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Dr. Jennifer Swainson is is a psychiatrist at the Misericordia Community Hospital in Edmonton with expertise in treating difficult mood disorders and their comorbid conditions. Dr. Swainson is certified by the American Board of Obesity Medicine and has interest in the reciprocal relationships between mood disorders, sleep, and obesity and their subsequent treatment considerations when they co-occur. Dr. Swainson has served on several advisory committees to the College of Physicians and Surgeons of Alberta (CPSA) in regard to CPSA tracking of high risk medications, and considerations for safe prescribing of ketamine for depression. Dr. Swainson is a co-author of the Canadian Network in Mood and Anxiety Treatments (CANMAT) 2023 Depression Treatment Guidelines and was lead author of the 2021 CANMAT Task Force Update on Ketamine for Depression. She is involved in clinical research and has authored numerous other publications focused on ketamine and esketamine for depression and has been an advocate for safe and accessible use of ketamine for mood disorders. Dr. Swainson is an active teacher of students and residents, and is a frequent speaker for family physicians on topics of mood and insomnia.

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DEPRESSION UPDATE: A BRIEFING ON THE CANADIAN MOOD AND ANXIETY DISORDER TREATMENT (CANMAT) 2023 DEPRESSION GUIDELINES AND ADVICE FOR THEIR APPLICATION IN PRIMARY CARE

Introduction

The Canadian Mood And Anxiety Disorder Treatment (CANMAT) guidelines for depression, last published in 2016, have now been updated with literature through to 2023, and have been recently published in 2024 (Lam et al , Canadian J Psych, In press 2024). This 92-page document thoroughly addresses aspects of depression management, using evidence based on the literature, and supplemented by an expert consensus of the 57 co-authors. While thorough, this document remains cumbersome for a busy primary care clinician to sort through and apply to everyday practice. Here, we present a summary of evidence for the treatment of depression, along with practical advice for clinical decision making in primary care.

Screening and Diagnosis

The CANMAT 2023 recommends screening patients with risk factors for depression with a validated self-rated instrument such as the Patient Health Questionnaire-2 (PHQ-2), and if positive, the PHQ-9. Risk factors cited in the CANMAT guidelines include a history of childhood adverse events, family history of mood disorders, chronic and non-psychiatric medical illnesses (including obesity as per Obesity Canada recommendations), psychiatric comorbidities, substance use disorders, insomnia and night shift work, female sex (especially during puberty, pregnancy, postpartum, perimenopause), recent stressful life events, job strain/income inequality, bereavement, peer victimization/bullying/cyberbullying, gender dysphoria, and a sedentary lifestyle/significant screen time.

(The PHQ-2 and PHQ-9 may be found here: https://www.albertahealthservices.ca/frm-19825.pdf)

A PHQ-9 score greater than 10 with both sensitivity and specificity rates of 88% is positive for major depression.[1] In addition to the total score, the frequency of symptoms must be considered. Major depressive disorder is suggested if 5 or more of the items are reported as occurring at least "more than half the days", but this must be followed up with a clinical interview to assess individual symptoms, as well as psychiatric and medical differential diagnoses that could be contributing to the symptoms.

Clinicians should consider screening patients with depression for bipolar disorder, because bipolar depression would require treatment with a mood stabilizer.[2] Antidepressant monotherapy in a patient with bipolar disorder is unlikely to be efficacious and may cause harm by eliciting mania or hypomania. The Rapid Mood Screener (RMS) is a 6-item self rated scale with an 88% sensitivity and an 80% specificity for bipolar I disorder.[3] Factors from a person's history that may point toward bipolarity include a family history of bipolar disorder, earlier age of first depressive episode (i.e. teens), atypical depressive features (e.g. hypersomnia, increased appetite), depression during pregnancy/postpartum, premenstrually related mood symptoms, pathological guilt, leaden paralysis, and psychotic depression.[4]

ADVICE: Screen at risk patients first with the PHQ-2:

- In the past two weeks, have you been bothered by having little interest or pleasure in doing things?
- In the past two weeks have you felt down, depressed, or hopeless?

If one answer is YES, proceed to the PHQ-9

If the PHQ-9 is positive, follow up with a clinical assessment

Treatment

Prompt treatment of depression is paramount as a longer duration of depression is associated with a greater resistance to treatment and a reduced likelihood of remission. Psychoeducation for patients to emphasize that returning for their follow up appointments is essential to ensure that their treatment can be optimized. Patients should receive psychoeducation about the fact that early treatment is most likely to have the best outcome.

Lifestyle Modification and Complementary and Alternative Medicines

Lifestyle and complementary and alternative medicines (CAM) treatments do not reach the level of evidence of pharmacotherapy; however, the CANMAT 2023 guidelines note that they could be used as monotherapy for mild depression (with a PHQ-9 score of 5–9) if this is the patient's preference. These treatments can be considered as adjunctive measures for moderate to severe depression (with a PHQ-9 of >9).

Lifestyle interventions, which include light therapy, healthy diet (Mediterranean style diet, or a "healthy" diet avoiding processed foods and added sugars), exercise, smoking cessation, and sleep hygiene, have all demonstrated a potential benefit in managing depression. Of these, light therapy and exercise have the strongest evidence. Supplements with some evidence for treating depression include Omega 3's[5] (CANMAT 2023) and Vitamin D.[5] CAM treatments with supporting evidence for treating depression include acupuncture, L-methyl folate, St. John's Wort (but not with antidepressants due to serotonin syndrome risk), S-adenosylmethionine, dehydroepiandrosterone, saffron, lavender, and roseroot.

ADVICE: *Mild depression with little functional impairment may be treated with lifestyle interventions/CAM and/or psychotherapy but ensure that the patient follows up with you to assess the efficacy of this treatment approach. Consider pharmacotherapy if the patient is not improving.*

Psychotherapy

Psychotherapy is often used in combination with pharmacotherapy for moderate-to-severe depression, but it may be effective on its own for mild depression. The strongest evidence is for Cognitive Behavioural Therapy (CBT), Interpersonal Therapy, or Behavioural Therapy occurring at least once, but preferably twice a week, and the CANMAT 2023 guideline note that there is little evidence for therapy occurring less than weekly in the acute phase of treatment. Barriers to accessing timely therapy are a reality, and despite having little evidence of support, potentially helpful guided digital health interventions, such as online CBT are listed in the guidelines as treatment options.

New additions to the guidelines include several second line psychotherapy options; mindfulness based cognitive therapy, short term psychodynamic therapy, and transdiagnostic psychological treatment of emotional disorders. A new listing as a third line of therapy is "Meta Cognitive therapy." While evidence does not support commonly practised eclectic uses of multiple forms of therapy (CANMAT 2023), non-standardized therapies are difficult, if not impossible, to study. From a practical standpoint, the optimal therapy may be what your patient can access, and the patient-therapist rapport has previously been noted to be the most predictive of positive outcomes.[6]

ADVICE: *In acute depression, frequent psychotherapy, provided once or twice a week, offers the most benefit. Establishing a positive patient rapport with the therapist is important.*

Pharmacotherapy

Within the CANMAT document, multiple pharmacotherapy options are included, and potential side effects are described. Here, treatment choices will be presented through a lens of balancing efficacy with side effects. In particular, the long-term risk of weight gain and metabolic effects are considered owing to the frequency of related comorbid conditions in primary care.

Antidepressant	Class	Typical Dose Range	Notes to Consider
Bupropion (most often used in XL form)	NDRI	150–300 mg	• Favourable side effect profile
Vilazodone	Multimodal	10–40 mg	• Favourable side effect profile
Vortioxetine	Multimodal	10–20 mg	• Favourable side effect profile
Desvenlafaxine	SNRI	50-100 mg	• Favourable side effect profile
Duloxetine	SNRI	60–120 mg	• Consider use if comorbid neuropathic pain, fibromyalgia
Levomilnacipran	SNRI	40–120 mg	
Venlafaxine-XR	SNRI	75–225 mg	• Significant discontinuation syndrome
Citalopram	SSRI	20–40 mg	• CANMAT flags QTc as a potential issue
Escitalopram	SSRI	10–20 mg	
Fluoxetine	SSRI	20–60 mg	
Fluvoxamine	SSRI	100–300 mg	
Paroxetine	SSRI	20–50 mg	• Associated with significant weight gain • Significant discontinuation syndrome
Sertraline	SSRI	50–200 mg	
Mirtazapine	NaSSA	30–60 mg	• Consider use if weight gain is desired (low body mass index)

Table 1. Potential first line anti-depressants and dosage ranges; *courtesy of Jennifer Swainson, MD.*

Abbreviation: QTc: Corrected QT interval

Choice of Initial Antidepressant

The CANMAT guideline list 17 first line antidepressants, 14 of which are available in Canada. The new first line additions since the 2016 guideline are levomilnacipran, a serotonin-norepinephrine reuptake inhibitor (SNRI), and vilazodone (multimodal). Another new addition (second line) is a combination of dextromethorphan and bupropion, approved in the United States but unavailable in Canada.

A recent meta-analysis of antidepressants found vortioxetine (multimodal antidepressant) to be the most efficacious and acceptable antidepressant, followed by escitalopram.[7] Amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine were reported to have slightly better efficacy but these overall differences were not felt to clearly distinguish these first line agents from the others (CANMAT 2024). Amitriptyline is considered as a second line treatment owing to its side effect profile.

Given the number of first line treatment options, the initial choice of antidepressant should be made in collaboration with the patient and with consideration of the side effect profile. Weight gain, sedation, and sexual side effects are frequently reported as long-term side effects that may lead to medication non-adherence and a lower quality of life, and in the case of weight gain, medical morbidity. Based on available data, and the CANMAT author consensus, only 4 of the 14 first line agents are described as having a favourable side effect profile in all 3 of those areas (**Table 1**). These include bupropion, a norepinephrine-dopamine reuptake inhibitor (NDRI), desvenlafaxine (SNRI),

vilazodone (multimodal antidepressant), and vortioxetine (multimodal antidepressant). The selective serotonin reuptake inhibitors SSRIS and duloxetine are generally associated with significant sexual side effects; thus, they may not be the optimal first choice of treatment. Mirtazapine and paroxetine are associated with the most significant weight gain, and mirtazapine is also associated with significant sedation. While any first line agent may be appropriate, and other factors such as cost, patient preference, comorbidities, and the potential for drug interactions must be considered, a simple and practical practice algorithm includes choosing one of the four antidepressants with the more favourable side effect profile (**Table 1**).

ADVICE: *Consider efficacy and tolerability when selecting an antidepressant. CANMAT identifies four first line antidepressants as having a more favorable side effect profile when considering long term risks of weight gain, sedation, and sexual side effects. There are antidepressants with better long-term side effect profiles than the commonly used SSRIs.*

Follow up of the First Antidepressant Trial

Follow up should occur 2–4 weeks after antidepressant initiation. At this time, both efficacy and tolerability should be assessed. If there is little response by 4 weeks after dose optimization, response or remission at 8–12 weeks is unlikely, and the patient should be assessed for factors contributing to the non-response including medication adherence, adequacy of dose and duration, comorbid psychiatric or medical factors, and ensuring a correct diagnosis.

After determining that the diagnosis of unipolar depression is correct, the decision for the next step should be made in collaboration with the patient. A dose increase may be considered if the initial treatment is well-tolerated. If the initial antidepressant has poor tolerability, there has been a lack of response, or if the patient prefers, the antidepressant may be switched. While the CANMAT reports that there is little data to support a preference for switching to a different class of antidepressant, it is a common practice to attempt an agent with a different mechanism, again considering the side effect profile.

If an optimized dose of an antidepressant elicits a partial response and is well tolerated, the next step would be to add an adjunctive medication. Repeated antidepressant switches are unlikely to be of benefit.

