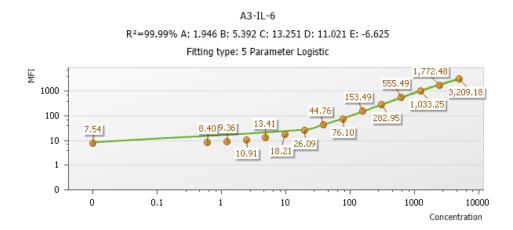
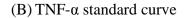
# Supplementary data

## The IL-6 and TNF-α standard sample

IL-6 and TNF- $\alpha$  standard samples ranged from 0.61 pg/mL to 5000.00 pg/mL, and their standard coefficient of determination (r<sup>2</sup>) were 0.999 and 0.998, respectively (Figure 1S).



(A) IL-6 standard curve



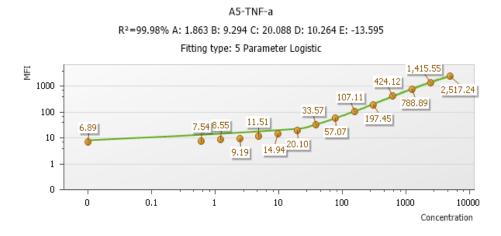
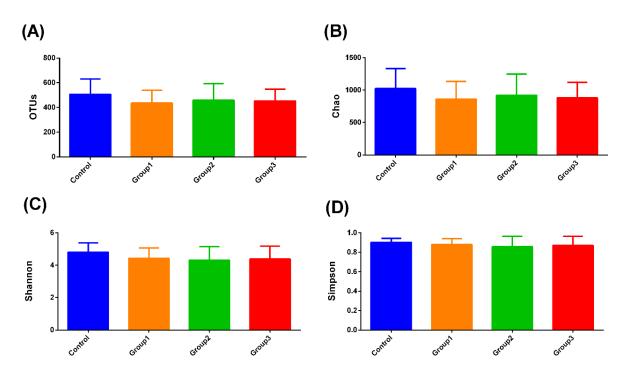


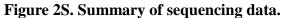
Figure 1S. IL-6 (A) and TNF-a (B) standard curves.

#### Characteristics of sequencing data

We obtained 36,700 clean reads from 20 faecal samples of the control group, 35,816 clean reads from 40 faecal samples of the Group 1, 36,550 clean reads from 23 faecal samples of the Group 2, and 35,919 clean reads from 30 faecal samples of the Group 3. We observed no statistically significant differences between clean reads among the control group and others. Good's coverage for each sample was >98%, indicating that the OTUs identified in each sample showed the majority of bacterial species identified in all samples. We found no statistically significant differences in OTUs among the control group and other groups (Figure 2SA). We examined the mean community diversity indices [Chao (Figure 2SB), Shannon (Figure 2SC) and Simpson (Figure 2SD)] after equalising library sizes to the minimum library size by random subtraction. We detected no statistically significant differences in community richness and diversity and Simpson index among the control groups.

Structurally, the gut microbiomes of the control group and other groups differed according to PCoA 1 and PCoA 2 (26.5% and 9.82%, respectively; Figure 3S).





Characteristics of sequencing data in the operational taxonomic units (OTUs) (A), the mean community diversity indices [Chao (B), Shannon (C) and Simpson (D)]. Control: patients with apnea–hypopnea index (AHI)  $\leq$  5 events/h were considered as non-OSAHS; Group 1: patients with 5 < AHI  $\leq$  15 were considered as mild OSAHS; Group 2: patients with 15 < AHI  $\leq$  30 were considered as moderate OSAHS; Group 3: patients with AHI  $\geq$  30 were considered as severe OSAHS.

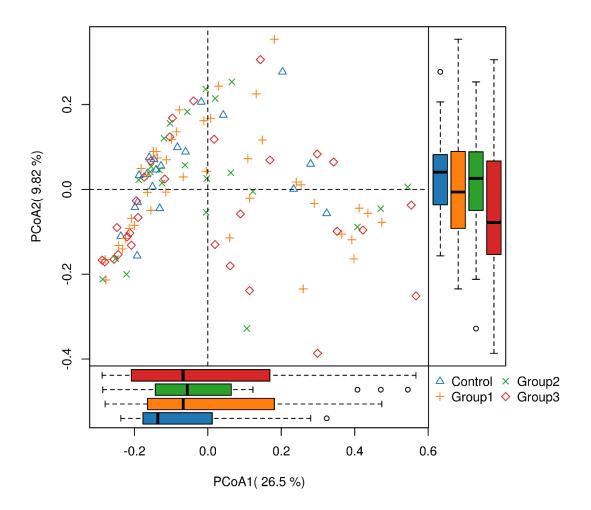


Figure 3S. The principal coordinate analysis (PCoA) based on the distance function of Bray–Curtis.

