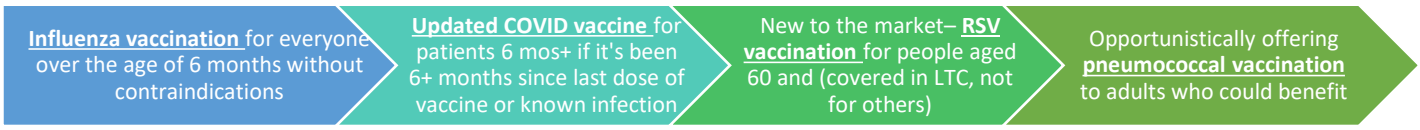
Thames Valley Family Health Team

The Dose Fall 2023

In This Issue…

Fall Vaccine Update: RSV, influenza, COVID, pneumococcal…oh my!

The peak season for respiratory viruses is nearly upon us, protect your patients by recommending the appropriate vaccines:



Do these four recommendations bring on more questions than answers? Continue reading below for more details.

Influenza

Continue to recommend seasonal influenza vaccination for all patients aged 6 months and older who do not have contraindications to vaccination[1].

Age Group	QIV (IIV4-SD) (FluLaval Tetra, Fluzone Quadrivalent)	QIV-HD (IIV4-HD) (Fluzone High- Dose Quadrivalent)	TIV-adj (IIV3-Adj) (Fluad)	Number of Doses
6 mos to 9 yrs	✓ 0.5mL IM			1 or 2*
9 yrs to 64 yrs	✓ 0.5mL IM			1
≥ 65 yrs	✓ 0.5mL IM	✓** **0.7mL** IM	✓** 0.5mL IM	1

IM = intramuscular injection

QIV = quadrivalent inactivated vaccine; QIV HD = high-dose quadrivalent inactivated vaccine; TIV-adj = adjuvanted trivalent inactivated vaccine

*Children 6 months to 9 years of age receiving flu vaccine for the first time in their lives should have a 2nd dose with a minimum interval of 4 weeks between doses.

✓=Recommended option

✓=Not preferred option but should still give if others are not available

= both QIV-HD and TIV-adj provide protection against influenza strains in older adults, there is insufficient evidence to recommend one over another, so choice based on vaccine availability in clinic. **Younger patients, even if they are in a high-risk group, are not indicated to receive the HD or TIV-adj vaccine.

Post-puncture shelf-life of QIV (IIV4-SD) multi-dose vials is 28 days

More info (in addition to references above): https://www.health.gov.on.ca/en/pro/programs/publichealth/flu/uiip/

COVID-19

For Fall 2023, NACI is recommending[2,3] vaccinating with a dose of the updated COVID-19 vaccine for persons 6 months and older if it has been **6 months since the later of the individual's last COVID-19 vaccination or known SARS-CoV-2 infection.** This reflects a shift in nomenclature from "booster" doses to "updated" or "yearly" doses, like the influenza vaccines.

Vaccination within a shorter interval (e.g. 3 months to < 6 months) is not known to pose a safety risk, rather the antibody response is greater with the longer dosing interval[7]. As of the date of publication of this newsletter, two updated COVID-19 vaccine has been approved, the **Spikevax® (Moderna) and Commirnaty® (Pfizer) Omicron XBB.1.5 subvariant vaccine**.[3,4,5]

> *From NACI[2,3]: Specifically consider recommending vaccination for those at higher risk of COVID-19 infection or severe disease, including individuals who are ≥ 65 years old, who reside in LTC or congregate living, with underlying complicating medical conditions, who are pregnant, who belong to First Nations, Metis, Inuit, racialized or equity-deserving communities, and those that provide essential community services.*

More info (in addition to references above):
https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_vaccine_administration.pdf

RSV

Arexvy® is a recombinant, adjuvanted respiratory syncytial virus (RSV) vaccine that has been approved this year for the prevention of lower respiratory tract disease (LRTD) caused by RSV infection. While it has been approved by Health Canada[6], the useability and recommendation for public coverage has not yet been determined by NACI. The use was reviewed by the American Advisory Committee on Immunization Practices (ACIP), and a majority of the committee supported use in the 65+ age group[7].

Who – indicated by Health Canada for individuals aged 60 and older.

What – A single-dose 0.5mL IM injection (need for additional doses not yet established). The product must be reconstituted prior to injection and must be administered within 4 hours of reconstitution.

