ACUTE PAIN MANAGEMENT FOR PEOPLE ON CHRONIC OPIOIDS/OPIOID AGONIST THERAPY

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Background

- It can be challenging to manage acute pain for people on chronic opioids because of opioid-related changes in the neural-reward pathway, tolerance, & hyperalgesia.
- It can also be challenging to manage acute pain for people with a hx of SUD (incl. opioid use disorder & people on opioid agonist therapy), chronic pain, anxiety, or depression because of a ↓ pain threshold, ↑ sensitivity to the pain experience, & ↑ distress in response to pain.[6]
- People with SUD may over-report pain due to fear of not being taken seriously **OR** under-report pain due to fear of being prescribed something that could cause a return to use.[18]
- Untreated acute pain may ↑ stress/suffering and cause ↑ in/return to opioid use (illegal/Rx).[13]

Clinical Pearls:

- Continue "baseline" opioid agonist therapy (OAT)/chronic opioid in most cases → **avoid "opioid deficit"**.
- A detailed med hx (prescribed & illegally obtained) can ↓ risk of opioid withdrawal & improve pain management.
- Optimize & emphasize non-opioid pharm & non-pharm strategies whenever possible.
- The presence of opioid use disorder (OUD) itself should not prevent the use of opioids to treat acute pain when opioids are indicated for severe pain.[8] Adding short-term opioids to OAT can be appropriate & may avoid triggering a return to use (i.e. relapse). Ensure tight control over opioid dispensing & taper off promptly when pain resolves. Pt may prefer a non-opioid approach. Discuss relapse prevention & create a relapse contingency plan, ideally together with an OAT prescriber.[13]
- If adding opioids for severe pain, establish sunset clause (i.e. discontinuation plan) based on expected pain duration.
- When adding opioids, higher than usual doses are often temporarily required to overcome tolerance.

General Principles

- Confirm which opioid taken, dose (any recent changes), route, interval/frequency (time last taken), reason for use (e.g. chronic pain, OUD), source (e.g. Rx, illegally obtained), frequency of witnessed ingestion, access to/presence of take home doses, & social situation/stability. Verify with primary care provider/community pharmacy as able. When establishing baseline needs, inquire about, document, & account for non-medical opioid use as appropriate.
- **Maintain baseline chronic opioid/OAT reqs** in most situations by continuing the current opioid dose (or similarly dosed if route not available/using from the illegal drug market). **The baseline dose provides negligible analgesia for acute pain.**
- **What is an "opioid deficit"?** When a patient has a physiological dependence on an opioid that is abruptly ↓/withdrawn, they will experience a net loss of opioid effect with subsequent symptoms of opioid withdrawal. This can be dangerous as it results in loss of opioid tolerance & may be followed by opioid overdose/death upon re-initiation of the prior opioid dose. Also, opioid withdrawal will ↑ the pain experience & may also ↑ post-op opioid requirements.[12] Goals are to avoid &/or treat opioid withdrawal, as well as to treat the pre-existing condition (usually with the prior home regimen) & temporarily add analgesia for the acute pain period.[5,6,7]
- Acute pain management should generally be approached the same as for patients not prescribed or using opioids; For mild-moderate acute pain, NSAIDs/acetaminophen are preferred over added opioids (risk > benefit).
- If concurrent opioid used for severe acute pain, generally avoid low potency opioids (e.g. codeine, tramadol) & **consider IR opioids on a scheduled** (esp useful if compulsive use) or PRN **short-term basis**; usually no role for adding SR opioids.

Approach to Acute Pain Using Non-Opioids

Non-opioid strategies are critical! See rxfiles.ca/PainLinks

What are the patient's:

- baseline pain levels?
- symptoms of opioid withdrawal (COWS), if any?
- preferences, goals, & expectations?
- respiratory depression/overdose risks (e.g. ↑ age, OSA)?

What has previously been helpful?

Follow condition-specific guidelines & develop flare management plans as appropriate (e.g. sickle cell disease, migraines).[15]

NSAIDs (oral/topical) & acetaminophen: FIRST LINE[24]

- Evidence[2020 SR] for benefit in acute MSK injury (non-low back). Opioids were no better than NSAIDs or acetaminophen → risk of opioids >> benefit.[14,28]
- NSAID + acetaminophen ≥ opioids for acute extremity pain[2017 RCT, 27] & most dental procedures.[21,22,28]
- Schedule (rather than PRN): NSAID (reassess after ~3 days) **combined with** acetaminophen (continue as long as added IR opioid, if used).[11]
- No evidence to suggest IV ketorolac > po NSAID (unless pt is unable to take po).[30] If used, 10mg likely as effective as 30mg IV dose.[31]

Co-analgesics / Adjuncts: (next pg for options unique to acute care settings)

- Gabapentinoids: caution → potential for abuse.
- Non-BZD muscle relaxants (e.g. baclofen, etc): short-term.[28,29]
- Non-NSAID topicals (lidocaine, capsaicin): little evidence.[23]
- Concurrent BZD/other CNS depressants: use with caution / avoid → risk of respiratory depression.

