## Risk models for mortality after acute myocardial infarction: development and validation based on HERO-2, a multinational clinical trial

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## Summary

Randomized clinical trials provide a rich source of data for developing risk factor models. We have developed risk-calibration strategies based on the HERO-2 trial, a large international randomized trial of two antithrombotic therapies—unfractionated heparin and bivalirudin—for the treatment of acute myocardial infarction (AMI). HERO-2 recruited 17 073 patients from 47 countries from Europe, North and South America and Asia, including Australia, New Zealand and Russia. For this reason the HERO-2 database provides an excellent opportunity to explore issues associated with developing, comparing and validating risk strategies for acute myocardial infarction. We discuss the ability of risk models to generalize to other populations from the context in which they were developed.

Risk indices developed using only western populations perform poorly, in terms of predicting individual risk, when applied to HERO-2 patients from other regions. Hence, either risk variables with region specificity need to be introduced or calibration is required to match the absolute level of risk in other regions. Statistical methods for recalibration in new settings are reviewed and methods for sample size calculation introduced. We present a risk index (HPI) with built-in region adjustment, which can be applied simply in clinical practice. HPI is very consistent with other risk-factor models developed in AMI, performed well in internal validation on statistical measures of ranking and calibration and was as accurate as a previous western population index in predicting risk in an external dataset of western patients; the new index needs to be tested in other non-western datasets. The HPI index applies well internationally and is likely to be widely applicable in non-trial settings

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