TIP: *If you switch antidepressants, do it only once before moving on to the addition of an evidence based adjunctive treatment.*

Adjunctive Treatments

The only 2 first line adjunctive agents are third generation atypical antipsychotics–aripiprazole and brexpiprazole (**Table 2**). A new addition to the guidelines is another third-generation atypical agent, cariprazine, which, though indicated as an adjunct therapy for depression in the United States, is considered off label in Canada for this use, and is considered a second line treatment in the CANMAT 2023. These third-generation antipsychotics are considered distinct from second generation antipsychotics owing to their mechanism of dopamine partial agonism, and the fact that they are less likely than several other atypical antipsychotics to be associated with weight gain, but they may be more likely to cause extrapyramidal side effects such as akathisia. Adjunctive therapies with the best evidence should typically be used first. To mitigate the weight gain risk of atypical antipsychotic adjuncts, the addition of metformin or glucagon-like peptide-1 (GLP-1) agonists may be considered.[8]

Other second line add-on strategies include antidepressants such as bupropion or mirtazapine, lithium, triiodothyronine, or modafinil. Risperidone and quetiapine have been newly relegated to the second line in the 2023 guidelines owing to concerns with metabolic effects, and failed trials for risperidone. Olanzapine remains a second line treatment owing to its significant metabolic effects.

ADVICE: *When using atypical antipsychotics as an adjunctive treatment, use aripiprazole, brexpiprazole, or cariprazine before risperidone, quetiapine or olanzapine owing to better evidence for efficacy and/or a better metabolic profile.*

Novel Adjunctive Approaches

Intravenous ketamine and intranasal esketamine are newly recognized in the 2023 guidelines as effective adjunctive treatments that are listed in the second line due to limitations with patient access. Both treatments must be administered and observed in a health care setting and are generally not conducive to most primary care practices. Additionally, the public mental health system offers limited opportunities for these treatments. Non-intravenous forms of ketamine are now considered a third line adjunct, however, data are limited for optimal dosing or frequency, thus careful consideration must be given before prescribing this form of treatment.[9] CANMAT has previously advised that non-intravenous ketamine should be used only by or in conjunction with specialist support.[9,10]Additionally, prescribing guidelines and monitoring requirements from provincial colleges may vary.

While there is much mainstream media and online discussions about psilocybin and "microdosing", psilocybin remains an investigational treatment and is not recommended to treat depression.[11] Cannabis is also not recommended owing to a lack of efficacy, and it has been

Line of Treatment	Adjunctive Agent	Target Dose[1]	Ease/Appropriateness of Use in Primary Care
First Line	Aripiprazole	2–10 mg	YES
	Brexpiprazole*	0.5–2 mg	YES
Second Line	Bupropion	150–450 mg	YES
	Intranasal esketamine*	56–84 mg intranasally	NO, needs to be administered and monitored
	Intravenous (IV) racemic ketamine*	0.5–1.0 mg/kg IV	NO, needs to be administered and monitored
	Olanzapine	2.5–10 mg	NOT routinely–weight gain
	Quetiapine-XR*	150–300 mg	NOT routinely–weight gain
	Risperidone*	1–3 mg	NOT routinely–Weight gain
	Lithium	600–1200 mg (therapeutic serum level: 0.5–0.8 mmol/L)	YES, but check TSH, CR, and note target Li level
	Cariprazine*	1.5–3 mg	YES
	Mirtazapine / Mianserin	30–60 mg/30–90 mg	YES–but note fatigue/weight gain
	Modafinil	100–400 mg	YES–cost may be an issue
	Triiodothyronine	25–50 mcg	YES
Third Line	Other antidepressants, including tricyclic antidepressants	Varies with the medication	YES, if comfortable prescribing
	Stimulants	Varies with the medication	YES–see CADDRA stimulant dose tables
	Lamotrigine*	100–300 mg	YES–start at 25 mg and increase weekly due to Stevens Johnsons risk
	Non-IV racemic ketamine*	Varies with the medication	NO
	Pramipexole*	1–2 mg twice daily	YES
	Ziprasidone	20–80 mg twice daily	YES, but rarely used in psychiatry due to limited clinical efficacy
Investigational	Psychedelic-assisted psychotherapy*	Moderate to high doses accompanied by psychotherapy	NO
Not Recommended	Cannabis* (insufficient evidence for efficacy; risk of harm)	NOT applicable	NOT applicable

Table 2. Adjunctive Treatment Options for Depression; *courtesy of Jennifer Swainson, MD.*

*Table adapted for primary care from the CANMAT 2023 depression guideline.

[1] Dose ranges are taken from product monographs; in clinical care, doses below and above the range may be used.

Abbreviations: CADDRA: Canadian ADHD Resource Alliance; **CANMAT:** Canadian Mood And Anxiety Disorder Treatment Guidelines; **CR:** creatinine; **IV:** intravenous; **Li:** lithium; **TSH:** thyroid stimulating hormone

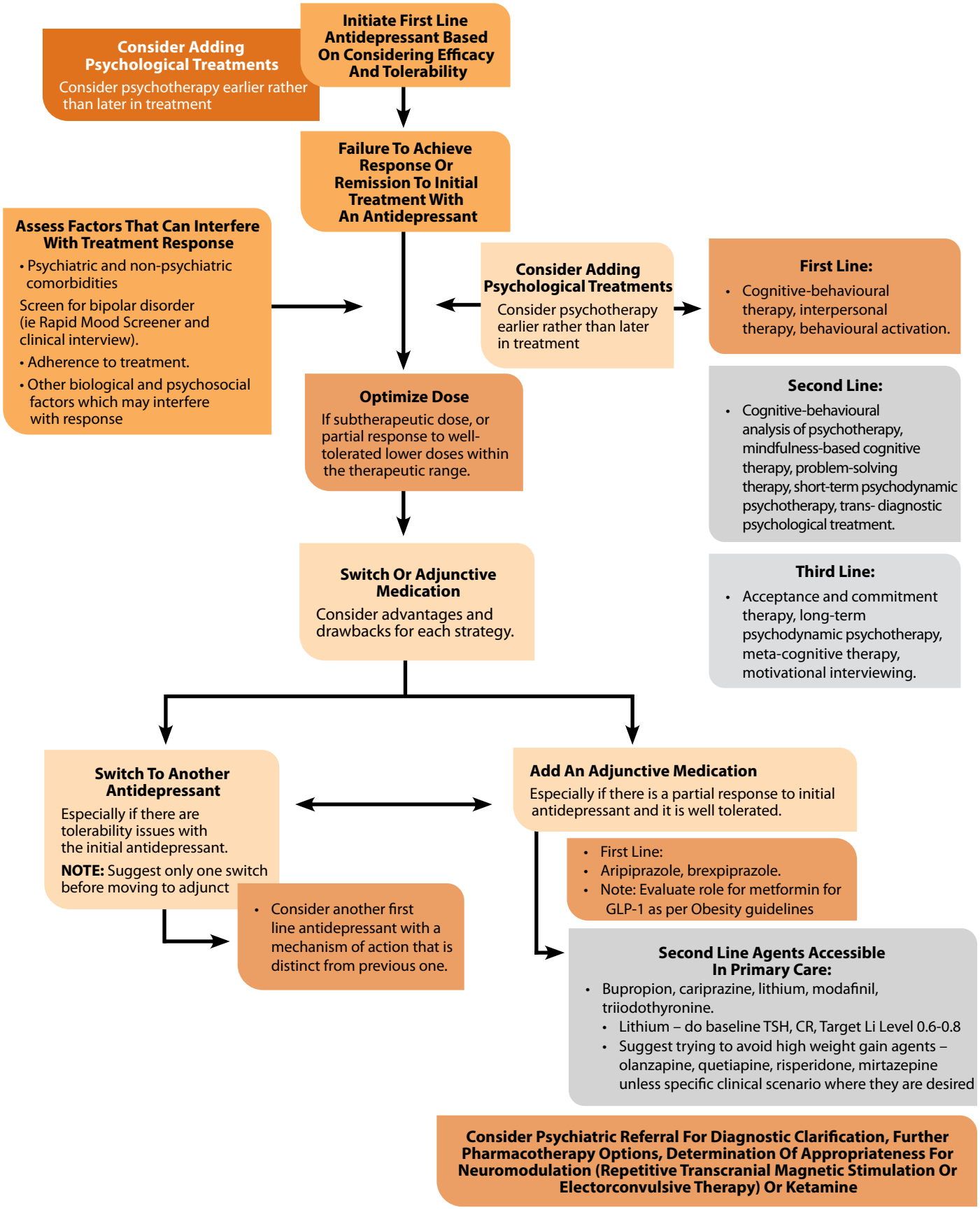

Figure 1. Algorithm for initial antidepressant treatment; *adapted from CANMAT paper.*

found to worsen the course of both depression and bipolar disorder.[12]

ADVICE: *Non-medical/self treatment with ketamine or psilocybin should be actively discouraged.*

Remission

Once a patient reaches remission after a first episode, the antidepressant should be continued for 6 to 12 months. If there is a history of multiple episodes or risk factors for recurrence, the antidepressant should be continued for 2 years or more. Risk factors include residual depressive symptoms, more severe depressive episodes, previous depressive episodes, comorbid medical or psychiatric illness, limited supports, life stressors, and a history of childhood maltreatment.

ADVICE: *If the patient required an adjunctive treatment to reach remission, the depression was more difficult to treat and would be at risk of recurrence.*

When to Seek Psychiatric Consultation

Trials of 2 antidepressants plus at least one adjunctive treatment should be tried before seeking psychiatric consultation. If the patient has not responded to this sequence of treatments, they can be considered to have treatment resistant, or difficult-to-treat depression, and may benefit from more complex pharmacotherapy, or interventions such as intravenous ketamine, or neuromodulation such as electroconvulsive therapy or repetitive transcranial magnetic stimulation. Psychiatric consultation may also help elucidate comorbidities or other factors contributing to a patient's non-response to treatment.

Conclusion

In a busy primary care practice, identifying depression with patient-rated screening tools can be of benefit. Depression treatment can include a combination of lifestyle modification, psychotherapy, and pharmacotherapy. Pharmacotherapy treatment options are many and can be simplified by considering the side effect profile and selecting agents that are least likely to carry long term side effect risks.

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Financial Disclosures

None declared.

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ASCVD=atherosclerotic cardiovascular disease; CI=cardiac index; LDL-C=low-density lipoprotein cholesterol; Q2W=every 2 weeks; QM=monthly

* LAPLACE-2 study design: Phase 3, 12-week, randomized, double-blind, placebo- and ezetimibe-controlled trial (N=1,896) in patients with primary hyperlipidemia (including 526 who had ASCVD) on maximum dose statin therapy. Patients were initially randomized to an open-label specific statin regimen for a 4-week lipid-stabilization period followed by random assignment to Repatha® 140 mg Q2W, Repatha® 420 mg QM or placebo for 12 weeks as add-on to daily statin therapy. Baseline LDL-C was 2.8 mmol/L, measured after the lipid stabilization period and before administration of first dose of Repatha®. Primary endpoint: Mean % change from baseline in LDL-C at week 12. Select secondary endpoint: Proportion of patients achieving LDL-C <1.8 mmol/L.[1,2]

References: 1. Repatha® (evolocumab injection) Product Monograph. Amgen Canada Inc., September 27, 2023. **2.** Robinson JG, *et al.* Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemia: The LAPLACE-2 randomized clinical trial. *JAMA* 2014;311(18):1870-82. **3.** Amgen Data on File.

