Medications for Opioid Use Disorder Treatment - Adult - Ambulatory
External Clinical Practice Guideline Endorsement

Note: Active Table of Contents – Click each header below to jump to the section of interest

Table of Contents

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Introduction

Opioid use disorder (OUD) is a chronic medical condition in which there is reduced control over opioid use that negatively impacts social functioning and results in tolerance and withdrawal.[1] OUD is a significant public health threat, affecting 1.6 million Americans in 2019 and causing significant adverse effects for the individual, their loved ones, and society as a whole.[2] Deaths due to opioid overdoses continue to escalate, having increased 51% between 2019 and 2021, and 5-fold since 1999.[3] As a result of these trends and a major gap between the number of people needing treatment for OUD vs. available services, and there is a critical need to expand access to effective treatments for OUD.[1,4] As with other chronic illnesses, ongoing patient-centered care across all healthcare settings is required to effectively treat symptoms, and achieve and maintain recovery.

To help increase access to safe and effective OUD treatment services, UW Health has implemented a Hub and Spoke model of care. In this care model, the Hub is capable of providing more complex, specialized services for OUD and unstable or uncontrolled psychiatric conditions. Centers of excellence within Primary Care can provide care for complex cases not requiring Addiction Psychiatry. Multiple Spoke sites (primary care offices) provide acute care for OUD with less complexity. More details on the Hub and Spoke services for OUD at UW Health can be found in in this overview. In this model, both types of locations offer medications for OUD (MOUD) as part of a comprehensive treatment plan.

Medications currently FDA-approved for use as part of MOUD include methadone, buprenorphine (including buprenorphine/naloxone combinations), and intramuscular naltrexone. Methadone can only be administered for OUD by federally certified treatment centers and is not currently offered through UW Health. A directory of federally certified opioid treatment programs (OTPs) is maintained on the SAMSHA website. Buprenorphine and naltrexone therapies are offered through the UW Health Hub and Spoke sites. Additional locations offering these services can be identified through the SAMSHA Behavioral Health Treatment Services Locator. Effective in 2023, a federal DATA waiver (or 'X 'DEA number) is no longer required to prescribe buprenorphine for OUD; only a standard DEA number (including Schedule III authority) is required and there are no limits to the number of patients that a prescriber may treat with buprenorphine. Effective in June 2023, new training requirements will be in place for all prescribers and this information will be available on the SAMHSA website. These changes were made in order to increase access to treatment. Risk Evaluation and Mitigation Strategy (REMS) program requirements also exist for the buprenorphine subcutaneous injection and implant formulations. Any medical provider with prescriptive authority can offer naltrexone.

The UW Health Hub and Spoke care team reviewed existing clinical practice guidelines[1,5,6] on the topic of OUD treatment and agreed to endorse the Medications for Opioid Use Disorder Treatment Improvement Protocol 63 (TIP 63) produced by the Substance Abuse and Mental Health Services Administration (SAMHSA).[1]

Scope

Intended User(s): Physicians, Advanced Practice Providers, Registered Nurses, Pharmacists, Peer support specialists

Objective(s): To provide evidence-based guidelines for the use of medications in the treatment of opioid use disorder (MOUD).

Target Population: Adults with an OUD diagnosis who are interested or would benefit from MOUD.

Clinical Questions Considered:

- Who should be offered MOUD?
- What medications should be offered as a part of MOUD?
- What patient-specific and medication specific considerations should be made when tailoring MOUD therapy?

Recommendations

UW Health endorses the recommendations and guidance found within the Medications for Opioid Use Disorder Treatment Improvement Protocol 63 (TIP 63) produced by the Substance Abuse and Mental Health Services Administration (SAMHSA).[1] Key components are summarized here and additional details and clarifications are provided as they relate to practices at UW Health, including UW Health evidence grading and recommendations, where necessary. An overall approach to MOUD care is outlined in Appendix A.

