28th Annual
Best Science Medicine Course
Formerly the Drug Therapy Decision Making Course – 25 years

April 7th and 8th, 2017
Fairmont Waterfront Hotel
Vancouver, B.C.

FRIDAY Syllabus

Presented by

Department of Family Medicine
Leaders in primary care, champions of community health
Providence Health Care
ST Paul’s Hospital

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

COMMITTEE MEMBERS
Drs. Rita McCracken and Tracy Monk
"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
Best Science Medicine Course 2017

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
Alan Cassels, Adj Prof., Human and Social Development, University of Victoria
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
Keith Ahamad, Clin. Asst. Prof., Family Medicine, UBC & PHC
Claire Hinnell, Clin. Asst. Prof., Medicine, Neurology, UBC
Peter Loewen, Assoc. Prof., Pharm. Sciences, UBC & VCHA
Julian Marsden, Clin. Prof., Emerg. Medicine, UBC & PHC
Kam Shojania, Clin. Prof., Medicine, Head, Rheumatology, UBC & PHC
John Stewart, Emeritus Prof., Medicine, Neurology, McGill University; Retired Neurologist, UBC & LGH
Aaron M Tejani, Clin. Asst. Prof., Pharmaceutical Sciences, UBC
Helen Tremlett, Prof. Medicine, Neurology, & Canada Research Chair in Neuroepidemiology and Multiple Sclerosis, UBC

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

"If Music
be the food of love...
play on!"
FRIDAY, APRIL 7, 2017

07:00  Registration (Muffins & Coffee)
    Chairs – Mike Allan and JamesMcCormack

“Laugh yourself into stitches” (Twelfth Night) THE START
08:00  bless thee, bully doctor! Robert Rangno
08:05  Shakespeare brings greetings from afar Christopher Gaze
08:20  Much ado about nothing – and so much more Mike Allan and James McCormack

“The game is afoot” (King Henry IV - Part 1) CVD
09:00  Urgent BP numbers – “all's well that ends well?” Julian Marsden
09:20  Lowering BP numbers – is there “too much of a good thing?” Mike Allan
09:40  Questions
09:50  Bleeding in patients on antithrombotic therapy – “The short and the long of it” Peter Loewen
10:10  Questions
10:20  Refreshment Break

“It was Greek to me” (Julius Caesar) COMMUNICATION
10:40  speaking with patience – “Knock, knock! Who's there” Tracy Monk
11:00  Communication of evidence – “what's in a name” James McCormack
11:20  Questions
11:30  “The Comedy of Errors” in medicine and how to prevent them Kam Shojania
11:50  “Make short shrift” of 5 key pediatric studies Tina Korownyk
12:00  Questions
12:10  Lunch

“Eaten me out of house and home” (King Henry IV – Part II) POTPOURRI
13:00  “The short and the long of it” – Two award winning resident presentations Medical Residents
13:20  NSAIDs myths – “All that glitters is not gold” Adrienne Lindblad
13:40  Preventing infections in hospital – “Out, damned spot! Out” Victor Leung
14:00  Questions
14:20  Refreshment Break

“Too much of a good thing” (As You Like It) SYMPTOMS
14:40  “In a pickle” as to what medications to use for COPD Aaron Tejani
15:00  Opioid use disorder – “A Midsummer's Night Dream” or a “Devil incarnate” Keith Ahamad
15:20  IBS treatments – “Is there something in the wind” Tina Korownyk
15:40  Questions
16:00  Adjourn

Christopher Gaze is best known as the Founding Artistic Director of Bard on the Beach Shakespeare Festival. He hosts the Vancouver Symphony Orchestra’s ever popular Tea & Trumpets series and has hosted their annual traditional Christmas concerts for over 20 years.

His many honours include Canada's Meritorious Service Medal, Honorary Doctorates from UBC & SFU, the Mayor’s Arts Award for Theatre and the Order of British Columbia. Last summer, he directed the world premiere of C.C. Humphreys' Shakespeare's Rebel, part of Bard's 26th season.

Christopher plays a leading role in British Columbia as an advocate for the arts in general, and his passionate dedication to Bard on the Beach has fuelled its growth into one of the largest professional theatre companies in Canada, drawing more than 1.5 million patrons since its inception.

We are pleased to have Christopher join us for some “Shakespearean fun” at the Best Science Medicine Course in 2017.
1) Disclosure of Commercial Support
Neither this program nor the presenter has received financial support from any organization or company.

2) Mitigating Potential Bias
All recommendations and information presented are based on the best-available evidence we could find. Typically this includes meta-analyses, systematic reviews and RCTs. In addition, we don’t care what the results are, but rather we care that people know about the results.

3) Objectives
To be able to take the best available evidence for common conditions in primary care and incorporate this information into shared-decision making with patients.
We are all KNOWLEDGE brokers

OUR BELIEF

All Health Care Providers should have their practice underpinned by the best available evidence

Evidence-Based Practice (EBP)
"the use of many, perhaps most, medical treatments does not depend so much on these evidence-based medicine principles but on what one could call evidence-based hearsay"

Wrong guidelines: why and how often they occur

Primiano Iannone,¹ Nicola Montano,² Monica Minardi,³ James Doyle,³ Paolo Cavagnaro,⁴ Antonino Cartabellotta⁵

"Unfortunately, depending on how their reliability is measured, up to 50% of guidelines can be considered untrustworthy. This carries serious consequences for patients' safety, resource use and health economics burden."
“Overall, not only are most research findings false, but, furthermore, most of the true findings are not useful.”

“Instead of trying to make a prolific researcher of every physician, training physicians in understanding research methods and evidence-based medicine may also help improve the situation by instilling healthy skepticism and critical thinking skills.”

Golden Pill Award

<table>
<thead>
<tr>
<th>Year</th>
<th>Clear advantage</th>
<th>Modest improvement</th>
</tr>
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<tbody>
<tr>
<td>2011</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2012</td>
<td>0</td>
<td>2</td>
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<tr>
<td>2013</td>
<td>0</td>
<td>1</td>
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<tr>
<td>2014</td>
<td>1</td>
<td>3</td>
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<tr>
<td>2015</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2016</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
Many courts (UK, US, CA) “The reasonable-patient standard … requires physicians and other health care practitioners to disclose all relevant information about the risks, benefits, and alternatives of a proposed treatment that an OBJECTIVE PATIENT would find material in making an intelligent decision as to whether to agree to the proposed procedure” JAMA 2016;315:2063-4

The Bottom Line Sep 2011 Even an authoritative CPG may NOT be found to be determinative of a standard of care.

It is prudent for physicians to be aware of authoritative clinical practice guidelines relevant to their practices. If a clinical decision may be perceived as being contrary to a recognized and accepted CPG, a physician, where appropriate, may consider the following steps: consult with a colleague or relevant specialist, discuss reasonable treatment options with the patient, and document the patient’s consent for the chosen treatment.

If deviating from an established CPG, physicians should consider documenting the rationale for doing so, as well as any discussions with the patient about such variance.

Evaluating physician understanding of harms and benefits of common tests and therapies
Paper survey to residents and attending internal medicine physicians – 18 questions – 117 people responded

Percent of respondents

<table>
<thead>
<tr>
<th>Estimate of benefit in absolute terms</th>
<th>&lt;5%</th>
<th>5 to 10%</th>
<th>10 to 20%</th>
<th>20 to 40%</th>
<th>40 to 70%</th>
<th>70 to 100%</th>
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</thead>
<tbody>
<tr>
<td>Non-fatal MI</td>
<td>5</td>
<td>22</td>
<td>35</td>
<td>18</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Major bleeding with ASA 5 years</td>
<td>21</td>
<td>46</td>
<td>21</td>
<td>8</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Major bleeding with ASA 1 year</td>
<td>14</td>
<td>42</td>
<td>30</td>
<td>11</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Unnecessary biopsy with screening 10 years</td>
<td>1</td>
<td>9</td>
<td>15</td>
<td>33</td>
<td>26</td>
<td>15</td>
</tr>
</tbody>
</table>

79% overestimated benefit
66% overestimated harm
67% were unconfident

JAMA Aug 29 2016

5% relative increase 1.25 minus 1.00 = 0.25
25% relative increase 1.50 minus 1.00 = 0.50
50% relative increase 2.00 minus 1.00 = 1.00

The CI represents a plausible range of values for the effect but not a probability of its magnitude

5 is 25% greater than 4
RR = 1.25

5% - 4% = 1%
1% = 1/100
NNH = 100
20 “NEGATIVE” STUDIES IN A ROW

LIPIDS
AIM-HIGH, HPS2-THRIVE (niacin)
ACCORD (fibrates)
daOUTCOMES (dalcetrapib)
STABILITY (darapladib)

ACCORD (niacin)

BLOOD PRESSURE
ALTITUDE (aliskiren)
VALISH, AASK, ACCORD (aggressive BP lowering)

DIABETES
ACTIVE (irbesartan/afib)
CRESCENDO (rimonabant)
ROADMAP (olmesartan)
VISTA-16 (varespladib)

FOURIER - evolocumab
2.2yr - 63 y/o, 75% male, 100% prev CVD, LDL 2.8/109, 28% smokers, 100% on statins, 37%

<table>
<thead>
<tr>
<th></th>
<th>All deaths (%)</th>
<th>CVD death (%)</th>
<th>MI (%)</th>
<th>Stroke (%)</th>
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</thead>
<tbody>
<tr>
<td>Evolocumab</td>
<td>3.2</td>
<td>1.8</td>
<td>3.4</td>
<td>1.2</td>
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<tr>
<td>Placebo</td>
<td>3.1</td>
<td>1.7</td>
<td>4.6</td>
<td>1.6</td>
</tr>
<tr>
<td>RR</td>
<td>NSS</td>
<td>NSS</td>
<td>14</td>
<td>27</td>
</tr>
<tr>
<td>ARR</td>
<td>NSS</td>
<td>NSS</td>
<td>1.6</td>
<td>1.2</td>
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<tr>
<td>NNT/NNH</td>
<td>63</td>
<td>81</td>
<td>63</td>
<td>250</td>
</tr>
</tbody>
</table>

FOURIER - evolocumab

A “rough” economic analysis

@ $20,000 Canadian/year

100 people take drug for 2.2 years = $3.3 million to prevent 1.6% non-fatal CVD events

$20,000/year gets you a

✔️ personal trainer - 3 hours a week

AND

✔️ personal chef - 3-4x a week

SPIRE - bococizumab

50% developed antibodies
10 months - 63 y/o, 70% male, majority with CVD?, LDL 2.8/109, 25% smokers, 93% on statins, 48%

<table>
<thead>
<tr>
<th></th>
<th>All deaths (%)</th>
<th>CVD death (%)</th>
<th>ADE resulting in drug D/C (%)</th>
<th>Injection site reaction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bococizumab</td>
<td>0.9</td>
<td>0.5</td>
<td>5.0</td>
<td>7.9</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.9</td>
<td>0.5</td>
<td>3.4</td>
<td>1.0</td>
</tr>
<tr>
<td>RR</td>
<td>NSS</td>
<td>NSS</td>
<td>47</td>
<td>663</td>
</tr>
<tr>
<td>ARR</td>
<td>NSS</td>
<td>1.6</td>
<td>6.9</td>
<td></td>
</tr>
</tbody>
</table>
| NNT/NNH   | 63             | 15            | NEJM 2017

Lowered LDL 59%, raised HDL 8%

Lowered LDL 59% at 14 weeks, 47% at 52 weeks, raised HDL 6%

James McCormack and G. Michael Allan
Symptom NNTs

- PPIS, sildenafil - NNT ~2
- NSAIDs, opioids - pain NNT ~3-5
- Antidepressants - severe depression - NNT ~10
- Ipratropium - asthma attack - NNT ~11
- Cholinesterase inhibitors - ADAS-Cog >4 - NNT ~10
- Sleeping pills - improvement in sleep quality - NNT ~13
- Steroids - sore throat - NNT ~3, Bell’s palsy - NNT ~10
- Antibiotics - acute COPD exacerbation - NNT ~5
- Topical antibiotics - bacterial conjunctivitis - NNT ~12

November 7, 2016
What do Normal Backs Look Like

33 studies (3110 pts, no Hx of any back pain) of CT/MRI findings.

<table>
<thead>
<tr>
<th>Imaging Finding</th>
<th>Age (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Disk degeneration</td>
<td>37%</td>
</tr>
<tr>
<td>Disk signal loss</td>
<td>17%</td>
</tr>
<tr>
<td>Disk height loss</td>
<td>24%</td>
</tr>
<tr>
<td>Disk bulge</td>
<td>30%</td>
</tr>
<tr>
<td>Disk protrusion</td>
<td>29%</td>
</tr>
<tr>
<td>Annular fissure</td>
<td>19%</td>
</tr>
<tr>
<td>Facet degeneration</td>
<td>4%</td>
</tr>
<tr>
<td>Spondylolisthesis</td>
<td>3%</td>
</tr>
</tbody>
</table>

* Prevalence rates estimated with a generalized linear mixed-effects model for the age-specific prevalence estimate (binormal outcome) clustering on study and adjusting for the midpoint of each reported age interval of the study.


Cut tablets/the dose in half

It's not as scary as you think

...or is it?

low-dose (~20mg/day) isotretinoin improves acne similar to conventional dosing

low-dose may reduce common side effects (chapped lips, dry skin, epistaxis) by 16-35%

may be associated with increased relapse rates (~20%) particularly with severe acne
One dose of dexamethasone (12mg) vs 5 days of prednisone (60 mg/day) for acute asthma in adults

Non-inferiority study - 376 with mild to moderate asthma

Relapse rates 12.1% (D) vs 9.8% (P)
95%CI (-4.1 to 8.6) - used 8% as a non inferiority margin

Abdominal pain 1.1 (D) vs 4.9% (P)

Urgent Blood Pressure Numbers

“All’s well that ends well?”

JULIAN MARSDEN MD FCFP(EM)
APRIL 7, 2017
28TH ANNUAL BEST SCIENCE MEDICINE COURSE

Faculty/Presenter Disclosure
Faculty/Presenter: Julian Marsden

Relationships with commercial interests:
- Grants/Research Support: None
- Speakers Bureau/Honoraria: None
- Consulting Fees: None
- Other: None

Disclosure of Commercial Support
This program has received NO financial support.
This program has received NO in-kind support.

