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Article

Keywords:

Posted Date: July 15th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1794670/v1>

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Pulse Oximetry Values from 33,080 Participants in the Apple Heart & Movement Study

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June 29, 2022

1 Abstract

Wearable devices that include pulse oximetry (SpO₂) sensing afford the opportunity to capture oxygen saturation measurements from large cohorts in unconstrained living conditions spanning all hours of the day. We report here a cross-sectional analysis of 72 million individual SpO₂ values collected from 33,080 individual participants in the Apple Heart and Movement Study, stratified by age, sex, body mass index, home altitude, and other demographic variables. Measurements were aggregated by hour of day for each individual to produce subject-specific 24-hour SpO₂ profiles, which were then grouped according to demographic variables for downstream analysis. 24-hour SpO₂ profiles exhibited similar circadian patterns for all subgroups, being approximately sinusoidal with nadir near midnight local time, zenith near noon local time, and mean 0.8% lower saturation during overnight hours.

Using SpO₂ measurements averaged for each subject into mean nocturnal and daytime SpO₂ values, we employed multivariate ordinary least squares regression to quantify population-level trends according to demographic factors including age, BMI, home altitude, and assigned (birth) sex. For the full cohort, regression coefficients obtained from models fit to daytime SpO₂ were in close quantitative agreement with the corresponding values from published reference models for awake arterial oxygen saturation measured under controlled laboratory conditions. Compared with daytime SpO₂, nocturnal SpO₂ regression models yielded higher coefficients of determination and emphasized the effects of age, BMI, and altitude in all subgroups.

Sex-specific subgroup analysis revealed significantly different regression coefficients for age and BMI for females compared with those of males (for both daytime and nocturnal SpO₂) although constant terms and altitude regression coefficients did not differ between sexes. Subgroup analysis according to self-reported race/ethnicity was accomplished using two strategies. Incorporating categorical variables encoding self-reported race/ethnicity into the full-cohort linear regression models identified small but statistically significant differences in daytime SpO₂ (largest coefficient corresponding to 0.13% lower SpO₂ for Hispanic study participants compared to White participants), but no significant differences between groups for nocturnal SpO₂. Additional subgroup analyses comparing separate regression models fit independently to subjects of each race/ethnicity were suggestive of small differences in age- and sex-related trends between groups, but indicated no significant difference in constant terms between any groups for either daytime or nocturnal SpO₂.

The diverse study population, automated background SpO₂ measurement collection spanning full 24-hour circadian cycle, and study design utilizing a single smartwatch-enabled sensor type enables the establishment of healthy population reference trends outside of clinical settings. Compared with daytime SpO₂ measurements, nocturnal SpO₂ measurements are systematically lower and emphasize the impact of both demographic factors and altitude. Additionally, the large subject pool in this study supports the detection of small but significant differences in age-dependent decline in SpO₂ between sexes under naturalistic conditions.

2 Introduction

Arterial blood oxygen saturation (SaO_2) is the fraction of hemoglobin containing bound oxygen relative to the total functional hemoglobin, and represents a key parameter indicative of cardiopulmonary function. Direct SaO_2 measurement necessitates an invasive arterial blood draw and blood gas analysis. Pulse oximetry enables non-invasive measurement of blood oxygen saturation (SpO_2) and provides a convenient estimate of SaO_2 that does not require arterial blood removal. The SpO_2 measurement relies upon quantifying changes in optical attenuation at two separate wavelengths (typically one red and one infrared), with signal content arising from pulsatile arterial blood modulation in response to individual heartbeats. Depending on design, pulse oximeters may operate in either transmissive mode, with the interrogating light propagating across a thin section of capillary rich tissue (commonly fingertip, earlobe, or toe), or in reflectance mode wherein the interrogating light scatters back in the direction of the optical illuminator. Reflectance SpO_2 is employed by consumer smart watch devices such as the Apple Watch (selected models) as well as selected products from Fitbit, Garmin, Samsung, Withings, and other manufacturers.

Oxygen saturation determined from SaO_2 or SpO_2 is often considered a "fifth vital sign" due to its relative ease of capture and high clinical utility [1, 2]. As a physiological metric, arterial oxygen saturation directly impacts systemic oxygen delivery in conjunction with cardiac output and hemoglobin concentration. Among healthy awake individuals, typical SpO_2 values lie in the range of 95-99%. Low blood oxygen saturation can arise from impaired lung function (e.g. reduced diffusion capacity), ventilation-perfusion mismatch, cardiac shunt, low cardiac output, or low oxygen concentration in the inspired air (e.g. due to altitude). No single universal SpO_2 threshold is applied in all medical use cases, but values less than 92% from individuals breathing room air at sea level generally prompt further investigation, with values remaining persistently below 90% indicating hypoxemia. Oxygen saturation is utilized to guide management of cardiopulmonary conditions such as chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), and obstructive sleep apnea (OSA).

Cross-sectional studies involving single-setting SpO_2 or SaO_2 measurements from nominally healthy individuals at constant altitude have consistently reported negative correlation of blood oxygen saturation with both age and body mass [3, 4, 5, 6, 7]. Studies incorporating multiple altitudes or a range of barometric pressure consistently report a positive linear relationship between awake arterial oxygen saturation and barometric pressure, in agreement with expectations based on the alveolar gas equation. [3, 8, 9]. Less consistently, some studies have also reported positive correlation between SpO_2 and female sex [5, 10, 11], although others have reported negative or insignificant SpO_2 findings with respect to sex [12]. A similar mix of conclusions has been published with respect to tobacco smoking status, with some studies reporting lower SpO_2 values for current smokers [6] and others reporting no significant relationship [5].

In the context of clinical screening and risk estimation for chronic cardiopulmonary disease, single-point SpO_2 measurements below 95% saturation have been reported as predictive of a variety of cardiopulmonary conditions and outcomes [13, 14, 15, 16, 17, 18]. The Tromsø Study examined single-event SpO_2 values and 10-year outcomes for cardiopulmonary disease, reporting significant elevated risk for values $\leq 92\%$ and 93-95% saturation, compared with 96-100% saturation [14]. Daytime SpO_2 has been reported as a significant independent predictor of hypertension [13], as well as circulatory impairment in the form of impaired left ventricular filling [15]. Mean overnight SpO_2 has also been reported as predictive of both absolute waking blood pressure and magnitude of morning blood pressure surge [16]. Studies examining overnight SpO_2 in the context of atherosclerotic cardiovascular risk have produced inconsistent findings, with some reporting significant relationships between mean overnight SpO_2 and presence of carotid artery plaque [17], and others reporting no significant relationship after adjusting for demographic variables and other known risk factors [18].

In this study we analyzed systematic variation in mean daytime and nocturnal SpO₂ captured by wearable devices, stratified by age, gender, body mass index (BMI), home altitude, and other self-identified demographic factors including race and ethnicity. We employed linear regression models to quantify these trends and enable comparison with existing published reference equations developed from smaller studies utilizing arterial blood gas analysis [3, 19] and pulse oximetry [20].

