted Survival Curves
for Patients with Heart Failure with Reduced or Preserved Ejection Fraction during the Year after the First Hospital Admission.





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Bhatia S, Liu P, *et al., N Engl J Med* 2006; 355:260-9

Mustafa Toma

Common Precipitants for Decompensation

- Adherence (Meds)
- Adherence (Salt)
- Adherence (Fluid?)
- Concurrent Infections
- Drugs/toxins: NSAIDs, BB/CCB, EtOH
- Arrhythmias
- Acute coronary syndrome
- Severe hypertension
- Pulmonary embolism
- Renal Failure

Key Points

- Evidence-based medications (EBM) are a major cornerstone in HF treatment
- Clinical tools exist to help improve the application of EBM in HF to front-line practitioners. For example the app can form the underpinning of a collaborative practice arrangement between nurses/physicians/pharmacists

Smart Phone App - CCS: MED-HF

Medications in HF: Patients

"Medications don't work in patients who don't take them"

- C. Everett Koop

Mustafa Toma

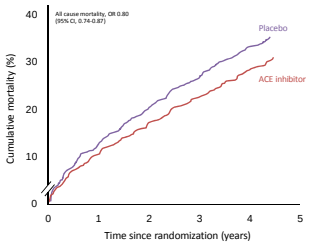
Medications in HF: Providers

Medications don't work in patients:

- whose Health Care Professionals don't prescribe them
- whose HCP don't prescribe them optimally
- whose HCP don't prescribe them safely

Clinical Effects Of ACE Inhibitors On HF

Overview of 5 Trials
(SAVE, AIRE, TRACE, SOLVD prevention, SOLVD treatment)



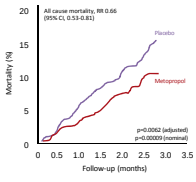
Large, prospective, randomized trials have consistently demonstrated a significant reduction in mortality

Overall, ACE inhibitors reduced risk of death by 20%
(p<0.0001)

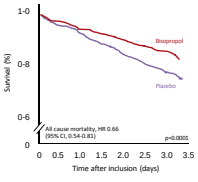
Treatment of 100 patients could prevent 7 major events (death/CHF readmission/MI)
ACE, Angiotensin-converting-enzyme.
Flather MD, *et al. Lancet*. 2000;355(9215):1575-1581.

Key Evidence Supporting Beta-Blockers In HF

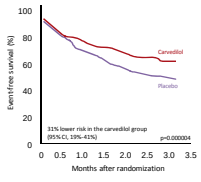
MERIT-HF
Cumulative percentage of total mortality*



CIBIS II
Survival curves**

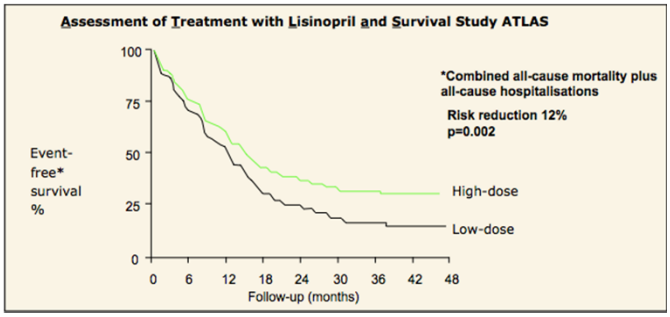


COPERNICUS
Time to death or hospitalization***



- *MERIT-HF Study Group. Lancet 1999;353:2001-7.
- ** CIBIS II Investigators. Lancet 1999;353:9-13.
- ***Packer M *et al. Circulation* 2002;106:2194-9.
- Arnold JMO, Liu P *et al. Can J Cardiol* 2006;22(1):23-45.

Medication Titration



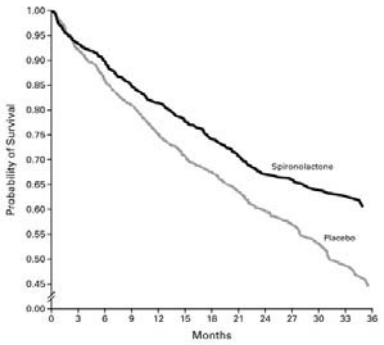
ATLAS Trial
Circulation 1999; 100:2312-18

Mustafa Toma

When to Use Spironolactone

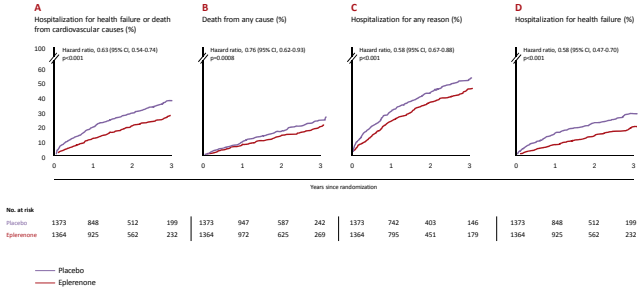
INCLUSION:
- NYHA III/IV
- On ACE-I and diuretic
- EF < 35%

EXCLUSION:
- Valvular heart disease
- UA
- Cr > 221 umol/L
- K > 5.0



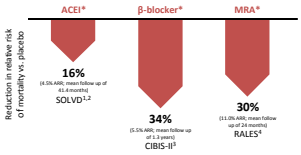
Pitt B et al. N Engl J Med 1999;341:709-717.

EMPHASIS-HF: Eplerenone Improve Survival Among NYHA II HF Patients



Zannad F *et al. N Engl J Med.* 2011;364(1):11-21.

Mortality In HFrEF Remains High Despite The Introduction Of New Therapies That Improve Survival



Survival rates in chronic HF have improved with the introduction of new therapies[1]

However, significant mortality remains – ~50% of patients die within 5 years of diagnosis[6–8]

- *On top of standard therapy at the time of the study (except in CHARM-Alternative where background ACEI therapy was excluded) patient populations varied between trials and as such relative risk reductions cannot be directly compared. SOLVD (Studies of Left Ventricular Dysfunction), CIBIS-II (Cardiac Insufficiency Bisoprolol Study II) and RALES (Randomized Aldactone Evaluation Study) enrolled chronic HF patients with LVEF≤35%. CHARM-Alternative (Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity) enrolled chronic HF patients with LVEF≤40%.
- ACEI=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; HF=heart failure; HFrEF=heart failure with reduced ejection fraction; LVEF=left ventricular ejection fraction; MRA=mineralocorticoid receptor antagonist
- 1. McMurray *et al.* Eur Heart J 2012;33:1787–847; 2. SOLVD Investigators. N Engl J Med 1991;325:293–302; 3. Granger *et al. Lancet* 2003;362:772–6; 4. CIBIS-II Investigators. Lancet 1999;353:9–13; 5. Pitt *et al. N Engl J Med* 1999;341:709-17;–50; 6. Go *et al. Circulation* 2014;129:e28-e292; 7. Yancy *et al. Circulation* 2013;128:e240–327; 8. Levy *et al. N Engl J Med* 2002;347:1397–402

Targeting Residual Risk In Systolic HF

- Through:
1. Combined Neprilysin and Renin-Angiotensin System Inhibition
   - The PARADIGM-HF trial (sacubtril/valsartan)
2. Heart Rate Reduction
   - The SHIFT trial (ivabradine)

Sacubitril/valsartan

Health Canada approved indication:
- Treatment of heart failure with reduced ejection fraction (HFrEF) in patients with NYHA Class II or III, to reduce the incidence of cardiovascular death and heart failure hospitalisation

Ivabradine

Approval by Health Canada obtained in Feb 2017

- 3

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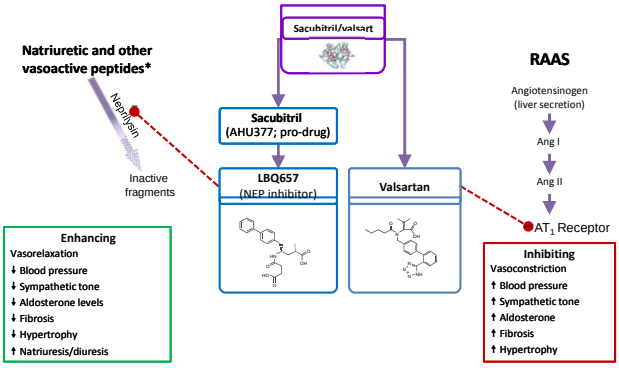
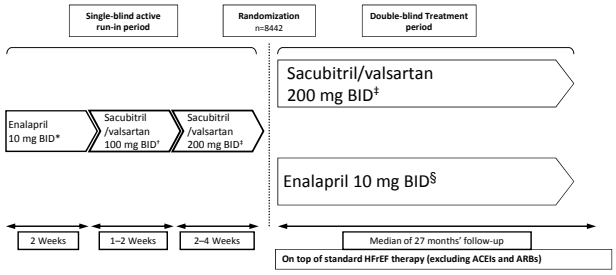
Sacubitril/valsartan simultaneously inhibits NEP and blocks the AT_1 receptor (via valsartan)



PARADIGM-HF: Study Design



Note: Health Canada approved corresponding doses for Sacubitril/valsartan are as follows:
Sacubitril/valsartan 100 mg: 48.6 mg sacubitril / 51.4 mg valsartan
Sacubitril/valsartan 200 mg: 97.2 mg sacubitril / 102.8 mg valsartan

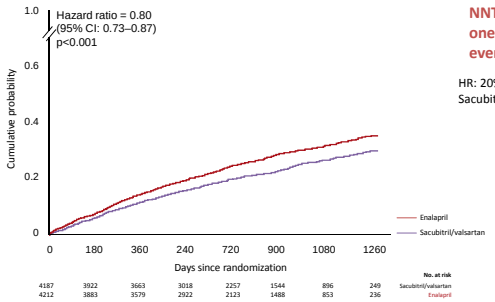
- *Enalapril 5 mg BID (10 mg TDD) for 1–2 weeks followed by enalapril 10 mg BID (20 mg TDD) as an optional starting run-in dose for those patients who are treated with ARBs or with a low dose of ACEI; †200 mg TDD; ‡400 mg TDD; §20 mg TDD.
- McMurray et al. Eur J Heart Fail. 2013;15:1062–73; McMurray et al. Eur J Heart Fail. 2014;16:817–25; McMurray et al. N Engl J Med 2014;371(11):993–1004.

PARADIGM-HF: Key Inclusion Criteria

- Chronic HF NYHA FC II–IV with LVEF ≤40%*
- BNP (or NT-proBNP) levels as follows:
  - ≥150 (or ≥600 pg/mL), or
  - ≥100 (or ≥400 pg/mL) and a hospitalization for HFrEF within the last 12 months
- ≥4 weeks' stable treatment with an ACE inhibitor or an ARB#, and a β-blocker
- Aldosterone antagonist should be considered for all patients
  (with treatment with a stable dose for ≥4 weeks, if given)

*The ejection fraction entry criteria was lowered to ≤35% in a protocol amendment
#Dosage equivalent to enalapril ≥10 mg/day
McMurray et al. Eur J Heart Fail. 2013;15:1062–73

PARADIGM-HF: Primary Endpoint: Death From CV Causes Or First Hospitalization For HF



NNT to prevent one primary event: 21

HR: 20% difference favoring Sacubitril/valsartan

- *The numbers of patients who would need to have been treated (NNT) to prevent one primary event was evaluated over the duration of the trial
- McMurray et al. N Engl J Med 2014;371(11):993–1004.

