Non-Inferiority Trials

Several Medical Letter readers have asked about the meaning of non-inferiority trials. A non-inferiority trial is a comparison with an active control to determine whether the difference in response between the new drug and the active control is small enough (less than some pre-specified margin) to demonstrate that the new treatment is not less effective (or is only slightly less effective) than the control in achieving the primary outcome.1,2 Non-inferiority trials are appropriate when a proven effective treatment already exists and assigning some patients to a placebo group would be unethical because the treatment is life-saving or prevents irreversible injury.3 The FDA recently issued guidelines on how to interpret a non-inferiority trial, how to choose a non-inferiority margin and how to analyze the results.4