Patient Eligibility

A diagnosis of OUD is made when an individual uses opioids and demonstrates at least 2 of the 11 DSM-5 OUD criteria within a 12-month period. The severity of OUD is considered mild when 2-3 symptoms are present, moderate with 4-5 symptoms, and severe when 6 or more symptoms are present. Of note, patients receiving chronic opioid therapy for pain are exempted from the criteria of tolerance and withdrawal unless other signs of OUD are present.[7]. These criteria are outlined on the DSM-5 OUD checklist (pg. 2-35).

In considering MOUD treatment options, comprehensive assessment is necessary including:

- Complete medical and social history
- Substance use history and previous treatments
- Review of the prescription drug monitoring program (PDMP)
- A targeted physical exam for signs of opioid withdrawal, intoxication, injection, and other medical consequences of misuse
- Appropriate laboratory tests in addition to those recommended by the non-treating provider (e.g., urine fluid drug tests, liver function tests, hepatitis B test, hepatitis C, HIV test, urine pregnancy test).

This assessment is intended to establish the diagnosis and severity of OUD. Additionally, this information is necessary to identify potential medication contraindications, other medical conditions requiring treatment, and any mental health or social issues in need of support.

Medications

All patients with a diagnosis of moderate to severe OUD should receive counseling about the risks and benefits of all FDA-approved MOUD options and be offered treatment as clinically appropriate: 1) methadone, 2) buprenorphine and buprenorphine/naloxone formulations, 3) naltrexone. (*UW Health Moderate Quality of evidence, Strong recommendation*).

Compared to the use of no medications, MOUD therapies have demonstrated significant reductions in mortality, illicit opioid use, risk of overdose, and increased retention in treatment[8-15]. Comparative effectiveness data for buprenorphine, extended-release naltrexone, and methadone are somewhat limited, but overall suggest comparable effects on retention in

treatment and reduction in illicit opioid use when comparing currently recommended dosing strategies[11,12,16-18]. Both buprenorphine and naltrexone are available through the UW Health Hub and Spoke sites.

Buprenorphine is a partial opioid receptor agonist with a ceiling effect and activates the receptors enough to relieve withdrawal symptoms and cravings.[1] Buprenorphine binds very tightly to opioid receptors, which leads to blunting or blocking the effects of illicit opiates (which bind less tightly) and reduces the risk of overdose. Buprenorphine co-formulated with naloxone is most commonly utilized. The naloxone is not absorbed sublingually or buccally, but if the medication is misused via the intranasal or injectable route, naloxone will blunt the effects of buprenorphine and other opioids administered, thereby reducing the chance for misuse. Multiple formulations of buprenorphine are available including buccal, sublingual (SL), and subcutaneous extended-release injections (monthly). The dermal implant formulation was discontinued in the U.S. market in 2020. Use of the buccal formulations is very limited, as the FDA-approved formulation was also discontinued from the U.S. market. The sublingual form of buprenorphine can be used for treatment induction as well as maintenance treatment for OUD. The extended-release subcutaneous injection of buprenorphine (Sublocade®) may be considered for maintenance treatment after patients have received buccal or sublingual form for at least 7 days. Buprenorphine is a controlled substance (C-III) and in order to prescribe buprenorphine products for OUD, only a standard DEA number with Schedule III authority is required.[1]

Naltrexone is an opioid receptor antagonist with no misuse or diversion potential.[1] Due to this mechanism, the euphoric effects of illicit opioids are blocked, opioid cravings are reduced, and overdose is less likely. Patients need to have abstained from short-acting opioids for 7-10 days and long-acting opioids (such as buprenorphine and methadone) for 10-14 days prior to initiating naltrexone in order to avoid precipitating withdrawal. Naltrexone can therefore be used to prevent relapse and opioid misuse following medically supervised withdrawal or in patients not physically dependent on opioids. The extended-release formulation for intramuscular injection (given monthly) has demonstrated effectiveness and is the primary dosage form recommended for use; this agent is best for patients who are unlikely to drop out of treatment and are determined to stop opiates all together. Once naltrexone is stopped, there is no protection against overdose. Oral naltrexone is generally not recommended due to adherence concerns and limited evidence for effectiveness; however, it may be considered in select cases when other options are not practically available, and use can be supervised. Naltrexone is not a controlled substance and any medical practitioner with prescriptive authority can prescriber or administer naltrexone for OUD.[1]