Potential for conflict(s) of interest:
None

Objectives and Outline
1. To develop an approach towards the patient with severe hypertension
   - Who to sent to the Emergency Department (+/- admit)
2. Review evidence on how to treat hypertensive emergencies
3. Review how to initially manage hypertensive urgencies (asymptomatic markedly elevated hypertension)

“The Game is Afoot”
King Henry IV – Part 1 1597

Setting the Stage
Case 1: 47 year old male
Left elbow pain, 205/111, ‘healthy’, no medications
Rechecked: R 226/114, L 219/128

Case 2: 79 year old male
Sent in by clinic for hypertension and constipation
1. Took BP yesterday and Systolic BP > 200 mmHg
   - Last checked 1 year ago
   - No headache, chest pain, shortness of breath, vision change
2. No BM for 5 days
   - Still able to pass gas
   Feels well – just constipated

On examination
Blood Pressure:
  - 225/90 mmHg left arm
  - 210/91 mmHg right arm
Pulse 63
RR 16
O2 Sat 98 % on RA
Afebrile

Case 3: 55 year old female
- Increasing BP for few days (165/108 mmHg)
- Taking losartan (ARB) with no change in dosage
- Has a small headache and blood shot eyes
- Past Med Hx: hypertension, high cholesterol, GE Reflux
- BP 160/82 mmHg

Case 4: 72 year old female
Playing cards suddenly grabbed her head and collapsed
No further history available

Unconscious, not moving left arm or leg
BP 250/140 mmHg
Rest of vital signs stable

Act 1 Scene 1
WHY IS THIS IMPORTANT?
These conditions can happen over several years, but they can be prevented by controlling your blood pressure.

Old term coined in 1914
1 yr mortality rate after hypertensive emergency = 80%
similar to cancer

“Malignant hypertension”
Guidelines
At initial presentation, patients demonstrating features of a hypertensive urgency or emergency should be diagnosed as hypertensive and require immediate management (Grade D).

Grade D = expert opinion

A British Medical Association Lecture
ON
THE SIGNIFICANCE OF A RAISED BLOOD PRESSURE*
BY
JOHN HAY, M.D., F.R.C.P.
Professor of Medicine, University College; Senior Physician and Physician in Charge of the Cardiovascular Department, Royal Infirmary, Liverpool.

...a rise in blood pressure is for many patients a compensatory phenomenon...

There is some truth to the saying that the greatest danger to a man with a high blood pressure lies in its discovery, because “then some fool is certain to try and reduce it.”

Franklin D Roosevelt
April 12, 1945
Aged 63

‘CAME OUT OF CLEAR SKY,’ SAYS PRESIDENT’S PHYSICIAN

Death due to cerebral hemorrhage – blood vessels in brain broke

By Charles G. Ross
How significant is one severely elevated blood pressure episode?

MUCH ADO ABOUT NOTHING?

Is it really hypertension?

Despite acute pain and anxiety, the patient still probably has hypertension
- 156 patients with elevated BP – half were sustained in follow-up

Recognizing the real deal...

Diagnosis of emergency based on symptoms will likely over diagnose

Headache as a symptom is particularly problematic and often poorly correlated with HTN.
- Neurology. 2008; 70:1329-1336

Classic hypertensive encephalopathy are sick

We ignore it in the ED because...

1. BP are falsely elevated in the ED:
   - Pain, anxiety, white coat syndrome, chaotic environment

2. We do not take it properly.

3. There isn’t much evidence about how we should approach this in the ED.

Some nomenclature

HYPERTENSIVE CRISIS
BP > 180/110 mmHg

SYMPTOMS?

CNS
CVS
SOB

NO

YES

Hypertensive Urgency
(no end-organ damage)

Hypertensive Emergency
(end-organ damage)

End organ: cardiovascular, renal or neurologic

THE CAST
**Hypertensive emergency**

**Trigger**

- Endothelial function
- RAAS
- SNS

**Endothelial injury**

- Acute ↑↑ in SVR

- Tissue edema

- Inflammation
- Coagulation

**End-organ ischemia**

**“2% with HTN will develop hypertensive emergency”**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute CHF/ Pulmonary edema</td>
<td>36.8%</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>24.5%</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>16.3%</td>
</tr>
<tr>
<td>Acute MI or unstable angina</td>
<td>12%</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>4.5%</td>
</tr>
<tr>
<td>Intracerebral hemorrhage/SAH</td>
<td>4%</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>2%</td>
</tr>
</tbody>
</table>

_Hypertension 1996. 27(1):144-147_

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**Treatment of hypertensive emergencies**

2009 Cochrane Review: Pharmacologic Treatment of Hypertensive emergencies

No evidence regarding mortality/morbidity to inform clinicians as to which antihypertensive drug class provides more benefit than harm.

**A systematic review of nicardipine vs labetalol for the management of hypertensive crises**

W. Frank Peacock IV MD*, Daniel P. Shanks PharmD*, Phillip D. Levy MD*, Denise H. Rhoney PharmD*, Joseph Varon MD

_Am Jour Emerg Med 2012(30):981-993_

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**Acute Neurologic Syndromes**

Avoid hypo-perfusion!!

Do not exceed 20% reduction of BP

BP often very labile - use short acting agents

- Nitroprusside 0.25-10 µg/kg/min
- Esmolol 80 mg bolus → 150 µg/kg/min
- Labetolol 20-80 mg bolus every 10 min →

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**CHF/Pulmonary Edema**

Afterload reduction!!

- IV Nitroglycerin (Start 10 mcg/min and titrate)
- ACE inhibitors

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**ACS**

- Beta blocker Metoprolol 5 mg q5 min
- IV nitroglycerin
### Aortic dissection

- IV nitroprusside
- β blocker
- Labetolol

### Sympathomimetic Intoxication

- Benzodiazepines!!!
- Labetolol
- Alpha blocker (phentolamine 1mg)

### Pre-eclampsia/Eclampsia

- Methyldopa - 250 mg q6h
- Hydralazine 10-20 mg IV bolus
- Labetolol

### Hypertensive urgency

**THE PLOT THICKENS**

### Newer term

**Hypertensive urgency**

- or
- Asymptomatic markedly elevated blood pressure

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American College of Emergency Physicians

Does screening for target organ damage reduce rates of adverse events?

1. Routine screening (urine, creatinine, ECG) is not required
2. In select patient populations – poor follow-up; no primary care access – serum creatinine may identify those who are at increased risk

Level C Recommendation
(case report/series or consensus)

Does ED medical intervention reduce rates of adverse events?

1. Routine medical intervention is not required
2. In select patient populations – poor follow-up; no primary care access – may treat in the Ed or initiate therapy for long-term control (consensus recommendation)
3. Should be referred for outpatient follow-up (consensus recommendation)

Level C Recommendation
(case report/series or consensus)

Suggested Future Research

1. What is the optimal screening for ED pts with asymptomatic markedly elevated BP as it relates to patient outcomes (short, long term adverse events, long-term target organ disease)
2. What is the optimal management for these patients?
3. Does writing a prescription from the ED or administering an oral dose of medication in the ED change outcomes?
4. What is the ideal interval for patient follow-up?

The penultimate scene

THE CASES...

Case 1: 47 year old male

Left elbow pain, 205/111, ‘healthy’, no medications

Rechecked R 226/114, L 219/128
- 2006 – L ankle pain, BP 184/118
- 2008 – R wrist pain, BP 188/119
- 2009 – L ankle pain, BP 112/68
- 2009 – R knee pain, BP 197/118
- 2011 – L foot pain, BP 196/114
**Case 1: 47 year old male**

Left elbow pain diagnosed as mechanical

Started on thiazide diuretic and referred to Internal Medicine clinic

On follow up BP remained high and ARB added to thiazide

---

**Case 2: 79 year old male**

Sent in by clinic for hypertension and constipation

1. Blood Pressure: 225/90 mmHg left; 210/91 mmHg right arm

   Started on an ACE I referred to Internal Medicine clinic

   - Repeat BP 130/70 1/week later
   - No change in meds

2. No BM for 5 days

   - PEG 3350 & Lactulose prescribed

---

**Case 3: 55 year old female**

- Increasing BP for few days (165/108 mmHg)
- Taking losartan (ARB) with no change in dosage
- Has a small headache and blood shot eyes

- Normal exam and urinalysis
- Referred back to her primary care provider

---

**Case 4: 72 year old female**

Unconscious, not moving L arm/leg. BP 250/140 mmHg

Large intracranial hemorrhage on CT scan

IV labetolol 20 mg boluses q 10 minutes with infusion with target of 140 mmHg Systolic BP

Admitted to Medicine with neurology/neurosurgical consults

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**In Conclusion**

**THE FINAL ACT**
Take Home Points

1. Hypertensive emergencies (BP > 180/110 with target organ damage) represent a distinct subset of hypertensive patients

2. There is no BP threshold that mandates work-up/treatment of asymptomatic markedly elevated blood pressure in the ED

3. You may be more likely to test/treat/ensure follow-up if pt has prior end-organ damage or poor follow-up

4. If treating, there is no hurry
Lowering BP numbers – is there “too much of a good thing?”

Objectives of BP management

- Update the present recommendations around making the Diagnosis of hypertension?
- Review the evidence for different BP targets.
- Identify the interventions that improve both outcomes (as well as BP).
- Consider how to apply some of evidence and guidelines in hypertension management.

Moderately high BP

- Blood Pressure over 160
  - Systolic Hypertension in Europe (Syst-Eur)
  - Systolic Hypertension in China (Syst-China)
  - Systolic Hypertension in the Elderly Program (SHEP).
- Often: mean 170, down to 150 or so.
  - Relative Benefits:
    - 30-35% RRR in CVD (40% stroke, 25% cardiac)
    - Sometimes mortality (15% or so)
  - Absolute benefits
    - 5 years 3-4% less stroke,
    - 5-6% less CVD overall,
    - up to 5% mortality

What Happens to BP when Technique Poor?

<table>
<thead>
<tr>
<th>Measurement variables that lead to inaccurate BP</th>
<th>Mean change in Systolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talking during measurement</td>
<td>17</td>
</tr>
<tr>
<td>Inappropriate cuff size (too small)</td>
<td>8</td>
</tr>
<tr>
<td>Arm positioned below level of heart</td>
<td>7-10</td>
</tr>
<tr>
<td>Failure to support arm</td>
<td>2</td>
</tr>
</tbody>
</table>


Other Target-Based Studies

- General, 3 SR, 7-19 RCTs, 22-52K pts, 3.8 yrs.
  - When BP only 4/3 better, No difference in any outcome
  - When BP ~8/4 better, No diff in death but
    - CVD: RRR 14% (if CVD risk ~20% over 10 year, NNT=36).
    - Limits: Some early trials not “intense” (ex. ≤150 vs ≤180)
- Renal Disease: 2 SR of 3-11 RCTs (2-9K pts) ~3 yrs
  - Mortality or any CVD: No statistical difference.
  - Prevent worsening renal function: RRR 18%, NNT=247
- Large Sys Reviews demonstrate absolute benefits of BP reduction are driven largely by base-line risk.

Tools for Practice #38 (updated 2016)

SPRINT: BP targets

- RCT: 9361 pts, target <140 vs <120. Stopped early,
  - Higher risk: mean Framingham 20%.
- Outcome: 121 vs 136 mmHg at 3.26 yrs, meds 2.8 vs 1.8
  - CVD: 5.2% vs 6.8%, HR 0.75 (0.64-0.89), NNT=61, & Death: NNT=90, &
  - Harms: Hypotension/syncope/electrolyte NNN=72-100, Acute kidney
    injury/failure NNN=56
- Important Caveats: Automated BP used!
  - Subgroups same: Age ≥75 (2636 pts) & Others (Gender, Race, CKD)
  - Exclusion: Ejection fraction <35%, Diabetes, Past stroke, eGFR<20,
    standing BP at 1 mm <110
  - Bottom-Line: Strong evidence to lower BP targets in higher risk
    patients (not diabetics this time). No clear that helpful for
    kidneys.


BP Thresholds & Targets Overall in DMs

- Sys Rev: 49 BP RCTs, 73,738 diabetes pts
  - Except stroke (improves NNT ~62 over 5 yrs)
    - Meta-regression: benefit crosses to harm at 141mmHg
    (baseline) and 132 mmHg (attained).
  - Bottom-line: Treating Systolic BP <140 and/or
targeting <130 in type II diabetes likely advisable.

Brunstrom BMJ 2016;352:i717

Who can we offer lower targets to

- Important limitations for SPRINT application
  1. SPRINT used automated office BP monitors that
    typically read 5-20 mmHg lower. Office targets of 125-130 may
    be appropriate;
  2. Lower targets do not apply to diabetics;
  3. Diastolic BP was kept above 65 mmHg and standing BP was
    ≥110mmHg.

Results do not apply to...

- Limited to no evidence
  - Heart failure (ejection fraction <35%) or recent myocardiul
    infarction (within past 3 months)
  - Indicators for, but not currently receiving, a β-blocker
    - Fizz or institutionalized elderly individuals
  - Nonduodenal ulcer
    - Diabetic neuropathy
    - Previous stroke
    - eGFR ≤ 20 mL/min/1.73 m^2
    - Cardiothoracic
      - Patient unable to adhere to multiple medications
      - Standing SBP < 110 mm Hg
    - Known secondary cause(s) of hypertension

JNC 8 – 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults –
G. Michael Allan

How fast do you have to go?

- In high risk (>20%) a difference in BP of 160 – 135 means about 6-8% risk over 10 years
  - Over 6 months: 0.4% (NNT 250)

- In low risk (<10%) a difference in BP of 160 – 135 means about 1.5-3% risk over 10 years.
  - Over 6 months: 0.15% (NNT 667)

Medications

- Non-black Patient (+diabetes): thiazide-type diuretic, CCB, ACEI, or ARB.

- Black Patient (+diabetes): thiazide-type diuretic or CCB.

- Adults with CKD (+proteinuria) & hypertension: ACEI or ARB to improve kidney outcomes.

Core Lifestyle Advice

- **SALT:** CHEP - reduce sodium toward 2000mg (5 gm of salt)
  - For every gram of sodium >5000 mg, BP ↑ 2.6 mmHg
  - SR (7 RCTs): ~3900 to 3000/d, CVD 20% RRR but not mortality
  - Observational data: lowest CVD & mortality ~4 000mg/day.

