## Abstract

## Introduction

Inflammatory bowel disease (IBD) is a group of chronic relapsing-remitting autoimmune condition(s) that involves a complex interplay of genetic and environmental factors. Sleep is likely to be impaired by symptoms of active IBD, and IBD-related pro-inflammatory cytokines may also influence sleep quality. Chronic sleep insufficiency, such as through sleep deprivation or obstructive sleep apnoea, has been linked to several adverse health outcomes including cardiovascular disease and worse all-cause mortality. Despite this, little is understood about the relationship between IBD activity and sleep quality, or the relationship between sleep quality and outcomes in IBD such as poor mental health, fatigue and quality of life (QoL).

#### Aims

The aims of this thesis were to:

1. Determine the presence and significance of the effect of IBD activity on sleep quality.

2. Determine whether there are relationships between sleep in IBD and mental health conditions and/or other patient-reported outcomes such as fatigue and QoL.

#### Methods

Systematic reviews and meta-analyses were conducted examining available data on IBD activity and sleep quality, prevalence of poor sleep in IBD and sleep quality in inactive IBD. A prospective observational study was conducted to determine the relationship between objective sleep quality—in the form of polysomnography—and objective IBD activity, assessed by endoscopy, magnetic resonance imaging or faecal calprotectin. A cross-sectional study explored the relationship between sleep, mental health conditions, fatigue and QoL in people with IBD. A structural equation modelling approach was used to understand the relationship between sleep and fatigue and other factors. A latent profile analysis was undertaken to identify latent profiles of fatigue.

### Results

The pooled prevalence of poor sleep in people with IBD was 56%. Examination of objective sleep quality via polysomnography demonstrated shorter sleep duration in objectively active IBD than remission. A further meta-analysis found that sleep quality in people with IBD in remission was worse than healthy controls. Use of opioids was associated with worse sleep

quality—as was infliximab (a TNF- $\alpha$  inhibitor)—although the relationship with infliximab was confounded by weight. In people with IBD, insomnia was associated with abdominal pain, IBD activity and depression and anxiety.

Sleep quality was associated with worse QoL with this effect independent of the influence of mental health conditions or IBD activity. The magnitude of reduction in QoL seen with insomnia was similar to that seen with active IBD. Worse IBD-related disability was seen in people with concurrent insomnia.

A structural equation model of fatigue suggests that sleep is a mediating variable for other factors, and showed that depression was a high-value target for intervention. Latent profile analysis of fatigue identified four profiles of fatigue, with one profile defined by poor mental health and little to no significant depression or anxiety seen outside of this profile.

# Conclusions

Objective sleep quality is worse in objectively active IBD than in remission. Sleep quality, typically not assessed in IBD clinics, is associated with reduced QoL and should be considered part of routine clinical care, especially in those in remission. Depression represents a high-value treatment target in fatigue and should be considered in any presentation of fatigue. Further research should consider determining the role of IBD-related pro-inflammatory cytokines in sleep quality and the longitudinal significance of objectively measured sleep quality.