

Newsletter: February, 2023

Dear all,

We would like to thank all who have taken part, are currently enrolled in our Trial of ondansetron as a Parkinson’s HAllucinations Treatment or are supporting the study in other ways. Since recruitment began in 2021, we have recruited 111 people (see Figure 1) and have set up 35 recruiting sites across the UK.

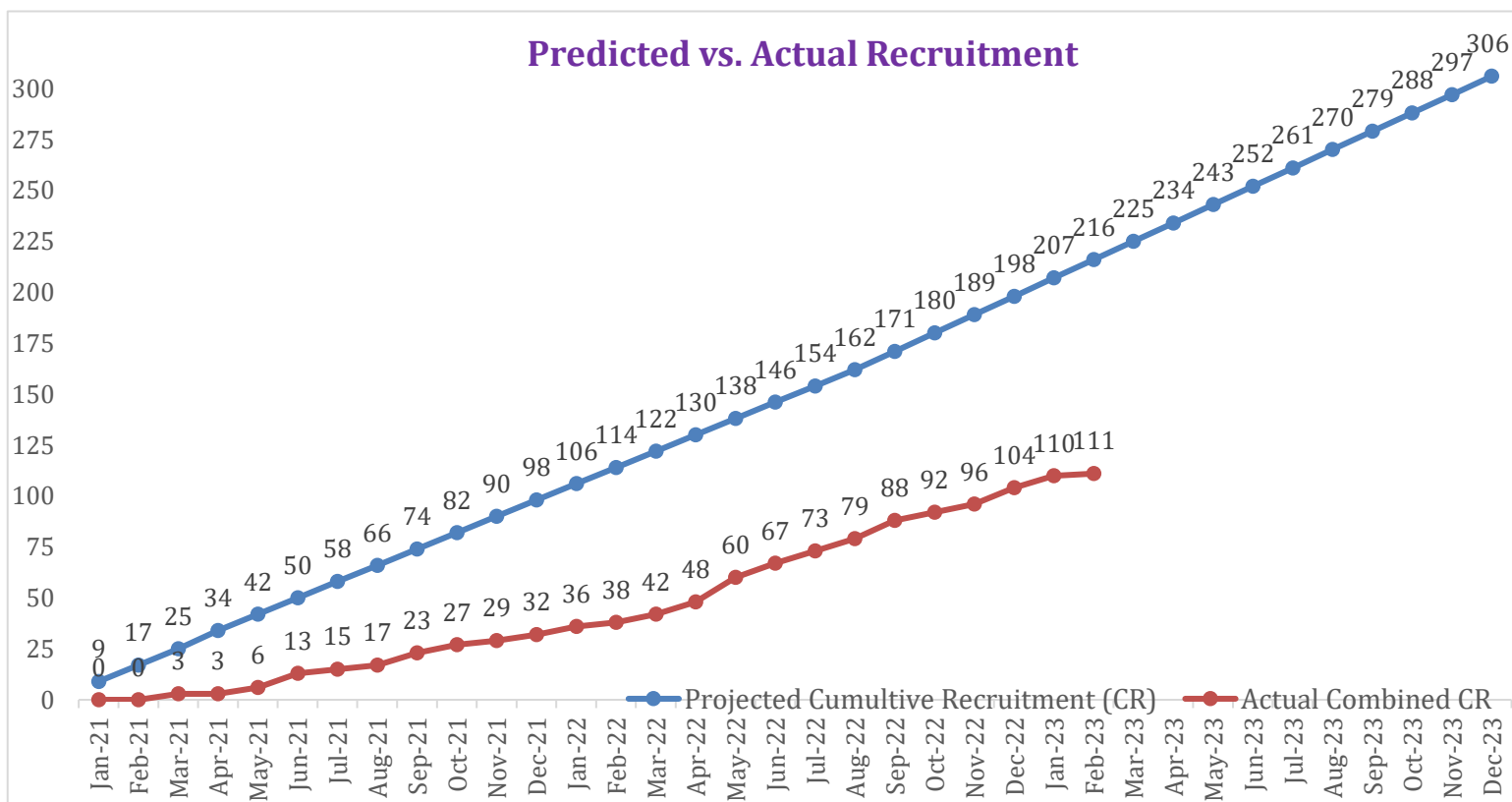


Figure 1: Total number of people recruited into the trial since the start of recruitment. The predicted number of recruits (blue) and the actual number of recruits (red) are shown.

