**Temporal relationship between night-time gastro-oesophageal reflux events and arousals from sleep: SUPPLEMENTAL DIGITAL CONTENT**

**METHODS**

**Protocol**

Participants attended the Respiratory Sleep Disorders Clinic at Sir Charles Gairdner Hospital in the morning for insertion of a 24-hour pH-impedance catheter after which they left the hospital to carry out their usual daily activities. To assist with interpretation of pH data, each participant was asked to keep a diary of all activities throughout the day, including periods of recumbency, meals, medications and any GER symptoms they experienced. They returned to the clinic in the evening and were fed a standardised meal consisting of meat/fish, mixed vegetables, bread and ice cream, following which they were set up for PSG and simultaneous pH/impedance monitoring.

### All participants were required to: cease any proton pump inhibitors (PPIs) and H2-receptor antagonists 7 days prior to the study; cease any antacids 24 hours prior to the study and remain off them for the duration of the study; and fast for a minimum of 6 hours prior to catheter insertion.

**Specific techniques**

Polysomnography

In-laboratory PSG was conducted according to the American Academy of Sleep Medicine recommendations(26) and included monitoring of EEG, left and right EOG, submental and tibial EMG, electrocardiogram (ECG), abdominal and thoracic motion; nasal and oral airflow; nasal pressure; oxygen saturation; body position and sound (Grael, Compumedics, Melbourne, Australia).

Classification of sleep stage, arousals and respiratory events were performed according to standard criteria.(27) The severity of sleep-disordered breathing was defined by the apnea-hypopnea index (AHI), which is the average number of apneas and hypopneas per hour of sleep. Arousals and awakenings from sleep were also defined using standard criteria.(26) Briefly, an arousal was an increase in EEG frequency that lasted from 3-15 seconds and an awakening was a shift in EEG frequency lasting for >15 seconds.

Esophageal pH/impedance monitoring

Prior to insertion of the pH/impedance catheter the location of the lower esophageal sphincter was identified manometrically. To do this a pressure catheter with four solid-state pressure transducers (Gaeltec, CTO-4; Dunvegan, Isle of Skye, Scotland; O.D. 2.7mm) was inserted via the nares and positioned with the sensors in the stomach. The location (depth) of the proximal border of the lower esophageal sphincter was identified using a slow pull-through technique. (28)

Esophageal pH/impedance monitoring was conducted using a pH/impedance catheter (VersaFlex pH-Z Catheters, Sierra Scientific, Los Angeles, USA), positioned with the pH sensor 5cm above the proximal border of the lower esophageal sphincter. The pH/impedance catheter was attached to a portable recording device (Digitrapper pH-Z system, Sierra Scientific, Los Angeles, USA). Recordings were analysed using the Accuview Analysis Software (Sierra Scientific, Los Angeles, USA) and automatic analyses were adjusted manually when required.

Questionnaires

The Gastroesophageal Reflux Questionnaire (GERQ) was used to define frequency of daytime and nighttime symptoms of GER.(29, 30) GER symptoms were classified as follows: heartburn or acid regurgitation experienced at least once in the last 12 months was defined as any GER and, if experienced at least once a week was defined as frequent GER. The term GER symptoms refers to symptoms experienced at any time during the day or night, while night-time GER (nGER) symptoms specifically refers to symptoms which woke the patient from sleep.(31)

Statistical Analysis

Sample size was determined based on past studies comparing those with and without OSA, a difference in ACT of 15% with a standard deviation of 10%. This requires a sample size of 7 per group to obtain significance between groups with an alpha of 0.05 and power of 0.8. Our overall sample size of 33 exceeds this and therefore compensates for any attrition which occurred.