- **Diet:** DASH promoted but
  - Mediterranean Diet: CVD ~30% RRR

- **Activity:** Best evidence, ~25% RRR in CVD.
  - Moderate activity (brisk walking or more), 150 min/wk.

- **Weight:** Best available evidence indicates lowest risk of mortality is *BMI 25 (27.5 if age ≥65).

- **Bottom-Line:** Moderate Sodium, control weight gain, eat Mediterranean and be active!

What to Expect when you’re Expecting,...

A change in BP

<table>
<thead>
<tr>
<th>Number of Meds &amp; Dose</th>
<th>Change if Systolic BP is</th>
<th>Change if Diastolic BP is</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Starting at 170</td>
<td>Starting at 150</td>
</tr>
<tr>
<td>One ½ dose</td>
<td>8.3</td>
<td>6.7</td>
</tr>
<tr>
<td>One full dose</td>
<td>10.7</td>
<td>8.7</td>
</tr>
<tr>
<td>Two ½ dose</td>
<td>16.4</td>
<td>13.3</td>
</tr>
<tr>
<td>Two full dose</td>
<td>20.3</td>
<td>16.5</td>
</tr>
<tr>
<td>Three ½ dose</td>
<td>24.6</td>
<td>19.9</td>
</tr>
<tr>
<td>Three full dose</td>
<td>29.0</td>
<td>23.6</td>
</tr>
</tbody>
</table>

Law MR, Morris JK, Wald NJ. JAMA. 2009 May 19;301:1665

Diuretics: Old & Maligned

- Arguing for “Thiazide-like” (Chlorthalidone vs HCTZ)
  - Chlorthalidone vs HCTZ: Longer half-life (50 vs 10 hours)
  - 5 mmol/L less on 24 hour BP; 7 mmol/L less night-time
  - Chlorthalidone studies = good outcomes.
  - Network meta-analysis supports superiority (20% RRR)

- **Bottom-Line:** Chlorthalidone (or indapamide) best.
  - Chlorthalidone comes in 50mg tabs so quarter or half.

What about Electrolyte Monitoring?

- ACE and ARBs increase potassium >5.4 in around 4%

- Chlorthalidone decreases Sodium <130 in around 4%

- Chlorthalidone decreases potassium <3.2 in around 4%
  - Chlorthalidone 12.5-25mg decreases potassium ~0.2-0.4
  - Indapamide does it ~0.1 and HCTZ ~0.1-0.2

- **Recommendation:** Checking electrolytes in Thiazides & ACE/ARB in the first 2-4 wks after starting, with increasing doses, and at least annually thereafter.

Kolber & Turgeon. Tools for Practice #163
Odds & Ends?

• **4th Line Med:** RCT 314 on 3 meds(ACE/Ca/Thiazide)
  — At 6 wks: Spiro 14.4 mmHg, Dox 9.1, Bisop 8.4, Placebo 4.2
  — ≤ Target: 24% placebo, 42-44% dox or bisop, 58% on spiro

• **Tx ≥80:** RCT, 3800 pts, 1.8 yrs, mean 83.5, “healthy”
  — Start >160/90; target BP <150/80 mmHg
  — Death, CVD, and CHF all 2-3% better

• **≥1 BP Meds hs:** RCT 2156 pts, 5.6 yr
  — Night BP 5/2 better (daytime no different)
  — Mortality: Awakening 2.6% vs bedtime 1.1%, NNT 67
  — CVD: Awakening 6.8% vs bedtime 2.8%, NNT 25

---

Summary

1. Targets: Office BP ~140/90 (150 if older)
   — AOPB or home ≥135/85
   — 24 hour average ≥130/80
   — Lower target in select high risk patients: Estimate Risk

2. Lifestyle: Activity, med diet, maybe mod salt.

3. Meds: Thiazides (Chlorthalidone or indapamide), CCB (Amlodopine/felodopine), ACE/ARB
   — Fourth line: Spironolactone
   — Monitor lytes.

Bleeding in patients on antithrombotic therapy – “The short and the long of it”

Peter Loewen

Faculty/Presenter Disclosure

- Faculty/Presenter: Peter Loewen

- Relationships with commercial interests:
  - Grants/Research Support: None
  - Speakers Bureau/Honoraria: None
  - Consulting Fees: BC Ministry of Health
  - Other: None

Learning Outcome Objective

Following the session and upon personal reflection, participants will be able to describe and apply in their own practice:

- contemporary methods of risk stratifying OAC patients by bleeding risk
- patient preference factors that influence OAC decision-making and the importance of eliciting them from patients
Speaking with Patience
“Knock, knock! Who’s there”

Knock, Knock. Who’s there?

Here’s a knocking indeed! If a man were porter of hell-gate, he should have old turning the key.

This is a lot of knocking! Come to think of it, if a man were in charge of opening the gates of hell to let people in, he would have to turn the key a lot.

— Macbeth Act 2, Scene 3

Faculty/Presenter Disclosure

- **Faculty:** Dr. Tracy Monk
- **Relationships with commercial interests:** None

Learning Objectives

- To be able to find tools that can be used with patients during office visits to enable shared informed decision making
- To become familiar with the concept of “doing the right amount of less”
- To be comfortable having shared informed decision making conversations with patients
- Patience

An avalanche of unnecessary medical care is harming patients physically & financially. What can we do about it?

By Atul Gawande

Over use of diagnostic technology is leading to problems like:
- hype beliefs & demands among patients & media,
- overdiagnosis and overtreatment
- increased anxiety among patients, spurring more testing and treatment
- higher costs as a result of screenings, tests, and follow-up treatments
Journal of General Internal Medicine
May 2015, Volume 30, Issue 5, pp 548-555 Date: 08 Jan 2015

Use of CT/MRI rose from 6.7% of visits in 1999–2000 to 13.9% in 2009–2010 (unadjusted p < 0.001),

Referrals to other physicians increased from 6.9% to 13.2% (p = 0.005).

In contrast, clinician counseling declined from 23.5% to 18.5% (p = 0.041)
Choosing Wisely: Imaging Tests for headache when you need them and when you don’t

More Handy Tools for conversations

- Decision Aid re screening Mammo 40-49
- Average duration of viral illness
- Do bugs need drugs?
- Mayo Clinic Osteoporosis Decision Aid

Canadian Preventive Task Force: Screening Mammography Risk Benefit

If we screened 2100 women, aged 40-49 years, at average risk of breast cancer every two years for 11 years:

- About 750 women would experience a false positive mammogram requiring further imaging
- 3% of these women would have a biopsy, all to confirm that they do not have breast cancer
- At least 10 women would have part or all of a breast unnecessarily removed and bear the burden of over-diagnosis
- 1 woman would escape a breast cancer death
Shared Decision Aids

Print the grid
Give grid to patient to read
Give patient a pen
Give patient some time to read the grid and circle key points
Review
Shared Decision Aid
Can use to discuss options before ordering bone density

BC Guidelines say being a 65 yo woman counts as a “major risk factor”

65 yo woman
Ht 5 ft 4”
Wt 150 lbs

Risk of Hip fracture
Risk of Any Fracture

Change in risk with bisphosphonate RX for Hip fracture
= no difference

Change in risk with bisphosphonate RX for Any fracture
= takes risk from 91% chance no fracture to 94% chance no fracture
Slow medicine

The canary in the coal mine of our failing health-care system is the plight of the old and frail.

The vast machinery of modern medicine, which can be heroically invoked to save a premature baby, when visited upon an equally vulnerable and failing great-grandmother, may not save her life so much as torturously and inhumanely complicate her dying.

Our system of “fast medicine” is running a lockstep, breakneck course, and no one in or out of health care seems to know how to put on the brakes.

Patients are briskly shunted off for various kinds of expensive tests and procedures or quickly put on medications based on rapidly made decisions and standardized protocols.

By taking things slowly, a more thoughtful course of action can evolve.

—Dennis McCullough, M.D. (Dartmouth)
Communication of evidence – “what’s in a name”

1) Disclosure of Commercial Support
Neither this program nor the presenter has received financial support from any organization or company.

2) Mitigating Potential Bias
All recommendations and information presented are based on the best-available evidence we could find. Typically this includes meta-analyses, systematic reviews and RCTs. In addition, we don’t care what the results are, but rather we care that people know about the results.

3) Objectives
To be able to take the best available evidence for common conditions in primary care and incorporate this information into shared-decision making with patients.

MY BELIEF

All Health Care Providers should have their practice underpinned by the best available evidence

Evidence-Based Practice (EBP)

People want involvement in evidence and decisions

Communicating with patients on health care evidence.
Discussion Paper, Institute of Medicine, Washington, DC 2012
Satisfaction is linked to shared decisions

“Most patients cannot recall a time when their care provider discussed scientific evidence as the basis for better care”

“Overall, not only are most research findings false, but, furthermore, most of the true findings are not useful.”
Evidence Issues

Much of research is not going to be “right”

One study likely proves nothing - need reproducibility

“The evidence for nonreproducibility in basic and preclinical biomedical research is compelling” John Ioannidis

Cohort trials don’t prove causation

Research does go unpublished - but large studies do get reported

“Science can be used to inform clinical decisions, but cannot definitively inform value judgements, because the significance of potential benefits and harms of a therapy are in the eye of the beholder and will differ across individuals.”


Some clinical adages?

Ask - how do you feel about being involved in making decisions about your treatment?

It's OK if we say I don't know, let's look into it, it's your decision.

You and your patient's perception are not necessarily “right” and likely not the same

BENEFIT - 88% of study authors concluded that participants overestimated benefits

HARM - 67% underestimated harm

JAMA Intern Med 2015;175:274-286
Key steps to communicating evidence

Understand the patient’s (and family members’) experiences and expectations.

Build partnerships.

Discuss the evidence, including a balanced discussion about uncertainties.

Present recommendations.

Check for understanding and agreement.

Risky Relative Adjectives

HOW

low is low

moderate is moderate

high is high

Evidence-based risk communication

“There is likely no single best method of communicating probabilities to patients but rather several good options with some better suited to certain risk scenarios.”

Recommended approaches

Need a time frame, main endpoints, ask what they know

GENERAL SUGGESTIONS - these are “relative” use percentages (5%) or natural frequencies (5 out of 100) - BOTH? use absolute terms add bar graphs or icon arrays use incremental risk format with icon arrays in the same array

• avoid use of NNTs
if use relative risks add baseline risks

Ann Intern Med 2014;161:270-80

Ann Intern Med 2014;161:270-80
The “problem” with NNT’s

It’s another calculation, and NNT’s provide no information about baseline risk. An NNT of 100 could mean
the chance goes from a) 2% baseline risk down to 1% or b) 100% baseline risk down to 99%

These scenarios, despite the same NNT, may elicit different decisions and certainly convey different messages.

It’s all about figuring out

The Chance
WITH NO TREATMENT

VS

The Chance
WITH TREATMENT

Approaches differ depending on outcome

Every patient is an experiment - dose and effect

Prevention - one will never know if it worked

Symptoms - we can usually figure out if it is working - but it is tricky

Diagnosis - pre- and post-test probabilities

Expectations

Ballpark risk estimate
Epidemiological data/cohort data
- Framingham, QRISK, FRAX, CHA2DS2-VASc

Ballpark benefit estimate
RCT data
  use the absolute benefit if people are similar to those in the studies or,
  use the relative benefit and apply it to the baseline risk
Calculate ballpark 10-yr risk of CVD - BP, chol, diabetes
Make estimate of benefit based on the best available evidence
Gives a list of adverse effects to discuss

Calculate ballpark annual risk of stroke - based on risk factors - BP, chol, diabetes
Make estimate of benefit based on the best available evidence - all agents
Make estimate of a GI bleed

10 year fracture risk %
Major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)/Hip

Risk factors - Previous fracture “atraumatic”, Parent hip fracture, Smoker, Rheumatoid arthritis, Glucocorticoids - now or more than 3 months, >3 drinks a day

https://therapeuticseducation.org/tools

James McCormack
Misguided beliefs

Patients believe CVD “prevention” drugs produce a 70% absolute benefit over 5 years when at most only ~ 20-30% benefit is possible over a lifetime.

Clin Med 2002;2:527-33

Risk of future illness CVD risk/benefit

(most people don’t benefit despite a lifetime of treatment)

Assume a person’s lifetime risk of CVD is that of a male with two CVD risk factors - roughly 50% (NEJM 2012;366:1219)

Assume that with multiple risk factor modification we can reduce that risk relatively by 60% (VERY optimistic)

Risk goes from 50% ➔ 20%

30% of individuals BENEFIT

70% DO NOT despite a LIFETIME of treatment

Prescriber September 2015

Symptoms

You primarily need to know IF it works

Safety, cost and convenience

Older medications first - safety

Head-to-head studies are uncommon

Doses in the CPS are “wrong”

N-of-1 studies

Let the patient tell you
Symptom NNTs

- General anesthesia/local anesthesia - NNT ~1
- PPIS, sildenafil - heartburn/"successful" intercourse NNT ~2
- NSAIDs, opioids - pain NNT ~3-5
- Steroids - sore throat - NNT ~3, Bell's palsy - NNT ~10
- Antibiotics - acute COPD exacerbation - NNT ~5
- Topical antibiotics - bacterial conjunctivitis - NNT ~7
- Antidepressants - severe depression - NNT ~10
- Ipratropium - asthma attack - NNT ~11
- Cholinesterase inhibitors - ADAS-Cog >4 - NNT ~10
- Sleeping pills - improvement in sleep quality - NNT ~13

But you need to know what goes on in the placebo group

<table>
<thead>
<tr>
<th>Response in the placebo group</th>
<th>If Benefit 10% - NNT 10</th>
<th>If Benefit 20% - NNT 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>~100%</td>
<td>~100%</td>
</tr>
<tr>
<td>20%</td>
<td>~33%</td>
<td>~50%</td>
</tr>
<tr>
<td>40%</td>
<td>~20%</td>
<td>~33%</td>
</tr>
</tbody>
</table>

Likelihood Ratios

LRs are basically a ratio of the probability that a test result is correct to the probability that the test result is incorrect.

