# Outcomes vary in global heart failure trials by geographic region

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A comparison of several international clinical trials of beta-blocker drugs has shown there are notable differences in how well the drugs prevent deaths in heart failure patients, based on where the patients were treated. In this study, U.S. patients apparently had a lower survival rate with beta-blocker treatment compared to patients outside the U.S.

The analysis is published online today in the *Journal of the American College of Cardiology*.

"Our analysis showed the survival rate associated with beta-blocker therapy in heart failure patients was reduced in U.S. patients," said Christopher O'Connor, M.D., the study's lead author and Director of the Duke Heart Center. "In contrast, the survival rate was much more significant in patients treated in the rest of the world."

"The findings point to a consistent pattern of geographical differences within clinical trials that needs to be addressed," O'Connor said.

The dissimilarity in multi-national heart failure trial findings is being published at a time when globalization of clinical trials is on the rise. "Global clinical trials enable researchers to achieve enrollment goals within a reasonable time frame, and ensure new therapies are adequately tested in broad populations who will likely be exposed to them once market approval has been obtained," O'Connor said. "But researchers must be aware that geographical discrepancies in results may exist, and future trials must be adapted accordingly."

O'Connor and his author team analyzed results from several randomized, double-blind, placebo-controlled, multi-center studies that evaluated survival following beta-blocker treatment in heart failure patients. Of the 8,988 patients enrolled in the four trials, 4198 patients (46.7%) were from the U.S.

Three of the studies showed similar significant reductions in mortality with beta-blocker treatment compared to placebo, including the Metoprolol Controlled-Release Randomized Intervention Trial in Heart Failure (MERIT-HF); Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS); and Cardiac Insufficiency Bisoprolol Study (CIBIS-II).

In contrast, the Beta-Blocker Evaluation of Survival Trial (BEST), which enrolled patients from the U.S. and Canada (97.7% and 2.3% respectively), showed a non-significant 13% risk reduction in patients treated with the beta-blocker bucindolol versus placebo.

O'Connor says several factors may contribute to the geographic discrepancies in clinical outcome, including population differences, genetics, and cultural, social, or administrative differences in disease management. O'Connor says the results may also reflect how different population groups, including ethnicities, respond to the drugs, as well as differences in standards of care and the use of evidence-based therapies that may have contributed to differences in patient outcomes.

"Our study reflects the need to reevaluate the conduct, methodology and analysis of multi-national trials to ensure the study findings can be generalized accurately," he said.

Provided by Duke University Medical Center