Benefit – In the double-blind placebo-controlled phase 3 clinical trial with follow-up time over two RSV seasons, vaccine efficacy at preventing confirmed RSV-associated LRTD was 82% in the first year and 56% in the second year after a single dose[7]. They estimate the 2-year benefit at ~75% as the trial was only 18 months in duration. The trial was not powered to estimate efficacy in the older (≥ 75 years) and frail populations, who tend to be at greater risk of severe illness; was also not powered to determine the differences in hospitalization rates, severe illness requiring respiratory support and death due to RSV illness[2].

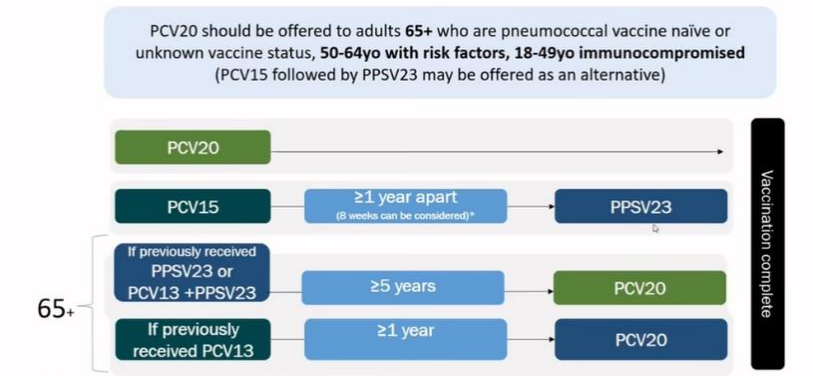
Safety – Usual vaccine side effects (myalgia, fatigue, injection site reaction or pain, headache) are common as the vaccine is adjuvented[6]; Guillain-Barre syndrome, acute disseminated encephalomyelitis and atrial fibrillation have also been observed but causality is not established. May be co-administered with the influenza vaccines (co-administration was studied in a Phase 3 study and did not find evidence of statistically significant interference in immune response or safety concerns)[8].

Cost – The Ontario Ministry of Health and Long Term Care has announced a plan[9] to fund the RSV vaccine this year for persons 60 years and older living in long-term care homes, Elder Care Lodges, and for some retirement home residents. Details of this roll-out are still pending. For all others, Arexvy® is now available in pharmacies. The out-of-pocket cost is approximately
$280-340 (variable, dependent on pharmacy markup and fees). There may be the opportunity for clinics to order directly from GSK at cost for their patients (must set up an account with GSK). A second RSV vaccine by Pfizer is also in development.

More info (in addition to references above): https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html

Adult Pneumococcal Vaccination

Current NACI recommendation for Pneumococcal vaccination in Adults[10]:



** Ontario does not pay for PCV-20 (Prevnar 20) or PCV15 (Vaxneuvance).
Prevnar 20 costs ~$116+ mark up + dispensing fee
Vaxneuvance costs ~$106 + mark up + dispensing fee

Why the recommendation for the 5-year interval between PPSV-23 (Pneumovax-23) and Prevnar 20?

- takes advantage of the estimated effectiveness duration of PNEU-P-23 and the boosting anticipated with PCV-20
- may also maximize the total duration of protection against pneumococcal infection.
- **ACIP (American) recommendation[11] is different:** either PCV15 or PCV20 ≥1 year after PPSV23

Why is PCV 20 given ≥1 year for those previously vaccinated with PCV13 (Prevnar-13)?

- expanded serotype coverage in a time effective manner
- the interval between vaccines can be as short as 8 weeks if needed (ie high risk)
- However, It should be noted that the **ACIP (American) have a different recommendation "incremental public health benefits of providing PCV15 or PCV20 to adults who have received PCV13 only or both PCV13 and PPSV23 have not been evaluated. These adults should complete the previously recommended PPSV23 schedule**"

Why is PCV-20 recommended over PCV15 +PPSV23?

- Cost Utility model done by NACI (lots of assumptions) favored PCV 20 for cost effectiveness.
- Current efficacy data is seroconversion for each serotype for PCV15 and PCV20 compared to PCV13
- **There are no clinical end points studied with either of the PCV15 or PCV20.**

On giving multiple vaccines…

There is no contraindication to concurrent administration of combinations of the influenza, pneumococcal and COVID-19 vaccines. As stated above, the RSV vaccine may be concurrently administered with the influenza vaccines.