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IDENTIFYING THE OPTIMAL BIRTH CONTROL FOR PATIENTS

Introduction

Despite decreases in pregnancy and abortion rates over the past few decades, unintended pregnancy remains a personal and public health challenge.[1] In the 1960s, the first birth control pills (progestin only and combined) revolutionized contraceptive effectiveness despite their high estrogen doses. In the 1980s, safety became front of mind, as older intra-uterine devices (IUDs) and implants were removed from the market, leading to the development of newer, safer options we enjoy today. In the 1990s, pill-related venous thromboembolism (VTE) scares led to surges in unintended pregnancy rates in the United Kingdom and Europe, only to be repeated in the 2000s. In the 2010s, long-acting reversible contraception (LARC) was hailed as the path forward for reducing pregnancy rates and, indeed, this has contributed to modest reductions in unintended pregnancy and abortion rates.

This decade has seen two major shifts in contraceptive care: the transition to blended models of service delivery (especially virtual and subscription-based options) and a transition toward "needs-based" counselling.

A Needs-based Approach to Contraception Counselling

The goal of needs-based counselling is to center the patient in the contraceptive discussion.[2] Patients want information about risks, benefits, and side effects, however, they wish to make the final decision. The jumping off point in needs-based contraception counselling is to invite the patient to suggest a method. While intuitive, this is a surprisingly significant departure from most approaches (e.g., pill-first or effectiveness-first).

Contraceptive choices are often based on social networks (what friends and family members are using). As first-generation LARC users become parents to sexually-active youth, there is a much greater degree of comfort with LARCs in teens and young adults than in previous generations. In addition to social networks, social media provides patients access to innumerable educational videos and reviews of birth control experiences, both positive and negative. While imperfect, the quality of birth control information being shared online is a significant improvement over schoolyard whispers and parent conversations. As a result, they tend to come to clinic more informed and motivated.

The Tic-Tac-Toe Approach

Needs-based counselling need not be difficult. Most patients seeking birth control have some sense of what they want to use, and want to know if it is a "good" option for them. Others may not know what to use, but the list of options can be rapidly narrowed with a few questions. The tic-tac-toe method has served me well over thousands of consultations. The first three questions are as follows:

1. What would you like to try?
2. What other benefits do you hope to receive from your birth control? (Indications)
3. Screen for method contraindications

If appropriate, prescribe an appropriate therapy. If the patient is unsure about the method, ask the next three questions:

4. What is your timeline to a future pregnancy (if ever)?
5. Which of these methods is acceptable?
6. Check cost/coverage issues.

Start by understanding the patient's timeline to pregnancy in order to initiate the conversation around a short-acting or long-acting method. Thereafter, review methods focusing on administration, effectiveness and side effects. Last, confirm coverage/affordability and make use of patient support resources that lower costs.

With so many methods, routes of administration and side effect profiles, it can be overwhelming for patients (and providers) to select a method. **Figure 1** shows a typical starting point for a patient who needs a full contraception consult. **Figure 2** summarizes the approach to short-acting methods. This paper will discuss troubleshooting methods as we work to find the optimal birth control for each patient.

Approach to Long-acting Methods

There are now four LARC methods available on the Canadian market, each with similar characteristics of high effectiveness, easy adherence, and high patient confidence. As all LARC methods have failure rates of less than 1%, the key to LARC counselling is to focus on the differences between each method, and less so its similarities.[3]

Copper IUDs

A copper IUD is more likely to be a second- or last-line option, but is an excellent option for many. A LARC user who wants the reassurance of a menses, has relatively light cycles prior to placement, and/or who wants a truly hormone-free option will be happiest with this device. There are nearly 20 options available. Keep in mind that three-year devices may have higher failure rates if used for longer. Five-year and 10-year devices can easily be extended, especially in patients who are over age 35 at the time of insertion.

Hormonal IUDs[4]

As the 52 mg hormonal IUD has therapeutic indications, the Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends it as the first-line LARC where bleeding control is required. Due to the relative ease of placement of a smaller-framed 19.5 mg device, this is the preferred option in younger and nulliparous patients (and those anxious about their first IUD placement). In patients who are both young/nulliparous with heavy menses, clinical experience suggests that a 52 mg device will provide the best outcome. However, in some cases I initiate with a 19.5 mg device if the patient is very concerned about pain with placement. Side effect profiles are similar in Phase III studies, therefore switching to a lower-dose IUD is unlikely to improve levonorgestrel side effects.

Implants

With nearly four years on the Canadian market, clinicians are still trying to determine the optimal place for implants in their counselling algorithms. The most obvious is for patients who wish to avoid (or had a negative experience with) an IUD. The simplicity of placement and removal make implants a favourable option for clinicians who are not comfortable with pelvic exams. The most frequent question I am asked at medical presentations is "What else can implants be used for?". The short answer is that they are intended for contraception only, however they may be a good option for patients with dysmenorrhea, transgender patients on testosterone, and in patients willing to try an implant for bleeding improvement prior to using a hormonal IUD.

Short-acting Methods: Sorting Through the Options

Most patients will use a short-acting birth control method as their contraceptive of choice at least once in their lifetime, and most new contraceptive users will initiate a combined oral contraceptive pill (COC). For this reason, clinicians reflexively initiate birth control with pills before transitioning to other options, and patients may not be aware of alternatives to these. Reviewing preference for LARC methods, estrogen-free options and non-oral options first, will quickly inform the patient of alternatives, and ensure that a pill is the best fit for them. A review of specific patient groups appears below.

Youth. When selecting a pill for a teenager, a higher estrogen-containing pill is recommended by the Canadian Paediatrics Society. Almost immediately, clinicians and parents face cognitive dissonance about hormone exposure in youth. The main reason to initiate a teen on a 30 mcg ethinyl estradiol. ([EE] or E4)-containing COC is for bone density preservation. Peak bone mineral

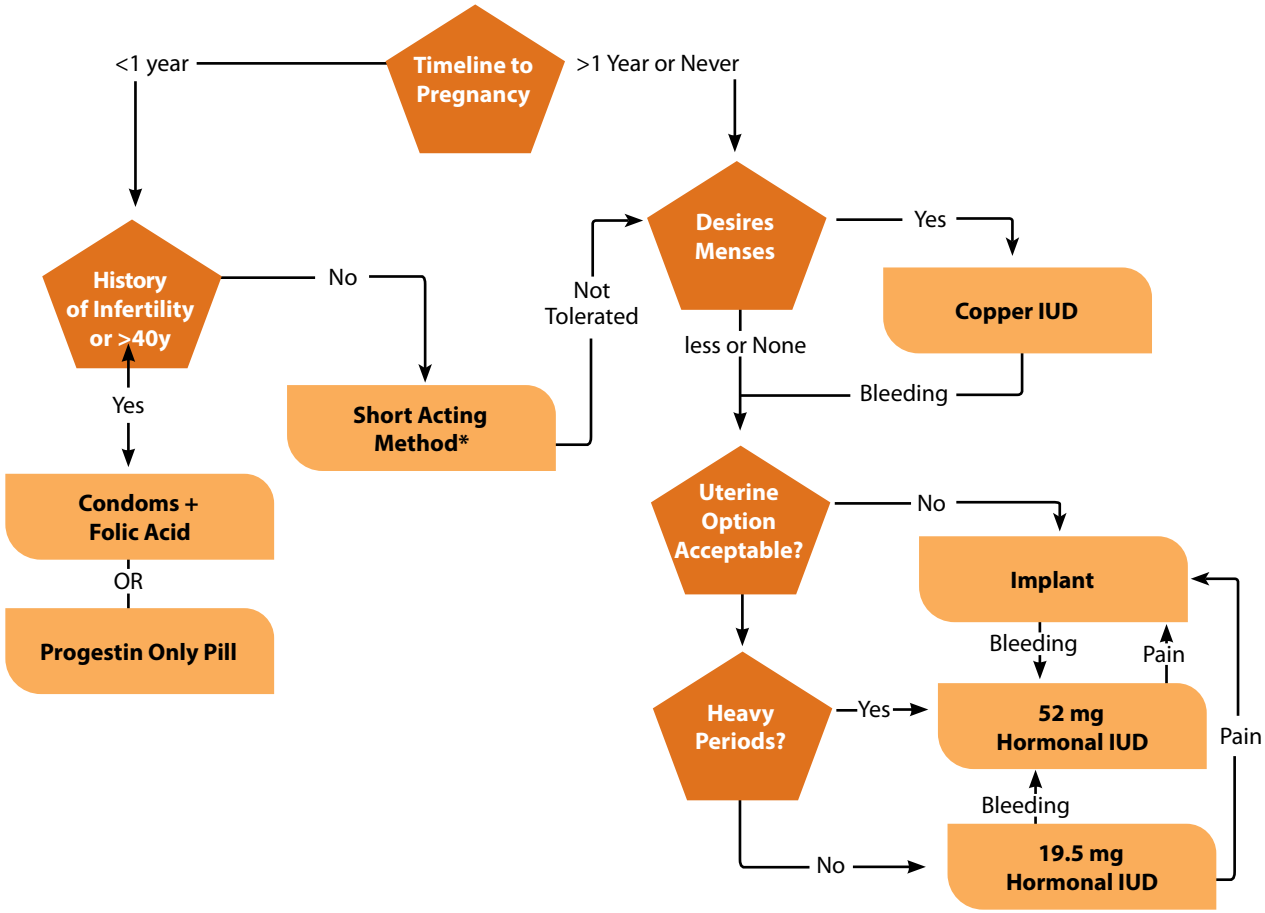

Figure 1. Simplified counselling algorithm and long-acting reversible contraceptive counselling; *courtesy of Dustin Costescu, MD, MS, FRCSC.*

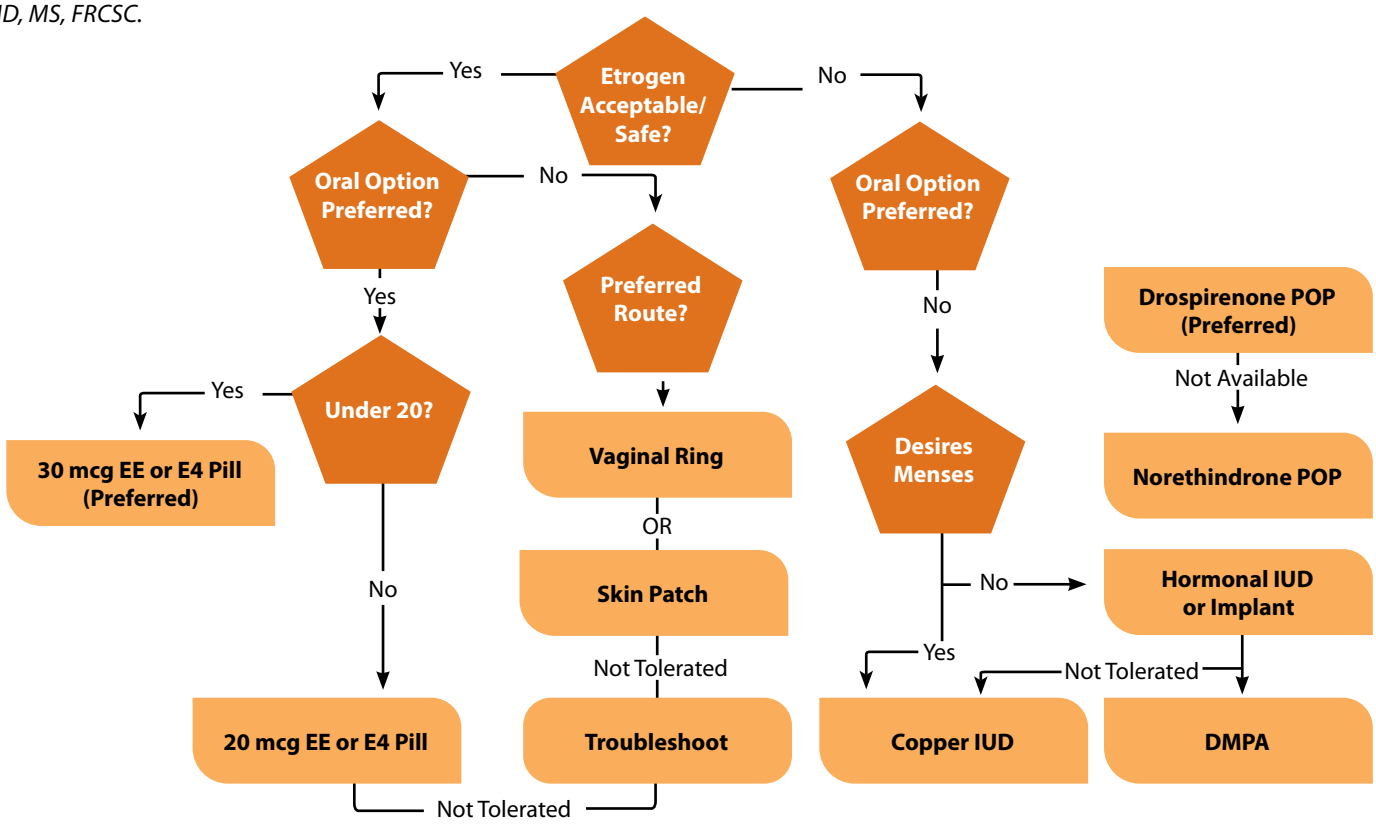

Figure 2. An approach to initiating short-acting contraception; *courtesy of Dustin Costescu, MD, MS, FRCSC.*

