



β -Blockers for hypertension

Nadia Khan and Finlay McAlister¹ conclude that β -blockers are efficacious for hypertension in younger but not in older patients, but their conclusions are based on questionable statistical methods.

In their Methods section, Khan and McAlister state that “Meta-analyses for all outcomes were performed using random-effects models.” When I tried to reproduce their results by entering data into Review Manager (the Cochrane Collaboration’s software for conducting reviews; version 4.2 for Windows), I also observed a significant reduction of cardiovascular events in younger patients (relative risk [RR] 0.86, 95% confidence interval [CI] 0.74-0.99), but this result was based on a fixed-effects model. With the “true” random-effects model, the CI was wider and included the value 1 (RR 0.86, 95% CI 0.75-1.00). Relative to other antihypertensive drugs, β -blockers seemed to increase the risk of cardiovascular events in older patients (RR 1.06, 95% CI 1.01-1.10), but again in a fixed-effects model. With a random-effects model, the CI includes 1 (RR 1.07, 95% CI 1.00-1.14).

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DOI:10.1503/cmaj.106018

Nadia Khan and Finlay McAlister¹ defined the primary outcome for their meta-analysis as the composite cardiovascular outcome of death, nonfatal myocardial infarction or nonfatal stroke. Unfortunately, this definition is unclear; as a result, for some studies only cardiovascular deaths and for other studies all-cause deaths were included in the analyses. We checked the values presented for all trials in Figs. 2A and 2B against the original publications and found several discrepancies (see Appendix 1 available at www.cmaj.ca/cgi/content/full/176/7/971-a/DC1). We recommend recalculating the results and rethinking the interpretation.

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DOI:10.1503/cmaj.106019

Nadia Khan and Finlay McAlister¹ re-examined our meta-analysis² of β -blockers in primary hypertension but came to a different conclusion than we did. We would like to clarify why the conclusions differ.

First, we examined the effect of β -blocker treatment on the incidence of myocardial infarction (MI), stroke or death separately, whereas Khan and McAlister focused on the composite end point of all 3 conditions. However, antihypertensive drugs do not have the same relative effect on stroke incidence as on MI or death.

Second, we excluded the results of the Captopril Prevention Project (CAPP) trial,³ because it is impossible to retrieve data on how many patients in that study were receiving

β -blockers.² CAPP had a PROBE design (prospective, randomized, open treatment with blinded end-point evaluation),³ as well as some other major quality concerns; for example, randomization was imbalanced, with more high-risk patients receiving captopril than conventional treatment (diuretics and/or β -blockers), and suboptimal use of captopril once daily was encouraged in an unknown number of patients. There is no way of extrapolating from other Scandinavian trials the percentage of patients in the CAPP study who were treated with β -blockers, since both investigators and patients differed among these trials.

Finally, cardiovascular outcome after treatment of primary hypertension in subjects under 60 years of age is poorly documented. Therefore β -blockers cannot be recommended for any age group.

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3. Hansson L, Lindholm LH, Niskanen L, et al. Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPP) randomised trial. *Lancet* 1999;353:611-6.

DOI:10.1503/cmaj.1060205

[The authors respond:]

Falk Hoffman asserts that the conclusions in our meta-analysis were incorrect, as the random-effects confidence intervals for Figs. 1A and 2B appeared to include the value 1 when the analyses were repeated with Review Manager software. However, unlike Hoffman, we conducted our random-effects analyses using a soft-