

## Title of Study: The effect of autonomic modulation on visceral pain hypersensitivity in patients with non erosive reflux disease (NERD).

REC reference number: **15/LO/1454**

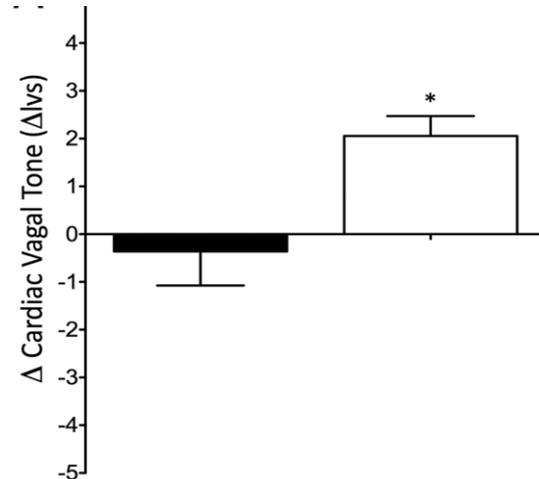
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### Introduction

Gastro oesophageal reflux disease (GORD) is defined by the Montreal definition as a condition that develops when the reflux of gastric content causes troublesome symptoms or complications(1). Patients with no evidence of oesophageal injury at gastroscopy are deemed to have a symptomatic syndrome. Patients with the symptomatic syndrome of GORD are defined as having non-erosive reflux disease (NERD). Of patients with GORD, those diagnosed with NERD make up 70%(2).

There are several pharmacological and therapeutic approaches to treat NERD, including pharmacological agents such as proton pump inhibitors (PPIs) and Histamine Receptor 2 Antagonists (H2RAs)(3). Surgical and newer endoscopic measures are another option in carefully selected patients with NERD. Despite the above, there remains a proportion of patients who gain only partial benefit from pharmacological therapies, and a smaller proportion that do not gain any benefit at all from these therapies. The prevalence of these patients is estimated at 30% in the tertiary setting(4).

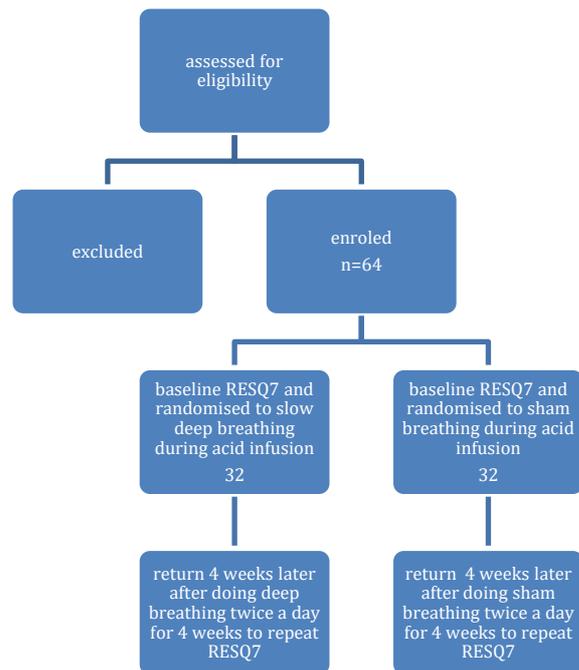
There is some evidence for efficacy of psychological interventions in patients with non-cardiac chest pain, which is most often oesophageal in origin. Slow deep breathing is often a component of these therapies(5). Our group has shown reduction in acid induced oesophageal pain hypersensitivity in healthy volunteers(6).



**Figure 1: The effect of sham/un-paced breathing (shaded black) and deep breathing (unshaded) on cardiac vagal tone (mean±SE) (parasympathetic tone) (sympathetic tone). \*Statistically significant at  $p < 0.03$ (6)**

The efficacy of slow deep breathing in patients with NERD has not been studied before and this is being investigated in our present study. We are evaluating the effect of slow deep breathing vs sham breathing on oesophageal pain hypersensitivity and symptoms. We are also evaluating lag time to perception of oesophageal discomfort after distal oesophageal acid infusion (simulation of reflux).

## Study protocol



### Objectives

*Primary objective:* To evaluate the effect of slow deep breathing and sham breathing on oesophageal pain hypersensitivity to experimental acid infusion in patients with NERD.

*Secondary objective:* A pilot follow-up study to evaluate the effect of slow deep breathing as a self-administered therapeutic measure for oesophageal symptoms in patients with NERD.

### Study endpoints

*Primary endpoint:* Difference in lag time to first sensation of discomfort following oesophageal acid perfusion after deep/sham breathing between the slow deep breathing group and the sham breathing group.

### Secondary endpoints

- Change in reflux symptoms questionnaire, anxiety and depression scores before and after 4 weeks of using slow deep breathing or sham breathing as a self-administered therapeutic measure for oesophageal pain in patients with NERD.
- Investigate the correlation of personality traits and anxiety/depression states with ANS response and pain perception (lag time) to deep breathing and sham breathing.
- Difference in APSS (acid perfusion sensitivity score) following oesophageal acid perfusion after deep/sham breathing between the slow deep breathing group and the sham breathing group.
- Confirm ANS changes before and after slow deep breathing/sham breathing.

### Current progress

At present 32/64 participants have completed the trial protocol. We have applied to ethics for permission to carry out an interim analysis in order to assess progress at present and to determine if any amendments are required as the study progresses. We anticipate we will require another 4-6 months to complete the study.

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