Mustafa Toma

PARADIGM-HF: Prospectively Defined Safety Events

Event, n (%)	Sacubitril/ valsartan (n=4,187)	Enalapril (n=4,212)	p value
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<0.001
Symptomatic with SBP <90 mmHg	112 (2.7)	59 (1.4)	<0.001
Elevated serum creatinine			
≥2.5 mg/dL	139 (3.3)	188 (4.5)	0.007
≥3.0 mg/dL	63 (1.5)	83 (2.0)	0.10
Elevated serum potassium			
>5.5 mmol/L	674 (16.1)	727 (17.3)	0.15
>6.0 mmol/L	181 (4.3)	236 (5.6)	0.007
Cough	474 (11.3)	601 (14.3)	<0.001
Angioedema (adjudicated by a blinded expert committee)			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	0.19
Catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	0.52
Hospitalized without airway compromise	3 (0.1)	1 (<0.1)	0.31
Airway compromise	0	0	—

Fewer patients in the Sacubitril/valsartan group than in the enalapril group stopped their study medication because of an Adverse Events (AE) (10.7 vs. 12.3%, p=0.03)

- McMurray et al. *N Engl J Med* 2014;371(11):993–1004

Canadian Cardiovascular Society Recent Recommendations For HFrEF

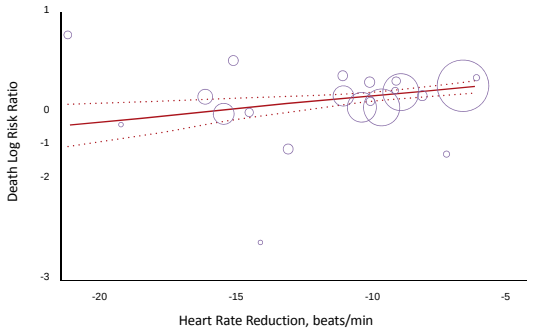
- **Recommendation**
- We recommend that in patients with mild to moderate HF, an EF < 40%, an elevated NP level or hospitalization for HF in the past 12 months, a serum potassium < 5.2 mmol/L and an eGFR ≥ 30 mL/min and treated with appropriate doses of guideline-directed medical therapy, they should be treated with Sacubitril/valsartan in place of an ACE inhibitor or an angiotensin receptor blocker, with close surveillance of serum potassium and creatinine (Conditional Recommendation, High-Quality Evidence).

- **Values and Preferences**
- This recommendation places high value on medications proven in large trials to reduce mortality, HF rehospitalization, and symptoms. It also considers the health economic implications of new medications.

- and

Heart Rate And Mortality In Chronic Heart Failure (CHF)

Meta-analysis: Beta-blocker Dose, Heart Rate Reduction, And Death In Patients With CHF



- McAlister F, Armstrong P, *et al. Ann Intern Med* 2009;150:784-794

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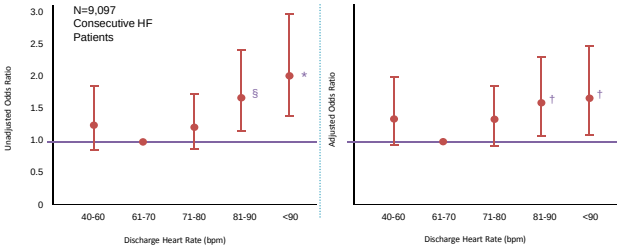
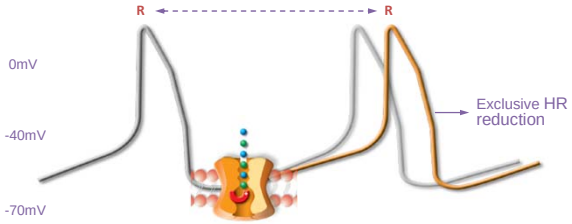
Discharge HR And Risk Of Adjusted 30 Day Mortality In Patients With CHF



- § p <0.05
- † p <0.01
- * p <0.001
- Habal, Liu, Lee. Circulation HF 2014; 7:12-20

Ivabradine Inhibits The I_f Current

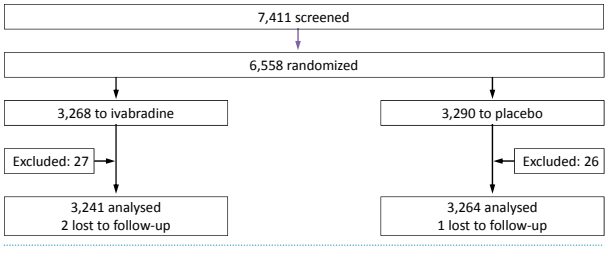


Ivabradine inhibits the *If* current by blocking the I_f channel, thus decreasing the depolarization slope and reducing heart rate.

Ivabradine reduces spontaneous action potential frequency; there is no impact on action potential threshold or shape.

- Thollon C *et al.* Br J Pharmacol. 1994;112:37-42
- DiFrancesco D. HCN current and its inhibition Curr Med Res Opin. 2005

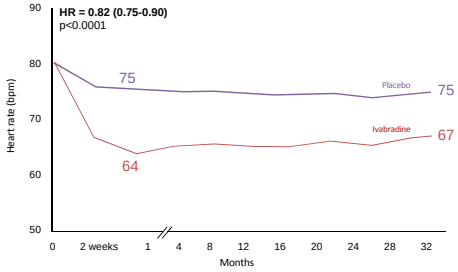
SHIFT Trial: Design And Follow Up



Median study duration: 22.9 months; maximum: 41.7 months

- Swedberg K. *et al.* SHIFT Investigators. Lancet. 2010;376(9744):875-85.

SHIFT Trial: Mean Heart Rate Reduction



Mean ivabradine dose:

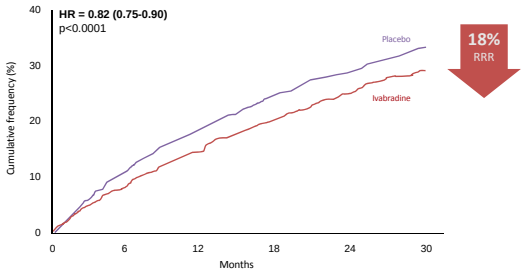
6.4 mg bid at 1 month

6.5 mg bid at 1 year

- Böhm M. *et al. Lancet.* 2010;376(9744):886-894.

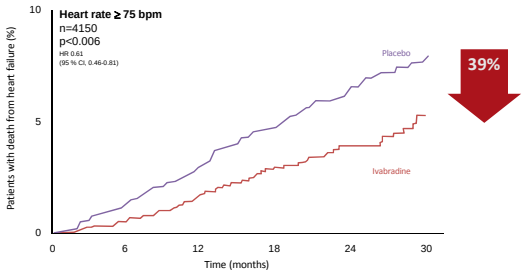
Mustafa Toma

SHIFT Trial: Primary Endpoint CV Death Or Hospital Admission For Worsening CHF



- Swedberg K, *et al.* SHIFT Investigators. Lancet. 2010;376(9744):875-85.

SHIFT Trial: Ivabradine Reduces The Risk Of Death For Heart Failure



- Böhm M *et al. Clin Res Cardiol.* 2012;102(1):11-22.
- Ivabradine or placebo is given on top of guideline-recommended therapy including ACE inhibitor, ß-blocker, mineralocorticoid receptor antagonist

Heart Rate Reduction

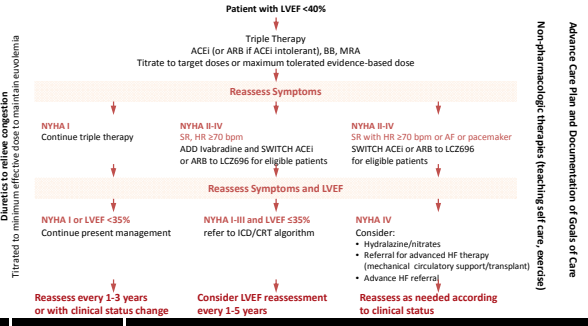
- Beta blockers (BB) are first line
  - Often residual heart rate is high or there is another intolerance
  - For those in NSR with HR > 70, up to 13% of HF population
- Ivabradine on top of BB will improve:
  - Morbidity if HR > 70 bpm
  - Mortality if HR > 75 bpm
- available in Canada Mar 2017

New HF Rx

- Sacubitril/valsartan
  - Combo drug
  - NYHA II-IV, LVEF < 40%, GFR > 30
- Ivabradine
  - Heart rate lowering
    - Only works in sinus rhythm
  - NYHA II/III, LVEF < 35%, HR > 77 bpm (?70 bpm)

Mustafa Toma

CCS HF Algorithm: Therapeutic Approach To Patients With CHF And Reduced Ejection Fraction



BC's HEART FAILURE NETWORK
Quality care for quality life.

New Provincial Heart failure Medication Process for Prescribing sacubitril/valsartan (ENTRESTO™)

UBC HF Symposium 2018

- Jun 1st/2nd in Vancouver
- www.bchfsymposium.ca

Conclusions

- HF on the rise
- Collaborative care between GP/IM/Cardiologists crucial
- Triple Rx to start for HFrEF
- New therapies:
  - Sacubitril/valsartan, ivabradine

Adrienne Lindblad

Generalized Anxiety Disorder

"Once you start down the dark path, forever it will dominate your destiny, consume you it will."

Adrienne J Lindblad
Knowledge Translation and Evidence Coordinator, Alberta College of Family Physicians
Associate Clinical Professor, Family Med, UofA

Faculty/Presenter Disclosure

- **Faculty/Presenter:** Adrienne Lindblad
- **Relationships with commercial interests:**
  - **Grants/Research Support:** *None*
  - **Speakers Bureau/Honoraria:** *None*
  - **Consulting Fees:** *None*
  - **Other:** *Employee of Alberta College of Family Physicians*

Treating anxiety feels like banging your head against a wall

Learning Objectives

- At the end of this presentation, participants will be able to:
  1) List the frequency of GAD without concurrent psychiatric conditions
  2) Discuss the efficacy and safety of various medications in GAD, including:
     a. Antidepressants
     b. Benzodiazepines
     c. Atypical antipsychotics
     d. Pregabalin
     e. Buspirone
  3) Review the effects of caffeine in GAD

Adrienne Lindblad

How do patients present?

- 13% of GAD patients present with anxiety symptoms as CC
- 48% present with somatic symptoms (pain, sleep problems, depression)

J Clin Psychiatry. 2002;63(suppl 8):24-34.

Canadian Guidelines on Screening

BMC Psychiatry. 2014;14(suppl 1):S1

Quick Screen?

Question: In the last 3 months, have you:	Sensitivity	Specificity
Had a spell or panic attack where all of a sudden you felt frightened, anxious or uneasy (Panic)?	0.92	0.75
Been bothered by nerves or feeling anxious or on edge (GAD)?	1.00	0.59
Would you say that being anxious or uncomfortable around people is a problem in your life (SAD)? (Does fear of embarrassment cause you to avoid doing things or speaking to people?)	0.76	0.77
Had recurrent dreams or nightmares of trauma or avoidance of trauma reminders (PTSD)?	0.68	0.81
Felt down, depressed or hopeless, felt little interest or pleasure in doing things for a week or more (MDD)?	0.84	0.69

Gen Hosp Psychiatry. 2006;28:108-18.

Treating GAD

Adrienne Lindblad

Can we trust the data?

- Studies short, small and often industry sponsored
- Blinded, randomization processes and allocation concealment rarely described
  - Example: 34 studies: 1 described randomization or allocation concealment
    - 10/25 reported blinding process
    - 11/16 high risk selective reporting

CDSR. 2016;9:CD011567

Antidepressants in GAD

- Overall NNT for response: 6 over ~13 weeks.
- Response ~60-70% versus 40-50%

CDSR 2003;2:CD003592. JAMA 2009;301:295-303.
J Clin Psych. 2006;67:874-81.
Am J Psych. 2004;161:1647-9.

Benzodiazepines

- Versus placebo: Systematic Review of 23 RCTs (n=2326):[1]
  - BZDs ↓ all-cause withdrawals (RR=0.78, 0.62-1.00)
  - BZDs ↓ withdrawals due to no efficacy (RR=0.29, 0.18-0.45)
    - Calculated NNT=7 over 4-6 weeks.[2,3]
  - BZD ↑ w/dr from AE (1.54, 1.17-2.03)
- Vs TCAs: SR of 3 RCTs (n=617):[4]
  - Similar efficacy (1 RCT), or TCAs better for psychiatric symptoms (2 RCTs), BZDs better for somatic symptoms (1 RCT)
  - BZDs have similar (1 RCT) or fewer adverse effects (2 RCTs)
- Vs newer antidepressants (paroxetine/venlafaxine): SR of 2 RCTs (n=709):[5]
  - Similar efficacy
  - Adverse effects :
    - Not reported in larger study of paroxetine vs lorazepam[6]
    - More with venlafaxine XR (9-13%) than diazepam (2%)[7]
      - NNH 9-14 over 8 weeks

[1]J Psychopharmacol 2007;21:774-82. [2]Psychopharmacol 1991;104(4):439-43. [3]Psychopharmacol 1991;105(3):428-32. [4]Psychother Psychsom. 2013;82:355-62. [5]Psychother Psychosom. 2013;82:355-62. [6]CNS Neurosci Ther. 2009;15:12-8. [7]Eur Psychiatry 2003;18:182-7.

