22nd ANNUAL DRUG THERAPY DECISION MAKING COURSE

Encouraging Healthy Skepticism

April 1st and 2nd, 2011

Fairmont Waterfront Hotel
Vancouver, B.C.

Saturday Syllabus

SKEPTICEMIA

When skepticism gets into your blood

There is no cure

Sponsored by

The THERAPEUTICS EDUCATION COLLABORATION
In Cooperation with the
DEPARTMENT OF FAMILY MEDICINE and
FACULTY OF PHARMACEUTICAL SCIENCES
UNIVERSITY OF BRITISH COLUMBIA

COURSE DIRECTORS
DR'S. ROBERT RANGNO, JAMES MCCORMACK and
MICHAEL ALLAN

“A truth's initial commotion is directly proportional to how deeply the lie was believed. It wasn't the world being round that agitated people, but that the world wasn't flat. When a well-packaged web of lies has been sold gradually to the masses over generations, the truth will seem utterly preposterous, and its speaker a raving lunatic."

- Dresden James

Course Directors

Bob Rangno, Emeritus Prof., Med./Pharmacology, UBC & SPH
James McCormack, Prof., Pharm. Sciences, UBC

Guest Faculty

G. Michael Allan, Assoc. Prof., Fam. Practice, University of Alberta
& Medical Director, Towards Optimized Practice
Mike Kolber, Assoc. Prof., Family Med., University of Alberta
Tina Korowynk, Asst. Prof, Family Med., University of Alberta
Mark McConnell, Internal Medicine, LaCrosse, Wisconsin

Local Faculty

Martin Dawes, Prof. and Head, Dept. of Family Practice, UBC
William Honer, Prof., Psychiatry, UBC, BC Mental Health and Addictions Research Institute
Val Montessori, Clin. Assoc. Prof., Medicine, Infectious Diseases, UBC & SPH
Bob Nakagawa, Asst. Deputy Minister, Pharmaceutical Services, B.C. Ministry of Health
Natasha Press, Clin. Assoc. Prof., Med., Infectious Diseases, UBC & SPH
John Sloan, Clin. Prof., Family Practice, UBC
Adil Virani, Assoc. Prof, Pharm. Sciences, UBC, & Director, Pharmacy Services, FHA

FHA – Fraser Health Authority
SPH – St. Paul's Hospital
UBC – University of British Columbia

22nd Annual
Drug Therapy Decision Making Course
Saturday, April 2, 2011

07:30 Registration coffee and muffins

Chair - Bob Rangno and James McCormack

"Fool's Gold"

08:30	Insulins – Bantering about what is Best	Mike Allan
08:50	Target shooting and target dosing – Bullseye or BS	James McCormack and Mike Allan
09:20	Questions	
09:40	Refreshment Break	

"A Fool and His Money are Soon Partying"

10:00	Screening – if you think you're healthy you haven't had enough tests	Mark McConnell, Tina Korownyk, Mike Allan, Mike Kolber
10:40	Questions	
11:10	Academic detailing - the alternative rep	Bob Nakagawa
11:30	Questions	
11:50	Lunch	

Chair - Bob Rangno and James McCormack

"Fool's Overture"

13:00	Patience with Patients – discussing evidence around risks, benefits, and side effects	Mark McConnell, Mike Allan, Mike Kolber, Tina Korownyk, Bob Rangno, James McCormack, Adil Virani
14:30	Questions	
15:00	The End	

Insulin:
Bantering about what is Best

G. Michael Allan
Associate Professor, University of Alberta,
Director, Evidence & CPD, ACFP

Conflict of Interest

- Family Doctor for >12 yrs
- Academic 8 years

- Pay from U of A and Alberta Health
- Research and Speaking Fees
  - Non-Profit Sources (ACFP, , IHE, etc)
  - No funding from Industry

What is he talking about now?

- Long Acting Insulin Analogues:
  - What is the evidence?
  - What are the limitations?
- Starting insulin:
  - What is the evidence?
  - How do we do it?
- The focus will be Type II diabetics

Long-Acting Insulin: Analogues vs NPH

- Comparing long-acting insulin analogues Glargine and Detemir vs NPH.
- The primary outcomes are A1C, hypoglycemia
- Secondary outcomes are weight gain, quality of life, risks.

Long-Acting Insulin: Analogues vs NPH

- Glargine vs NPH (6 studies) – 2902 pts
  - A1C pretty much the same
  - Hypoglycemia*: Severe, No diff
    - Symptomatic, NPH worse (52.9% vs 62.8%, NNT 11)
    - Nocturnal, NPH worse (25.1% vs 37.8%, NNT 8)
- Detemir vs NPH (2 studies) – 980 pts.
  - A1C favors NPH 0.1% (stat sign, but ? Clinically)
  - Hypoglycemia*:Severe, No diff
    - Overall, NPH worse (55.7% vs 71.1%, NNT 7)
    - Nocturnal, NPH worse (22.5% vs 39.3%, NNT 6)
- No diff in morbidity, mortality, quality of life,

All event rates and NNTs are off meta-graphs? Cochrane 2007; 2 : CD005613

Long-Acting Insulin: Analogues vs NPH Evidence Issues

1 Understanding hypoglycemia as an outcome?

- Hypoglycemic symptoms are non-specific, variable, heterogeneous, and weaken with increasing age.[1]
- Symptoms have a poor correlation with biochemical hypoglycemia[2] (and some have suggested they are unrelated).[3]
- Blood glucose measurements are required to diagnosis hypoglycemia.[2]

1) Diabet Med. 1991;8(3):217-22. 2) J Intern Med. 1990;228(6):641-6. 3) BMJ. 1990;300(6716):16-8.

Long-Acting Insulin: Analogues vs NPH Evidence Issues

- Other Issues

2 Unblinded: Everyone knew who was on which insulin. This may have biased in favor of the new product.

3 Unconfirmed. All trials allowed unconfirmed hypoglycemia to be included (including severe). This has the ability to bias the results, particularly when combined with the above.

4 Other concerns: AC missing in about 4, many non-inferiority design so per protocol preferred but done in only 2.

Long-Acting Insulin: Analogues vs NPH

- CMAJ review[1] (summary of CADTH report[2]
- 49 studies (many cross-over)
  - Hypoglycemia: ≥1 event for dichotomous outcomes & rate ratio to account for frequency
- Most studies poor quality (for examples: unblinded & unclear AC in > 90% of trials)
- Outcomes: A1C
  - No difference in those attaining A1c<7%
  - Most not stat sign, those that are
    - NPH < Glargine (if no oral): 0.28%
    - NPH < Detemir (with oral): 0.13%

1) CMAJ 2009;180(4):385-97 2) http://www.cadth.ca/media/pdf/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf

Long-Acting Insulin: Analogues vs NPH

- Glargine
  - With oral meds (most 24 wks or more)
    - Severe Hypoglycemia: NS
    - Overall: 0.87 (0.81-0.93), pts with ≥1 episode
      - Glar 47.2% vs NPH 55.9%, AR 8.7%, NNT 12
      - Rate ratio: ns
    - Nocturnal: 0.56 (0.47-0.68), pts with ≥1 episode
      - Glar 18.8% vs NPH 33.1%, AR 14.3%, NNT 7
      - Rate Ratio: 0.41 (stat sign)
  - Without oral meds
    - Nocturnal: 0.78 (0.62-0.98)

1) CMAJ 2009;180(4):385-97 2) http://www.cadth.ca/media/pdf/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf

Long-Acting Insulin: Analogues vs NPH

- Detemir
  - With oral meds
    - Severe Hypoglycemia & Overall: ns
    - Nocturnal: 0.53 (0.31-0.91), pts with ≥1 episode,
      - Det 19.5% vs NPH 33.3%, AR 13.8%, NNT 8
      - Rate Ratio: 0.48
  - With short-acting
    - Severe Hypoglycemia: ns
    - Nocturnal: 0.54 (0.30-0.97)

1) CMAJ 2009;180(4):385-97 2) http://www.cadth.ca/media/pdf/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf

Long-Acting Insulin: Analogues vs NPH

- CDR review of detemir (in 2009): 7 trials vs NPH
  - Most excluded patients with history of major hypo
  - Overall, A1C better in NPH.
- CDR review of Glargine (in 2006): 9 trials vs NPH.
  - Need to consider A1C with hypo: no convincing evidence glargine reduced A1C and hypo together better than NPH
- No benefit on quality of life data.