From NACI[1]– when giving more than one injection at a single clinic visit, it is preferred to administer in different limbs. If that is not possible, injection sites in one limb should be separated by at least 2.5cm (1 inch). Separate needles and syringes should be used for each injection.

FAQs about simulants for adult ADHD

My adult ADHD patient is finding their long-acting stimulant is not lasting through their longer work day, what can I do?

- Consider an alternative product with a longer duration of action;
    - Foquest (methylphenidate CR) has the longest duration of action (13-16h), followed Vyvanse (lisdexamfetamine dimesylate) (13-14h), followed by Adderall (mixed amphetamine salts) and Biphentin (methylphenidate XR) (10-12h)[1]
- Or, add a second dose of a short acting product (methylphenidate IR or Dexedrine) in the afternoon – this can be dosed regularly or PRN for longer days. Monitor for changes in sleep.

(continued on following page)

How do I switch between stimulants?

- When switching between methylphenidate products, switch to the same daily dose, rounding down where necessary[2]
- When switching from a methylphenidate to an amphetamine based product, switch to half the dose[3]
- When switching any other agent to Vyvanse, switch to 20-30mg and titrate up[2]
- Tapers are not necessary when pausing treatment, and gradual up-titration is not needed when resuming[3]

How can I tailor a patient's medication regimen if they are concerned about cardiovascular safety?

- The evidence is conflicting regarding the risk of sudden CV death and arrythmia with stimulant medication. Several large observational studies found no evidence of increased risk of MI, stroke or sudden cardiac death[4]
- On average, stimulants are expected to increase SBP 1-6 mmHg and HR 1-10 bpm, though higher in some[4]
    - In patients with existing hypertension or CVD monitor heart rate and blood pressure regularly
- Consider the patient's individual risk factors – e.g. family history of sudden cardiac death or arrhythmia
    - Refer patients with structural abnormalities or long QT syndrome to cardiology for assessment
    - In patients with other cardiac risk factors, monitor ECG periodically
- Be aware that non-stimulant ADHD medications are not without cardiac side effects. For example, atomoxetine can increase QT/BP/HR, guanfacine and clonidine can cause decreased BP/HR and abrupt stopping of these meds can cause rebound increases in BP/HR[4].

The CADDRA Medication Table is an excellent quick resource about the properties of the ADHD medications

A different approach – targeted naltrexone for alcohol use disorder

Have you heard of targeted naltrexone therapy ("the Sinclair method") for alcohol use disorder (AUD)?

Naltrexone daily treatment is an effective first line treatment for any severity of AUD, used to achieve abstinence or to reduce consumption of alcohol. The cost of a 50mg dose is approximately $3 per day. Daily dosing of naltrexone is considered one of the first-line treatments for all severities of AUD, the other is acamprosate[1,2].

Targeted naltrexone therapy is an "as needed" approach, where it is taken 50mg once daily PRN when the patient feels strong cravings or 1-2 hours before expected drinking/trigger exposure[1]. While this approach is off label (all the second-line AUD treatments are off-label) and less widely studied, it can provide an alternative to no treatment if a patient cannot afford or is resistant or non-compliant to daily dosing. The small trials that have been published (primarily in men, younger individuals) showed a reduction in the number of heavy drinking days in a month, and the likelihood of intoxication[2,3,4,5]. Other studies have shown less effect, demonstrating why this is not necessarily a first line treatment approach[6].

Recall that opioid use in the past 7-10 days, acute hepatitis, liver failure and elevated liver enzymes are contraindications to using naltrexone in any dosing approach[1].

Risks of naltrexone include GI adverse effects (may be worse for women, patients who do not completely abstain from alcohol), headache, dizziness, and increase of AST/ALT – monitoring of LFTs is recommended at baseline and periodically (e.g. at 1, 3, 6 months of treatment)[1].

So it's time to stop testosterone…

Consider this scenario: you and your patient have decided it is time to stop testosterone replacement therapy – perhaps it is no longer effective at treating their symptoms, or it no longer aligns with their goals of care, or they are experiencing adverse effects. Whatever the reason, consider the following tips for tapering off testosterone replacement therapy, a practice that can have its nuances.