Non-Pharmacological Strategies:

- Shared decision-making: feeling of control can ↓ pain & suffering.
- "5M approach": combine **m**ind, **m**ovement, **m**edication, **m**odalities, & **m**anual therapies (e.g. ice/heat, physical techniques, TENS, behavioural strategies, deep breathing). Consider a "Comfort Menu."
- Expectation management: communicate goal of "tolerable discomfort," not pain elimination.[5]
- Collaboration: multi-disciplinary involvement useful.
- Flexibility: it can be difficult to predict pain needs.
- Offer reassurance: *"I am taking an approach that treats both this new pain & your chronic pain condition / OUD."*

Approach to Managing Severe Acute Pain Using Opioids

An Advantage | A Disadvantage | A Large Disadvantage

codeine, fentanyl, heroin, hydromorphone, morphine, oxycodone, tapentadol, tramadol

(Rx or from illegal drug market)

Generally, continue to meet baseline opioid requirements with scheduled dosing (account for use of illegally obtained opioids→inpt settings). May require opioid rotation to ~equivalent MED.

Option A. Add 10% of MED (of same baseline opioid if appropriate/possible), given at appropriate intervals, po preferred (may schedule & encourage pt to refuse if not needed as inpt). Amount of tolerance can be variable → follow closely to adjust/titrate.[17]

Option B. If on PRN opioids only, consider changing PRN dose to ↑ by 1.5x (e.g. home dose morphine 10mg po QID PRN→Rx morphine 15mg po QID PRN).[17]

Option C. Some suggest taper baseline opioid prior to elective procedures. **X** VERY limited evidence[observational studies] suggests association between dose & outcomes. Further study needed.[16]

methadone

DO NOT STOP METHADONE – restarting can be challenging[15]

Option A. Add other short-term opioids (e.g. morphine, hydromorphone) as above, po preferred.
✓✓ Quick onset to assess effect & adjust PRN.
X Risk misuse, Rx in small, controlled quantities.

Option B. Divide daily methadone dose to TID-QID: analgesic effect lasts ~6-8hrs.[8]
✓✓ Useful if stable daily dose & in recovery.
XX Avoid in initiation phase or if outpt.

Option C. If divided dosing insufficient & other opioids **CI** (e.g. confirmed severe allergy), may use methadone dosed up to 10% of total daily dose TID PRN. **XX** Avoid: risk of accumulation & overdose.[19]

buprenorphine

Dosing equivalencies:[5]
buprenorphine-naloxone (**SUBOXONE**, g) 8mg/2mg sublingual tab/film daily

is approximately equivalent to:

PROBUPHINE 320mg intradermal implant q6mos

SUBLOCADE 100mg subcut q1mos.

Note: Maximum dose of bup transdermal (**BUTRANS**) is 20 mcg/hr patch q7d, provides bup 0.48mg/d. **Much** < 8mg bup-nal SL.

DO NOT STOP BUPRENORPHINE-NALOXONE – restarting can be challenging[6,7,8]

Approach is controversial → concern that buprenorphine's high affinity for the mu-opioid receptor & long $t_{½}$ might block the effect of other opioids, particularly at doses >8-12mg/day. No RCTs available to direct approach. Doses of ≤8mg (or equivalent, see left) are not expected to block the effects of other opioids & should be continued through an acute pain episode. Case reports suggest pain can be well managed even while bup-nal dose >8-12mg is maintained.[6]
Risk of changing bup-nal often > benefit esp if using for OUD. If bup-nal is stopped completely to treat acute pain with other opioids, create a plan for bup-nal re-initiation to avoid precipitating withdrawal upon restarting.

Option A. Divide bup daily dose to TID-QID: analgesic effect may last ~4-8hrs; debated, off-label.[7,8] May also ↑ daily dose by 20-25%,[ASAM 2020] OR use small (e.g. 2mg) PRN doses (CDN max 24mg, FDA max 32mg).[7,8]
✓✓ Useful if stable dose, in recovery, taking bup for chronic pain, & emergent mild acute pain.
X If daily dose >12mg may limit ability to trial other opioids due to mu-receptor occupancy.

