

**TCS/21/04 - A single-centre, randomised, open label, blinded end-point, safety and efficacy trial of conventional versus higher dose acetylcysteine in patients with paracetamol overdose. (The High SNAP Trial).**

Paracetamol overdose is very common. Someone presents to hospital following an overdose every 5 minutes across the UK. This rate is the same as for heart attacks. Despite having an effective antidote called acetylcysteine, 1 in 10 patients go on to develop liver damage. Acetylcysteine causes side-effects such as allergic reactions that are unpleasant for the patient and result in this essential treatment being stopped. In this field, there is a lack of reliable evidence to guide patient care. It is unknown whether increasing the dose of acetylcysteine is more effective at preventing liver damage partly because, until recently, dose increases have not been possible due to the side-effects. To address this, we designed a new protocol for giving acetylcysteine (the SNAP regimen) that is now used in hospitals across the UK and has dramatically reduced the risk of patients experiencing side-effects. The improved safety of the SNAP regimen allows us to assess the potential benefits of treating patients with higher acetylcysteine doses. This trial will determine whether increasing the acetylcysteine dose results in an increase in the breakdown of paracetamol, without causing an unacceptable rate of side-effects. Paracetamol breakdown will be assessed by measurement of the breakdown products (metabolites) in the blood. Side-effects will be assessed using the questionnaire approach we developed and validated in the SNAP Trial. The results of this trial are essential information for the next step, a UK-wide trial to determine whether a higher dose of acetylcysteine improves the outcome for patients.