density (BMD) is around age 21 and comparative studies show that there is impairment in peak BMD in low dose users (under 30 mcg). LARCs do not have adverse impact on bone health, nor do progestin only pills (POPs). If a mid-range pill is not tolerated due to estrogen side effects, a lower dose can be selected next.

Older users. Patients over the age of 35 may acquire additional health conditions for which estrogen is contraindicated.[6] In light of this, special consideration should be taken when prescribing any combined hormonal contraceptive in this population. The decision to use an estrogen-containing option vs an estrogen-free option is far more important than the dose of estrogen, if used. When uncertain about estrogen contraindications, the SOGC follows the CDC-US Medical Eligibility Criteria for Contraceptive Use (US-MEC).[7] There is an app available that outlines a large number of medical conditions and assigns a four-point score based on risk. If the condition ranks as 1 or 2, prescribe without consultation. If a 3 or 4, do not prescribe and consider expert consultation.

Amenorrhea. While LARCs are well known for inducing amenorrhea (Depot medroxyprogesterone acetate [DMPA] over 60%, 52 mg IUD 40%, 19.5 mg IUD 24%, and implant 24%), certain short-acting methods are more likely than others to cause amenorrhea as well. While amenorrhea is often desired or accepted, it is critical to forewarn patients that this is normal. Specifically, there is no association with amenorrhea on oral contraceptive pills and premature ovarian insufficiency.

As a general rule, pills with a shorter hormone interval (24/4 and 24/2/2), and lower-dose COCs are associated with a higher rate of amenorrhea than standard 21/7 pills. The pill associated with the highest rate of amenorrhea is the 10 mcg EE/norethindrone acetate (NETA) pill (35%), followed by E4/drospirenone (DRSP) (11%), then other 24/4 formulations. While amenorrhea is common with NETA POP, it is uncommon with DRSP POPs. Patients with amenorrhea should undertake a pregnancy test and, if negative, can be reassured that this is normal.

Approximately 60% of pill users will skip hormone-free intervals to avoid menstruation during times of travel, holy pilgrimages, anticipated sexual activity, or simply to enjoy amenorrhea. This is safe and does not increase the risk of VTE. Patients using pills on a continuous basis will eventually develop spotting from an atrophic lining. If this occurs, stop the pill for 4 days and resume.[6]

Unscheduled bleeding. A major advantage of estrogen-containing contraceptives is stabilization of the endometrium and an overall reduction in bleeding. However, many patients will experience unscheduled bleeding (bleeding which occurs outside of expected menses). As a general rule, progestin- only pills and lower-dose (20 mcg EE and less) pills are associated with a greater rate of unscheduled bleeding. E4/DRSP has a relatively low rate of unscheduled bleeding, and may reflect differences in endometrial receptivity vs ethinyl estradiol. Patients experiencing unscheduled bleeding should switch to an E4 or 30 mcg+ EE pill. Exercise caution when switching pills as many are similar to each other, and occasionally a patient will simply switch brands of the same pill, without improvement. Continued unscheduled bleeding may warrant a discussion about alternatives, especially if adherence is the problem.

Acne. Estrogen-containing pills reduce acne by two main mechanisms: estrogen reduces sebum production and LH blockade by progestins reduce androgen levels. Drospirenone and cyproterone-containing pills also have direct antiandrogenic effects at the receptor-level. A common marketing tool in the 1990s, debate exists as to whether or not the "androgenicity" of the progestin in a pill contributes to acne and side effects. In acne studies, however, pills containing cyproterone and drosperinone are less comedogenic, followed by desogestrel (and its first level metabolite etonogestrel), and finally norethindrone, norgestimate and levonorgestrel (LNG).[6]

Mood. Hormone-related mood effects are poorly understood and under-reported. Taking a careful history, including whether or not mood is worse during the hormone-free interval or when taking pills, and the type of mood concern, are essential. Estrogens tend to cause activating symptoms, whereas progestins and hormone withdrawal mood disorders tend to aggravate depressive symptoms. The EE20/DRSP pill is approved in the United States for the treatment of premenstrual dysphoric disorder. Apart from that, unfortunately, finding a good mood pill is a trial and error endeavour. For patients with cyclical mood issues, a hormonal IUD may not help, as most patients ovulate with a hormonal IUD.[4]

Headache. Patients with pre-existing headache should be evaluated for the presence of migraine with aura (particularly non-visual aura). Many patients who report migraines do not have true migraine headache and do not have focal neurological deficit. Patients with non-aura migraines can use estrogen-containing contraceptives, although caution should be considered in those over age 35.

Pill-associated headaches occur either from estrogen dosing or estrogen withdrawal. Patients with migraines in the hormone-free window (so called menstrual migraines) can continue their method and possibly reduce or eliminate the hormone-free interval semi-continuously or altogether. Patients experience headache on COCs almost always due to estrogen content. Therefore, reducing the estrogen content or switching to a progestin-only method should be considered if patients experience headaches when taking active medication.[6]

Estrogenicity Theory and Venous Thromboembolism

No contraception review is complete without a discussion of VTE, the most serious complication from estrogen-containing contraceptives. The attributable risk of death from provoked chronic traumatic encephalopathy is approximately 3 per million pill users, with most occurring in those with an inherited or acquired thrombophilia. This risk must be interpreted in the context of VTE from pregnancy or puerperium, which is 10–100 times higher. Therefore, prevention of pregnancy also greatly reduces a patient's chances of developing a VTE.[6]

The Estrogenicity Theory is born of the observation that progestins alone are not thrombogenic, but may differ in their ability to mitigate some of the VTE risk of the estrogen component of the pill. Initially, the rationale was that "Estrogenicity = Estrogen Dose – Androgenicity of Progestin". With the advent of better hematological testing, in particular activated protein C resistance assays, it appears that anti-thrombotic activity is independent of androgenicity.[8]

Therefore, in order to alter the VTE-causing potential of a combined hormonal contraceptive (CHC), we can change either the estrogen dose, the estrogen type, or progestin.

It is well-known that there is a dose-dependent relationship between estrogen and VTE. Estrogens promote both clotting factor production and Protein C and S resistance (reducing the antithrombotic effects of these proteins). In population-based studies, pills with 50 mcg EE or higher are associated with an increase in VTE compared to those with lower doses. Below 50 mcg, it is not clear that further reductions lower VTE risk.[9]

Ethinyl estradiol is a highly bioavailable and metabolically active estrogen, with high liver activation and high thrombogenicity. It also has high persistence via enterohepatic circulation, so even transdermal preparations of EE are associated with high rates of VTE and are no safer than oral options. A new COC option containing estetrol is much less thrombogenic (based on Phase III and in vitro data). Therefore, if a CHC is desired, E4/DRSP should be considered, followed by a 20 mcg pill containing LNG or NETA.

Among pills, patches and rings containing EE, there are slight differences (<3 per 10,000) in VTE risk between different progestins. Older pills containing LNG or NETA are less thrombogenic than those containing desogestrel (DSG) or DRSP. If a patient is sufficiently concerned about VTE risk to choose a pill brand that is less thrombogenic, they should be informed about progestin-only options as an alternative.[10]

DMPA is associated with a two-fold increase in VTE compared to the incidence of VTE among non-users. However, DMPA is often (and can be) used in patients with VTE risk factors, especially given limited alternatives.

Next and Last Line Options

Satisfaction and Switching. Patient satisfaction with birth control, like many preventative medications, is difficult to measure. Success from the provider perspective is prevention of unplanned pregnancy, but patients often don't recognize the value of prevention. Patients measure satisfaction based on adherence, tolerability and "switching intention" – the degree to which they wish to try a different method. Adherence refers to the ability to use a method consistently and correctly as often as possible – using a condom each time, taking a pill each day, changing a ring each month, getting an injection every season, and so on. However, adherence is more than remembering – adherence is affected by convenience, access, confidence that the method will work, and acceptability of side effects attributable to the method. Patients may be more interested in switching methods than you think. Switching intention is highest (about 50%) among users of less effective options, such as condoms, especially if there has been a condom failure or adherence is a challenge. Users of short-acting methods also report high switching intention, either because of contraceptive failure, lack of confidence in the method (or adherence to dosing), a long timeline to pregnancy, or side effects. LARC users report the lowest switching intention, reflecting both high satisfaction but also limited alternatives. At the conclusion of any contraception consult, raise the option of discussing alternatives at a follow-up visit if there is room for improved side effects or there is interest in switching methods.[11]

Last line options. Conspicuously absent from the treatment algorithms are two important options: Injectable DMPA and permanent contraception. DMPA is an important contraceptive because, in many cases, it is the treatment of last resort for patients who have not tolerated other options, those with repeated contraceptive failures, and those requiring therapeutic amenorrhea. The delay to fertility return and weight gain are the main reasons why it is not offered early in the algorithm, but this option is safe, minimally thrombogenic, and should be considered when other options have not been acceptable.

Permanent contraception remains a human right. In Canada, more couples rely on vasectomy than salpingectomy, however it is an outlier when compared to global statistics. Permanent contraception should be offered to patients who are certain they desire no (or no further) children. It should not be offered because a

patient cannot access reliable reversible contraception, or because of a lack of tolerance of reversible methods. Surgical backlogs have made tubal ligation surgeries less accessible with significantly longer wait times and the risk of unintended pregnancy while waiting. Ensure that patients have alternative methods while on the surgical waiting list.

Conclusion

Unintended pregnancy is a fact of life, but there is a method of contraception available for each patient. The best method of birth control is the one the patient wants to use, is able to use, is well-tolerated, and that the patient trusts. Good counselling and clever troubleshooting are the keys to finding the appropriate method when a first-line option does not fit. Focusing on patient needs leads to higher satisfaction and better outcomes.