Methadone is a controlled substance (C-II) that can only be administered for OUD through federally certified OTPs and is not available through UW Health. Methadone may be administered or continued in a hospital setting but cannot be prescribed for OUD and take away doses are not permitted. As a result, Chapter 3B of the SAMHSA TIP 63 document does not pertain, except for general information related to methadone therapy for patients who may be receiving this medication through another provider or for a different indication. Methadone is a full opioid agonist that is used for medically supervised withdrawal and maintenance treatment. Daily doses are administered from a structured dosing clinic and over time patients can earn take-away doses. Advantages of methadone include the structured daily routine and acceptability by patients interested in continuing opioid use and gradually using less as their methadone dose is increased. Disadvantages are that patients must go to the clinic daily, there is no protection from overdose, and complex pharmacokinetics and drug interactions exist.[1]

Medication Selection Considerations

In addition to the medication-specific considerations noted above, medication adverse effects, treatment availability and accessibility, costs, patient history and patient preferences must all be taken into account to facilitate shared-decision making. Multiple helpful summaries of medication considerations are provided in the SAMHSA TIP 63 guideline, including:

- Exhibit 2.14 Comparison of OUD Medications to Guide Shared Decision Making (pg. 2-19)
- Exhibit 2.15 Treatment Setting Based on Patient's Choice of OUD Medication (pg. 2-21)
- Exhibit 3A.1 OUD Medications: An Overview (pg. 3-6)
- Exhibit 3A.5 OUD Medications: Formulations (pg. 3-14)

When buprenorphine is selected, there are some important considerations regarding its use in induction and maintenance therapy such as timing of initiation, dosing, symptom monitoring, and treatment duration. Buprenorphine induction can be office- or home-based depending on the patient-specific considerations and experience of the provider. The traditional buprenorphine induction strategy requires discontinuation of the full opioid agonist and the presence of mild to moderate withdrawal symptoms (assessed using COWS) before initiating buprenorphine.[1] Of note, the SAMHSA TIP 63 provides general recommendations for traditional induction dosing of buprenorphine products, which is effective for many individuals. However, alternative approaches to initiation exist and merit consideration depending on the clinical context. For example, a low-dose (aka micro-dosing) initiation strategy involves the use of lower initial doses of buprenorphine with gradual titration in order to avoid precipitated withdrawal while continuing the full opioid agonist.[19-21]. This micro-dosing strategy may be considered when patients aren't able to tolerate the withdrawal severity needed for traditional induction, when patients are transitioning from higher doses of methadone (e.g. >30mg) to buprenorphine, or for patients using illicit fentanyl. Alternatively, a high-dose rapid induction strategy has also been explored in which patients using heroin, fentanyl, or highly potent synthetic opioids require and receive higher doses of SL buprenorphine after experiencing mild to moderate opioid withdrawal; if SL buprenorphine is tolerated, then options include either continuation of high doses SL buprenorphine or rapid transition to subcutaneous extended release buprenorphine.[22-25] Succinct summaries of buprenorphine considerations can be found in the following quick start guides available through SAMHSA listed below. A buprenorphine home dosage schedule worksheet is also provided.

- Buprenorphine Quick Start Guide (samhsa.gov)
- Buprenorphine Quick Start Pocket Guide (samhsa.gov)
- Buprenorphine/Naloxone Home Dosage Schedule (pg. 3-77)

Following selection of an MOUD therapy, a treatment agreement must be completed by the patient (or their representative) and the treating provider.

Medical Management Visits and Drug Testing in MOUD Care

As a part of ongoing MOUD care, two important components are medical management visits and incorporation of drug testing. The approach to both visits and drug testing should be tailored to the patient's acuity and level of care, generally occurring more frequently at the initiation of treatment and less frequently as the patient becomes more stable. UW Health has available a Smart Set [#8103] titled "Primary Care Medication for Opioid Use Disorder", which includes office visit note templates and many helpful pre-built orders to facilitate MOUD care.