3 Methods

This study examined data from the Apple Heart and Movement Study, an ongoing research study beginning November 19, 2021 conducted in partnership with American Heart Association and Brigham and Women’s Hospital that was designed to explore the links between physical activity and cardiovascular health. Study participants were all Apple Watch users at least 18 years old residing in the United States, and provided informed consent electronically in the Apple Research app. The study was approved by the Advarra Central Institutional Review Board, and registered to ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT04198194) [21]. All data collection, both raw measurements and metadata, was accomplished using the using the Apple Research app.

Subjects were selected for inclusion in downstream analysis based on use of a Series 6 Apple Watch and contribution of sufficient SpO₂ measurements during the study period as described in the flowchart in Figure 1. Subject demographic distributions including age, body mass index, estimated home altitude, and self-reported race and ethnicity are summarized in Figure 2. Geographic information was based on zip (postal) code, with 3-5 zip code digits available depending on total participant count in that location (for privacy purposes, zip codes containing few subjects were reported with the trailing two digits redacted). Approximate home altitude was determined by associating the zip code information with USGS mean surface elevation in the corresponding geographic area. Due to comparatively small numbers of individuals self-reporting ethnicity of ‘American Indian or Alaskan Native’, ‘Middle Eastern or North African’, ‘Native Hawaiian or other Pacific Islander’, and ‘None of these fully describes me’, these subjects were combined into a single race/ethnicity group (‘Other’) when used for downstream subgroup analysis. Body mass index was determined from height and weight, and mean barometric pressure was calculated from home altitude using the reference NOAA Pressure Altitude equation [24]. Tabulated summary statistics and statistical comparisons are shown in Table 1.

All individual SpO₂ measurements from Series 6 Watches collected between January 1 2021 and September 15 2021 were aggregated from active study participants, along with self-reported demographic information. Blood oxygen saturation values were measured using the Apple-developed SpO₂ sensor available on some Apple Watch models (only data from Apple Watch Series 6 devices is utilized in the present study). SpO₂ values were acquired both on-demand (initiated by the watch wearer), as well as passively via background measurements attempted automatically under low-motion conditions at roughly 30-minute cadence. The Apple Watch SpO₂ measurement has been reported to have accurate agreement with reference clinical fingertip pulse oximetry on both individuals with cardiopulmonary disease as well as healthy controls [22, 23]. Histograms of all individual SpO₂ values (ranging from 60-100% saturation with integer values) collected from the full study cohort are shown in Figure 3.

Individual SpO₂ values were labeled with timestamps corresponding to wall clock time in the subject’s local time zone. All downstream analysis utilized data from subjects contributing at least 30 individual SpO₂ measurements during typical mid-sleep hours (local wall clock time 01:00-04:59) as well as at least 30 individual SpO₂ measurements during typical awake daytime hours (local wall clock time 11:00-18:59). For subjects satisfying these selection criteria (Figure 1) all SpO₂ measurements collected during the study period were retained, with no outlier rejection, thresholding, filtering, or other removal of individual SpO₂ values. This data aggregation yielded 33,080 unique subjects contributing over 72.2 million individual SpO₂ values

(median 1,772 values/subject) spanning all hours of the day. A complete dataset for each subject consisted of mean daytime and nocturnal SpO₂, approximate home altitude inferred from zip code information, and self-reported age, assigned sex, height, weight, and race/ethnicity.

Individual SpO₂ values from each subject were grouped and averaged by hour of the day, yielding a single 24-hour mean SpO₂ profile per subject, irrespective of the subject’s total number of collected SpO₂ measurements or their hourly distribution throughout the day. Subject 24-hour profiles were then averaged over either the full cohort or various subgroups (for example subjects grouped by decade of age or BMI category). The 24-hour SpO₂ profile mean and standard deviation for the general cohort is shown in Figure 4, and 24-hour SpO₂ profile means and 99.5% confidence interval profiles for subgroups stratified by age, BMI, home altitude, and sex are shown in Figure 5. This method for aggregating hourly SpO₂ values for the full cohort and subgroups minimizes bias due to the number of individual measurements per subject, and has been reported in prior literature for circadian analysis of blood pressure profiles stratified by various demographic variables [25].

Per-subject mean daytime oxygen saturation (dSpO₂) and mean nocturnal oxygen saturation (nSpO₂) were calculated for each individual by averaging all SpO₂ values occurring between 11:00-18:59 local clock time, and 01:00-04:59 local clock time, respectively. Mean day-night oxygen saturation difference (dnΔSpO₂) for each individual was determined from the difference between these two metrics (dSpO₂ - nSpO₂), with positive values of dnΔSpO₂ corresponding to lower average blood oxygen saturation overnight than during the daytime. Full-cohort distributions of dSpO₂, nSpO₂ and dnΔSpO₂ are shown in Figure 6.

3.1 Statistical Analysis

Plotting and data visualization were performed using the Python packages Seaborn [29] (version 0.11.0) and Matplotlib [30] (version 3.2.2). Ordinary least squares linear regression modeling (OLS) was performed using the Python statsmodels module [26] (version 0.11.1) to quantify systematic factors impacting measured blood oxygen saturation at the population level. Dependent variables consisted of dSpO₂ and nSpO₂ separately. Various sets of independent variables were used for fitting linear regression models, with all reported models summarized in Table 2.

For direct comparison with the arterial oxygen saturation reference equation reported by R. Crapo, *et al.* [3], dSpO₂ and nSpO₂ were modeled using a combination of age, height, weight, assigned sex and inferred barometric pressure (estimated from home altitude). This reference model employing height and weight separately in place of BMI, and barometric pressure in place of home altitude, is referred to as M_{Ref} in subsequent discussion. For subjects residing at low altitude (below the dataset median of 155m) we fit a simple univariate model (M_{Age}) for dSpO₂ using only age as the independent variable, for comparison against the univariate regression model reported by R. Crapo, *et al.*, for low-altitude measurements [3].

For additional full-cohort analysis we fit dSpO₂ and nSpO₂ using model M_1 , which employed linear terms for the following independent variables: age, BMI, estimated home altitude, assigned sex (categorically encoded using 1 corresponding to male sex and 0 corresponding to female sex), and self-reported race/ethnicity group (categorically encoded using dummy variables, with ‘White’ race/ethnicity used as the reference category based on greatest subject count in this subgroup). Quadratic terms were evaluated but did not produce models with meaningfully different goodness-of-fit metrics compared to models using only linear terms, and so were not utilized for further analysis. For model M_1 , age and BMI variables were adjusted by subtracting 40y and 25.0 BMI points from each data point. This adjustment has no quantitative impact on the measured regression coefficients, but improves interpretability of the model’s constant terms (constants may be interpreted as the population-mean SpO₂ for a 40-year-old White female with BMI 25.0 residing at sea level).