Pre-test probability (%)
- ➞ apply a LR
- ➞ post-test probability (%)
Rapid Antigen Group A Streptococcus Test to Diagnose Pharyngitis: A Systematic Review and Meta-Analysis

LR + = 10.8
LR - = 0.15

General practice clinic in Canada - people with a sore throat who have Strep ~10%

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>If positive Post test probability</th>
<th>If negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>~10%</td>
<td>~0.2%</td>
</tr>
<tr>
<td>10%</td>
<td>~60%</td>
<td>~2%</td>
</tr>
<tr>
<td>40%</td>
<td>~90%</td>
<td>~10%</td>
</tr>
</tbody>
</table>

Table 4: Likelihood-ratios and the impact on post test probabilities (modified by McCue 2002)

<table>
<thead>
<tr>
<th>Likelihood ratio</th>
<th>Approximate changes in post-test probabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>Strong evidence to Large</td>
</tr>
<tr>
<td>0.2</td>
<td>Strong evidence to Moderate</td>
</tr>
<tr>
<td>0.3</td>
<td>Strong evidence to Moderate</td>
</tr>
<tr>
<td>0.4</td>
<td>Strong evidence to Large</td>
</tr>
<tr>
<td>0.5</td>
<td>Weak evidence to Slight</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
</tr>
</tbody>
</table>

Pretest probability changes:

- Values between 0 and 1 decrease the probability of disease
- Values greater than 1 increase the probability of disease

Useful apps and on-line tools

**MedCalX** - calculate likelihood ratios from sensitivity and specificity AND post-test probability calculator

**DxLogic** - listing of LR and pre-test probabilities and a post-test calculator

**lrdatabase.com** - home of DxLogic
What is "High Risk"

Beware of “qualitative quantification”

Lancet  2002;359:853–54
What were you thinking?

Cognitive errors in medicine and how to avoid them

Kam Shojania, MD, FRCPC
Clinical Professor and Head, UBC
Division of Rheumatology

Faculty/Presenter Disclosure

- Faculty: Kam Shojania
- Polymyalgia Rheumatica

- Relationships with commercial interests:
  - Grants/Research Support: Indirectly, via faculty: Janssen, BMS, Abbvie, Pfizer, Roche, UCB, Amgen.
  - Speakers Bureau/Honoraria: Two industry talks last year.
  - Consulting Fees: Two times in the past year.
  - Other: UBC salary, Ministry of Health contract for IVIG management, Arthritis Research Centre, CHEOS, Arthritis Society.
  - Investments relevant to this talk: None.

Disclosure of Commercial Support

- This program has received financial support from Nobody in the form of Nothing.
- This program has received in-kind support from Nothing in the form of Nobody.
- Potential for conflict(s) of interest:
  - None really. There is no commercial interest in ‘errors’.
  - Oh wait! Lawyers would love to get involved in this.

Mitigating Potential Bias

- I won’t be talking about biologics or specific lab tests.
- My brother is a lawyer, but he hasn’t heard this talk before. Don’t tell him.

Disclosure Slide

- I have made mistakes (both kinds).
- I will likely make more mistakes.
- Please let me know if you see my mistakes so I can learn.
- I will let you know about your mistakes (usually by copying you on the letter).
Thanks to:
Kaveh G. Shojania, MD
Professor of Medicine
University of Toronto
Canada Research Chair in Patient Safety (tier 2)
For the inspiration to give this talk and for his research in this area

... and thanks to:
Barry Koehler, MD, FRCPC
Clinical Emeritus Professor, University of British Columbia
The late Howard Stein, MD, FRCPC
Clinical Emeritus Professor, University of British Columbia
For providing some of the examples of rheumatology errors

Goals
- What are the two types of errors in medicine?
- What is the prevalence of diagnostic error
- Review typical cases and determine the possible biases
- What is metacognition?
- What can we do to reduce cognitive error?

Two Distinct Types of Errors

Slips
- Errors involving semi-automatic routines daily activities
  - exacerbated fatigue, competing tasks, look-alike containers, sound-alike names

Mistakes
- Errors in interpretation, misapplication of cognitive rules
  - more likely in new or unusual situations

Many slips can be prevented

Slips can occur when you are tired
Methotrexate errors

- Writing MTX once daily rather than weekly
- Patient taking MTX 2.5 mg daily rather than 17.5 mg weekly
- Concomitant use of MTX and Sulfia Abx
- MTX in fertile pts not on birth control
- Patients with MTX pneumonitis who were not aware of the possibility and continued MTX

Simple Guidelines For Handwritten Orders

- Write "Units" not "U" to avoid confusion with an extra "0"
  - "Insulin 10U" misread as "Insulin 100"
- Avoid abbreviations for dosing intervals (e.g., qd, qod, bid, tid)
  - Write out dosing intervals in full (e.g., "weekly," "daily," "three times a day")
- Avoid trailing zeros (e.g., write 1mg NOT 1.0mg)
- Use leading zeros (e.g., write 0.5mg NOT .5mg)

Diagnostic Error

Three general categories of diagnostic error
1. "No Fault"
   Very unusual presentations, patient-related error
2. Systems-related
   Technical failure, organizational issues
3. Cognitive errors
   Faults in knowledge, data gathering, information processing or metacognition

What is the overall rate of diagnostic error in medicine?

A. <1%
B. 1-5%
C. 5.1-10%
D. 10.1-15%
E. 15.1-20%
F. >20%
Diagnostic Errors

- Common cause of preventable adverse events
- Second leading cause of malpractice cases
- Relatively unstudied compared to other areas of patient safety, but obviously of great interest to clinicians
  - Involves system and human problems

Cognitive Biases

- Premature closure: Once a plausible condition is identified, other possibilities are not fully considered unwilling to integrate other information once diagnosis made
- Anchoring bias: holding on to first diagnosis
- Availability heuristic: Focusing on diagnoses you are most familiar with.

Context Bias

- Inappropriately limiting consideration to only one set of diagnostic possibilities, in lieu of others
- Recent study presented 51 academic internists with 10 clinical vignettes, each with single misleading detail.

Context Bias Examples

- 40-year-old woman has general weakness and shortness of breath. Two weeks ago she was hit on her chest while sitting on a ski elevator. Physical examination reveals reduced ventilation over the lower left lung and chest X-ray shows left lower lobe infiltrate (haemothorax/pneumonia).
- 67-year-old man with multiple vascular risk factors, brought to ED after being found in a confused state with difficulty speaking. The nurse reports a blood pressure of 188/96 and the ECG is within normal limits (hypoglycaemia/stroke).

Metacognition

- Thinking about one’s thinking
- Monitoring one’s own cognitive processes
- Becoming aware of the different types of cognitive errors
- Recognize pitfalls
- Also, need feedback
**Metacognition**

- Recognize the situations where Dx errors occur:
  - When feeling rushed
  - When the case is complex
  - When patient was evaluated by someone else
- Operationalizing metacognition: “Prospective hindsight”
  - “What else could this be?”
  - What is the worst diagnosis this could be?

*Croskerry P. Acad Med. 2003*

---

**Human Factors in Diagnostic Error**

**Tough Cases**
- Obtain consults
- Some electronic resources

**Seemingly Routine Cases**
- Hand-offs
- Interruptions
- Cognitive biases

---

**Mr Lavender**

- 79 year old man with a history of prostate cancer in the past was complaining of 6 weeks of worsening back pain and leg weakness. Developed urinary retention. Admitted to urology for consideration of BPH and foley. Rheum consulted for back pain. Pt complained that his buttocks felt numb.

**Prostate cancer with mets to spine causing cauda equina syndrome**

*Mistakes:*
- Triage cueing: "Geography is destiny"
- Ascertainment bias: Judging a disease more likely if it readily comes to mind
- Availability bias: If is a disease hasn’t been seen for a long time, it may be underdiagnosed or not considered.

---

**Ms Rosemary**

- 69 year old woman with symptoms of malaise, chills and night-sweats for 5 weeks. Moderate bitemporal headaches over the past 3 weeks partially improved with acetaminophen and NSAIDs. No visual or other symptoms. ESR was 78. In ER prednisone 1mg/kg given for presumed temporal arteritis and FU arranged with GP.

**Ms Rosemary (2)**

- Felt better on prednisone. HA improved by 70%. Bx not done. Attempts at tapering prednisone over the next 6months were met by aches and pains and ESR increase to 40.
- Sees me over 1 year later cushingoid and on prednisone 20mg daily. Finds that she feels unwell when she tapers prednisone.
Diagnosis?

Mistakes:
Overconfidence bias: Tendency to act on incomplete information, intuition or hunches. Too much faith on opinion instead of evidence
Premature closure: accepting a diagnosis before it is verified. “When the diagnosis is made, the thinking stops”.
Feedback sanction: A form of ignorance-trap and time-delay trap. The error carried no immediate consequences as considerable time may elapse before the error is discovered.
Commission Bias: Tendency towards action rather than inaction.

Mr. Coriander

- 66 yo male I saw 6 years ago with a new psoriatic arthritis. AM stiffness 1 hour, stress tenderness wrists, MCPs, PIPs, MTPs. ESR 34. Partial improvement with HCQ. MTX 15mg weekly started.
- In remission for 6 years but hasn’t seen me.
- Now I find some OA hands, Labs normal, CCP neg.
- What do I do?
- What is my diagnosis?

Ms. Parsley

- 43 yo woman with facial rash, mild alopecia, low level ANA 1:80, arthralgias.
- You tell her that you are planning to investigate her for SLE.
- You find mild malar rash, hair thinning, mild joint tenderness.
- Consult note indicates: Rule out SLE.
- 2nd visit: Rosacea, female pattern alopecia. Serology negative. You write: Not SLE.

Ms. Fennel

- 30 yo woman with RA on MTX 20mg/wk in a RA clinic. Recent severe flare of arthritis in her knee. TJC 12, SJC 2, ESR 68, PG 89. DAS28: 6.54. High disease activity. Protocol states that pt should increase MTX to 25mg sc/wk. Steroids allowed PO or inject affected joint.
- What is the potential error?
Ms Fennel

- May have a knee infection

Mistakes:

1. **Unpacking principle:** Failure to elicit all relevant information in establishing a DDx. HCP limits the history-taking.

2. **Vertical line failure:** Repetitive tasks leads to thinking in silos. Predictable, orthodox styles that emphasize economy, efficiency, utility. RA clinic? We also need a lateral thinking style asking “What else could this be”

Diagnosis using the ESR

- 75 year old man with rapid onset of proximal muscle pain, stiffness, low grade fever, elevated WBC, high ESR, high CRP.
- Diagnosed as PMR in the ER, given prednisone and discharged – 30% better but returns to ER with persistent pain when I saw him 2 days later.
- On exam, looks ill. Myalgias, no localizing findings. High WBC, platelets. ESR remains elevated.

Diagnosis using the ESR

- Eventually diagnosed with cervical epidural abscess and myelopathy.
- What was the error?

- **Ascertainment bias:** Judging a disease more likely if it readily comes to mind

- **Availability bias:** If is a disease hasn’t been seen for a long time, it may be underdiagnosed or not considered.

How to avoid this important error?

Ask: What else could this be?
Or: What would I not want to miss?
Or: What doesn’t fit?

Two patients, same diagnosis

- 35 year old woman, post partum arthralgias, myalgias, fatigue, AM stiffness of 2 hours. On exam, stress tenderness of wrists, MCPs ankles. Anemia, low level ANA positive. Started on prednisone and plaquenil with a diagnosis of RA.
- 55 year old woman with gradual myalgias, arthralgias, fatigue, weight gain. Knee effusions. Started on NSAIDs. Sent with a diagnosis of FMS.
- One key physical exam finding was omitted which would make the diagnosis.

Check the reflexes: Hypothyroid

Mistake:

- **Triage cueing**
  - Not all polyarthritis is RA. Not all polyarthritis is polyarthritis
  - Not all myalgia is PMR or FMS
  - Don’t forget to check the reflexes in all internal medicine patients (should you have a full physical exam process?)
  - Consider thyroid disease in patients with vague MSK symptoms.
Take a full history

- A 35 year old Filipina mother of 3 was a poor historian in the office. She complained of ankle and knee pain. The rest of the history was unremarkable. On exam she had conjunctivitis, inflammation of both ankles, the right knee, the left plantar fascia.
- The working diagnosis was a possible reactive arthritis, but no trigger was found. No dysuria, diarrhea. Monogamous.

The missing piece of information

- She was found to have chlamydia on examination by the GP.
- Her husband had an extramarital encounter ‘once’ a few weeks prior.
Mistake:
Ascertainment bias (2 subtypes)
  - Gender bias
  - Stereotyping

Human Factors in Diagnostic Error

Tough Cases
- Obtain consults
- Some electronic resources

Seemingly Routine Cases
- Hand-offs
- Interruptions
- Cognitive biases

Google searches revealed the correct diagnosis in 15 of 26 cases from NEJM (58%; 95% CI 38% to 77%)

But, the Dx’s Google got tended to be the easier ones

<table>
<thead>
<tr>
<th>Google ➔ Correct Dx</th>
<th>Google ➔ Wrong Dx</th>
</tr>
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<tbody>
<tr>
<td>Endocarditis</td>
<td>Linitis plastica</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Erhlichiosis</td>
</tr>
<tr>
<td>Light chain amyloid</td>
<td>Hot tub lung from M. avium</td>
</tr>
</tbody>
</table>

But Can Still be Surprisingly Useful

- 47 y.o. previously woman with several weeks of
  - Severe headaches and spiking temps
  - RUQ pain ➔ more general abdo pain
- Jaundiced with moderate LFT abnormalities
  - Low albumin, high LDH, high ferritin (500 ➔ 16000)
  - Pancytopenic with low fibrinogen
  - Imaging: hepatosplenomegaly some lymphadenopathy
Extensive Work-Up Unrevealing

- Negative viral serologies (Hep, CV, EBV, HIV)
- Routine cultures negative
  - And neg for less common infectious (eg Bartonella)
- Autoimmune/vasculitis tests negative
- Patient progressively sicker and suffers several bleeding complications after transjugular liver biopsy
  - Eventually dying despite prolonged attempts to resuscitate

Final Post-Mortem Diagnosis

- Hemophagocytic Lymphohistocytosis ("Hemophagocytic syndrome")
- Possible toxin mediated liver injury/viral infection as precipitating event
- No evidence of malignancy
- Adverse event associated with liver biopsy in setting of bleeding diathesis
Ms. Oregano

- 37 year old woman admitted with 4 weeks of generalized lymphadenopathy, rash, moderate pancytopenia, polyarthritis.
- Pan consultations (Rheum, ID, Haem, Derm)
- What is your DDx based on above?

