A Hybrid World:
Developing Versatile Materials for Maximum Impact

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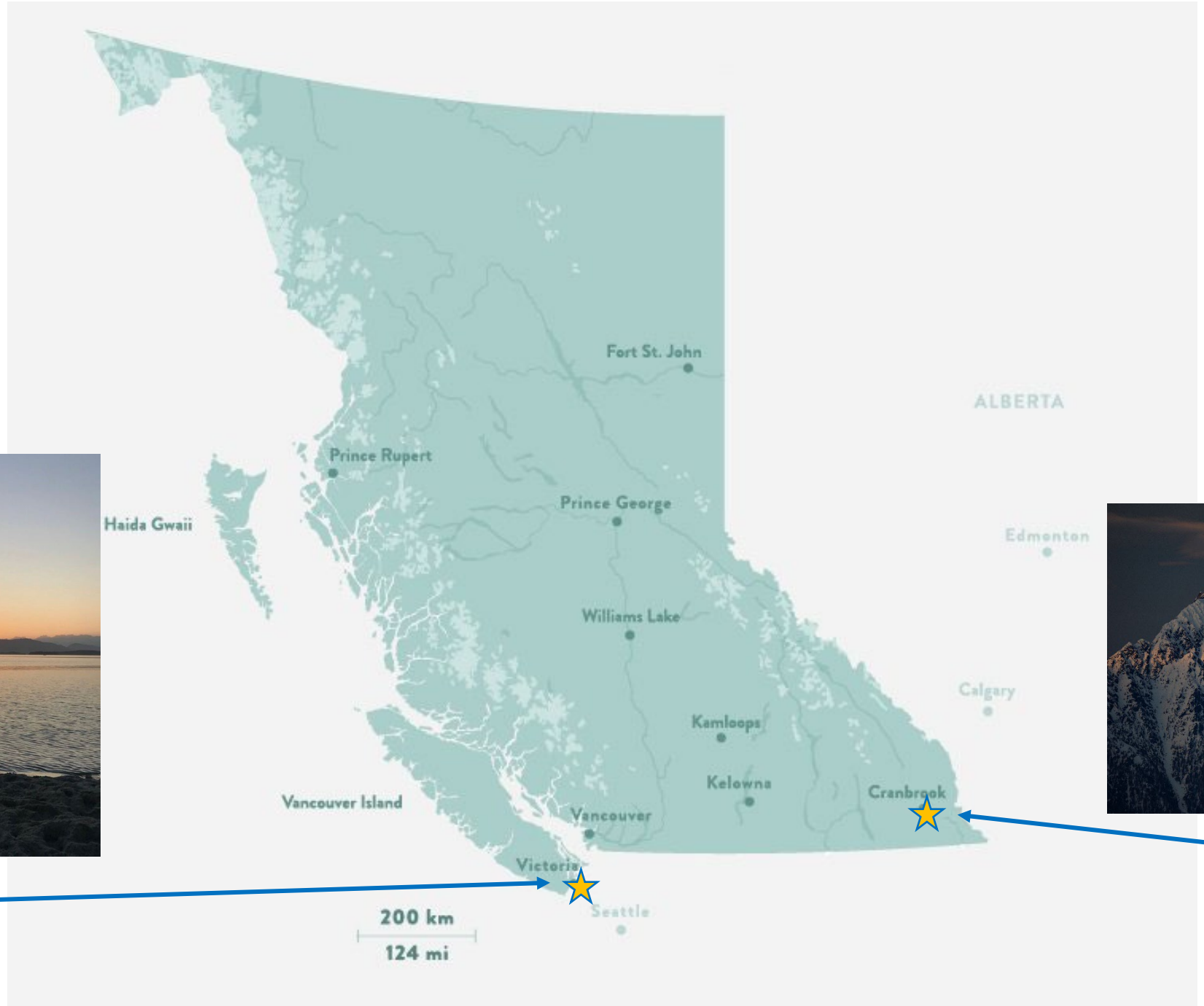
Where Jen lives!



Where Kyle lives!

Disclosures and Financial Support

- British Columbia's Ministry of Health's Pharmaceutical, Laboratory and Blood Services Division provides Island Health and Interior Health funding for the purpose of delivering the BC Provincial Academic Detailing Service.

- We have no other conflict of interests.

Background

- Providing only virtual details during the COVID-19 pandemic, our established BC PAD team required **new creativity in developing our materials**
- **We shifted** from detailed Word documents to PowerPoint slides for TEAD
- Moving forward in a hybrid world we are **still learning** what works well to create a single document which can be used either in-person or virtually

Objectives

Employ the concept of less vs. more when creating detailing materials

Examine key features of detailing materials that affect their usefulness

Implement detailers' views on materials they find effective to translate knowledge to practice

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Our Teams Approach

Where We Were:

- Pre-pandemic: mostly in-person sessions
- Detailed handouts

Our teams approach

Where We Were:

- Pre-pandemic: mostly in-person sessions
- Detailed handouts

= More

What effect does intensifying therapy in COPD have on the risk of exacerbation or death?