In order to evaluate the presence of systematic factors impacting measured SpO₂ as a function of subject sex, race or ethnicity, we performed the following subgroup analysis using dSpO₂ and nSpO₂ as dependent variables:

- Model coefficients and confidence intervals corresponding to sex and race/ethnicity variables were examined, for the M₁ model fit to the full subject cohort.
- Linear regression models were fit separately for male and female participants using model M_{1,sex} and the resulting coefficients and confidence intervals were compared between groups.
- Linear regression models were fit separately for participants in each race/ethnicity group using model M_{1,race-ethn.} and the resulting coefficients and confidence intervals compared between groups.

In accordance with recent recommendations regarding use of p-values in statistical analysis [27], we have used a threshold of p<.005 (rather than p<.05) to determine statistical significance. Correspondingly, we report uncertainty for fitted model coefficients using 99.5% confidence intervals, and all plotted error bars correspond to 99.5% confidence interval (the or equivalent of 2.81*SEM in Figure 5). All p-values were calculated using the SciPy stats package [28] (version 1.5.0). P-values reported for linear regression coefficients correspond to two-sided t-tests under the null hypothesis that the coefficient is equal to zero. In subgroup analysis, p-values reported for comparing coefficients between separate linear regression models fit to independent data subsets (for example data from females vs. males) were determined using Welch’s unequal variances t-test, under the null hypothesis that the two coefficients are equal. For race/ethnicity subgroup analysis, when comparing coefficients between subgroups we utilized a Bonferroni-corrected p-value threshold of <.0005 to account for multiple pairwise comparisons.

4 Results

Figure 5 shows 24-hour SpO₂ profiles (mean ± 99.5% confidence interval) stratified by decade of age, BMI group, gender, and location-inferred home altitude. All subgroups exhibited systematic 24-hour variation in SpO₂ with lowest mean values occurring during nocturnal hours (nadir approximately 01:00 local time), and highest mean values occurring during mid-day hours (zenith approximately 11:00, with a broad elevated plateau spanning 10:00-18:00). The general cohort (Fig. 4) exhibited a mean diurnal range of approximately 1% saturation. Subgroups having lower mean daytime SpO₂ tended to yield a larger mean 24-hour range of SpO₂ and disproportionately lower nocturnal SpO₂, examples of which can be observed for older subgroups (Fig. 5a) and for subjects residing at >1000m altitude (5c).

Histograms of dSpO₂ and nSpO₂ are shown in Figure 6. In the full cohort, mean dSpO₂ was 96.17 [SD 1.28]%; mean nSpO₂ was 95.38 [SD 1.47]%; and mean dnΔSpO₂ was 0.78 [SD 0.98]%. Both dSpO₂ and nSpO₂ were significantly correlated with age, BMI, and altitude, and exhibited a monotonic decreasing trend with each of these variables. Figure 7 shows 2D histograms for these metrics overlaid with the corresponding univariate linear regression line, slope and Pearson correlation coefficient. In all cases, both the absolute slope and the correlation coefficients were greater for nSpO₂ than for dSpO₂. For daytime SpO₂, measured slopes with respect to each of these variables were in good quantitative agreement with existing publications [3, 8, 9]. Table 3 compares the slopes and intercepts for simple univariate regression of daytime SpO₂ using only age as the independent variable (for subjects with home altitude below the study median of 155m) with the equivalent low-altitude univariate model reported by R. Crapo, *et al.* [3].

Linear regression results for model M_{Ref} fit to both daytime and nocturnal SpO₂ using the full subject cohort are summarized and compared with the reference results reported by R. Crapo, *et al.* in Table 4. For daytime SpO₂ the fitted constant term (89.25%, 99.5% CI 88.68–89.83) differs by less than 0.2% saturation compared with the constant term from the reference SaO₂ model. The value of this constant term is not physiologically interpretable as it corresponds to the predicted oxygen saturation at zero age, weight, and

barometric pressure, but instead provides an indication of absolute calibration agreement between the SaO₂ and SpO₂ sensors used by the two studies. For daytime SpO₂ the model coefficients for age, weight, and barometric pressure all have 5-20% smaller absolute magnitude compared with the corresponding reference model coefficients. In contrast, for nocturnal SpO₂ the fitted model coefficients have 5-20% greater magnitude compared with reference model coefficients. Additionally, on our data set the nocturnal SpO₂ model fit yields a statistically significant term for sex (0.16% higher nSpO₂ for males, 99.5% CI 0.11–0.22, $p = 2.7 \times 10^{-16}$), and both daytime and nocturnal SpO₂ model fits yield statistically significant coefficients for height, in contrast to the published reference SaO₂ model which did not report significant fit coefficients for sex or height.

Linear regression results for model M₁ fit to the full subject cohort for dSpO₂ and nSpO₂ are listed in Table 5. For both dSpO₂ and nSpO₂, all M₁ regression coefficients for age, BMI, and home altitude are highly significant. For nocturnal SpO₂, no coefficients corresponding to categorical variables were identified as significant. However, M₁ fit using daytime SpO₂ produced significant coefficient for sex (0.05% higher SpO₂ for females, 99.5% CI 0.01–.09, $p = 4.1 \times 10^{-4}$), Asian race/ethnicity compared with White race/ethnicity (0.10% higher SpO₂ for White participants, 99.5% CI 0.03–0.17, $p = 1.2 \times 10^{-4}$), and for Hispanic race/ethnicity compared with White race/ethnicity (0.13% higher SpO₂ for White participants, 99.5% CI 0.07–0.19, $p = 4.8 \times 10^{-10}$).

For the purposes of sex-specific subgroup analysis, we compared M_{1,sex} models fit for male and female subjects separately with M₁ models fit for full cohort. The fitted model coefficients and confidence intervals are plotted in Figure 8 to facilitate visual comparison, with the results also tabulated in Supplementary Table S.1. For both sexes as well as the full subject cohort, coefficients of determination (R^2) were higher for models fit to nSpO₂ compared with dSpO₂. Additionally the fitted model coefficients for age, BMI, and altitude variables all exhibited significantly larger absolute magnitudes for nSpO₂ compared to dSpO₂ (implying a greater impact on SpO₂ from each these variables at night). This phenomenon of greater impact on SpO₂ from each of these variables overnight is also observable in the grouped 24-hour mean profiles shown in figures 5a-5c, in which the separation between subgroup 24-hour profiles is consistently larger during nocturnal hours.