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↓**20**%

(HR 0.80; 95% CI [0.66, 0.98])

(event n=174 vs. 213)

Non-fatal MI†

↓**30**%

(HR 0.70; 95% CI [0.59, 0.82])

(event n=237 vs. 332)

Non-fatal stroke†

↓**29**%

(HR 0.71; 95% CI [0.54, 0.94])

(event n=85 vs. 118)

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Relevant warnings and precautions:

- Not recommended in combination with or substituted for other products that contain omega-3 fatty acids
- Increased incidence of bleeding
- Increased risk of atrial fibrillation or flutter requiring hospitalization
- Potential for anaphylactic reaction to fish and/or shellfish
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*8,179 statin-treated adult patients with elevated serum triglyceride levels (≥1.5 mmol/L to <5.6 mmol/L) who were also at high risk for atherothrombotic events. Patients either had established CVD or were at high risk for CVD and were randomized to either Vascepa® or placebo. Patients with established cardiovascular disease were at least 45 years of age and had a documented history of coronary artery disease, cerebrovascular or carotid disease, or peripheral artery disease. Patients with other risk factors for cardiovascular disease were at least 50 years of age and had diabetes and at least one additional major cardiovascular risk factor. 5-point MACE was defined as time to first occurrence of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. Most patients at baseline were taking at least one other cardiovascular medication including anti-hypertensives (95%), anti-platelet agents (79.4%), beta blockers (70.7%), angiotensin-converting enzyme (ACE) inhibitors (51.9%), and angiotensin receptor blockers (ARB) (27.0%), with 77.5% taking either an ACE inhibitor or ARB. At baseline, while on stable background lipid-lowering therapy, the median LDL-C was 1.9 mmol/L.

†Incidence rates of CV events per 100 patient years (Vascepa® vs. placebo): cardiovascular death, 1.0 vs. 1.2; non-fatal myocardial infarction, 1.4 vs. 2.0; non-fatal stroke, 0.5 vs. 0.7.

‡CV death includes adjudicated cardiovascular deaths and deaths of undetermined causality.

§Comparative clinical significance has not been established.

CCS, Canadian Cardiovascular Society; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular event.

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MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA IN 2024

Background

Benign prostatic hyperplasia (BPH) is a condition involving the proliferation of smooth muscle and epithelial cells within the transition zone of the prostate. The process by which this takes place is not precisely known. It does require that testosterone and 5-alpha reductase convert it to dihydrotestosterone (DHT) which is the active androgen within the prostate. The growth of the prostate results from an imbalance between cell growth and cell death. Obstruction occurs via compression of the urethra by the resulting hyperplastic nodules, as well as increased smooth muscle tone and resistance within the enlarged gland. It is an almost universal process in men beginning in their 40's; it increases to a prevalence of 60% by age 60 and 80% by age 80.[1] This results in progressive bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTs). Patients can range from being asymptomatic to severely symptomatic. In the most extreme cases, it can result in complete urinary retention and renal dysfunction. The annual economic impact of BPH has been estimated at nearly $4 billion in the Unites States.[2]

Diagnosis

History

The initial management phase requires taking a history. Patients may experience a variety of symptoms which can be broadly divided into those that involve storage (e.g., frequency [urination eight or more times per day] and urgency [the inability to delay urination]) and emptying (slow flow; which may include trouble starting/maintaining a urine stream). The International Prostate Symptom Score (IPSS) is a validated questionnaire that is recommended in order to provide an objective measure of the severity of a patient's condition (**Figure 1**). Furthermore, it allows for a standardized method to monitor patients and gauge the success of any therapeutic interventions.

It is important to note that not all LUTS in men are due to BPH. Overactive bladder is a condition that results in storage symptoms. It can occur as a primary condition separate from BPH or it can be a secondary condition induced by BOO-caused by BPH. Interstitial cystitis (IC) and chronic prostatitis can be a source of LUTs and are associated with chronic pelvic pain. In the case of IC, patients often experience pelvic pain that is relieved by urination. Patients with prostatitis typically have perineal pain and may also have pain with ejaculation.

Urethral stricture should be considered in younger patients who have slow urinary flow, especially in the context of a history of urethral trauma or sexually transmitted infection. Distal ureteral stones may cause a combination of storage and emptying LUTs, including urinary retention in some circumstances. This would generally occur in the setting of typical renal colic. Isolated nocturia may be a sign of untreated sleep apnea and a sleep study should be considered in these patients.

Finally, behavioural factors can cause significant LUTs. The amount, type and timing of fluid intake can have

INTERNATIONAL PROSTATE SYMPTOM SCORE SHEET

Dr. Name: _____ **Address:** _____

Patient Name: _____ **Address:** _____

Date: _____

Age Group: 40-49 ☐ 50-59 ☐ 60-69 ☐ 70+ ☐

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
1. INCOMPLETE EMPTYING Over the past month, how often have you had an occurrence of not emptying your bladder completely after you finished urinating	0	1	2	3	4	5	
2. FREQUENCY Over the post month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. INTERMITTENCY Over the past month, how often have you found you stopped and morted several trees when you urinated?	0	1	2	3	4	5	
4. URGENCY Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. WEAK STREAM Over the past month, how often have you had a very weak urinary stream?	0	1	2	3	4	5	
6. STRAINING Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
7. NOCTURIA Over the past month, how many times did you most typically get up to urinate from the time you went to bed of night until the same you got up in the morning?	0	1 **1** time	2 **2** times	3 **3** times	4 **4** times	5 **5** or more times	

Which of the above do you regard as most troublesome (1.7) _____

TOTAL PROSTATE SYMPTOM SCORE _____

	Delighted	Pleased	Mostly satisfied	About half the time	More than half the time	Almost always	Terrible
QUALITY OF LIFE DUE TO URINARY SYMPTOMS If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that? (pick one).	0	1	2	3	4	5	6

Figure 1. IPSS (International Prostate Symptom Score Sheet).

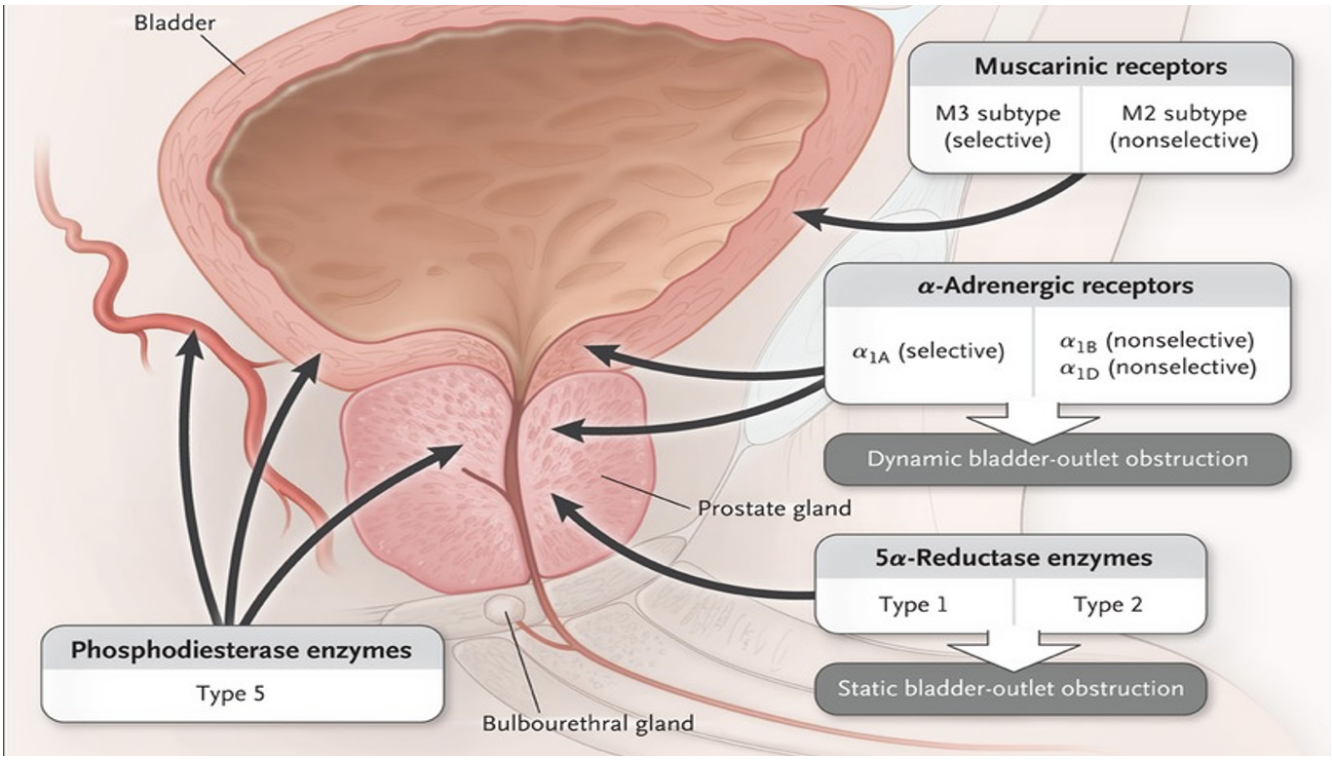

Figure 2. Classes of medication for the treatment of LUTs and site of action within the lower urinary tract; *adapted from Sarma AV, Wei JT. Benign prostatic hyperplasia and lower urinary tract symptoms. N Engl J Med. 2012;367:248-57.*

a significant effect on LUTs. Caffeine and alcohol act as diuretics and can exacerbate voiding symptoms. Furthermore, consumption of fluids in the evening and/or throughout the night can be a source of nocturia.

Physical Examination

It is recommended to perform a digital rectal exam (DRE) as part of the evaluation.[3] DRE provides useful information including an estimate of prostate size and detection of palpable irregularities. A tender prostate may be a sign of prostatitis.

Laboratory Tests

A urine analysis is important to rule out underlying conditions such as infection or hematuria. It is also recommended that a prostate-specific antigen (PSA) be performed in appropriate patients.[3] This includes men between the ages of 50-70 with at least 10 years of life expectancy or starting at age 45, and those who are at an increased risk of prostate cancer.[4] PSA screening decreases the risk of prostate cancer mortality in this patient population and can also provide a surrogate marker for prostate size. In 2012, the United States Preventive Services Task Force (USPSTF) recommended against using PSA to screen for prostate cancer and this was followed by a similar recommendation by the Canadian Task Force on Preventive Health Care. Since that time there has been an increase in the incidence of patients presenting with late-stage prostate cancer. This resulted in the USPSTF revising their statement and recognizing that there is a net benefit to PSA-based screening for prostate cancer.[5]

Serum creatinine and post-void residual measurement are optional tests that can help to rule out underlying renal dysfunction or significant urinary retention. Transrectal ultrasound is not recommended as a routine investigation but can be useful in cases where surgical intervention is being considered.[3]

Treatment

The treatment options for BPH can be divided into watchful waiting, medical therapy and surgery. The option selected depends on the degree of bother and, to a large degree, on patient preference. Therefore, there is no defined sequence required when treating BPH. Those with significant LUTs as defined by the IPSS may elect to proceed with watchful waiting. Patients who prefer to avoid long-term medical therapy may wish to proceed directly to surgery. It is important to provide patient counselling with respect to these options.

Watchful Waiting

Patients who are asymptomatic, have low bother from their symptoms or who wish to avoid medication and surgery can be observed. It is worthwhile to review reversible factors that could contribute to LUTs-caused by BPH such as the timing of fluid consumption, the use of decongestants and antihistamines, and the intake of caffeine and alcohol.

Pharmacotherapy

Various classes of medication are available for the treatment of LUTs related to BPH which act on various parts of the lower urinary tract **(Figure 2)**.