Option B. Add other short-term IR opioid (e.g. hydromorphone ?preferred due to ↑affinity)
✓✓ For moderate-severe pain - evidence & clinical experience suggest analgesia often sufficient with this approach.[7]
X No evidence to support addition of IR opioids in ambulatory care.[8] Limit to 3d supply (?daily dispensed), if using.[25]

Option C. Lower/taper bup daily dose to 8-12mg/day (to free up mu-receptors) ~2-3 days pre-procedure & add regular IR opioid.[2,3] Usually resume home bup-nal dose ~3 days post-op.[26]
✓✓ Useful if stable dose, **severe pain anticipated** (i.e. elective surgery), **&** pt taking it for chronic pain.
XX May destabilize a person with OUD. Limited evidence[8] & little utility for unplanned acute pain.
If ↓ bup & adding another opioid, **must monitor closely for overdose over next 72hr** (as bup slowly wears off & is replaced by a more strongly activating (full agonist) opioid on the mu-receptor).

How long should additional opioids generally continue? (≤3d often sufficient)[11,15]

Expected Severity	Duration
Mild: Nonspecific acute LBP, sprains, strains, appendectomy, limited cellulitis, dental procedures, minor fracture (wrist, ankle, foot) ORIF, migraine/headache (caution: medication-overuse HA)	**1-2 days** (if at all)
Moderate: Limited 2nd degree burns, trauma, minimally invasive sx, noncompound fractures, most laparoscopic procedures	**3-5 days**
Severe: Major abdominal, thoracic, & maxillofacial surgeries, CABG, hip/compound fractures, most TJA (hip, shoulder, ankle), laminectomy	**7-14 days**
Long-term recovery may be needed for: Amputations, major plastics (e.g. infection debridement), & spine procedures (e.g. lumbar fusion)	**14 days** (or more)

- People on chronic opioids may require longer duration than those who are not - yet infrequently need >14 days.[17]

What is a sunset clause?

Pre-emptively communicates a plan for discontinuing / tapering opioids based on expected duration of pain & condition-specific guidelines.

- Generally, aim to return to baseline dose & taper added opioids if using regularly >5-7 days.
- If needed, ER/acute care might provide concurrent short opioid outpt Rx (e.g. 3-7d), which may warrant tapering/follow-up by the primary care provider.[7]
- In most cases, dispensed Rx quantities should be structured / tightly controlled, given at frequent intervals in small amounts / part fills, with close follow-up, & tapered as soon as able.

Concerns about Problematic Chronic Opioid Use:

- If concerned about problematic opioid use by people taking opioids chronically for pain, assess for OUD (see RxFiles: Concomitant Chronic Pain and Opioid Use Concerns chart).
- Avoid stigmatizing people on chronic opioids by undervaluing their expression of pain &/or placing labels such as "drug-seeking." Pre-existing tolerance may mean using higher than usual opioid doses for analgesia.

Considerations Specific to Acute Pain for People with Opioid Use Disorder (OUD):

For patients with OUD & acute pain who are on OAT: Maintain OAT in most cases. The risks of changing (lowering or stopping) OAT **can lead to dangerous outcomes** & generally outweigh benefit.
Risks can include:[7]

- destabilization & return to use (i.e. relapse).
- unintentional **overdose & death** (resulting from return to use after loss of tolerance).
- ↑ patient anxiety, ↓ trust/loss of therapeutic alliance.
- dose conversion challenges (e.g. medication errors).
- ↑ pain & other opioid requirements.
- challenges restarting (e.g. loss to follow-up, overlooked/lack of community coordination at discharge, precipitated withdrawal[if bup stopped then restarted]).[6]

If additional opioids are indicated, hydromorphone po/IV (or fentanyl IV[caution]) may be preferred while on bup due to its potency & ↑ mu-receptor affinity. Discussion with the patient may identify specific opioids they wish to avoid (e.g. due to their concerns about the prior opioid of use & potential for relapse).

For patients with OUD & acute pain who are interested in starting OAT: Offer OAT concurrently. Methadone may be preferred if severe pain with use of concurrent opioids,[8,9] though some clinicians initiate bup-nal using a low-dose initiation (i.e. "microdosing")[32] approach to target dose bup 8-12mg while using concurrent IR opioids during the acute pain episode[(expert opinion)]. If delaying the start of OAT, plan to initiate immediately after acute pain resolved (bup-nal preferred when other opioids are no longer indicated and have been discontinued).

For patients with OUD & acute pain who are not currently interested in starting OAT: Goals are to reduce acute pain (optimize non-opioid analgesics & non-pharm strategies), minimize harms, alleviate opioid withdrawal, & establish therapeutic relationship.

