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Appendix E

Individual Interview Guide

Study to Explore Healthcare Providers' Practices, Perspectives, and Experiences Prescribing/Co-Prescribing Benzodiazepines and Opioids

Breakdown of the 30 One-on-One Interviews

- 9 interviews among primary care physicians (PCPs) who have **NOT** prescribed MOUD/buprenorphine
- 3 interviews among PCPs who **have** prescribed MOUD [i.e., their main practice is general primary care, but they have prescribed MOUD/buprenorphine to patients for opioid use disorder]
- 2 interviews among PCP specialists in Mental Health who have **NOT** prescribed MOUD/buprenorphine
- 2 interviews among PCP specialists/psychiatrists who **have** prescribed buprenorphine products for OUD in the past 3 months
- 2 interviews among PCP specialists in Neurology who have **NOT** prescribed MOUD/buprenorphine
- 2 interviews among PCP specialist in Emergency Medicine who have **NOT** prescribed MOUD/buprenorphine
- 2 interviews among PCP specialists in Pain Medicine (may have prescribed buprenorphine products for OUD in the past 3 months)
- 2 interviews among PCP specialists in Addiction Medicine who **have** prescribed buprenorphine products or dispensed methadone for OUD in the past 3 months
- 2 interviews among primary care nurse practitioners (NPs) who have **NOT** prescribed MOUD/buprenorphine
- 2 interviews among primary care physician assistants (PAs) who have **NOT** prescribed MOUD/buprenorphine
- 1 interview with a NP specialist in Mental Health who have **NOT** prescribed MOUD/buprenorphine
- 1 interview with a PA specialist in Mental Health who have **NOT** prescribed MOUD/buprenorphine

Goal Timing: 60 minutes (on average)
Actual Timing:

Section Title	HCPs who have NOT prescribed MOUD	HCPs who HAVE prescribed MOUD
Introduction to Study and Ground Rules	7	7
Prescribing Practices	30	35
Experience with Clinical Guidelines and FDA Warnings	15	15
Resources and Training / Wrap Up	8	3
Total with all questions in place	60	60

1. Introduction (7 minutes)

a. Introduction of Moderator

Welcome and thank you for participating in [today's/tonight's] interview. My name is _____, and I am from Lake Research Partners, a national research firm. You have been asked to participate in this discussion because you are a healthcare provider who prescribes benzodiazepines, opioids, or medications for opioid use disorder. The Food and Drug Administration wants to understand healthcare professionals' perspectives about these medications and has contracted with Lake Research Partners to conduct this series of focus groups.

I'm interested in hearing your experiences and opinions. I am not a medical professional or an expert in the topics we will be discussing. As a result, I may have follow-up questions and ask you to explain things that may seem obvious to you but will be new to me.

b. Overview of moderator's ground rules, including the following:
   i. Before we begin, I want to go over a few ground rules for our discussion, which will last 60 minutes. Your participation is voluntary, and you have the right to withdraw at any time without penalty.
   ii. If at any time you are uncomfortable with a question, you can choose not to answer.
   iii. Our discussion will be video and audio recorded. The recording will be transcribed and will help us write a final report summarizing the feedback from the groups. By signing the consent form prior to our conversation today you have agreed to this.
   iv. Everything we discuss today will be kept private to the extent permitted by law - meaning what you say will not be tied back to you individually and the recording, transcription, and reports will be scrubbed of any identifying information. Use only your first name or a nickname in the interview. Only the recruiters have your full name and contact information. It will not be given to anyone at the FDA and no one will contact you after this discussion is over.
   v. I ask that you not share anything that is discussed today with anyone outside of the interview, and if you are speaking about someone else, that you do not share their name or other identifying information.
   vi. Some members of the study team from Lake Research Partners and the FDA are observing the discussion remotely. They want to hear directly from you and may take notes, but they will not interact with you in any way.
   vii. I am looking for active participation for the full 60 minutes we'll be together.
   viii. There are no right or wrong answers, and we are not looking for consensus. I want to hear all of your opinions, so don't hold back on giving me your honest thoughts.

