Sleep apnoea syndrome (SAS) is a common sleep disorder. Continuous Positive Airway Pressure (CPAP) is the cornerstone of SAS treatment. Several studies have shown that CPAP therapy can effectively reduce upper airway obstruction and improve daytime sleepiness [1-2]. But on a long term basis and despite good adherence, RES can persist in 12% to 18% of patients. Predictors of RES in correctly titrated and observant CPAP-treated patients are: i) poor sleep; ii) co-morbid sleep disorders; or iii) other co-morbid medical conditions [3-4]. Although previously hypothesized, long-term sleepiness effects associated with treatment materials (device and mask), particularly leak-parameters, have not been evaluated.

In this context, mouth-leaks are associated with arousals during the lighter stages of sleep that interfere with progression to deeper stages, compromising sleep quality and disrupting sleep architecture. In 2011, a 3 month trial of CPAP among mouth breather patients treated with nasal masks demonstrated no difference in sleep architecture as compared with nasal breathers despite lower CPAP compliance. As underlined by the 2013 American Thoracic Society statement, one of the difficulties for performing leak measurements in CPAP patients is the incorrigibility of device-measured leak parameters. Complicating matters, each manufacturer uses their own definitions and thresholds for leaks, which have not been subject to independent scientific validation using strong criteria such as compliance, quality of life, and quality of sleep [5]. The only study evaluating the link between mouth leaks and various patient-reported outcomes failed to find a significant statistical relationship between the two. Interestingly, the impact of the latter patient-reported leaks on RES was not investigated.

The primary objective of the Sleepiness-leaks (SLEEPLEAKS) study, is to assess the impact of CPAP-reported leaks (CPAP leaks) on the RES of a large population of apnoeic patients undergoing long term CPAP therapy in real life conditions. The secondary objectives are to evaluate the impact of patient self-reported leaks (patient leaks) on RES, to determine if a patient leaks threshold can predict RES and to determine if CPAP leaks are predictive of patient leaks.

SLEEPLEAKS is a non-randomized InterfaceVent study:
- Prospective real life study
- Adult cohort undergoing at least 3 months of CPAP for SAS.
- Clinical information collected:
  - Anthropometrics
  - Material (interface and CPAP)
  - QOL - EQ-5D-3L and Eworth sleepiness scale
- Self-reported leaks:
  - An 11-point visual analogue scale question: Do leaks around the mask bother you?
  - An 11 point visual analogue scale question: Do you have dry mouth?
- Machine leaks:
  - Leaks variables as reported by each manufacturer were included in the analysis (leak variables differ according to each manufacturer’s CPAP).
- Statistical analysis:
  - Normality test, median IQR, Linear and logistic regression, ROC curve, spline modelling
- Participants:
  - 1494 patients were included (72% male). Median age was 67 ±0.8 years, median body mass index was 30.8 ±27.6 kg/m², median AHI was 39.1 (0.7) h. The median duration of the CPAP treatment was 4.8 (2.2-10.2) years and the median CPAP use was 6.75 (5.5-7.5) h/day
  - 1,244 patients were treated with an oronasal interface, 54.4% with a nasal interface, 17.2% with nasal pillows, and 87.1% with non-CPAP
  - The median ESS was 5.9 (3.9). The prevalence rate of ESS score of 11 was 16.7%, and 12.1% had an apnoea/hypopnoea index (AHI) ≥15
  - measured. A logistic regression analysis revealed that a younger age (p<0.0001), a higher level of education (p<0.0001) and the absence of a previous history of hypertension (p=0.0005) were associated with lower ESS scores.
  - In contrast, the ESS was strongly and positively associated with CPAP use (p<0.0001), CPAP treatment time (p<0.0001), and the percentage of patients with a leaky device (p=0.0005).

RESULTS

- Identification of patients in the database:
  - Adult patients (21, 18 years old)
  - With at least 3 months of CPAP treatment

- Excluded patients:
  - Interface issues (n=71)
  - Questionnaires not available (n=17)
  - Did not consent (n=120)

- Patients included in the analysis:
  - N=1484

RESULTS

- The current study is the first large cohort to assess the impact of factors related to treatment itself on the RES of apnoeic patients undergoing long term CPAP therapy. The main results of this study are that in multivariable logistic regression analysis, patients leaks are a significant factor of RES, and in contrast, CPAP leaks pressure levels, PAP mode and type of interface are not. In addition, younger age, lower CPAP adherence, a lower quality of life (EQ-5D-3L, health status and anxiety/depression) and patients leaks are associated with RES.

- PAP level variations during auto-CPAP treatment have been demonstrated to potentially alter sleep continuity and quality. In our study, we were unable to find a difference between fixed-CPAP and auto-CPAP, nor demonstrate an effect of pressure levels on RES. We hypothesize that manufacturer-determined algorithm differences or improvements introduced results, as Marrone previously discussed [8].

- Our results suggest that patients leaks but not CPAP leaks are significantly associated with RES. The 2013 American Thoracic Society Statement underestimated that mouth leaks may impair CPAP effectiveness, but measurement and reporting terminology are inconsistent [7]. This statement is a reflection of the need for standardization of the use of compatible leak measures and a quantification of mouth leaks. Five years after this statement, leak characterization remains manufacturer-dependent. In our cohort, bench tests have demonstrated that certain manufacturer’s leak measures may be inaccurate [9, 10]. To date, in long term correctly CPAP treated patients, there is no scientifically recognized device-leakage threshold associated with strong criteria such as quality-of-life or observation [7, 11, 12].

- We observed the absence of relationship between CPAP leaks and patients leaks.

- Patient self-reported mouth dryness was the only significant factor associated with patients leaks at the multivariable level. Mouth dryness potentially be the consequence of mouth leaks (although we cannot overcome other confounding factors in our study such as medical prescriptions and comorbidities). Of course, mouth dryness is not sufficient for the accurate evaluation of mouth opening and new tools are required. Recently, the suitability of a mandibular movement sensor for evaluating mouth opening effects on unintentional leaks was demonstrated and may respond to this need in the future.

CONCLUSION: Before proceeding with telemedicine initiatives, it is necessary to validate the diagnostic potential of target device-generated data before they are implicated in a decision making process. Sometimes, simply requesting patient self-reported data may be more pertinent.

"Take home" message: In Apnoeic, long-term CPAP patients, patient-reported leaks (contrary to device-reported leaks) are associated with residual excessive sleepiness. Mouth dryness (contrary to device-reported leaks) is associated with patient-reported leaks.