#### Alteration in the taxa among groups

The relative abundance of the class *Gammaproteobacteria* (p = 0.030) was lower in the control group than in the Group 2 (post hoc analysis p = 0.048) (Figure 4SA).

The relative abundances of the order *Spirochaetales* (p = 0.046) and *Gammaproteobacteria* (p = 0.038) were higher in the Group 2 than the Group 1 (post hoc analysis p = 0.048) and the Group 3 (post hoc analysis p = 0.039), respectively; *Betaproteobacteria* (p = 0.020) was higher in the control group than in the Group 2 (post hoc analysis p = 0.047) and the Group 3 (post hoc analysis p = 0.029), respectively (Figure 4SB).

The relative abundances of the families *Ruminococcaceae* (p = 0.032) was lower in the Group 3 than in the Group 2 (post hoc analysis p = 0.048) and the control group (post hoc analysis p = 0.047), respectively; *Acidaminococcaceae* (p = 0.033) was lower in the control group than in the Group 1 (post hoc analysis p = 0.029); *Clostridiales* (p = 0.021) was lower in the Group 1 than in the Group 3 (post hoc analysis p = 0.036); *Rikenellaceae* (p = 0.024) was higher in the control group than in the Group 3 (post hoc analysis p = 0.018); *Comamonadaceae* (p = 0.016) was lower in the Group 1 than in the Group 2 (post hoc analysis p = 0.030); *Aerococcaceae* (p =0.026) was lower in the control group than in the Group 3 (post hoc analysis p =0.047); *Spirochaetaceae* (p = 0.046) was the highest in the Group 2, than the control group (post hoc analysis p = 0.019), the Group 1 (post hoc analysis p = 0.016), and the Group 3 (post hoc analysis p = 0.014); *Burkholderiales* (p = 0.035) was lower in the control group than in the Group 3 (post hoc analysis p = 0.035); are control group than in the Group 3 (post hoc analysis p = 0.014); *Burkholderiales* (p = 0.035) was lower in *Gammaproteobacteria* (p = 0.038) was lower in the Group 3 than in the Group 2 (post hoc analysis p = 0.050); *Betaproteobacteria* (p = 0.020) was higher in the control group than in the Group 2 (post hoc analysis p = 0.046) and the Group 3 (post hoc analysis p = 0.029), respectively (Figure 4SC).

The relative abundances of the following genera significantly differed among groups: Faecalibacterium (p = 0.044), Megamonas (p = 0.046), Ruminococcaceae (p= 0.048), Clostridiales (p = 0.021), Alistipes (p = 0.024), Bifidobacterium (p = 0.037), Dialister (p = 0.007), Oscillibacter (p = 0.008), Erysipelotrichaceae (p = 0.025), Anaerotruncus (p = 0.043), Cronobacter (p = 0.006), Aquabacterium (p = 0.033), *Gammaproteobacteria* (p = 0.038), *Synergistaceae* (p = 0.032), *Betaproteobacteria* (p= 0.020), and *Micrococcus* (p = 0.007). The post hoc analysis, the relative abundances of the genera Megamonas (p = 0.047), Ruminococcaceae (p = 0.044), Alistipes (p = 0.044), (0.018), Dialister (p = 0.006), Oscillibacter (p = 0.004) and Betaproteobacteria (p = (0.020) were higher in the control group than in the Group 3; *Erysipelotrichaceae* (p = (0.022) was lower in the control group than in the Group 1; *Anaerotruncus* (p = (0.037)) was higher in the Group 2 than in the Group 3; *Faecalibacterium* (p = 0.040), Cronobacter (p = 0.041), and Micrococcus (p = 0.021) were higher in the Group2 than in the Group 3; *Clostridiales* (p = 0.036) was higher in the Group 1 than in the Group 3, whereas *Dialister* (p = 0.022) was lower in the Group 1 than the control group; *Bifidobacterium* (p = 0.046) was higher in the control group than in the Group 3; Aquabacterium (p = 0.031) was higher in Group 3 than in the Group 1; Synergistaceae (p = 0.038) was higher in the Group 2 than in the Group 1 (Figure 1C).