BZDs as adjunct to antidepressants

Adrienne Lindblad

Atypical Antipsychotics

- Systematic Review of 9 RCTS, n=4387, up to 12 weeks:
- Monotherapy vs placebo:
  - Response: Odds ratio: 2.21 (1.10, 4.45), Number Needed to Treat (NNT)=6. Inconsistent results.
  - Remission compared to placebo: OR 1.83 (1.07, 3.12), NNT=10. Inconsistent results.
  - Stopping early for adverse effects: OR 3.76 (2.64, 5.34). NNH=9.
  - 1 long-term study (n=433) using as adjunct to prevent relapse: no difference in stopping early, NNT to prevent relapse=4.
- Monotherapy vs antidepressants:
  - no difference in any efficacy outcome (2 RCTs published as conference proceedings), but more likely to drop out due to adverse effects (NNH=11).
- As adjunct to antidepressants (quetiapine, risperidone and olanzapine) versus placebo:
  - no differences, but olanzapine improved one anxiety rating.

CDSR 2010;12:CD008120.

Pregabalin

- Systematic review of 4 RCTs:[1]
  - Vs placebo: response rates (1 RCT, n=271), not different
    - AE: 67% placebo, 73% 50mg PGB, 89% 200mg PGB, 91% lorazepam
  - Vs BZD: response rates (1 RCT, n=454): 61% vs 43% alprazolam, other RCT found no difference in HAM-A scores from lorazepam
- One open-label RCT vs SSRI (sertraline) (not in SR):[2] no difference HAM-A or # AE. Response rates not reported.
- As adjunct: Industry-sponsored DB, R, PCT of 356 patients with GAD.[3]
  - If inadequate response to antidepressant, randomized to pregabalin 150-600 mg/d or placebo
  - After 8 weeks: Mean change in HAM-A: 1.2 (SS, not clinically different)
    - Response (HAM-A): 48% versus 35%, NNT=8.
    - Response (CGI-I): No difference
    - Remission: No difference
  - Stopped due to AE: 4.4% versus 2.3%, NNH=47
- Several studies show onset within 1 week, but usually not clinically relevant.[4-6]

[1]Clin Evid. 2011;10:1002. [2]Eur Rev Med Pharmacol Sci. 2015;19(11):2120-4. [3]Int Clin Psychopharmacol. 2012;27:142-50. [4]Int Clin Psychopharmacol. 2009;24(2):87-96. [5]Br J Psych. 2008;193(15):389-94. [6]Am J Psychiatry. 2003;160:533-40.

Buspirone

- Systematic review, 36 RCTs, n=5908, most 4-8 weeks[1]
- Efficacy: inconsistent, remission rates not reported
  - Not always better than placebo on scales
  - # respond often not reported
- Largest RCT: patients and MD found more improvement with BZD[2]
- No difference in overall improvement compared to venlafaxine (1 RCT, n=271)[1]
- 1 single blind study in Iran (n=271): no difference in anxiety score[3]

[1]CDSR. 2006;3:CD006115. [2]J Clin Psychiatry. 1986;47:409-12.
[3]Psychiatry Clin Neurosci. 2010;64:128033

Which drug is best?

- Indirect comparison meta-analysis of 27 RCTs (funding: escitalopram)
  - Only 6 direct comparisons
- Probability of response: fluoxetine, lorazepam, duloxetine*, sertraline, paroxetine, pregabalin, venlafaxine, escitalopram, tiagabine
- Remission: fluoxetine, escitalopram, venlafaxine*, paroxetine, sertraline, duloxetine, tiagabine
- Withdrawal: lorazepam, duloxetine, escitalopram, venlafaxine, tiagabine, paroxetine, fluoxetine, pregabalin*, sertraline*

BMJ 2011;342:d1199.

Adrienne Lindblad

Does Caffeine Make Anxiety Worse?

- Systematic review of 8 studies: All showed association between panic disorder and caffeine challenge.
- "Provocative tests": abstain from caffeine for ≥ 1 week
- Then give blinded, large dose caffeine
- Example: baseline caffeine intake: 200-250 mg/day
- Dose: 480mg or 10 mg/kg

Exprt Rev Neurotherapeutics. 2011;11(1):1185-95. Arch Gen Psych. 1985;42(3):233-43.

Caffeine and Anxiety

- 8 SS differences, 27 no difference. [1]
  - Including sweating went from -11 to 28 (GAD) and from -2 to 15 health controls. No other numbers given.
- Abstain from caffeine for 1 week, then drink 480 mg in 15 minutes.[2]
  - "Panic attack": 48% panic disorder, 0% controls
  - Symptoms: inconsistent.
- Anxiety patients felt significantly more nervous and anxious after being given caffeine than controls.[3]

[1]Arch Gen Psych. 1992;49:867-9. [2]Depress Anxiety. 2008;25:847-53.
[3]Arch Gen Psych. 1985;42(3):233-43

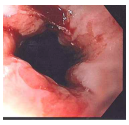
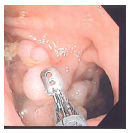
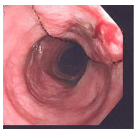
Caffeine Bottom Line

- Advise patients with panic disorder to avoid abstaining from caffeine for a week and then consuming the equivalent of 4-5 cups of coffee in 15 minutes.
- Reasonable caffeine use likely ok.

Summary

- Antidepressants 1st line (NNT~6 over 13 weeks)
- Antipsychotics: inconsistent results, but not as well tolerated as antidepressants. No real benefit as adjunct.
- Pregabalin: inconsistent, might be helpful, but not much evidence. Only 1 study as adjunct.
- BZD: similar efficacy to antidepressants, possible better short-term tolerability; NNT compared to placebo=7 over 4-6 weeks.
- Buspirone: efficacy at best, similar to antidepressants and BZD; likely better than placebo (NNT=5), but effects inconsistent.
- Caffeine: be reasonable

Mike Kolber

A GI potpourri
"I've got a bad feeling about this."
Mike Kolber MD, CCFP, MSc
BS Medicine Vancouver May 2018

Faculty/Presenter Disclosure

- **Faculty/Presenter:** Mike Kolber
  - Rural FP with special interest in GI: Peace River
  - PEER Group, University of Alberta Department of Family Medicine
- **Where get Personal $:** U of Alberta Department of FM
- **Where get Grant/ Program $:** Alberta College of FPs, Toward Optimized Practice
- **Relationships with commercial interests:**
  - **Grants/Research Support or Speakers Bureau:** None
  - **Consulting Fees:** Not applicable
  - **Other:** **emprss**: U of A spin off, quality metrics in medical procedures
- **Intellectual COI:** Alberta Government Expert Drug Committee

2

Experiential COI

- I enjoy helping patients feel better
- I am a drugectomist
- My nickname in med school was "Coupons"

On the Menu

- PPIs: "the good, the bad, the costly"
- Canadian H. Pylori guidelines
  - "Evidence, who needs evidence"
- What the $%#* is a FODMAP diet?
- 4 ways to improve constipation management
- GI Lab tests simplified: Fecal calprotectin, ATTG, FIT

"Go Ahead… Give me a PPI"

Proton Pump Inhibitors (PPIs)
The Good
The Bad
The Labs and…
The Costly

PPIs the Good: They work!

Disease	Outcome	NNT vs Placebo
Uninvestigated GERD	Symptoms	2
Erosive Esophagitis	Healing or symptoms	2
Endoscopic Negative Reflux	Symptoms	4
1' prevention PUD in NSAID users	Peptic ulcers (endoscopic)	4-9
Non ulcer dyspepsia	Symptoms	10

Rxfiles 2015: accessed Jan 2017

Mike Kolber

How many Canadians take PPIs?

- 27 million Rxs, 18% adults (CIHI 2016)
- 50% may not have appropriate indication
  - 40% medicine admit for "stress ulcer"
  - LT care[3]: 18% last week of life!
- Asthma, cough, atypical ENT symptoms: RCT evidence → PPIs don't work[4,5]

http://www.canadianhealthcarenetwork.ca/pharmacists/news/special-reports/top-100-drugs-19660/4 *BMJ 2008;336:2,* [2]*Ann Pharmaco* 2006;40:1261, [3]*J Am Geriatr Soc 2010: 58; 880,* [4]*NEJM 2009;360:1487,* [5]*Chest 2005; 128:1128,* [6]Dig Dis Sci (2015) 60:2280 *CMAJ* 2015. DOI:10.1503

PPIs - The "Bad"

Outcome	Patients / Outcome	Study Type	Results
Diarrhea	All cause	RCT	3-8%
CDAD	Community	Cohort	1/10,000 → 2/10,000
CDAD	**Inpatients + Abx**	**Cohort**	**8-10%**
CDAD	**Recurrent**	**Cohort**	**~7% ARI (20 →27%) in 3m**
CAP (pneumonia)	All	Cohort	1% ARI per year
CAP (pneumonia)	**Recurrent**	**Cohort**	**4% ARI (8-12%) in 5 years**
Osteoporotic #	Women	Cohort	NNH 2000 for 1 additional # over 8 years
Plavix plus PPI	CVD patients	Cohort	↑ recurrent CVE
Plavix plus PPI	CVD patients	RCT	**No difference CVE**

Please see handout for references

PPI associated Adverse Events Possibly Due to residual confounding

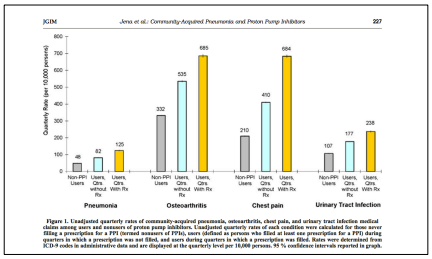


Figure 1. Unadjusted quarterly rates of community-acquired pneumonia, osteoarthritis, chest pain, and urinary tract infection medical claims among users and nonusers of proton pump inhibitors. Unadjusted quarterly rates of each condition were calculated for those never filling a prescription for a PPI (termed nonusers of PPIs), users (defined as persons who filled at least one prescription for a PPI) during quarters in which a prescription was not filled, and users during quarters in which a prescription was filled. Rates were determined from ICD-9 codes in administrative data and are displayed at the quarterly level per 10,000 persons. 95 % confidence intervals reported in graph.

J Gen Intern Med 2012; 28(2):223

PPI – The Labs

- **VB12:**[1]
  - Case-control: (25K cases, 180k controls)[1]:
    - Odds VB12 deficient: ~1.7Xs greater on PPI
    - >65 yo: 10% (baseline) → 17% on PPI
- **Magnesium:**[2-5]
  - case control, cohort, re-challenge
  - SR: 9 heterogeneous studies; 18-27% in ~5 years
    - Especially if taking diuretics

Long term PPIs and > 65 yo → check Vb12
Long term PPIs and on diuretics → check Mg

[1]JAMA. 2013;310(22):2435 [2]Aliment Pharmacol Ther 2012; 36: 405, [3]Am J Kidney Dis. 66(5):775
[4]PLoS ONE 2015; 9(11): e112558. [5]Expert Opin. Drug Saf. 2013; 12(5):709

Are PPIs equally effective?