Comparing female- and male-specific models shows no meaningful differences for constant terms and altitude coefficients between sexes, in either dSpO₂ models (Fig. 8a, 8d) or nSpO₂ models (Fig. 8e, 8h). However, the coefficients for age differ significantly between the sex-specific models for both dSpO₂ ($p = 1.4 \times 10^{-24}$, Fig. 8b) and nSpO₂ ($p = 4.5 \times 10^{-18}$, Fig. 8f), with females producing a larger magnitude for age coefficients (implying greater decline in SpO₂ with age) for both measurement periods. Additionally, BMI coefficients also differ significantly between sex-specific models for both dSpO₂ ($p = 1.1 \times 10^{-3}$, Fig. 8c) and nSpO₂ ($p = 1.9 \times 10^{-10}$, Fig. 8g), with males producing a larger coefficient magnitude (implying greater decline in SpO₂ with increasing BMI).

For additional subgroup analysis we fit model M_{1,race-ethn.} separately for subjects in each of the five race/ethnicity groups reported in the study demographics (Table 1). All race/ethnicity subgroup regression results are plotted in Figure 9 to facilitate visual comparison, with results tabulated in Supplementary Table S.2. Comparing regression coefficients between subgroup models using Welch’s unequal variances t-test, and employing the Bonferroni-corrected p-value threshold of .0005 to determine statistical significance, identified the following significant pairwise coefficient differences (p-values for significance tests are shown; individual coefficient values and confidence intervals are listed in Supplementary Table S.2):

- Age coefficients (daytime SpO₂): Significant group differences for Asian participants compared with Other participants ($p = 4.7 \times 10^{-6}$), and for Asian compared with White participants ($p = 3.7 \times 10^{-6}$).

- Age coefficients (nocturnal SpO₂): Significant group differences for Asian compared with Hispanic participants ($p = 7.6 \times 10^{-6}$), for Asian compared with Other participants ($p = 2.7 \times 10^{-7}$), and for Asian compared with White participants ($p = 9.2 \times 10^{-8}$).
- Altitude coefficients (nocturnal SpO₂): Significant group differences for Hispanic compared with Other participants ($p = 1.6 \times 10^{-4}$), and for Hispanic compared with White participants ($p = 2.4 \times 10^{-4}$).
- Sex coefficients (daytime SpO₂): Significant group differences for Asian compared with Black participants ($p = 2.8 \times 10^{-5}$), and for Black compared with White participants ($p = 3.0 \times 10^{-7}$).
- Sex coefficients (nocturnal SpO₂): Significant group differences for Asian compared with Black participants ($p = 3.8 \times 10^{-4}$).

All other pairwise group comparisons, including all comparisons for constant terms and BMI coefficients, were not determined to be significant.

5 Discussion

5.1 Diurnal Variation of SpO₂

All subgroups in our data set exhibited diurnal variation with similar circadian profiles, consisting of nadir during typical overnight sleep hours and zenith in mid-day (Fig. 4 and 5). Few prior studies have examined systematic 24-hour circadian variation in oxygen saturation for healthy adult individuals under naturalistic conditions. Existing studies examining overnight SpO₂ compared with daytime awake SpO₂ have typically focused on cohorts presenting with a chronic cardiopulmonary disease such as COPD or sleep apnea. However, findings reported in existing publications regarding circadian and diurnal variation in blood oxygen saturation are in general agreement with both the scale and phase of SpO₂ variation observed in our data set. A study of 77 healthy pediatric subjects from whom SpO₂ values were collected at 2-hour cadence for 24 hours reported systematic sinusoidal variation having an average amplitude of 2% saturation, with lowest values during mid-sleep and highest values in early afternoon hours [31]. Similarly, a study of diurnal variation in arterial oxygen saturation among 22 healthy young adult individuals (mean age 20y) living at 2600m altitude found that lowest values consistently occurred between hours 01:00 and 03:00 [32]. Circadian variation independent of sleep status has also been reported for pulmonary function metrics measured from healthy subjects under controlled conditions, with lowest measured pulmonary function occurring typical sleep hours even while subjects remained awake [33, 34]. Combined with prior studies of both healthy individuals and individuals with chronic pulmonary disease which reported no significant differences arterial oxygen pressures for sitting vs. standing and supine positions [35], this suggests that the lower mean SpO₂ observed during nocturnal hours is driven primarily by endogenous variation in cardiopulmonary parameters in concert with sleep/wake cycle, rather than by typical recumbent body positions during sleep.

For linear regression models fit to the full subject cohort and for every subgroup (Table 5 and Supplementary Tables S.1 and S.2) we have measured consistently stronger effects from age, BMI, and altitude (as well as higher coefficients of determination) for nocturnal SpO₂ values compared with daytime SpO₂ values. These phenomena are not specific to the two time windows we have chosen to define daytime and nocturnal measurement periods, but occur consistently for clock hours typically associated with sleep vs. waking and transitional periods (illustrated in Supplementary Figure S.1). The larger effect size at night for these systematic drivers of SpO₂, combined with the superior model fits for nocturnal SpO₂, suggests that sleeping conditions provide the best opportunity to resolve meaningful physiological differences as well as avoid potential confounds due to daytime behavior.

Additionally, as can be observed in 24-hour mean SpO₂ profiles for various cohorts (Fig. 5), subgroups with lower daytime SpO₂ also tend to exhibit a greater decline in SpO₂ during overnight hours. The three independent variables that most strongly influence daytime and nocturnal SpO₂ (age, BMI, and altitude) are also significant predictors of the change in SpO₂ from day to night (dnΔSpO₂). The correlation between dnΔSpO₂ and these three independent variables is illustrated in Supplementary Figure S.2. Identifying and quantifying additional unexplained factors driving systematic nocturnal changes in SpO₂ (specifically instances with overnight decline) merits further investigation.

5.2 Age-Related Effects on SpO₂

The age-dependent average decline in oxygen saturation measured for the full subject cohort (-0.031 %/year for dSpO₂) is in close quantitative agreement with trends published previously by other researchers (-0.036 %/year reported by R. Crapo *et al.* [3], -0.027 %/year reported by R. Perez-Padilla, *et al.* [20], -0.020 %/year reported by E. Klæstrup, *et al.* [19]). Progressive decline in pulmonary function with age has been described extensively in research literature, with quantitative trends reported for spirometry metrics, respiratory muscle function, gas exchange metrics, and physical lung tissue properties such as elastic recoil and alveolar size [36]. Age-related lung tissue changes include progressive remodeling of the collagen fibers that surround and support the alveoli, contributing to increased average alveolar size and loss of elastic recoil. Combined, this results in a tendency for smaller airways of older lungs to close during breathing even under resting conditions [37]. The closure of these airways translates into mismatch between alveolar ventilation and pulmonary capillary perfusion (V/Q mismatch) which hampers the diffusion of inhaled oxygen into the arterial blood stream [38]. Additionally, alveolar enlargement reduces total alveolar surface area, which further impairs gas exchange and contributes to increasing alveolar-arterial O₂ gradient [36]. Collectively these age-related changes cause a progressive decline in arterial oxygen saturation that is approximately linear with age, even in the absence of overt lung disease [39, 3, 19].