ix. Given the number of areas we want to cover in the short amount of time we'll be together, I may need to move on – please don't be offended.
x. Please silence your devices and minimize any distractions for the next 60 minutes.
xi. If technical assistance is needed, reach out to our technical support team by direct messaging them in the chat or using the phone number or email address you see on screen. (moderator to paste this information in the chat: call 615-732-7752, or email support@qualmeeting.com)
xii. Do you have any questions before we begin?

c. You have been invited to participate in this interview because you are a [primary care physician OR (medical field) specialist OR nurse practitioner OR physician assistant]. Before we dive into the questions, let's quickly do self-introductions. Please tell me your first name and in which state you currently practice.

We will spend the rest of our time talking about your experiences prescribing benzodiazepines and opioid analgesics [**HCPs WHO HAVE PRESCRIBED MOUD:** and buprenorphine-containing medications for opioid use disorder [**FOR ADDICTION MEDICINE SPECIALISTS**: and dispensing methadone].

2. **Prescribing Practices (30 minutes for HCPs who have NOT prescribed MOUD; 35 minutes for HCPs who HAVE prescribed MOUD)**

a. Which benzodiazepines do you prescribe and for what conditions? What are the reasons you prescribe those benzodiazepines? Do you see any differences among those and other benzodiazepines and if so, in what way(s)?

i. When you think about prescribing a benzodiazepine to a patient, what factors do you consider? [**LISTEN FOR VOLUNTEERED ANSWERS, THEN PROBE ON FOLLOWING FACTORS:**]

1. Patient characteristics
    a. Indication for which the medication is prescribed (**if needed:** medical condition of patient like anxiety, insomnia, etc.)
    b. Medical history of patient (**if needed:** mental health, physical health, history of abuse or addiction?)
    c. Prescription history (**if needed:** other medications the patient may be taking? Other healthcare providers the patient may be seeing?)
    d. Other life situations or lifestyle attributes

2. Characteristics of the benzodiazepine being prescribed (e.g., short- or long-acting; dose; duration of the prescribed benzodiazepine treatment, such as short- or long-term; and risk of misuse, abuse, or other potential issues)

3. Previous or other treatment options

4. Regulatory or legal considerations (**if needed:** prescribing guidelines; federal, state, or local laws, etc.)

ii. How have your benzodiazepine prescribing practices changed over time? Why have they changed?

b. Which opioid analgesics do you prescribe, and for what conditions?

i. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] What is your experience prescribing buprenorphine-containing medications for opioid use disorder (OUD)?

1. **Note to moderator**: Please note for participant that from here forward, I'll be referring to opioid use disorder as OUD.

ii. When you think about prescribing an opioid analgesic to a patient, what factors do you consider?

[**LISTEN FOR VOLUNTEERED ANSWERS, THEN PROBE ON FOLLOWING FACTORS**]

1. Patient characteristics

a. Indication for which the medication is prescribed (**if needed**: medical condition of patient like acute and chronic pain)
b. Medical history of patient (**if needed**: mental health, physical health; history of abuse or addiction?)
c. Prescription history (**if needed:** other medications the patient may be taking? Other healthcare providers the patient may be seeing?)
d. Other life situations or lifestyle attributes

2. Characteristics of the opioid analgesic being prescribed (e.g., immediate release or extended release/long-acting; abuse-deterrent formulation or not; dose; and duration of the prescribed opioid analgesic treatment, such as short or long-term)

3. Previous or other treatment options

4. Regulatory or legal considerations (**if needed:** prescribing guidelines; federal, state, or local laws, etc.)

[**FOR HCPs WHO HAVE PRESCRIBED MOUD; ASK AS APPROPRIATE AFTER GETTING INITIAL READ ON OPIOID ANALGESIC FACTORS**:] How do these factors compare to those you consider when prescribing a buprenorphine-containing medication for OUD?

iii. How have your prescribing practices for opioid analgesics changed over time? Why have they changed?

1. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] How have your prescribing practices for buprenorphine-containing products for OUD changed over time? Why have they changed?

c. In what situations have you co-prescribed benzodiazepines and opioid analgesics?

i. Which benzodiazepines and opioid analgesics have you prescribed together?

ii. When co-prescribing benzodiazepines and opioid analgesics, what factors do you consider? [**LISTEN FOR VOLUNTEERED ANSWERS, THEN PROBE ON FOLLOWING FACTORS FOR BOTH OPIOID ANALGESICS AND BUPRENORPHINE FOR OUD AS APPROPRIATE:**]

1. Patient characteristics

a. Indication(s) for which the medications are prescribed (**if needed**: medical condition of patient (acute and chronic pain))
b. Medical history of patient (**if needed**: mental health, physical health, history of abuse or addiction?)
c. Prescription history (other medications the patient may be taking? Other healthcare providers the patient may be seeing?)
d. Other life situations or lifestyle attributes

2. Types of opioids and benzodiazepines being prescribed, dose or duration of prescriptions (e.g., immediate release or extended release/long-acting; abuse-deterrent formulation or not; dose; and duration of the prescribed opioid analgesic treatment, such as short or long-term).

3. Regulatory or legal considerations (opioid prescribing guidelines; federal, state, or local laws, etc.)

iii. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] In what situations have you co-prescribed benzodiazepines and a medication for OUD?

1. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] How do the factors you mentioned for opioid analgesics compare to when you co-prescribe a benzodiazepine and a buprenorphine-containing medication for OUD, including when a patient is receiving one or the other medication from another prescriber?

2. **[FOR ADDICTION MEDICINE SPECIALISTS ONLY IF SOMEONE SPECIFICALLY MENTIONS METHADONE:**] How do those factors compare to when you are treating a patient for OUD using methadone and the patient is also being prescribed a benzodiazepine?

iv. What concerns do you think about when co-prescribing benzodiazepines and opioid analgesics? To what do you attribute these concerns? **Probe if not mentioned**:

1. Concerns about the boxed warning risks (i.e., profound sedation, respiratory depression, coma, death).
2. Concerns around risk of addiction, dependence, misuse, withdrawal, and/or overdose.
3. Concerns around potential lack of communication between different healthcare providers a patient may see.
4. Regulatory or legal considerations (**if needed:** prescribing guidelines; federal, state, or local laws, etc.).

    a. **Probe if needed:** Are your concerns a result of the dangers inherently associated with the substances themselves or a result of patient misuse?

v. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY:**] How do the concerns you think about differ when co-prescribing benzodiazepines with a buprenorphine-containing medication for OUD, and why do they differ?

1. **[FOR ADDICTION MEDICINE SPECIALISTS ONLY IF SOMEONE SPECIFICALLY MENTIONS METHADONE:**] How do those concerns compare to when you are treating a patient for OUD using methadone and the patient is also being prescribed a benzodiazepine?

vi. Describe a situation in which you have discontinued or tapered a co-prescribed opioid analgesic and/or a benzodiazepine, the reasons for doing so, and the outcomes, including challenges. How did you determine how to discontinue or taper these medications and was the patient involved? [**IF NEEDED**:] e.g., use tapering guidelines (whose), develop an individualized tapering plan, etc.?

vii. [**NOTE TO MODERATOR**: If there is no response to the actual experiences question, then follow with:] Describe a situation in which you might determine that discontinuing or tapering co-prescribed opioid analgesics and benzodiazepines is necessary and the reasons.