Oral capsules	Absorption is highly variable. Most will have very little absorption unless taken with a high fat meal. Can taper by reducing dose and frequency but stopping cold turkey may also be a reasonable option
Topicals	Androgel pump delivers 1.25g/pump (most expensive, but easiest for administering incremental doses), otherwise available as 2.5g or 5g packets (cannot easily split dose) • Androgel is now available as a generic, which is about 2/3rds of the cost of brand name Testim available as 5g tubes, these are easier to use partial doses than the Androgel packets, but it is not an exact way of delivering a dose (however accuracy of dosing may not be very important with a taper) Testosterone patch discontinued 2022, Axiron (axillary testosterone) no longer available
Nasal	Nasal gel (Natesto) – one pump (5.5 mg) in each nostril BID-TID; taper by adjusting frequency of dosing
Intramuscular injectables	Trough usually occurs at 2-3 weeks after last dose. Usually dosed every 2 weeks, but doses may be reduced and/or spread out to every 3-4 weeks during a taper Adjusting frequently causes a yo-yo effect (supratherapeutic in first week after injection)

Considerations for converting between testosterone products:

IM testosterone cypionate & enanthate (Delatestryl® 200 mg/mL and Depo-testosterone® 100 mg/mL) have a 1:1 equivalency
Be wary of <u>administration errors</u> as the concentrations are different

Approximately 10% of testosterone in transdermally applied gels is absorbed. (e.g. 50 mg testosterone gel delivers approximately 5mg of absorbed drug)

The bioavailability of oral testosterone undecanoate is about 7% provided it is taken with a meal. However, as mentioned above, this is highly variable.

While engaging in shared decision-making regarding testosterone replacement, consider sharing some of these facts which may help to provide context for patients.

Potential Benefits of testosterone replacement:
- Increased quality of life by 3.4/85-point scale
- Increased sexual function/libido = ~1 extra sexual encounter with partner each month
- Less benefit than PDE5 inhibitors on erectile dysfunction
- Other purported small benefits: improved grip strength, physical function, BMD, lean body mass (however the ACP does not recommend initiating treatment with testosterone with the primary goal of improving energy, vitality, physical fitness or cognition)

Potential Harms of testosterone replacement:
- Erythrocytosis - NNH 53 over <12 months
- Increased PSA - NNH 26 at 12 months
- Increased acne, mood changes, blood pressure
- Other harms are likely (e.g. stroke, MI, VTE, possibly prostate cancer), but trials are too short to quantify

Also consider investigating possible reversible causes of low testosterone including use of alcohol, opioids, anabolic steroids, estrogen, GnRH inhibitors, corticosteroids, spironolactone, cimetidine, cyproterone, ketoconazole, phenytoin, and chemotherapy

Tool Spotlight: PEER Decision Aids

PEER (Patients, Experience, Evidence, Research) is a group of primary care providers who work in collaboration with the Alberta College of Family Physicians (AFPC) to, in their words, "provide optimal health care in the context of Patient preferences and values, physician Experience and scientific Evidence from relevant Research reflecting patient oriented outcomes". They offer a variety of valuable resources, including the decision aids below.

- **Diabetes Decision Aid**: https://decisionaid.ca/diabetes/
- Calculates 10-year risk of complications of diabetes given patient specific factors
- Estimates the impact of treatment on the 10-year risk
- Factors in a shared decision making talking point to focus on the risk factors that matter most to your patient
- Offers the ability to generate a summary of the discussion that can be shared or uploaded into an EMR

- **Pain Calculator (C-TOP Tool)**: https://pain-calculator.com/
- Visually depicts the impact of various treatments (medication by class and other non-pharmacological interventions) for diferent pain conditions
- 3 calculators: for neuropathic pain, osteoarthritis or low back pain
- Opportunity to input the patient's current pain score (on 10-point visual scale) to estimate what the impact on score would be with therapy

Pharmacy practice update: minor ailments expansion

As of October 1, 2023, pharmacists in Ontario are permitted to prescribe treatment for the following new minor ailments:

- Acne (mild)
- Aphthous Ulcers (canker sores)
- Diaper dermatitis
- Vulvovaginal candidiasis (yeast infection)
- Pinworms and threadworms
- Nausea and vomiting of pregnancy

Another change to minor ailments in Ontario this month is that eligible medications are no longer designated based on the American Hospital Formulary Service classification. The eligible medications which can be prescribed for minor ailments are now designated by a list in the regulations to the Pharmacy Act. This list is available on the Ontario College of Pharmacists website in two formats, linked here – chart and list.