Alpha Blockers

Alpha blockers act by relaxing the smooth muscle at the bladder neck and within the prostate, and aid in improving urinary flow. Those used in the treatment of BPH include terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin. This class of medication is the primary first-line option for pharmacologic management of BPH.[3] The most common side effects include dizziness, nasal congestion and retrograde ejaculation. Floppy iris syndrome can be seen with alpha blocker therapy and may be an issue for patients undergoing eye surgery. It is a condition involving loss of muscle tone in the iris and results in pupil constriction, despite pre-operative dilation. Increased awareness by ophthalmologists has resulted in effective management.[6]

Non-selective alpha blockers such as terazosin and doxazosin have demonstrated higher rates of hypotension and dizziness. The alpha-1A receptor subtype has greater expression at the bladder neck and prostate, and is involved in the contraction of these structures; it has minimal effect on blood pressure.[7] The selective alpha-blockers target the alpha-1A receptor and include tamsulosin, alfuzosin, and silodosin. This selectivity results in a greater effect on the lower urinary tract while minimizing the impact on blood pressure. It also results in a greater incidence of retrograde ejaculation which is highest with tamsulosin and silodosin. Retrograde ejaculation occurs less with alfuzosin so this may be a better option in patients where ejaculatory dysfunction is a greater concern.[1]

These five agents have similar clinical effectiveness so there is little benefit in switching to other alpha-blockers if a patient has not responded to one initially. However, it is reasonable to try a different alpha-blocker in the event a patient is having intolerable side effects with their current alpha-blocker.[8]

5-alpha Reductase Inhibitors (5-ARIs)

5-ARI's, including finasteride and dutasteride, act by inhibiting the conversion of testosterone to DHT. Finasteride inhibits the type 1 5-alpha reductase isoenzyme while dutasteride acts on type 1 and type 2 isoenzymes. DHT is the active androgen within the prostate and inhibition of its production results in a decrease in prostatic growth. Therefore, benefit is seen in larger prostates with a volume of 30 cc or greater and it is reasonable to consider 5-ARI monotherapy in such patients. This class of medication decreases the size of the prostate by approximately 25% after 6 months. As such, symptomatic improvement is not immediate, and patients should be counselled that it may take months for them to notice any change in symptoms. Unlike other BPH medications, 5-ARI's can alter the natural progression of the condition resulting in a lower risk of urinary retention and the need for surgical intervention.[9] Although dutasteride decreases DHT within the prostate to a greater degree, it does not appear to result in a significant decrease in clinical response when compared with finasteride.[10] Side effects of 5-ARI's include erectile dysfunction, decreased libido, ejaculatory disorders, and gynecomastia. Rarely, post-finasteride syndrome can occur, in which side effects persist despite medication cessation.[11]

It is important to note that as the size of the prostate decreases, it is expected that serum PSA levels will decrease. After 1 year of being on the medication it should be assumed that the true PSA is twice that which is being measured.[12] A lack of decrease in PSA or a rising PSA while on a 5-ARI represents a concern for underlying prostate cancer. A higher incidence of advanced prostate cancer has been described in patients taking 5-ARI but this may be secondary to the failure to account for the expected effects of this medication class on PSA results rather than being a causative factor.[1]

Combination therapy (alpha-blockers and 5-ARI's)
In general, given their side effect profile and onset of action, alpha-blockers are the first option for pharmacotherapy in symptomatic BPH. In patients with an incomplete response and an enlarged prostate (volume > 30 cc) adding a 5-ARI has been shown to improve symptom control more than with either medication alone. This was shown in two landmark studies for both finasteride (MTOPS trial) and dutasteride (CombAT trial).[13,14] After 9 months of combination therapy, stopping the alpha-blocker and continuing with 5-ARI monotherapy is tolerated in many patients.[15]

Phosphodiesterase-5 inhibitors

While Phosphodiesterase-5 inhibitors (PDE-5Is) are first-line treatment for erectile dysfunction they have also been shown to provide clinically significant benefit in improving LUTs secondary to BPH.[16] Because of the prolonged duration of action of tadalafil, it is the agent typically used at a dose of 5 mg/day. This is an option for patients being treated for BPH and erectile dysfunction concurrently.

Antimuscarinic and Beta-3 Agonist Medication

Urinary storage symptoms seen in the context of BPH can be challenging to treat. While there may be relief with medications targeting bladder outlet obstruction, it may also represent a component of underlying bladder overactivity. Therefore, medications targeting overactive bladder may be helpful either as monotherapy or in combination with alpha-blockers and/or 5-ARI. It is important to note that these medications may increase the risk of urinary retention, especially in those who already demonstrate incomplete bladder emptying.

Phytotherapy

There are a number of herbal medications marketed for BPH. However, they lack consistent formulation, predictable pharmacokinetics and regulatory oversight. Furthermore, in multiple clinical studies they have not demonstrated a benefit over placebo. Therefore, they are not recommended as standard treatment.[3]

Surgery

Surgery is considered in patients with symptoms such as urinary retention who do not respond to pharmacologic therapy. It is also indicated in those who experience intolerable side effects from medications or if there is a desire to avoid medication entirely.

The standard procedure is a transurethral resection of the prostate (TURP). This involves a transurethral endoscopic approach to the obstructive prostate tissue growing into the prostatic urethra and bladder neck. Risks of the procedure include infection, bleeding, urinary retention and rarely, incontinence. A high proportion of patients also experience retrograde ejaculation. Laser vaporization of the prostate involves a similar approach in which the obstructive prostate tissue is vaporized rather than resected. It has the benefit of causing less bleeding and is generally performed as an outpatient procedure.

With increasing prostate size, TURP and laser vaporization may be less efficacious and carry a higher risk of bleeding. For very large prostates (i.e., >100 cc) simple prostatectomy is an option. Traditionally, this involves an open surgical approach to the prostate in which the exterior capsule is opened, and the obstructive adenoma is excised from inside of it. More recently this has been achieved through laparoscopic and robotically-assisted approaches.

Laser enucleation of the prostate in which a transurethral endoscopic approach is taken offers an alternative to simple prostatectomy. A laser incision is carried out in the plane between the adenoma and prostatic capsule thereby enucleating the prostate from the inside. The enucleated adenoma is then placed in the bladder and subsequently removed by morcellation.

More recently, a number of minimally invasive, clinic-based procedures have gained popularity. They involve short periods of sedation or local anesthetic in some cases. They tend to cause minimal bleeding and less risk of sexual and ejaculatory dysfunction. These procedures include prostatic urethral lift (UroLift), water vapour energy ablation (Rezum), robotic water jet ablation (Aquablation), and a temporary implantable nitinol device (iTind).

Prostatic artery embolization is a procedure performed through interventional radiology. It can be an effective treatment for intractable hematuria. However, in terms of BPH treatment, it has demonstrated a lack of long-term durability.[3]

Conclusion

BPH is a common condition effecting millions of men globally. There are a number of treatment options available that can be tailored to an individual's symptoms and objectives.

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None declared.

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PRACTICAL IMPLEMENTATION OF DIABETES CANADA GUIDELINE UPDATES FOR TYPE 2 DIABETES MANAGEMENT IN PRIMARY CARE

Introduction

Type 2 diabetes (T2DM) is a growing global health epidemic identified by the World Health Organization (WHO) as a major public health challenge of the 21st century.[1] By 2050, it is estimated that 1.31 billion people worldwide could be living with T2DM.[1] Across Canada, T2DM affects >9% of our population (i.e., >3.6 million individuals), and age-adjusted prevalence is also increasing at an alarming rate averaging 3.3% per year.[2] More than 90% of people living with diabetes have T2DM, and most of these individuals are cared for in the primary care setting. With rising rates of obesity and metabolic risk factors, along with an aging Canadian population, the burden of T2DM facing primary care is only expected to increase over time.

T2DM care is complex, tailored to the individual, and rapidly advancing. A May 2023 survey commissioned by Diabetes Canada estimated that over one-third of family practitioners' time is spent treating diabetes, and that most healthcare providers find T2DM challenging to treat.[3] The Diabetes Canada Clinical Practice Guidelines (DCAN CPG) provides useful and practical guidance on T2DM management. It has recently shifted its update structure from a comprehensive overhaul every five years, to a select few focused chapter updates each year in recognition of the rapidly shifting body of evidence. More recently, updated chapters of the DCAN CPG include a Pharmacologic Glycemic Management of Type 2 Diabetes in Adults chapter in 2020; Blood Glucose Monitoring in Adults and Children with Diabetes chapter in 2021; Remission of Type 2 Diabetes special article in 2022; and Hypoglycemia in Adults chapter and Position Statement on DIY Automated Insulin Delivery special article in 2023. The purpose of this review is to provide a pragmatic overview of these recent chapter updates and to highlight priorities for T2DM management in primary care.

Priority #1: Screening at-risk individuals, individualizing treatment targets, and delivering person-centred care

It is estimated that over 1.2 million Canadians live with undiagnosed T2DM.[4] Untreated and suboptimally treated T2DM are associated with significant comorbidities and increased risks of microvascular and macrovascular complications.[5] Screening for prediabetes and T2DM by fasting plasma glucose (FPG) or hemoglobin A1c (HbA1c) is therefore recommended every three years by Diabetes Canada guidelines for anyone over the age of 40 or at high risk for T2DM using a risk calculator such as CANRISK.[6,7] Earlier screening should also be considered for people with additional risk factors such as a first-degree relative with T2DM; high-risk ethnicity (e.g., African, Arab, Asian, Hispanic, Indigenous, or South Asian); history of gestational diabetes mellitus (GDM); or those at very high risk based on a risk calculator.[6]

Once a diagnosis of T2DM is established, the choice of initial and subsequent management strategies and targets of glycemic control should be individualized based on patient characteristics; the presence of established atherosclerotic cardiovascular (CV) disease or renal disease; the presence of CV risk factors; medication cost and coverage considerations; and the patient's preference.[8] While for most adults with T2DM it is recommended to target HbA1c ≤7.0%, in select individuals at low risk of hypoglycemia based on class of medications utilized and other characteristics, it is reasonable to target HbA1c ≤6.5% to reduce the risk of chronic kidney disease and retinopathy.[9] A higher HbA1c target should be considered with HbA1c 7.1%-8.0% for individuals who are functionally dependent, and HbA1c 7.1%-8.5% for individuals with recurrent, severe hypoglycemia, especially if accompanied by hypoglycemia unawareness, limited life expectancy, or in the frail elderly with dementia.[9]

In the 2022 Diabetes Canada Special Article on Remission of Type 2 Diabetes, the above individualized HbA1c targets have been expanded to include the option of T2DM remission.[10] Remission is defined as achieving the following HbA1c ranges without any antihyperglycemic medications for ≥3 months, with remission to prediabetes defined as HbA1c 6.0%-6.4% and remission to normoglycemia defined as HbA1c <6.0%.[10] The ideal candidate for whom remission is an option is a person with a diagnosis of T2DM <6 years; with overweight or obesity; without significant eating or mental health disorders; without microvascular or macrovascular complications of T2DM; and who is inclined and able to engage in sustained weight loss by either bariatric surgery, a low-calorie total dietary/meal replacement diet, or a structured exercise program combined with a calorie-restricted diet.[10] Once remission is achieved, HBA1c should continue to be performed every six months to assess the persistence of remission and monitor for relapse.[10] The User's Guide accompanying this special

article provides practical examples of commercially available low-calorie meal replacement options and a checklist clinicians can use to guide discussions and shared decision-making with patients.[11]

Priority #2: Optimizing pharmacotherapy to prevent complications and improve outcomes

Newer antihyperglycemic agents approved and available for use in Canada, including sodium-glucose cotransporter-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP1-RAs), have been shown to have CV benefits in people living with T2DM in CV outcome trials. In recognition of this rapidly advancing body of evidence, Diabetes Canada published a 2020 Chapter Update on Pharmacologic Glycemic Management of Type 2 Diabetes in Adults.[8] In this chapter update, the selection and adjustment of antihyperglycemic pharmacotherapy shifted away from a glucocentric approach aimed at meeting HBA1c targets to a more holistic approach. It recommended that the choice of antihyperglycemic medications be individualized according to a multitude of factors including degree of hyperglycemia; efficacy of agents for reducing T2DM complications and blood glucose; medication effects on the risk of hypoglycemia; body weight; concomitant medical conditions; the ability to adhere to the regimen; affordability of medications; and patient values and preferences.[8]