There is an absence of high-quality evidence regarding the effect of intensifying inhaled therapy (ie, progressing to LAMA+LABA and LAMA+LABA+ICS) on the risk of COPD exacerbation and death.

- In people with persistent exacerbations (defined by GOLD as: ≥ 2 exacerbations per year or 1 leading to hospitalization), the 2017 GOLD COPD guideline recommends the following:[4]
  1. monotherapy: LAMA (rather than LABA)
  2. progression to double therapy: LAMA+LABA (rather than ICS+LABA, unless asthma diagnosis)
  3. progression to triple therapy: LAMA+LABA+ICS (addition of ICS to LAMA+LABA)

Table 2: Relevant Evidence from Cochrane Systematic Reviews: Exacerbations, Total Mortality

LAMA vs PLACEBO[6]	Effect of tiotropium compared to placebo		22 RCTs, N=23,309
Exacerbations: number of people with one or more	PLACEBO = 44 per 100 vs LAMA = 38 per 100		3-48 months (range)
	OR 0.78, 95%CI 0.70-0.87 SS	High quality	22 RCTs, N=23,309
Mortality (all cause)	OR 0.98, 95%CI 0.86-1.11 NSS	Moderate quality	22 RCTs, N=23,309
LAMA vs LABA[10]	Effect of tiotropium compared to LABA		7 RCTs, N=12,223
Exacerbations: number of people with one or more	LABA = 29 per 100 vs LAMA = 26 per 100		3-12 months (range)
	OR 0.86, 95%CI 0.79-0.93 SS	Moderate quality	6 RCTs, N=12,123
Mortality (all cause)	OR 0.82, 95%CI 0.60-1.13 NSS	Very low quality	6 RCTs, N=12,123
LAMA+LABA vs LAMA[7]	Effect of adding LABA to tiotropium		10 RCTs, N=10,894
Exacerbations: number of people with one or more	RCTs were not pooled	Ungraded	3-12 months (range) 7 RCTs, N=6391
Mortality (all cause)	OR 1.24, 95%CI 0.81-1.90 NSS	Low quality	8 RCTs, N=9633
LAMA+LABA+ICS vs LAMA+LABA[11]	Effect of adding ICS to tiotropium + LABA		1 RCT, N=293
Exacerbations: number of people with one or more	LAMA+LABA = 65 per 100 vs triple = 60 per 100		12 months
	OR 0.81, 95%CI 0.51-1.30 NSS	Ungraded	1 RCT, N=293
Mortality (all cause)	OR 1.02, 95%CI 0.32-3.24 NSS	Ungraded	1 RCT, N=293

Notes:
Exacerbation outcome COPD exacerbations are not consistently defined, counted, analyzed in clinical trials which affects interpretability[12-14]
Placebo other COPD medications permitted (eg, salbutamol) as long as they were not one of the randomized treatments
RCTs randomized controlled trials; **N** number of participants; **OR** odds ratio; **95%CI** 95% confidence interval
SS statistically significant difference; **NSS** not statistically significantly different
High quality evidence Cochrane authors are very confident that the true effect lies close to the estimate of the effect
Moderate quality evidence Cochrane authors are moderately confident that the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different
Low quality evidence Cochrane authors' confidence in the effect estimate is limited, the true effect may be substantially different
Very low quality evidence Cochrane authors have very little confidence in the effect estimate, the true effect is likely substantially different
LAMA+LABA provided as separate inhalers;[7] LAMA+LABA provided as combination inhaler Cochrane review is at the protocol stage;[8] results for the exacerbation outcome were not pooled in the LAMA+LABA vs LAMA comparison due to heterogeneity between the studies, however the number of people with exacerbations was not reduced in the 3 subgroups (formoterol, olodaterol, or salmeterol when added to tiotropium)[7]
LAMA+LABA+ICS triple therapy provided as ICS+LABA (combination inhaler) + LAMA (second inhaler);[11] Cochrane authors did not grade the quality of evidence but conclude that there were not enough patients to draw firm conclusions;[11] Cochrane review of triple therapy provided as LAMA+LABA (combination inhaler) + ICS (second inhaler) did not identify any relevant studies[15]

ICS+LABA vs LABA[16]	Effect of adding ICS to LABA		14 RCTs, N=11,794
Exacerbations: number of people with one or more	LABA = 47 per 100 vs ICS+LABA = 42 per 100		12 months (median)
	OR 0.83, 95%CI 0.70-0.98 SS	Moderate quality	6 RCTs, N=3357
Mortality (all cause)	OR 0.92, 95%CI 0.76-1.11 NS	Moderate quality	10 RCTs, N=10,681

Notes:
ICS+LABA provided as combination inhaler twice daily;[16] the exacerbation outcome does not include TORCH 2007 (N=6184) or SUMMIT 2016 (N=16,590);[17,18] the mortality outcome does not include SUMMIT 2016 (N=16,590)[18]
ICS+LABA vs LAMA+LABA Cochrane review is at the protocol stage[19]
ICS+LABA once daily vs LABA Cochrane review is at the protocol stage[20]
ICS+LABA twice daily vs tiotropium Cochrane authors conclude that the relative efficacy & safety of ICS+LABA vs tiotropium is uncertain[21]
ICS+LABA once daily vs LAMA Cochrane review is at the protocol stage[22]