Caring for trans patients in primary care part 2: feminizing hormone therapy

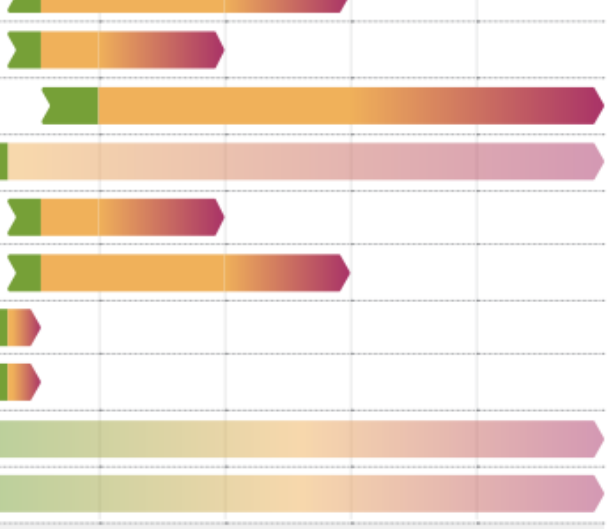
We are continuing with our series of highlights of elements of the Rainbow Health Ontario guides for providing gender-affirming care for trans patients in primary care with **feminizing hormone therapy**.

Feminizing hormones are used in gender-affirming care for *transfeminine* patients (those who were assigned male at birth but who identify with the feminine spectrum). This therapy includes estrogens and anti-androgens. There is no consensus about the timing of initiation of these medications – in some cases, the anti-androgen is initiated 1-3 months prior to the estrogen, and in others they are started and titrated simultaneously. The goal is to reduce the effects of testosterone and promote the development of feminine secondary sex characteristics (keeping in mind individual patient's goals). The expected time course to full effect of physical changes is variable, see the graphic below for a summary.

EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES

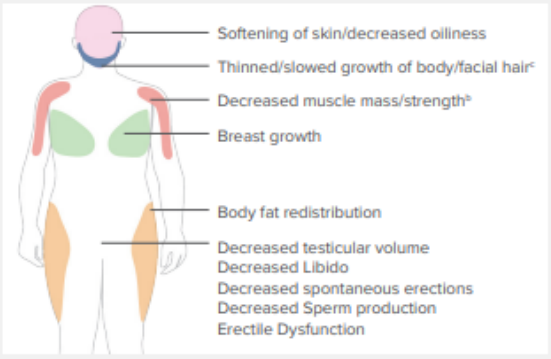
The degree and rate of physical effects are largely dependent on patient-specific factors such as age, genetics, body habitus and lifestyle, and to some extent the dose and route used (selected in accordance with a patient's specific goals and risk profile).[8]

Physical Effects	Reversibility	Onset[a]	Expected maximal effect[a]
Softening of skin/ decreased oiliness	Reversible	3-6 months	Unknown
Body fat redistribution	Reversible/ Variable	3-6 months	2-3 years
Decreased muscle mass/strength[b]	Reversible	3-6 months	1-2 years
Thinned/slowed growth of body/facial hair[c]	Reversible	6-12 months	>3 years
Scalp hair loss (loss stops, no regrowth)	Reversible	1-3 months	Variable
Breast growth	Irreversible	3-6 months	1-2 years
Decreased testicular volume	Variable	3-6 months	2-3 years
Decreased libido	Variable	1-3 months	3-6 months
Decreased spontaneous erections	Variable	1-3 months	3-6 months
Decreased sperm production	Variable	Variable	Variable
Reduced erectile function	Variable	Variable	Variable



Keep in mind: Use patient preferred terminology. "Testicular" and "erections" may be upsetting to some but not all. Physical changes related to androgen blockade and estrogen may take months to appear and are generally considered to be complete after 2-3 years on hormone therapy. Breast growth is an aspect of feminization to which many transfeminine patients assign great importance. The degree of breast development is dependent on many factors, but most transfeminine patients experience modest breast development (average cup size <A, at a developmental Tanner stage of 2-3).[9,10] Feminizing therapy does not affect the pitch of the voice in transfeminine patients.

a) Estimates represent unpublished clinical and published observations[8,12,13]
b) Significantly dependent on amount of exercise;
c) Complete removal of facial hair requires electrolysis, laser treatment, or both



Source: Guidelines for Gender Affirming Primary Care with Trans and Non-Binary Patients: A Quick Reference Guide for Primary Care Providers[1]