- Depends who takes you golfing!
- Individual patient responses

Khan, Cochrane Systematic Reviews 2007, CD003244

PPIs the Costly

- Consider lower(est) cost alternative
- $225 million annual savings: Rabeprazole switch

Generic Name	Brand name	Strength	Dosing	90 Day Cost (unless otherwise noted)	Coverage
GASTROINTESTINAL					
***As of October 1, 2016, Maximum Allowable Cost (MAC) pricing exists for PPIs paid for by Alberta government sponsored drug programs. The drug plan will only pay the cost of rabeprazole 10mg for low dose PPI and will only pay the cost of pantoprazole magnesium for high dose PPI.					
Proton Pump Inhibitors (PPIs) ***					
Rabeprazole	Pariet	10mg	QD	**$25**	BC / IA covered
Pantoprazole	Pantoloc/Tecta	40mg	QD	**$30**	BC / IA covered
Omeprazole	Losec	20mg	QD	**$55**	BC / IA covered
Lansoprazole	Prevacid	30mg	QD	**$60**	BC / IA covered
Esomeprazole	Nexium	40mg	QD	**$230**	NC by BC or IA
Dexlansoprazole	**Dexilant**	30mg	QD	**$230**	NC by BC or IA

Price Comparison of Commonly Prescribed Pharmaceuticals in Alberta 2018

Mike Kolber

Alberta Government **Bulletin**
Alberta Health Care Insurance Plan

Number: Med 189	Date: January 16, 2017	Page: 1 of 2
Subject: REMINDER: Change to coverage for proton pump inhibitors takes effect February 1, 2017	Reference: *Alberta Drug Benefit List*	

Active ingredient	Least cost alternative/Maximum allowable cost price
LANSOPRAZOLE 15 MG	*Lower dose – The price will be set at the lowest price for rabeprazole sodium 10 mg.*
OMEPRAZOLE 10 MG	
RABEPRAZOLE SODIUM 10 MG	
LANSOPRAZOLE 30 MG	*Higher dose – The price will be set at the lowest price for pantoprazole magnesium 40 mg.*
OMEPRAZOLE 20 MG	
PANTOPRAZOLE MAGNESIUM 40 MG	
PANTOPRAZOLE SODIUM 40 MG	
RABEPRAZOLE SODIUM 20 MG	

DRUG CATEGORY	MAXIMUM ALLOWABLE COST (MAC) PRICE THRESHOLD	DRUGS WITHIN MAXIMUM ALLOWABLE COST (MAC) PRICE THRESHOLD	DRUGS NOT WITHIN MAXIMUM ALLOWABLE COST (MAC) PRICE THRESHOLD
Proton Pump Inhibitors	$0.20 per tablet	Generic versions of: • pantoprazole magnesium (Tecta®) • generic versions of rabeprazole (Pariet®) *	Brand and generic versions of: • esomeprazole (Nexium®) • lansoprazole (Prevacid®) ** • omeprazole (Losec®) ** • pantoprazole sodium (Pantoloc®)

Modernized Reference Drug Program
Proton Pump Inhibitors (PPIs)

BRITISH COLUMBIA

Fully Covered (Reference Drugs)		Partially Covered (Non-Reference Drugs)			
• **Rabeprazole** 10 or 20 mg	• **Pantoprazole magnesium** 40 mg	• **Esomeprazole** 20 or 40 mg	• **Lansoprazole** 15 or 30 mg	• **Omeprazole** 20 mg	• **Pantoprazole sodium** 40 mg

Information provided is not intended as a substitute for professional judgement.

Alberta Blue Cross LCA 2017, Sask MAC 2016, BC Pharmacare RDP 2016

Can patients stop PPIs?

- Yes ~25% successfully stop
  - Another 30-50% decrease dose
- 2 cluster RCTs: academic detailing or patient information vs standard care [6,7]

Study	Patients	Recruitment	Intervention	Proportion successful DC
Bjornsson[1] 2006	97 (mostly GERD)	Pharmacy survey	Gastroscopy (normal)	27% @ 1 year
Krol 2004[6]	113 dyspepsia	GPs EMR	GP letter	13% @ 5 months
Murie 2012[4]	166 NUD, GERD	GP EMR	HP tx, educate, self tx plan,	34% @ 1 year
Walsh 2016[5]	46 mostly GERD	EMR pre-PHE	Reminder / tool for GP	26% @ 10 weeks

[1]*Aliment Pharm 2006 ;24: 945* [2]*Am J Gastro* 2009; 104:S27, [3]*Family Practice*, 2014; 31: (6): 625, Quality Primary Care 2012; 20: 141 , J PRIM HEALTH CARE 2016;8(2):164, AP&T 2004; 19: 917; [7]Ann Fam Med. 2015;13:545

Taper PPIs

PPI DEPRESCRIBING

Approaches for stopping or dose reduction of PPIs in those who may not need lifelong treatment

April 2015

Rx FILES

PPI Deprescribing	Evidence for Deprescribing of PPIs

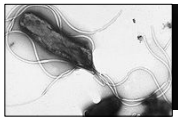
↑interval between doses (ex q 2 days x 2-4 weeks), then DC

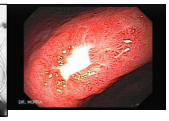
www.rxfiles.ca

PPI Teaching Points

- Good: PPIs work: 3-6-9 GERD rule
- Bad: PPIs associated with potential AEs:
  - C Diff: Hospital admit, needs Abx → try to stop PPI
  - C Diff or Pneumonia: stop PPI (↓recurrence)
- Costly: use cheapest!
- Stopping PPIs: ~25% successful: taper then DC
  - Don't stop in patients with BE, Endoscopic GERD, stricture

4 words





How to choose Hp treatment?

- Effectiveness:
  - determined by macrolide resistance (< 20% ok)
    - Avoid macrolide if recent use
  - 80% success was 'benchmark standard'
- Keep it Simple: improves adherence
- Cost: double length of therapy = double cost

TFP 2011, 2015 Bugs and Drugs 2012

Mike Kolber

Network MA BMJ 2015

Therapy	Eradication (%)	Adverse events (%)	# Pills
Triple therapy 7d	73	21	56
Triple therapy 10-14 day*	81	24	112
Sequential 10 days	87	22	70
CLAMET 7 days**	94	26	84
CLAMET 14 days	No evidence	No evidence	168
Quadruple: 10 - 14 days	85	23	336 (14 d)

*Cochrane 2013: 10-14 vs 7 day TT ~10% AR Increase eradication

**CLAMET: based on 1 low quality study of 119 Japanese patients: Clarithro resistance > 20%, no studies directly comparing 10 or 14 days to 7 days TT

BMJ 2015;351:h4052, Cochrane 2013, Issue 12. Art. No.: CD008337
World J Gastro Pharmacol Ther 2012; 6; 3(1): 1-6

Network MA BMJ 2015

Therapy	Eradication (%)	Adverse events (%)	# Pills
Triple therapy 7d	**73**	21	56
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BMJ 2015;351:h4052, Cochrane 2013, Issue 12. Art. No.: CD008337
World J Gastro Pharmacol Ther 2012; 6; 3(1): 1-6

Canadian Hp Eradication Rates

- 17 trials of CAN patients: diff tx lengths
- Eradication:
  - –Triple (PAC): 84% (79-90)
  - –Quadruple: 87% (80-95)

Rogers, Can J. Gastro 2007; 21(5): 295

2016 Canadian HP Guidelines *14 days Treatment*

- 1st line: CLAMET: PPI, **CL**arithro, **A**moxil, **MET**ro
- 2nd line: QUAD: PPI, bismuth, Tetra, Metro
- 3rd line: LEVOQUIN: PPI, amoxil, Levoquin
- *Removed: triple and sequential therapy!*

CONSENSUS STATEMENT

The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults

Gastroenterology 2016;151:51

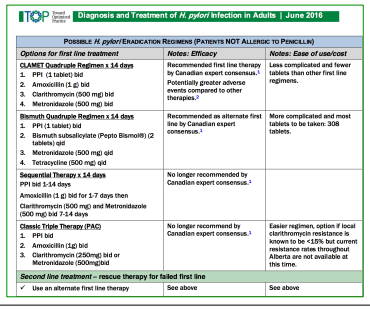
2016 HP Guidelines

- 14/15 statements: "*strongly recommended*"
- 14 /15 statements: supported by *very low or low quality* evidence

"The lack of availability of data on local susceptibility patterns and eradication success rates was a knowledge gap that has a major impact on the choice of therapy and hence best management"

Gastroenterology 2016;151:51

TOP Alberta 2016 HP Guidelines



TOP Toward Optimized Practice — Diagnosis and Treatment of *H. pylori* Infection in Adults | June 2016

Possible *H. pylori* Eradication Regimens (Patients NOT Allergic to Penicillin)

Options for first line treatment	Notes: Efficacy	Notes: Ease of use/cost
CLAMET Quadruple Regimen x 14 days 1. PPI (1 tablet) bid 2. Amoxicillin (1 g) bid 3. Clarithromycin (500 mg) bid 4. Metronidazole (500 mg) bid	Recommended first line therapy by Canadian expert consensus.[1] Potentially greater adverse events compared to other therapies.[2]	Less complicated and fewer tablets than other first line regimens.
Bismuth Quadruple Regimen x 14 days 1. PPI (1 tablet) bid 2. Bismuth subsalicylate (Pepto Bismol®) (2 tablets) qid 3. Metronidazole (500 mg) qid 4. Tetracycline (500 mg) qid	Recommended as alternate first line by Canadian expert consensus.[1]	More complicated and most tablets to be taken: 308 tablets.
Sequential Therapy x 14 days PPI bid 1-14 days Amoxicillin (1 g) bid for 1-7 days then Clarithromycin (500 mg) and Metronidazole (500 mg) bid 7-14 days	No longer recommended by Canadian expert consensus.[1]	
Classic Triple Therapy (PAC) 1. PPI bid 2. Amoxicillin (1g) bid 3. Clarithromycin (250mg) bid or Metronidazole (500mg)bid	No longer recommend by Canadian expert consensus.[1]	Easier regimen, option if local clarithromycin resistance is known to be <15% but current resistance rates throughout Alberta are not available at this time.
***Second line treatment* – rescue therapy for failed first line**		
✓ Use an alternate first line therapy	See above	See above

Teaching Point: If fail HP eradication → use different regimen

Mike Kolber

HP 2018 Summary

- In Canada: until local resistance known…no need to change HP regimens
  - Triple Therapy: 10-14 days ~80% success (7d = 70%)
  - Sequential 10 days: ~90% success
  - Quadruple Therapy x 14 days = 336 pills!
- If fail one treatment: use a different regimen

Kolber personal communication 2016, TOP HP guidelines 2016, Helicobacter 2017, Laine Gastro 2016;151:9

What the $%&# is a FODMAP DIET (and what's the evidence for IBS)?

Fermentable oligo-, di-, monosaccharides, and polyols [FODMAPs]

FODMAP Evidence

(All from Secondary Care)

- Best RCT[1]: 6 weeks Danish, open label, 123 IBS pts
  - IBSS: FODMAP ↓ 150 > probiotics >> normal diet
  - Sub-group: only worked in diarrhea IBS
- Other RCTs[2-4]: small #s, time (2 days), COI ($)
- 2016 RCT IBS-D:[5] FODMAP vs mNICE diet
  - frequent small meals, avoid triggers, alcohol, caffeine
  - Adequate pain relief: 4 weeks: FODMAP 52 vs 41% (NSS)
  - ↓abdominal pain: 51 FODMAP vs 23% (NNT =4)

[1]World J Gastro 2014;20(43):1621 [2]Gastroenterology 2014;146:67 [3]J Nutr 2012:142:151 [4]J Gastro Hepatol. 2010;25:1366 TFP #142 / Can Fam Phys 2015, 691. [5]Am J Gastro 2016; 111(12):1824.

