

Assignment of Subjects to Clinical Studies

By Norman M. Goldfarb

Clinical studies randomly assign subjects to study arms. Random assignment prevents bias – intentional or unintentional – and protects the statistical validity of the study.

However, what if a potential subject qualifies for two or more competing studies? How does the site balance statistical validity vs. fairness to the study sponsors vs. welfare of the subject vs. welfare of the study site?

- Clinical research is experiment, not treatment, so statistical validity is essential. However, statistical validity is blind to the special interests of subjects, sponsors and sites.
- Making the potential subject's welfare the top priority is appealing, but likely to introduce bias, e.g., because more seriously-ill subjects may be assigned to the study that the investigator believes has the more-likely cure.
- Unless the site has told one sponsor that its study is low priority, random assignment seems like a good approach to the required fairness. However, if five subjects just dropped out of one study, should the site assign the next five to bring the studies into balance?
- If one study is more difficult to enroll, it is tempted to assign a qualified subject to that study in order to create a satisfied customer and the prospect of future business for the site.
- If the site prefers one study over another because it is easier to conduct, pays more, or the sponsor is nicer, is it legitimate to favor that study?
- Allowing the subject to choose the study is likely to introduce bias and not satisfy any of the other criteria.

The following procedure balances these competing criteria. The balance can be adjusted by changing the order of the assignment rules. For example, if statistical validity is the only criterion, skip straight to the last step.

1. If a candidate is eligible for more than one study, offer only one study to him/her. If he/she declines to participate, wait at least one week before offering another study (to avoid letting the subject know there was a choice).
2. The first study to offer is the one that generated the contact.
3. If it is not possible to determine which study generated the contact, decide based on the potential subject's welfare.
4. If there is no preference based on the potential subject's welfare, offer the study based on fairness (as defined by the site) to the sponsors. (Sites benefit indirectly when they treat customers fairly.)
5. As a last resort, assign the subject to a study randomly. Flip a coin for 50:50 randomization. For other ratios, use the last two digits in the serial number of the first dollar bill that comes to hand. For example, 01-33 = Study A, 34-66 = Study B, 67-99 = Study C, and 00 = use another bill.

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