Long-Acting Insulin: Analogues vs NPH

- Long-acting analogues not cost effective[1]
- Weight Gain: Mean over 7 studies = 0.18 kg more with NPH[2]
- Cancer risk: Some concern about insulin glargine but observational and not conclusive[3]
- Quality of Life: Rarely measured but not statistically significant when measured.[4]

1) CMAJ 2009;180(4):400-7 2) http://www.cadth.ca/media/pdf/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf 3) http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Glargine-cancer-RapidRx-10Jul09.pdf 4) Detemir http://www.cadth.ca/media/cdr/complete/cdr_complete_Levemir_Resubmission_Adults_August_20-2009.pdf AND Glargine http://www.cadth.ca/media/cdr/complete/cdr_complete_Lantus_Oct25-06.pdf

Long-Acting Insulin: Analogues vs NPH

- Quotes from others:
- "The improved glycemic control, reduced risk of hypoglycemia and improved quality of life achieved with insulin analogues versus conventional insulins are at best minor and of clinically debatable relevance."[1]
- "Our analysis suggests, if at all only a minor clinical benefit of treatment with long-acting insulin analogues for patients with diabetes mellitus type 2 treated with "basal" insulin regarding symptomatic nocturnal hypoglycaemic events. Until long-term efficacy and safety data are available, we suggest a cautious approach to therapy with insulin glargine or detemir."[2]

1) CMAJ 2009;180(4):369-70. 2) Cochrane 2007; 2: CD005613.

Long-Acting Insulin: Analogues vs NPH

- Bottom-line: Hard to separate A1C from hypoglycemia. Trials poor with lots of potential bias to exaggerate hypoglycemic advantage of analogues. Hypoglycemic events uncommon. Sub-group of patients with hypoglycemic problems on NPH never studied.

Starting Insulin

- Evidence: 4 reasonably-sized RCT on initiating insulin in Type 2 diabetes (starting A1c ≥7 or 7.5 or 8).
- 4-T study[1]: 708 patients for 3 yrs on either: long-acting basal OD, biphasic mixed BID or prandial insulin with meals.[1]
  - HbA1c levels were not significantly different between the three groups
    - Significantly more patients in the basal and prandial groups attained a HbA1c ≤7.0% (63% & 67% vs 49% biphasic).
  - Basal insulin had significantly
    - Less weight gain (3.6kg) than prandial (6.4kg) or biphasic insulin (5.7kg),
    - Fewer hypoglycemic events/person/yr (1.7 basal vs 3.0 biphasic, vs 5.7 prandial)
    - More patients requiring a second type of insulin (82% basal, 74% prandial and 68% biphasic)
    - Higher total dose of insulin (by weight).
  - Size, duration and three comparator arms makes the primary study.

Starting Insulin

- The 3 remaining studies (APOLLO[2], INITIATE[3] and JDDM 11[4]) followed 160 to 418 patients (total 811) for 6 months to almost a year and compared basal to prandial,[2] basal to biphasic,[3] biphasic to prandial[4] insulin.
  - HbA1c was generally similar except biphasic improved HbA1c 0.5% more than basal in one study and got more people to a HbA1C ≤7.0%[3]
  - Basal insulin had significantly less hypoglycemia (than prandial[2] or biphasic[3]) and weight gain (than biphasic[3]).

Starting Insulin

- 4-T study[1] is given priority because it is the largest, longest and compares the 3 options. Fortunately, the remaining studies[2-4] generally support those findings.
- INSIGHT[5] found initiating basal insulin in poorly controlled type 2 diabetes resulted in significantly lower HbA1C than continued oral hypoglycemic agents
  - Mean HbA1c and hypoglycemic rates were not different between patients of family practitioners or diabetes experts[6]
- Specialists are five times more likely to initiate insulin than family practitioners.[7]

Starting Insulin

- Bottom-line: In type 2 diabetes poorly controlled with oral agents, initiating basal insulin results in similar HbA1c reductions compared to starting with prandial or biphasic insulin and may cause less weight gain and hypoglycemia. Family practitioners who start insulin are as effective as specialist.

Starting Insulin

- To initiate basal insulin, prescribe: NPH 10 units QHS, increasing by 1 unit each night until Fasting Blood Glucose (FBG) = 4-7 mmol/L (5.5), remembering to educate the patient regarding hypoglycemia.[8]

1. N Engl J Med 2009;361(18):1736-47. 2. Lancet 2008; 371(9640): 1073–84. 3. Diabetes Care 2005; 28 (2): 260-5. 4. Diabetes Res Clin Pract. 2008;79(1):171-6. 5. Diabet Med 2006;23:736-42. 6. Can Fam Physician, April 2008; 54: 550 – 558. 7. Diabetes Care 2005;28(3):600-6. 8. Diabetes Care. British Columbia Guidelines and Protocols Advisory Committee. September 2010. Available at: http://www.bcguidelines.ca/gpac/pdf/diabetes.pdf Insulin Prescription. Ontario College of Family Physicians. June 2010. Available at: http://www.ocfp.on.ca/local/files/Insulin Prescription_Rev1.pdf

Evidence for Targets

Cholesterol
SANDS trial - 3 years - 499 American Indian men and women aged 40 years or older with type 2 diabetes and no prior CVD events
Results - surrogates improved - no change in clinical outcomes

Blood pressure
Less than 135/85 "Despite a -4/-3 mmHg greater achieved reduction in systolic/diastolic BP, attempting to achieve "lower targets" instead of "standard targets" did not change total mortality, MI, stroke, CHF, major CV events or ESRD"

Cochrane Review 2009;Issue 3:CD004349

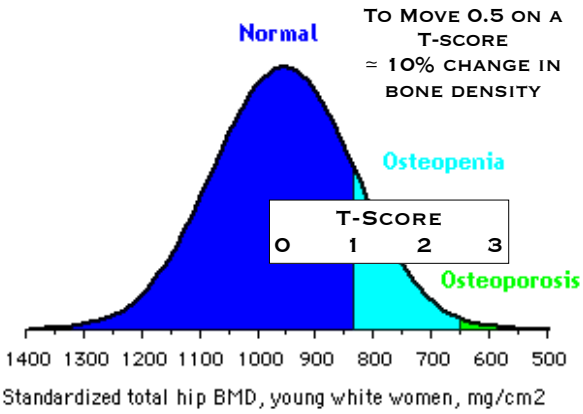
Criticism
Did not include UKPDS
Cardio-Sis - 1,111 non diabetics - 2 years - SBP 140 vs 130 - Death from any cause, MI, stroke, TIA, atrial fibrillation, admission for heart failure, angina, or coronary revascularisation (9.4% vs 4.8%) - BUT numbers driven by cardiovascular revascularization and A fib -
Lancet 2009;374:525–33

Evidence for Targets

Diabetes
Annals: 5 trials (27,802 pts), 3.4-10.7 years
Non-fatal MI (AR 0.9%, NNT 112) x 5 years
Combined CVD (1.5%, NNT 67)

Lancet meta-analysis (using PROACTIVE found similar thing)

Ann Intern Med 2009;151:394-403; Lancet 2009;373:1765–72



How are "we" doing?

Many population surveys find practicing physicians are not adequately hitting the targets identified from guidelines.
From the Third National Health & Nutrition Exam Survey (NHANES) of DM in the US,
In total: 93% DM pts did not hit all targets.
Cholesterol Targets in US
68% not at the 3 Cholesterol Targets

JAMA 2004;291:335-42
J Manag Care Pharm 2006;12;745-51

Do the RCT's hit Targets?

Small RCT to hit targets in BP, Chol & sugar[1]
only 1 hit all targets
BUT ↓ mortality (NNT 5) & CVD events (4)

Review: CVD pts, highest dose of statins[2]
<50% actual get an LDL < 2 mmol/L (80 mg/dL)

1) N Engl J Med 2003;348:383-93;N Engl J Med 2008;358:580-91, 2) CMAJ 2008;178:576-84

Target DOSES

ACE inhibitors, betablockers, ARBs - CHF
Class 1 recommendation "with a special focus on adherence, persistence, and uptitration to recommended doses of ACE inhibitor/ARB and beta-blocker medication"

2009 Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: Developed in Collaboration With the International Society for Heart

ACE inhibitors

NETWORK trial – Eur H J 1998;19:481-9

1,532 patients with class II to IV heart failure

receive either 5,10, or 20 mg of enalapril for 6 months

No difference in deaths, worsening of heart failure or hospitalization for heart failure

ACE inhibitors

ATLAS - Circ 1999;100:2312-8

3164 patients with class II to IV heart failure

either 2.5 to 5.0 mg daily or 32.5 to 35 mg daily of lisinopril

approx 4 years

No difference in mortality

Mortality plus hospitalization for any cause reduced from 83.8% to 79.7%

Worsening heart failure reduced from 44%to 38%

Dizziness ARI of 7%, hypotension of 4% and worsening renal function of 3%

Carvedilol

6 months n = 345 (ACE intolerant)	Hospitalizations (%)	Death (%)	Dizziness (%)	Bradycardia (%)
Placebo	22	16	23	1
6.25 BID	11	6	24	1
12.5 BID	13	7	33	11
25 BID	11	1 (n=1)	38	11

Circulation 1996;94:2807-2816

Carvedilol - japanese

3 years n= 364	Hospitalizations / death (%)	Dose reduction needed (%)
2.5 mg	23	1
5 mg	19	4
20 mg	21	23

JCHF trial - unpublished - Nov 18, 2009

Meta-analysis: β-Blocker Dose, Heart Rate Reduction, and Death in Patients With Heart Failure

Finlay A. McAlister, MD, MSc; Natasha Wiebe, MMath, PStat; Justin A. Ezekowitz, MD, MSc; Alexander A. Leung, MD; and Paul W. Armstrong, MD

"no statistically significant relationship between B-blocker dosing achieved and the magnitude of all-cause mortality reductions"

Ann Intern Med 2009;150:784-794

Losartan - heaal

5 years n = 3,846	HF admisssion (%)	Death (%)	Hypotension (%)	Hyperkalemia (%)	Angioedema (%)	Renal impairment (%)
50 mg	23	35	8	7	0	17
150 mg	26	33	11	10	0.3	24

No difference in CV death, all-cause admission
No difference in adverse events leading to D/C

Lancet 2009;374;1840-8

Panel - M. McConnell, T. Korownyk, M. Allan, M. Kolber

Screening - if you think you're healthy you haven't had enough tests

Screening – What criteria should we use?