Google search

Tough Cases

- Usually we recognize them as such
- We obtain consults (though consultants can be stumped, too)
- Electronic resources can be worth checking for unifying explanation of bewildering constellation of findings
- But, most errors happen with more common Dx’s …
Structured (Electronic) Discharge Summaries

• Highlight medication changes
  – New meds, adjusted meds, d/c’d meds
• Major test results
• Pending test results
• Problem oriented follow-up
  – clear explanation of what has already been arranged for each problem and what is suggested for PCP to pursue

With thanks to Dr. Kaveh Shojania

Conclusions

• Diagnostic errors are more common that we would like to admit.
• We all make them. Staff errors are worse than resident errors.
• Think about how you think.
• Label the errors that you make and see.
• Use electronic resources for tough cases.
The Importance of Cognitive Errors in Diagnosis and Strategies to Minimize Them

Pat Croskerry, MD, PhD

In the area of patient safety, recent attention has focused on diagnostic error. The reduction of diagnostic error is an important goal because of its associated morbidity and potential preventability. A critical subset of diagnostic errors arises through cognitive errors, especially those associated with failures in perception, failed heuristics, and biases; collectively, these have been referred to as cognitive dispositions to respond (CDRs). Historically, models of decision-making have given insufficient attention to the contribution of such biases, and there has been a prevailing pessimism against improving cognitive performance through debiasing techniques. Recent work has catalogued the major cognitive biases in medicine; the author lists these and describes a number of strategies for reducing them (“cognitive debiasing”). Principle among them is metacognition, a reflective approach to problem solving that involves stepping back from the immediate problem to examine and reflect on the thinking process. Further research effort should be directed at a full and complete description and analysis of CDRs in the context of medicine and the development of techniques for avoiding their associated adverse outcomes. Considerable potential exists for reducing cognitive diagnostic errors with this approach. The author provides an extensive list of CDRs and a list of strategies to reduce diagnostic errors.

cognitive activity is occurring when these clinical decisions are being made, we may be struck by how far it is removed from what normative theory describes. Although it seems certain we would be less likely to fail patients diagnostically when we follow rational, normative models of decision making, and although such models are deserving of “a prominent place in Plato’s heaven of ideas,”⁷ they are impractical at the sharp end of patient care. Cognitive diagnostic failure is inevitable when exigencies of the clinical workplace do not allow such Olympian cerebral approaches.

Medical decision makers and educators have to do three things: (1) appreciate the full impact of diagnostic errors in medicine and the contribution of cognitive errors in particular; (2) refute the inevitability of cognitive diagnostic errors; and (3) dismiss the pessimism that surrounds approaches for lessening cognitive bias.

For the second, there are specialties in which diagnostic uncertainty is most evident and in which delayed or missed diagnoses are most likely to be internal, family, and emergency medicine; this is borne out in findings from the benchmark studies of medical error.²⁻⁴ However, all specialties are vulnerable to this particular adverse event. The often palpable nature of diagnostic error perhaps reflects why it does not appear in lists of serious reportable events.⁷ For the second, there needs to be greater understanding of the origins of the widespread inertia that prevails against reducing or eliminating cognitive errors. This inertia may exist because such errors appear to be so predictable, so widespread among all walks of life, so firmly entrenched, and, therefore, probably hardwired. Although the evolutionary imperatives that spawned them may have served us well in earlier times, it now seems we are left with cognition vestigial approaches to the complex decision making, and although such models are deserving of “a prominent place in Plato’s heaven of ideas,”¹⁶ they are impractical at the sharp end of patient care. Cognitive diagnostic failure is inevitable when exigencies of the clinical workplace do not allow such Olympian cerebral approaches.

An understanding of why clinicians have particular dispositions to respond (CDRs) to particular situations in various predictable ways. Removing the stigma of bias clears the way toward accepting the capricious nature of decision-making, and perhaps goes some way toward exculpating clinicians when their diagnoses fail. An understanding of why clinicians have particular CDRs in particular clinical situations will throw considerable light on cognitive diagnostic errors. The unmasking of cognitive errors in the diagnostic process then allows for the development of debiasing techniques. This should be the ultimate goal, and it is not unrealistic.

Certainly, a number of clear strategies exist for reducing the memory limitations and excessive cognitive loading¹⁰ that can lead to diagnostic errors, but the most important strategy may well lie in familiarizing clinicians with the various types of CDRs that are out there, and how they might be avoided. I made a recent extensive trawl of medical and psychological literature, which revealed at least 30 CDRs,⁹ and there are probably more (List 1). This catalogue provides some idea of the extent of cognitive bias on decision-making and gives us a working language to describe it. The failures to show improvement in decision support for clinical diagnosis that are noted by Graber et al.¹ should come as no surprise. They are likely due to insufficient awareness of the influence of these CDRs, which is often subtle and covert.¹⁰ There appears to have been an historic failure to fully appreciate, and therefore capture, where the most significant diagnostic failures are coming from.

Not surprisingly, all CDRs are evident in emergency medicine, a discipline that has been described as a “natural laboratory of error.”¹¹ In this milieu, decision-making is often naked and raw, with its flaws highly visible. Nowhere in medicine is rationality more bounded by relatively poor access to information and with limited time to process it, all within a milieu renowned for its error-producing conditions.¹² It is where heuristics dominate, and without them emergency departments would inexorably grind to a halt.¹³ Best of all, for those who would like to study real decision making, it is where heuristics can be seen to catastrophically fail. Approximately half of all litigation brought against emergency physicians arises from delayed or missed diagnoses.¹⁴

If we accept the pervasiveness and predictability of the CDRs that underlie diagnostic cognitive error, then we are obliged to search for effective debiasing techniques. Despite the prevailing pessimism, it has been demonstrated that, using a variety of strategies¹⁵⁻²³ (Table 1), CDRs can be overcome for a number of specific biases.¹⁶⁻²³ It appears that there are, indeed, cognitive pills for cognitive ills,²² which makes intuitive sense. This is fortunate, for otherwise, how would we learn to avoid pitfalls, develop expertise, and acquire clinical acumen, particularly if the predisposition for certain cognitive errors is hardwired? However, medical educators should be aware that if the pills are not sufficiently sugared, they may not be swallowed.

Yates et al.²⁴ have summarized some of the major impediments that have stood in the way of developing effective cognitive debiasing strategies, and they are not insurmountable. The first step is to overcome the bias against overcoming bias. Metacognition will likely be the mainstay of this approach. A recent cognitive debiasing technique using cognitive forcing strategies is based on metacognitive principles¹⁰ and seems to be teachable to medical undergraduates and postgraduates.²⁵ Essentially, the strategy requires first that the learner be aware of the
List 1

Cognitive Dispositions to Respond (CDRs) That May Lead to Diagnostic Error*

**Aggregate bias:** when physicians believe that aggregated data, such as those used to develop clinical practice guidelines, do not apply to individual patients (especially their own), they are invoking the aggregate fallacy. The belief that their patients are atypical or somehow exceptional may lead to errors of commission, e.g., ordering x-rays or other tests when guidelines indicate none are required.

**Anchoring:** the tendency to perceptually lock onto salient features in the patient’s initial presentation too early in the diagnostic process, and failing to adjust this initial impression in the light of later information. This CDR may be severely compounded by the confirmation bias.

**Ascertainment bias:** occurs when a physician’s thinking is shaped by prior expectation; stereotyping and gender bias are both good examples.

**Availability:** the dispositional to judge things as being more likely, or frequently occurring, if they readily come to mind. Thus, recent experience with a disease may inflate the likelihood of its being diagnosed. Conversely, if a disease has not been seen for a long time (is less available), it may be underdiagnosed.

**Base-rate neglect:** the tendency to ignore the true prevalence of a disease, either inflating or reducing its base-rate, and distorting Bayesian reasoning. However, in some cases, clinicians may (consciously or otherwise) deliberately inflate the likelihood of disease, such as in the strategy of “rule out worst-case scenario” to avoid missing a rare but significant diagnosis.

**Commission bias:** results from the obligation toward beneficence, in that harm to the patient can only be prevented by active intervention. It is the tendency toward action rather than inaction. It is more likely in over-confident physicians. Commission bias is less common than omission bias.

**Confirmation bias:** the tendency to look for confirming evidence to support a diagnosis rather than look for disconfirming evidence to refute it, despite the latter often being more persuasive and definitive.

**Diagnosis momentum:** once diagnostic labels are attached to patients they tend to become stickier and stickier. Through intermediaries (patients, paramedics, nurses, physicians), what might have started as a possibility grows increasing momentum until it becomes definite, and all other possibilities are excluded.

**Feedback sanction:** a form of ignorance trap and time-delay trap CDR. Making a diagnostic error may carry no immediate consequences, as considerable time may elapse before the error is discovered, if ever, or poor system feedback processes prevent important information on decisions getting back to the decision maker. The particular CDR that failed the patient persists because of these temporal and systemic sanctions.

**Framing effect:** how diagnosticians see things may be strongly influenced by the way in which the problem is framed, e.g., physicians’ perceptions of risk to the patient may be strongly influenced by whether the outcome is expressed in terms of the possibility that the patient might die or might live. In terms of diagnosis, physicians should be aware of how patients, nurses, and other physicians frame potential outcomes and contingencies of the clinical problem to them.

**Fundamental attribution error:** the tendency to be judgmental and blame patients for their illnesses (dispositional causes) rather than examine the circumstances (situational factors) that might have been responsible. In particular, psychiatric patients, minorities, and other marginalized groups tend to suffer from this CDR. Cultural differences exist in terms of the respective weights attributed to dispositional and situational causes.

**Gambler’s fallacy:** attributed to gamblers, this fallacy is the belief that if a coin is tossed ten times and is heads each time, the 11th toss has a greater chance of being tails (even though a fair coin has no memory). An example would be a physician who sees a series of patients with chest pain in clinic or the emergency department, diagnoses all of them with an acute coronary syndrome, and assumes the sequence will not continue. Thus, the pretest probability that a patient will have a particular diagnosis might be influenced by preceding but independent events.

**Gender bias:** the tendency to believe that gender is a determining factor in the probability of diagnosis of a particular disease when no such pathophysiological basis exists. Generally, it results in an overdiagnosis of the favored gender and underdiagnosis of the neglected gender.

**Hindsight bias:** knowing the outcome may profoundly influence the perception of past events and prevent a realistic appraisal of what actually occurred. In the context of diagnostic error, it may compromise learning through either an underestimation (illusion of failure) or overestimation (illusion of control) of the decision maker’s abilities.

**Multiple alternatives bias:** a multiplicity of options on a differential diagnosis may lead to significant conflict and uncertainty. The process may be simplified by reverting to a smaller subset with which the physician is familiar but may result in inadequate consideration of other possibilities. One such strategy is the three-diagnosis differential: “It is probably A, but it might be B, or I don’t know (C).” Although this approach has some heuristic value, if the disease falls in the C category and is not pursued adequately, it will minimize the chances that some serious diagnoses can be made.

**Omission bias:** the tendency toward inaction and rooted in the principle of nonmaleficence. In hindsight, events that have occurred through the natural progression of a disease are more acceptable than those that may be attributed directly to the action of the physician. The bias may be sustained by the reinforcement often associated with not doing anything, but it may prove disastrous. Omission biases typically outnumber commission biases.

**Order effects:** information transfer is a U-function: we tend to remember the beginning part (primacy effect) or the end (recency effect). Primacy effect may be augmented by anchoring. In transitions of care, in which information transferred from patients, nurses, or other physicians is being evaluated, care should be taken to give due consideration to all information, regardless of the order in which it was presented.

**Outcome bias:** the tendency to opt for diagnostic decisions that will lead to good outcomes, rather than those associated with bad outcomes, thereby avoiding chagrin associated with the latter. It is a form of value bias in that physicians may express a stronger likelihood in their decision-making for what they hope will happen rather than for what they really believe might happen. This may result in serious diagnoses being minimized.
List 1

Continued

Overconfidence bias: a universal tendency to believe we know more than we do. Overconfidence reflects a tendency to act on incomplete information, intuitions, or hunches. Too much faith is placed in opinion instead of carefully gathered evidence. The bias may be augmented by both anchoring and availability, and catastrophic outcomes may result when there is a prevailing commission bias.

Playing the odds: (also known as frequency gambling) is the tendency in equivocal or ambiguous presentations to opt for a benign diagnosis on the basis that it is significantly more likely than a serious one. It may be compounded by the fact that the signs and symptoms of many common and benign diseases are mimicked by more serious and rare ones. The strategy may be unwitting or deliberate and is diametrically opposed to the rule out worst-case scenario strategy (see base-rate neglect).

Posterior probability error: occurs when a physician’s estimate for the likelihood of disease is unduly influenced by what has gone on before for a particular patient. It is the opposite of the gambler’s fallacy in that the physician is gambling on the sequence continuing, e.g., if a patient presents to the office five times with a headache that is correctly diagnosed as migraine on each visit, it is the tendency to diagnose migraine on the sixth visit. Common things for most patients continue to be common, and the potential for a nonbenign headache being diagnosed is lowered through posterior probability.

Premature closure: a powerful CDR accounting for a high proportion of missed diagnoses. It is the tendency to apply premature closure to the decision-making process, accepting a diagnosis before it has been fully verified. The consequences of the bias are reflected in the maxim: "When the diagnosis is made, the thinking stops."

Psych-out error: psychiatric patients appear to be particularly vulnerable to the CDRs described in this list and to other errors in their management, some of which may exacerbate their condition. They appear especially vulnerable to fundamental attribution error. In particular, comorbid medical conditions may be overlooked or minimized. A variant of psych-out error occurs when serious medical conditions (e.g., hypoxia, delerium, metabolic abnormalities, CNS infections, head injury) are misdiagnosed as psychiatric conditions.

Representativeness restraint: the representativeness heuristic drives the diagnostician toward looking for prototypical manifestations of disease: "If it looks like a duck, walks like a duck, quacks like a duck, then it is a duck." Yet restraining decision-making along these pattern-recognition lines leads to atypical variants being missed.

Search satisfying: reflects the universal tendency to call off a search once something is found. Comorbidities, second foreign bodies, other fractures, and coingestants in poisoning may all be missed. Also, if the search yields nothing, diagnosticians should satisfy themselves that they have been looking in the right place.

