

Study Title: A randomized double-blind multicenter double-dummy non-inferiority trial of inhaled loxapine and intramuscular haloperidol + intramuscular lorazepam
PI (researcher): Michael Wilson
Institution: University of Arkansas for Medical Sciences
Sponsor: Emergency Medicine Foundation

University of Arkansas for Medical Sciences Informed Consent Form

- **We are asking you to be in a research study.**
- **You do not have to be in the study.**
- **If you say yes, you can quit the study at any time.**
- **Please take as much time as you need to make your choice.**
- **You can still get your medical care from UAMS even if you are not in the study.**

Why am I being asked to be in this research study?

- Sometimes people become very excited in the emergency department, and speak with loud voices, move a lot, or even throw things. This is called agitation.
- We want to learn more about how medications help people with certain kinds of agitation from schizophrenia or bipolar disorder. Although you are not agitated now, we are asking for permission to give you government-approved medications for agitation should you need treatment in the UAMS emergency department within the next 3 years.
- This study will help us learn more about how people with agitation respond to certain medications and whether some medications work as well as others.
- We are asking people like you with either schizophrenia or bipolar 1 disorder to help us. Approximately 140 people at two sites between 18 & 64 years of age will be part of this study. At least half of these participants, maybe more, will come from UAMS.
- No matter which medications you receive – either haloperidol (also known as Haldol) + lorazepam (also known as Ativan) or loxapine (also known as Adasuve), these medications are government-approved for agitation.

What if I don't understand something?

- This form may have words you don't understand. Research staff will read it with you, if you like.
- You may ask as many questions as you like before you decide whether you want to be in this study.

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- You are free to ask questions at any time before, during, or after you are in the study.

What if I say yes, I want to be in this study?

We first will see if you qualify to be in the study. We will:

- Ask you some questions about yourself, including about your medical problems.
- We will ask about your allergies.
- We will ask if you mind being randomly assigned (like flipping a coin) to receive either of the study medications (haloperidol/lorazepam or inhaled loxapine) should you ever need them in the emergency department.

If you qualify, we will do these things:

- give you an electronic form with questions about your health and allergies.
- read the questions out loud and fill out the form with you, if you like.

If you are accepted into the study, we will do these things:

- If you do not need treatment for agitation in the UAMS emergency department right now, then nothing will happen now, and nothing will happen unless you need that treatment.
- If you are in the UAMS emergency department and your physician decides that you need treatment for agitation, you will receive both a medication that you breathe in (an inhaler) and an injection. Either the inhaler or the injection, but not both, will contain medication. We will not know in advance which group you will be in, and we cannot promise that you will receive one medication or the other.
 - ✓ For half of the people in the study, the injection will contain normal saline (a placebo, which has no medication, like salt water) but the inhaler will contain loxapine (also known as Adasuve). Loxapine is an inhaled medication that helps people calm down and think more clearly. You should not use loxapine if you have any allergy to medications called antipsychotics. You should also not use loxapine if you have asthma, COPD (a type of lung disease), if you are pregnant, if you are nursing an infant, or if you are over 64 years of age.
 - ✓ For the other half of the people in the study, the inhaler will contain nothing (a placebo) but the injection will contain 5 milligrams of haloperidol (also known as Haldol) and 2 milligrams of lorazepam (also known as Ativan).

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Haloperidol is a type of medication which helps people calm down and think more clearly.

- ✓ Lorazepam is a type of medication called a benzodiazepine. This medication helps people calm down and feel less anxious. You should not use either haloperidol or lorazepam if you have an allergy to antipsychotics or benzodiazepines, if you are pregnant, if you are nursing an infant, if you are over 64 years of age, if you have breathing difficulties, or if you have glaucoma.

- Please note that your chance of being in either group is random “like a flip of a coin toss,” although we will not use a coin for this. Since your group assignment is unknown to the nurses or the doctors, they will also not know which group you will be in. If you somehow figure out what group you are in, we ask you not to tell the nurses or doctors so that they will not know either. If it ever becomes necessary for your doctor to know what drug regimen you were given, that information will be made available to him or her.
- The total amount of time you will be observed in the emergency department is approximately 2.5-3 hours. We are going to check on you frequently no matter which medication you receive. You may have your vital signs taken and be asked how you feel from the medication afterwards, but you will not need to do anything else. You do not need to answer these questions if you don’t feel like it.
- After you leave the emergency department, we will look in your medical chart for other things, including the total length of time you stayed in the emergency department, whether your doctor decided that you needed other medications for agitation, whether you have any other medical problems, whether you had any side effects from the medication, and whether you were admitted to the hospital or discharged home.

How long will this study take?

If you need treatment in the emergency department and are administered medication, the total length of time you will be observed is approximately 2.5-3 hours.

Who will see the information about me that is collected?

- The local study team will know your name and have access to your information.
- We will do our best to make sure no one outside the study knows you are part of the study.

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- We will take your name off information that we collect from you during the study.
- When we share the results of the study in medical journals, we will not include your name or any other information that allows people to identify you personally.
- There are people who make sure the study is run the right way. These people may see information from the study about you including information that identifies you. They are:
 - ✓ The Emergency Medicine Foundation, who sponsored the research.
 - ✓ OHRP (Office for Human Research Protections), a federal agency
 - ✓ UAMS Institutional Review Board, which reviews all UAMS research
 - ✓ Other institutional oversight offices
 - ✓ Your study information will be sent to our research colleagues at Hennepin Medical Center in Minneapolis, but this information will include a code number instead of your name.
- State law requires we tell the authorities if we learn
 - ✓ about possible child or adult abuse
 - ✓ that you might hurt yourself or someone else

Where and how long will my information be kept?