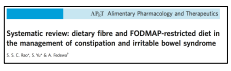
FODMAP diet for IBS

- TFP 142: "**Low FODMAP diet may improve symptoms for patients with primarily diarrhea subtype IBS. However, most studies were low quality (small #s, short duration)"**
- **More high quality studies are needed.**

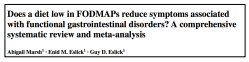
TFP #142, 2015, Can Fam Phys 2015, 691

3 FODMAP Meta-Analysis = 3 Different Conclusions

"More research required to establish LT efficacy[1]"



"… is efficacious in treating functional GI symptoms[2]"



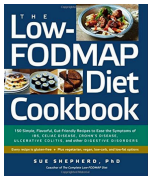
"….FODMAP diet RCTS characterized by high risk of bias…risk that effects reported are driven primarily by a placebo response."[3]

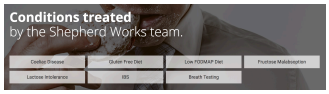
Systematic review: quality of trials on the symptomatic effects of the low FODMAP diet for irritable bowel syndrome

[1]Aliment Pharm Ther 2015; 41: 1256, [2]Eur J Nutr 2015; DOI 10.1007 [3]Aliment Pharma Ther. 2017;1

FODMAP diet Summary

- May improve symptoms in diarrhea predominant IBS patients
- Healthy Skepticism: possibly n of 1 trial





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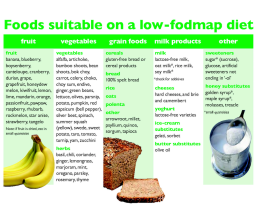
FODMAP Diet: Stanford



Reduce: diet pops (artificial sweeteners) , wheat, dairy and FARTY FOODS (cabbage, onions, beans)

Google: "Stanford FODMAP"

4 Things to do for Constipation

1. Hold the Colace!

- 5.6 million Rx 2015: BC, ONT, NB, PEI
- ***TFP 2016: "Docusate ~placebo in increasing stool frequency and inferior to other products for treating…constipation."***
- 'Best' RCTS:
  - 74 Palliatives: senna + docusate vs placebo → No diff in BM / sx
  - 74 hospitalized (1960s): docusate or placebo: over 30 days
    - Docusate ↑ BMs by ~ 1/week (Limitations: 26% LTFU)
- Other RCTs: comatose patients, poor quality, unblinded
- Post-op patients: Senna + docusate vs:
  - Placebo: 1st BM ~1 day sooner – due to senna
  - PEG: 1st BM 1-2 days sooner with PEG.

TFP #161 April 25, 2016. CADTH 2014 Docusate (Calcium or Sodium) for the Prevention or Management of Constipation

2. Use Osmotic Agents (PEG)

- *TFP 2015: "In adult and pediatric patients with chronic constipation, PEG more effective than other agents. Compared to placebo, it relieves constipation in 1in every 2-3 patients and adds 1-3 BMs / week"*
- PEG vs lactulose: ↑ stool frequency and ↓ interventions (especially in peds)
- Starting Doses:
  - Adults: 17 grams daily
  - Peds: 0.6 grams/kg/day (or 5-12 grams/day)

TFP #45 2011, updated 2015, *Am J Gastro 2007;102:1436 [2]Gut 2011; 60: 209 Cochrane 2010 CD007570, [2]Arch Dis Child 2009;94:156, Cochrane* 2012, CD009118

3. Consider a clean out

- 1-2 litres x 2-4 days

Primary Care Network PEACE REGION

Peace River Gastrointestinal Clinic
c/o Associate Medical Clinic
Box 7590 Peace River, AB T8S 1T2
Ph: 780-618-4322 Fax: 780-624-4015

GOLYTELY/Co-Lytely (4 litre) Preparation Instructions

The day before your colonoscopy:

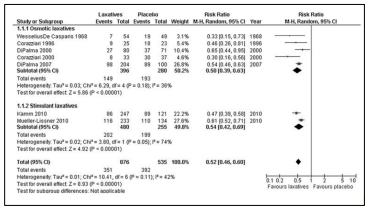
Clear fluids only: clear fluids are fluids you can see through (see examples below). Some patients (previous poor bowel preparation, chronic constipation or constipating medications), may require 2 days of clear fluids.

Prepare the preparation: as per the instructions on the bottle. Use only water to mix the solution. You may add flavouring (like ginger ale) after mixing. Put the bottle in the fridge (is easier to drink when it's cold).

Between 5 – 8 pm: drink 2 litres of the bowel prep solution over 2 hours. Drink about one cup (250 mL) every 10 -15 minutes.

Evidence Free Zone

4. Ok to Use stimulants



Global symptom improvement: NNT = 3

Ford, Gut 2011;60:209

Mike Kolber

Comparative Shopping Price per Poop

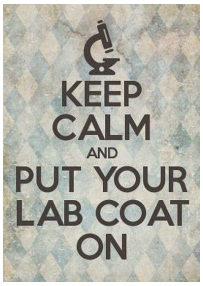
- **Bisacodyl:** 10 mg od = $10 /month = **$0.65 /poop**
- **Lactulose*:** 15ml qd = $12 /month = **$1.00 /poop**
- **PEG 3350**: 17g qd = $20 /month = **$1.70 /poop**
- **Linaclotide:** 145ug qd = $120 /month = **$10 /poop**
- **Prucalopride**: 2mg qd = $125 / month = **$30 /poop**
- **Methylnaltrexone (Relistor)** = **$55 / inj**

*covered by Alberta Blue Cross

Price Comparison of Commonly Prescribed Pharmaceuticals in Alberta 2017

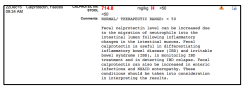
Alberta College of Family Physicians

GI Labs 2018
Fecal calprotectin



Fecal Calprotectin (adults)

- Evidence limited; small studies, tertiary care, in known (or high prevalence) IBD patients*
- If < 50: LR- = <0.1 → helps rule out IBD
- If > 50 LR+ = 7-15 → helps rule in IBD
  - **If >250: LRs >10**
  - If 50-250: LRs: ~2-5

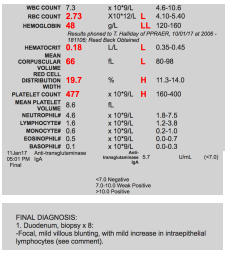


*Needs Canadian primary care study

BMJ 2010;341:c3369, Health Technol Assess 2013;17(55)

Anti-Tissue Transglutaminase (ATTG)

- 250 / day in N. Alberta: 2-3% positive



FINAL DIAGNOSIS:
1. Duodenum, biopsy x 8:
-Focal, mild villous blunting, with mild increase in intraepithelial lymphocytes (see comment).

65 y.o. minimally traumatic ankle #, myalgias, ↓ calcium, Vb12 and coagulopathy

PEIP 2016 Higgins, Am J Gastro 2013; 108:656

Anticipated findings: FIT +

Spanish RCT: FIT vs colon: 55K pts, 50-69 yo average risk[1]
- 75ng/ml cutoff (same as AB) → 7.2%+
- CRC = 1/180 colon, **1/18 FIT+**

BC cohort: 50-74 yo, 2 FITs q 2 years[2]: 1555 colons
- 8.6%+, **1/20 FIT+ = CRC,** 8 FIT- had CRC @ 2.5 years
- 3 perforations, 6 bleeds

Calgary cohort[3]: 10k average risk, 4k FIT colons
- ADR: **FIT+ =60%**, Average risk screen =30%

AFPEE cohort: 422 FIT + colons

[1]*NEJM 2012;366:697,* [2]*CMAJ Open* 2016. DOI:10.9778, [3]*Am J Gastro 2016* doi:10.1038

Summary

- PPIs: the good, the bad, and the costly
- HP eradication: Sequential x 10, Triple x 14
  - Use different regimen if fail eradication
- Constipation: no colace, use osmotics +/- stimulants, try clean out, no new meds
- Fecal Calprotectin, ATTG, FIT

Mike Kolber

Questions

- mkolber@ualberta.ca

G. Michael Allan

Is it High-Time for Medical Cannabis: Doobie-ous Evidence or Smokin' Results?

"The force is strong with this one."

Mike Allan
Evidence & CPD Program, Alberta College of Family Physicians
Department of Family Medicine, University of Alberta

Faculty/Presenter Disclosure

- **Faculty/Presenter: Mike Allan,**
- **Where we get Personal $:** U of A, Alberta Health, College of Family Physicians of Canada
- **Where we get Grant/ Program $:** Alberta College of Family Physicians, Other Colleges of Family Physicians, Toward Optimized Practice, Other non-profit organizer

- **Relationships with commercial interests:**
  - **Grants/Research Support:** Not applicable
  - **Speakers Bureau/Honoraria:** Not applicable
  - **Consulting Fees:** Not applicable
  - **Other:** None

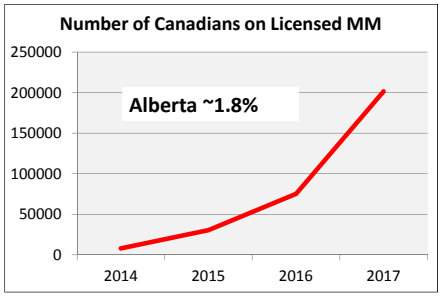
Objectives

1) Understand the lack of evidence around Medical Cannabinoids for most indications.
2) Review the weaknesses in medical cannabinoid research.
3) Learn the benefits of medical cannabinoids for 4 possible indications:
   a) Neuropathic pain
   b) Cancer/end-of-life Pain
   c) Chemotherapy-induced nausea and vomiting
   d) Spasticity due to MS
4) Apply this information based on up-coming primary care / national guidelines (suggesting Medical Cannabinoids are only consider in rare case for the above indications.

What is presently happening,…

- Canada: Any Cannabis Use 43% and this year ~12%.
- Patients with conditions like chronic pain or MS, ~15-20% use Cannabis.
- Most common reason: Pain (58-84% of medical use).

Health Rep. 2015 Apr;26(4):10-5. Drug Alcohol Depend. 2017;177:1-13.



Health Canada. Market Data. Government of Canada. 2017.

G. Michael Allan

Some of the promoted medical uses for Cannabinoids

1. Tourette Syndrome
2. Amyotrophic Lateral Sclerosis
3. Huntington's Disease
4. Parkinson's Disease
5. Dystonia
6. Glaucoma
7. Traumatic Brain Injury/Intracranial Hemorrhage
8. Addiction
9. Anxiety
10. Depression
11. Sleep Disorders
12. Posttraumatic Stress Disorder
13. Schizophrenia and Other Psychosis
14. Osteoarthritis
15. Fibromyalgia
16. Neuropathic Pain
17. HIV Pain
18. Dementia
19. Cancer
20. Chemotherapy-Induced Nausea and Vomiting
21. Anorexia and Weight Loss
22. Irritable Bowel Syndrome
23. Epilepsy
24. Spasticity Associated with Multiple Sclerosis or Spinal Cord Injury
25. Tourette Syndrome

Examples of Poor Research

- Gluacoma: 1 RCTs with 6 people (no effect)
- Anxiety: 1 RCT of 24 patients tested for simulated public speaking found more improvement on mood visual analogue scale.
- IBS: 1 RCT of 36 pts given dronabinol for 2.5, 5mg or placebo BID x2 days: Focused on transit times.

JAMA. 2015;313(24):2456-2473. National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Press. doi: 10.17226/24625.

Two Primary Problems.

- Blinding: Attempted but rarely tested
  - In 2 Inhaled cannabis cross-over RCTs
    - 1st: 57% identified all 6 phases
    - 2nd: 90% identified active vs cannabis cigs without THC/CBD
  - Dronabinol, 95% of patients identified active (as did 85% of nurses. (nabilone study similar)
- Inclusion: Previous users often focused on.
  - Of 6 inhaled RCTs: 3 required past use, 2 no limitation and 1 did not report.
  - In Nausea/vomiting, previous use led to great response
  - Naive users (not past report psychosis).
- Together, these introduce profound bias

Can Fam Physician 2018 (submitted)

Pain Outcomes: 30% pain reduction & others

Type of Pain	Risk Ratio	Cannabis	Placebo	NNT
Chronic Pain	1.23 (0.98-1.56)	37%	31%	~19
Smoked, Neuropathic	1.62 (1.24-2.12)	47%	29%	6
Neuropathic	1.34 (1.04-1.74)	38%	30%	14
Cancer	1.35 (0.63-2.09)	NR	NR	NR
Palliative	1.34 (0.96-1.86)	30%	23%	~15
Chronic Pain	**1.37 (1.14- 1.64)**	**39%**	**30%**	**11**

- On a 0-10 point scale: Baseline ~6/10.
  - Placebo reduces things ~0.8
  - Cannabinoids: 0.2 to 0.8

Can Fam Physician 2018 (submitted). JAMA. 2015;313:2456-73. J Pain 2015;16:1221-32. Schmerz 2016; 30: 62-88. Medwave 2016;16 Suppl 3:e6539. Curr Med Res Opin 2007;23:17-24. Der Schmerz 2016;30:25-36.