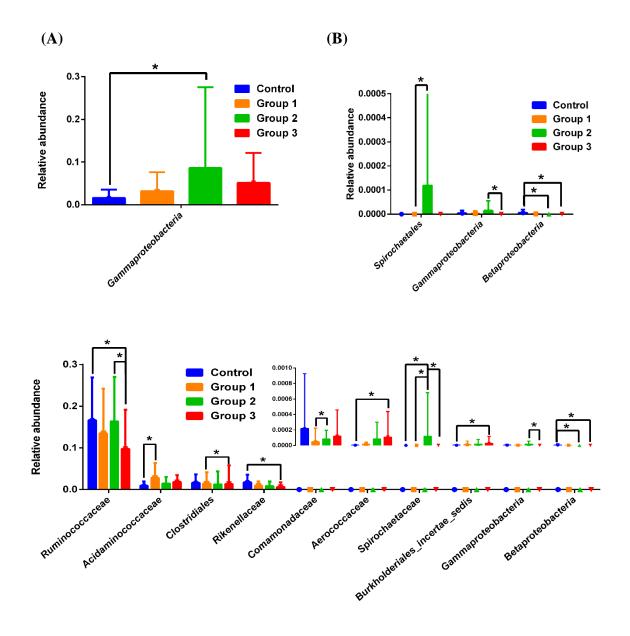


Figure 4S. There were differences in the faecal microbiome at class (A), order (B), family (C) levels.

Statistical analysis was performed by Wilcoxon tests. \* p<.05, \*\* p<.01 compared with the control group or OSAHS groups.

Control: patients with apnea–hypopnea index (AHI)  $\leq$  5 events/h were considered as non-OSAHS; Group 1: patients with 5 < AHI  $\leq$  15 were considered as mild OSAHS;

Group 2: patients with  $15 < AHI \le 30$  were considered as moderate OSAHS; Group 3: patients with  $AHI \ge 30$  were considered as severe OSAHS.

### **Enterotypes analysis**

For enterotype 1, the relative abundances of the following genera significantly differed among groups: *Lachnospiraceae* was higher in the Group 3 than the Group 2 (p = 0.041); *Phascolarctobacterium* was higher in the Group 1 than the control group (p = 0.027); *Bifidobacterium* was higher in the control group than the Group 3 (p = 0.043); *Dialister* was higher in the control group than the Group 1 (p = 0.005) or the Group 3 (p = 0.037); *Burkholderiales* was higher in the control group than the Group 1 (p = 0.023); *Oscillibacter* was higher in the control group than the Group 3 (p = 0.016); *Erysipelotrichaceae* was lower in the control group than the Group 1 (p = 0.002) or Group 3 (p = 0.020); *Acidaminococcus* was higher in the control group than the control group than the Group 1 (p = 0.005) or Group 2 (p = 0.033); *Cronobacter* was lower in the control group than the control group than the Group 1 (p = 0.025) or Group 2 (p = 0.028) (Figure 3B).

For enterotype 2, the relative abundances of the following genera significantly differed among groups: *Sutterella* (p = 0.015) and *Raoultella* (p = 0.050) were higher in the Group 1 than the Group 3; *Collinsella* (p = 0.018) and *Bacteroidetes* (p = 0.033) were higher in the Group 2 than the Group 3; *Methylobacterium* was higher in the control group than the Group 2 (p = 0.047) or the Group 3 (p = 0.048); *Prevotellaceae* was higher in the control group than the Group 1 (p = 0.047) or the Group 3 (p = 0.034). Moreover, *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* was not found in the Group 1; *Prevotellaceae* and *Methylobacterium* and *Prevotellaceae* and *Methylobacterium* and *Prevotellaceae* an

were not found in the Group 2 and *Bacteroidete*, *Raoultella*, and *Victivallis* were not found in the Group 3 (Figure 3C).

For enterotype 3, the relative abundances of the following genera significantly differed among groups: *Howardella* [p = 0.004 (Control vs. Group 1), p = 0.014 (Control vs. Group 2), p = 0.003 (Control vs. Group 3)], *Synergistes* [p = 0.004 (Control vs. Group 1), p = 0.014 (Control vs. Group 2), p = 0.003 (Control vs. Group 3)], and *Brevibacterium* [p = 0.004 (Control vs. Group 1), p = 0.014 (Control vs. Group 1), p = 0.014 (Control vs. Group 2), p = 0.003 (Control vs. Group 3)] were higher in the control group than in the OSAHS groups (Figure 3D).