COPD Update: Focus on Intensifying LABA, LAMA and ICS Therapy

B.C. Provincial Academic Detailing Service **February 2017**

Antidepressants for Major Depressive Disorder:
Drug Information to Support Drug Therapy Decisions

B.C. Provincial Academic Detailing (PAD) Service **March 2020**

Antidepressant Clinical Trials

The most common efficacy measures used in antidepressant randomized controlled trials are symptom severity scales (clinician administered), eg:[1-3]

- Hamilton Depression Rating Scale (17 item) (HDRS-17: score range 0 to 52), and the
- Montgomery Asberg Depression Rating Scale (MADRS: score range 0 to 60).

Antidepressant trials have often excluded people with:[2,4-7]

- less severe depression scores (eg, HDRS < 19),
- depression with psychotic features,
- suicidal ideation,
- substance use disorder, or
- serious medical comorbidity.

In the largest dataset of published and unpublished trials, (522 trials; 116,477 participants):[2]

- mean age was 44; two-thirds were women,
- mean HDRS-17 score was 26 at baseline, and the
- median duration of the trials was 8 weeks.

Efficacy is often reported as a:

- continuous outcome: mean difference in depression severity scores achieved in the antidepressant group compared to the placebo group, or a
- dichotomous outcome: proportion of people achieving at least a 50% improvement in symptom severity scores.

Antidepressant Onset of Effect

Health Canada and the US Food and Drug Administration generally do not detail the time course of treatment response for antidepressants, but:[24-57]

- meta-analyses demonstrate evidence of improvement in depression symptom scales within the first 1 to 2 weeks, and[58,59]
- the effect appears largely maximized by 6 to 8 weeks.[24,59,60]

Antidepressant Dose Response

Antidepressants are generally approved by Health Canada and the US Food and Drug Administration:

- with a defined dosage range, but
- the relationship between dose and response is often not well characterized.[24-57]

For several antidepressants, efficacy appears optimized below the maximum approved dose, and:

- there is a more consistent relationship between higher doses and adverse events leading to drug discontinuation (See Table 1).[61,62]

Antidepressant Meta-Analyses & Systematic Reviews

The mean difference in improvement achieved in the antidepressant group as compared to the improvement achieved in the placebo group is:

- approximately 2 points (HDRS-17),[3,8,9]
- eg, in one meta-analysis: mean 9.6 point improvement in the antidepressant group versus 7.8 point improvement in the placebo group.[8]

Proportion of people achieving at least a 50% improvement in their symptom severity score (median 8 weeks):

- 45-50%* in the antidepressant group, and
- 35% in the placebo group.[2,10]

*citalopram, escitalopram, fluoxetine, paroxetine, sertraline, vilazodone, vortioxetine, venlafaxine, desvenlafaxine, duloxetine, levomilnacipran, mirtazapine, bupropion

In short-term (6 to 12 week) antidepressant trials:

- approximately 1 in 3 people discontinue treatment (antidepressant or placebo).[11]

Systematic reviews and network meta-analyses of antidepressant comparisons:

- do not claim substantial differences in efficacy;[2,12-22]
- the largest network meta-analysis did not identify high quality evidence for comparisons.[2]

Direct comparisons of recently marketed antidepressants (eg, levomilnacipran, vilazodone, vortioxetine) to more commonly prescribed antidepressants are limited.[2,21,22]

Evidence is incomplete for functional outcomes, quality of life, specific and serious* adverse events.[2,9-23]

*eg, death, disability, hospitalization

Combining Antidepressants

When response to initial antidepressant therapy is considered inadequate, available evidence does not reliably inform next drug therapy steps:[2,63,64]

- switching antidepressants,
- adding another antidepressant, or
- adding a non-antidepressant.

Combining antidepressants with dissimilar pharmacologic profiles has been proposed (eg, adding mirtazapine or bupropion to an SSRI or SNRI), but:

- few methodologically rigorous trials have examined the efficacy and safety of these combinations.[63,65-68]

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pad

Antidepressants for Major Depressive Disorder:
Drug Information to Support Drug Therapy Decisions

B.C. Provincial Academic Detailing (PAD) Service **March 2020**

Handout for in-person detailing

Antidepressant Efficacy

Single Slide for Virtual Detailing

Antidepressant Meta-Analyses & Systematic Reviews

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Our Teams Approach

Where We Are Headed:

- Post-pandemic: a hybrid of virtual and in-person sessions
- PowerPoint slides (can be made into a handout)

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= less

ADHD Medications: Translating efficacy from clinical trials

Factors to consider when translating efficacy from ADHD medication clinical trials to clinical practice:[1-6]

- The objective of drug-approval trials submitted to Health Canada & the US Food and Drug Administration is to show a statistically-significant reduction in core ADHD symptoms versus placebo (inattention, hyperactivity, impulsivity).
- Most trials are short-term (i.e., ≤ 12 weeks); there is insufficient data to assess outcomes at 26 & 52 weeks.
- The symptom scales used in these trials can vary; this makes meta-analyses difficult to translate clinically (e.g., the statistical difference is reported but not the absolute benefit).
- There is no consensus definition for a clinically-important difference or of 'responder' which could inform the calculation of a number-needed-to-treat (NNT).
- In a 2018 network meta-analysis with 101 comparisons (drug versus placebo & drug versus drug), the certainty of evidence was assessed as high quality for one comparison, moderate for 12, low for 38, and very low for 50.