G. Michael Allan

What factors influence Cannabinoid pain effect?

Comparison	Subgroup	Risk Ratios	Difference
Type of Cannabinoid	Inhaled	1.52 (1.17-1.99)	P=0.34
	Buccal	1.28 (1.02-1.61)	
Size of RCT	<150	1.56 (1.26-1.92)	P=0.03
	>150	1.09 (0.86-1.39)	
Duration of RCT	<1 week	1.58 (1.13-2.20)	P=0.01
	2-5 wks	1.79 (1.32-2.43)	
	9-15 wks	1.07 (0.87-1.32)	

Bottom-Line: When you examine higher quality studies (larger & longer), cannabinoids do not appear to have an effect on pain.

Can Fam Physician 2018 (submitted)

Additional Variables in Pain

- Research mostly Nabiximol + some inhaled.
- Nabilone (oral): 2 best trials
  - RCT Fibromyalgia 40 patients, 1mg PO BID x4 wks
    - 14.6 more than placebo on 100mm VAS.
  - RCT: 73 x3 wks, 500 µg v 60 mg dihydrocodeine QID.
    - 10 on 100mm VAS: 19% dihydrocodeine vs 5% nabilone.
- Rheumatologic Pain: Insufficient evidence
- Acute Pain: decrease (1), worse (1) & no effect (5)
- Function not reported and QoL unchanged.

J Pain. 2008; 9(2):164-73. BMJ. 2008 Jan 26;336(7637):199-201

Absence Nausea & Vomiting from Chemotherapy

Comparator	Outcome	Rate Ratio	Cannabis	Control	NNT
Vs Placebo	Control Sx*	3.60 (2.55 - 5.09)	47%	13%	3
	Pt Preference	4.82 (1.74-13.36)	72%	18%	2
		5.67 (3.95 - 8.15)	76%	13%	2
Vs Neuroleptics	Control Sx*	1.85 (1.18 - 2.91)	31%	16%	7
	Pt Preference	2.76 (1.88 - 4.03)	63%	19%	3
		2.39 (2.05 - 2.78)	61%	26%	3

* Done by us

JAMA 2015; 313:2456-73. Cochrane Database Syst Rev 2015; (11) CD009464. Eur J Cancer Care 2008:17:431-43 BMJ 2001:323(7303):16-21.

Additional Variables

- Most trials followed patients 1 day (after chemo)
- Patient preference higher than effectiveness (preference ~75% while effectiveness 47%)
  - Maybe preference based on more than effectiveness
- Medical Cannabinoids for nausea/vomiting are primarily oral agents like Nabilone (& delisted dronabinol).

JAMA 2015; 313:2456-73. Cochrane Database Syst Rev 2015; (11) CD009464. Eur J Cancer Care 2008:17:431-43 BMJ 2001:323(7303):16-21.

G. Michael Allan

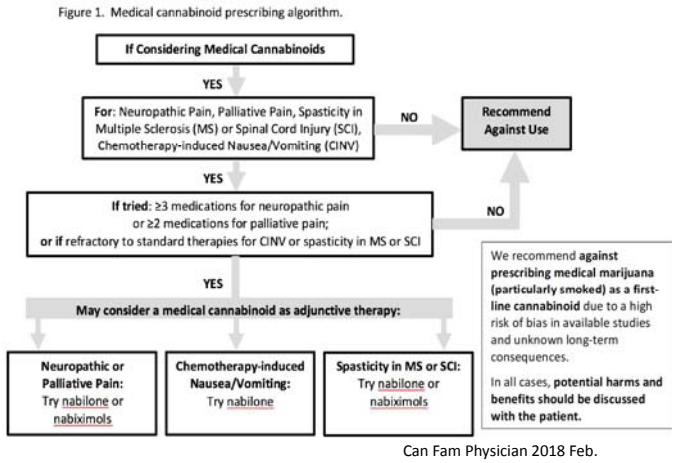
Spasticity: How well it works

	Rate Ratio	Cannabis	Placebo	NNT
≥30% Improvement in Spasticity	1.43 (0.99-2.08)	35%	24%	~10
	1.37 (1.07-1.76)	35%	25%	10
Global Impression of Change (by us)	1.45 (1.08 – 1.95)	50%	35%	7

- Spasticity score from 0-10, Mean score: 6.2,
  - Placebo improved spasticity 0.95
  - Cannabinoid improved spasticity, over placebo, by 0.31 – 0.76

JAMA 2015; 313(24):2456-73. BMJ 2001;323(7303):16-21.

Type of Adverse Event	Cannabinoid Event Rate	Placebo Event Rate	NNH
Overall	81%	62%	6
Withdrawal	11%	~3%	14
Ataxia/Muscle Twitching	30%	11%	6
Blurred Vision/ Visual Hallucination	6%	0%	17
Central Nervous System	60%	27%	4
Disorientation/Confusion	9%	2%	15
Dissociation/ Acute Psychosis	5%	0%	20
Disturbance attention/ disconnected thought	17%	2%	7
Dizziness	32%	11%	5
Dysphoria	13%	0.3%	8
Euphoria	15%	2%	9
"Feeling High"	35%	3%	4
Hypotension	25%	11%	8
Impaired Memory	11%	2%	NS (12)**
Numbness	21%	4%	6
Psychiatric	17%	5%	9
Sedation	50%	30%	5
Speech Disorders	32%	7%	5



Can Fam Physician 2018 Feb.

Last Thoughts: Smoked

- Prescribing guides recommend max 9% THC
  - 1 inhalation ("drag") = 100mg once a day
  - Titrate up to QID = ~half a "joint"/day (400mg/day)
- What is being used:
  - In Canada: 27% THC is maximum but many ~15%,
  - Can smoke 5 grams/day (~6 "joints")
- Presently patients can easily attain 20x the recommended dose. (cost $500/month)

Can Fam Physician. 2014 Dec;60(12):1083-90.

MRSA and what do we need to treat – how long ABX
"I've got a bad feeling about this."

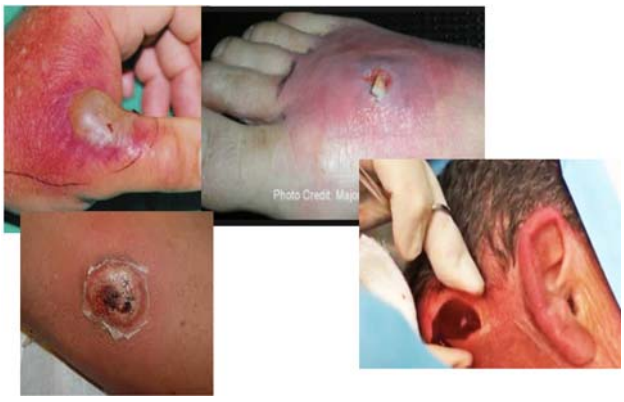
Natasha Press
ID, St. Paul's Hospital

"I've got a bad feeling about this…"

- is probably the second or third most-iconic line in all of Star Wars, coming in after Darth Vader's "I am your father" and Admiral Ackbar's "It's a trap!"
- Has been spoken by everyone from Han Solo to C-3PO.
- Precede some calamity
- e.g. caught by your enemies, bound to a pole, and they're about to eat you

www.starwars.com

MRSA ➔ "I have a bad feeling about this"



Faculty/Presenter Disclosure

- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** Merck, Pfizer (>2 years ago)
  - **Consulting Fees:** None
  - **Other:** None
  - **Potential for conflict(s) of interest: None**

Natasha Press

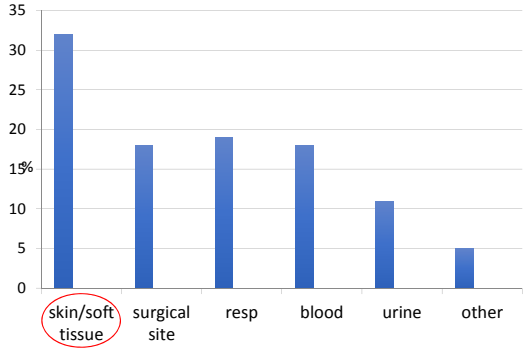
Learning objectives

- To understand the epidemiology of MRSA skin and soft tissue infections
- To know when antibiotics are needed
- To understand which antibiotics to use
- To recognize how long to treat

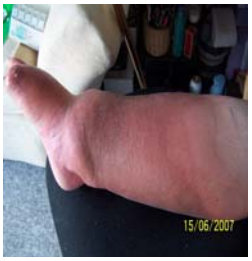
What is MRSA?

- *Staphylococcus aureus:*
- MSSA (methicillin susceptible *S. aureus*)
  - cephalexin, cloxacillin
- MRSA (methicillin resistant *S. aureus*)
  - TMP-SMX, doxycycline, clindamycin

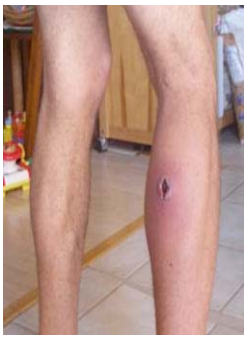
MRSA Infections, 2008-12



Canadian Nosocomial Infection Surveillance Program



- Non-purulent Cellulitis
- (no wound or abscess)
- **Group A Streptococcus**

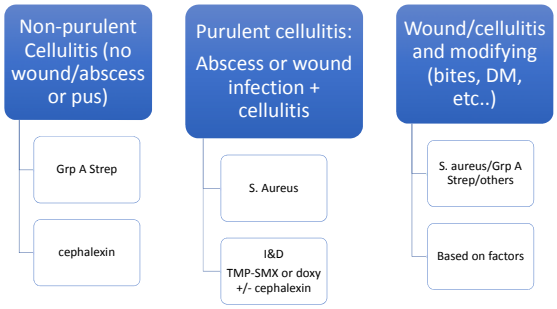


Purulent Cellulitis with wound or abscess

DDx: – **S. aureus**
– Gp A Streptococcus
– others

Natasha Press

SSTIs: Oral treatment



Non-purulent cellulitis (*Grp A Strep*)

- Choice of abx: cephalexin or penicillin
- Duration of therapy: 5 days
- Longer if infection has not improved (strong)
- Elevate affected area (strong)

2014 IDSA Update of SSTIs at www.idsociety.org

Recurrent non-purulent cellulitis

- Up to 20% recurrence within a year (legs)

Recurrent non-purulent cellulitis

- Decrease risk factors: (strong/moderate)
- Maintain skin integrity
  - Treat athlete's foot
  - Treat eczema/dry skin
- Decrease edema –
  - Venous insufficiency/lymphedema - compression stockings
- Maintain healthy body weight

IDSA guidelines 2014

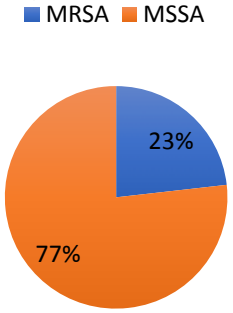
Natasha Press

Purulent cellulitis

- *S. aureus* >> β-hemolytic strep
- Empiric abx for MRSA (strong)
- Probably don't need to treat Grp A Strep (strong)
- Duration of therapy: (strong)
  - 5-10 days
  - Depends on clinical response

Lui. Clinical Infect Dis. 2011

BC Data (2014)



2014 AMR Trends Report www.bccdc.ca

BC data: antibiotic susceptibility

	MSSA	MRSA	Group A Strep
Clindamycin	79%	63%	88%
TMP-SMX (septra)	96%	93%	Not reliable
Doxycyline	95%	89%	Not reliable

2014 AMR Trends Report www.bccdc.ca

Outpatient purulent cellulitis: empiric abx for MRSA

Antibiotic	Dose (Adult)	Evidence
TMP-SMX	1-2 DS BID	strong
Doxycycline, minocycline	100 BID	strong
Linezolid	600 BID	strong
(Clindamycin)	(300-450 TID)	strong

Lui. Clinical Infect Dis 2011

Natasha Press

Abscess

- Incision and drainage (strong) → C&S
- Galen (AD 129–199): concept of "laudable pus" became unshakeable for almost 15 centuries.
  - ➔ If pus is about, let it out

- Galen of Pergamon
- (AD 129–199)
- Greek Physician

- Galen Erso
- Of Star Wars
- Coerced into using kyber crystals to enhance energy yields to create the Death Star's superlaser

Abscess

- Incision and drainage (strong) → C&S

- What's the role of antibiotics?
  - Shift in practice in last 5 years
  - IDSA guidelines on MRSA Infections 2011
  - IDSA guidelines on Skin and Soft Tissue Infections 2014
  - 2015-2017: Three Randomized Controlled Trials published in New Engl J Med

Antibiotic therapy is recommended for abscesses associated with: (strong)

- Severe, extensive, progressive disease with cellulitis/septic phlebitis
- Sx of systemic illness
- Comorbidity, immunocompromise
- Extremes of age
- Difficult to drain area (e.g. face, hand, genitalia)
- Failure of prior I&D

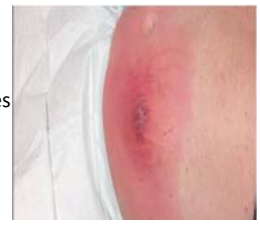
Liu. Clinical Infect Dis. 2011.

