Survival after acute myocardial infarction has been enhanced by treatment with thrombolytic agents, aspirin, and beta-adrenoceptor blockade. However there remains a substantial subgroup of patients who manifest clinical evidence of heart failure despite the first two of these treatments, and for whom beta-adrenoceptor antagonists are relatively or absolutely contraindicated. These patients have a greatly increased risk of fatal and non-fatal ischaemic, arrhythmic, and haemodynamic events. In this selected high-risk subset of patients we investigated the effect of therapy with the angiotensin converting enzyme (ACE) inhibitor ramipril, postulating that it would lengthen survival. 2006 patients who had shown clinical evidence of heart failure at any time after an acute myocardial infarction (AMI) were recruited from 144 centres in 14 countries. Patients were randomly allocated to double-blind treatment with either placebo (992 patients) or ramipril (1014 patients) on day 3 to day 10 after AMI (day 1). Patients with severe heart failure resistant to conventional therapy, in whom the attending physician considered the use of an ACE inhibitor to be mandatory, were excluded. Follow-up was continued for a minimum of 6 months and an average of 15 months. On intention-to-treat analysis mortality from all causes was significantly lower for patients randomised to receive ramipril (170 deaths; 17%) than for those randomised to receive placebo (222 deaths; 23%). The observed risk reduction was 27% (95% CI 11% to 40%; p = 0.002). Analysis of prespecified secondary outcomes revealed a risk reduction of 19% for the first validated outcome (i.e., first event in an individual patient)—namely, death, severe/resistant heart failure, myocardial infarction, or stroke (95% CI 5% to 31%; p = 0.008). Oral administration of ramipril to patients with clinical evidence of either transient or ongoing heart failure, initiated between the second and ninth day after myocardial infarction, resulted in a substantial reduction in premature death from all causes. This benefit was apparent as early as 30 days and was consistent across a range of subgroups.