Systematic Review & Network Meta-Analysis (Lancet Psychiatry 2018)[6,7]

133 trials; 14,346 children & adolescent participants; 10,296 adult participants

Outcomes: efficacy & acceptability at 12 weeks	Medications* statistically-significantly better than placebo			
	Children & Adolescents		Adults	
ADHD core symptoms: reduction in symptoms rated by clinicians	methylphenidate amphetamines atomoxetine guanfacine		methylphenidate amphetamines atomoxetine	
Acceptability: discontinuation for any reason, encompasses efficacy & tolerability	methylphenidate		amphetamines	
Clinician impression of improvement: proportion of participants much or very much improved from baseline**	placebo: 25%	methylphenidate: 65% amphetamines: 72% atomoxetine: 43% guanfacine: 55%	placebo: 25%	methylphenidate: 51% amphetamines: 62%

* Medications approved by Health Canada for ADHD

**Clinical Global Impression-Improvement (CGI-I) 7-point scale: very much improved, much improved, minimally improved, no change, minimally worse, much worse or very much worse relative to baseline state; does not indicate the degree of participants' clinical severity at the end of the trial; proportion of participants 'much or very much improved' was estimated by converting the reported odds ratio to a risk ratio which was then applied to the placebo response rate (25%)

[1]Health Canada Drug Product Database; [2]Health Canada Drug Health Product Register; [3]US Food and Drug Administration FDA Approved Drugs; [4]WONG Lancet Psychiatry 2019:6:528-37; [5]Cochrane Database Systematic Reviews CD007813, CD009885, CD009996, CD012857, CD013011; [6]CORTESE CIPRIANI Lancet Psychiatry 2018:5:727-38 & 871-73; [7]FARAONE CORTESE Molecular Psychiatry 2022:27:212-19

Objectives

Employ the concept of less vs more when creating detailing materials

Examine key features of detailing materials that affect their usefulness

Implement detailers' views on materials they find effective to translate knowledge to practice

Our Teams Approach

Feedback from the PAD team

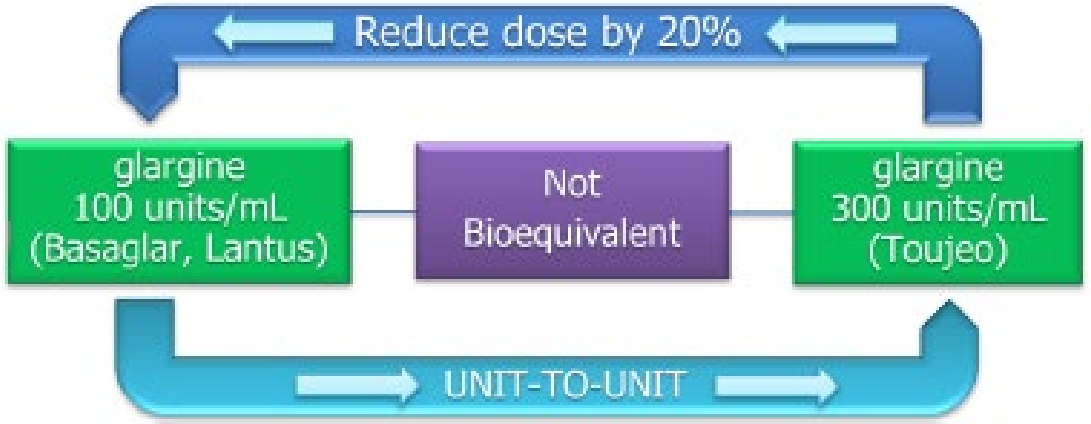
Feedback

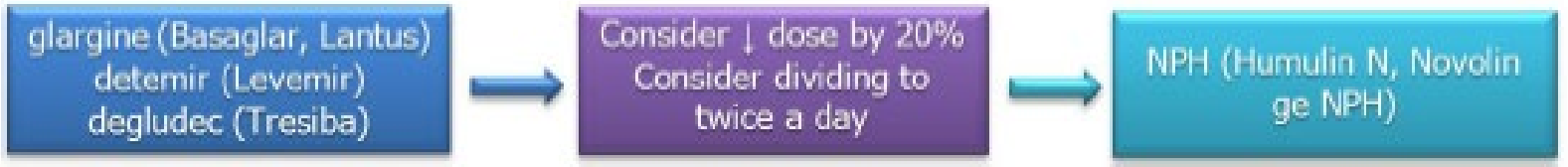
Cristi:

