STATISTICAL ANALYSIS PLAN

Study name	Understanding Non-Response in Spine Fusion Surgery
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Version	3

AIM 1

We will assess baseline covariates with respect to the primary outcome, the Oswestry Disability Index (ODI) failure to achieve at least a 15% improvement (minimal important clinical difference as established by the Food and Drug Administration [FDA]) in the ODI score which ranges from 0 to 100 where 0 indicates not disability and 100 indicates complete disability when comparing baseline to six months after surgical procedure, reporting proportions for categorical variables and means and other measures of central tendency for continuous variables. We will use a multivariate logistic regression model with robust standard errors to evaluate these covariates and the primary outcome. A latent class analysis will be used to identify clusters of traits (e.g., patients with depression, anxiety, and catastrophizing) that tend to be grouped together within patient subtypes. This technique assumes there are distinct patterns and that individuals can be grouped into a small number of clusters representing each outcome path (the "latent classes"). The association between clusters and non-response will be described using logistic regression models accounting for repeated testing. As a sensitivity analysis, we will repeat the latent class analysis on the raw percentage change of the primary outcome measure to examine the robustness of variables that define latent classes. We will also conduct a sensitivity analysis looking for different degrees of change in the primary outcome beyond the 15% threshold defined by the FDA. We will also conduct a missing data analysis to describe and characterize enrolled participants who do not provide further outcome measures due to attrition. We will conduct sensitivity analyses using 10-fold multiple imputation to assess the robustness of the results. We will create an imputation model with variables found to be predictive of missingness and data will be imputed to create 10 complete data sets. The results will then be combined across data sets with the using STATA (i.e., MI) statistical software packages.

As a sensitivity analysis, we will repeat the latent class analysis on the raw percentage change of the primary outcome measure to examine the robustness of variables that define latent classes. We will also conduct a sensitivity analysis looking for different degrees of change in the primary outcome beyond the 15pts threshold defined by the FDA. We will also conduct a missing data analysis to describe and characterize enrolled participants who do not provide further outcome measures due to attrition. We

will conduct sensitivity analyses using 10-fold multiple imputation to assess the robustness of the results.

We will assess baseline covariates with respect to ODI non-improvement at 60 days, reporting proportions for categorical variables and means and other measures of central tendency for continuous variables. A multivariate logistic regression model with robust standard errors will be used to evaluate these covariates and the primary outcome: ODI non-Improvement at 60 days.

Use a latent class analysis to identify clusters of traits (e.g., patients with depression, anxiety, and catastrophizing) that tend to be grouped together within patient subtypes. This technique assumes there are distinct patterns and that individuals can be grouped into a small number of clusters representing each outcome path (the “latent classes”). The association between clusters and non-response will be described using logistic regression models accounting for repeated testing.

AIM 2

For responders and non-responders, we will perform a descriptive analysis of radiographic characteristics and compare proportions for categorical variables and means for continuous variables. We will explore the associations between radiographic measures and non-response using conditional logistic regression models, as appropriate for matched case-controls studies with multiple controls.