In most cases:	If managing as an outpatient:	If managing as an inpatient:
• Confirmatory UDS. • Offer take home naloxone kit & other harm reduction options. • Consider screening for HIV, Hep B/C, STIs, pregnancy as appropriate.	• Communicate concern about OUD alongside open offer to discuss OAT options. • Consider short structured opioid course (e.g. daily dispensing) with sunset clause based on expected duration of severe pain (consult with primary provider).	• Assess withdrawal (monitor COWS, baseline & often q4hr while awake until score consistently ≤12). • Estimate & replace baseline opioid reqs to treat withdrawal symptoms & pain (IV may be preferred for ease of administration/ comfort/titration if IV access & pt was using IV as outpt[expert opinion]). • Offer concurrent pharmacological opioid withdrawal adjuncts (e.g. clonidine, loperamide, NSAIDs, dimenhydrinate, hydroxyzine).

Considerations Specific to Acute Pain in the Emergency Department/Acute Care Settings:

- People taking opioids chronically may need to be admitted for pain control for procedures that would otherwise be tolerated as outpts for those not on chronic opioids.
- If patient with untreated OUD is admitted, treat acute pain & withdrawal concurrently (monitor COWS). Offer OAT. Generally, prefer methadone if not planning to continue as outpatient.[8,9] Consult pain/addiction medicine specialist PRN.
- When possible, involve the patient & their primary prescriber in making a clear, proactive plan for structure, support, & opioid discontinuation.
- Be aware of treatment agreement in place with other prescribers. If opioids used, this should be communicated to the primary prescriber.
- Conduct a pre-procedural assessment, when possible, to assess risk of postoperative increases in pain/persistent opioid use,[11] & risk of respiratory depression / overdose / peri-operative complications (e.g. screen for OSA) as well as to establish early recovery after surgery protocols.
- Consider using the **Clinically Aligned Pain Assessment (CAPA) Tool**[20] to ask about: comfort, change in pain severity, pain control, functioning, & sleep.

Medication History:

- Communication with community pharmacist is helpful to confirm med hx (verify if patient receives daily dispensed/directly observed therapy or take home doses), as well as to ↓ risk of diversion (medications may be dispensed to patient/others while hospitalized & receiving doses as an inpatient).
- Be aware of & continue prior subcutaneous, trans- & intra-dermal formulations of buprenorphine the patient has been prescribed.
- If CNS/resp depression occurs when given opioid equivalent to "home doses," consider potential for 1) outpt diversion, 2) outpt non-adherence, 3) concurrent illness (e.g. infection, AKI, brain injury), &/or 4) medications (e.g. alcohol, BZD, other sedatives) decreasing opioid requirements/increasing adverse effects.
- Reversal of buprenorphine overdose may require ↑ naloxone doses (e.g. 2mg IM/IV q2-3min PRN) relative to other opioids.

Adjunctive Agents & Additional Opioids:

- Consider use of adjuncts unique to acute care/supervised settings: single dose corticosteroids (e.g. methylprednisolone, dexamethasone), NMDA antagonists (e.g. ketamine, nitrous oxide), alpha-2 agonists (e.g. dexmedetomidine, clonidine), IV lidocaine. Utilize regional and neuraxial anesthesia to minimize other pharmacotherapies, if available & appropriate.
- If additional opioid deemed necessary for a patient on high potency chronic opioids/OAT, likely will need 2nd structured opioid regimen with higher & more frequent dosing to overcome receptor affinity & tolerance.[1,8] Consider additional bowel care as warranted.
- Oral routes generally preferred to IV for post-operative analgesia whenever possible.[24] However, note conditions that affect GI function/warrant NPO. Switch to most equivalent baseline opioid dose if prior dosage form not feasible (e.g. change from po because IV required). If switching to a different opioid, ↓ dose (e.g. by 25-50%) for incomplete cross-tolerance.
- Offer PCA (bolus only, once initial dose determined) if available for severe pain → provides sense of control. Reassess pain control/dose frequently. Transition to equivalent po dosing (if this was the route taken prior to admission) as soon as able.
- Parenteral fentanyl can be a short-term option for severe/incident pain (in closely monitored settings) due to potency & quick onset/offset (parenteral formulation may also be administered SL).
- Use caution when calculating doses to switch back to home regimen from parenteral dosing. Often start with scheduled doses, though may encourage patient to refuse doses that are above the baseline opioid requirements if analgesia is sufficient (reminder: avoid causing opioid deficit). Adjust subsequent dose/interval accordingly.[17]

Discharge Planning:

- Determine Rx at discharge based on prior 24hr requirements (no Rx if not used in 24hrs). Consider patient's ability to attend follow-up appointments and pharmacy access. Coordinate with community prescriber and pharmacist. Ensure patient has access to take home naloxone page 132.

"What happens if I have acute pain while on bup-nal?" – addressing patient concerns

Acknowledge concern:

- Other opioids may not work as well for pain when taking higher doses of bup-nal (e.g. >12mg).