5.3 Obesity and Body Mass Effects on SpO₂

Our findings regarding the continuous linear relationship between increasing body weight and decreasing arterial oxygen saturation (measurable even between non-obese BMI categories) is in close quantitative agreement with prior published work. The linear regression model for daytime SpO₂ fit to the full subject cohort in our data set (Table 5) yields a slope of -0.046 %/BMI-point for dSpO₂, compared with -0.036 %/BMI-point reported by Perez-Padilla *et al.* [20].

Bodyweight-associated changes in pulmonary function and arterial oxygen saturation have been studied most commonly in the context of severe obesity (BMI>40) [40, 41, 42, 43], although some published research has reported significant trends in spirometry metrics as a function of BMI even for normal and overweight (non-obese) categories [44, 45, 46, 47]. Researchers have consistently reported a negative correlation between arterial oxygen saturation and BMI or weight, even in the absence of obstruction or pulmonary co-morbidities. The hypothesized mechanisms of interaction between body composition and pulmonary function include both direct mechanical effects such as lung unit closure and atelectasis (reducing functional lung capacity, and increasing V/Q mismatch), as well as adiposity-mediated pulmonary tissue inflammation [48, 49]. Further, these obesity-related effects on pulmonary function and oxygen saturation are expected to have a greater impact during nocturnal sleep hours compared with awake daytime hours [50], which may explain the slightly larger effect size for BMI we have measured for nSpO₂ vs. dSpO₂ in the full cohort and all subgroups (-0.046 %/BMI-point for dSpO₂ vs. -0.056 %/BMI-point for nSpO₂ fit using the full subject cohort).

5.4 Sex-Dependent Effects on SpO₂

The sex-specific regression models (summarized in Figure 8) and Supplementary Table S.1) support two conclusions regarding systematic differences in SpO₂ trends between sexes. First, SpO₂ tends to decline more rapidly with increasing BMI for males than females. Additionally, SpO₂ tends to decline more rapidly with

increasing age for females than males. Although some existing blood oxygen saturation studies have reported small but significant relationships between measured SpO₂ and female sex (exclusively as additive sex-specific offsets [5, 10, 11]), to our knowledge no prior published work has quantified differing sex-dependent trends for age and BMI.

The sex-specific difference in SpO₂ trend vs. BMI (Fig. 8c) may be attributable to systematic variation in body fat distribution between males and females. Males tend to have disproportionately higher abdominal and visceral adipose tissue than females, even accounting for BMI and total body fat percentage [51]. In light of the reported inverse relationships between abdominal body fat and pulmonary function [42, 40], the disproportionate accumulation of abdominal and visceral body fat among males may explain the greater decrease in SpO₂ with each incremental increase in BMI.

The significant sex-dependent trends for SpO₂ vs. age observed in our data (Fig. 8b and 8f) have not been reported previously among healthy cohorts. However, some pathological lung conditions such as asthma, COPD and pulmonary hypertension display prevalence trends that vary with sex, potentially mediated through the influence of sex hormones on lung function [52]. The transition from regular menstrual status to post-menopause is associated with acceleration of age-related decline in lung function, as quantified by lung capacity metrics such as forced vital capacity. [53]. Additionally, sex-dependent differences in age-related trends have been reported for some cardiovascular metrics including blood pressure [54, 25].

In conjunction with the significant difference in age-related SpO₂ trends between males and females, it is also important to note that the constant terms do not differ statistically between the sexes. Controlling for altitude and BMI, sex-specific differences are small or negligible for young individuals, although with advancing age mean SpO₂ declines faster for females than males. This effect can be observed visually in Figure 5d, which overlays male and female mean 24-hour SpO₂ profiles for moderate-BMI, low-altitude subgroups of two different age groups (20-30 years and 60-70 years). In the younger age group males and females present nearly equal mean SpO₂ across all hours of the day, however for older ages the SpO₂ profiles diverge and females exhibit lower SpO₂ across all hours.

5.5 Altitude Effects on SpO₂

The decline in SpO₂ with increasing altitude is well-established, and occurs as a direct result of the reduced oxygen partial pressure in the ambient environment. Because of the nonlinear (though monotonic) relationship between altitude and mean atmospheric pressure [24], and the sigmoid shape of the oxygen-hemoglobin dissociation curve [55], the theoretical trend for arterial oxygen saturation with altitude is not expected to be perfectly linear. However, significant deviation from a consistent linear trend only occurs at high altitudes (>2500m) [56], and therefore for altitude range evaluated in our data set a linear approximation is adequate.

5.6 Skin Tone and Race/Ethnicity Effects on Measured SpO₂

Given the optical basis for the function of pulse oximeter devices, which employ both infrared and visible wavelengths of light, many researchers and clinicians have raised valid concerns regarding the accuracy of pulse oximetry measurements across the full spectrum of human skin tone. Three recent studies utilizing large hospital-gathered data sets consisting of opportunistic paired SpO₂ and arterial blood gas measurements have reported significant differences in SpO₂ measurement accuracy depending on patient race and ethnicity at low oxygen saturation values. [57, 58, 59, 60]. These inaccuracies among in-hospital SpO₂ measurements disproportionately impact patients of non-White race/ethnicity [58], particularly Black individuals [57, 59, 60].

On the data set reported here, subgroup analysis according to self-reported race/ethnicity (Figure 9 and Supplementary Table S.2) does not indicate the presence of any significant or meaningful systematic bias in SpO₂ measurements between race/ethnicity groups. For both dSpO₂ and nSpO₂, regression models fit to subjects of each race/ethnicity group yield constant terms with no significant differences between groups (figures 9a and 9e). Additionally, for regression models incorporating categorical variables encoding each race/ethnicity group fit to female subjects, male subjects, and the full subject cohort (rightmost four columns of Table 5 and Supplementary Table S.1), race/ethnicity coefficients correspond to differences smaller than $\pm 0.15\%$ saturation between White and non-White subgroups in our dataset. Combined, this suggests the absence of a clinically meaningful SpO₂ measurement bias with skin tone over the range of saturation values collected in this study. However, because this data set consists of nominally healthy individuals outside of clinical settings, the range of measured SpO₂ values is heavily weighted toward non-hypoxic conditions. Just 2.5% of all collected SpO₂ values fall below 90% saturation, and 0.29% fall below 85% saturation (Fig. 3). Therefore using this data set we are not able to confirm or refute the systematic race/ethnicity differences reported from clinical SpO₂ data sets that include hypoxic values [57, 58, 59].

For further inspection of differences in mean SpO₂ according to race/ethnicity, we also compared dSpO₂ and nSpO₂ distributions by race/ethnicity group after linear adjustment all individual data points (using sex-specific regression model fits) to correspond to subject age of 40 years, BMI of 25.0, and sea level home altitude. The resulting distributions show no statistically significant differences between race/ethnicity groups based on two-sample Kolmogorov-Smirnov tests, either over the full SpO₂ range or if the distributions are clipped at 94% saturation to emphasize the hypoxic SpO₂ range. An example comparison of adjusted nSpO₂ distributions for Black and White subjects is shown in Supplementary Figure S.3.

