Where unblinding occurs, or is not implemented in the first place, this can influence how the patient reports the disease. For example, if a patient believes that she is in the study drug arm, she may tend to report that she is recovering. If a subject learns that he or she is receiving the study drug, and not placebo, the subject may try to please the doctor by exaggerating the improvement, and conversely, a subject learning that he is in the placebo group may tend to view their experiences more negatively, as he may feel deprived of treatment (38). Unblinding can also influence how the patient conforms to the study protocol. For example, if a patient believes (rightly or wrongly) that he is in the placebo group, he may fail to take his drugs on time. Unblinding can also influence the tendency of a subject to drop out of the study. If a subject believes that she is in the placebo group, she may be tempted to drop out of the study. Unblinding can also influence the tendency to become lost to follow-up. If a subject believes that she was in the placebo group, she may fail to provide information to the investigator, in the years following the study. If a study subject learns that he has been assigned to the placebo group, he may be more willing to drop out of the clinical trial, once it is under way (39). Disproportionate dropout rates from one study arm, relative to another study arm, can influence the interpretation and outcome of clinical trials.

According to the ICH Guidelines (40), blinding can prevent the following sources of bias:

(1) Subjects on active drug might report more favorable outcomes because they expect a benefit or might be more likely to stay in a study if they knew they were on active drug.

(2) Observers might be less likely to identify and report treatment responses in a no-treatment group or might be more sensitive to a favorable outcome or adverse event in patients receiving active drug.

(3) Knowledge of treatment assignment could affect vigor of attempts to obtain on-study or follow-up data.

(4) Knowledge of treatment assignment could affect decisions about whether a subject should remain on treatment or receive concomitant medications or other ancillary therapy.

(5) Knowledge of treatment assignment could affect decisions as to whether a given subject's results should be included in an analysis.

In observing the uneven quality of reporting on methods for allocation and blinding, as it has occurred in publications of clinical trials, D.C. Bauer (41), an editor of a

[38] Krogsbøll LT, Hróbjartsson A, Gøtzsche PC. Spontaneous improvement in randomised clinical trials: meta-analysis of three-armed trials comparing no treatment, placebo and active intervention. *BMC Med Res Methodol.* 2009;9:1.

[39] Forder PM, Gebski VJ, Keech AC. Allocation concealment and blinding: when ignorance is bliss. *Med J Aust.* 2005;182:87–89.

[40] ICH Harmonised Tripartite Guideline. Choice of control group and related issues in clinical trials E10. (Step 4 version, July 2000), 33 pages.

[41] Bauer DC. Randomized trial reporting in general endocrine journals: the good, the bad, and the ugly. *J Clin Endocrinol Metab.* 2008;93:3733–3734.