1. How did you decide to discontinue or reduce the dose of the opioid analgesic versus the benzodiazepine?

2. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY:**] Describe a situation in which you have discontinued or tapered a co-prescribed benzodiazepine and/or medication for OUD, the reasons for doing so, and the outcomes, including challenges. How did you determine how to discontinue or taper these medications and was the patient involved? **[IF NEEDED**:] e.g., use tapering guidelines (whose), develop an individualized tapering plan, etc.?

    a. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY:**] How did you decide to discontinue or reduce the dose of the medication for OUD versus the benzodiazepine?

3. How do the considerations compare when one healthcare provider co-prescribes both an opioid analgesic and a benzodiazepine to a patient versus when more than one provider is prescribing these medications?

    a. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY:**] How do the considerations compare when one healthcare provider prescribes a benzodiazepine and medication for OUD versus when more than one provider is prescribing them?

4. How do the considerations compare when you think about prescribing a benzodiazepine if an opioid analgesic has already been prescribed?

5. How do the considerations compare when prescribing an opioid analgesic if a benzodiazepine has already been prescribed?

viii. When a benzodiazepine and an opioid analgesic are being prescribed by multiple providers, how do you ensure good communication among providers and with the patient?

1. **Probe if needed:** What do you discuss with other prescribers when co-prescribing a benzodiazepine and an opioid analgesic?

2. **Probe if needed:** What do you discuss with your patients when co-prescribing a benzodiazepine and an opioid analgesic?

3. **[HCPs WHO HAVE PRESCRIBED MOUD ONLY:**] How does this compare to when benzodiazepines and medication for OUD are being co-prescribed by different healthcare providers?

ix. What issues or barriers have you experienced when communicating with patients who are receiving a benzodiazepine and/or an opioid analgesic from another healthcare provider?

x. What issues or barriers have you experienced when communicating with other healthcare providers who are prescribing a benzodiazepine and/or an opioid analgesic to a patient to whom you are prescribing these medications?

1. How can these communication issues between healthcare providers be avoided or addressed?

a. **Probes if needed**: prescription drug monitoring programs, alternative therapies, tapering or discontinuation, shorter prescription times, more coordination between different healthcare providers who prescribe medication?

2. What general strategies do you use to decrease risks when co-prescribing a benzodiazepine and an opioid analgesic?

a. **Probes if needed**: length of time of prescription, evaluation before renewing prescriptions, reduction in dose for one or both of the drug classes; co-prescribing naloxone; recommending patients seek additional care such as counseling; monitoring the patient for misuse/abuse of these 2 medications, use of other substances, or development of a use disorder?

xi. When co-prescribed with an opioid analgesic, how do the risks compare between benzodiazepines and other sedative hypnotics or sleep drugs like zolpidem (Ambien), eszopiclone (Lunesta), and zaleplon (Sonata)?

d. Next, I'd like to ask what you have done or would do in a few different situations. If there are specific tools or strategies you might use in the given scenario, please identify them.

i. What have you done when you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine is misusing the medication?

1. [**If no experience**:] What would you do if you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine is misusing the medications?

ii. What have you done when you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine is experiencing withdrawal from the medications?

1. [**If no experience**:] What would you do if you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine is experiencing withdrawal from the medications?

iii. What have you done when you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine has developed an addiction?

1. [**If no experience**:] What would you do if you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine has developed an addiction?

iv. What have you done when you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine has taken an overdose?

1. [**If no experience**:] What would you do if you suspected or learned a patient who is co-prescribed an opioid and a benzodiazepine has taken an overdose?

3. Experience with Clinical Guidelines and FDA Warnings (15 minutes)

a. How do clinical guidelines related to co-prescribing benzodiazepines and opioid analgesics inform or guide your prescribing decisions?

i. What kind of clinical guidelines are you following, and why are you using those particular ones?

ii. How do clinical guidelines inform or guide your prescribing decisions when multiple healthcare professionals may be prescribing these medications to the same patient?

iii. What risks are clinical guidelines not sufficiently addressing for patients who are being prescribed a benzodiazepine and an opioid concomitantly?

b. How have your practices co-prescribing benzodiazepines and opioids changed over time?

c. Are you aware of a Boxed Warning related to benzodiazepines?

i. **If yes:** What do you know about the Boxed Warning?

