



Nurse-led titration of drug doses in chronic heart failure

A Cochrane review found that in people with chronic heart failure, titration of beta-blockers, angiotensin-converting-enzyme inhibitors and angiotensin-II-receptor antagonists by nurses rather than by doctors was associated with a lower rate of hospital admissions and mortality.

Overview:

- In people with heart failure, nurse-led titration of doses of beta-blockers, angiotensin-converting-enzyme inhibitors and angiotensin-II-receptor antagonists was associated with lower rates of hospital admission than titration by doctors.
- Nurse-led titration of these drugs was also associated with lower all-cause mortality.
- This Cochrane review highlights the value of nurse-led titration, but more robust studies are required to examine safety and cost effectiveness before this strategy can be recommended over usual care.

Background: Heart failure due to left ventricular systolic dysfunction (also known as heart failure with reduced ejection fraction) can be treated with beta-blockers or angiotensin-converting-enzyme (ACE) inhibitors, with angiotensin-II-receptor antagonists (ARBs) a second-line option ([NICE 2010](#)).

These drugs have a dose-dependent effect, so the dose a person receives should be titrated up to an optimal level. However, there can be some reluctance in primary care doctors to increase doses ([Philips et al. 2004](#)). An alternative approach is titration of doses by nurses, which has been shown to improve outcomes in people with heart failure ([Jain et al. 2005](#))



Current advice: The NICE guideline on [chronic heart failure in adults](#) (currently [being updated](#)) recommends offering both ACE inhibitors and beta-blockers licensed for heart failure to all people with heart failure due to left ventricular systolic dysfunction. Clinical judgement should be used when deciding which drug to start first.

Therapy with ACE inhibitors should be started at a low dose and titrated upwards at short intervals (for example, every 2 weeks) until the optimal tolerated or target dose is achieved. Beta-blockers should be introduced in a 'start low, go slow' manner.

An ARB licensed for heart failure may be considered as an alternative to an ACE inhibitor for people who have intolerable side effects or who remain symptomatic despite optimal therapy with an ACE inhibitor and a beta-blocker.

The NICE pathway on [chronic heart failure](#) brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: A Cochrane review by [Driscoll et al. \(2015\)](#) compared nurse-led titration of drug doses with titration by doctors in people with heart failure.

The review identified 7 randomised controlled trials on titration of beta-blockers, ACE inhibitors and ARBs in 1684 adults with chronic heart failure due to left ventricular systolic dysfunction. Nurse-led titration took place in an outpatient clinic in 4 studies; the remaining 3 studies considered nurse-led titration in primary care, via telephone follow-up and in a residential care facility. Follow-up ranged from 6 months to 18 months.

In a pooled meta-analysis of 4 studies (3 on beta-blockers and 1 on beta-blockers and ACE inhibitors, n=560), nurse-led titration was associated with a lower risk of hospital admission for any cause than titration by a doctor (risk ratio [RR]=0.80, 95% confidence interval [CI] 0.72 to 0.88, p=0.00022).

Nurse-led titration was also associated with a lower rate of hospital admission related to heart failure (RR=0.51, 95% CI 0.36 to 0.72, p=0.00012; 2 studies on beta-blockers and 2 on beta-blockers and ACE inhibitors, n=642).

Meta-analysis of 6 studies (n=902) showed that people who received nurse-led titration were less likely to die from any cause than those who had titration by a doctor (RR=0.66, 95% CI 0.48 to 0.92, p=0.015). The authors estimated that approximately 56 deaths could be avoided in every 1000 people if everyone with heart failure had nurse-led titration of their drug doses.

Limitations of this analysis include that all the studies could not blind participants and study personnel to group allocation. In addition, only 2 studies reported on adverse effects of titration (1 of which reported no adverse events and the other reported an adverse event in the nurse-led titration group but did not specify type or severity).

Commentary by Dr Clare J Taylor, General Practitioner and NIHR Academic Clinical Lecturer, University of Oxford:

“The benefits of ACE inhibitors, beta-blockers and ARBs in people who have heart failure with reduced ejection fraction have been known for many years. Guidelines globally advocate the use of these drugs, but the effect of the type of healthcare professional managing the up-titration has not been described.

“This Cochrane review assessed the effect of nurse-led titration, compared with titration by a doctor (usual care), on the outcome of people who had heart failure with reduced ejection fraction. The review found that all-cause mortality and hospitalisations were lower in the nurse-led titration group. However, data on the number of participants who achieved target dose and on the frequency of adverse events are lacking, or from low quality evidence. This is a major weakness of the review and limits the applicability of the findings.

“Randomised controlled trials assessing the effectiveness of ACE inhibitors, beta-blockers and ARBs have reported large positive effects on hospitalisation and survival rates. Yet in clinical practice, people with heart failure often receive substantially less than the target dose.

“Doctors may be reluctant to up-titrate for two reasons. Firstly, people with heart failure may have several chronic diseases, and doctors may choose not to initiate or up-titrate drugs that may exacerbate other conditions. For example, heart failure and chronic kidney disease often coexist. Initiating or increasing the dose of an ACE inhibitor in a person with these 2 conditions can,

usually temporarily, worsen renal function. Secondly, the participants in the clinical trials supporting the use of these drugs were significantly younger than the real-world patient population and with few or no comorbidities. This disparity means some doctors feel the evidence from the trial populations may not be applicable to the people they manage.

“Nurse-led clinics are already an integral part of many heart failure services within the NHS. The clinics tend to focus solely on heart failure treatment and aim to achieve the target dose required to optimise benefit, according to a disease-specific protocol. Initiation and up-titration of several drugs is resource intensive, and nurse-led clinics have more capacity to see people frequently to optimise treatment.

“This Cochrane review highlights the value of nurse-led titration, but more robust studies are required to examine safety and cost effectiveness before this strategy can be recommended over usual care.”

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