5.7 Study Limitations

This study has several important limitations. Although the Apple Heart & Movement Study represents a large total subject pool, it contains significant demographic imbalances as illustrated in Figure 2d and Table 1. For example 53% of the cohort used in the analysis reported here is White and male. Additionally all subject metadata including age, body measurements, geographic location (from which elevation and barometric pressure are inferred), sex, and race/ethnicity have been provided by subject self-report without independent verification.

This study did not exclude any subjects based upon cardiovascular or pulmonary disease risk factors, behavior (including alcohol and smoking habits), or self-reported chronic health conditions that may significantly impact blood oxygen saturation (such as COPD, emphysema, and sleep apnea). The study period also occurred in the midst of the COVID-19 pandemic (spanning the timeframe when vaccination became widely available in the US), during which an unknown fraction of the study population may have experienced acute respiratory infection. As such, the aggregated data inevitably includes some measurements collected under pathological conditions and this may influence the resulting population-scale observations and statistical models.

All data in the study was collected in uncontrolled naturalistic conditions, and therefore contains a large variety of unknown measurement contexts and use conditions which may influence the measured SpO₂ values. Additionally, the grouping of measurements into nocturnal vs. daytime average values is determined by referencing against local clock time, as opposed to grouping according to subject-specific physiological measures such as sleep or activity state. This grouping likely introduces a mix of both awake and asleep measurements into each subject’s dSpO₂ and nSpO₂ values. However, fitting and comparing linear model coefficients for individual clock hours does not reveal significant variability between adjacent hours, but rather a smooth circadian variation for each coefficient value (results shown in Supplementary Figure S.1).

Lastly, because the AppleWatch Series 6 sensor is not a CO-oximeter it is unable to measure or account for the presence of non-oxygen-carrying dyshemoglobin compounds such as carboxyhemoglobin, sulphemoglobin, and methemoglobin.

6 Acknowledgements

The authors acknowledge the important data contributions provided by all participants in the Apple Heart & Movement Study, without whom this research would not be possible. We also thank the following individuals for their thoughtful discussion, helpful guidance, and other valuable effort in support of this work: Marni Bartlett, David Tsay, Asha Chesnutt, Jen Block, Laura Rhodes, Paul Mannheimer, Mai Le, Mohsen Mollazadeh, Aditya Dua, Max Akhterov, Chris Brouse, and Angela Spillane.

7 Competing Interests

I.S., J.S., and M.O. are employees of Apple, Inc. and own Apple, Inc. stock. C.M. received grant funding from the American Heart Association for this work. The Apple Heart & Movement Study receives funding from Apple, Inc. and the American Heart Association.

8 Author Contributions

I.S. analyzed the data, interpreted the results, and drafted the manuscript. J.S. analyzed the data and interpreted the results. C.M. designed the study. M.O. was responsible for the critical revision and final approval of the manuscript.

9 Data Availability

The aggregated data that support the findings of this study can be made available on request from the corresponding author (M.O.). Request for data will be evaluated and responded to in a manner consistent with the specific language in the study protocol and informed consent form.

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10 Figures and Tables

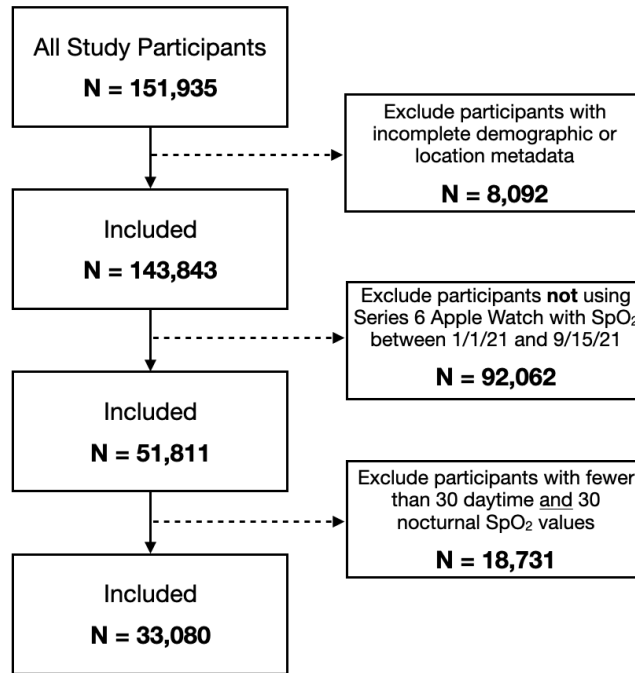


Figure 1: Subject inclusion/exclusion criteria flowchart.