Offer reassurance:

- We have evidence that in many cases, an anti-inflammatory +/- acetaminophen work just as well, if not better, than opioids for mild to moderate pain. This means most pain can be well managed with non-opioid medications & strategies.
- When severe pain does occur, in most cases the bup-nal can be continued at the same dose & the pain can be treated with other opioids layered on top for a short time. This may require using higher than usual opioid doses.

Recognize choice:

- There are options for how to approach the acute pain episode, especially for planned procedures where severe pain is anticipated.
- Though stopping the bup-nal during an acute pain episode is generally discouraged, we could consider temporarily adjusting the dose to help with the pain. This might include lowering, increasing or splitting the dose for a brief period of time.

Offer & invite collaboration:

- Encourage the patient to discuss any questions or concerns they have about their pain management, breaking a treatment agreement, or returning to use (i.e. relapse).
- Invite patients to proactively create pain & relapse contingency plans together with their care providers.

AKI=acute kidney injury **bup**=buprenorphine **BZD**=benzodiazepines **CABG**=coronary artery bypass graft **CDN**=Canadian **CI**=contraindicated **CNCP**=chronic non-cancer pain **CNS**=central nervous system **COX-2**=selective cyclooxygenase inhibitor **d**=day **def**=deficiency **ER**=emergency room **esp**=especially **FDA**=approved Food & Drug Admin. **HA**=headache **hx**=history **inpt**=inpatient **IR**=immediate release **IV**=intravenous **LBP**=low back pain **MED**=morphine equivalent dose **mos**=months **nal**=naloxone **NMDA**=N-methyl-D-aspartate **NPO**=nothing per orem **OAT**=opioid agonist therapy **ORIF**=open reduction internal fixation **OSA**=obstructive sleep apnea **outpt**=outpatient **PCA**=patient-controlled analgesia **pg**=page **po**=per orem **pt**=patient **reqs**=requirements **Rx**=prescription **SL**=sublingual **SR**=sustained release **subcut**=subcutaneous **SUD**=substance use disorder **sx**=surgery **TJA**=total joint arthroplasty **TKA**=total knee arthroplasty

High Blood Pressure Clinical Guidelines

Blood pressure (BP) is a common chronic cardiovascular condition in the United States and dentistry can play an important role in screening patients for hypertension and is an important vital sign to consider in providing dental treatment.

Definitions:

- Acute Hypertension: Can result from stimuli such as physical exertion, anxiety, or stress and generally normalizes once the stimuli is gone.
- Chronic Hypertension: Is blood pressure that remains consistently higher than normal.

Blood Pressure should be taken on patients with an upper arm BP monitor (provided in clinic – manual and/or automatic). Wrist BP monitors can be used if a upper arm BP monitor is not able to be used as determined by the faculty/provider. However, wrist BP monitors/cuffs are not as accurate as the Upper Arm BP monitors and should be limited in use.

- Always utilize the appropriate size cuff (e.g., small, medium, large) based on the patient's age and size to take the BP.
- A manual and/or automatic upper arm BP cuff should be used. If an automatic BP cuff is used and high BP readings are attained, a manual upper arm BP cuff may need to be used.
- If high BP readings are obtained that would preclude treatment, the BP measurement should be repeated after the patient has sat quietly for 5 minutes with their feet flat on the floor and their arm supported at the level of their heart. If the BP decreases to a recommended level allowing treatment to proceed (see section 6.22.4.1) should be in conjunction with clinical judgement.

Recommendations for when to take BP

- Patient on anti-hypertensive medications and/or previous history of cardiac event, such as, but not limited to, myocardial infarction or stroke;
- Comprehensive Oral Evaluation (D0150), Periodic Oral Evaluation (D0120), or Limited Oral Evaluation (D0140);
    - Pediatric/minor patients: provider should evaluate and determine if taking BP is appropriate given review of Health History.
- Before surgical procedures and those involving sedation (oral, IV or Nitrous Oxide); and/or,
    - Nitrous Oxide: Pediatric/minor patients: provider should evaluate and determine if taking BP is appropriate given review of Health History.
- Before vasoconstrictors in local anesthetics are used in patients, especially in patients with a cardiac event history and/or taking anti-hypertensive medication(s), or contributory health history.

References: https://www.ada.org/resources/research/science-and-research-institute/oral-health-topics/hypertension#.Y0A1K9dhE6E.link

High Blood Pressure Treatment Guidelines

The following BP treatment guidelines are recommendations and should be used in conjunction with a provider(s) clinical judgement taking into consideration, but not limited to, the multifactorial functional capacity and risk stratification tool, the clinical situation (including the need for emergent care), health history, dental history, prescription and non-prescription medications, Illicit substances, anxiety, risks to the patient, acute vs. chronic hypertension, written guidance from a physician, and/or individual patients' clinical situation. The provider, given this information, has the clinical autonomy to make treatment decisions in the best interest of the patient.