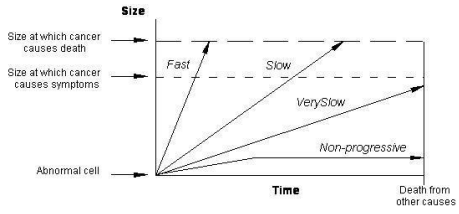
- The *burden of suffering* caused by the disease (severity and frequency)
- The *quality of the screening test* (sensitivity, specificity, cost, simplicity, safety, lead-time)
- The quality (effectiveness, safety, cost) of the *treatment* available for the disease

Screening Test Biases

- **Over-Diagnosis** – Over-diagnosis of a "normal" state as early form of disease. This may inflate the number of conditions found, and also *may inflate survival statistics*
- **Compliance** – compliant pts tend to have better prognosis regardless of screening, *thus those who tend to volunteer for a screening programs will likely have better results*

Screening Test Biases

- **Length Bias** – screening tests are likely to find slow growing tumors b/c they are present long before they cause symptoms.
- Fast growing tumors are more likely to cause symptoms and lead to diagnosis between screening intervals. *Thus, screening tends to find tumors with inherently better prognosis.*



Screening Test Biases

Lead-time bias – Lead time is the interval between the detection of a medical condition by screening and when it ordinarily would be diagnosed because of symptoms

Two men, lung CA begins at age 65:
Bob - CT scan picks up lung CA at age 65
Larry - No screening, becomes symptomatic at 66
Both die at age 67 from lung CA

Can be reported in two ways:
1)Screening improved Bob's survival from time of diagnosis (2 yrs vs 1yr)
2)Screening increased "disease time" for Bob, and did not decrease mortality

Canadian Cancer Stats 2010
Mortality of the "Big Four"

1. INCIDENCE AND MORTALITY BY CANCER TYPE

Table 1.2
Estimated Deaths and Age-Standardized Mortality Rates for Cancers by Sex, Canada, 2010

	Deaths 2010 Estimates			Deaths per 100,000 2010 Estimates		
	Total*	M	F	Total*	M	F
All Cancers	**76,200**	**40,000**	**36,200**	**170**	**204**	**146**
Lung†	20,600	11,200	9,400	47	57	39
Colorectal	9,100	5,000	4,100	20	25	16
Breast	5,400	50	5,300	12	<0.5	21
Prostate	4,300	4,300	—	22	22	—

Panel - M. McConnell, T. Korownyk, M. Allan, M. Kolber

Canadian Cancer Stats 2010
Incidence of "Big Four"

1. INCIDENCE AND MORTALITY BY CANCER TYPE

Table 1.1
Estimated New Cases and Age-Standardized Incidence Rates for Cancers by Sex, Canada, 2010

	New Cases 2010 Estimates			Cases per 100,000 2010 Estimates		
	Total*	M	F	Total*	M	F
All Cancers	**173,800**	**90,000**	**83,900**	**403**	**455**	**366**
Prostate	24,600	24,600	—	123	123	—
Lung†	24,200	12,900	11,200	55	66	48
Breast	23,300	180	23,200	53	1	102
Colorectal	22,500	12,400	10,100	51	62	41

Lung Cancer Screening

- Patient: "Should I be screened?"
- Provider: "Should I screen?"
- In the US there are three questions:
  - Does the patient want it?
  - Does their insurance pay for it?
  - Do I recommend it?
- Factors: Costs, Risk, Anxiety
- The difference with Lung Cancer:
  - Smoking related for 85-90% of the cases

What is the risk of having the disease?

Table 2 Currently active randomized trials on lung cancer screening with computed tomography

Study	Reference	Country	Start	*N*[a] screened	Age	Rounds planned	Baseline screen: Percentage abnormal[b]	Baseline screen: LC	Baseline screen: Percentage
NLST (CT/CXR)	http://www.cancer.gov/nlst/what-is-nlst	USA	2002	26726/26735	55–74	3	–	–	–
DANTE	[23••]	I	2001	1276	60–74	5	15	28	2.19
ITALUNG	[24•]	I	2004	1406	55–69	5	30	20	1.5
DLCST	[18•]	DK	2004	2052	50–70	5	8.7	17	0.8
NELSON	[19••]	NL-B	2004	7757	50–74	3	20.8	70	0.9
MILD	http://www.capolmone.org	I	2005	2208[c]	49–75	5	–	–	–
LUSI	[25]	D	2007	2000[c]	50–69	5	–	–	–

LC, lung cancer.
[a] Patients with any abnormality in their baseline computed tomography scan.
[b] Planned accrual.
[c] 2 : 1 randomization scheme, 1400 controls (U. Pastorino, personal communication).

About 1-2%

Infante, Pedersen; Curr Opin Pulm Med 16:301–306

Cohort Trials

	Cancer	# patients	Prevalence
NY	124	6295	1.9%
COSMOS	91	4815	1.8%
Canada I-ELCAP	20	1000	2%

Mazzone, Current Oncology Rep (2010) 12:226-234

RCTs

	Cancer	# patients	Prevalence
French	8	621	1.3%
NELSON	17	~2000	0.9%
DANTE	20	1000	2% Deaths were equal

Mazzone, Current Oncology Rep (2010) 12:226-234

Mazzone, Curr Oncol Rep (2010) 12:226-234

	CA found	Mortality
French	1%	NR
Danish	0.8%	NR
DANTE	4.7% vs 2.8%	20 deaths in each group
ITALUNG	0.6%	NR

"In the CT arm it appeared that 1 cancer was found for every 200 CT scans per year (1 in 65 over the course of 3 years). 300 people went through the entire screening program for each live saved" – personal communication

Panel - M. McConnell, T. Korownyk, M. Allan, M. Kolber

Summary: CXR

- About 2% have abnormal studies
- About half of those have cancer
- About half of those are Stage 1

- NNS about 50 to find an "abnormality"
- NNS about 100-200 to find cancer
- NNS about 200-400 to find resectable

Cancer Found (LDCT)

	Study Onset	# of cases	Stage I	At One Year
LDCT	2%	40	50%	0.5%
CXR	0.5%	20	40%	0.7%

About 1%

The Lung Screening Study Research Group. Lung Cancer (2005) 47, 9-15

LSS (2004)

- If positive (= 5mm non calc nodule) then work up by PMD
  - False Negative? <5mm not worked up?
  - 31/39 CA in same lobe: 5 were not!
  - Is ">5mm" more or less sensitive than private?
- LDCT detects more early CA
- Do we need to? (overdiagnosis)
- Do we save net lives? (risk of w/u, tx)

NLST website

- over 6 years (the average follow up for the CT vs CXR groups)
  - lung ca death: 1.3% vs. 1.6%
  - any death: 6.5% vs. 6.9%

- NNS with CT instead of CXR to prevent 1 lung cancer death over 6 years is 312
- Recommendation from DSMB is to halt study

NLST website

Table 3: Interim Analysis of Primary Endpoint Reported on October 20, 2010

Trial Arm	Person years (py)	Lung cancer deaths	Lung cancer mortality per 100,000 py	Reduction in lung cancer mortality (%)	Value of test statistic	Efficacy boundary
LDCT	144,097.6	354	245.7	20.3	−3.21	−2.02
CXR	143,363.5	442	308.3			

Mortality:
1.4% LDCT vs 1.7% CXR

- "The NCI recently announced randomized trial evidence for mortality reduction benefit with low-dose CT screening"
- "The Date (sic) Safety and Monitoring Board found a 20.3% reduction in lung cancer mortality, which fulfilled criteria for completion of the trial"
- (expired website)
- Referencing the preliminary NLST

Editorial, Lung Cancer 71 (2011) 247-8. (Elsevier)

Panel - M. McConnell, T. Korownyk, M. Allan, M. Kolber

Clinical Question:
What are the consequences of a screening program for lung cancer?

