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Title

Representativeness of antihypertensive trials: analysis of Serious Adverse Events

Priority 1 (Research Category)

Hypertension

Presenters

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Abstract

Context: Representativeness of 'standard' antihypertensive drug trials is uncertain, with limited recruitment of older people. Some trials specifically recruit older participants to address this. Trials are obliged to report hospitalizations and deaths, regardless of cause, as Serious Adverse Events (SAEs). If older-people's trials are representative, we would expect rates of SAEs in trials to be similar to the rate of hospitalisation and death in the community, and higher than standard trials. Objective: To compare the rate of SAEs in hypertension trials to rates of hospitalisation and death among people taking similar treatments in the community. Study Design: Observational study comparing trial populations to a community cohort. Dataset: We identified trials of Renin-Angiotensin-Aldosterone system (RAAS) drugs for hypertension from clinicatrials.gov. We identified a community comparison population of people with hypertension starting RAAS drugs using primary care data from the Wales, UK (SAIL databank). Population studied: Trial participants from 110 RAAS hypertension trials (11 older-people's trials, mean age 73, and 99 standard trials, mean age 56). Community cohort of people with hypertension (n=56,036, mean age 60) starting RAAS drugs. Outcomes: SAEs in trials (mostly accounted for by hospitalizations or deaths) and all-cause hospitalizations/deaths in the community comparison. SAE rates in older-people and standard trials were compared, adjusting for trial characteristics. The community rate was used to calculate the expected rate of hospitalizations/deaths given the age/sex distribution of each trial. We then compared the expected rate with the observed rate of SAEs in each trial. Results: Older-people's trials had higher SAEs rate than standard trials (0.18 versus 0.11 events/person/year, adjusted IRR 1.74, 95% CI 1.03-2.92). The hospitalisation and death rate in the community for those taking RAAS antihypertensives was much greater than the rate of SAEs reported in standard (ratio 3.70 (3.12-4.55)) and older-people's trials (4.35 (2.56-7.69)), adjusting for age and sex. Conclusion: Trials report substantially fewer SAEs than expected from rates of hospitalisations and deaths among similar-aged people receiving equivalent treatments in the community. SAE rates may be a useful metric to assess trial representativeness. Clinicians should be cautious when applying trial recommendations to older people, even when trials focus on older people.