Official Title: HiLo: Pragmatic Trial of Higher vs Lower Serum Phosphate Targets in Patients Undergoing Hemodialysis

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HiLo: Pragmatic trial of higher vs lower serum phosphate goals in patients undergoing hemodialysis

Study Summary

Your dialysis unit is participating in the HiLo research study designed to find out how patients feel, how often they are hospitalized, and how long they live based on the level of phosphate in their blood. The study will compare two phosphate targets. Patients in the "Hi" group will aim to keep their blood phosphate level at or above 6.5 mg/dl. Patients in the "Lo" group will aim to keep their blood phosphate level less than 5.5 mg/dl. If you participate in the study, your dietitian and nephrologist may adjust your phosphate binder dose and give you advice about your diet in order to keep your phosphate at the target level for your group.

There are no extra tests or dialysis sessions required for the study. If you agree to participate, your dialysis unit will send information from your medical record about your phosphate levels, other blood test results, dialysis treatments, blood pressure, weights, and hospitalizations to the HiLo study team. Depending on when you join the study, you will be in HiLo for up to 45 months.

There are risks to this study that are described in this document. If you are interested in learning more about this study, please continue reading below.

You are being asked to voluntarily consider participating in a research study called HiLo. The information below explains the study so you can decide if you want to take part. Please read this form and other informational materials about the study carefully. The study team will provide you with written materials that summarize what your participation in the study involves. You can share these summaries with your Primary Care Physician and other physicians and health care teams that you visit.

If you decide you do not want to participate in this research, there will be no consequences and you will not be treated differently or lose any benefits to which you are entitled.

Feel free to talk this over with your family, friends, and doctor. If there is anything you do not

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understand or if you have questions, be sure to call the phone number at the end of this form to speak with a member of the research team or email any questions or concerns to the project team at HiLo@duke.edu."

Why is the HiLo trial being done?

- Although dialysis has been used for more than 50 years, the ***best*** phosphate level in the blood for people with kidney failure is not known. The HiLo study is being done to compare how patients feel, how often they are hospitalized, and how long they live based on the level of phosphate in their blood. The study compares two groups: Patients assigned to the "Hi" group will aim to keep their blood phosphate level at or above 6.5 mg/dl. Patients assigned to the "Lo" group will aim to keep their blood phosphate level less than 5.5 mg/dl. Our goal is to learn more about phosphate levels so that we can better determine what the ***best*** phosphate levels are for patients with kidney disease.

Why are phosphate levels in the blood high in patients with kidney disease?

- Phosphate is a substance that is important for bone health and many other processes in the body. When the kidneys are not working, phosphate levels in the blood can get high. The approaches that dialysis teams use to decrease phosphate levels in the blood include asking patients to decrease their intake of foods that have high amounts of phosphate and prescribing phosphate binder pills that bind to phosphate in food and prevent it from being absorbed into the blood. Dialysis also removes some of the phosphate from the blood.

- At this time, the best phosphate level in the blood for people with kidney failure is not known.

What are the pros and cons of keeping phosphate levels low?

- Aiming for a low phosphate level less than 5.5 mg/dl *might* be better for patients, but we are not sure because no study like HiLo has been done before.

- Aiming for a low phosphate level can also have downsides. For example, strict diets are often needed. These strict diets can be difficult to follow and can decrease the amount of protein patients eat and lead to poor nutrition. To reach a low phosphate level, patients usually need to take many phosphate binder pills. This can be difficult for patients since they may already need to take a lot of other medications.

Who is doing this study?

- HiLo is being funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). DaVita, Inc. is one of the dialysis providers participating in HiLo. The study director is Dr. Myles Wolf, a nephrologist at the Duke Clinical Research Institute (DCRI). The HiLo trial is being overseen by the DCRI. Your dialysis unit is participating in the HiLo study.

What happens in the HiLo trial?

- If you participate in this study you will be randomly assigned to either the Hi group or the Lo group. You will have an equal chance of being assigned to either of these groups – like what happens with flipping a coin. Neither you nor the researchers can choose which group you are assigned to. Before you decide to participate, you should think about whether you would be okay with being assigned to either group.

- If you are assigned to the Hi group you will aim to keep your blood phosphate level at or above 6.5 mg/dl. This is higher than the usual phosphate goal at your dialysis unit. Your dietitian and nephrologist will adjust your phosphate binder dose and give you advice about your diet in order to keep your blood phosphate level at the goal of 6.5 mg/dl or higher. For many patients, being assigned to the Hi group will mean that they can take fewer phosphate binders and have a less restrictive diet.

  If you are assigned to the Lo group you will aim to keep your blood phosphate level less than 5.5 mg/dl. This is the same goal that is already being used by your dialysis unit. Your dietitian and nephrologist may adjust your phosphate binder dose and give you advice about your diet in order to keep your blood phosphate level less than 5.5 mg/dl.

- Your dialysis unit will send information about your phosphate levels, other blood test results, dialysis treatments, blood pressure, weights, and hospitalizations to the HiLo study team at DCRI and to the NIDDK.

- The research team at the DCRI will receive information such as your name in case we need to contact you about the study. Other information that can identify you, such as your medical record number, dates of service and date of birth will also be sent to DCRI.

- We will collect information from your medical records about your health history and test results from before you entered the study, and also information that is already collected about you by the Centers for Medicare & Medicaid Services (CMS) and the United States Renal Data System (USRDS). CMS is a government agency that provides health insurance for many patients receiving dialysis. The USRDS is another government agency that monitors national trends in dialysis treatment.