Category	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)	Dental Treatment recommendations	Referral to Physician
Normal	<120	and	<80	Elective care	No
Elevated	120-129	and	<80	Elective care	No
Hypertension					
Stage 1	130-139	or	80-89	Elective care	No
Stage 2	140-159	or	90-99	Elective care	No
Stage 2	>160	and/or	>100	• Wait 5 minutes and reassess. • If the BP decreases below 160/100 or within written guidance from a physician treatment may proceed in conjunction with clinical judgement. • If dental symptoms, pain, and/or anxiety contribute to HTN, initiate emergency care with BP monitoring • If BP does not decrease <160/100, utilize the Functional Capacity and Risk Stratification framework to determine if treatment can be safely completed	Yes
Hypertensive Crisis	>180	and/or	>120	• Utilize the Functional Capacity and Risk Stratification framework to determine if treatment can be safely completed • If dental symptoms, pain, and/or anxiety contribute to HTN, provider may initiate emergency care in conjunction with clinical judgement with BP monitoring. • Refer to physician as soon as possible or send for urgent medical evaluation, if symptomatic. This should be in conjunction with clinical judgement and using the Functional Capacity and Risk Stratification. • Consider deferring elective care after risk stratification.	Yes

- Dental Management of the Medically Compromised Patient, James W. Little et al, Seventh Edition., *and* <https://www.ada.org/en/member-center/oral-health-topics/hypertension> (July 20, 2021)
- https://www.ada.org/resources/research/science-and-research-institute/oral-health-topics/hypertension#.Y0A1K9dhE6E.link

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Functional Capacity Determination and Risk Stratification

Patients with an elevated blood pressure, less than 180/110, with no active cardiac conditions is not an indication to cancel a dental procedure without considering the potential risks and benefits of delaying the procedure. In conjunction with the risk/benefit analysis, It is recommended that the clinician utilize the multifactorial risk stratification based on the American College of Cardiology Foundation and American Heart Association taskforce on practice guidelines to determine if the dental procedure should be delayed.

Providers should use the following risk stratification: One (1) "yes" answer in Section 1 and in Section 2 one (1) "yes" answer for both category A and B.

Section 1: Determination of Metabolic Capacity	
The patient should be "Yes" to at least one of the following	• Can you do light work around the house like dusting or washing dishes?
	• Can you climb a flight of stairs or walk up a hill?
	• Can you walk on level ground at 4 miles per hour?
	• Can you run a short distance?
	• Can you do heavy work around the house, like scrubbing floors, or lifting or moving heavy furniture?
	• Can you participate in golf, bowling, dancing, doubles tennis, or throwing a baseball or football?

Section 2: Risk Stratification	
Category A	• Is the patient taking antihypertensive medication and did they take it this day?
	• Does the patient have a health care provider managing their hypertension and have they been seen in the past 6 months?
	• Does the patient appear anxious, acknowledge anxiety about the procedure, or have a heart rate >100 beats per minute?
Category B	• Did the patient take public transportation or drive and walk in for the procedure?
	• Does the patient take care of their own house or apartment?
	• Does the patient state they can walk up a flight of stairs?
There must be a one (1) "yes" answer to category A and B	

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Comparison of GLP-1 Agonists

(full update August 2024)

This chart compares GLP-1 agonists (including the "twincretin" tirzepatide) in regard to A1c reduction, weight loss, dosing, tolerability, clinical outcomes (e.g., cardiac or kidney benefit), how supplied, cost, and storage. For a review of class **adverse effects**, see **footnote f**.

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Dulaglutide (*Trulicity*) A1c: -1.09% (mean across trials)[1] Weight loss: 0.73 kg (mean across trials)[1]	Single dose pen (autoinjector): 0.75, 1.5, 3 (US), 4.5 mg (US) US: $977.42 Canada: ~$250 (1.5 mg/week) Store at 2°C to 8°C, or room temp (≤30°C) for ≤14 days.	**Initial**: 0.75 mg once weekly. **Max**: may increase to 1.5 mg once weekly, then by 1.5 mg weekly every four weeks to a max of 4.5 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤1.5 mg.[15]	• Added to standard DM treatment in patients with CV disease or risk factors, over ~5.4 years reduced the composite of nonfatal MI, nonfatal stroke, and death from CV or unknown causes (NNT = 71).[4] For individual outcomes, only nonfatal stroke was significantly reduced. • Reduced a composite of new macroalbuminuria, 30% decrease in eGFR, or need for dialysis/transplant (NNT= 40), driven by prevention of macroalbuminuria (exploratory analysis).[5] • Discontinuation due to adverse GI effects (1.5 mg): ~1 in 15 patients[3]
Exenatide (*Byetta* [US]) A1c: -0.7% (10 mcg BID monotherapy)[a,c] Weight loss: -1.5 kg (10 mcg BID monotherapy)[a,c]	Sixty (60)-dose pen: 5, 10 mcg (needles not included) US: $849.95 Store at 2°C to 8°C. In-use pens can be stored at ≤25°C for up to 30 days.	**Initial**: 5 mcg BID within 60 min before the two main meals (≥6 hours apart). **Max**: may increase to 10 mcg BID after four weeks. **Comparative dose**: see footnote g. **Missed dose**: skip missed dose **Kidney impairment**: Not recommended if CrCl <30 mL/min. Use 10 mcg BID with caution if CrCl 30 to 50 mL/min. Use caution in kidney transplant.	• Discontinuation due to adverse GI effects (10 mcg BID): ~1 in 24 patients[3]

