$$PA_i \sim Q + MMRC + Smoking\ status + Country + Gender + Day\ group + FEV1 + Age + BMI + (1|patient\ ID) + (1|Day\ group{:}\ patient\ ID) + \varepsilon. \textit{(1.2)}$$

This kind of analysis was chosen to focus on differences between effects, while accounting simultaneously for different sources of variance (i.e. controlling for several confounding factors and distinguishing between weekdays and weekend days/nights) and repeated measurements.

Moreover, applying linear mixed effects models on the time-specific data, we assessed the association of sleep quality with physical activity levels during the following day taking into account repeated measurements of sleep and physical activity for each participant without disregarding between-subject variations.

To construct the models we used the lmer function of the package lme4 in R [109]. Least squares means (LS-means) and differences of LS-means of the fixed effects were calculated to present the results. Degrees of freedom and p-values for significant differences (significant if $p<0.05$) were computed using Satterthwaite's approximation [110]. Comparisons of demographic and clinical characteristics between included and excluded patients were evaluated by Mann-Whitney U-test for continuous variables and Chi-square test for categorical variables.

Analyses were carried out using MATLAB R2015a (The MathWorks, Inc., Natick, Massachusetts, United States) and R (R Core Team, 2012) software.

5.4 Results

In total 932 patients with COPD were eligible for analysis. Figure 32 shows the flow of participants through the study. Patients excluded due to irregular sleeping patterns and not enough time in bed had significantly lower FEV_1% predicted compared with included patients (46.6±19.4 vs. 50.8±20.5, $p<0.05$). No significant differences between included and excluded patients were observed for age, gender, body mass index (BMI), smoking status and MMRC. The median number of days analysed per patient was six (four weekdays + Saturday and Sunday), resulting in a total of 5646 valid assessed days, of which 3788 (67%) were weekdays. Demographic and clinical characteristics of the patients included in the study are presented in Table VIII, those of excluded patients can be found in Table IX. Comparisons of demographic and clinical characteristics between included and excluded patients were evaluated by Mann-Whitney U-test for continuous variables and Chi-square test for categorical variables.

Patients excluded from the study because of irregular sleeping patterns and too short time spent in bed during the night (column II, Table IX) had lower FEV_1 compared to included patients. Accordingly, the excluded sample had a higher percentage of patients in GOLD 3 and GOLD 4 and a lower percentage in GOLD 1 and GOLD 2. This is line with the findings of this study showing that patients with impaired sleep had worse COPD severity.

The sample excluded due to missing data (column III, Table IX) had a higher percentage of males, lower percentage of smokers, older age, higher BMI, higher percentage of patients in GOLD 1and GOLD 3, and a lower percentage of patients in GOLD 2 and GOLD 4 compared to the sample of included patients.