With respect to medical visits, a frequency of approximately once a week is recommended (keeping in mind potential treatment barriers) until significant reductions in or abstinence from illicit substance use is demonstrated.[1] During these visits, key goals include assessing:

- Patients' clinical needs and challenges
- Medication effectiveness and side effects
- Functional status (e.g., home, work, school)
- Cravings
- Stress coping strategies and potential triggers for return to substance use
- Adherence to the prescribed MOUD regimen and responsible handling of the medication
- Use of alcohol and illicit drugs and ensuring adequate therapeutic dosing (e.g., opioid blockade if there is ongoing illicit opioid use and adherence to medication)
- Follow up on any referrals made, such as adjunctive counseling, recovery support groups, or other psychosocial services
- Discussion of harm reduction approaches

The frequency of office visits may be reduced as patients demonstrate adherence to the treatment plan, reduced use of illicit substances, and as expected drug tests[1]. As visits become less frequent, consider random urine drug testing, medication counts (buprenorphine tablets or films), and involvement of network supports if available. Indications that a patient may be ready for less frequent visits include[1]:

- Sustained (several weeks) illicit opioid abstinence (per self-report and drug test results)
- Adherence to appointments and treatment plan
- No ongoing drug use that may risk patient safety
- Absence of significant medication side effects
- Stable mental health and medical conditions
- Responsible handling of medication
- No unexpected controlled medication prescriptions from other providers in the PDMP

Incorporation of drug testing in the ongoing clinical monitoring is part of best practice. It should be explained to patients that testing is intended to help them meet treatment goals, assess adherence to treatment, guide adjustments to treatment plans, and is not performed for punitive reasons[1].

The following principles should be considered with respect to the frequency and approach to use of drug testing[1]:

- Drug testing frequency should be individualized, taking into account the risk of relapse and patient-specific considerations.
    - In general, it should be performed at least at the time of the initial evaluation and initiation of MOUD, and at a frequency consistent with office visits (e.g., weekly initially)
- Periodic random testing is considered best practice
- Confirmed drug test results can be used to adjust the patient's individualized treatment plan

It is important to note the complexities of drug testing options that are available, the limitations of what they detect and the associated time windows for detection, and that they are an additional therapeutic tool to augment MOUD care. For additional details on drug testing

considerations, the American Society of Addiction Medicine (ASAM) Consensus Statement on Appropriate Use of Drug Testing in Clinical Medicine serves as a recommended resource.[26]

Duration of medication use

Medication for OUD should be continued as long as it is providing a benefit, and may be continued long-term. There is no evidence suggesting any particular duration of therapy, although it is recognized that the risk of relapse upon discontinuation of MOUD therapy is significant. Any decision regarding if and how to taper off of MOUD therapy needs to be highly individualized.[1]

Additional Aspects of OUD Care

While a detailed review of all aspects of OUD care is beyond the scope of this guideline, it is important to note that medications for OUD are only one important component of care. Other critically important aspects of care include:

- Providing brief supportive education and counseling
- Referring to ancillary psychosocial services
- Offering harm reduction measures
- Naloxone prescription for overdose treatment
- Referring to psychiatric and medical care if not directly provided by the healthcare professional prescribing or administering OUD medication
- Assessment and treatment of other substance use disorders
- Offering counseling and other recovery support services

A valuable resource for UW healthcare providers seeking guidance in treating their patients' substance use disorder is the UW Addiction Consultation Hotline. Through this resource, addiction specialists can provide advice on the medical management of substance related issues.

Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Conflicts of Interest

All guideline workgroup members are expected to follow institutional policies and procedures around conflicts of interest. Actions in which a guideline member discloses a conflict of interest relevant to the guideline topic may include, but is not limited to, abstaining from voting, dismissal during comment and voting period, or recusal from requesting and/or participation in the decision-making process.