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Exenatide (*Bydureon BCise* [US]) A1c: -0.64% (adults); -0.71% (pediatrics)[a,c] Weight loss: 0.92 kg	Single dose pen (autoinjector): 2 mg US: $827.45 Store at 2°C to 8°C, or room temp (≤30°C) for ≤4 weeks.	For patients 10 years and older: 2 mg once every seven days **Comparative dose**: see footnote g. **Kidney impairment**: Not recommended if eGFR <45 mL/min/1.73 m^2. Use caution in kidney transplant. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.	• Once-weekly exenatide added to standard DM therapy in patients with or without CV disease had a neutral CV effect, but was associated with a reduction in death from any cause compared to placebo (NNT = 341).[6] • Discontinuation due to adverse GI effects: ~1 in 22 patients.[3] • Highest rate of injection site reactions among once-weekly GLP-1s.[3] • Required mixing immediately before injection.
Liraglutide (*Saxenda*) Indicated for weight loss. Weight loss: 3.7 to 5.2 kg (3 mg once daily x 56 weeks)[a,c]	Dial-a-dose pen: 18 mg/3 mL (pen needles not included) US: $1,349.02 Canada: ~$450 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	For patients 12 years and older: 3 mg **once daily** (start with 0.6 mg once daily, increase dose weekly by 0.6 mg to goal of 3 mg once daily). For adults, discontinue after 16 weeks if <4% (after 12 weeks if ≤5% [Canada]) weight loss achieved. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	• See *Victoza*, below for information on clinical outcomes in type 2 DM. • ~44% to 62% of patients met weight loss goal (≥5%) at 56 weeks compared to 16% to 34% with placebo. • Discontinuation due to adverse effects: ~1 in 11 patients.[c]

Drug/ A1c decrease/ Weight loss	Availability Cost[b] Storage[c]	Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]	Comments (e.g., clinical outcomes, tolerability)
Liraglutide[d] (*Victoza*) A1c: -1.04% (adults); -1.06 (pediatrics)[1,a,c] Weight loss: 1.33 kg[1]	Dial-a-dose pen: 18 mg/3 mL (needles not included) US: $815.27 Canada: $336.10 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	For patients 10 years and older: **Initial**: 0.6 mg once daily for one week, then 1.2 mg once daily. (Pediatric patients may achieve control with 0.6 mg once daily.) **Max**: may increase to 1.8 mg once daily after one week. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	• Added to standard care in patients with type 2 DM with CV disease or at high CV risk over ~4 years reduced:[7] o death from CV causes, nonfatal MI, or nonfatal stroke, NNT = 53; death from CV causes, NNT = 77; death from any cause, NNT = 71. o new macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73m^2, need for dialysis/transplant, or death from kidney causes (NNT =67), driven by prevention of macroalbuminuria (NNT = 83). o Did not reduce the individual rates of MI, nonfatal stroke, or HF-related hospitalizations. • Discontinuation due to adverse GI effects (1.8 mg): ~1 in 18 patients[3]
Semaglutide (*Ozempic*) A1c: -1.4% (1 mg weekly as monotherapy)[a,c] Weight loss (1 mg): 3.5 kg[a,c] *Continued…*	Multi-dose pen: 0.25 or 0.5 mg (four 0.25 mg doses or two 0.5 mg doses), 1 mg (4 doses), 2 mg (4 doses [US]) (includes needles) US: $1,291.36 Canada: ~$235 (1 mg/week) Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤56 days.	**Initial**: 0.25 mg once weekly for four weeks, then 0.5 mg once weekly, **Max**: may increase to 1 mg once weekly after four weeks. After four weeks on the 1 mg dose, may increase to 2 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 remain, administer the missed dose. If two or more consecutive doses are missed, consider starting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, or 0.25 mg if ≥5doses are missed..[15]	• In type 2 DM patients with CV disease, CKD, or CV risk factors, reduced the combined endpoint of CV death, nonfatal MI, or nonfatal stroke (NNT = 44 for ~ 2 years). For individual outcomes, only nonfatal stroke was significant. A composite of new onset macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73m2, need for dialysis/transplant, or death from kidney causes was reduced (NNT = 44), driven by prevention of macroalbuminuria.[8] • In type 2 DM with CKD, reduced a composite of major kidney events (kidney failure, ≥50% reduction in eGFR, kidney or CV death) (NNT = 20 over 3 years). Kidney function declined more slowly, and the risks of major CV events and all-cause mortality were reduced.[21]