Our recruitment rate increased in 2022 and we are hoping that this will continue as we add more recruiting centres.

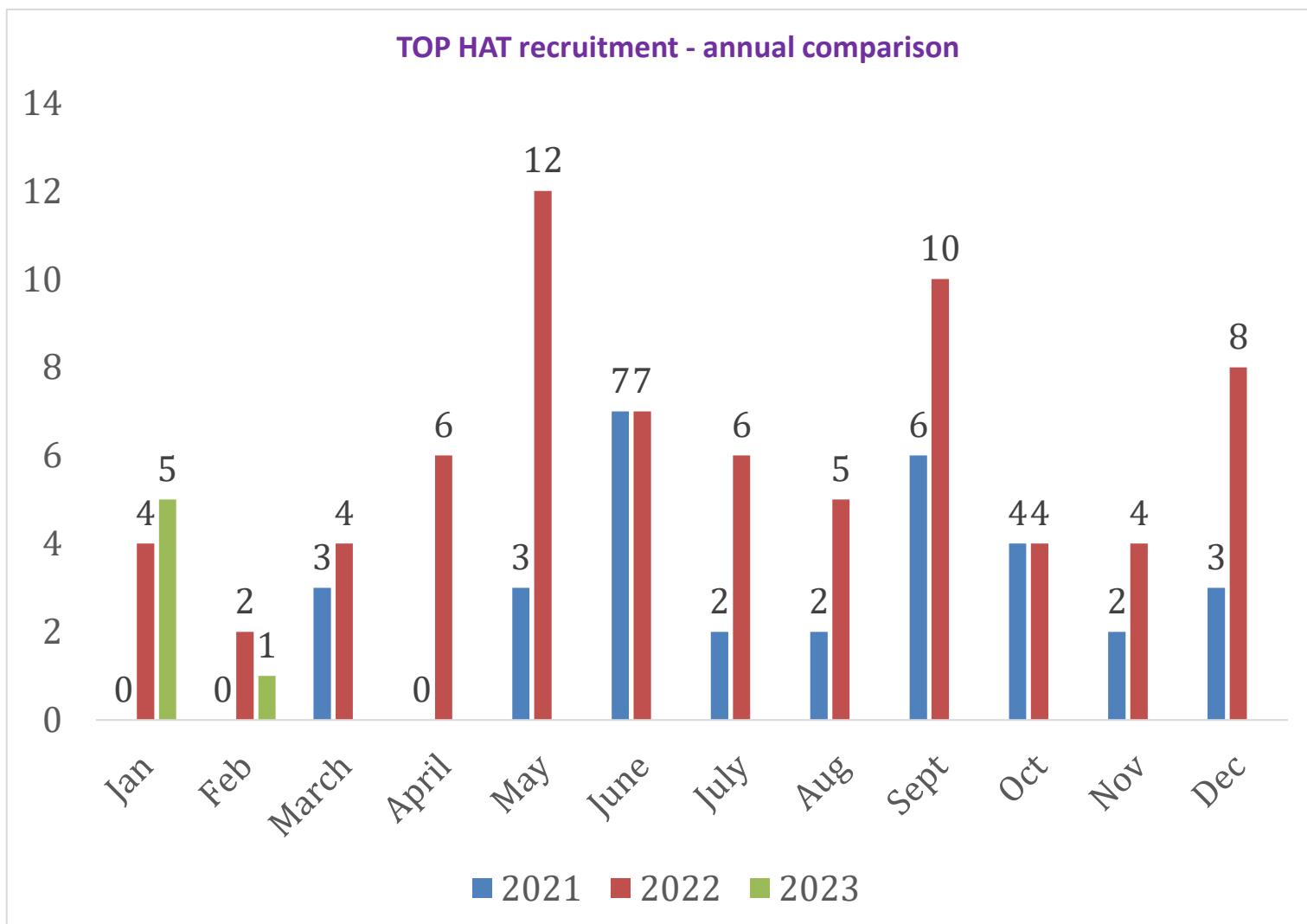


Figure 2: The total number of participants recruited each year since the start of recruitment in 2021.