- Early data from NELSON: CT as a screening test for lung cancer.
- Baseline CT followed by repeat at 1 year and 3 years.
- Mean age = 59 years/ 42 pack-years of smoking/ 84% were male.
- Nodules are very common!
- Patients with a positive nodule were referred to a thoracic surgeon for further evaluation and those with an indeterminate nodule were scanned 3 months later; if the nodule had a doubling time of less than 400 days, they were also considered positive and referred.
- Of the 7557 patients 19% had a nodule:
  - 70 had lung cancer (0.9%)
- Of the 7361 patients with negative baseline CT:
  - 20 had lung cancer(0.3%)

van Klaveren RJ, et al. Management of lung nodules detected by volume CT scanning. N Engl J Med 2009;361(23):2221-2229.

MDCT: Multidetector Row CT

- 459 participants, healthy, age 60-69
- 41% had a finding; 23% needed f/u
- Most common: pulmonary nodule
- "The net risks and benefits of looking for non-cardiac abnormalities during MDCT should be rigorously evaluated."

- Arch Int Med, vol 168, No. 7, April 14,2008

Risk

- Cost (Scan, visits, accidents, insurance)
  - $1800 (CT)
- Cancer: One for every 1000-2000 scans
- Invasive work up
- Anxiety

What are the consequences of a screening program for lung cancer?

Lung cancer screening with high-resolution computed tomography (CT) has a 36% positive predictive value and 99.7% negative predictive value during the first round of screening, but results in many biopsies and significant radiation exposure. For every 1000 to 2000 chest CT scans in an adult, we cause 1 solid tumor. Since this group had a total 17,000 scans over 2 years, the screening program caused an additional 12 to 18 solid tumors. It is not clear how many of these early-stage cancers would have progressed to become clinical cancers or harm the patient; the answer to that will have to await the comparison with the control patients who were not screened.

Arch Intern Med 2009;169:2078

USPSTF

- Grade I
- "evidence is insufficient to recommend for or against screening asymptomatic patients for lung cancer"
- Can detect cancer at an earlier stage
- "Poor evidence that any screening strategy for lung cancer decreases mortality."
- "USPSTF could not determine the balance between the benefits and harms of screening for lung cancer"

Risk Chart for Men (current and never smokers)*

Find the line closest to your age and smoking status. The numbers tell you **how many of 1000 men will die in the next 10 years from...**

		Vascular Disease		Cancer			Infection			Lung Disease	Accidents	All Causes Combined
Age	Smoking status	Heart Disease	Stroke	Lung	Colon	Prostate	Pneumonia	Flu	AIDS	COPD		
35	Never smoker	1	1						2		5	15
	Smoker	**7**	**1**	**1**		Less than 1 death			**2**		**5**	**42**
40	Never smoker	3	1	1	1				2		6	24
	Smoker	**14**	**2**	**4**	**1**				**2**	**1**	**6**	**62**
45	Never smoker	6	1	1	1				2		6	35
	Smoker	**21**	**3**	**8**	**1**		**1**		**2**	**1**	**6**	**91**
50	Never smoker	11	1	1	2	1	1		1		5	49
	Smoker	**29**	**5**	**18**	**2**	**1**	**1**		**1**	**3**	**5**	**128**
55	Never smoker	19	3	1	3	2	1		1	1	5	71
	Smoker	**41**	**7**	**34**	**3**	**1**	**2**		**1**	**7**	**4**	**178**
60	Never smoker	32	5	2	5	3	2		1	1	5	115
	Smoker	**56**	**11**	**59**	**5**	**3**	**3**		**1**	**16**	**4**	**256**
65	Never smoker	52	9	4	8	6	3			3	6	176
	Smoker	**74**	**16**	**89**	**7**	**6**	**5**			**26**	**5**	**365**
70	Never smoker	87	18	6	10	12	6			5	7	291
	Smoker	**100**	**26**	**113**	**9**	**10**	**9**			**45**	**6**	**511**
75	Never smoker	137	32	8	13	19	11			6	11	449
	Smoker	**140**	**39**	**109**	**11**	**15**	**16**			**60**	**9**	**667**

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Risk Chart for Women (current and never smokers)*

Find the line closest to your age and smoking status. The numbers tell you **how many of 1,000 women will die in the next 10 years from...**

		Vascular Disease		Cancer					Infection			Lung Disease	Accidents	All Causes Combined
Age	Smoking status	Heart Disease	Stroke	Lung Cancer	Breast Cancer	Colon Cancer	Ovarian Cancer	Cervical Cancer	Pneumonia	Flu	AIDS	COPD		
35	Never smoker	1			1						1		2	14
	Smoker	**1**	**1**	**1**	**1**						**1**		**2**	**14**
40	Never smoker	1			2	1	Less than 1 death				1		2	19
	Smoker	**4**	**2**	**4**	**2**						**1**	**1**	**2**	**27**
45	Never smoker	2	1	1	3	1	1				1		2	25
	Smoker	**9**	**3**	**7**	**3**	**1**	**1**				**1**	**2**	**2**	**45**
50	Never smoker	4	1	1	4	1	1						2	37
	Smoker	**13**	**5**	**14**	**4**	**1**	**1**					**4**	**2**	**69**
55	Never smoker	8	2	2	6	2	2	1	1			1	2	55
	Smoker	**20**	**6**	**26**	**5**	**2**	**2**	**1**	**1**			**9**	**2**	**110**
60	Never smoker	14	4	3	7	3	3	1	1			2	2	84
	Smoker	**31**	**8**	**41**	**6**	**3**	**3**	**1**	**2**			**18**	**2**	**167**
65	Never smoker	25	7	5	8	5	4	1	2			3	3	131
	Smoker	**45**	**15**	**55**	**7**	**5**	**3**	**1**	**4**			**31**	**3**	**241**
70	Never smoker	46	14	7	9	7	4	1	4			5	4	207
	Smoker	**56**	**25**	**61**	**8**	**6**	**4**	**1**	**7**			**44**	**4**	**335**
75	Never smoker	89	30	7	11	10	5	1	8			6	7	335
	Smoker	**99**	**34**	**58**	**10**	**9**	**4**		**14**			**61**	**7**	**463**

*A never smoker has smoked less than 100 cigarettes in her life and a current smoker has smoked at least 100 cigarettes or more in her life and smokes (any amount) now. The numbers in each row do not add up the chance of dying from everything combined, because there are many other causes of death besides the ones listed here.

Summary

- We can find cancer
- But not many
- And not much more than in "usual care"
- Slightly earlier (stage)
- We will do a lot more: CT, PET, Biopsy
- And we don't know if patients will benefit
  - Await NLST and PLCO (about 2015)

Recommendations

- Policy?: Pay people to stop smoking?
- Stop smoking and consider checking for Radon if you can afford to move
- Individual decision
  - Can you afford it?
  - And all the potential tests?
  - Risk of complications, CA & losing insurance?
- *Unless, of course, a celebrity has their "life saved" by screening*

ultimately…

"I'm never going to that doc again! I asked to have a chest x-ray to check for lung cancer…I used to smoke…and she said "we don't screen for that"

Selected references

- The Cochrane Collaboration, 2010 issue 1
- Lung Cancer; 71 (2011) 247-8
- Curr Oncol Rep (2010) 12:226-34
- NEJM 2009; 361(23):2221-9
- Am J Respir Crit Care Med; 2009, vol 180:445-53
- JNCI; 2010; 102:722-31
- Radiology; Jan 2011; 258:243-53
- Lung Cancer; (2005) 47:9-15
- Arch Intern Med; 2009;169(22)
- J Natl Cancer Inst 2008;100:845-853

Colorectal cancer Screening

Mike Kolber

DTC 2011

Panel - M. McConnell, T. Korownyk, M. Allan, M. Kolber

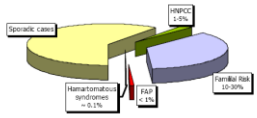
Declaration

- I am an evidence biased POLYP REMOVER!
- Evidence + experience + patient expectations = clinical decision

Who gets CRC?

3.3 Familial and genetic factors in colorectal cancer

Fig. 1 Familial risk factors and colorectal cancer



Average risk. The risk of CRC increases with age and family history. Colorectal cancer is rare before the age of 50, but after that threshold, the incidence of CRC increases dramatically. Those with no family history are considered to be at average risk.

Colorectal Cancer Screening Goals

- Take a FHx → save a life
- Population screen all average risk 50 -75 yrs
  - "Filter first" (FOBT, FIT ("I am FIT for CRC screening")
- Detect and remove adenomas
- Earlier diagnosis of CRC (get a better grade!)