Feminizing Therapy	Formulation	Starting Dose	Usual Dose	ODB/OHIP+ Coverage
ANTI-ANDROGENS*				
Spironolactone	Oral	50mg daily-BID	100mg BID	✓
Cyproterone	Oral	12.5mg q2d-daily	12.5mg-25mg daily	✓
ESTROGENS **				
Estradiol	Oral	1-2mg daily	4mg daily or 2mg BID	✓
Estradiol	Transdermal Patch	50mcg daily (patch applied 2X/week)	Variable, up to 200mcg daily (patch applied 2X/week)	X
Estradiol	Transdermal Gel	2.5g daily (2 pumps)	Variable, up to 6.25g (5 pumps) daily	X
Estradiol Valerate	IM Injection	3-4mg weekly or 6-8 mg q 2 weeks	Variable, up to 10mg weekly	X

*should a patient choose to pursue surgical interventions, androgen suppression is not required in most transfeminine patients following orchiectomy (+/- vaginoplasty)

**once a patient is over the age of 50 and has been on estrogen for several years, doses of estrogen treatment can be reduced to those used in post-menopausal cis women (e.g. starting doses listed here, or transition to low dose topicals)

Safety and Monitoring

Safety of both feminizing and masculinizing hormone therapy for trans patients is considered by the Endocrine Society to be “safe without a large risk of adverse effects when followed carefully for a few well-documented medical concerns”. For both transfeminine and transmasculine patients, lab monitoring is recommended at 3, 6 and 12 months after initiation of therapy, and yearly thereafter (for a full list of recommended labs, see the Rainbow Health quick reference). Checklists for ongoing preventative care are also available in the full guidelines.

Gender Journeys

Gender Journeys is a new program being offered by TVFHT in collaboration with the London Intercommunity Health Centre. It is a safe space for individuals age 16+ in the beginning stages of transition to explore questions of gender identity and belonging. We welcome those just thinking about transition and those who may have already taken early steps towards their transition, as well as those who are gender-questioning.

This program is 8 weekly sessions, 2 hours each, in person in East London. It is not walk-in, and is expected that participants will attend all the sessions.

For more information or to register - https://thamesvalleyfht.ca/programregistration/gender-journeys/

References

Vaccines

1. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-10-influenza-vaccine.html
2. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-use-covid-19-vaccines-fall-2023.html
3. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-addendum-guidance-use-covid-19-vaccines-fall-2023/statement.pdf
4. https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/moderna.html
5. https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/pfizer-biontech.html
6. Arexvy Product Monograph. Aug 4 2023. Accessed online at https://pdf.hres.ca/dpd_pm/00071904.PDF
7. ACIP Evidence to Recommendations for Use of GSK Adjuvanted RSVPreF3 Vaccine (AREXVY) in Adults Ages 60 and Older. July 2023. Accessed Online at https://www.cdc.gov/vaccines/acip/recs/grade/GSK-Adjuvanted-RSVPreF3-adults-etr.html
8. Chandler R, Montenegro N, Llorach C, Quinn D, Noriega-Aguirre L, Bensellam M, De Schrevel N, Kuriyakose S, Lambert A, Olivier A, Hulstrøm V. 2139. Immunogenicity, reactogenicity and safety of a Respiratory Syncytial Virus prefusion F (RSVPreF3) candidate vaccine co-administered with the seasonal quadrivalent influenza vaccine in older adults. Open Forum Infect Dis. 2022 Dec 15;9(Suppl 2):ofac492.1759. doi: 10.1093/ofid/ofac492.1759. PMCID: PMC9752441.
9. https://news.ontario.ca/en/release/1003504/connecting-ontarians-to-the-tools-they-need-to-stay-healthy-this-respiratory-illness-season
10. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html
11. https://www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm

ADHD Troubleshooting

1. CADDRA Medication Chart https://www.caddra.ca/wp-content/uploads/Nov-2022-Medication-laminate-1.pdf
2. Clinical Resource, Comparison of ADHD Medications (Canada). Pharmacist's Letter/Prescriber's Letter. May 2018.
3. Pharmacist's Letter Canada. September 2019, No. 350918. Solve Common Dilemmas With ADHD Stimulants
4. A Soubolsky, M Bishara. ADHD Drug Comparison Chart. In RxFiles Comparison Charts (Online). Updated Aug 2023. Accessed online at www.rxfiles.ca

