External applicability of blood pressure-lowering drug trials to real-world patients with manifest cardiovascular disease

Authors:
NE Bonekamp¹, W Spiering¹, HM Nathoe², LJ Kappelle³, GJ De Borst⁴, FLJ Visseren¹, J Westerink¹, ¹University Medical Center Utrecht, Department of Vascular Medicine - Utrecht - Netherlands (The), ²University Medical Center Utrecht, Department of Cardiology - Utrecht - Netherlands (The), ³University Medical Center Utrecht, Department of Neurology - Utrecht - Netherlands (The), ⁴University Medical Center Utrecht, Department of Vascular Surgery - Utrecht - Netherlands (The),

On behalf: The UCC-SMART Study Group

Topic(s):
Hypertension: Pharmacotherapy

Background: Randomised controlled trials (RCTs) are the main source of evidence for clinical treatment guidelines. However, there are concerns that strict eligibility criteria for participant selection may limit applicability of trial results to real-world patients.

Purpose: To assess the applicability of blood pressure-lowering drug trials in real-world secondary preventive care in stable coronary artery disease, peripheral artery disease and cerebrovascular disease.

Methods: Eligibility criteria from the largest guideline-informing RCTs on blood pressure-lowering drugs, the EUROPA, PEACE, HOPE-PAD, PROFESS and PROGRESS trials, were applied to three subcohorts within the UCC-SMART study with coronary artery disease (n=5155), peripheral artery disease (n=1487) and cerebrovascular disease (n=2515). Baseline differences between would-be trial eligible and ineligible patients were estimated. Differences in all-cause mortality and a composite major adverse cardiovascular event (MACE) outcome of cardiovascular death, myocardial infarction and stroke were calculated and adjusted for age, sex and cardiovascular risk factors using Cox proportional hazard models.

Results: Seventy-five percent of UCC-SMART patients with the appropriate cardiovascular disease were eligible for EUROPA, 84% for PEACE, 59% for HOPE-PAD, 17% for PROFESS and 100% for PROGRESS. Across trials, the main reasons for UCC-SMART patients’ ineligibility were age younger than 50 or 55 years and cardiovascular history. On average, eligible patients were older (range 1.4–14.6 years across trials). Incidence rates for all-cause mortality and MACE were higher for trial eligible patients (Figure 1). After adjustment for age and sex, EUROPA and PEACE eligible patients had a lower risk of mortality (EUROPA: hazard ratio (HR) 0.68 95% confidence interval (CI) 0.59-0.77, PEACE: HR 0.52 95%CI 0.43-0.64) and MACE (EUROPA: HR 0.88 95%CI 0.76-1.01, PEACE: 0.56 95%CI 0.46-0.69), while differences between HOPE-PAD and PROFESS eligible and ineligible patients were not statistically significant.

Conclusion: The results from the landmark trials on blood pressure-lowering drugs, specifically RAASi, in patients with peripheral artery and cerebrovascular disease are widely applicable to real-world patient populations. Although the majority of coronary artery disease patients is eligible for the EUROPA and PEACE trial, the results of these trials should be applied to trial ineligible patients with caution.
External applicability of blood pressure-lowering drug trials to real-world patients with manifest cardiovascular disease

Authors: NE Bonekamp, W Spiering, HM Nathoe, LJ Kappelle, GJ De Borst, FLJ Visseren, J Westerink

1 University Medical Center Utrecht, Department of Vascular Medicine - Utrecht - Netherlands (The)
2 University Medical Center Utrecht, Department of Cardiology - Utrecht - Netherlands (The)
3 University Medical Center Utrecht, Department of Neurology - Utrecht - Netherlands (The)
4 University Medical Center Utrecht, Department of Vascular Surgery - Utrecht - Netherlands (The)

On behalf: The UCC-SMART Study Group

Topic(s): Hypertension: Pharmacotherapy

Background: Randomised controlled trials (RCTs) are the main source of evidence for clinical treatment guidelines. However, there are concerns that strict eligibility criteria for participant selection may limit applicability of trial results to real-world patients.

Purpose: To assess the applicability of blood pressure-lowering drug trials in real-world secondary preventive care in stable coronary artery disease, peripheral artery disease and cerebrovascular disease.

Methods: Eligibility criteria from the largest guideline-informing RCTs on blood pressure-lowering drugs, the EUROPA, PEACE, HOPE-PAD, PRoFESS and PROGRESS trials, were applied to three subcohorts within the UCC-SMART study with coronary artery disease (n=5155), peripheral artery disease (n=1487) and cerebrovascular disease (n=2515). Baseline differences between would-be trial eligible and ineligible patients were estimated. Differences in all-cause mortality and a composite major adverse cardiovascular event (MACE) outcome of cardiovascular death, myocardial infarction and stroke were calculated and adjusted for age, sex and cardiovascular risk factors using Cox proportional hazard models.

Results: Seventy-five percent of UCC-SMART patients with the appropriate cardiovascular disease were eligible for EUROPA, 84% for PEACE, 59% for HOPE-PAD, 17% for PRoFESS and 100% for PROGRESS. Across trials, the main reasons for UCC-SMART patients' ineligibility were age younger than 50 or 55 years and cardiovascular history. On average, eligible patients were older (range 1.4–14.6 years across trials). Incidence rates for all-cause mortality and MACE were higher for trial eligible patients (Figure 1). After adjustment for age and sex, EUROPA and PEACE eligible patients had a lower risk of mortality (EUROPA: hazard ratio (HR) 0.68 95% confidence interval (CI) 0.59-0.77, PEACE: HR 0.52 95%CI 0.43-0.64) and MACE (EUROPA: HR 0.88 95%CI 0.76-1.01, PEACE: 0.56 95%CI 0.46-0.69), while differences between HOPE-PAD and PRoFESS eligible and ineligible patients were not statistically significant.

Conclusion: The results from the landmark trials on blood pressure-lowering drugs, specifically RAASi, in patients with peripheral artery and cerebrovascular disease are widely applicable to real-world patient populations. Although the majority of coronary artery disease patients is eligible for the EUROPA and PEACE trial, the results of these trials should be applied to trial ineligible patients with caution.