- We will code your information and keep the code in a locked file.
- Only the researchers will have access to the code for your information.
- We will store your information for 7 years
- Your medical record will contain information that you received one of the drugs in the study.
- We will put a copy of this form in your medical record.

What if I say no, I do not want to be in this study?

- Nothing bad will happen. You may still get one of these drugs if you are agitated in the emergency department, but we will not observe your reaction to this. We will not collect research information about how you responded to this medication.
- You can still get medical care at UAMS.

What happens if I say yes, but change my mind later?

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- If you are signing this form in clinic and not in the ER, it will be valid for 3 years, but if you come to the ER during that time and decide you don't want to be in the study after all then you don't have to join.
- You can stop being in the study at any time, and you can ask us not to observe you when you are in the emergency department.
- Nothing bad will happen.
- You can still get medical care at UAMS.
- If you decide to stop being in the study, call Dr Wilson at 501-686-5515 or send him a letter at the UAMS Department of Emergency Medicine, 4301 West Markham Street, slot #584, Little Rock, Arkansas, 72205. He will do everything possible to remove your information. However, this may be impossible in some cases if the data has already been reported.

Can I be taken out of the study even if I want to continue?

Yes, the study doctor (or head researcher) can take you out of the study if:

- You do not follow study instructions.
- It is not in your best interest to continue or if you bring a family member who objects to you being in the study.
- The study is stopped for any reason.
- The study drugs are unavailable, or if there is any other reason that we cannot administer you these medications and then observe you.

If I stop being in the study, what will happen to any information collected from me in the study?

- We may be able to remove your information if it has not already been reported or sent, without identifiers, to a central site. We will not be able to remove you if we have already shared your information.

Will my information from the study be used for anything else, including future research?

- No. Your information will be used only in this study.

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Will it cost me anything to be in the study?

The study drugs haloperidol + lorazepam or inhaled loxapine will be provided to you free of charge. You and/or your insurance company will be billed for your regular medical care in the usual manner for your disease.

Will I be paid?

No. You will not be paid for being in this study.

Will being in this study help me in any way?

Being in the study may help you because you will get treatment for your agitation, although it may not help you more than if you got similar treatment for your agitation outside of this study. We think that being in the study will help people with agitation in the future. What we learn may help in the following ways:

- We may learn how individuals with agitation respond to the study medications.

What are the risks of being in this study?

The risks are:

- Someone could find out that you were in the study and learn something about you that you did not want others to know. We will do our best to protect your privacy.
- The questions could make you sad or upset.
- You may be allergic or have a bad reaction to the study drugs. Although these drugs have been approved by the United States government agency called the Food & Drug Administration (or FDA), you may have a different reaction to them. In the case of loxapine, these risks could include hypersensitivity (serious skin reactions), wheezing or difficulty breathing, increased chance of death or stroke if you are over 65, low blood pressure, passing out, seizures, impairment of thinking or motor skills, or urinary retention. Please note that these risks would be the same if you use loxapine outside of this study. In the case of haloperidol & lorazepam, these risks could include increased chance of death if you are over 65, QT prolongation (a type of heart rhythm disturbance), increased motor movements or abnormal contractions of muscles, increased chance of pneumonia, impairment of thinking or motor skills, possible disturbance of white blood cells (the cells in your body that fight off infection, also termed leukopenia/neutropenia),

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fast heart rate, worsening of glaucoma (if you have this disease), and low blood pressure or high blood pressure.

- In addition, this study may involve other risks that are not currently known to you or your embryo or fetus if you are pregnant. Please let us know whether you are pregnant before you get any study drugs.

What if I get sick or hurt while I'm in this study?

- If you get hurt when you are here for the study, we will help you get the care you need. This may include first aid, emergency care and/or follow-up care.
- If you are not here and get hurt or sick, and think it is because of the study, do these things:
 - ✓ tell your doctor or ER staff
 - the name of this study (say “the Adasuve study”)
 - the name of the head researcher for this study (Dr Wilson)
 - a copy of this form if you have it
- This treatment may be billed to you or your insurance company in the normal manner. Normally, no other form of payment is available.
- You will not give up any of your legal rights by signing this form.

What are the alternatives to being in this study?

You do not have to be in this study. If you do not want to be in this study, your options are:

- To not be in the study. In this case, you may still receive these medications. However, we will not observe your response to them, and we will not collect information about you.

What if new information comes up about the study?

- We want you to know about anything that may change your mind about being in the study.
- The researcher will let you know by:
 - ✓ telling you in the emergency department

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Where can I find more information about this clinical trial?

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website any time.

What if I have questions?

- Please call the head researcher of the study, Dr Wilson at 501-686-8729, if you:
 - ✓ have any questions about this study
 - ✓ have questions about your rights
 - ✓ feel you have been injured in any way by being in this study
- You can also call the office that supervises research (UAMS Institutional Review Board) at 501-686-5667 if you
 - ✓ have questions about this study
 - ✓ have questions about your rights
 - ✓ can't reach the study team
 - ✓ need to speak to someone not directly involved with this study

What should I do if I want to be in the study?

Sign this form. We will give you a copy of this form to keep.

By signing the document, I am saying:

- I understand that joining this study is voluntary.
- I agree to be in the study.
- Someone talked with me about the information in this document and answered all my questions.

I know that:

- I can stop all parts of the study at any time and nothing bad will happen to me.

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- I can call the office that supervises research (UAMS Institutional Review Board) at 501-686-5667 if I have any questions about the study or about my rights.
- My decision will not change my medical care at UAMS.

I agree to be part of this study:

Your name (please print)

Your signature

Date

Name of legally responsible person (please print)

Signature of legally responsible person

Relationship to you: _____

Name of person obtaining consent (please print)

Signature of person obtaining consent

Date