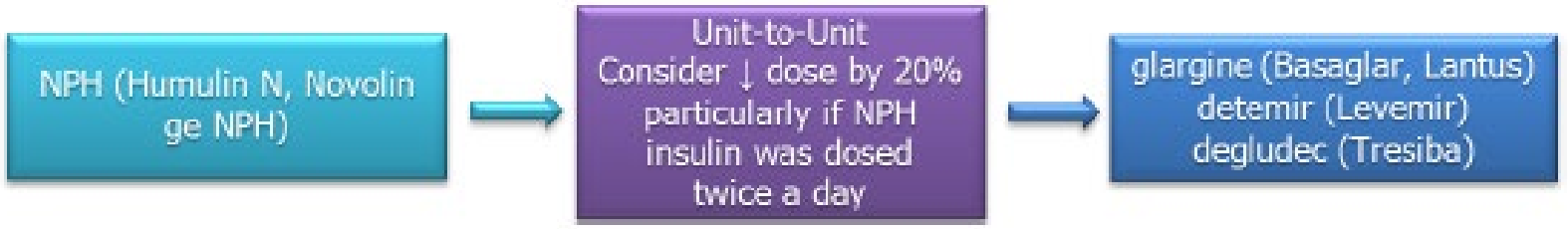
"This is a very difficult thing to balance: a handout that includes a lot of useful and important information but is also easy to use virtually."

"My favorite topic to detail on virtually was basal insulin. There were not many medications to cover, lots of practical information, and simple tables or visuals that could be copied into a PowerPoint. Even simply using the PDF as a detailing aid worked."


glargine
100 units/mL
(Lantus)
Unit-to-Unit
glargine biosimilar
100 units/mL
(Basaglar)


Reduce dose by 20%
glargine
100 units/mL
(Basaglar, Lantus)
Not
Bioequivalent
glargine
300 units/mL
(Toujeo)
UNIT-TO-UNIT


glargine (Basaglar, Lantus)
detemir (Levemir)
degludec (Tresiba)
Consider ↓ dose by 20%
Consider dividing to
twice a day
NPH (Humulin N, Novolin
ge NPH)


NPH (Humulin N, Novolin
ge NPH)
Unit-to-Unit
Consider ↓ dose by 20%
particularly if NPH
insulin was dosed
twice a day
glargine (Basaglar, Lantus)
detemir (Levemir)
degludec (Tresiba)

Feedback

Cristi:

"We have different detailing styles which adds complexity when creating materials. I like simple, visual slides, with key words or charts/bar graphs/images that people can remember. I build a conversation around these, vs. complex slides with every detail on them. However, I know others prefer the opposite and simple, bare slides don't make good handouts."

Aron:

"It is really difficult as some physicians need high level overview of a topic, and others enjoy the minutiae. Designing a handout to enable both situations is understandably difficult."

ADHD Medications: BC PharmaCare coverage

Regular Benefit Drug
minimum 1 week trial at adequate dose

methylphenidate
immediate or sustained release
Ritalin IR generics§, Ritalin SR generics§

dextroamphetamine
immediate or sustained release
Dexedrine*, Dexedrine Spansules*, generics

If unsatisfactory trial or intolerance to EITHER class above and patient requires 12 hours of continuous medication coverage, can apply for Special Authority for a long-acting stimulant

methylphenidate
extended release
Concerta*, generics

amphetamine mixed salts
extended release
Adderall XR generics†

lisdexamfetamine
Vyvanse**

If unsatisfactory trial or intolerance to BOTH a methylphenidate AND an amphetamine above (at least one extended release or long acting), can apply for Special Authority for atomoxetine

atomoxetine
Strattera generics†

Unsatisfactory trial or intolerance defined as no demonstrated effectiveness for symptoms of ADHD or functional impairment secondary to ADHD after a minimum 1 week trial at adequate dose(s)

§Ritalin brand name no longer marketed in Canada
*Concerta and Dexedrine brand formulations reimbursed up to the cost of generic formulations
**Vyvanse capsules are Limited Coverage, chewable tablets are a Non-Benefit
†Adderall XR and Strattera brand formulations are Non-Benefits

Feedback

Aron:

"Big picture thru two topics: Great goal to have short info dense handout slides. Also, would be useful to design detailing slides which do better job highlighting key points, as opposed to asking detailers to chop up and personalize dense slides."

"Examples: the T2DM overview slide 3 and insomnia prescribing principles slides are fabulous for detailing. The drug info slides are not fabulous for detailing, but great references. I think keep making the detailed reference slides, and design useable visually appealing simpler detailing versions from them in advance."

Medications for Insomnia: Prescribing Principles

Ask patients "What do you hope to achieve with insomnia treatment?"[1]

Review for medications that can cause insomnia & consider the potential for prescribing cascades.

Implement non-pharmacologic strategies.[1-3]

Use low starting doses and note changes to the maximum doses intended to reduce the risk of next day impairment with benzodiazepine receptor agonists.[4]

Decisions about effectiveness can be made early. The drug approval process requires evidence of efficacy within the first 1 to 2 nights of use.[5,6]

Limit prescriptions of benzodiazepines & benzodiazepine receptor agonists to intermittent or short-term use.[4,7,8]

Review for interacting medications that could narrow the therapeutic window.

Recognize the harms associated with off-label medications including low doses of quetiapine and trazodone.

