

Memo

1. How many controls should sites recruit per case? What are the priorities for recruiting controls?

The site should continuously make every attempt to bring in any **affected** blood relatives and any **identical** (affected or unaffected) siblings.

In addition, ACP would request sites to bring in 1-2 controls per case, based on the following prioritization:

1. Both parents – if not available, then →
2. One parent and one sibling – if not available, then →
3. A sibling, as close in age to the case as possible – if not available, then →
4. An adult child – if not available, then →
5. A half sibling – if not available, then →
6. A matched unrelated control (gender, age, race, geographically matched)

The first year the focus should be on recruiting related controls unless a case has no relatives to refer (then they could refer a matched unrelated control).

2. Please clarify the phrase “unrelated subjects who are suitable controls for subjects with demyelinating diseases” (section 4 of protocol). Who would qualify as an appropriate unrelated control?

An appropriate unrelated control would be an age, race, gender matched control who grew up in the same area as the case (within 50 miles). Additionally, they would need to pass the inclusion/exclusion criteria for controls in order to be included in the study.

3. If a potential case subject cannot refer any controls, can they still be enrolled in the study?

Yes. There is no **requirement** that every case subject have one or more controls per the previously mentioned hierarchy. It is **desirable** but not **required**. A case subject may be enrolled without associated controls.