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Response to the letter from Wong *et al.*

James W. Dear[1*], Paul I. Dargan[2,3], Michael Eddleston[1], Ruben H. Thanacoody[4], Simon H.L. Thomas[4]

[1] *Pharmacology, Toxicology and Therapeutics, Centre for Cardiovascular Science, University of Edinburgh, UK*
[2] *Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust, London, UK*
[3] *Faculty of Life Sciences and Medicine, King's College London, London, UK*
[4] *Medical Toxicology Centre, Institute of Cellular Medicine, Newcastle University, Newcastle NE2 4HH, UK*

Dear Editor

With interest, we read the letter from Dr. Wong and colleagues [1] regarding our recent paper titled *'Safety and Efficacy of the SNAP 12-hour Acetylcysteine Regimen for the Treatment of Paracetamol Overdose'* [2].

The authors raise concerns about patients not having had blood drawn at both 10 and 20 hours after the commencement of the 12h SNAP acetylcysteine regimen for treatment of paracetamol overdose. There are a number of important points, which need to be clarified.

1. In this patient group there will be self-discharges. This would be expected to occur with the 2-bag 20h acetylcysteine regimen advocated by the authors of the letter. In comparison with current practice using the standard 21h acetylcysteine regimen, patients treated with the SNAP regimen have an extra blood sample at 10h after starting acetylcysteine. This provides valuable information with regard to the risk associated with a patient taking their discharge against medical advice. Furthermore, this allows the treating doctor to identify patients in whom treatment could be stopped after 12h of acetylcysteine (as advocated in the protocol briefly described by Dr Wong). Only with the SNAP regimen will the full licenced dose of acetylcysteine (300mg/kg) have been administered to the patient after completing 12h of treatment.

In our paper in *EClinicalMedicine* all patients had blood sampling at 10h after starting treatment and Edinburgh patients were followed after discharge for hospital re-admission, liver failure and death using the Scottish Health Record Linkage system. This provides a comprehensive data set for analysis. No patients were readmitted due to a complication of their paracetamol poisoning, which supports the SNAP regimen being clinically effective.

2. The authors imply that a patient with an ALT activity of 961U/L was one of only 6 out of 1137 patients with an ALT increase from baseline without 20h blood sampling. This is an incorrect assumption. This patient presented 5 days after a single acute overdose. Their admission ALT activity was 1427U/L. At 10h their ALT had fallen, INR 1.1 and paracetamol <5mg/L. This indicates a low risk of subsequent liver failure.

3. The authors suggest we excluded patients with hepatotoxicity from our analysis. Again, this is incorrect. As clearly stated in the legends, the primary analysis in Figure 1 and Table 2 includes all patients audited in this study with no exclusions.

The SNAP regimen substantially reduces adverse reactions and has comparable clinical effectiveness to the standard treatment regimen. As noted in the commentary that accompanied our paper [3], this regimen allows both low risk patients to have a shortened duration of treatment with the full licenced dose of acetylcysteine and higher risk patients to receive a higher dose. It is the only regimen to offer all these advantages backed up by a robust evidence base [4].

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* Corresponding author.
E-mail address: james.dear@ed.ac.uk (J.W. Dear).

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