**Supplemental Methods A – Post-hoc Analysis: Excluding patients using multiple laxatives**

To explore the relationship between laxative use and various objective sleep metrics (TST, SE, SOL, WASO, and AI), we constructed multivariable linear regression models. In our models, we included age, sex, BMI, and laxative use (TST, SE, SOL, WASO, and AI), as well as clinically relevant comorbidities such as prior stroke, diabetes, Parkinson’s Disease, and opioid use. All variables were assessed for multi-collinearity (defined as a variance inflation factor > 2.5) before the construction of each model[1](#_ENREF_1). All fully adjusted models controlled for the effect of total recording time due to its influence on sleep continuity variables[2](#_ENREF_2). To relax the assumption of linearity, all continuous variables were modeled as restricted cubic splines with three knots[3](#_ENREF_3). As recommended, knots were placed at the 10th, 50th, and 90th percentiles of each predictor[3](#_ENREF_3). Homoscedasticity was visually assessed using the residuals versus fitted values plot. Normality was visually assessed using a residual Q-Q plot; however, no outcome transformations were applied as such transformations can bias model estimates, and models constructed with a large sample size (i.e. where the number of observations per parameter is > 10) are generally robust to the normality assumption[4](#_ENREF_4).

Statistical significance was set to P < 0.05. All data analyses were performed in R (version 4.2.0) using the “rms” package. Model validation was performed using the “0.632 Bootstrap” method to assess the overfitting of the models.

**Supplemental Results A**

After removing patients using multiple laxative types at once, 73 patients were available for our analysis. Of these patients, 22 were using stimulant laxatives, 38 were stool softener users, 9 patients were osmotic laxative users, and 4 patients were using an unspecified laxative.

In our fully adjusted model, laxative users (all types) had 8.5% lower sleep efficiency (p<0.001), 31.1-minute greater wake after sleep onset (p<0.001), and 35.3-minute lower total sleep time (p<0.001) than non-laxative users. Stool softener users had 8.7% lower sleep efficiency (p=0.002), 36.3-minute greater wake after sleep onset (p<0.001), and 36.8-minute lower total sleep time (p=0.001) than those not using stool softeners. Stimulant and osmotic laxative use was not significantly associated with changes in sleep metrics in our fully adjusted models (Table S1).

**Table S1. Linear regression models examining the association between laxatives (and subtypes) and sleep metrics while controlling for the impact of various covariates.** In our adjusted models, covariates were age, sex, BMI, diabetes, stroke, Parkinson’s Disease, opioid use, total recording time and laxative use. **p<0.05 (bolded)**

|  |  |
| --- | --- |
|  | **Adjusted Models** |
| *Variables* | *β* | *CI (95%)* | *p-Value* |
| Laxative (All types) |  |  |  |
|  SE | -8.49 | -12.44 – -4.54 | **<0.001** |
|  SOL | 4.68 | -2.14 – 11.50 | 0.179 |
|  WASO | 31.11 | 17.14 – 45.07 | **<0.001** |
|  TST | -35.32 | -51.71 – -18.94 | **<0.001** |
|  AI | 2.09 | -1.81 – 5.98 | 0.294 |
| Stool Softeners |  |  |  |
|  SE | -8.74 | -14.16 – -3.32 | **0.002** |
|  SOL | 1.20 | -8.14 – 10.55 | 0.801 |
|  WASO | 36.34 | 17.20 – 55.48 | **<0.001** |
|  TST | -36.77 | -59.24 – -14.31 | **0.001** |
|  AI | 3.18 | -2.15 – 8.52 | 0.242 |
| Osmotic Laxatives |  |  |  |
|  SE | -9.57 | -20.37 – 1.24 | 0.083 |
|  SOL | 5.84 | -12.78 – 24.45 | 0.539 |
|  WASO | 35.19 | -3.02 – 73.41 | 0.071 |
|  TST | -40.79 | -85.62 – 4.04 | 0.075 |
|  AI | 7.24 | -3.38 – 17.87 | 0.182 |
| Stimulant Laxatives |  |  |  |
|  SE | -6.76 | -13.87 – 0.34 | 0.062 |
|  SOL | 11.42 | -0.81 – 23.65 | 0.067 |
|  WASO | 16.64 | -8.49 – 41.76 | 0.194 |
|  TST | -28.00 | -57.47 – 1.46 | 0.063 |
|  AI | -5.27 | -12.25 – 1.72 | 0.140 |