Natasha Press

New studies: Is I&D enough? Should we use abx too?

- Clindamycin versus TMP-SMX for Uncomplicated Skin Infections.
  - N Engl J Med 2015
- TMP-SMX versus Placebo for Uncomplicated Skin Abscess.
  - N Engl J Med 2016
- A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses.
  - N Engl J Med 2017

Clindamycin vs TMP-SMX N Engl J Med 2015



- Outpatients (adults and kids)
- Large (>5 cm) abscess or multiple abscesses
- PLUS cellulitis
- I&D as required
- Randomized to: Clindamycin or TMP-SMX
- Similar cure rates = 80%
- No placebo arm

Miller et al. N Engl J Med 2015; 372: 1093.

TMP-SMX vs. placebo N Engl J Med 2016

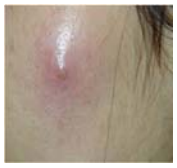
- Uncomplicated abscess ➔ I&D
- Randomized to TMP-SMX 2 DS po bid x 7 days vs. Placebo
- TMP-SMX (80.5%)
- Placebo (73.6%)

Talan DA et al. N Engl J Med. 2016; 374 (9): 823

- MRSA subgroup:
- Results at one week: TMP-SMX better than placebo (86.5% vs 74.3%)
- Results at 6 weeks: TMP-SMX better than placebo (82.4% VS. 70.2%)

Talan DA et al. Ann Emerg Med. 2018; 71 (1):21.

Clindamycin vs. TMP-SMX vs. Placebo N Engl J Med 2017



- Outpatients (adults and kids)
- Abscess <5 cm
- I&D
- Randomized to clindamycin vs TMP-SMX vs placebo (x 10 days)
- Cure rates: Clindamycin [83%] =TMP-SMX [82%] > placebo [69%]
- Recurrence: Clindamycin [7%] < TMP-SMX [13%] = placebo [12%]
- Adverse events: Clindamycin [22%] > TMP-SMX [11%] = placebo [12%]
- Conclusion: I&D plus abx improve short-term outcomes but have side-effects

Daum RS et al. N Engl J Med. 2017;376(26);2545.

Natasha Press

Which antibiotic to use?

- TMP-SMX or doxycycline
- Clindamycin: ↑ resistance, ↑ adverse events
- If recurrent: base on patient's previous culture results

How long to treat?

- Antibiotics add benefit to I&D
- But how long to treat?

"The antibiotic course has had its day"

- BMJ July 26, 2017
- Challenges "Always complete the full prescription, even if you feel better, because stopping treatment early promotes the growth of drug-resistant bacteria"

  Antibiotic Awareness Week 2016 WHO
- We have no evidence to support that stopping antibiotic treatment early encourages antibiotic resistance
- We have lots of evidence that taking antibiotics for longer than necessary increases the risk of resistance

BMJ 2017; 358:j3418

Natasha Press

"The antibiotic course has had its day"

- Key point: clinical trials are required to determine the most effective strategies for optimizing duration of abx therapy
- There are clinical syndromes where you should complete the course even if you feel better e.g. MRSA bacteremia
- Duration of abx for MRSA purulent skin and soft tissue infections:
  - 5-14 days
- "Don't have to finish the course"

Management of Recurrent MRSA SSTIs

- Personal Hygiene/Wound Care (strong)
- Cover draining wounds
- Hand hygiene
- No sharing personal items (e.g. towels)
- Clean environment high-touch surfaces (weak)
- Decolonization (weak)

Lui. Clinical Infect Dis. 2011

IDSA recommended regimens for decolonization

- 1. mupirocin ointment to nares bid x 5-10 days (weak)
- 2. mupirocin + Chlorhexidine body washes x 5-14 days (weak)
- 3. mupirocin + bleach baths

De-Staphing with bleach baths

- RCT n= 300 patients with SSTI and *S. aureus* colonization
- Eradication of colonization at 4 months:
- Only regimen more effective than education alone was mupirocin plus beach baths (71% versus 48%)

Fritz et al Infect Control Hosp Epidemiol, 2011;32(9):872

Natasha Press

Bleach baths

- Children:
- add 5 ml of household bleach (e.g. Clorox-Regular 6.0% hypochlorite) for every gallon of water.
- 15 minutes 2x/week
- Apply a moisturizer following the bath

- Adults: Add ¼ cup of bleach to the tub

Decolonizing household contacts

- 43% of household contacts had identical MRSA strain as case[1]
- If household transmission suspected, consider de-staphing asymptomatic household contacts (weak)[2]
- Decolonization in large community settings has not worked[3]

[1]Johansson et al. Scan J Infect Dis. 2007;39(9);764
[2]Liu. Clin Infect Dis. 2011
[3]Ellis et al. Clin Infect Dis. 2014; 58(11): 1540.

Conclusion

- Let's change the "I have a bad feeling about this" to "I have a good feeling"
- MRSA Purulent skin and soft tissue infection:
  - I&D➔ C&S
  - Treat empirically for MRSA (TMP-SMX or doxycycline)
  - If C&S result available ➔ use it to guide abx
  - Duration of treatment is variable – until the patient is better
  - If recurrent: consider decolonization (mupirocin ointment to nares and bleach baths)
  - Reduce risk factors: wash hands, wash gym clothes, maintain good skin integrity

R2-D2 and C-3PO

Silly Studies: Objectives

1. Learn how research is done by people with opinions that are seeking to validate
2. Understand some social aspects of medicine that have gained public attention
3. Learn some novel treatments that are being trialed throughout the globe.

Disclosure of Commercial Support

Neither this program nor the presenter has received financial support from any organization or company.

Gut, 1971, **12**, 713-716

Influence of diet on flatus volume in human subjects

P. J. DAVIES

From the Department of Gastroenterology, Central Middlesex Hospital, London

SUMMARY Ten flatulent but otherwise healthy subjects were studied while consuming two or three different diets. Flatus collections showed that a bean-containing, high crude-fibre diet produced more flatus (mean 49·4 ml/hr) than either a diet with a restricted crude-fibre content (mean 26·7 ml/hr) or a liquid chemically defined diet (mean 10·9 ml/hr). There was a close correlation between the crude-fibre content of the diet and the production of flatus. The results are consistent with the conclusion that flatus is not the result of swallowing air, but arises mainly from bacterial fermentation of indigestible carbohydrate, eg, cellulose, passing into the colon.

R2-D2 and C-3PO

J Fam Pract. 1994 Nov;39(5):441-5.

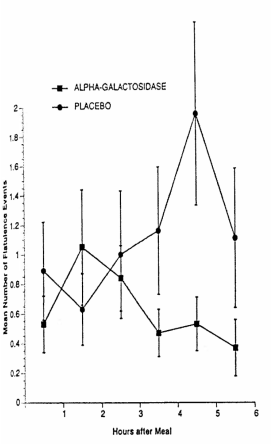
Does Beano prevent gas? A double-blind crossover study of oral alpha-galactosidase to treat dietary oligosaccharide intolerance.

Ganiats TG[1], Norcross WA, Halverson AL, Burford PA, Palinkas LA.

METHODS: Nineteen subjects were randomized into two groups and fed test meals of meatless chili. At the first test meal, group 1 received eight drops of alpha-galactosidase solution and group 2 received eight drops of placebo. After the meal, subjects were asked to keep a careful record of gastrointestinal symptoms, including occurrences of intestinal gas passage, for the next 6 hours. One week

The test meal, prepared by one of the authors, consisted of meatless chili (made with navy, pinto, and kidney beans, cabbage, broccoli, cauliflower, and onions), corn bread, and water. Each meal was made using the same

- New knowledge
  - Flatulence peaks at 5 hours post-farty meal
  - Beano prevents about 1 fart per hour for 3 hours
  - NNnF : not available



Effects of Two Weeks' Mandatory Snack Consumption on Energy Intake and Energy Balance

Results: Daily energy intakes increased from 10.4 MJ (control) to 11.1 MJ (low-energy) and 11.5 MJ (high-energy) ($p < 0.001$), resulting in a trend (not significant) for body weight gain. Energy balance was more positive when sub-

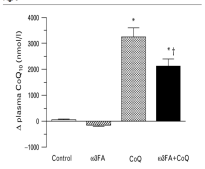
- New Knowledge:
  - If you are forced to eat, your intake will increase.
  - This might lead to weight gain

OBESITY Vol. 15 No. 3 March 2007 673

Will giving Q10 increase your Q10 levels?

proposed. The aim of this study was to assess the effect of CoQ_{10} on metabolic control in 23 type 2 diabetic patients in a randomized, placebo-controlled trial. Treatment with CoQ_{10} 100 mg bid caused a more than 3-fold rise in serum CoQ_{10} concentration ($p < 0.001$). No correlation was observed between serum CoQ_{10} concentration and metabolic control. No significant changes in metabolic parameters were observed during CoQ_{10} supplementation. The treatment was well tolerated and did not

Fig. 3



Changes in plasma CoQ_{10}. General linear model analysis tested for treatment effects on postintervention values adjusted for baseline value. Treatment effect $P < 0.0001$. Post-hoc comparisons used the Tukey test. *$P < 0.0001$ denotes a significance vs. control and ωΔFA groups; †$P = 0.005$ denotes a significance vs. CoQ. ωΔFA, omega-3 fatty acid; CoQ, coenzyme Q_{10}.

- New Knowledge
  - If you give anything that the body absorbs (like Q10), you can find higher levels in the serum

BioFactors 9 (1999) 315–318.

R2-D2 and C-3PO

Investigated the horrors of,…

Reusable Shopping Bags

Assessment of the Potential for Cross Contamination of Food Products by Reusable Shopping Bags

Gerba CP, Williams D, Sinclair RG (2010). Assessment of the potential for cross contamination of food products by reusable shopping bags.

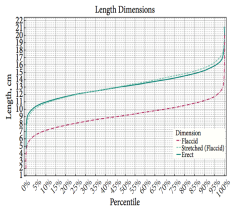
- **New Knowledge,**
  - **If you pour meat juice in bags &leave them in hot place (trunk), bacteria can grow.**

range of enteric bacteria, including several opportunistic pathogens. When meat juices were added to bags and stored in the trunks of cars for two hours the number of bacteria increased 10-fold indicating the potential for bacterial growth in the bags. Hand or machine washing was

Does Length Matter?