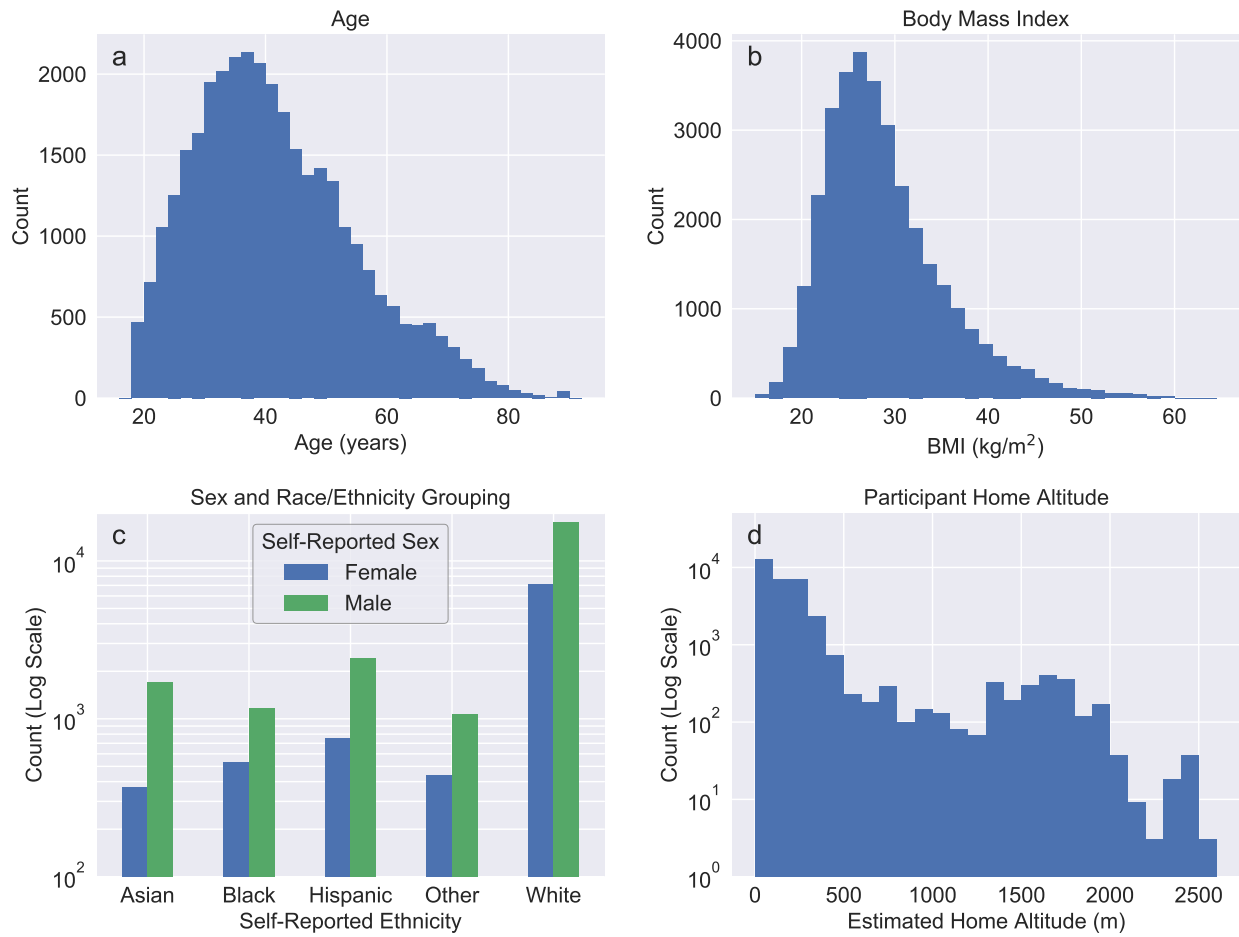


Figure 2: Demographic variable distributions for all subjects used in the analysis. Note that for Age (a) and Body Mass Index (b) the y-axis representing subject counts uses a linear scale, while for sex and race/ethnicity groups (c) and estimated home altitude (d) the y-axis uses logarithmic scale for clarity.

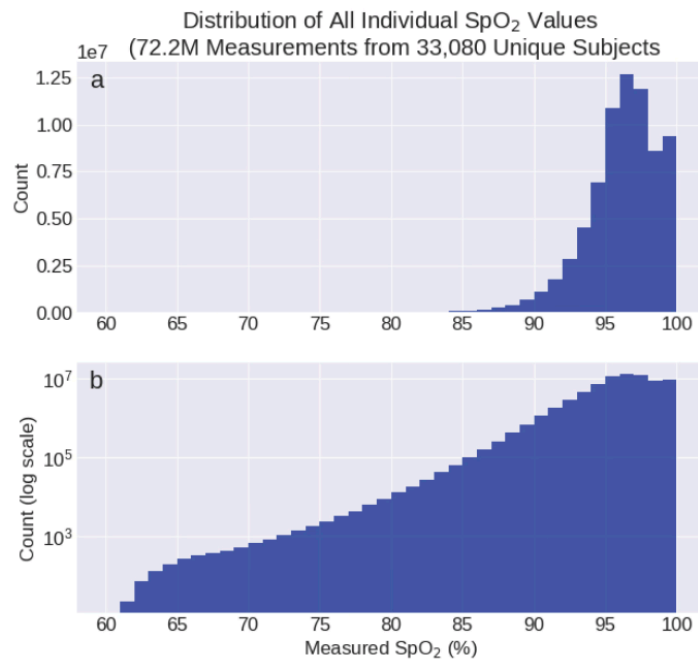


Figure 3: Histograms of all individual SpO₂ values collected from the full subject cohort, shown with linear y-scale (top) and logarithmic y-scale (bottom). The two histograms represent identical data, but with differing y-scales to enable useful visualization of the value distribution for SpO₂<85%.

Subject Group	N (%)	Age, yr. (mean \pm std. dev.)	BMI, kg/m ² (mean \pm std. dev.)	Home Altitude, m (mean \pm std. dev.)	Daytime SpO ₂ , % (mean \pm std. dev.)	Nocturnal SpO ₂ , % (mean \pm std. dev.)
Full Cohort	33080 (100.0%)	41.0 \pm 13.2	28.9 \pm 6.5	260.4 \pm 392.9	96.2 \pm 1.3	95.4 \pm 1.3
Female Assigned Sex	9169 (27.7%)	40.3 \pm 13.1	29.5 \pm 7.6	268.6 \pm 384.7	96.2 \pm 1.4	95.4 \pm 1.4
Male Assigned Sex	23911 (72.3%)	41.3 \pm 13.2	28.7 \pm 6.1	257.3 \pm 395.9	96.2 \pm 1.3	95.4 \pm 1.3
Asian Race/Ethnicity	2063 (6.2%)	37.8 \pm 11.8	26.3 \pm 4.8	179.2 \pm 309.6	96.4 \pm 1.2	95.8 \pm 1.2
Black Race/Ethnicity	1687 (5.1%)	39.4 \pm 11.8	30.8 \pm 7.3	198.3 \pm 311.6	96.2 \pm 1.3	95.4 \pm 1.3
Hispanic Race/Ethnicity	3162 (9.6%)	36.9 \pm 11.1	29.6 \pm 6.6	254.9 \pm 410.6	96.2 \pm 1.3	95.5 \pm 1.3
Other Race/Ethnicity	1501 (4.5%)	39.9 \pm 12.0	29.3 \pm 6.8	244.1 \pm 366.6	96.2 \pm 1.4	95.5 \pm 1.4
White Race/Ethnicity	24667 (74.6%)	42.0 \pm 13.5	28.8 \pm 6.5	273.2 \pm 401.9	96.2 \pm 1.3	95.3 \pm 1.3

Table 1: Summary of dataset statistics for the full cohort and demographic groups used for subgroup analysis.

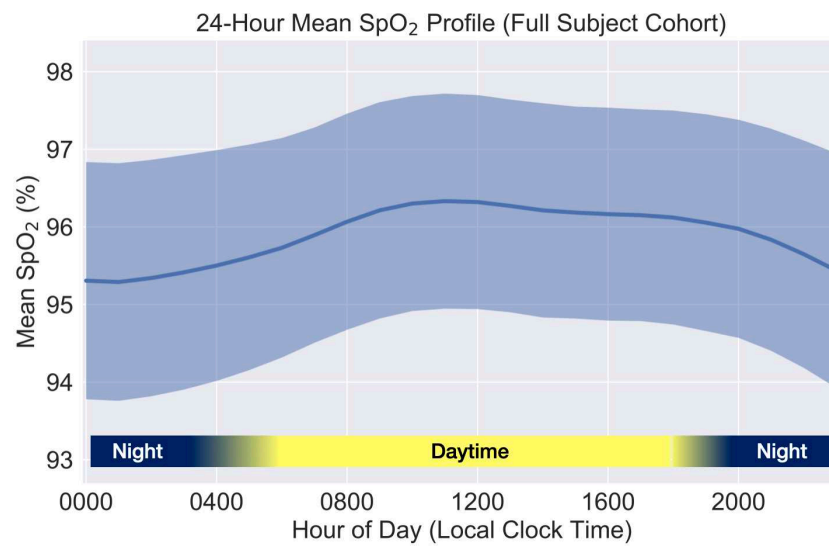


Figure 4: 24-hour SpO₂ variation for the full study cohort, shown as the mean \pm standard deviation after subject-level hourly profile aggregation as described in Methods section.