How many people will participate?

- There will be approximately 4400 people taking part in this study. The study is taking place at approximately 120-150 dialysis units across the United States.

What will you be asked to do if you are in HiLo?

- You will be asked to work with your dietitian and nephrologist to keep your blood phosphate level at the assigned target through adjustments (if needed) in phosphate binders and diet.

- The data from your medical record will be shared with the HiLo study team.

- There will not be any extra blood collection or any extra tests for the study.

- Northwestern University, in partnership with the HiLo study team, is also collecting information about how kidney disease has affected the lives of patients and whether control of blood phosphate levels has resulted in gastrointestinal symptoms. The study team will obtain this information in the form of a survey completed either online or over

the phone. You can still participate in HiLo without taking part in the survey. If you choose to participate in the survey you will be asked to complete the survey at 3 different time points in your first year of participating in HiLo. If you chose to complete the surveys by phone, a member of the Northwestern University study team will contact you.

How long will you be in HiLo?

- You will be in HiLo for up to 45 months. This study is expected to end in 2024.
- You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor and dietitian first.
- If you become pregnant while in the study, you will be withdrawn from the study.

Are there any risks from being in HiLo?

- High phosphate levels might contribute to health problems in the heart, blood vessels and bones, but we do not know for certain if this is true. Keeping phosphate levels low might lead to poor nutritional status because of the strict diets required. Keeping phosphate levels low might also lead to too much calcium in the blood vessels and tissues because phosphate binders that are needed to keep the phosphate level low often contain calcium.
- We understand that you may have questions about the phosphate targets for this study. You are encouraged to review the study website along with the other informational materials that are provided to you. Please also speak with your dietitian or someone from the research study team about your questions/concerns.
- There is a risk of loss of confidentiality of your study data.

Are there any benefits from being in HiLo?

- There will not be any direct benefits to you from being in HiLo, but we hope that the

information we learn from this study will help other people with kidney disease in the future.

What are the alternatives to being in HiLo?

- If you do not participate in HiLo, your phosphate target will be determined by your dietitian and nephrologist.

What happens to data that are collected in the study?

- The data collected from you will be used for this study and may be shared with other researchers in the future for their research related to dialysis.

- If you sign this consent form, your study data will be shared with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). After the study is over, the NIDDK will put your information – along with information from the other study participants – into the NIDDK Data Repository. The NIDDK Data Repository is a data bank of health information from all NIDDK studies. Other scientists may use the information from the databank for further research.

  Before we share your information with the NIDDK Data Repository, we will remove your name, address, date of birth and dialysis unit. The information we share may include your age, race and sex. Anyone who uses the information must promise not to try to re-identify any individual study participant. But it is still possible someone could try to identify you based on the data.

Will my information be kept confidential?

- Your privacy is very important to us. When we put your data into the database, we will remove your name and other identifiers, and we will replace these with a code number. There will be a master list linking the code numbers to names, but we will keep it separate and secure. There is a risk that someone could get access to study information we have stored about you and misuse it. We think the chance of this is very small, but

we cannot make guarantees.

- People working for and with DCRI, HiLo, DaVita, Inc. or the participating federal government agencies may review study records to make sure we are doing things the right way.

  A Certificate of Confidentiality to protect the identity of research participants from 'forced disclosure' will be applied to this study. Avoiding forced disclosure means that doctors, researchers, and other staff involved in this study cannot be forced to provide any subjects' identities in any federal, state or local, civil, criminal, administrative, legislative or other legal proceeding. This Certificate of Confidentiality was issued by the National Institutes of Health, which is a United States federal government agency.

What are my rights as a research participant?

- You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data will be collected for study purposes. All data that have already been collected will still be used by the research team.

What if I have injuries related to the research?

- If you have any medical concerns or injuries you should contact your doctor or go to the emergency room.

- Because this study is being overseen by Duke Clinical Research Institute, immediate necessary medical care is also available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., your Duke physicians, or DaVita, Inc. to provide monetary compensation or free medical care to you in the event of a study-related injury.

- You can call the DCRI research team for questions about a research-related injury, or if you have problems, concerns, questions or suggestions about the research using the

following toll-free telephone number: 1-888-973-1596

What are my costs related to the research?

- All costs that are part of your usual medical care that you could have incurred regardless of your enrollment in this study will be billed to you or your healthcare insurance.

Is my participation in HiLo voluntary?

- Yes, it is up to you to decide whether to participate.

What happens to information about me after the study is over or if I cancel my permission?

- After the study, study data will remain in the secure computer systems (servers) at DCRI and the NIDDK Repository.

Will I be told about the results of the HiLo study?

- The study has a website (www.hilostudy.org) that will have information on the study's progress and what we are learning from the study. When the study is completed and the results have been analyzed, a summary of what we learned will be posted on this site. You can discuss the summary with your nephrologist and dietitian to discuss how the results might affect your care.

- A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by US 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 at any time.

Who can I contact if I have questions about HiLo?

- You can call the DCRI research team for questions about a research-related injury, or if you have problems, concerns, questions or suggestions about the research using the following toll-free telephone number: 1-888-973-1596

- For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.
- You can also visit the study website for additional information at www.hilostudy.org.

Thank you for reading this information about the HiLo study. If you agree to participate, please review and sign the electronic version of this consent form (eConsent) that was presented to you.

By signing the electronic consent (eConsent), I acknowledge that:

- The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction.
- I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research.
- I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time.
- I have been told that I will be given a copy of this consent form.
- I agree to share my study data with the NIDDK Data Repository.