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EDITORIALS

β blockers for heart failure

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End under-prescribing for women and older adults

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In their linked article, Kotecha and colleagues (doi:10.1136/bmj.i1855) present a meta-analysis of individual patient data (IPD) and conclude that β blockers reduce all cause mortality and admission to hospital related to heart failure in patients with heart failure with reduced ejection fraction (HFrEF) and in sinus rhythm, irrespective of age and sex.[1] These findings reinforce the recommendations of current clinical guidelines.[2 3] In daily clinical practice, however, prescription rates of β blockers and the doses taken are lower than might be expected based on the available evidence. β blockers seem to be underused, especially in women and older adults of both sexes. Studies from secondary care clearly show suboptimal prescribing, although reported prescription rates vary considerably.[4 5] In primary care, uptake of β blockers is even lower.[6 7]

Kotecha and colleagues included nearly all the available evidence from trials comparing β blockers with placebo, with individual data from 13 833 patients including 3283 women and more than 4000 adults aged 70-80. Use of β blockers significantly reduced mortality hazard ratios ranged from 0.65 in the third quarter of the age distribution (median age 68) to 0.77 for the highest quarter (median age 75). Sex did not modify these effect estimates. Similarly, β blockers reduced the number of admissions related to heart failure in all age and sex subgroups.

The authors should be applauded for also focusing on age and sex specific discontinuation rates and prescribed dose of β blocker (as a percentage of the maximum recommended dose). These data provide important information on intolerability of β blockers; an important cause of suboptimal prescribing particularly among older adults who have a high prevalence of comorbidity and polypharmacy. Interestingly, both discontinuation rates and the dose reached were similar across age and sex subgroups; about one in every six to seven patients discontinued treatment with a β blocker and patients received 70-75% of the maximum dose, including those in the oldest age group. Importantly, these numbers were similar in the placebo groups, indicating that when possible side effects occur during treatment with β blockers, they might not be caused by the drug.

Why do we need this IPD meta-analysis? Apparently, clinicians are more hesitant to prescribe β blockers in older patients and in women, although clinical guidelines recommend treatment irrespective of age and sex.[2 3] Perhaps, this is because individual trials do not show convincing benefit of β blockers in women and older adults. Indeed, both groups are under-represented in trials. In daily practice the mean age of patients with HFrEF is around 75, and about 50% of patients are women. Yet, the mean age of patients included in this IPD meta-analysis was 63 and only 23% were women.[8] Consequently, firm conclusions about effectiveness in patient subgroups are difficult from individual trials, forcing readers to make unsubstantiated assumptions that effects will be similar. Subgroup analyses in individual trials are rarely powerful enough to generate reliable results. This is illustrated by the inconsistent relative effects in men and women observed in subgroup analyses from the individual β blocker trials.[1]

Meta-analysis of individual patient data is a powerful tool to reliably explore whether interventions work better (or worse) in clinically relevant subgroups including men, women, and older adults.[9] The identification of subgroups is enhanced in all meta-analyses, but IPD meta-analyses, however, have several important advantages over analyses of aggregate data, including the ability to harmonise definitions of subgroups (such as age groups) or outcomes and to adjust for baseline differences.[9 10] The work by Kotecha and colleagues illustrates these advantages: the findings show conclusively that β blockers are beneficial for patients with HFrEF, irrespective of age or sex. The authors confirmed the robustness of their findings in elaborate sensitivity analyses.

This IPD meta-analysis reports important information for patients and clinicians. Clinicians should offer β blockers to all men and women with HFrEF and in sinus rhythm, irrespective of their age. Patients should expect this equity of approach. When typical side effects occur, both prescribers and patients should realise that adults given placebos in trials of β blockers report side effects at comparable rates.

IPD meta-analysis adds value to both individual trials and regular meta-analysis.[11] This one shows once again that subgroup

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analyses from individual trials should be interpreted with caution or, even better, not performed at all when they are underpowered. Trialists should carefully document their data from individual patients and agree to share it with researchers conducting IPD meta-analyses (perhaps encouraged by funders and leading journals) as these collaborations have great power to change practice for the better and improve outcomes for patients.

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