Drug efficacy in older people with multimorbidity

A US cohort study found that warfarin, beta-blockers, calcium channel blockers, renin–angiotensin system blockers, statins and thiazides reduced mortality when used for an indicated condition in older people with multimorbidity.

**Overview:**
- Warfarin, beta-blockers, calcium channel blockers, renin–angiotensin system (RAS) blockers, statins and thiazides reduced mortality when used for an indicated condition in older people with multimorbidity.
- Clopidogrel, metformin, selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) did not reduce mortality in older people with multimorbidity.
- These findings imply that using common cardiovascular drugs indicated for single diseases is of benefit in people with multimorbidity.

**Background:** Multimorbidity is the combination of 1 chronic disease with at least 1 other disease (acute or chronic), biopsychosocial factor or risk factor (NICE 2014). It is often defined more simply as the coexistence of 2 or more long-term conditions.

Many drugs trials focus on people who have only the disease of interest and exclude people with comorbid conditions (Boyd et al. 2012). As a result, it is not clear whether drugs are as effective in people with other chronic diseases as well as the indicated condition.

In addition, guidelines for chronic conditions often recommend drugs on the basis of their effect on that specific condition (Uhlig et al. 2014). Following guideline recommendations for each condition in a person with multimorbidity can mean that the individual receives a number of different drugs concurrently (polypharmacy). Taking a large number of drugs can reduce adherence, increase the burden of treatment and raise the likelihood of adverse effects (King’s Fund 2013).
Current advice: The NICE guideline on medicines optimisation recommends that healthcare professionals consider carrying out a structured medication review for some groups of people, when a clear purpose for the review has been identified. These groups include:

- adults, children and young people taking multiple medicines
- adults, children and young people with chronic or long-term conditions
- older people.

A medication review is defined as ‘a structured, critical examination of a person’s medicines with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste’.

NICE is currently preparing guidance on multimorbidity, which has an anticipated publication date of September 2016.

The NICE pathway on medicines optimisation brings together all related NICE guidance and associated products on the area in a set of interactive topic-based diagrams.

New evidence: A cohort study by Tinetti et al. (2015) assessed the effects of common drugs on mortality in older people with multiple chronic conditions.

Participants were identified from people who took part in the US Medicare Current Beneficiary Survey. This analysis looked at people aged 65 years or more who had at least 2 of 9 chronic conditions: atrial fibrillation; coronary artery disease; chronic kidney disease; depression; diabetes; heart failure; hyperlipidaemia; hypertension; and thromboembolic disease.

Survey data were used to determine whether these people took any of 9 oral prescription drugs for their conditions, as recommended by US national guidelines for the disease. These drugs were: beta-blockers; calcium channel blockers; clopidogrel; metformin; RAS blockers; SSRIs or SNRIs; statins; thiazides; and warfarin. Some drugs, such as beta-blockers and statins, were indicated for more than 1 condition.

The study cohort comprised 8578 participants with a mean age of 77.4 years. The authors compared mortality in people with multimorbidity who were taking a guideline-recommended drug for an indicated condition and people who had the condition and other chronic diseases but were not taking the drug. A total of 1287 (15%) participants died during follow-up (median duration=24 months).

Warfarin was associated with a reduced risk of death among people with atrial fibrillation or thromboembolic disease and other chronic conditions (aHR=0.69, 95% CI 0.56 to 0.85 and aHR=0.44, 95% CI 0.30 to 0.62, respectively). Beta-blockers, calcium channel blockers, RAS blockers, statins and thiazides all also reduced mortality.

Clopidogrel was not associated with a reduced risk of death in participants with atrial fibrillation or coronary artery disease plus other chronic conditions (adjusted hazard ratio [aHR]=1.26, 95% confidence interval [CI] 0.94 to 1.67 and aHR=0.94, 95% CI 0.76 to 1.16, respectively). Beta-blockers, calcium channel blockers, RAS blockers, statins and thiazides all also reduced mortality.

Metformin did not significantly lower mortality in people with diabetes plus other chronic conditions compared with those who did not take the drug (aHR=0.85, 95% CI 0.68 to 1.05). Likewise, SSRIs and SNRIs did not reduce mortality in people with depression and other chronic conditions (aHR=0.95, 95% CI 0.79 to 1.15).

Strengths of this study include that it used a large cohort that reflected the heterogeneous older adult population in the USA. Limitations include that the authors did not have information on duration, dose or adherence of drug treatment. The observational design of the study means that the possibility of unmeasured confounders cannot be ruled out.
Commentary by Professor Stewart Mercer, Professor of Primary Care Research, University of Glasgow:

“Multimorbidity is now the norm rather than the exception as populations age. However, the evidence base on how best to manage people with multimorbidity is sparse, and guidelines almost always take a single disease focus based on trials in which people with multimorbidity are excluded. Thus there is a substantial evidence gap in multimorbidity, leaving practitioners and physicians to ‘muddle through’ the management of such people.

“This research by Tinetti et al. (2015) is a welcome addition to the evidence base on the management of people with multimorbidity. The authors used a cohort design to try to show whether commonly prescribed drugs were as effective at reducing mortality in people with multiple conditions as in those without. They found that commonly used drugs in cardiovascular disease – warfarin, beta-blockers, calcium channel blockers, RAS blockers, statins and thiazides – all reduced mortality in people with multiple chronic conditions. This is reassuring news because it implies that using such drugs indicated in single disease guidelines in people with multimorbidity is of benefit.

“UK clinicians, including GPs, tend to adhere to cardiovascular guidelines even though they have not been specifically designed for people with multimorbidity, but worry about polypharmacy and treatment burden. In addition, many are concerned as to whether or not the drugs remain effective in people with multimorbidity: the current study will help to reassure doctors that they are.

“The lack of effect of clopidogrel was perhaps surprising, but the lack of effect of the other drugs on mortality is perhaps less so. Further work would be required to show if metformin, SSRIs, or SNRIs had any effects on morbidity and quality of life rather than mortality.

“Finally, we should remember that all clinical decisions in people with multimorbidity should be patient centred. For certain people at certain stages of life, a tailored approach to their medication management will be required. Thus shared decision-making and putting the person before their conditions remains crucial.”

Study sponsorship: US National Institute on Aging.

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