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Answers to Frequently Asked Questions

Randomized Trial of Endotracheal Tubes to Prevent Ventilator-Associated Pneumonia – PreVent 2 Study

Who is sponsoring this research?
The National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) is the source of funding for the PreVent 2 Study.

What is the purpose of this study?
Pneumonia (infection in the lungs) is a common and serious problem in patients who are critically ill and require the support of a breathing machine (mechanical ventilation) through a breathing tube.
The purpose of this study is to identify ways to reduce the risk of pneumonia in critically ill patients that require mechanical ventilation.

One of the causes of pneumonia in patients on mechanical ventilation is the leakage of secretions that are contaminated with germs from the mouth and throat down into the lungs. These secretions tend to leak around regular breathing tubes. However, there are specialized tubes that are designed to prevent leakage of secretions into the lungs. One of these tubes has an extra small channel that allows saliva and other secretions to be suctioned out of the back of the throat, before they can leak down into the lungs. However, it is not clear if this tube (compared to a regular tube) is more effective or safe in preventing pneumonia. Both tubes are approved for use by the Food and Drug Administration, they have good safety profiles, and are commonly used in clinical practice.

For the PreVent 2 Study, we are trying to see if the specially designed breathing tube helps preventing the development of pneumonia, in comparison with regular breathing tubes. Pneumonia can make patients very sick by reducing the oxygen in the blood and the oxygen supply to the brain. It can also cause an inflammatory response that can affect brain function with a long-term decline in thinking abilities. This study will evaluate if preventing pneumonia improves the quality of life and ability to think at six months after the placement of the breathing tube.

How is this study designed?
This is a single-site study randomized, controlled, phase 2 trial that will be conducted under the Exception from Informed Consent regulations. The study is designed to compare the safety long-term patient quality of life, and cognitive function of patients who undergo emergency tracheal intubation with one of two different endotracheal tubes. The study will take place at Oregon Health and Science University Hospital.

What research procedures will occur?

- Eligible patients who require emergency intubation will randomly receive the standard tube or the special tube in the hospital
- The research team will follow the patient's care on a daily basis to see if symptoms of pneumonia develop
- When the patient's breathing tube is removed at the hospital, the research team will review their medical record to see if there is any evidence of injury/safety issues
- The research team will record details about your past medical history and your current illness from the medical record. We will also record the time you spent on the breathing machine, time in the ICU, time in the hospital, and collect data from your medical record about your medical care for up to 6 months after you are discharged from the hospital.
- Patients will be contacted at approximately six months post intubation to see if quality of life and thinking abilities, or any problems that might be related to the breathing tubes, are different

Who will be included in the study?

This study involves critically ill adult patients that are being cared for at OHSU Hospital. Patients may be enrolled in this study if they:

- Require endotracheal intubation in the emergency department or in the hospital AND
- Are admitted to the ICU and receive mechanical ventilation

How are participants enrolled in the study?

The PreVent 2 Study will enroll patients who require emergency placement of a breathing tube at the Oregon Health and Science University (OHSU) Hospital. The decision to place the breathing tube will be made by the caregivers (doctors and paramedics), and is not affected by the study. When a patient requires the insertion of a breathing tube, they can receive either the specialized or the standard tube. However, since insertion of the breathing tube will occur in an emergency, in most cases patients will not be initially asked for informed consent to participate in a research study. The research team will review hospital reports twice daily basis to identify eligible patients

Which treatments will be evaluated in this study?

Endotracheal tubes allow a ventilator to fill the lungs and prevents secretions from going into the lungs. The balloon sits in the windpipe (trachea) and seals the upper airways from the lungs. The special tube was developed with a hole above the balloon and an additional port to allow secretions pooling above the cuff to be sucked out. Two different tubes will be evaluated in this study as follows:

Standard tube: PVC-ETT

Special tube with suctioning: EVAC-PU-ETT

What is known about the risks and benefits of these two tubes?
Both the standard and the special tubes are FDA-cleared for tracheal intubation. Both tubes are used in many hospitals and carry the same types of risks. Patients who require tracheal intubation may experience side effects from the breathing tube. There are no known increased medical risks between the two tubes being studied. There is some evidence that the special tube may help prevent pneumonia. It is not possible to know now if the study tube will prevent pneumonia compared to the usual breathing tube

Where will the study be conducted?
The study will be conducted at a single site, OHSU, a 576-bed hospital with four ICUs and an emergency department.

How many patients will be enrolled in the study?
A total of 1,074 individuals will be enrolled at OHSU.

When will the study start?
The first patient is expected to be enrolled in the summer of 2019. The start time will depend on when the study receives approval to begin by the OHSU Institutional Review Board (IRB).

How long will it take to complete the study?
The study enrollment is expected to last approximately three years.