Testosterone Tapering

1. Jensen K. Injectable and Oral Testosterone Shortage. In MedSask Medication Information Service. Updated 20 Jan 2023. Accessed online at https://medsasklive.usask.ca/sites/medsask/files/2023-02/testosterone-v.51.pdf
2. Paty B. University of British Columbia. Appropriate testosterone testing for male hypogonadism. In This Changed My Practice. Updated 21 Jan 2020. Accessed online at https://thischangedmypractice.com/testosterone-testing-male-hypogonadism
3. Crawley A, Regier L. Testosterone Drug Comparison Chart- Andropause. In RxFiles Comparison Charts (Online). Updated Aug 2021. Accessed online at www.rxfiles.ca
4. Qaseem A, Horwitch CA, Vijan S, Etxeandia-Ikobaltzeta I, Kansagara D; Clinical Guidelines Committee of the American College of Physicians; Forciea MA, Crandall C, Fitterman N, Hicks LA, Lin JS, Maroto M, McLean RM, Mustafa RA, Tufte J. Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians. Ann Intern Med. 2020 Jan 21;172(2):126-133. doi: 10.7326/M19-0882. Epub 2020 Jan 7. Erratum in: Ann Intern Med. 2023 Apr;176(4):584. PMID: 31905405.
5. Grober ED, Krakowsky Y, Khera M, Holmes DT, Lee JC, Grantmyre JE, Patel P, Bebb RA, Fitzpatrick R, Campbell JD, Carrier S, Morgentaler A. Canadian Urological Association guideline on testosterone deficiency in men: Evidence-based Q&A. Can Urol Assoc J. 2021 May;15(5):E234-E243. doi: 10.5489/cuaj.7252. PMID: 33661092; PMCID: PMC8095276.

Targeted Naltrexone

1. C Coons, M Jin, J Bareham. Alcohol Use Disorder (AUD) Comparison Chart. In RxFiles Drug Comparison Charts (Online). Updated July 2023. Accessed online at www.rxfiles.ca
2. UpToDate Online. Alcohol use disorder: Pharmacologic management https://www.uptodate.com/contents/alcohol-use-disorder-pharmacologic-management?search=targeted%20naltrexone&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#
3. Bold KW, Fucito LM, Corbin WR, DeMartini KS, Leeman RF, Kranzler HR, O'Malley SS. Daily relations among affect, urge, targeted naltrexone, and alcohol use in young adults. Exp Clin Psychopharmacol. 2016 Oct;24(5):367-375. doi: 10.1037/pha0000090. PMID: 27690505; PMCID: PMC5111359.
4. Epler AJ, Sher KJ, Loomis TB, O'Malley SS. College student receptiveness to various alcohol treatment options. J Am Coll Health. 2009 Jul-Aug;58(1):26-32. doi: 10.3200/JACH.58.1.26-32. PMID: 19592350; PMCID: PMC2818496.
5. Santos GM, Ikeda J, Coffin P, Walker J, Matheson T, Ali A, McLaughlin M, Jain J, Arenander J, Vittinghoff E, Batki S. Targeted Oral Naltrexone for Mild to Moderate Alcohol Use Disorder Among Sexual and Gender Minority Men: A Randomized Trial. Am J Psychiatry. 2022 Dec 1;179(12):915-926. doi: 10.1176/appi.ajp.20220335. Epub 2022 Oct 26. PMID: 36285404; PMCID: PMC10072332.
6. Kranzler HR, Tennen H, Armeli S, Chan G, Covault J, Arias A, Oncken C. Targeted naltrexone for problem drinkers. J Clin Psychopharmacol. 2009 Aug;29(4):350-7. doi: 10.1097/JCP.0b013e3181ac5213. PMID: 19593174; PMCID: PMC3184851.

Feminizing Therapies for Trans Patients

1. Guidelines for Gender Affirming Primary Care with Trans and Non-Binary Patients: A Quick Reference Guide for Primary Care Providers. https://www.rainbowhealthontario.ca/resource-library/qrg
2. Sherbourne Health's Guidelines for Gender-Affirming Primary Care with Trans and Non-Binary Patients. 4th Edition. 2019. https://www.rainbowhealthontario.ca/resource-library/sherbourne-healths-guidelines-for-gender-affirming-primary-care-with-trans-and-non-binary-patients/