Salford Royal and Dorset are our top recruiting sites, with Sherwood Forest and UCLH in second place and snapping at their heels to also reach the top spot!

In May 2021, we widened the trial eligibility criteria to include people with Lewy Body dementia, as they experience similar visual experiences to people with Parkinson's and may also benefit from ondansetron.

Information from people with Lewy Body dementia will be analysed separately from those with Parkinson's, as they may differ in their response or susceptibility to any side effects of

the drug. 87 of those recruited so far have Parkinson’s and 24 are with Lewy Body dementia (see Figure 3.).

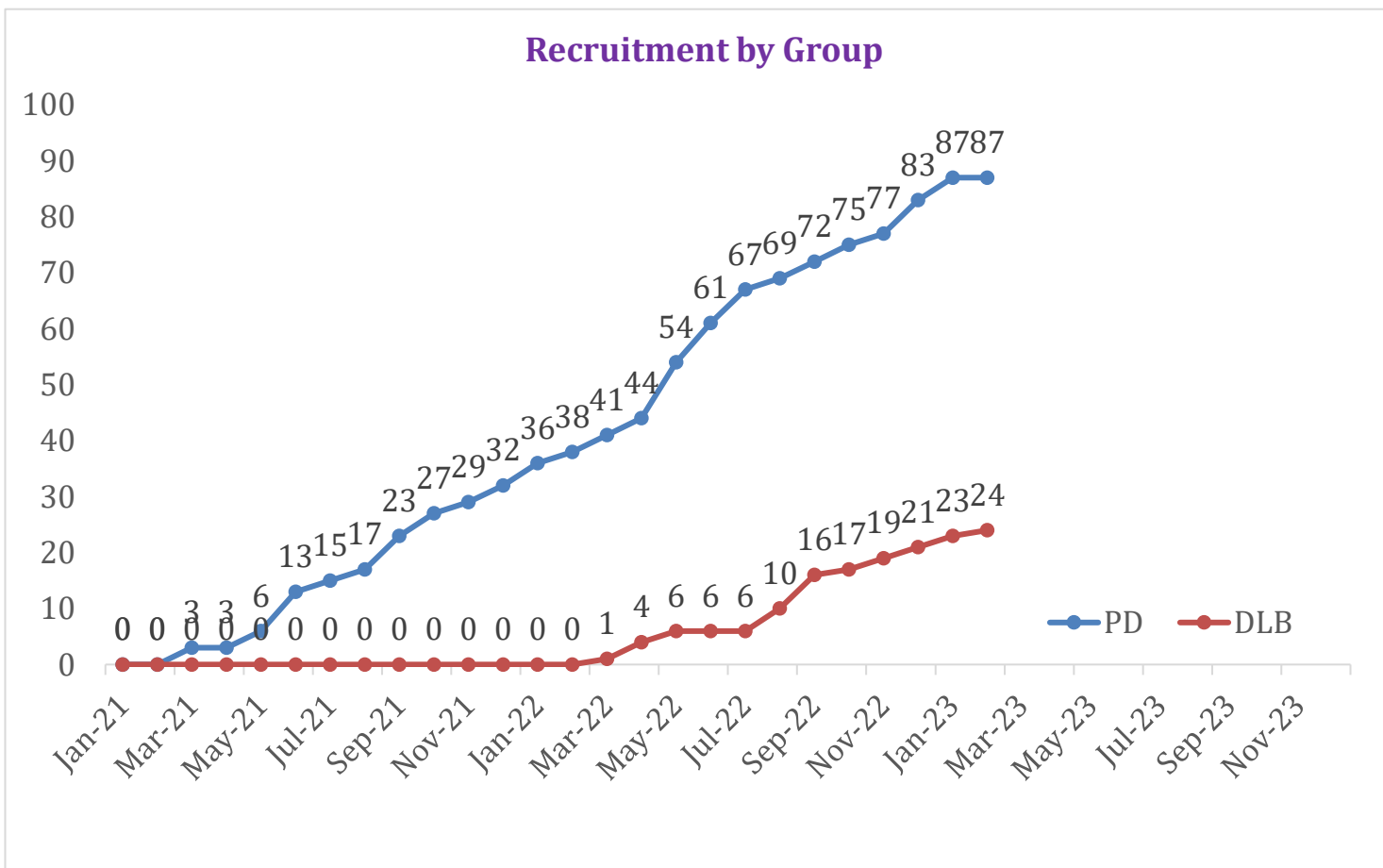


Figure 3: Number of participants with Parkinson’s (blue) and Lewy Body dementia (red) that have been recruited to the trial.