1. **Listen for:** mentions of 2016, 2017, and/or 2020 changes.

ii. How did you hear about these updates?

iii. How, if at all, did these warnings influence your prescribing?

1. **Probe if needed**: How did the warnings influence your prescribing practices for benzodiazepines? For opioid analgesics? For medications in the two drug classes together?

2. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] How have these warnings informed or guided your co-prescribing of benzodiazepines and medication for OUD?

[**Note if needed**:] To make sure we're on the same page, benzodiazepines have a Boxed Warning (sometimes referred to as a "black box" warning) that taking benzodiazepines at the same time as opioids can lead to profound sedation, respiratory depression, coma, and death. In 2020, the FDA added warnings about the risks of misuse, abuse, addiction, physical dependence, dangerous withdrawal symptoms and overdose with benzodiazepines, especially when they are combined with medicines such as opioid analgesics.

iv. For those of you who were not previously aware of these warnings, how do you think knowing about them might influence your future prescribing?

v. What barriers are there to reducing the co-prescribing of benzodiazepines and opioid analgesics?

vi. **[HCPs WHO HAVE PRESCRIBED MOUD ONLY**:] What barriers are there to reducing co-prescribing of benzodiazepines and medications for OUD?

4. Resources and Training (8 minutes; 3 minutes for HCPs WHO HAVE PRESCRIBED MOUD)

To wrap up today's conversation, I want to talk about resources and training on the topic of co-prescribing benzodiazepines and opioids [**HCPs WHO HAVE PRESCRIBED MOUD:** including buprenorphine-containing medication for OUD.

a. [**SKIP FOR HCPs WHO HAVE PRESCRIBED MOUD**] Outside of any training you may have received in medical school, residency, fellowship, or equivalent training, what continuing education have you received related to co-prescribing opioid analgesics and benzodiazepines?

i. What was helpful in these trainings to address your information needs and inform your prescribing behaviors?

ii. How have they helped you keep up with the science and changing recommendations?

1. How have the trainings impacted your practices of co-prescribing an opioid and a benzodiazepine?

2. How have the trainings impacted your considerations of alternative treatments when prescribing a benzodiazepine alone or in combination with an opioid?

iii. What non-training related information or resources have you received related to co-prescribing an opioid and a benzodiazepine?

b. [**HCPs WHO HAVE PRESCRIBED MOUD ONLY**] What training have you received related to co-prescribing medications for OUD and benzodiazepines?

c. What additional resources or materials would be helpful for healthcare providers on the topics we've been discussing today? What kinds of training would be helpful?

d. From what sources do you want to receive information and/or trainings on these topics? How would you feel about receiving information on this topic from the FDA?

e. [**SKIP FOR HCPs WHO HAVE PRESCRIBED MOUD**] You told us during the recruitment screening that you had not prescribed buprenorphine-containing products during the past 3 months. The current administration released new practice guidelines that exempt many prescribers from federal certification requirements, including training, that are part of the process for obtaining a waiver to treat up to 30 patients with buprenorphine for opioid use disorder. Given this exemption, would you consider prescribing buprenorphine if you had patients with OUD?

i. [**IF TIME:**] Why or why not?

Before I let you go, I'd like to check with my colleagues to see if they have any last questions or clarifications. [**MODERATOR CHECK CHAT FOR QUESTIONS AND ASK IF TIME**]

Those are all of my prepared questions for you. Is there anything else that you would like to add about the topics we discussed today? Is there anything else you would like to tell the FDA about co-prescribing benzodiazepines and opioids [**HCPs WHO HAVE PRESCRIBED MOUD ONLY:** or medications for OUD specifically]?

Thank you for your time and attention throughout this conversation. Have a nice day/evening!