How long will an individual participant be in the study?
The expected duration of the study is 6 months. Most data will be collected in the hospital until an individual is discharged. Then, 6 months after the clinical intubation, a member of the research team will contact each participant to collect additional information for the study.

Why can't participants give permission before enrolling in the study?
Patients in this study will require emergency endotracheal intubation in the Emergency Department or in-hospital for respiratory distress or failure. Respiratory distress or failure occurs unexpectedly, and because of the inability to predict when respiratory distress or failure is going to occur, a person cannot sign up ahead of time. The window of time (called the therapeutic window) to perform an emergency endotracheal intubation is very short. It may be seconds to minutes. In most cases, patients will be too sick to make health care related decisions during this time. Patients will almost always be unconscious (unable to speak or hear) when they are enrolled in the PreVent 2 trial. Life-supporting interventions must be given immediately without delay. Emergency intubation cannot be delayed waiting to obtain consent for this study.

How can research be done on a person without the person's permission?
There are serious medical emergency situations where patients are unconscious or too sick to give permission to be enrolled in a study. Respiratory distress or failure is one of those situations. The PreVent 2 study will be conducted under federal regulations that allow an exception from informed consent (EFIC).

What is exception from informed consent?
In 1996, the Food and Drug Administration (FDA) developed specific regulations to permit emergency research without prospective consent under carefully controlled circumstances. This is in recognition of the unique kind of emergency medical situations in which patients or family members cannot give informed consent before treatment as well as the need to allow emergency care to advance through research.

According to FDA regulations, to qualify for Exception from Informed Consent (EFIC), the research study must involve participants suffering from a life-threatening disease process or injury for which the current standard of care is associated with a very high failure or mortality rate. In addition, there must be reasonable evidence that the research has the potential to provide real and direct benefit to the patient. Studies must be held to the highest ethical standards. The PreVent 2 study has undergone many independent rigorous reviews to ensure it meets these standards.

The use of a randomized clinical trial such as this is the "gold standard" for determining what works best for people. For treatments that must be given immediately to be effective, EFIC research is considered appropriate by federal regulatory bodies and many ethicists who study this field. The obligation to improve standard treatments that yield poor results in life-threatening conditions is also considered an ethical imperative, as is maintaining individual rights of citizens. In EFIC trials, citizens receive standard treatment in addition to research treatment. To be tested in this fashion, the research treatment has to have shown promise in earlier or smaller studies.

If a family member is present when the patient has respiratory distress or failure, why is the family not asked for permission?
In most cases, there will not be time. In order to give permission to participate in a study, it is important that the person giving permission understands what is being said to them, and can make a well-informed decision. Family members are usually very upset during a medical emergency such as respiratory distress or failure and are not able to concentrate or comprehend what is being said during the emergency. Respiratory distress or failure is an extreme emergency during which the patient could potentially die if treatment is not begun immediately. Patients suffering respiratory distress or failure are usually unconscious and any time taken to discuss their treatment with family can deprive the patient of immediately starting life-saving measures.

If it is possible, we will make efforts to contact the patient's legally authorized representative (LAR) to ask for consent rather than proceed without consent

In addition, before intubation, there may be signs that a patient does not wish to participate in a study. For example, a LAR or family member may communicate the patient's unwillingness to be in research, or

a patient is wearing a "No Study" bracelet. If we learn of opposition to participating in research before intubation, then the patient will not be randomized and will instead receive a non-study standard tube.

Will the research team attempt to inform the patient and/or family members of the study at some point?

Yes. The research team will make several attempts to obtain informed consent from the patient's legally authorized representative or directly from the patient, if possible. Attempts to obtain consent will happen at the earliest possible opportunity before (if feasible) and during the study, up until hospital discharge. Participants will remain in the study for the duration of the placement of the endotracheal tube and will be followed up to six months. The patient, the patient's legally authorized representative or family member will be given the opportunity to withdraw the patient from further study participation and will be provided instruction for how to do so. During the informed consent process, the LAR or patient will be provided information about the endotracheal tubes, study procedures, potential risks and benefits already described above. The consent process will include information that the FDA may inspect subject records for this study.

Are there any risks to the patient?

Because a breathing tube is required for clinical care, we expect a participant will be exposed to the same clinical risks if they were not in this study. These are clinical risks and not a result of participation in this research study. There are no known increased medical risks between the two tubes being studied. There may be some risks that the investigators do not yet know about.

Can a person opt out of this research?

Yes. We will provide an opt-out "No Study" bracelet for those people who do not want to be enrolled in the study. You can contact us by calling the PreVent 2 Study team at 503-494-9545 or email apomocean@ohsu.edu.

Who can I contact if I have more questions?

For more information about this study, please feel free to visit our website at apomocean.ohsu.edu/prevent2. You can view a copy of the informed consent document here.

You may also contact the study coordinator, Mike Kampp, directly phone at 503-494-5224 or email kamppm@ohsu.edu