prove more important in the interpretation of some outcomes (e.g., chest pain) than of others (e.g., mortality). If possible, of course, it is better to keep both subjects and investigators ignorant of the treatment status, as this will minimize the possibility of actions on the part of either group that could bias the results. When complications of disease or therapy arise that necessitate knowledge of the specific therapy to which the patient has been assigned, this information usually can be given to one or more physicians external to the study who can decide on the proper course of action. If the therapy under study is a drug, the blinding is generally done simply by preparing a placebo identical in appearance to the active agent. However, one study in which the identical appearance of drug and placebo was achieved, but blinding was not, is instructive to review here:

Example. In the early 1970s, healthy adults were enrolled in an experimental study in which they were asked to take either vitamin C (3 g/day) or a lactose placebo for 9 months, during which time the incidence of colds was monitored (Karlowski et al., 1975). Because during the follow-up period some subjects indicated that they were biting into and tasting the preparation that they had been given, the investigators asked all subjects at the conclusion of the study to guess the group to which they had been assigned. Of the 102 who attempted a guess, 79 were correct (77%). The following table summarizes the incidence of colds in persons assigned to each of the two treatment groups, as well as in the subgroup of subjects who guessed incorrectly:

Treatment guessed	Treatment received	No. of subjects	No. with ≥2 colds
Vitamin C	Placebo	11	2 (18%)
—	Vitamin C	101	36 (36%)
Placebo	Vitamin C	12	8 (67%)
—	Placebo	89	42 (47%)

In the group assigned to receive placebo, there was an overall excess (47% vs. 36%) in the percentage of subjects with two or more colds. However, a larger difference was associated with a subject's believing he or she was assigned to a particular group: 36% of subjects assigned to receive vitamin C had two or more colds, twice the incidence in persons who, though they actually were taking placebo, thought they were taking vitamin C. A similar difference was found for persons receiving the vitamin but believing it was a placebo—their incidence was higher than persons receiving placebo (67% vs. 47%). Since a subject's suspicion of the group to which he or she had been assigned so strongly influenced the results, and since a subject's suspicion was much more often right than wrong, the validity of the vitamin C-placebo comparison was seriously compromised.

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