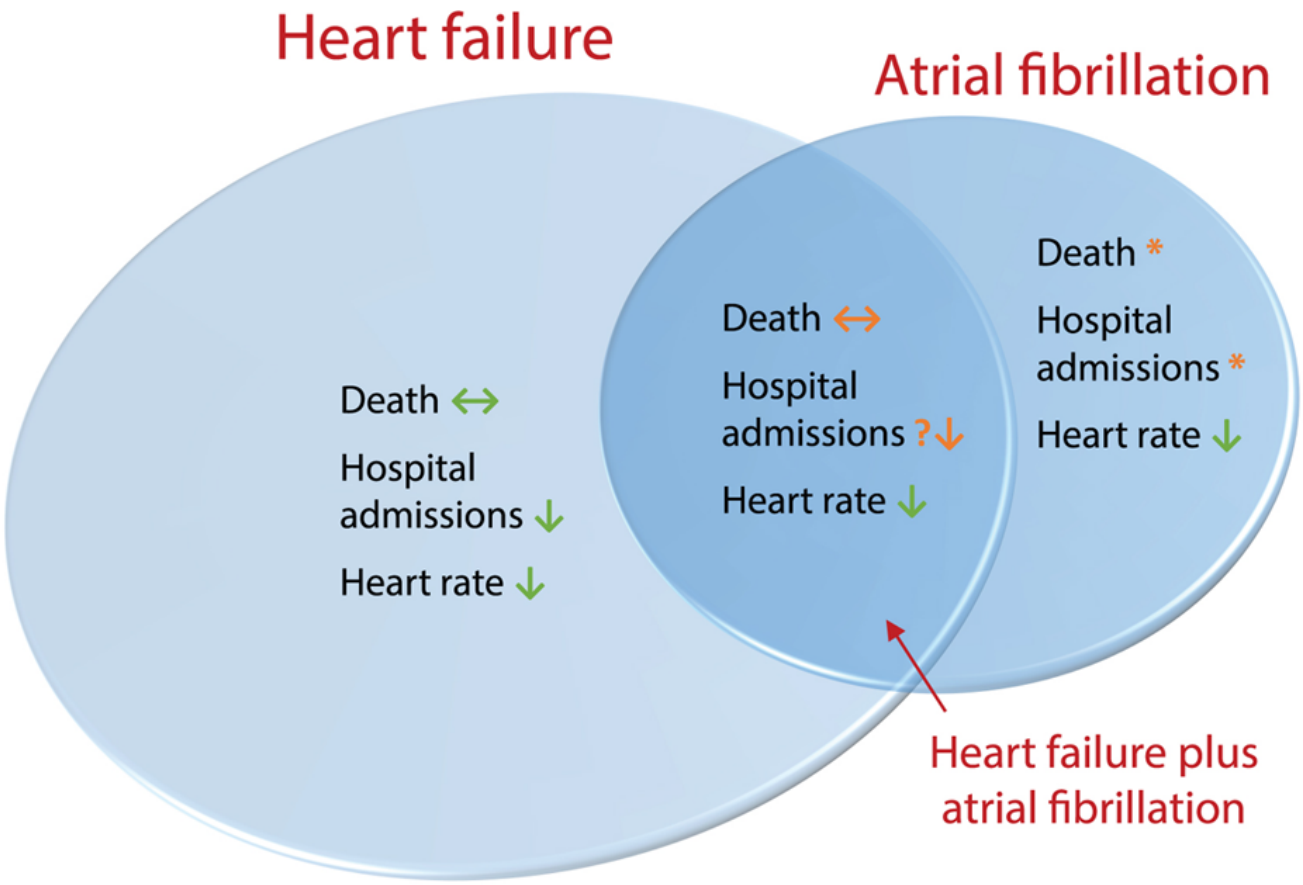
Is digoxin safe?

Digoxin is a medication commonly used in patients with heart disease. It is extracted from the foxglove plant and was first described in 1785. During the last few centuries it has become an established treatment in patients with heart failure to increase the function of the heart, and those with atrial fibrillation to reduce heart rate. Heart failure is where the function of the heart is not sufficient to meet the body's needs. It has many causes, such as previous heart attacks, and leads to symptoms of breathlessness and lethargy. Patients with heart failure have a much higher risk of dying or being admitted to hospital. Atrial fibrillation is a common heart condition that causes an irregular and often rapid heart rate. Patients with atrial fibrillation are typically older and often have a number of other medical conditions, including high blood pressure and heart failure. Atrial fibrillation causes every 4th stroke and patients suffer from frequent hospital admissions, early death and reduced quality of life. We can expect twice as many people to have this condition over the next 20 years.

Although digoxin is frequently used in heart failure and atrial fibrillation, there have been surprisingly few clinical trials investigating the benefits and risk of therapy. Good quality clinical trials are important (particularly where the treatments are randomly assigned) as this reduces the bias of a doctor choosing treatments they feel may work better. In one major study of patients with heart failure (the DIG trial), digoxin did not reduce the risk of death, but did reduce the likelihood of being admitted to hospital. A series of studies have followed which have not randomly assigned treatment – these often show that unlike the clinical trials, digoxin increases the risk of death. Our objective in this study was to comprehensively and systematically assess all studies published on digoxin in order to better appreciate whether digoxin improves or worsens clinical outcomes in heart failure, atrial fibrillation and the combination of these two conditions.



Evidence for digoxin:

- Randomized controlled trials and observational data
- Observational data only

↔ = Consistent data on neutral effect with digoxin
↓ = Lower with digoxin therapy
* = Unable to comment (biased observational data only)

Our results confirm that in clinical trials where treatments are randomly assigned, digoxin does not increase or reduce the risk of death. In patients with heart failure, digoxin reduced the need for hospital admissions. Unfortunately, there was very little good quality data in patients with atrial fibrillation, highlighting the need for further clinical trials in this area. We also identified that studies just observing what happens in normal clinical practice (without randomly assigning treatments) should not be used to look at the treatment effects of medications. In these studies, there was clear indication of bias due to marked differences in the type of patients who receive digoxin (they are usually much older, with more diabetes and worse heart failure, all of which are themselves associated with an increase in the risk of death). In summary, our review of all published data on

digoxin suggests that it does not cause death, may reduce the need for hospital admission and should continue to be considered as a treatment option in patients with heart failure and atrial fibrillation (pending further trials).

***Dipak Kotecha**, MBChB PhD MRCP FESC FHEA*

UNIVERSITY OF BIRMINGHAM

Publication

Safety and efficacy of digoxin: systematic review and meta-analysis of observational and controlled trial data.
Ziff OJ, Lane DA, Samra M, Griffith M, Kirchhof P, Lip GY, Steeds RP, Townend J, Kotecha D
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