Revisit ongoing use with an individualized & practical plan based on treatment goals (eg, dose reduction, less frequent use, or tapering & deprescribing).[8,9]

1. VA DoD 2019 Guideline; 2. AASM 2017 Guideline; 3. ACP 2016 Guideline; 4. Health Canada Drug Product Database;
5. US FDA 2009 Doxepin Review; 6. US FDA 2019 Lemborexant Review; 7. Therapeutics Initiative 1995 Letter 11;
8. Canadian BZRA Use Disorder 2019 Guideline; 9. Deprescribing.org BZRA Deprescribing 2018 Guideline

Feedback

Jen:

"Overall, slide 3 from both decks are my absolute favorites, you can have entire conversations from both of these or go into more detail with subsequent pages as participants need it. As both Aron and Cristi have stated, it's a fine balance of too much or too little on a handout."

"Personally, I like the small details for clinicians to refer back to and, yes, lots of people tell me they do this. But I don't like to present virtually with them and only show parts or highlights of most pages."

Medications for Insomnia: Topics for Discussion

- GOALS
- MEDICATIONS CAN CAUSE INSOMNIA
- NON-PHARM
- DOSING
- DRUG APPROVAL PROCESS
- BZD'S & BZRA'S
- DRUG INTERACTIONS
- OFF-LABEL MEDICATION HARMS
- TAPERING

Feedback

Aron:

"Side by side comparison slide comparing the most relevant decision points would be really, really good. Even if price or duration of action is all we can highlight. But a one stop shop on how to decide is useful for discussion."

Tanya:

"For the T2DM topic, slide 3 was great, and I agree that side by side comparisons on a slide work well for discussion. Maybe we can try to incorporate more of this for our next topic."

Translating ADHD Medication Formulation Pharmacokinetics

- The US Food and Drug Administration states that for methylphenidate and amphetamines, there is a relationship between drug concentration and efficacy and adverse events; modification to drug pharmacokinetics may impact onset and duration of these effects.[1]
- There are differences in the pharmacokinetics between formulations but they are measured in small sample sizes and under varying conditions which makes it difficult to directly compare medications. This table provides our best estimates.
- Formulations which combine immediate and sustained-release features (eg, extended/delayed/controlled release) are principally designed to mimic the changing serum levels of immediate release formulations dosed multiple times a day, but avoid the need for a dose at school or work.[2,3,4]

Formulation		Tmax1	Tmax2	Duration of effect
Methylphenidate	**Drug Release Features**			
Ritalin tablets[2]	immediate release (IR) only	2 hours	none	12 hours (when dosed TID)
Ritalin SR tablets[2,3]	sustained release (SR) only	3.8 hours	not expected	8 hours
Concerta tablets[2]	biphasic: 22% IR, 78% SR	1 hour	6-10 hours	12 hours
Biphentin capsules[2,4,5]	biphasic: 40% IR, 60% SR	1-3 hours	6-7 hours	12 hours
Foquest capsules[2]	biphasic: 20% IR, 80% SR	1-2.5 hours	8.5-16 hours	16 hours
Amphetamines				
Dexedrine tablets[2,6]	immediate release (IR) only	3 hours	none	not provided
Dexedrine Spansule capsules[2,6,7]	biphasic: 40% IR, 60% SR	8 hours	information not provided	10-12 hours
Adderall XR capsules[2,3]	biphasic: 50% IR, 50% SR	5-7 hours		12 hours
Vyvanse capsules[2,6]	amphetamine prodrug	3.5-4.5 hours	not expected	12-14 hours

Feedback

Nancy:

"Links in the handouts were very appreciated practical tools (everything from CBTi, deprescribing.org handouts, sick day management etc)."

Insomnia

Non-Pharmacologic Strategies for Insomnia

Cognitive Behavioural Therapy for Insomnia (CBTi)[1-6]

- Guidelines strongly recommend CBTi for chronic insomnia.
- Involves cognitive therapy strategies along with behavioural strategies which include sleep restriction and stimulus control with or without relaxation techniques and sleep hygiene.
- Compared to inactive control, CBTi decreases time to fall asleep by ~12 minutes and decreases awake time after sleep onset by ~22 minutes.[5] Comparisons to drug therapy are limited.[1,3,6]

Brief Behavioural Therapy for Insomnia (BBTi)[2-6]

- Practical techniques if CBTi not possible.
- Involves sleep restriction and stimulus control with or without relaxation techniques and sleep hygiene.