Sexual Medicine — BJUI

Am I normal? A systematic review and construction of nomograms for flaccid and erect penis length and circumference in up to 15 521 men



"not possible to draw conclusions about race and length" *BJU Int 2015; 115: 978–986*
"1 cm smaller than self reported data"

A little-bit country: A lot sad

- 49 metropolitan areas in US.
- Examined association between proportion of airtime devoted to Country Music & social/ health issues
- Country music associated with (Correlation)
  - Living in the south (r=0.26)
  - Owning a gun (r=0.50)
  - Divorce (r=0.51)
  - Suicide (r=0.54)
    - But only among whites, others seem immune
- Bottom-Line: Country music linked to guns, divorce and suicide. Take That CMT.

Social Forces 1992;71: 211-8

Intractable Hic-cups: Ending with the End

- 27 y.o. man hic-cup x 72 hrs.
  - "DRE massage was then attempted using a slow circumferential motion." Ended within 30 seconds
- 60 y.o man, Tx, recurred 2 hr later, & Tx again
- Case Series (5 more not described): DRE worked
- Other options: Swallowing granulated sugar. Breathing into bag, Catheter stimulation of oro or nasopharynx, Carotid sinus massage, Traction on tongue, Ice water gargles, Drinking upside-down, Valsalva maneuver, Fright, Ocular compress

Ann Emerg Med. 1988;17:872.J Intern Med. 1990;227:145-6. Arch Otolaryngol Head Neck Surg. 1993;119:1383. Arch Otolaryngol Head Neck Surg. 1992;118:1115-9.

R2-D2 and C-3PO

Women, Men and Thinking clearly

- On two small studies (~50 males each)
  - Both studies had reduced cognitive performance for men when interacting women (but not reverse)
- 2 other studies (~80 participants)
  - Interacting via computer or even "future interaction"
  - When women involved (even possible interaction), men 0.5 sec slower cognitively (from 4.1 to 4.7 seconds)
- Bottom-Line: Women make men dumber.

Arch Sex Behav. 2012 Aug;41(4):1051-6. Arch Sex Behav (2012) 41:1051–1056

Can alcohol contribute to poor choices in sex?

- Meta-analysis of 12 observational studies.
- Adjusted analysis:
  - linear relationship: Alcohol & unprotected sex
  - Each 0.1 blood alcohol level = ~3% increase in unprotected sex.
- Bottom-Line: Country says it best
- "I Ain't Never Gone To Bed With An Ugly Man, But I Sure Woke Up With a Few"

Addiction. 2012 Jan;107(1):51-9.

You get what you pay for?

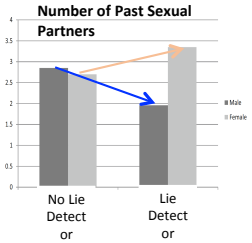
- 82 people, electric shock pain RCT. All Placebo
  - Group 1: pain pill worth $2.50 (similar to codeine) but faster etc.
  - Group 2: Pain pill worth $0.10, discounted medicine.
- Outcome: High cost = better mean pain ~12mm
  - 85% high cost got better vs 61% of discounted
- Bottom-Line: If it's expensive, it's better. (May explain some of patient complaints around generics).

JAMA. 2008 Mar 5;299(9):1016-7.

Honesty & Cultural Expectations

- 293 (55% female) college students, mean age 19.
  - ½ to lie detector & ½ to "anxiety" machine (neither functioning)

- Results:
  - Not many changed on lie detector. But some small changes around sex,..
- Bottom-Line: We're not honest about sex, in culturally acceptable directions.



Sex Roles (2013) 68:401–414

R2-D2 and C-3PO

Kissing Makes it all Better!

- Study 1: 30 allergic rhinitis & 30 atopic dermatitis
  - Age 29, 53% female, Japanese, "do not kiss habitually"
  - "kissed with lover or spouse freely for 30 min alone in a room with closed doors while listening to soft music"
  - The Beauty and the Beast, When You Wish Upon a Star, My Heart Will Go On, Love is a Many-Splendored Thing, Moon River, Sunrise Sunset, Can You Feel the Love Tonight.
  - Skin Prick Test
- Outcomes: 20-30% reduction in neurotrophins
  - Wheals: 8mm before & 5.4 after kissing (no diff if hugging)
- Bottom-Line: Kissing treats atopy. Dose and potency still unresolved.

Physiology & Behavior 80 (2003) 395– 398

"5 Second Rule"

- Dropped foods: 4 inoculated surfaces (steel, tile, wood, carpet), measured bacteria transfer
  - Contact time, food and surface type effected all bacteria transfer (watermelon ↑, carpet ↓)
- Coliform count on different household sites:

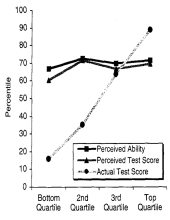
Surface	Coliforms / inch²
Toilet Seat	0.68
Kitchen Floor	2.75
Fridge Handle or Kitchen counter	~6
Toilet flush handle	34
Kitchen rag or sponge	20,000,000

Bottom-Line: Wash your rags!

Appl. Environ. Microbiol. doi:10.1128/AEM.01838-16
Carroll A, New York Times Oct 12, 2016, Journal of Applied Microbiology 1998, **85:** 819

Incompetent & unaware: Linked by Necessity

- 4 studies: humour, logic, grammar/reflection) & logic/training (Done 45-140 university students)
- Outcomes:
  - Bottom quartile estimated their ability ~65 percentile (above average).
  - Showing others work only did not help bottom-quartile self-assess.
  - Only training helped self-assess.
- Bottom-Line: If you are bad at something, you don't know it. "Ignorance more frequently begets confidence than does knowledge"



J Pers Soc Psychol. 1999 Dec;77(6):1121-34.

9 studies (but discussed many others)

Testing: hand grip strength, "mental health", blood samples, etc

If sex is within ≤2 hours before competition

"High-quality, randomized controlled studies are urgently needed."

Sexual Activity before Sports Competition: A Systematic Review

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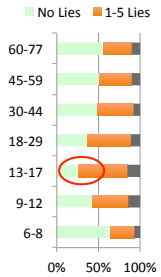
Sexual activity before competition has been considered as a possible cause for reduced performance since ancient Greece and Rome. Recently, the hypothesis that optimal sport performance could be influenced by a variety of factors including sexual activity before competition has been investigated. However, few scientific data are available, with the exception of anecdotal reports of individual experiences. The present systematic review focused on the current scientific evidence on the effects of sexual activity on sport performance regardless of sport type. Data were obtained following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, using PubMed/MEDLINE, ISI/Web of Science, the Cochrane Collaboration Database, Cochrane Library, Evidence Database (PEDro), Evidence Based Medicine (EBM) Search review, National Guidelines, ProQuest, and Scopus, all searched from inception further, to broaden the search, no time filter nor language restriction have been applied. Also, the gray literature was mined using Google Scholar. Only relevant scientific articles reporting outcomes of athletic performance after sexual activity were considered. The impact of sexual activity before a sport competition is still unclear, but most studies generally seem to exclude a direct impact of sexual activity on athletic aerobic and strength performance. The most important aspect seems to be the interval from the time of the sports competition that affects negatively the performance if it is shorter than 2 h. There are possible negative effects from some possible concurrent wrong behaviors such as smoking or alcohol abuse. There are no investigations about the effect of masturbation in this context. There is a need to clarify the effects of sexual activity on competition performance. The present evidence suggests that sexual activity the day before competition does not exert any negative impact on performance, even though high-quality, randomized controlled studies are urgently needed.

Keywords: athletes, abstinence, circadian rhythm, competition, performance, sex, time of day

Dishonesty: An age related skill

- Survey: 992 Dutch visiting a museum
  - Honesty lowest: pre-teen - young adult
- Other:
  - Lying may require a healthy frontal lobe (age & illness limit it)
  - Practice in lying makes it easier[2]
  - Gender varies, but maybe women lie for others & men lie for themselves.[3]
- **Bottom-Line**: Lying peaks in youth. Fortunately, practice improves & women are nicer liars



1) Acta Psychol (Amst). 2015;160:58-68. 2) Conscious Cogn. 2011 Sep;20(3):908-11. Bockstaele Frontiers in Psych. 3) IZA Discussion Paper No. 7946.
https://www.psychologytoday.com/

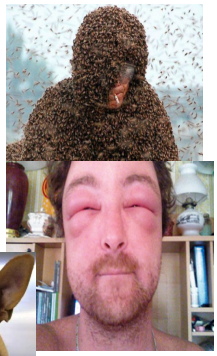
You know what they say about big feet?

- 104 men presenting to urology for unrelated cause (mean age 54)
  - Stretched flaccid penile length vs shoe size (UK)
- Results; Mean 13cm & UK size 9.
  - Correlation $r^2 = 0.012$ (p=0.28)
- Other: 64 found very weak correlation
  - 3100 males: no correlation (but self reported size)
- **Bottom-Line**: Maybe Donald Trump didn't need to worry about the size of his hands, ….

BJU International (2002), 90, 586–587. Ann Sex Res 1993; 6: 231–5. Edward R. Definitive Penis Size Survey, 6th edn. 2002. http://www.sizesurvey.com

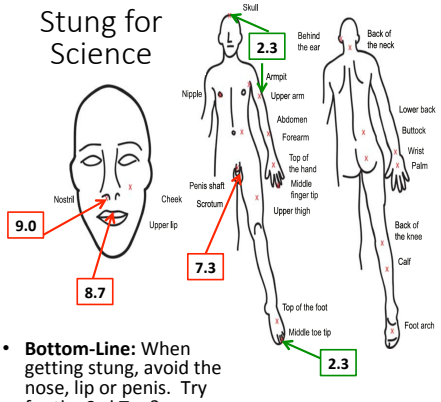
Stung for Science

- Grad student at Cornell
- Prep: Stung 5x/day for 3 months
- Then, 1 sting on 25 places, repeated 3x over 38 days.



PeerJ. 2014 Apr 3;2:e338

Stung for Science



- **Bottom-Line:** When getting stung, avoid the nose, lip or penis. Try for the 3rd Toe?

PeerJ. 2014 Apr 3;2:e338

R2-D2 and C-3PO

Finally, Good research in renal stones

- RCT 90 Turkish men with ≤6mm stones distal ureter
  - Sex 3-4/wk vs Tamsulosin 0.4mg/d vs control
  - "Sexual intercourse & masturbation prohibited in groups 2 & 3"
  - Passed by 2 wks: 84%, 48%, 35% (NN'T'≈2)
- RCT 56 Egyptian men with 5-10mm stones distal ureter
  - Sex ≥3-4/wk vs control. Followed 4 weeks.
  - Passed by 2 wk 82% v 53% (NNT=4); Days to expulsion 12 v 16
- **Bottom-Line**: "Practicing sexual intercourse for 3–4 times/wk for married male patients" may increase stone passage by 30-50%.

UROLOGY 2015; 86: 19-24. Int Urol Nephrol 2017; 49:27–30

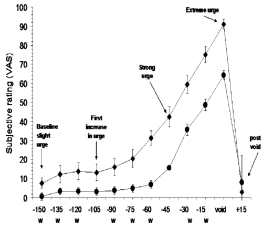
A hair's breadth closer to the truth

- #1: 25 men (10 shaved head), 59 evaluated:
  - only dominance diff 3.64/7 vs 4.14/7 (p=0.019).
- #2: 4 men +/- digitally removed hair, 344 evaluated:
  - dominance, masculinity, confidence, strength, even height rated slightly higher.
- #3. Short description of man with shaved, thinning or full hair, 552 evaluated:
  - Same results but thinning worse for all.
- **Bottom-Line**: The only hope for the Mikes are shaved heads.

Social Psychological and Personality Science 2012 00(0) 1-8

How well do we think when we need to pee?

- 8 pts (2 female), age ~34
  - 250 ml water q15 min
- 3 cognitive tests: 2 of 3 worse at "extreme urge
- Impairment similar to or worse than staying awake 24 or BAC 0.05%



- **Bottom-Line**: If you really need to pee: Go! Your cognition is impaired anyhow so you won't miss much.

Neurourology and Urodynamics 30:183–187 (2011)

Save the date!

The 30th Annual Best Science Medicine Course
will be held on
Friday, May 3rd and
Saturday, May 4th, 2019

Thanks for your questions and discussion.

Thank you for completing your course evaluations.

“I am one with the Force. The Force is with me.”

Rogue One: A Star Wars Story (2016)