Methodology

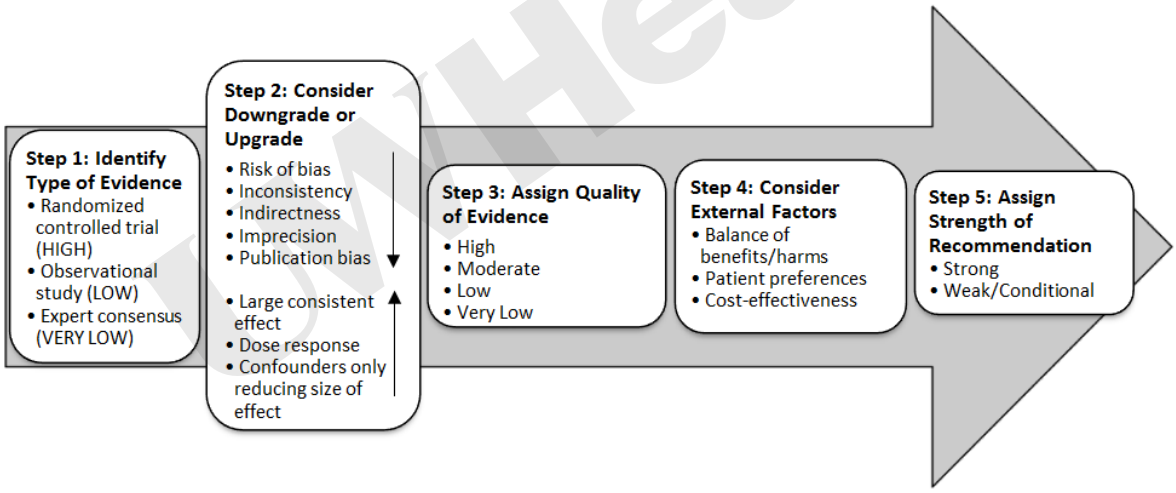
Development Process

Each guideline is reviewed and updated approximately every 3 years, in consideration of the primary literature and relevant practice changes. All guidelines are developed using the guiding principles, standard processes, and styling outlined in the UW Health Clinical Practice Guideline Resource Guide. This includes expectations for workgroup composition and recruitment strategies, disclosure and management of conflict of interest for participating workgroup members, literature review techniques, evidence grading resources, required approval bodies, and suggestions for communication and implementation.

Methods Used to Formulate the Recommendations:

Following a review and discussion of the literature along with expert opinion, the workgroup members agreed to adopt recommendations provided within the Medications for Opioid Use Disorder Treatment Improvement Protocol 63 (TIP 63), produced by the Substance Abuse and Mental Health Services Administration (SAMHSA).[1] All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate). Development of the SAMHSA TIP 63 content involved a consensus panel of clinicians, researchers, program administrators, patient advocates, and scientific reviewers with extensive expertise in MOUD. The draft content is then evaluated by field reviewers with front-line experience from each of the intended audiences for the guideline to facilitate modifications, resulting in the final version.[1]

GRADE Methodology adapted by UW Health



GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

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Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based guideline recommendations in everyday clinical practice.

Patient Assessment Tools
Clinical Opiate Withdrawal Scale (COWS)
Subjective Opiate Withdrawal Scale (SOWS)
Brief Addiction Monitor (BAM)
Vermont Treatment Needs Questionnaire

Patient Resources
Form: Agreement to treatment with buprenorphine
HFFY (ID 2023): How to give naloxone and respond to overdose

Healthwise Resources
Opioid Use Disorder
Opioid Use Disorder: Medication Assisted Treatment