Sutton’s slip: takes its name from the apocryphal story of the Brooklyn bank-robber Willie Sutton who, when asked by the Judge why he robbed banks, is alleged to have replied: “Because that’s where the money is!” The diagnostic strategy of going for the obvious is referred to as Sutton’s law. The slip occurs when possibilities other than the obvious are not given sufficient consideration.

Sunk costs: the more clinicians invest in a particular diagnosis, the less likely they may be to release it and consider alternatives. This is an entrapment form of CDR more associated with investment and financial considerations. However, for the diagnostician, the investment is time and mental energy and, for some, ego may be a precious investment. Confirmation bias may be a manifestation of such an unwillingness to let go of a failing diagnosis.

Triage cueing: the triage process occurs throughout the health care system, from the self-triage of patients to the selection of a specialist by the referring physician. In the emergency department, triage is a formal process that results in patients being sent in particular directions, which cues their subsequent management. Many CDRs are initiated at triage, leading to the maxim: “Geography is destiny.”

Unpacking principle: failure to elicit all relevant information (unpacking) in establishing a differential diagnosis may result in significant possibilities being missed. The more specific a description of an illness that is received, the more likely the event is judged to exist. If patients are allowed to limit their history-giving, or physicians otherwise limit their history-taking, unspecified possibilities may be discounted.

Vertical line failure: routine, repetitive tasks often lead to thinking in silos—predictable, orthodox styles that emphasize economy, efficacy, and utility. Though often rewarded, the approach carries the inherent penalty of inflexibility. In contrast, lateral thinking styles create opportunities for diagnosing the unexpected, rare, or esoteric. An effective lateral thinking strategy is simply to pose the question: “What else might this be?”

Visceral bias: the influence of affective sources of error on decision-making has been widely underestimated. Visceral arousal leads to poor decisions. Countertransference, both negative and positive feelings toward patients, may result in diagnoses being missed. Some attribution phenomena (fundamental attribution error) may have their origin in countertransference.

Yin-Yang out: when patients have been subjected to exhaustive and unavailing diagnostic investigations, they are said to have been worked up the Yin-Yang. The Yin-Yang out is the tendency to believe that nothing further can be done to throw light on the dark place where, and if, any definitive diagnosis resides for the patient, i.e., the physician is let out of further diagnostic effort. This may prove ultimately to be true, but to adopt the strategy at the outset is fraught with the chance of a variety of errors.

*The terms used to describe the various CDRs above are those by which they are commonly known in the psychology and medicine literature, as well as colloquially. Some, such as feedback sanction and hindsight bias, are indirect, reflecting more on processes that interfere with physician calibration. There is considerable overlap among CDRs, some being known by other synonyms. These, together with further detail and citations for the original work, are described in Croskerry P. Achieving quality in clinical decision making: cognitive strategies and detection of bias. Acad Emerg Med. 2002;9:1184–1204. The above list was based on material in that article and in an earlier work.27*
various cognitive pitfalls, and second that specific forcing strategies be developed to counter them.

Much of clinical decision making, as Reason \(^5\) notes, is where “the cognitive reality departs from the formalized ideal.” This cognitive reality is extremely vulnerable to error. The problem is that cognitive error is high-hanging fruit and difficult to get at, and there will be a tendency to pursue more readily attainable goals. There is a story about a jogger who came across a man on his knees under a streetlight one evening. He explained that he had dropped his wedding ring. The jogger offered to help him search, and he accepted. With no luck after a half hour, the jogger asked the man if he was sure he had dropped the ring at the place where they were searching. The man replied that he actually dropped it several yards away in the shadows. “Then why are we looking here?” asked the jogger. “Because the light is better,” came the reply.

Real solutions to cognitive diagnostic errors lie in the shadows, and they will be difficult to find. One very clear goal in reducing diagnostic errors in medicine is to first describe, analyze, and research CDRs in the context of medical decision making, and to then find effective ways of cognitively debiasing ourselves and those whom we teach. Not only should we be able to reduce many cognitive diagnostic errors, but we may also be pleasantly surprised to find how many can be eliminated.

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REFERENCES


Table 1

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Mechanism/Action</th>
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<tbody>
<tr>
<td>Develop insight/awareness</td>
<td>Provide detailed descriptions and thorough characterizations of known cognitive biases, together with multiple clinical examples illustrating their adverse effects on decision-making and diagnosis formulation.</td>
</tr>
<tr>
<td>Consider alternatives</td>
<td>Establish forced consideration of alternative possibilities e.g., the generation and working through of a differential diagnosis. Encourage routinely asking the question: What else might this be?</td>
</tr>
<tr>
<td>Metacognition</td>
<td>Train for a reflective approach to problem solving: stepping back from the immediate problem to examine and reflect on the thinking process.</td>
</tr>
<tr>
<td>Decrease reliance on memory</td>
<td>Improve the accuracy of judgments through cognitive aids: mnemonics, clinical practice guidelines, algorithms, hand-held computers.</td>
</tr>
<tr>
<td>Specific training</td>
<td>Identify specific flaws and biases in thinking and provide directed training to overcome them: e.g., instruction in fundamental rules of probability, distinguishing correlation from causation, basic Bayesian probability theory.</td>
</tr>
<tr>
<td>Simulation</td>
<td>Develop mental rehearsal, “cognitive walkthrough” strategies for specific clinical scenarios to allow cognitive biases to be made and their consequences to be observed. Construct clinical training videos contrasting incorrect (biased) approaches with the correct (debiased) approach.</td>
</tr>
<tr>
<td>Cognitive forcing strategies</td>
<td>Develop generic and specific strategies to avoid predictable bias in particular clinical situations.</td>
</tr>
<tr>
<td>Make task easier</td>
<td>Provide more information about the specific problem to reduce task difficulty and ambiguity. Make available rapid access to concise, clear, well-organized information.</td>
</tr>
<tr>
<td>Minimize time pressures</td>
<td>Provide adequate time for quality decision-making.</td>
</tr>
<tr>
<td>Accountability</td>
<td>Establish clear accountability and follow-up for decisions made.</td>
</tr>
<tr>
<td>Feedback</td>
<td>Provide as rapid and reliable feedback as possible to decision makers so that errors are immediately appreciated, understood, and corrected, resulting in better calibration of decision makers.</td>
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Objectives

- Review current evidence around common pediatric concerns including:
- Allergen exposure and allergy
- Television exposure
- Rehydration in mild dehydration
- Infant sleep training
- Optimal treatment duration & dosing

Hygiene Hypothesis
(Thumb Sucking & Nail-Biting)

- Cohort study 1037 pts born in Dunedin NZ 1972-1973
- Multiple follow up visits and questionnaires up to 38 yrs of age
- Association of thumb sucking & nail biting with atopic sensitization, asthma & hay fever

Peanut Exposure in Kids

- RCT, 640 infants (mean 7.8 mo), severe eczema, egg allergy or both, consume or avoid peanuts until 5 yrs of age.\(^1\)
- Primary outcome: proportion of pts with peanut allergy at 5 yrs as determined by oral food challenge
  - Peanut allergy = 1.9% consumption group, 13.7% in avoidance group
  - NNT = 9
- Bottom Line: AAP suggests early introduction of peanuts in high risk infants \(^2\)

Footnotes:
Screen Time

American Academy Of Pediatrics Lifts ‘No Screens Under 2’ Rule

15 months – 2 years: small studies suggests kids can learn new words from educational media if parents are present

Small studies show poorer language skills correlated with earlier solo viewing of educational videos

Language delays in children who watch more TV or start earlier.

Ages 2-5: 1 hr of screen time per day with an adult

Gastroenteritis Therapies:

• Systematic Review, 31 RCTs, mild to moderate dehydration from gastroenteritis, developed countries
• Oral versus IV Rehydration:
  – Hospitalization (3 RCTs): RR 0.80 (0.24-2.71)
  – Return to ED (3 RCTs): RR 0.86 (0.39-1.89)
• Ondansetron vs placebo:
  – Need for IV (3 RCTs): RR 0.38 (0.27-0.54)
  – Hospitalization (5 RCTs): RR 0.32 (0.18-0.57)

Word Learning From Baby Videos

• 96 children, 12-25 months, 6 weeks of in home DVD viewing
• Results:
  – No evidence that viewing educational videos improved vocabulary acquisition
  – Earlier exposure to videos associated with lower scores on measures of general vocabulary
  – No association between hours of viewing and general vocabulary development
• Bottom Line: Parents are still valuable


Hydrating Kids: Electrolyte solution?

• RCT 647 kids (mean 28 months, 51% male, 68% score 0 and 25% score 1-2 out of 8), daily f/u
  – ½-strength apple juice vs apple-flavored, sweetened Pediatric Electrolyte, each 2L given 5mL q2-5 minutes
• Outcomes: Tx failure 17% vs 25%, NNT ~12.
  – Mostly less return to care, hospitalization & IV rehydration
  – Rehydration equal if <24 months, ≥24 months ¾ AJ better
• Bottom-line: For kids with minimal dehydration, ½ strength AJ (or preferred fluids) as good as electrolyte solution. One small trial demonstrated improvement with frozen (NNT = 3), but only frozen was sweetened.


Does Osmolality Matter?

• WHO Previously: 311mmol/L
• WHO Now: <250 mmol/L
• Gatorade: ~350 mmol/kg
• Pedialyte: ~270 mmol/kg
• Apple Juice: ~700 mmol/kg
• Dilute Apple Juice: ~350mmol/kg
• Coca Cola: ~ 500mmol/kg

* Osmolality = mmol/kg, Osmolarity = mmol/L, you need the density of the fluid to convert L to Kg
Pediatric Migraine

• 361 children (8-17yrs) with migraine, randomized to amitriptyline (1mg/kg/d), topiramate (2 mg/kg/d) or placebo x 24 weeks
• Primary outcome: ≥50% relative reduction in the number of headache days
  – No diff: 52%, 55% vs 61%
  – Non significant outcomes for # days, % pts who completed treatment, disability score
• Amitriptyline s/es: Fatigue and dry mouth
• Topiramate s/es: paresthesia and weight loss
• **Bottom Line:** Trial stopped for futility


Infant Sleep Problems

• RCT 43 infants (6-16 mo), 63% girls
• Graduated extinction vs bedtime fading vs control (sleep education)
• Both interventions demonstrated:
  – Significant benefits in sleep latency (p<0.05)
  – Number of awakenings (p<0.0001)
  – Wake after sleep (p=0.01)
  – Significant reduction in maternal stress over 1st month
• 12-mo: no significant differences in emotional & behavioral problems, no significant differences in secure-insecure attachment styles.
• Non significant difference in cortisol levels


Treatment Options

• Extinction/ “Cry it out”
  – put the child to bed at a designated bedtime and then ignore the child until a set time the next morning
• Graduated Extinction/ controlled comforting
  – Ignore bedtime crying and tantrums for extended periods (ie q5mins, or progressively longer intervals) Check in and comfort child for brief periods (ie 15 to 60 seconds)
• Faded Bedtime
  – Take child out of bed for prescribed periods of time if child does not fall asleep. Bedtime is delayed (~15 mins per night) to ensure rapid sleep initiation
• Parent Education/ Prevention
  – Bedtime routines, sleep schedule, put baby to bed “drowsy but not asleep”

The Debate

• ↑ cortisol levels:
  – ?long-term consequences of infant helplessness
  – ? insecure parent-child attachments
  – ?emotional & behavioral problems
• Mothers of infants with a sleep problem
  – More likely to use physical punishment1
  – Increased risk of developing depression (OR>2)2,3
  – More likely to report intrusive thoughts of harming their child4

What do we already know?

• American Academy of Sleep Medicine reviewed 52 studies (2500 infants)
• 49/52 reported benefit with nighttime behavioral treatments
• Benefit seen on average in 82% of children
• Strongest evidence: Unmodified extinction (19 studies), gradual extinction (14 studies) and parental education (5 studies)
• Benefit in maternal mood and stress also seen

Infant Sleep Study

Community RCT, 328 families, controlled comfort or fading4
• Results:
  – Fewer sleep problems
    • 10 mo (56% vs 68%) NNT = 9
    • 12 mo (59% vs 55%) NNT = 7
  – Sustained reduction in maternal depression
    • 2 years (15% vs 26%) NNT = 10
5 year follow up, 225 (69%) families:2
• No significant difference in any of 20 outcomes
  – Child emotional or conduct behavior, cortisol measures
  – Child-parent relationship
  – Maternal mental health & parenting

**Bottom Line:** Sleep training improved infant sleep and maternal depression. No evidence of long term benefit or harms up to 5 yrs.

Sleep. 2006;29(10):1263–1276


In Canada...

- RCT, Vancouver Public Health Units, 235 families, infants 6-8 months
  Randomized to sleep training (controlled comfort) vs safety education
  1* outcome at 6 weeks:
  > 2 wakes per night: 31% vs 60% (NNT = 4)
  Severe sleep problems: 4% vs 14% (NNT = 10)
  Care provider improved depression, fatigue, sleep quality (statistically sign improvement)


Swaddling Risks

- Systematic review: cohort or case – control Swaddling and SIDS
- 4 studies, 760 Cases & 1759 Controls
- Removing most heterogeneous study,
- Risk of SIDS with swaddling
  - Overall: OR 1.38 (CI 1.05-1.80)
  - if > 6 mo of age: OR 2.53
  - if placed prone to sleep: OR 12.99
- Limitations: swaddling not clearly defined, not adjusted for confounders such as co-sleeping
  **Bottom Line: Not over 6 months, not prone**

Duration of Antibiotics

- RCT 515, age 6-23 months, AOM, 5 vs 10 days Clavulin, x14d.
  - Clinical Failure: 34% vs 16%, NNT 6. (Other outcomes similar)
  - Sum symptoms score minimally diff. Diarrhea & rash similar.
  - Bilateral AOM and exposure to ≤3 kids = worsening outcomes

**Bottom-Line: Antibiotic duration can be guided by symptoms in some conditions (like pneumonia) but simply shortening the course for some (like AOM) may not be wise.**


Optimal Dosing

- RCT in 3 urban pediatric clinics, 2110 parents
- Primary Outcome: Dosing Error
- 3 different doses, 3 different tools (9 in total)
  - 84% made ±1 dosing error (>20% deviation)
  - errors in 25% of trials (mean errors = 2.3)
  - Overdosing in 68.0% of errors
  - 21% made ±1 large error (>2x the dose)
  - More errors with
    - cups than syringes OR = 4.6
    - teaspoon only label OR 1.2
- **Bottom Line: syringes & millimeter dosing best.**
  Associated study reports 28% parents who view labels with tsp or teaspoon use non-standard dosing tools.2


Top 5

- First world problems: thumb sucking & nail biting
  Allergen sensitization, early peanut exposure may reduce allergies, screen time better with a parent
- Rehydration in mild dehydration: oral better than IV, pedialyte not necessary & preferred fluids better
- No as helpful: teething sx just what you think, no benefit for amitriptyline or topiramate for pediatric migraine
- Sleep: sleep training NNT ~7 for fewer night time awakenings, improved maternal mood, no swaddling over 6 mo & not facing prone
- Treatment duration & dosing: Longer is better for Antibiotics in AOM, fewer dosing errors with syringe
“The short and the long of it”
NSAID myths

“You have witchcraft in your lips”
-Shakespeare, Henry V.

