

**PREMIER Manual of Procedures**

**24. STUDY OUTCOMES AND ADJUDICATION**

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**Summary of Edits**

## **24. Study Outcomes and Adjudication**

In the event that Protocol rules relating to censoring and outcome determination do not clearly apply in a specific case, an Adjudication Committee reviews blinded individual participant data and makes a final resolution. This committee is comprised of study investigators and includes at least two clinicians and one statistician. The coordinating center tracks the activities of the Adjudication Committee and the outcome of its deliberations, and regularly reports back to the Steering Committee and DSMB.

Examples of issues that are likely to come to the Adjudication Committee include (but are not limited to) the following:

1. Blood pressure measurements are obtained outside the recommended time windows.

Although the Steering Committee voted not to exclude measurements just because they exceeded predetermined windows of acceptability, practical considerations may complicate the interpretation of such measurements. For instance, if the first follow-up blood pressure for a participant occurs at six months post randomization, should this really be treated as a three month blood pressure or should the three-month measurement be left missing and the observed measurement used as the first of the four six-month measurements? As noted in chapters 12 through 15, target and acceptable windows exist for all study measurements, and all observations falling outside of the acceptable windows are deferred to the Adjudication Committee for final consideration.

2. Intermittent use of blood pressure lowering medication.

Participants who are regularly taking antihypertensive medication(s) at the time of outcome assessment are classified as hypertensive and their BP data are considered censored at that time. If the use of antihypertensive medication(s) is intermittent, however, or if the participant had used such medications in the past but is not currently taking them, the case is referred to the Adjudication Committee to decide how to classify the participant in terms of hypertensive status and whether the BP measurements need to be censored.

3. Use of blood pressure lowering medication for reasons other than high blood pressure.

Occasionally a participant will be taking blood pressure lowering medications for reasons other than high blood pressure. For example, a participant may be advised to take a peripheral alpha antagonist (such as doxazosin, terazosin, trimazosin) for benign prostatic hypertrophy (BPH). If these medications are being taken on a regular basis, the participant's blood pressure measurements are censored at the time the medication was started. If use of such medications is irregular, or if they had been used in the past and since discontinued, the Adjudication Committee determines whether the measurements

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still need to be censored. In both cases, the Adjudication Committee determines the participant's hypertension status based on BP measurements obtained prior to starting this medication and any additional clinical information the committee chooses to obtain.

### 4. Exclusionary medications started after randomization.

Certain outcomes are censored as a result of starting exclusionary medications after randomization:

<b>Medication</b>	<b>Censored outcomes</b>
Insulin	Blood glucose, insulin
Oral diabetes meds	Blood glucose, insulin
Antihypertensive meds	Measured BP (hypertension status = HTN)
Oral steroids	BP, blood glucose, insulin. <i>(If BP is censored, hypertension status is based on BP measurements prior to start of the medication.)</i>
Oral breathing meds (other than inhalers)	BP <i>(If BP is censored, hypertension status is based on BP measurements prior to start of the medication.)</i>
Weight loss meds	All clinical outcomes

The Adjudication Committee does not need to review individual participant records if they are clearly taking an exclusionary medication on a daily basis and the above censoring rules apply. However, if use of exclusionary medication is intermittent or irregular, the Adjudication Committee reviews the individual case and decides if/what/when censoring should occur.

### 5. Cardiovascular Events

Persons may experience clinical events (MI or stroke) that affect blood pressure. In general, such events will not be considered as indicating hypertension. Blood pressure obtained during follow-up will be used in the analysis as long as the person remains off medications that influence BP. Still, there may be circumstances in which censoring may be appropriate.