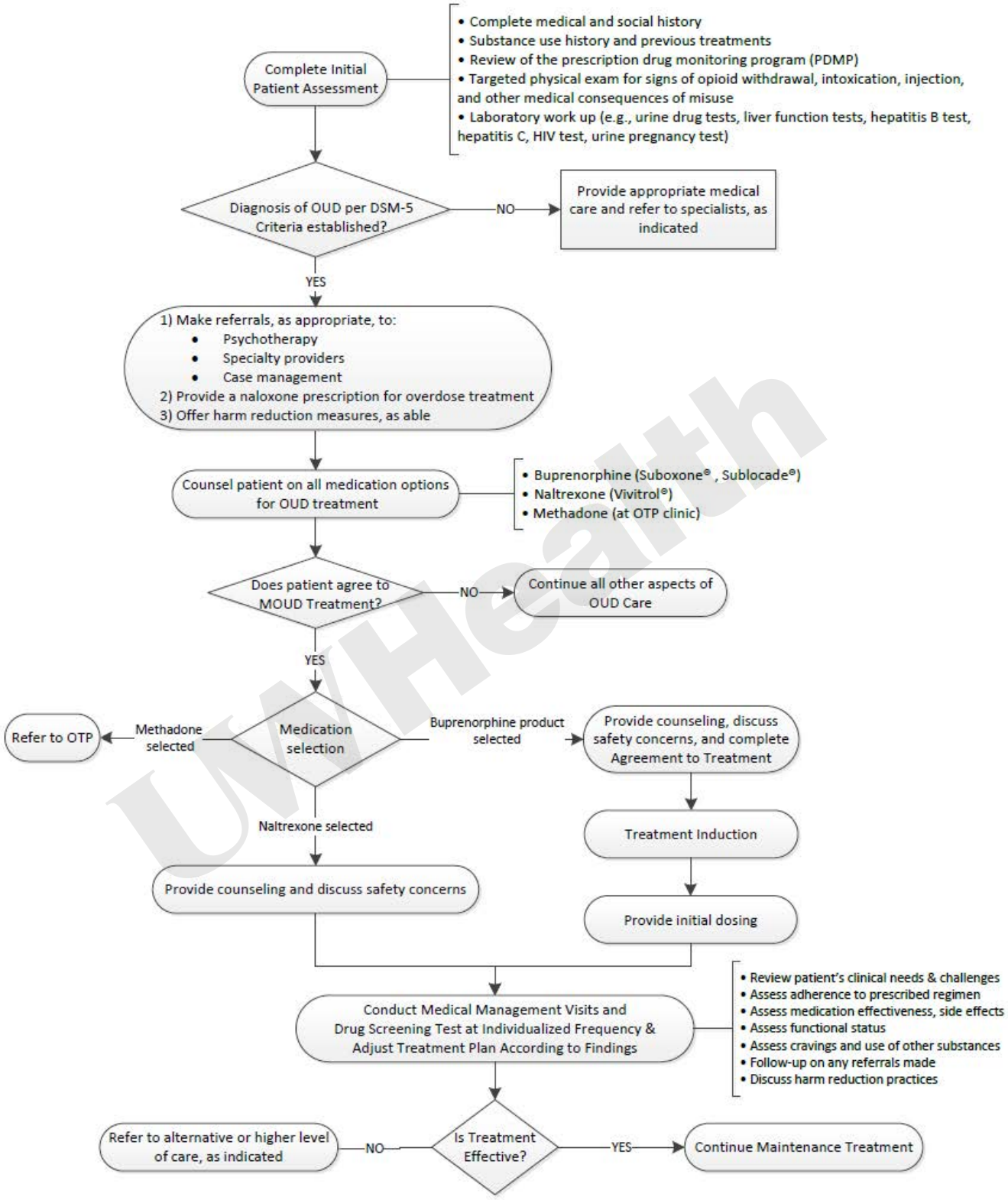
Buprenorphine (Injection – Sublocade)
Buprenorphine (oral/sublingual)
Buprenorphine and naloxone (oral/sublingual)
Naloxone (injection)
Naloxone (nasal)
Naltrexone (injection)
Naltrexone (oral)
Methadone (oral) [Not available through UW Health services]

Order Sets & Smart Sets
Primary Care Medication for Opioid Use Disorder Smart Set [8103]

Protocols
Naloxone for Opioid Overdose - Adult/Pediatric/Neonatal - Inpatient/Ambulatory/Emergency Department [126]

Metrics
- Patients are successfully discharged from Hub and Spoke Program
- Reduction in inpatient admissions, emergency room visits, urgent care visits among patients with OUD

Appendix A. MOUD Care Process



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