Adrienne Lindblad BSP ACPR PharmD
Knowledge Translation and Evidence Coordinator,
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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, other funds from non-profit organizations (Towards Optimized Practice)

Learning Objectives

By the end of the session, participants will be able to:
  • Discuss whether the best available evidence supports 5 common myths surrounding non-steroidal anti-inflammatory medications (NSAIDs), including:
    • Effects on fracture healing
    • Efficacy of topical NSAIDs
    • Efficacy compared to opioids in pediatric musculoskeletal pain
    • Efficacy compared to acetaminophen for osteoarthritis and back pain
    • Cardiovascular safety of various NSAIDs

Other Disclosure

• All Shakespeare quotes are from Google and I have no idea if they are real.

Insults you can throw at me

• I’ll beat thee, but I would infect my hands
  • Timon of Athens
• Poisonous bunch-backed toad
  • Richard III
• I’ll tickle your catastrophe
  • Henry IV
• You, minion, are too saucy
  • Romeo and Juliet
• Would thou wert clean enough to spit upon
  • Timon of Athens
• What, you egg?
  • MacBeth

Myth?

NSAIDs reduce inflammation and swelling in acute injury
Swelling

• 8 RCTs vs placebo (44-364 patients)
  • Knee injury (1 study): no swelling: 71% diclofenac vs 35%.
  • Ankle injury (6 studies): 3 found decreased swelling (~2-11%), rest no difference.
  • Hamstring (1 study): no difference.
• Systematic review (10 RCTs) vs other drugs:
  • most no difference
  • 1 reduced swelling by 6% vs dextropropoxyphene.
  • 1 increased swelling by 8% vs acetaminophen.

**Bottom Line**

• Unlikely to be any reliable effect on swelling.
• NSAIDs do improve pain for ~1 in 4 over one week.

Myth?

• NSAIDs inhibit fracture healing

NSAIDs and Fracture Healing

• Adults: 2 RCTs (n=140), Colles fractures, given flubiprofen, piroxicam or placebo
  • No difference recovery time, physiotherapy, malunion or nonunion, functional recovery or healing.
  • Quasi-RCT acetabular fractures: less serious injuries and different surgical approach analyzed in “non-NASAID” arm.
• Peds: 1 RCT (n=336), arm fractures, given ibuprofen or acetaminophen/codeine
  • No difference fracture nonunion at 1 year.
• Cohort data: Patients with nonhealing (painful) fractures likely use more analgesia.

So do NSAIDs impede fracture healing?

• Bottom Line:
  • To quote Hamlet, Act III, Scene 3, Line 87:

  “NO”

Myth?

• Topical NSAIDs aren’t as good as oral NSAIDs
Topicals

- Acute MSK pain:¹
  - Systematic review of 47 RCTs n=(5512)
  - Clinical success: 65% vs 43% placebo (NNT=5)
  - Included diclofenac, ibuprofen, ketoprofen and piroxicam
  - No difference adverse effects
  - Benefits decrease over time (NNT=10 at 9-14 days, possibly due to recovery)

- Chronic MSK pain:²-⁵
  - 4 systematic reviews
  - Short-term: NNT~5 compared to placebo
  - Long-term: NNT~11
  - Compared to oral: similar pain control (RR 1.1, 0.9-1.3)

Myth?

- Opioids are superior to NSAIDs for acute pediatric MSK injuries

Peds MSK

- Bottom Line: Ibuprofen better single-agent relief than acetaminophen or codeine, and is at least as good as acetaminophen with codeine and morphine for acute injury related pain, with fewer adverse effects.

Topicals

- Bottom Line:
  - In acute and chronic MSK pain, topical NSAIDs are better than placebo and equivalent to oral NSAIDs with similar tolerability.

Myth?

- Different NSAIDs have different cardiovascular risks
  - Or, NSAIDs “...art unfit for any place but hell”
    - Shakespeare, Richard III

Peds MSK

- RCT ibuprofen vs acetaminophen vs codeine (n=336, 54% fractures)¹
  - Ibuprofen greater pain reduction (~12 mm)
  - Morphine vs ibuprofen (n=134, all fractures): no difference in pain, but less nausea with NSAID²
  - Acet+codeine vs ibuprofen (n=336): no difference pain, but less AE³
  - Ibuprofen + codeine vs ibuprof alone (n=81): no difference⁴
  - Others: no difference (underpowered)⁵-⁸

Safety of Celecoxib vs other NSAIDs

• TFP #101: ~750 RCTs & 350,000 pts. Naproxen & low dose Ibuprofen lowest CVD risk
• Industry-sponsored RCT 24,081 pts with Arthritis (90% OA/10% RA) plus increased CVD risk x 2.8 yrs
  - Celecoxib 210mg/d, Naprosyn 852mg/d, Ibuprofen 2045mg/d
  - Combined CVD: 4.2% vs 4.3% vs 4.8% (not significant difference)
  - Serious (clinical) GI: 1.1% vs 1.5% vs 1.6% (celecoxib sign lower)
  - Pain (from 54mm): 9.3mm, 10.2mm, 9.5mm
  - 69% stopped taking the drug by study end.

CVD Risk

• Bottom Line:
  - Celebrex ~100mg BID is as safe as higher dose Naproxen or Ibuprofen.

Myth?

• Acetaminophen is just as good as NSAIDs for back pain or osteoarthritis

Acetaminophen vs NSAIDs

• Bottom Line:
  - NSAIDs are likely superior to acetaminophen for back pain and osteoarthritis (short-term and topical). Acetaminophen is not efficacious for back pain or osteoarthritis.

• Systematic review for acute back pain:
  - NSAIDs better ~7.5 points/100

• Systematic review for osteoarthritis:
  - NSAIDs improved pain ~6 points vs acetaminophen
  - Patient assessed global improvement in pain NNT=6

• Acetaminophen no better than placebo:
  - in one high-quality RCT, 5 systematic reviews of back pain
  - 5 systematic reviews of osteoarthritis: no meaningful change

Acetaminophen vs NSAIDs

• Systematic review for acute back pain:
  - NSAIDs better ~7.5 points/100

• Systematic review for osteoarthritis:
  - NSAIDs improved pain ~6 points vs acetaminophen
  - Patient assessed global improvement in pain NNT=6

• Acetaminophen no better than placebo:
  - in one high-quality RCT, 5 systematic reviews of back pain
  - 5 systematic reviews of osteoarthritis: no meaningful change

Acetaminophen vs NSAIDs

• Bottom Line:
  - NSAIDs unlikely to have much clinical effect on swelling in acute injury
  - NSAIDs do not impede fracture healing
  - Topical NSAIDs similar efficacy to oral
  - Ibuprofen for peds MSK pain
  - Celecoxib likely as safe as higher dose naproxen and ibuprofen on the heart
  - Hopefully nothing here quite as offensive as “villain, I have done thy mother”

Summary
Preventing Infections in Hospitals

"Out, damned spot! Out"

Faculty/Presenter Disclosure

- Faculty/Presenter: Victor Leung
- Relationships with commercial interests:
  - Grants/Research Support: Cubist
  - Speakers Bureau/Honoraria: Merck, Pfizer, Pendopharm, Sunovion
  - Consulting Fees: Merck, Pfizer, Pendopharm,
  - Other: None

Disclosure of Commercial Support

- This program has received financial support from the Best Science Medicine Course in the form of a speaker honorarium
- Potential for conflict(s) of interest:
  - None

Mitigating Potential Bias

- Not applicable

Learning Outcome Objective

Review evidence based practices to prevent hospital acquired infections.

Understand the role of hand hygiene in prevention hospital acquired infections.

Review pre/intra/post-operative interventions to reduce surgical site infections

Discuss the bundled approach to reducing device associated infections (e.g. central line associated bacteremias; ventilator associated pneumonia)

Can hand hygiene among health care workers be improved?
Clean care is safer care

- System change
- Training and education
- Observation and feedback
- Reminders in the hospital
- Hospital safety climate

World Health Organization 5 moments for hand hygiene

Comparative efficacy of interventions to promote hand hygiene in hospital: a systematic review and network meta-analysis

- Promotion of hand hygiene with WHO-5 is effective for increasing compliance in HCWs
- Addition of goal setting, reward incentives and accountability strategies can lead to further improvements

A pragmatic randomized controlled trial of 6-step vs. 3-step hand hygiene technique
Reilly et al., ICHE June 2016

- 6-step reduced bacterial counts more (2.58 CFU/ml vs. 2.88 CFU/ml)
- 6-step did not increase the total hand coverage area and required 15% more time.

Should annual influenza vaccination be mandated for healthcare workers?

- “We conclude there is no evidence that vaccinating HCWs prevents influenza in elderly residents in LTCFs.” — Thomas et al. Cochrane Database Syst Rev. 2010

- “Influenza vaccines have a modest effect in reducing influenza symptoms and working days lost. There is no evidence that they affect complications, such as pneumonia, or transmission.” — Jefferson et al. Cochrane Database Syst Rev. 2010

Influenza Vaccination of Healthcare Workers: Critical Analysis of the Evidence for Patient Benefit Underpinning Policies of Enforcement
De Serres et al. PLOS One 2017

“Given the poor scientific quality of the available evidence, we conclude that policies of enforcement lack a valid empirical underpinning and that current scientific data are inadequate to show substantial patient benefit as a requirement for their ethical implementation... We reiterate that, although current data are inadequate to support enforced HCW influenza vaccination, they do not refute approaches to support voluntary vaccination or other more broadly protective practices such as staying home or masking when acutely ill.”

Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and Clostridium difficile: the Benefits of Enhanced Disinfection study: a cluster-randomized, multicentre, crossover study.
Anderson et al. Lancet 2017

- Compared standard disinfection to
  - bleach,
  - UV-C
  - bleach + UV-C

- UV-C didn’t reduce C. difficile risk beyond using bleach

No touch disinfection with UV-C.
Does it work?
What is new for preventing *Clostridium difficile* infection?

Transmissibility of *Clostridium difficile* Without Contact Isolation: Results From a Prospective Observational Study With 451 Patients
Widmer et al., Clinical Infectious Diseases 2017

- “We discontinued contact precautions for patients with CDI, except for patients infected with hypervirulent ribotypes or with stool incontinence, to determine the rate of transmission”

- Results:
  - only 2 proven (and 4 probable) transmission events were documented using genome sequencing over the decade, and no outbreaks occurred

Key message

- When a patient who had cardiac surgery in the last 6 years is diagnosed with a vasculitis or a granulomatous disease, you should rule out *Mycobacterium chimaera* infection before starting steroids

Case

You are seeing a 70 year old man who had an aortic valve replacement 5 years ago and for the last three years has been suffering from fatigue, progressive weight loss and back pain. The consultant rheumatologist has diagnosed him with vertebral sarcoidosis and has advised initiation of steroids. Do you believe the diagnosis?

Mycobacterium chimaera infections associated with heater cooler units used for cardiac surgery

- Symptoms can occur months to years after cardiac surgery
- The most common symptoms reported by patients with this infection following open heart surgery are persistent fever, increasing or unusual shortness of breath, and unexplained weight loss.
- Other signs of a possible M. chimaera infection may include:
  - fatigue
  - persistent cough
  - night sweats
  - Arthralgias/myalgias
- Laboratory abnormalities: renal failure, hepatitis, cytopenias
Title:

“In a pickle” as to what medications to use for COPD?

Presented by:
Aaron M Tejani, BSc(Pharm), PharmD
Researcher, Therapeutics Initiative (UBC)
Email: aaron.tejani@ti.ubc.ca
www.ti.ubc.ca
Twitter: @amtejani @Drug_Evidence

Link to Slides (Active on April 7, 2017):
http://prezi.com/9j2c6uceftaf/?utm_campaign=share&utm_medium=copy

Faculty/Presenter Disclosure

• Faculty/Presenter: Aaron M Tejani
• Relationships with commercial interests:
  — Grants/Research Support: None
  — Speakers Bureau/Honoraria: None
  — Consulting Fees: None
    — Other: Received payment for Medical Legal consultation services, honoraria for UBC/Divisions of Family Practice (BC)/Best Science Medicine course/College of Pharmacists of BC/Canadian clinician groups (BCNPA, Yellowknife doctors) in for teaching. Received honoraria for peer review of manuscripts from Elsevier Publishing.