How have people with Parkinson’s and Lewy Body dementia and their families helped us?

Prior to trial set up

A focus group, recruited by Parkinson’s UK Research Support Network, comprised of people with Parkinson’s and those with experience of caring for a family member with Parkinson’s hallucinations, was involved early in the study planning process.

You may have read on our website that the group made important contributions to the study design, including the timing and location of assessments, choice of outcome measures, and the inclusion of blood sampling to inform dosage strategies for clinical use.

The group supported a flexible dosing strategy, to reduce the risk of side-effects, and suggested use of a tablet, instead of a (larger) capsule, as people with Parkinson's can have swallowing difficulties.

A second group reviewed the trial materials, patient and caregiver information sheets and leaflets before we submitted an application for ethical approval.

They also contributed to our recruitment strategy, emphasising the importance of UK-wide coverage. We now have sites in England, Scotland, Wales and Northern Ireland!

During the first wave of the pandemic

Parkinson's UK Research Support Network helped us to recruit to a third focus group in May 2020, to seek feedback on our plans to adapt the trial procedures to reduce face to face contact and minimise exposure to coronavirus.

One of the changes we made was to use a hand held device to measure your heart rate, to avoid the need for you to go to hospital for a 12 lead ECG.

The other important change was to ensure the study drug would be delivered directly to your home, to avoid the need for a visit to the hospital pharmacy.

Autumn 2022

In the past 5 months, we have held a series of focus groups, to ask people with Parkinson's, Lewy Body dementia and their families what they would consider to be a 'meaningful change' in hallucinations.

We compared their opinions to those of expert clinicians who had taken part in an anonymised survey. People were recruited by the Parkinson's UK Research Support Network, by the Rare Dementia Support Group, and via the University College London Hospital team.

Some of the group shared their experiences. We heard that being tired or having an infection can increase the frequency of hallucinations, and that the medications used to treat Parkinson's can increase the frequency or quality of the hallucinations. We also learnt that rivastigmine, a medication that is used to improve memory in people with dementia, can be helpful.

One important theme was that people with Parkinson's and Lewy Body dementia are very sensitive to medication side effects and that it can be a difficult balancing act to treat hallucinations without worsening other symptoms.

The group felt that, when considering what would be a 'meaningful' change, it is important to take into account the quality and content of the hallucinations as well as their frequency, as some hallucinations are benign and others can be deeply upsetting.

When asked to comment on several made up scenarios, feedback from focus group participants was consistent with those of the clinicians we surveyed.

We aim to publish our findings as they will help us to interpret the findings of TOP HAT.

What are our plans for 2023

Once we have 12 week follow up data on the first 100 participants with Parkinson's, the statisticians will have an initial look at the data – it is described as an interim analysis.

There will not be sufficient numbers to definitively say whether or not ondansetron is significantly superior to placebo in treating hallucinations, but will provide us with valuable information on outcomes and safety.

Until the trial is complete and all the data has been analysed by independent statisticians, we will not be able to recommend the use of ondansetron beyond the 12 week treatment period, even if you think that it may have helped you. This is because everyone in the trial (you as the participants and us as the research teams) are all blinded to the treatment allocation that you have been randomised to (active or placebo). We will not be able to break this allocation and find out what group you were in without compromising the quality

of the data. Once the trial is complete and all the data has been analysed we will be able to say, with confidence, whether or not ondansetron was successful in reducing visual hallucinations.

We will update you on progress in our next letter, which will be at the end of August.

Suzanne Reeves and Olga Zubko
(Chief Investigator and Trial Manager)

<https://www.ucl.ac.uk/psychiatry/research/mental-health-older-people/top-hat>