Kolber's Rule #1:
Take a FHx → Save a Life!

Polyp – Cancer Sequence

- CRCs from pre - existing polyps (adenomas)
- Average "lag time" at least 10 years
- About 1% per year > 1 cm progress to cancer
- Remove polyps → prevent cancer

Bond, Endoscopy 2003; 35: 35-40
Levine, NEJM 2006; 355: 2551-7

Does screening for CRC make a Difference?

- FOBT:
  - ~1200 x 10 years to prevent 1 CRC death[1,2]
- Flex sigmoid:
  - ~200 x 11 yrs to prevent 1 CRC
  - ~500 x 11 years to prevent 1 CRC death[3]
- Colonoscopy:
  - no data to show prevents CRC death

[1] Towler, Cochrane 1998; [2]Hewitson, Cochrane 2007: CD001216
[3]Atkin et al, Lancet 2010; 375: 1624–33

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10,000 patients screened x 10 years with FOBT

- 9 fewer CRC deaths[1]
- 2800 colonoscopies[1]
- ~2 perforations
- Earlier grade of cancers[2]

[1]Towler Cochrane Reviews 1998 CD001216
[2] Hewitson Cochrane Reviews 2007 CD001216

FOBT: Accuracy

- Positive FOBT: 1-4% =
- Sensitivity: (those w CRC who FOBT test +) = 37-57%
- PPV: (test positive who actually have CRC) = 5-18% *(>80 are false positive)*

Hewitson, Cochrane Reviews 2007: CD001216
Young, Digestion 2007;76:26–33

Fecal Immune Testing (FIT)

- Antibodies to globin
- 2 stools (can be in toilet): poke (no spoon!)
- Detects only LGI bleeding (globin broken down in gut)
- No dietary or medication restrictions
- Quantitative
- ↑sensitivity (69%), ↑ participation cw FOBT

Young, Digestion 2007;76:26–33

Colorectal cancer screening Summary

- Principles of screening
  - Common, #2 mortality, earlier = better outcome
  - Better test coming "I am FIT for CRC screening"
- Evidence for FOBT, sigmoidoscopy*
- Take a Family history and save a life!

Preventative Measures

Factor	Effect on Breast Cancer
Combination HRT	RRI 24%[1]
Obesity	RRI 185% (comparing women > 82.2 kg with those < 58.7 kg in WHI cohort) [2]
Alcohol	No significant risk increase from one drink per day or less RRI 20% for 2 drinks vs. none RRI 40% for 3 drinks vs. None[3]
Diet	Most studies have found that a low-fat diet reduces risk
Smoking	Insufficient evidence
Physical Activity	RRR 30-40% if vigorous and more than 4 hours per week

1) **JAMA** 2002; 288(3):321-333. 2) **Cancer Epidemiol Biomarkers Prev** 2007; 16(12):2533-2547. **3) Ann Surg** 2003; 237(4):474-482. 4) **J Natl Cancer Inst** 2009; 101(6):384-398. 5) URL:http://www.cancer.gov/cancerinfo/pdq/prevention
McMaster Cancer Prevention Module 2010

Systematic Reviews

Age (years)	Trials Included, n	RR for breast Ca mortality (95%CI)	NNS to prevent one Ca death[1]
39-49	8	0.85 (0.75-0.96)	1904 (929-6378)
50-59	6	0.86 (0.75-0.99)	1339 (322-7455)
60-69	2	0.68 (0.54-0.87)	377 (230-1050)
70-74	1	1.12 (0.73-1.72)	N/A

2011 Cochrane review reported NNT 2000 women for 10 years to prevent one death

1) Ann Intern Med. 2009;151:727-737. 2) Cochrane Database Sys Rev

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Limitations of the Evidence

- RCTs from 1963 to 1991, population variation
- Many pts in control groups underwent mammography
- Inadequate reporting & inconsistent numbers published
- Overdiagnosis (Invasive CA & DCIS – significant number will never progress[2])
- Variation in treatment of breast cancer
  - Malmo found trend for ↑ risk breast CA mortality initially in younger screening group
  - Do recent improvements decrease screening benefit?
- Breast cancer mortality biased in favor of screening
  - mortality for other cancers significantly higher in the screened group
- **All-cause mortality not significantly ↓ in any trial**

1) Cochrane Database Syst Rev. 2011;1:CD001877 2) British Journal of Cancer 1987; 56(6):814–9.

Harms of screening

1) Pain

2) Psychological Distress - persistant anxiety/distress in women who have had false pos, despite further neg testing[1]

3) **False Reassurance -** Mammogram 95% specific[2]

4) Radiation exposure – Biennial screening from 40–80 yrs: radiation induced breast ca death 10-13/100 000 women[3,4]

Many women will require further imaging which may increase their exposure

5) **Overdiagnosis –** 1-52%. There may be 10 women unnecessarily diagnosed with cancer for each life saved[1]

1) Cochrane Database Syst Rev. 2011;1:CD001877 2) Ann Intern Med. 2008;148(9):671-9. 3) Radiology 2010;257(1):246-53. 4) Radiology 2011;258(1):98-105

Overdiagnosis

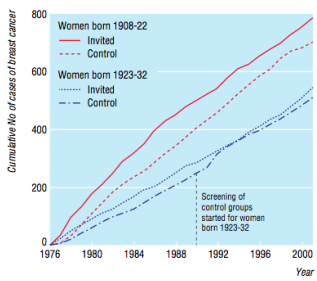

Fig 2 Cumulative number of all breast cancer cases (in situ and invasive) per year and group for total follow-up of women born during 1908-22 (unscreened control group) and 1923-32 (controls groups invited to screening from 1990 onwards)

BMJ. 2006;25:332(7543):689-92.

Screening Outcomes 1000 women x 10 years

Event over 10 years	Screening q2yr , Start at 50	No Screening
Recalled for more tests	242	
Extra Imaging	178	
Biopsy	64	
Breast CA of Any Kind	32.9	20.2
Develop Interval CA	10.4	
Die from Breast CA	4.0	5.9
Total who die	29.3	31.1

***Missing: Impact on quality of life**

1) BMJ. 2005;23:330(7497):936

Prostate Cancer Screening:

Reduction in Prostate Cancer Mortality

Time	Number Needed to Screen	Number benefiting per 1000 screened	Number Needed to Treat
9 yrs	1410	0.7	48
14 yrs	293	3.4	12

- Based on 2 high quality studies
- Not dissimilar to other adopted screening programs
  - Like them, No difference in over-all mortality

N Eng J Med 2009;360(13):1320-8. Lancet Oncol. 2010;11:725-32.

Are there problems with the test?

- Positive PSA (≥4ng/ml) per round, based on age
  - 4.8% at age 55, 7.5% at age 59,
  - 12.4% at age 63 16.5% at age 67.
- Positive PSA (<10ng/ml) are 70% false positive
- Positives (& false positives) accumulate with age.
  - After 4 rounds, ~1 in 6 chance of false positive
- A false positive: leads to a 20% increase in "worry about prostate cancer" 1 yr after (26% vs 6%)

Br J Cancer. 2010;102(3):469-74. Ann Fam Med. 2009;7(3):212-22.
J Gen Intern Med. 2006;21(7):715-21.

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What about Intervention?

- Biopsy: hematuria >3 days (23%), pain (7.5%), fever (3.5%, most require antibiotics), hospitalizations (0.5%) and urinary retention (0.4%).
  - 0.15% core-needle breast biopsies cause infections requiring antibiotics
- Treatment: every 10,000 men screened over 14 yrs,
  - 34 prostate cancer deaths will be prevented at the cost of
  - 120 more men with impotence or sexual inactivity
  - 25 more men with urinary incontinence.

