Bias in uncontrolled therapeutic trials in rheumatology due to selection of populations with extreme characteristics.

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Abstract
OBJECTIVE: To assess the prevalence of biases from selection of patients with extreme characteristics in recent uncontrolled therapeutic studies in rheumatology.

METHODS: We hand searched 4 major rheumatology journals for uncontrolled trials published in 1997 or 1998 that measured therapeutic efficacy by comparing one or more variables at followup vs at baseline. We evaluated the susceptibility to bias from random measurement error and natural variability for variables used for defining eligibility that overlap with those used for defining outcomes.

RESULTS: Twenty-five studies were analyzed. In 22 studies, the eligibility criteria were related to the outcome criteria and defined a patient population with extreme characteristics. Only 3 studies clearly reported that they had performed a baseline measurement separate from the screening (eligibility) measurement. The remaining 19 reports (76%) might be susceptible to bias: in 7, identical variables were used for eligibility criteria and outcomes; 3 used outcome variables that were also used for characterizing eligibility along with other criteria; 2 used specific eligibility variables that were part of composite outcome scores; and 7 selected patients on the basis of vague descriptors of disease severity, while disease severity was also the outcome.

CONCLUSION: Several recent uncontrolled trials of therapeutic interventions in rheumatology are subject to biases stemming from the selection of patients with extreme characteristics. Baseline evaluations separate from the screening measurements should be performed and eligibility criteria and outcomes should be carefully defined.

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