Patient Resources	
CBTi, BBTi	Kelty's Key Vancouver Coastal Health Online Therapy[7] Self help modules keltyskey.com/courses/insomnia/
Stimulus Control	Establishing the bedroom as a cue for sleep rather than wakefulness[3] Kelty's Key Module 5: Creating a Sleep Sanctuary[7] Stimulus Control Patient Fact Sheet (Australia)[8]
Sleep Restriction	Limit time in bed to actual sleep time followed by gradual adjustment as sleep efficiency improves[3] Kelty's Key Module 6: Setting Your Sleep Window[7] Sleep Restriction Patient Fact Sheet (Australia)[8]

Tips

- Some third party plans provide coverage for CBTi (with in-person or online therapists)
- Requires time, motivation, and encouragement
- Recommending sleep hygiene on its own has not been shown to be effective in treating chronic insomnia[3,4]
- Sleep restriction: caution in high-risk occupations due to potential for sleepiness during initial phase of sleep restriction[3]
- Book "Say Goodnight to Insomnia" (Gregg D. Jacobs)

1. ACP 2016 Guideline; 2. Alberta TOP 2015 Guideline; 3. VA DoD 2019 Guideline; 4. AASM 2006 Guideline; 5. AHRQ 2015 Evidence Report; 6. CADTH 2018 Evidence Review; 7. Kelty's Key Vancouver Coastal Health Online Therapy; 8. South Australia Drug and Alcohol Services

Objectives

Employ the concept of less vs more when creating detailing materials

Examine key features of detailing materials that affect their usefulness

Implement detailers' views on materials they find effective to translate knowledge to practice

Large Group Discussion:
Hearing From You

Consider 2 examples of BC PAD slides/handouts (**Hypertension and T2DM**)

1. **What works well for you? What does not?**
2. **How to balance too much information versus too little?**

Hypertension in Primary Care: Blood Pressure Goals for Adults Aged 60 and Older

B.C. Provincial Academic Detailing Service November 2017

Which sources of evidence contribute to recommendations for systolic blood pressure goals?

The American College of Physicians and the American Academy of Family Physicians 2017 weak recommendation for a SBP goal < 140 mmHg in adults aged 60 and older was informed by a systematic review which included SPRINT 2015 and five other RCTs comparing more intensive versus less intensive BP goals.[4,5]

WEISS 2017[5] authors' summation [6 RCTs, N=41,491; 2-5 years]: "Tighter control may prevent, on average, roughly 10 to 20 events for every 1000 high-risk patients treated over 5 years across a population, but more aggressive treatment is likely associated with greater medication burden and higher risk for adverse effects".

Trials comparing BP goals of < 140/≤ 85 mmHg versus < 150-160/≤ 90 mmHg were included.

Trials comparing more intensive SBP goals of < 120 mmHg versus < 140 mmHg were included.

WEISS 2017[5] Benefits and harms of intensive blood pressure in adults aged ≥ 60	6 RCTs; N=41,491	2-5 years

all-cause mortality	ARR 0.8%	**Roughly 10 to 20 fewer events for every 1000 high-risk patients treated over 5 years**	RR 0.86 [95%CI 0.69, 1.06] low quality
fatal and nonfatal stroke	ARR 0.5%		RR 0.79 [95%CI 0.59, 0.99] moderate quality
fatal and nonfatal coronary events	ARR 0.9%		RR 0.82 [95%CI 0.64, 1.00] low quality

Two RCTs contributed the most weight to WEISS 2017; both trials compared SBP < 120 mmHg versus SBP < 140 mmHg
- ACCORD-BP 2010: N=4733, 4.7 years follow up, type 2 diabetes with CV risk factors, CVD 34%, baseline BP 139/76 mmHg[6]
- SPRINT 2015: N=9361, 3.3 years follow up, CV risk factors but without diabetes, CVD 20%, baseline BP 140/78 mmHg[7]

Discordant results all-cause mortality
- ACCORD-BP 2010: HR 1.07 [95%CI 0.85, 1.35][6]
- SPRINT 2015: HR 0.73 [95%CI 0.60, 0.90][7]

Concordant results serious adverse events attributed to treatment
- ACCORD-BP 2010: ARI 2.0%; 20 more per 1000 [P < 0.001][6]
- SPRINT 2015: ARI 2.2%; 22 more per 1000 [P < 0.001][7]

Total serious adverse events [net benefit]: this systematic review did not analyze total serious adverse events

Hypertension Canada's strong recommendation for a SBP goal ≤ 120 in 'high-risk' adults [including those aged 75 and older] was defined principally by the SPRINT 2015 trial.[7,8]

SPRINT 2015[7] Randomized trial of intensive versus standard blood-pressure control	1 RCT; N=9361	3.3 years

Age ≥ 50 and SBP 130-180 mmHg with cardiovascular risk factors: A) age ≥ 75 [28%], or B) clinical or subclinical cardiovascular disease [20%], or C) chronic kidney disease with eGFR 20-59 mL/min/1.73 m^2 [28%], or D) Framingham 10-year cardiovascular risk score ≥ 15% [61%]

Without diabetes, prior stroke, heart failure, polycystic kidney disease, eGFR < 20 mL/min/1.73 m^2, adherence concerns, residence in assisted-living or long-term care facility, or standing SBP < 110 mmHg

mean age 68, 36% women	baseline 140/78 mmHg	91% receiving antihypertensives at baseline
SBP goal 135-139 mmHg	achieved 136/76 mmHg	# antihypertensives ≤ 2 = 77% | 3 = 17% | ≥ 4 = 7%
SBP goal < 120 mmHg	achieved 121/69 mmHg	# antihypertensives ≤ 2 = 45% | 3 = 32% | ≥ 4 = 24%

all-cause mortality	ARR 1.2%	**NNTB 63** [CV morb & mort] **NNTH 45** [serious adverse*]	HR 0.73 [95%CI 0.60, 0.90] single RCT
cardiovascular morbidity & mortality	ARR 1.6%		HR 0.75 [95%CI 0.64, 0.89] single RCT
serious adverse events*	ARI 2.2%		HR 1.88; P < 0.001 single RCT