Urology. 2002;60(5):826-30. Ann Intern Med. 2010;152(4):238-46.
Eur J Cancer. 2010 Nov 17. [Epub ahead of print]

Extra: Prostate Screening Studies

	Randomized to		Screening	Total F/U	Percent Screened*		Prostate Cancer Mortality (Rate Ratio unless noted)	
	Screening	No screening			Screened	Unscreened	Intention to Screen	Per Protocol
Norrkoping, Sweden[5,6]	1,494[†]	7,532	DRE q3 yrs x4 PSA q3 yrs x2[‡]	15 years (10 PSA)[‡]	83%[§]	na	1.04 (0.64, 1.68)[**]	na
Quebec City[7,8]	31,133	15,353	DRE + PSA PSA q yearly	11 years	23.6%	7.3%[††]	1.01 (0.76, 1.34)[‡‡] (risk ratio)	0.36 (0.19, 0.65) (risk ratio)
PLCO (USA)[9]	38,343	38,350	PSA q yr x 6 DRE q yr x 4	11.5 years	86%	52%	1.11 (0.83, 1.50)[§§] (risk ratio)	na
ERSPC (Europe)[10,11]	72,890	89,353	PSA q 4yrs (early DRE)	9 years	82.2%	15.4%[***]	0.80 (0.65, 0.98)	0.69 (0.51, 0.92)
Goteburg (Sweden)[12]	9,952	9,952	PSA q 2 yrs	14 years	76.1%	"low"	0.56 (0.39, 0.82)	0.44 (0.28, 0.68)

Bob Nakagawa

Academic Detailing:
The alternative rep

Bob Nakagawa, BSc(Pharm), ACPR, FCSHP
Assistant Deputy Minister, Pharmaceutical Services
BC Ministry of Health

22nd Annual Drug Therapy Decision Making Course
2 April 2011

Disclosure

- All presented work is funded by the BC Ministry of Health, Pharmaceutical Services Division

Outline

- Academic detailing
  - Definition
  - Rationale
  - Evidence
  - Comparison to other 'reps'
- BC PAD Service
  - Goals
  - Methods
  - Topics
  - Participants
  - Evaluation
  - Feedback

Academic detailing is…

Academic detailer, Vivian Yih, discussing a PAD topic

- educational method
- brief (10-30 minutes)
- 2-way; interactive
- credible source
- evidence-informed
- brief graphic print materials
- personalized to physician's needs
- practical alternatives

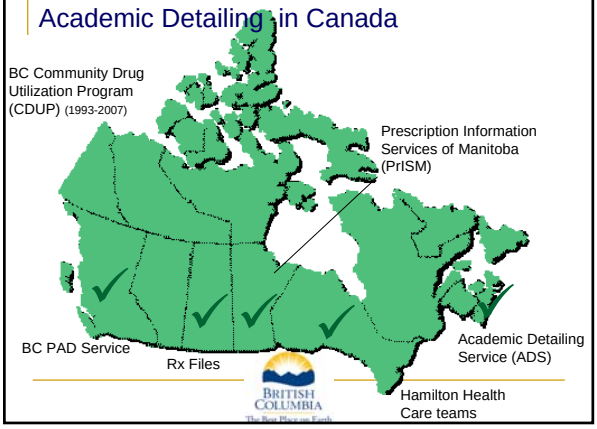
Soumerai SB. Avorn J. JAMA 1990;263:549-56

Evidence for academic detailing

- Cochrane Systematic Reviews 2007
  - 69 studies of 'educational outreach visits' prior to March 2007
  - "Educational outreach visits appear to improve the care delivered to patients. For prescribing, the effects were relatively consistent and small, but potentially important."

O'Brien MA, Rogers S, et al. Cochrane, Database of Systematic Reviews 2007, Issue 4

Academic Detailing in Canada



Bob Nakagawa

Provincial Academic Detailing (PAD) Service
Goals

- Improve the health of British Columbians
- Provide evidenced informed drug information to physicians and other health care professionals
- Encourage use of therapeutically equivalent cost effective drugs
- Evaluate the impact of academic detailing
- Collaborate with other educational initiatives and academic detailing groups across Canada

Provincial Academic Detailing (PAD) Service
Methods – Topic selection

- PAD Advisory Committee
  - Membership
    - Physicians (BCMA, CFP, UBC Faculty of Medicine)
    - Pharmacists (PSD pharmacists, HA rep, College of Pharmacists)
    - Researchers (UBC, PSD)
  - Reviews topic suggestions
  - Provides topic recommendations

Topic suggestions are welcome from participants!

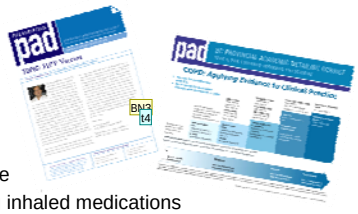
Provincial Academic Detailing (PAD) Service
Methods – Topic development

- External content expert
- Min. 2 peer reviewers
- Printed materials
  - Evidence summaries
  - Drug tables
  - Algorithms
  - Treatment ladders
  - Patient handouts

Provincial Academic Detailing (PAD) Service

Topics to date

- HPV Vaccine
- Anticoagulation in atrial fibrillation
- Antibiotics in community practice
- COPD: Optimizing inhaled medications
- Osteoporosis: Focus on bisphosphonates



Each topic is accredited for 1.0 Mainpro-M1 credit

The BC PAD Service team

Provincial Academic Detailing (PAD) Service

PAD services are available province-wide
- 11 academic detailing pharmacists (9.0 FTEs)
- Target: 2000 practitioners

- Sessions are also available using web-conferencing (Technology Enabled Academic Detailing)

Bob Nakagawa

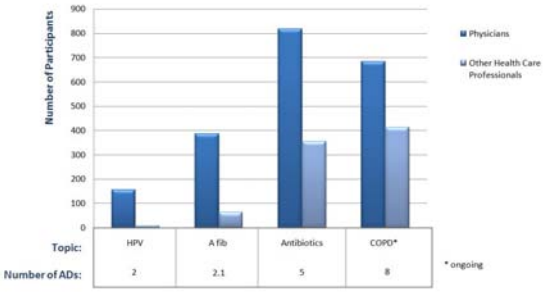
Slide 10

BN3 can we add a slide with the key messages for each of these, or is it too much info?
Bob Nakagawa, 3/8/2011

t4 I have added the KM for each topic...however, I think it is way too much information to cover in the time that you have. I have put the extra slides as the end. My suggstions would be use one as an example (antibitoics). I have put it after evaluation so that it cn be used as a lead in to another new slides which which illustrates physicians responses to how the KM's will impact their practice.
tnaumann, 3/9/2011

Bob Nakagawa

Participation in PAD



Provincial Academic Detailing (PAD) Service Evaluation

Qualitative analyses

- Program evaluation survey for each topic
- Focus groups and interviews
- Contribute to continuous quality improvement

Quantitative analysis

- Phased approach
- Pre and post, design delay

Physician feedback

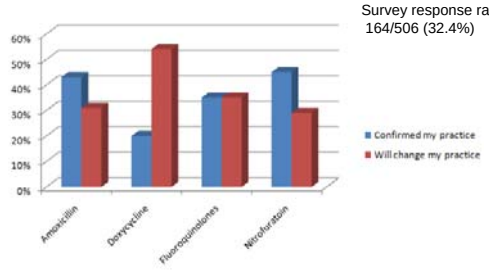
"Excellent program."
"Clear, precise, useful."
"Allowed for interaction."
"I would like these sessions on a regular basis".
"Really appreciate this service –up to date, non-biased info."
"Very valuable program. I like that it is short and to-the-point."
"The 'non-prescription' pad is fantastic!"
"The academic detailing visit was a valuable use of my time."

Antibiotics in Community Practice

Key messages

1. **Amoxicillin** is the first-line antibiotic for acute bacterial sinusitis and acute exacerbation of chronic bronchitis.
2. **Doxycycline** is the first-line antibiotic for community-acquired pneumonia.
3. **Fluoroquinolones** are reserved for patients with no other treatment options.
4. **Nitrofurantoin** is an appropriate first choice agent for uncomplicated urinary tract infections.

Practice change: Antibiotic topic



Survey response rate:
164/506 (32.4%)

Thank you

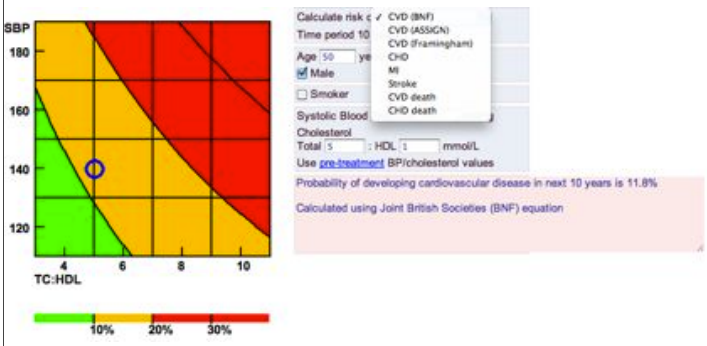
For more information about the PAD service, or to locate your nearest academic detailer, please contact

PAD@gov.bc.ca

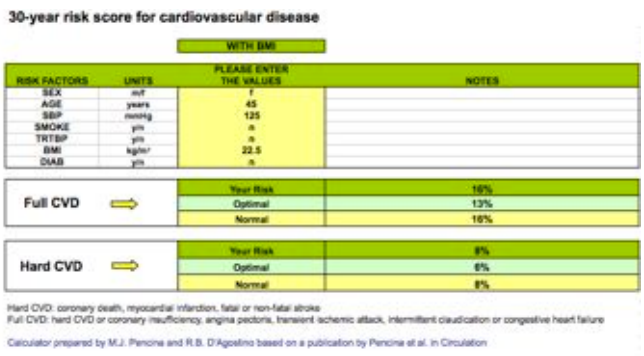
pad BC PROVINCIAL ACADEMIC DETAILING SERVICE
YOUR Rx FOR EVIDENCE-INFORMED PRESCRIBING