For instance, in people living with T2DM who have established atherosclerotic cardiovascular disease (ASCVD), either an SGLT2i or a GLP1-RA should be added to reduce major adverse cardiovascular events (MACE), and an SGLT2i be added to reduce hospitalization for heart failure and progression of nephropathy.[8] In people living with T2DM and chronic kidney disease (CKD), an SGLT2i is recommended to reduce the risk of progression of nephropathy, hospitalization for heart failure (HHF), and MACE, and GLP1-RA can be considered to reduce MACE.[8] Last, in people without ASCVD but age >60 with at least two CV risk factors, a GLP1-RA (dulaglutide, liraglutide, or subcutaneous semaglutide) should be considered to reduce MACE, and an SGLT2i (dapagliflozin or canagliflozin) should be considered to reduce HHF and progression of nephropathy.[8]

Oral semaglutide was notably not named in the chapter update as having comparable CV benefits as the injectable GLP1-RA options. This is because while oral semaglutide demonstrated CV safety in the PIONEER-6 trial compared to placebo, the trial was not designed to demonstrate superiority; this will be examined further in the upcoming SOUL trial.[12,13] As of March 2023, the once weekly injectable glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 co-agonist tirzepatide has also received Health Canada indication for use to improve glycemic control for the treatment of adults living with T2DM. The SURPASS trials have shown superiority of tirzepatide vs placebo, subcutaneous semaglutide, and insulin glargine in glycemic lowering and weight loss in this population. The upcoming SURPASS-CVOT will shed light on whether or not it carries the same CV benefit as GLP1-RA therapy.[14,15]

When using SGLT2i, there are several management considerations. First, although empagliflozin and canagliflozin each have two doses available, the lower dose is sufficient for most patients. This is because the cardiorenal benefits are not different between the two doses and often the lower dose is the only one studied in dedicated renal trials (e.g., CREDENCE and EMPA-KIDNEY.)[16,17] The dose response curve is also rather flat and a higher dose generally has only a small effect in further reduction in blood glucose. The exception to this rule is dapagliflozin, as 10 mg PO daily was the demonstrated cardiorenal protective dose used in the DAPA-HF and DAPA-CKD trials.[18,19] Second, although renal protective effects persist at low estimated glomerular filtration rate (eGFR) ranges, glycemic-lowering effects are blunted once eGFR is below 45. As such, although SGLT2i should still be initiated for cardiorenal protection in patients with eGFR <45 (canagliflozin 100 mg daily can be initiated for eGFR >30, dapagliflozin 10 mg daily can be initiated for eGFR >25, and empagliflozin 10 mg daily can be initiated for eGFR >20), additional glycemic control agents should be considered to reach HbA1c targets.[16,17,19] Last, due to the associated risks of diabetic ketoacidosis, patients should be counselled to temporarily withhold SGLT2i use during acute illnesses associated with risk for dehydration and prior to major surgical procedures for at least 48-72 hours.[8]

When it comes to using GLP1-RA therapy, there are also several management pearls. All GLP1-RA medications have the potential to cause gastrointestinal side effects, with nausea (25%-60%), vomiting (5%-15%) and diarrhea being the most common in clinical trials leading to discontinuation.[20] To minimize these side effects, all GLP1-RA medications are initiated at a low dose and titrated according to product monographs. Up-titration can be slowed to reduce the severity and frequency of side effects. Patients should also be counselled that these effects are transient and usually resolve with time, and on lifestyle management strategies that improve side effects including eating smaller meals, eating more slowly, stop eating prior to feeling full, and avoidance of fatty and spicy foods.[21] Last, GLP1-RAs are contraindicated in pregnancy and breastfeeding. Women of reproductive age being prescribed these medications should receive counselling on reliable contraception while taking them and advised to switch to alternative non-teratogenic options prior to planned pregnancy.

Priority #3: Promoting safety in T2DM care across the lifespan

Throughout the lifespan of a person living with T2DM, there are several important safety considerations to

address, including hypoglycemia and mental health. As primary care physicians provide comprehensive and longitudinal care, they are also uniquely positioned to be aware of important checkpoints for intervention in a patient's life that impact their T2DM management, such as family planning and preconception counselling for reproductive age women, and functional decline and deprescribing in the elderly.[22]

Hypoglycemia can occur in individuals treated with insulin or insulin secretagogues, and if occurring frequently, poses significant long-term health risks to the patient. The latest 2023 Diabetes Canada Chapter Update on Hypoglycemia in Adults defined severity of hypoglycemia not only by glucose levels but also severity of the associated symptoms.[23] While level 1 (glucose 3.0 mmol/L -3.9 mmol/L accompanied by autonomic symptoms) and level 2 (glucose <3.0 mmol/L accompanied by neuroglycopenic symptoms without significant impact on mental status) can be recognized and treated by the individual experiencing hypoglycemia, level 3 is defined as hypoglycemia of any degree that requires external assistance to treat.[23] Frequent hypoglycemia predisposes individuals to impaired awareness of hypoglycemia, which occurs when the threshold for development of autonomic warning symptoms is close to, or lower than, the threshold for neuroglycopenic symptoms.[23] Effective strategies to reduce hypoglycemia include psychoeducational training of patients and support persons in recognizing and reducing hypoglycemia; prescribing glucagon (intranasal, intramuscular or subcutaneous) and teaching family members on administration technique; transition to pharmacotherapies that reduce the risk of hypoglycemia (e.g., discontinue insulin and secretagogues in favour of incretin-based pharmacotherapy, consider second-generation basal insulin analogues insulin glargine-300 and degludec over insulin NPH, glargine-100, and detemir to reduce nocturnal hypoglycemia); and the use of continuous glucose monitoring (CGM) to identify episodes of hypoglycemia.[23]

Living with T2DM comes with significant mental and emotional burdens, and research has identified three T2DM-specific psychological syndromes.[24] Diabetes distress (DD) refers to the negative emotional burden of self-management related to living with T2DM. Psychological insulin resistance is the strong negative response from people with T2DM to the recommendation from healthcare providers that they should start insulin. Fear of hypoglycemia, usually a result of traumatic experiences of serious or nocturnal hypoglycemia, often results in patients adopting compensatory hyperglycemia as a prevention strategy for future hypoglycemia events.[24] All of these are underrecognized barriers to T2DM care and, if left unaddressed, can significantly impact the patient's ability to achieve glycemic targets, prevent complications, and achieve overall quality of life.[24] The 2023 Chapter Update on Diabetes and Mental Health provides detailed recommendations on the screening and management of mental health comorbidities in people living with T2DM, and how to differentiate DD from major depressive disorder.[24]

As the diagnosis of T2DM becomes increasingly common in younger age groups, the prevalence of pre-existing T2DM in pregnancy has also increased steadily over the past decade.[25] Among women with pre-existing T2DM, preconception care is known to improve maternal and fetal outcomes, and therefore it is paramount that women of reproductive age living with T2DM receive preconception counselling as part of healthcare visits for disease management. The Diabetes in Pregnancy chapter of the 2018 Diabetes Canada CPG outlines key components to preconception care.[25] This involves patient education about the importance of optimizing glycemic control prior to pregnancy, as hyperglycemia is teratogenic and increases risk of congenital anomalies in the first trimester.[25] Most antihyperglycemic medications (except metformin, insulin and glyburide), renal protective antihypertensives (e.g., angiotensin-converting-enzyme inhibitors and angiotensin-2 receptor blockers), as well as statins, are contraindicated in pregnancy.[25]. Patients treated with these medications must be counselled on the importance of reliable contraception or be transitioned to pregnancy-safe alternatives prior to conception.[25] Microvascular complications such as retinopathy and nephropathy can also worsen in pregnancy. Women with pre-existing T2DM should undergo retinopathy screening by a vision care specialist preconception, in the first trimester, and within the first year postpartum.[25] Nephropathy screening should be completed preconception, and women with albuminuria or CKD should be followed closely in pregnancy for the development of hypertension and preeclampsia.[25] Regarding T2DM management in older adults, care should be individualized taking into account the existence of other comorbidities and frailty. In functionally independent older people living with T2DM, who have life expectancy of >10 years, Diabetes Canada guidelines recommend following the same glycemic, blood pressure and lipid targets as younger people with T2DM.[26] However, in the older person with T2DM and multiple comorbidities or frailty, the priority should shift to strictly preventing hypoglycemia by transitioning patients off of antihyperglycemic agents that increase the risk of hypoglycemia in favour of alternatives with less risk of hypoglycemia (e.g., incretin-based therapies in place of sulfonylureas, modified-release gliclazide in place of shorter-acting glyburide, and the second-generation basal insulins, insulin glargine-300 or degludec in place of insulin NPH, detemir, or glargine-100).[26] In older adults on insulin or with impaired awareness of hypoglycemia, continuous glucose monitoring devices can be considered to assist with glucose monitoring and identification of hypoglycemia. Polypharmacy is common in older

adults living with T2DM, and deprescribing should be considered, especially in individuals with limited life expectancy, to reduce complexity of therapy, unwanted side effects and drug-drug interactions.[26]

Conclusion

T2DM is an increasingly prevalent and complex problem facing primary care physicians. With an abundance of effective pharmacotherapy agents coming to market, the approach to T2DM management needs be more holistic than glucocentric. Pharmacotherapy selection should also be tailored to the individual with factors such as presence of complications and comorbidities, body weight, cost and coverage, and patient preference taken into consideration during shared decision-making. The DCAN CPG chapters are an up-to-date, comprehensive yet succinct, and user-friendly resource available to guide clinicians navigating through this increasingly complex landscape.

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FROM THE FIRST BREATH TO THE GOLDEN YEARS: RESPIRATORY SYNCYTIAL VIRUS PREVENTION IN INFANTS AND OLDER ADULTS

Introduction

Respiratory syncytial virus (RSV) is one of the most common respiratory infections observed in primary care. Although many think of RSV as a 'common cold', it is a serious health threat to certain populations, including children, particularly infants who are 6 months of age or younger, those with comorbidities, and older adults.[1] With the increasing number of options to reduce the impact of RSV infections, including morbidity and mortality, it is important to recognize that primary care clinicians must be able to identify people at risk for RSV infection, effectively educate them on the potential impact of the condition, and identify strategies to lower the risk.

Respiratory Syncytial Virus

RSV is a single stranded RNA virus that is classified into two subgroups: type A (RSVA) and type B (RSVB).[2] The two transmembrane glycoproteins, F (fusion) and G (**Figure 1**), play critical roles in the entry of the virus into the host cell.[1] The G protein is the most varying structure among RSV strains, and this variability dictates the antigenic nature between RSVA and RSVB groups.[2]

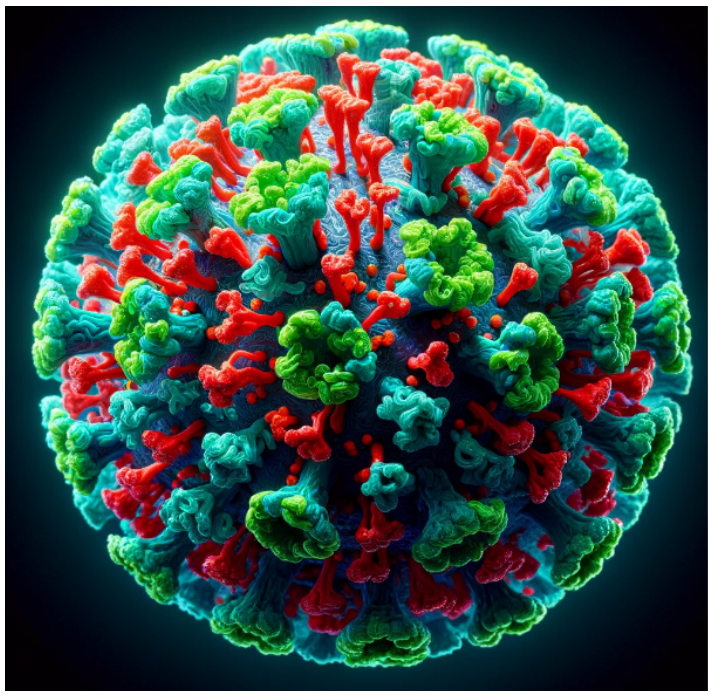

Figure 1. RSV with G and F transmembrane proteins.

