David Kosub: Hello, and welcome to another edition of NIH's All About Grants podcast. I'm your host, David Kosub, with the NIH's Office of Extramural Research. Our listeners are likely aware that sex and race may contribute to differences observed in health outcomes and physiologic conditions. But unfortunately, some of the findings from stratified analyses of these variables may not be readily available. To address this concern, NIH recently adapted an existing policy requiring that the results of valid analysis on sex, gender, race and ethnicity be reported to clinicaltrials.gov once an applicable NIH-defined Phase III clinical trial has completed. And that's what brings us here today. We have with us Ms. Dawn Corbet, who is NIH's inclusion policy officer, and she can help us explain more what we mean by valid analysis and the updates to the policy. Thank you for being here. So, let's jump right in and get a foundation under us. Dawn, can you explain what a valid analysis is?

Dawn Corbet: Sure. A valid analysis in this context, we're referring to what's commonly known as a stratified analysis. These analyses explore how well the intervention works among sex, gender, and racial ethnic groups. They may or may not be powered, but they help us understand important trends and inform the direction for future research questions.

David Kosub: And what about an applicable clinical trial?

Dawn Corbet: Applicable clinical trials, in general, study food and drug administration, regulated therapeutics, biologics, and devices. Third-party requirement we're discussing today pertains to a subset of these applicable clinical trials that are known as NIH-defined Phase III clinical trials, which are studies that evaluate an intervention in large groups of people by comparing the intervention to other standard or experimental interventions. NIH funds approximately 600 of these types of trials each year.

David Kosub: When are stratified analyses actually required? How many studies actually conduct them?

Dawn Corbet: Most NIH-defined Phase III clinical trials will require stratified analyses. There's an exception when there's strong evidence that no significant differences exist between sex and gender or racial ethnic groups. To determine if there's strong evidence of no significant differences, investigators that are conducting NIH-defined Phase III clinical trials are expected to review existing evidence to determine whether or not clinically important sex/gender, and race/ethnicity difference in the intervention are a factor to be expected. This information is described as prior evidence in the recent policy amendment and may include data from basic research or earlier phase studies, as well as clinical observations, metabolic studies, genetic studies, pharmacology studies, and other relevant studies.

David Kosub: Some of our listeners may be aware that NIH has required stratified analyses to be performed for decades. What exactly is new about this requirement?

Dawn Corbet: Well, you're right. Since 1994, NIH has required all NIH-defined Phase III clinical trials to provide plans for stratified analyses by sex, or gender, and race and ethnicity and to report on the progress of these analyses in annual progress reports. The new requirement that was described in the December 2017 Policy Amendment is that a subset of these trials that are also applicable clinical trials must also report the results of valid analyses by sex or gender and race and ethnicity in clinicaltrials.gov. This new reporting requirement applies to new and competing awards made on or after December 13th, 2017. Findings from the stratified analyses based on sex or gender and race and ethnicity from these applicable NIH-defined Phase III clinical trials must now be recorded in clinicaltrials.gov within one year of completion of data collection for the study's primary outcome measure. This builds on existing requirements for registering and reporting results at clinicaltrials.gov. If you have an applicable NIH-defined Phase III clinical trial that was already underway before the effective date, the requirement will not affect your current award.

David Kosub: Great, thanks for that explanation. I also wanted to jump back to a statement you made earlier indicating that stratified analyses may not need to be powered. Can you talk a little bit more about that, and how that may align with NIH's drive to have more rigorous and reproducible science?

Dawn Corbet: So that's right. Not all stratified analyses need to have a high statistical power for detecting a stated effect. NIH recognizes that some studies will not have sufficient statistical power to definitively answer whether or not there's clinically significant differences in how well the intervention works among sex or gender and racial and ethnic groups. However, even when the analyses are not powered, they still have value in informing future studies. For example, the data may be used in meta-analysis of related clinical trials that further explore potential differences in the effect by sex or gender, race and ethnicity. NIH expects investigators consider how data from valid analyses may inform future studies when they're designing their study, including their use of subsequent meta-analysis. And in some cases, NIH requires that an NIH-defined Phase III clinical trial be adequately powered to examine differences by sex or gender or race and ethnicity. When there's strong evidence that clinically important differences exist, when there is strong evidence from previously reported work that no clinically important differences exist among sex or gender and race and ethnicity groups, valid analyses by sex or gender and race and ethnicity are not required. Additional information about these requirements for stratified analyses based on prior evidence is available in the full NIH policy guidelines on inclusion of women and minorities as subjects in clinical research websites.

David Kosub: Great, thanks for that clarification. Any final words you'd like to leave with our listeners?

Dawn Corbet: When you're preparing to register your applicable NIH-defined Phase III clinical trial, NIH encourages you to identify which outcomes are relevant to sex or gender and race and ethnicity that you'll need to report at clinicaltrials.gov. Keep in mind that most studies will be expected to report results on sex or gender and race and ethnicity for all primary outcomes. NIH's inclusion of women and minorities website includes guidance that can help you to include your appropriate outcomes at clinicaltrials.gov registration and results reporting.

David Kosub: Fantastic. Thank you very much, Dawn. Greatly appreciate you taking the time to discuss stratified analyses with us, and also to reiterate what you just mentioned, for those interested, please do visit the NIH grants webpage on inclusion for more information. This has been David Kosub with NIH's All About Grants. Thank you.

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