Patience with Patients - Panel

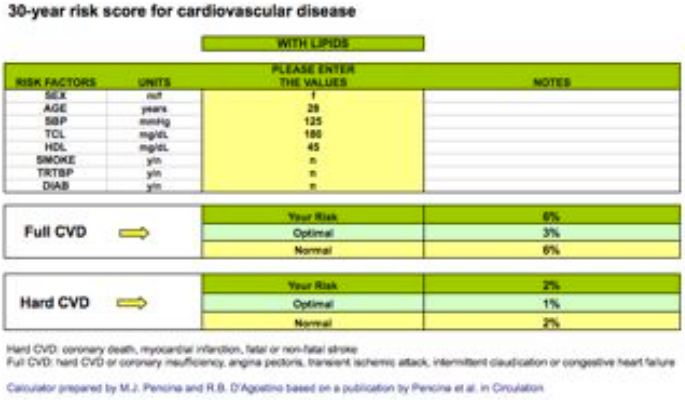
CVD risk calculators



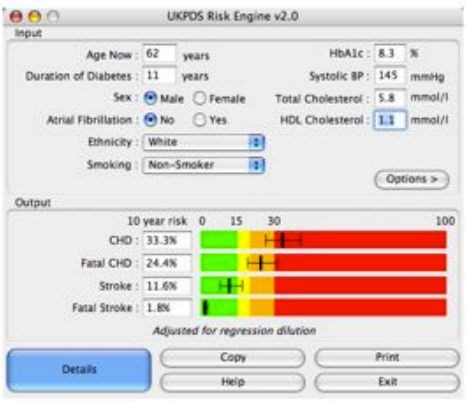
http://cvrisk.mvm.ed.ac.uk/calculator/calc.asp



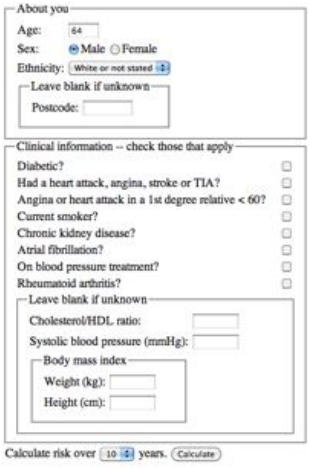
http://www.framinghamheartstudy.org/risk/



http://www.framinghamheartstudy.org/risk/

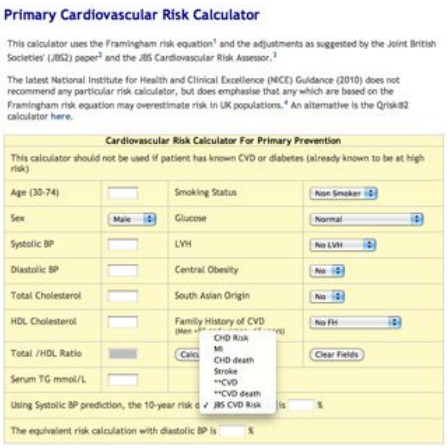


http://www.dtu.ox.ac.uk/riskengine/



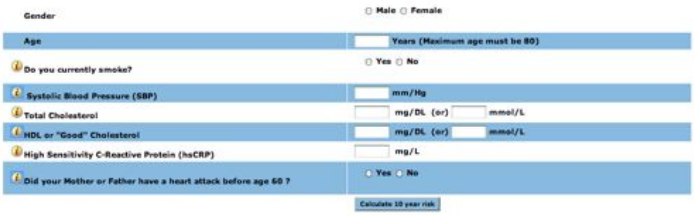
http://www.qrisk.org/

Patience with Patients - Panel



Qrisk as well

http://www.patient.co.uk/doctor/Primary-Cardiovascular-Risk-Calculator.htm



http://www.reynoldsriskscore.org/

55 YEAR-OLD MALE

NON-SMOKER, CHOL 5, HDL 1.25

10 YEAR RISK (%)

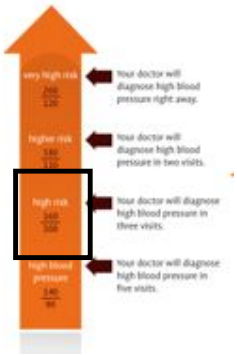
JNC 6	JNC 7	Systolic mm Hg	Non diabetic		Diabetic	
			CHD	Stroke	CHD	Stroke
Optimal	Normal	110	7	1	9	1
Normal	Prehtn	120	8	1	11	2
Borderline	Prehtn	130	9	2	12	3
Stage 1	Stage 1	140	10	2	13	3
Stage 1	Stage 1	150	11	3	15	4
Stage 2	Stage 2	160	12	4	16	6
Stage 2	Stage 2	180	15	5	19	9

YOU HAVE A "TYPICAL" MALE PATIENT WHO IS 50 YEARS OLD - YOU ARE DISCUSSING TREATING HIS BLOOD PRESSURE (160 /100 MMHG) - WHAT DO YOU TELL HIM IS THE BENEFIT?

THE "REALITY"

DRUG THERAPY CAN REDUCE THE OVERALL CHANCE OF HIM DEVELOPING CVD FROM 4% DOWN TO 3% OVER 5 YEARS

STAGE 2 HYPERTENSION - HIGH RISK



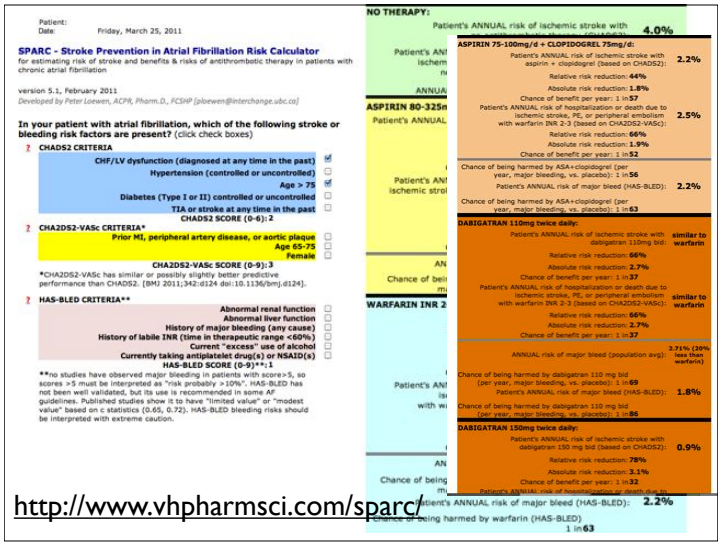
ABSOLUTE BENEFIT OF STATINS OVER APPROX. 5 YEARS

	Major coronary events (%)*	Death (%)	Strokes (%)	FROM WHAT CVD TO WHAT CVD (%)
Primary	1-1.5*	0.4	-	8-9 to 7
Diabetes	2	-	1-1.5	10 to 7
Secondary	4	2	1	20 to 15