Drug/ A1c decrease/ Weight loss	Availability Cost[b] Storage[c]	Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]	Comments (e.g., clinical outcomes, tolerability)
Ozempic, continued			• Discontinuation due to adverse GI effects (1 mg): ~1 in 10 patients[3]
Semaglutide (*Rybelsus*) A1c: -1.1% (as monotherapy, 14 mg/day)[a,c] Weight loss (14 mg): 3.8 kg[a,c]	3 mg, 7 mg, or 14 mg tablets. US: 968.52 Canada: 233.38	**Initial**: 3 mg once daily at least 30 minutes before the first food, beverage, or other oral medications of the day, with ≤120 mL of water (~half a glass). After 30 days, increase the dose to 7 mg once daily. **Max**: After 30 days on the 7 mg dose, may increase to 14 mg once daily. **Comparative dose**: patients taking *Rybelsus* 14 mg may switch to *Ozempic* 0.5 mg. Patients on *Ozempic* 0.5 mg can be switched to *Rybelsus* 7 mg or 14 mg (US). Also see footnote g. **Missed dose**: skip the missed dose	• ORAL semaglutide in patients with type 2 DM and CV disease, CKD, or CV risk factors had a neutral CV effect.[9] • Discontinuation due to adverse GI effects: ~1 in 15 patients[c]
Semaglutide (*Wegovy*) Indicated for weight loss. Weight loss: ~10.6 to 12.7 kg (2.4 mg once weekly at one year)[13,14]	Single-dose pen (autoinjector): 0.25, 0.5, 1, 1.7, 2.4 mg. US: $1,349.02 Canada: $419.73 Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤28 days.	For patients 12 years and older: 0.25 mg once weekly, increased every four weeks to 0.5 mg, 1 mg, 1.7 mg, then 2.4 mg once weekly. Canada: consider stopping if the patient is not showing progress after 12 weeks on the maintenance dose. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 hours remain, administer the missed dose. If two or more consecutive doses are missed, consider restarting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, and 0.25 mg if ≥5doses are missed.[15]	• Reduces CV risk (prevents 1 event for every 67 patients treated for ~ 3 years.[10] • 67% to 85% of patients met weight loss goal (≥5%) at 52 weeks compared to 30% to 48% with placebo.[13,14] • Discontinuation due to adverse effects: ~ 1 in 15 patients[c]

Drug/ A1c decrease/ Weight loss	Availability Cost[b] Storage[c]	Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]	Comments (e.g., clinical outcomes, tolerability)
Tirzepatide[e] (*Mounjaro*) A1c: -2.1%[1,a] Weight loss: 6.18 kg (as monotherapy, 15 mg/week).[a,c]	Single-dose vial or pen (autoinjector [US]): 2.5, 5, 7.5, 10, 12.5 (US), 15 mg (US) (vial does not includes needles or syringe) US: $1,069.08 Canada: ~$97 (10 mg vial) Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤21 days.	**Initial**: 2.5 mg once weekly for four weeks, then 5 mg once weekly. **Max**: may increase by 2.5 mg/week every four weeks to a max of 15 mg once weekly. **Comparative dose**: see footnote g. **Missed dose:** If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c] • Discontinuation due to adverse GI effects (15 mg): ~1 in 16 patients.[c]
Tirzepatide[e] (*Zepbound* [US]) Indicated for weight loss. Weight loss: ~18.8 kg (15 mg once weekly at week 72)[12,a]	Single-dose vial or pen: 2.5, 5, 7.5, 10, 12.5, 15 mg (vials do not include syringe or needle) US: $1,059.87 Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤21 days.	Start with 2.5 mg once weekly, increase dose every 4 weeks to 5 mg, 7.5 mg, 10 mg, 12.5 mg, then 15 mg. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c] • Discontinuation due to adverse effects: ~ 1 in 15 patients • Though no specific guidance is available, stopping after 12 weeks if <5% weight loss achieved is reasonable based on guidelines.[11] • 85% to 91% of patients met weight loss goal (≥5%) at 72 weeks compared to 35% with placebo.[12]

Abbreviations: BID = twice daily; CKD = chronic kidney disease; CV = cardiovascular; DM: diabetes mellitus; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; HF = heart failure; MI = myocardial infarction; NNT = number needed to treat; SCr = serum creatinine