Learning Objectives:

1. Describe a list of clinically important therapeutic goals (e.g. reduce risk/frequency of exacerbations, improve symptoms, prevent serious harm) for a typical patient with COPD.
2. Describe the main evidence base for use of long-acting bronchodilator/inhaled corticosteroid combinations (LABA-ICS) for COPD.
3. Understand the implications of attrition bias as it relates to COPD clinical trials.
4. Summarize the evidence for LABA-ICS for COPD patients as it relates to the aforementioned therapeutic goals.
5. Describe when one would expect to see an improvement in symptoms with LABA-ICS if it were to occur.
6. Outline simple prescribing principles for LABA-ICS.
7. Describe the differences/similarities of the evidence for long-acting antimuscarinic/long-acting bronchodilator combinations (LAMA-LABA) and LAMA monotherapy compared to LABA-ICS.
Best Science Medicine Course
April 2017

Provincial Guidelines for the Clinical Management of Opioid Addiction
Keith Ahamad, MD, CCFP
Clinical Assistant Professor, UBC
Lead for Addiction, Primary Care, PHC
Research Scientist, BC Centre on Substance Use

Faculty/Presenter Disclosure

• **Faculty:** Keith Ahamad

• **Relationships with commercial interests:**
  – Grants/Research Support: CIHR, NIH
  – Speakers Bureau/Honoraria: None
  – Consulting Fees: None
  – Other: BC Centre on Substance Use (MoH), Providence Health Care

Disclosure of Commercial Support

• I have NOT received financial support or in-kind support from any commercial interest.
• St Paul’s Addiction Medicine Fellowship is funded in part by Goldcorp Corporation

• **Potential for conflict(s) of interest:**
  – None

Mitigating Potential Bias

• No sources of bias

Learning Outcome Objective

• Describe step-wise approach to treating Opioid use disorder (OUD)
• Recognize potential harms of “detox only” strategies
• Understand why Buprenorphine/naloxone is recommended as 1st line treatment OUD
• Understand how and why Primary Care can treat OUD
BC has always had a guideline for how to prescribe methadone, but guidelines considering when to use methadone versus other treatments have been lacking.
A Guideline for the Clinical Management of Opioid Use Disorder

**Release date**
Jan 2017

**Rank** | **Type of Evidence**
--- | ---
1 | Systematic reviews of randomized controlled trials
2 a | Randomized clinical trials
2 b | Nonrandomized clinical trials
3 a | Observational studies with controls
3 b | Observational studies - no controls
4 | Expert consensus

---

**Treatment options for opioid use disorder**

- **Safety Considerations**
  - **Withdrawal Management Alone**
    - Detox can potentially be an important first point of contact and a bridge to other treatment options
    - However, *inpatient* detox alone associated with:
      - HIV-transmission (MacArthur et al., 2012)
      - High rates of relapse (Strang et al., 2003)
      - Morbidity and Mortality (Luty 2003, Simpson and Friend, 1988)
    - Outpatient slow tapers
    - **THN Training**

---

**Low**
- Systematic reviews of randomized controlled trials
- Randomized clinical trials
- Observational studies with controls
- Expert consensus

**High**
- Observational studies - no controls
- Nonrandomized clinical trials

---

**Treatment options for opioid use disorder**

**Withdrawal Management**
- Tapered methadone, buprenorphine, or alpha2-adrenergic agonist
- Psychosocial treatment
- Residential treatment
- Oral naltrexone

**Agonist Therapies**
- Buprenorphine/naloxone
- Methadone

**Alternative Approaches**
- Slow-release oral morphine

**Treatment Intensity**
- LOW
  - If opioid use continues, consider treatment intensification
- HIGH
  - Where possible, simplify treatment

---

**Safety Considerations**

- Detox can potentially be an important first point of contact and a bridge to other treatment options
- However, *inpatient* detox alone associated with:
  - HIV-transmission (MacArthur et al., 2012)
  - High rates of relapse (Strang et al., 2003)
  - Morbidity and Mortality (Luty 2003, Simpson and Friend, 1988)
- Outpatient slow tapers
- **THN Training**
**Agonist Treatment | Methadone**

**MMT vs. no opioid replacement therapy (Mattick et al., Cochrane Review 2009)**

- Methadone significantly more effective than non-pharmacological approaches in:
  - Retention in treatment
  - Suppression of heroin use

**Agonist Treatment | Buprenorphine/naloxone**

**Buprenorphine vs. Methadone Maintenance Therapy (Mattick et al., Cochrane Review 2014)**

- At medium/high doses bup/nx is not markedly different from methadone in terms of treatment retention
- No difference between bup/nx and MMT in reducing illicit opioid use

**Indicators of Buprenorphine and Methadone Use and Abuse: What Do We Know?**

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<th>Year</th>
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<th>Methadone Deaths</th>
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</tbody>
</table>

Source: National Poison Data System, American Association of Poison Control Centers.
US Safety Data

- Post marketing surveillance (RBK) 2002-2013 (OUD patients)
  - 464 death related to Bup
  - Average of 33/yr

- CDC reported in 2008
  - Prescription Opioid deaths 14,800

---

**US Safety Data**

- Post marketing surveillance (RBK) 2002-2013 (OUD patients)
  - 464 death related to Bup
  - Average of 33/yr

- CDC reported in 2008
  - Prescription Opioid deaths 14,800

---

**CBC INVESTIGATES | Fentanyl crisis: Easier access to Suboxone urgently needed, experts say**

"Wells Fargo has taken a stand" even after 2.5-fold increase in B.C. fentanyl deaths

- Equal efficacy
- Bup = safer
  - 1st Line
  - Take home dosing schedule?
  - Random pill counts
  - Random UDS
Annals of Family Medicine

Treating Opioid Addiction With Buprenorphine-Naloxone in Community-Based Primary Care Settings


Abstract

Buprenorphine-Naloxone (B-N) is a medication used to treat opioid addiction. This medication is typically administered in specialized addiction treatment centers. However, there is a growing interest in providing B-N in primary care settings. This study aimed to evaluate the feasibility and efficacy of providing B-N in primary care settings.

Methods

A randomized controlled trial was conducted involving 100 patients with opioid addiction. Patients were randomly assigned to either the intervention group (B-N in primary care) or the control group (B-N in specialized addiction centers).

Results

The results showed that patients in the intervention group had a significantly higher likelihood of achieving remission compared to those in the control group.

Conclusion

Buprenorphine-Naloxone can effectively be provided in primary care settings, offering a promising option for the treatment of opioid addiction.

Acknowledgements

• Evan Wood
• BCCSU Staff
• CRISM
• MoH
IBS

"Is there something in the wind?"

Tina Korownyk
Dept of Family Medicine, UofA

Learning Outcome Objective

Review best evidence around IBS management, including medical and lifestyle interventions.

FODMAP DIET
what is it & does it work?


FODMAP DIET
what is it & does it work?


Faculty/Presenter Disclosure

- Faculty/Presenter: Christina Korownyk
- Where we get Personal $: U of A, Alberta Health
- 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

IBS

Physician

Must Most Other

Symptoms

Referral

Etiology

Treatment

Patient

IBS

Most Bothersome

Symptoms

Referral

Etiology

Treatment


Patient-Provider Agreement

IBS

LOW FODMAP DIET

 Eliminate foods containing fodmaps

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

“A Novel Mind-Body Management Study”
Placebo & IBS

• 80 patients [70% female]
• Randomized:
  – Open labeled placebo pill bid + 3 visits (intervention)
  – Positive framing “placebo is powerful, the body can immediately respond, a positive attitude helps”
  – Warm supportive GP relationship
• IBS global improvement (7 point Likert scale):
  – ↑ 1 point placebo vs no ↑ control
• IBS-SSS: ↑ 92 placebo vs 46 control
  – 50 is MCID
• Adequate relief: 59% placebo vs 35% control
  – NNT = 5
• Bottom Line: Placebo Works
  “I liked that my feeling about the intensity of the problem was validated and was taken seriously... was able to discuss my IBS”

Anti-spasmodics

• Compared to placebo, anti-spasmodics improve:
  – Abdo pain: 58% vs 46% (NNT = 8)
  – Global assessment: 57% vs 39% (NNT = 5)
  – Symptom score: 37% vs 22% (NNT = 7)
• Meds that work: dicyclomine (Bentyl), peppermint oil, pinaverium (Dicetel), trimebutine (Modulon)
• Nothing from primary care

Anti-depressants

• Compared to placebo, anti-depressants improve:
  – Abdo pain: 54% vs 37% (NNT = 6)
  – Global assessment: 59% vs 39% (NNT = 5)
  – IBS symptom score: 53% vs 26% (NNT 4)
• SSRIs: improve global assessment
• TCAs: improve abdo pain, global assessment and symptom score

Peppermint Oil

• Systematic Review
  – 5 placebo controlled RCTs, 392 patients
  – 1 trial reported IBS subtype (IBS-D 75%)
• Quality: most studies ≤ 4 weeks, no North America
  – Most studies – enteric coated capsules tid
• Significant improvement in abdominal pain RR 2.14
• Global improvement IBS Symptoms:
  – 136/197 (69%) peppermint
  – 60 / 195 (31%) placebo
  – NNT = 3
• Most common adverse effect: Heart Burn

IBS Treatments

<table>
<thead>
<tr>
<th>Agent</th>
<th>Outcome</th>
<th># Trials</th>
<th>Intervention</th>
<th>Control</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antispasmodics&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Global Assessment</td>
<td>22</td>
<td>60%</td>
<td>39%</td>
<td>5</td>
</tr>
<tr>
<td>Peppermint Oil&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Improved Sx</td>
<td>4</td>
<td>69%</td>
<td>31%</td>
<td>3</td>
</tr>
<tr>
<td>Antidepressants&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Global Improvement Sx</td>
<td>56%</td>
<td>35%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulking Agents&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Global Assessment</td>
<td>11</td>
<td>60%</td>
<td>49%</td>
<td>NS</td>
</tr>
<tr>
<td>Placebo&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Adequate Relief</td>
<td>1</td>
<td>59%</td>
<td>35%</td>
<td>5</td>
</tr>
<tr>
<td>Laxatives&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Adequate Relief 9/12 weeks</td>
<td>2</td>
<td>40%</td>
<td>20%</td>
<td>5</td>
</tr>
<tr>
<td>Chinese Herbal Medicine&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Global Sx Improvement</td>
<td>7</td>
<td>73%</td>
<td>45%</td>
<td>4</td>
</tr>
</tbody>
</table>


1) Kaptchuk, Plus one 2010; 5: e15591
Linaclotide

2 multicentre (phase 3) RCTs (803 and 805 pts)\(^1,2\)
• Linaclotide 290mcg VS placebo in IBS-C
  – 2 systematic reviews
  – Both RCTs have strikingly similar baseline demographics and outcomes\(^1,2\)
  – Mean age 44, 90% & 91% female, 77% & 78% white.
  – Both trials:
    • Baseline abdominal pain ~5.6 on 11-point scale,
    • Complete spontaneous bowel movements 0.2/week

Primary Outcome – FDA “responder” at 12 weeks:
  – ≥ 30% reduction in abdominal pain + increase of 1 complete spontaneous BM for 6/12 weeks\(^1,2\)
  • 34% vs 21% and 34% vs 14%
  • Number needed to treat (NNT) = 7

Linoclotide

• Secondary outcomes at 12 weeks:
  • 2.7-2.8 additional spontaneous BMs/week (above placebo)\(^1,2\)
  • Average pain reduction in both trials:
    – 1.9 on 11-point numeric rating scale
    – Minimally clinically significant difference (2.2)\(^3\)

• Adverse outcomes:
  – Diarrhea resulting in discontinuation\(^1,2\)
    • 5-6% vs 0.2-0.3%
    • Numbers needed to harm (NNH) = 23

• Limitations: unclear recruitment, run in which excluded non-compliers and
  ➢ 40% of patients who did not meet strict inclusion criteria
  ➢ Some inconsistent data between abstracts and peer reviewed publications,\(^3,8\)
  including primary authors

The dark history of inside your bowel...

• 5-HT\(_3\) Agonist Alosetron (Lotronex): Ischemic colitis
• 5-HT\(_4\) Agonist Cisapride (Prepulsid), Tegaserod (Zelnorm): CV events
• Prucalopride (Restoran): Approved in Canada but NOT US due to concerns of 5-HT\(_4\) class of drugs
• Linoclotide (Constella): selective agonist at the guanylate cyclase-C (GC-C) receptor on the luminal surface of intestinal enterocytes
Tina Korownyk

Treat the Constipation

**Prucalopride (Restoran)**

- Middle aged women with 0.5 BM “*weekly*”
  - weekly BMs to: 1 (placebo) & 2 (prucalopride)
- PEG vs Prucalopride:*
  - PEG “non-inferior” for primary outcome
  - PEG superior to prucalopride in majority of secondary outcomes
- Systematic Reviews Prucalopride:
  - Unfunded: “no evidence that effective”
  - Industry Affiliated: “efficacy on patient important outcomes and a favorable safety profile support the use of high selectivity 5-HT4 agonists”
- **Bottom Line: No better than PEG, two 5-HT4 agonists previously removed due to increased CV events.**

**PEG**

- At least 8 systematic reviews
  - PEG vs other laxatives and/or placebo
    - range 5-19 trials, 594-1,443 participants 2-52 weeks long
- Adults outcomes, statistically significant:
  - PEG versus placebo:
    - Relief of constipation: NNT=2-3
    - Increased stool frequency: 2-3 more/week
  - PEG versus lactulose:
    - Increased stool frequency and reduced need for additional interventions
- **Bottom Line:** In adults and pediatric patients with chronic constipation, PEG is as or more effective than other agents. Adult starting dose 17g/day.

**Colace**

- Best RCTs:
  - 74 palliative pts on senna: Add docusate vs placebo
  - No diff in BM or Symptoms in 10 days
  - 74 hospitalized patients: Cross over RCT docusate vs placebo over 30 days
  - Docusate increased BMs by ~1/week
  - Limitations: 26% lost to follow-up in 1960s
- Other studies: pts comatose, poor quality, unblinded
  - Post op pts: Senna + Docusate vs:
    - Placebo: 1st BM ~1 day sooner – likely due to senna
    - PEG: 1st BM 1-2 days sooner with PEG
- **Bottom Line:** Docusate appears similar to placebo in increasing stool frequency and is inferior to other products for treating constipation

![Image](https://www.tinakorownyk.com)

**Comparative Shopping:**

- Bisacodyl 10mg qd = $10/mo = $0.65/poop
- Lactulose 15mg qd = $12/mo = $1.00/poop
- PEG 3350 17g qd = $20/mo = $1.70/poop
- Linaclotide 290ug qd = $180/mo = $17/poop
- Prucalopride 2mg qd = $125/mo = $30/poop

![Price Comparison](https://www.tinakorownyk.com)

**Summary**

- Patients want reassurance & validation
  - Clinicians & Patients not always on the same page with regards to management
- Variety of patients, variety of responses
  - Treat bothersome symptoms (GI and non GI)
  - Use what works for them
- Interventions (including placebo) work in some people some of the time
  - Common sense:
    - Diarrhea: TCAs, peppermint oil
    - Constipation: SSRIs, PEG
    - Pain: Anti-spasmodic

![Image](https://www.tinakorownyk.com)


TPF #161 A placebo pill for soft poops April 25, 2016

TPF #45 Polyethylene glycol (PEG) for Pediatric and Adult Chronic Constipation Mar 10, 2015
Thanks for your questions and discussion.

Thanks for completing your course evaluations.