*Nocturnal hypoxic burden as a measure of OSA severity*

The total area under the ventilation curve, compared to eupneic ventilation, can be used to quantify the total ventilation deficit caused by obstruction in the airway. However, due to the differences in airflow measurement methodologies (e.g. nasal pressure airflow, thermal airflow, respiratory belts) and lack of standardization across clinical and cohort studies, pulse oximetry may be used as a more standard and readily available surrogate of airflow ventilation. Therefore, instead of the area under ventilation curve, the area under the desaturation curve associated with the respiratory events was used to quantify sleep apnea severity. We derived a measure of sleep-related “hypoxic burden” aimed at capturing the total amount of respiratory event-related hypoxemia over the sleep period. The hypoxic burden was defined as the total area under the respiratory event-related desaturation curve. For each individually identified apnea or hypopnea (obstructive and central regardless of associated desaturation), the pre-event baseline saturation was defined as the maximum SpO2 during the 100 seconds prior to the end of the event. The area under this baseline value was calculated over a subject-specific search window (Figure 1) for each event. For a robust area calculation (particularly for the events without SpO2 recovery to the baseline value), the subject-specific search window was obtained from an averaged desaturation curve. The average desaturation curve for each participant was determined by overlaying SpO2 signals with respect to the end of events (Figure 1). The hypoxic burden was then obtained by adding these individual desaturation areas and dividing the total area by the sleep duration, with the units of hypoxic burden being (%·min)/hr. For example, a hypoxic burden of 20 (%·min)/hr is equivalent to 20 minutes of 1% desaturation per hour or 5 minutes of 4% desaturation per hour.

Figure 1: Example of hypoxic burden calculation for an individual respiratory event (Resp. Event). Panel A demonstrates the nasal cannula airflow and annotated respiratory events. Panel B shows the overlaid oxygen saturation signals (SpO2) associated with all respiratory events for one individual. These signals were synchronized at the termination of respiratory events (time zero) and averaged to calculate the search window (the time between two peaks). The search window was used to calculate the hypoxic burden for individual events. That is, the area under saturation curve within the search window (Panel C). The total hypoxic burden was defined as the sum of individual burdens divided by total sleep time.