**Supplemental Methods B – Post-hoc Analysis: PLMI and Laxative Use**

To explore the relationship between laxative use and Periodic Limb Movement Index (PLMI), we constructed multivariable linear regression models. In the first minimally adjusted models, demographic variables such as age, sex, BMI, and laxative use (all types, stool softener, osmotic, or stimulant) were included in our analyses. In the second fully adjusted models, we included age, sex, BMI, and laxative use as well as clinically relevant comorbidities such as prior stroke, diabetes, Parkinson’s Disease, and opioid use. All variables were assessed for multi-collinearity (defined as a variance inflation factor > 2.5) before the construction of each model[1](#_ENREF_1). All fully adjusted models controlled for the effect of total recording time due to its influence on sleep continuity variables[2](#_ENREF_2). To relax the assumption of linearity, all continuous variables were modeled as restricted cubic splines with three knots[3](#_ENREF_3). As recommended, knots were placed at the 10th, 50th, and 90th percentiles of each predictor[3](#_ENREF_3). Homoscedasticity was visually assessed using the residuals versus fitted values plot. Normality was visually assessed using a residual Q-Q plot; however, no outcome transformations were applied as such transformations can bias model estimates, and models constructed with a large sample size (i.e. where the number of observations per parameter is > 10) are generally robust to the normality assumption[4](#_ENREF_4).

Statistical significance was set to P < 0.05. All data analyses were performed in R (version 4.2.0) using the “rms” package. Model validation was performed using the “0.632 Bootstrap” method to assess the overfitting of the models.

**Supplemental Results B**

Our adjusted models revealed PLMI was not significantly associated with laxative use of any type (Table S2).

**Table S2. Linear regression models examining the association between laxatives (and subtypes) and Periodic Limb Movement Index while controlling for the impact of various covariates.** In our adjusted model, covariates were age, sex, BMI, diabetes, stroke, Parkinson’s Disease, opioid use, total recording time and laxative use. **p<0.05 (bolded)**

|  |  |
| --- | --- |
|  | **Impact on PLMI - Adjusted Models** |
| *Laxative Type* | *β* | *CI (95%)* | *p-Value* |
| All Laxatives | 4.64 | -0.83 – 10.11 | 0.097 |
| Stool Softeners | 7.77 | 0.96 – 14.59 | **0.260** |
| Osmotic  | -2.52 | -15.41 – 10.37 | 0.701 |
| Stimulant | 2.91 | -5.16 – 10.99 | 0.480 |

Bibliography

1. Johnston R, Jones K, Manley D. Confounding and collinearity in regression analysis: a cautionary tale and an alternative procedure, illustrated by studies of British voting behaviour. Qual Quant. 2018;52:1957-1976. doi:10.1007/s11135-017-0584-6

2. Maurer LF, Espie CA, Omlin X, et al. Isolating the role of time in bed restriction in the treatment of insomnia: a randomized, controlled, dismantling trial comparing sleep restriction therapy with time in bed regularization. Sleep. 2020;43doi:10.1093/sleep/zsaa096

3. Harrell FE. Regression modeling strategies : with applications to linear models, logistic regression, and survival analysis. Springer series in statistics. Springer; 2001:xxii, 568 p.

4. Schmidt AF, Finan C. Linear regression and the normality assumption. J Clin Epidemiol. 2018;98:146-151. doi:10.1016/j.jclinepi.2017.12.006