* JUST IN MALES AND NO DIFFERENCE IN OVERALL SERIOUS ADVERSE EVENTS

Atrial fib calculator

Patience with Patients - Panel



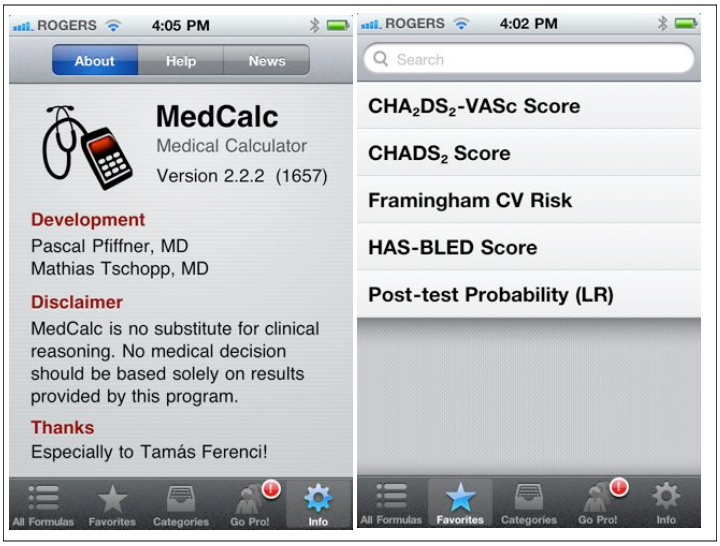
http://www.vhpharmsci.com/sparc/

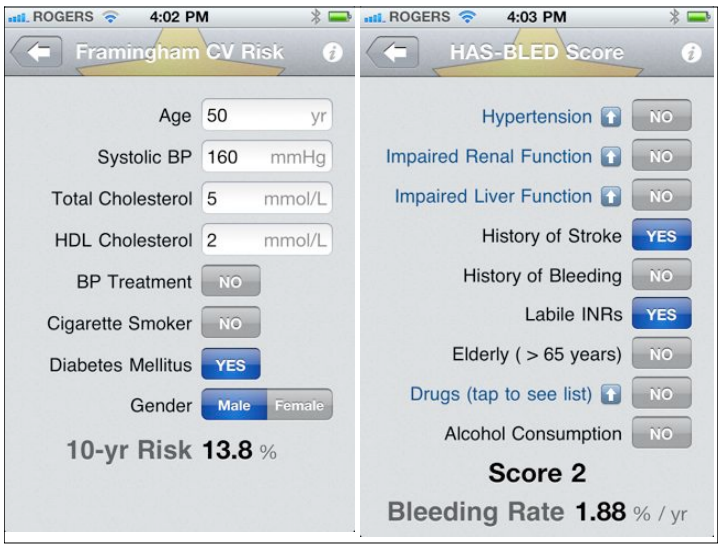
A SIMPLE A FIB TABLE

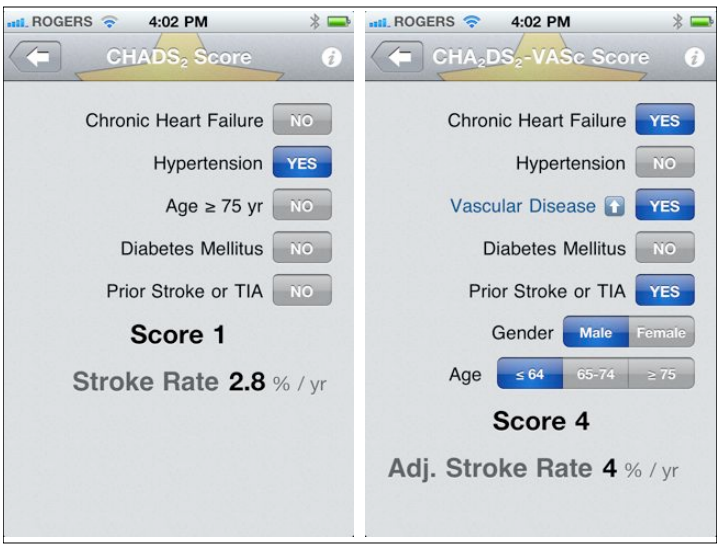
$CHADS_2$ Score	Patient's ANNUAL risk (%) of ischemic stroke			Difference in benefit between ASA and OAC
	No therapy	ASA	OAC	
0	1.9	1.5	0.6	0.9
1	2.8	2.2	0.9	1.3
2	4	3.1	1.3	1.8
3	5.9	4.6	1.9	2.7
4	8.5	6.6	2.8	3.8
5	18	14	6	8

BLEED RISK/YR- ASPIRIN 1%, WARFARIN 2-3%, DABIGATRAN 2%

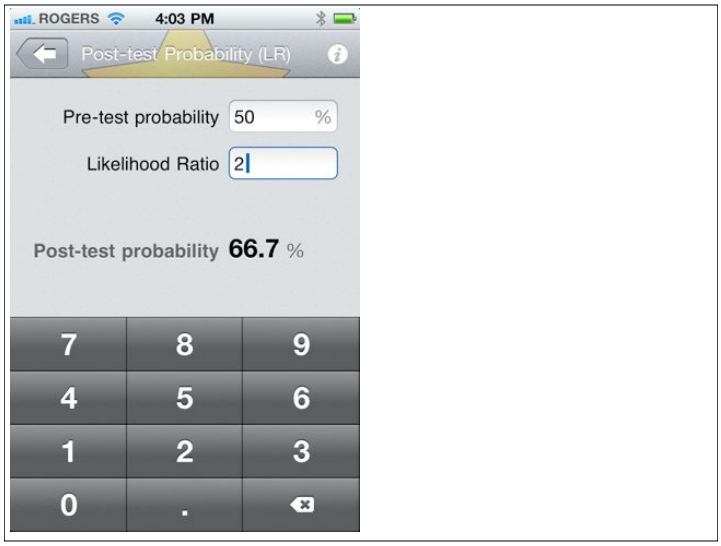
iPhone Apps

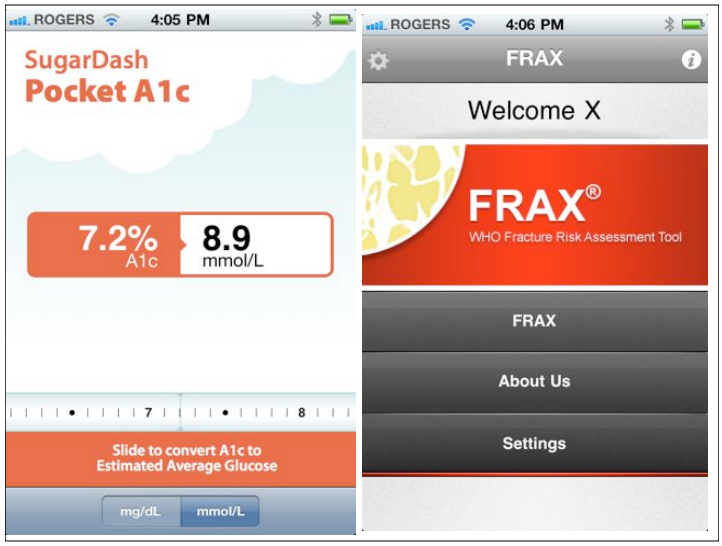




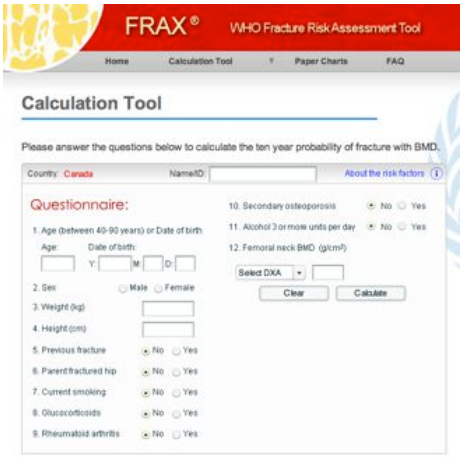


Patience with Patients - Panel





Fracture risk calculators



http://www.sheffield.ac.uk/FRAX/

Does your patient have osteoporosis?

(Osteoporosis Self-assessment Tool)

Age – weight (kg) = ????
Chance of osteoporosis
> 20 – approx 50-60%
0-20 – approx 15-20%
<0 – less than 5%

An example
60 years old
130 lbs = 60 kg
Score = 0

Valid in men as well

Mayo Clin Proc 2003;78:723-7

Mayo Clin Proc. 2002;77:629-637
The Singapore Family Physician Jul-Sep 2003;29:12
MOH Osteoporosis clinical practice guidelines - Singapore Mar 2002

5 year chance of fractures - without knowing BMD

Age	Age 65-69 (Baseline)	% to add to baseline for each factor*
% chance of any non-vertebral fx	10	3
% chance of vertebral fx	1	2
% chance of hip fx	0.5	1

*For each 5 year increment above age 65-69
History of broken bones after age 50
Mother with hip fracture
Smoke
Less than 125 lbs

Osteoporos Int 2001;12:519–28

Patience with Patients - Panel

10 year probability of a fracture

(hip, forearm, humerus, clinical vertebral)

SD	1	0	-1	-2	-2.5	-3	-4
Women							
AGE							
50	2	4	6	9	11	14	21
55	3	4	7	11	13	17	26
60	3	5	8	13	16	20	31
65	4	6	10	16	19	24	36
70	4	7	12	18	23	28	42
75	4	7	12	19	25	31	46
80	5	8	13	21	26	32	46
85	5	7	12	19	24	30	43

CMAJ 2002 167: S1-S34, Ost Int 2001 12:989-95

Relative and absolute benefits from using alendronate for 2-3 years

	Vertebral fractures		Non-vertebral fractures	
	Prim	Sec	Prim	Sec
Relative	45	45	?	20
Absolute	2	6	?	2

Cochrane Library

Side effects - words versus numbers

Qualitative descriptor	EU assigned frequency	Mean frequency estimated by participants (n=200)
Very common	>10%	65% (24·2)
Common	1–10%	45% (22·3)
Uncommon	0·1–1%	18% (13·3)
Rare	0·01–0·1%	8% (7·5)
Very rare	<0·01%	4% (6·7)

Values are mean (SD).

Table 1: Recommended qualitative descriptions with EU assigned frequency bands, and participants' estimates from the pilot study

Lancet 2002;359:853–54

Thanks for your questions and discussion.

Thanks for completing your course evaluations.

HAVE A SAFE TRIP HOME

We hope to see you next year!