Primary cardiovascular composite outcome first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure or cardiovascular death

Serious adverse events possibly or definitely related to the intervention*: ↑ hypotension, syncope, electrolyte abnormalities, acute kidney injury | Total serious adverse events intensive treatment group = 38.3%; standard treatment group = 37.1% [HR 1.04; P = 0.25]

BP measurement method average of 3 automated office readings while seated after 5 minutes of quiet rest; the American College of Cardiology/American Heart Association 2017 high blood pressure guideline identifies that this may limit confident extrapolation of an SBP goal < 120 mmHg to general clinical practice if the same BP measurement method is not used[9]

SBP goal < 120 mmHg achieved by < 50% participants in the intensive group | Unscheduled clinic visits 30% more in intensive group[10]

Baseline SBP ≥ 160 mmHg = 10% [N=976][11] | Older adults age ≥ 75 = 28% [N=2636] age ≥ 80 = 12% [N=1159][12]

Early trial termination 3.3 years versus planned 5 years | Open label | Lost to follow up or withdrew consent 5.5% [N=520]

RCT=randomized controlled trial; ARR=absolute risk reduction; ARI=absolute risk increase; RR=relative risk; HR=hazard ratio; 95%CI=95% confidence interval N=number of participants; NNTB=number needed to treat for an additional beneficial outcome; NNTH=number needed to treat for an additional harmful outcome

Type 2 Diabetes: Non Insulin Medications Overview

Non Insulin Medications

Available in Canada

- metformin
- sulfonylureas: gliclazide, glyburide, glimepiride
- acarbose
- repaglinide
- thiazolidinediones: pioglitazone, rosiglitazone
- DPP4 inhibitors: linagliptin, sitagliptin, saxagliptin, alogliptin
- SGLT2 inhibitors: empagliflozin, canagliflozin, dapagliflozin
- GLP1 agonists: semaglutide subcut, semaglutide oral, liraglutide subcut, dulaglutide subcut, exenatide subcut, lixisenatide subcut

Annual drug cost *approx*	
metformin	< $50
gliclazide	< $150
DPP4 inhibitors	$900-$1300
SGLT2 inhibitors	$1100
GLP1 agonists	$2800-$3800

Drug Class Indications Beyond HbA1c Lowering

Health Canada
US FDA

	DPP4 inhibitors	SGLT2 inhibitors	GLP1 agonists	Clinical Outcome Trial Doses
Type 2 Diabetes with Cardiovascular Disease		+	+	empagliflozin 10 or 25 mg PO once a day* canagliflozin 100 or 300 mg PO once a day* dapagliflozin 10 mg PO once a day* semaglutide 0.5 or 1 mg subcut once a week semaglutide 14 mg PO once a day liraglutide 1.8 mg subcut once a day* dulaglutide 1.5 mg subcut once a week*
Type 2 Diabetes with Multiple Cardiovascular Risk Factors		+	+	
Diabetic Nephropathy		+		canagliflozin 100 mg PO once a day*
Chronic Kidney Disease		+		dapagliflozin 10 mg PO once a day*
Heart Failure		+		empagliflozin 10 mg PO once a day* dapagliflozin 10 mg PO once a day*
Chronic Weight Management			+	liraglutide 3 mg subcut once a day* semaglutide 2.4 mg subcut once a week*

* Denotes which SGLT2i or GLP1a has a Health Canada indication as of September 2021

PharmaCare Coverage British Columbia

regular benefit	metformin	glyburide				
limited coverage	gliclazide	linagliptin	saxagliptin	pioglitazone	empagliflozin	semaglutide subcutaneous

Large Group Discussion:
Hearing From You

Consider 2 examples of BC PAD slides/handouts (**Hypertension and T2DM**)

3. **What do you think clinicians prefer:**

   a) a lot of detailed information to reflect back on or high-level overview with a couple of key messages to take home?

   b) simple handouts or detailed handouts and then a core set of simple slides for detailing? (ex. antidepressants)

Breakout Sessions:
We'll see you in 25 minutes!

Describe ONE feature of the BC PAD Hypertension or T2DM materials that stood out to you as helpful or a hindrance in providing details in a hybrid setting (in-person or virtual).

Think about your team's current approach. Discuss an example of your materials (or share!) and discuss:

1. Based on a recent topic you have delivered or one you are preparing, what is working well? What is not?
2. What would you try differently based on today's discussion?
3. How are you trying to balance too much/too little information?
4. What feedback can your group offer other academic detailing teams?

Summary and Closure

- In a hybrid world, it is more important than ever to make materials work for both the detailer and clinician in a **variety of settings**

- It is useful to **explore concepts and examples** of detailing materials from the academic detailing community to help teams develop and refine their knowledge translation materials

Please rejoin the main room now by clicking on the link in the chatbox.