The F protein is critical for infecting the host cell.[1] Unlike the G protein, the sequence of the F protein is highly conserved between RSVA and RSVB, with less than 10% sequence diversity between the two groups.[2] The F protein exists in two major forms based on its fusion to the host cell, the less stable prefusion (Pre-F) and the stable post-fusion (Post-F).[1] The F protein, specifically PreF, plays an important role in immunity and is the target for currently available vaccines and monoclonal antibodies.

Did you know?
Prior to the COVID-19 pandemic, RSV infections followed a seasonal pattern of peaking during late fall or early winter (mid-December to early February).[3] A low number of RSV infections had occurred during the first year of the pandemic, along with increases in RSV cases out of season.[1] This may be explained by reduced RSV exposure during the first year of the pandemic, creating an 'immunity debt', making the population more vulnerable to another RSV infection.[1]

Epidemiology and Burden of Disease Infants

Most children will experience at least one RSV infection by 2 years of age.[3] In fact, RSV is the leading cause of lower respiratory tract infection (LRTI) in Canadian children.[4] LRTI affects more than one in three children in the first 2 years of life and is the most common cause of hospital admission in their first year of life.[4] Hospitalization rates due to RSV have increased from 1% to 3% of all infants.[4] Mortality due to RSV is rare among children receiving supportive care, with an estimated case-fatality rate of less than 0.5%.[5]

Older Adults

RSV is increasingly recognized as a significant cause of severe respiratory disease in older adults.[6] Older adults experience a variety of factors (e.g. immunosenescence, weaker respiratory muscles, and lower lung compliance) associated with a higher risk of complications from RSV.[2]

The incidence of RSV LRTI in people ≥65 years has been estimated to be 6.7 cases per 1000 people per year.[1] Although the individual risk of severe RSV LRTI is lower in older adults than in infants, the impact of this infection in this group is significant.[1] A recent publication, compared outcomes of individuals aged ≥ 60 years hospitalized for COVID-19, influenza, or RSV.[6] They reported that RSV was associated with a lower risk of hospitalization, when compared to influenza and COVID-19; however, it had a higher risk of requiring:[6]

- Supplemental oxygen
- Mechanical ventilation
- ICU admission

Patients infected with RSV also report a lower quality of life, including an increase in fatigue, difficulty in social functioning, and limitations due to emotional problems.[8]

Practice Pearl
One Canadian study found that adults aged ≥65 years comprised only 22% of all RSV-related hospitalizations, yet were associated with 85% of RSV-related deaths.[9] Findings of the study indicated that 1 in 9 older adults hospitalized due to RSV, die from this infection and its complications.[9]

Clinical Presentation and Diagnosis

Patients infected with RSV will typically experience mild to moderate nasal congestion and low-grade fever within a few days of exposure and transmission, followed within a few days by a productive cough.[2] A portion of infected individuals will progress to LRTI and develop symptoms requiring hospitalization.[2] The timeline for a typical RSV infection is illustrated in **Figure 2**.

The clinical presentation of RSV cannot be distinguished from other respiratory viruses, including influenza.[10] The challenge in older adults is that the clinical signs of RSV overlap with signs of heart failure and chronic obstructive pulmonary disease (COPD).[10]

Did you know?
Repeat infections with RSV are common throughout life.[3] Approximately 30–75% of children <2 years of age who have been infected with RSV in their first 12 months of life will experience a reinfection the following season. When reinfected with RSV, most older children and adults will typically present with an upper respiratory tract infection.[3]

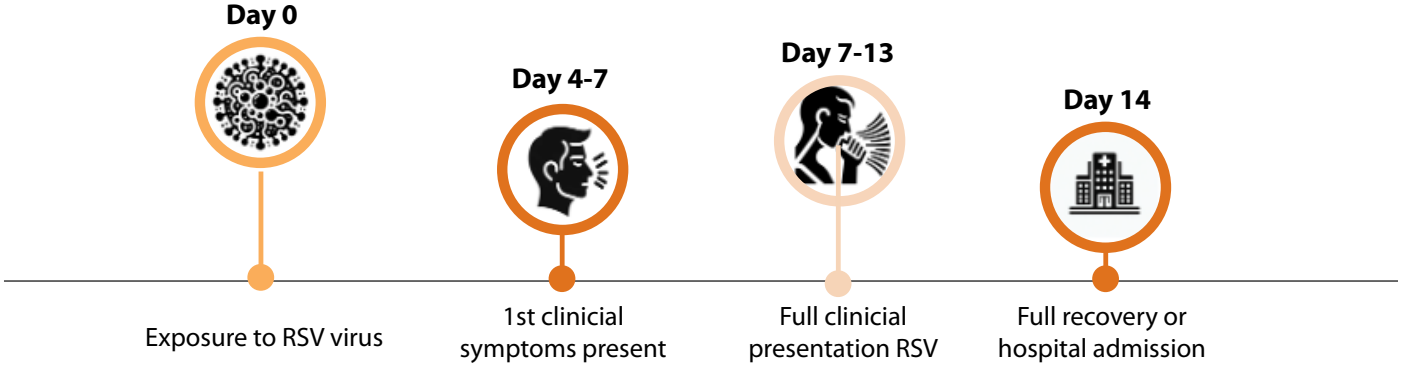

Figure 2 - Median Timeline for an RSV Infection; *adapted from Kaler et al.*[2]

Vaccine	Components	Dose	Efficacy – prevention of medically attending LRTI*	Safety	Other
Arexvy® (GSK)	Antigen: 120 µg PreF3 Adjuvant: $AS01_E$	0.5 mL IM (deltoid)	77.5% (57.9–89.0) for season 1 and interim season 2	**Common:** Pain at the injection site (61%), Fatigue (34%), Myalgia (29%) Headache (27%)	**Optimal timing for vaccine:** Onset of fall and winter RSV season, though could be administered any time **Coadministration:** ACIP recommends coadministration with other vaccines at the same visit
Abrysvo® (Pfizer)	Antigen: 60 µg PreF A 60 µg PreF B	0.5 mL IM (deltoid)	81.0% (43.5–95.2) for season 1 and interim season 2	**Common:** Fatigue (16%), Headache (13%), Pain at the injection site (11%)	

Table 1. Summary of Subunit RSV Vaccines[13-15]

Abbreviations: ACIP: Advisory Committee on Immunization Practices; **IM:** intramuscular; **LRTI:** lower respiratory tract infection; **PreF3:** Pre-fusion protein 3; **RSV:** respiratory syncytial virus.

*LRTI prompting one or more inpatient or outpatient healthcare services

Vaccine	Contains	C	Efficacy	Safety	Other
Sinagis® (Palivizumab)	Monoclonal antibody targeting the F protein	50mg for infants <5 kg 100 mg for infants ≥5 kg Single IM injection in anterolateral aspect of thigh	38 to 86% reduction in the risk of RSV hospital admissions	**Common:** Rash Pyrexia	Option in premature infants who will not benefit as significantly from maternal RSV vaccination Nirsevimab has been used in the second RSV season in those at high risk NACI has advised to consider these options in infants at elevated risk due to prematurity or comorbid illness
Beyfortus® (Nirsevimab)		15 mg/kg of body weight IM in anterolateral aspect of thigh every 28–30 days during RSV season	79% reduction in the risk of medically attended RSV LRTI	**Common:** Rash Pyrexia	

Table 2. Summary of Subunit RSV Monoclonal Antibodies.[5,20–22]

Abbreviations: IM: intramuscular; **LRTI:** lower respiratory tract infection; **NACI:** National Advisory Council on Immunization; **RSV:** respiratory syncytial virus

Did you know?
The shedding of RSV is highly variable and begins within a day of exposure and can persist for 3–7 days for adults, up to 14–21 days for infants, and up to several months for immunocompromised individuals.[2]

Risk Factors for Severe Respiratory Syncytial Virus Infection and Hospitalization

A variety of factors are associated with a higher risk of severe RSV infections. In children, these higher risk groups include prematurity, chronic lung disease of prematurity, congenital heart disease, trisomy 21, and neuromuscular disease.[3] In older adults, age and comorbidities (e.g. asthma, diabetes, coronary heart disease, heart failure, and COPD) increase the risk of severe RSV outcomes.[11]

Practice Pearl
It is challenging to predict which infants and older adults will develop severe RSV infections. At least half of all infants hospitalized with RSV were previously healthy without any of the established risk factors.[3]

Respiratory Syncytial Virus Prevention – Vaccination

Older Adults

Two subunit vaccines have been developed to prevent lower respiratory tract disease caused by RSV in adults aged ≥60 years. The two vaccines contain a stabilized version on the RSV Pre-F protein.[12] The National Advisory Committee on Immunization (NACI) has not provided recommendations for RSV immunization in older adults. The CDC recommends clinicians consider vaccination in adults aged ≥60 years using shared decision making. A summary of these two vaccines is provided in **Table 1**.

Infants

Immunization during pregnancy is another common strategy to reduce the risk of infectious disease in infants. The administration of Abrysvo® in pregnant persons between 24 and 36 weeks of pregnancy was evaluated to determine the efficacy in reducing RSV infections in infants.[16] Administration of the vaccine reduced the risk of:[17]

- The baby being hospitalized for RSV by 68% and having a healthcare visit for RSV by 57**%** within 3 months after birth
- The baby being hospitalized for RSV by 57% and having a healthcare visit for RSV by 51% within 6 months after birth
- Severe RSV disease by 82% within 3 months and by 69% within 6 months after birth

The most common adverse effects reported were similar to those reported in older adults, with pain at the injection site, headache, myalgia, and nausea.[17] More preterm births occurred when the vaccine was administered during 24 through 36 weeks of pregnancy; however, the difference was not statistically significant.[17] An increase in preterm births was not observed when the vaccine was administered between weeks 32 through 36 of pregnancy.[17]

ACIP recommends pregnant people between 32 through 36 weeks of pregnancy receive the RSV vaccine during the RSV season.[17] The vaccine is approved in Canada for the active immunization of pregnant individuals from 32 through 36 weeks gestational age. They also state that coadministration of the RSV vaccine with other adult vaccines including Tdap, COVID-19 and influenza can occur at the same visit, when recommended.[17]

Respiratory Syncytial Virus Prevention – Monoclonal Antibodies

Another strategy to reduce the risk of severe RSV in infants is the administration of monoclonal antibodies targeting the F protein. These antibodies provide passive protection to high-risk infants who are at risk of severe RSV outcomes.[18] These monoclonal antibodies bind to the F protein of RSV, thus preventing a key component of human cell infection by the virus.[19] These antibodies are used in infants at high-risk of infection such as those who are premature, and those with risk factors discussed above. **Table 2** provides a summary of these therapies.

Role of the Primary Care Clinician

Until recently, the options to reduce the impact of RSV infections in patients at risk were limited to public health interventions (e.g. social distancing, masking, and handwashing). With the introduction of vaccines and monoclonal antibodies, clinicians have options to reduce the impact of RSV in vulnerable patients. The key is to identify patients who can benefit from these interventions in clinical practice. Having a discussion with the patient about the benefits and risks of prevention options can help clinicians recommend the most effective strategies to reduce the patient's risk.

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