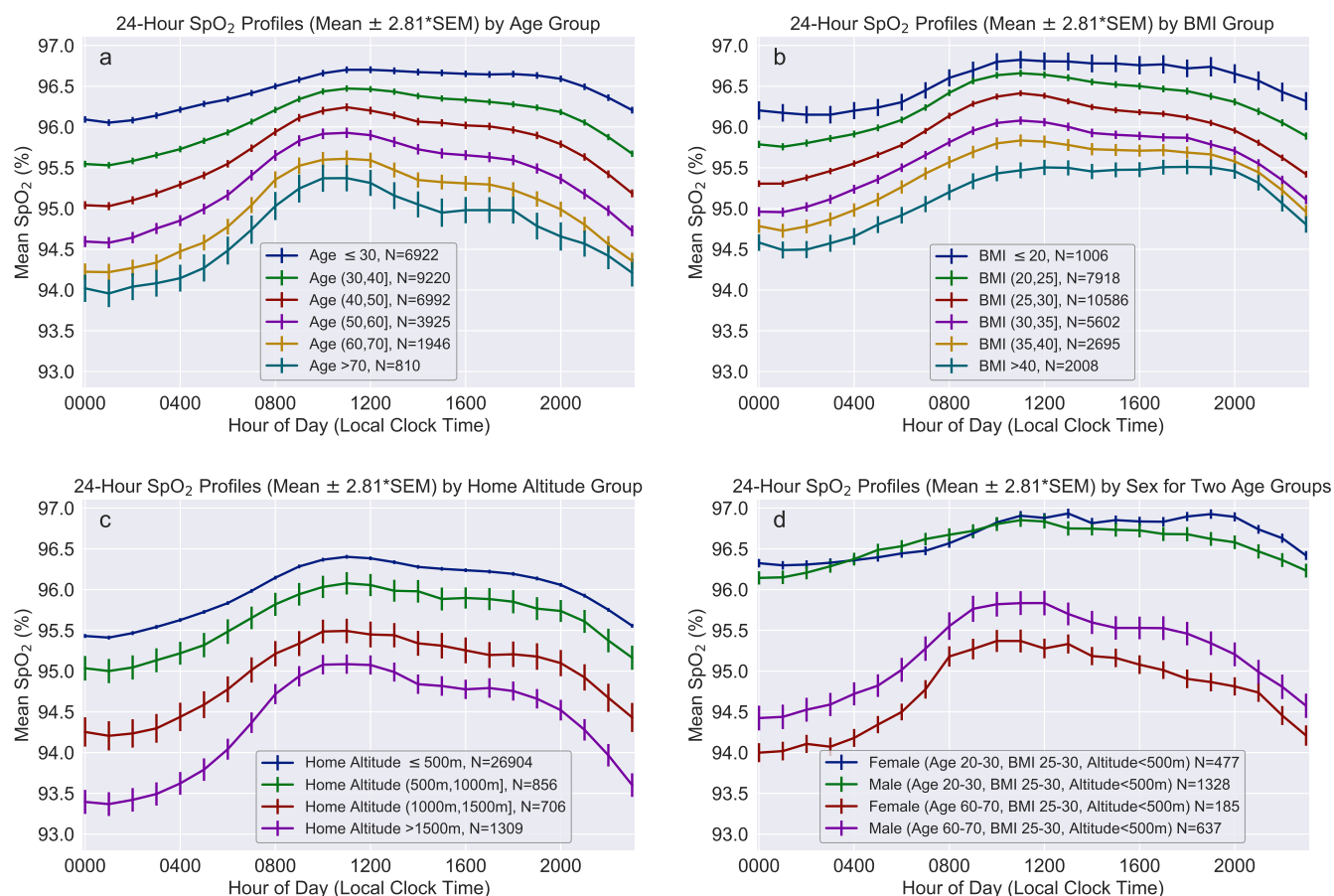


Figure 5: Twenty-four-hour group mean SpO₂ profiles grouped according to (a) age, (b) body mass index, (c) home altitude and (d) assigned sex for two age groups with limited range of BMI and home altitude. Solid lines indicate group mean value for each hour, with whiskers indicating ± 2.81 times the SEM (equivalent to 99.5% confidence interval for the mean value) for each hour. Group profiles were determined by first generating the hourly SpO₂ profile for each subject, then calculating the mean and SEM across subjects for each hour as described in the Methods section.

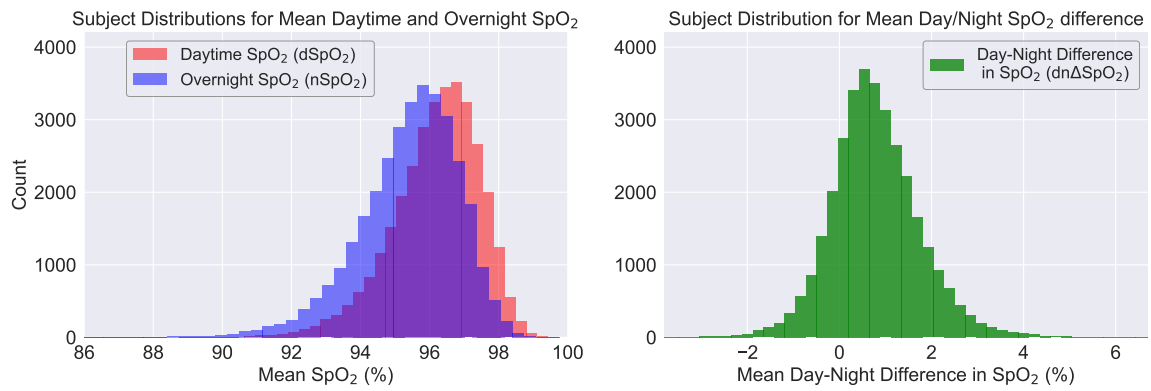


Figure 6: Distribution of daytime mean saturation (dSpO₂, left), nocturnal mean saturation (nSpO₂, left) and mean day-night SpO₂ difference (dnΔSpO₂, right) for the full study cohort. Positive values for dnΔSpO₂ correspond to lower measured SpO₂ at night.

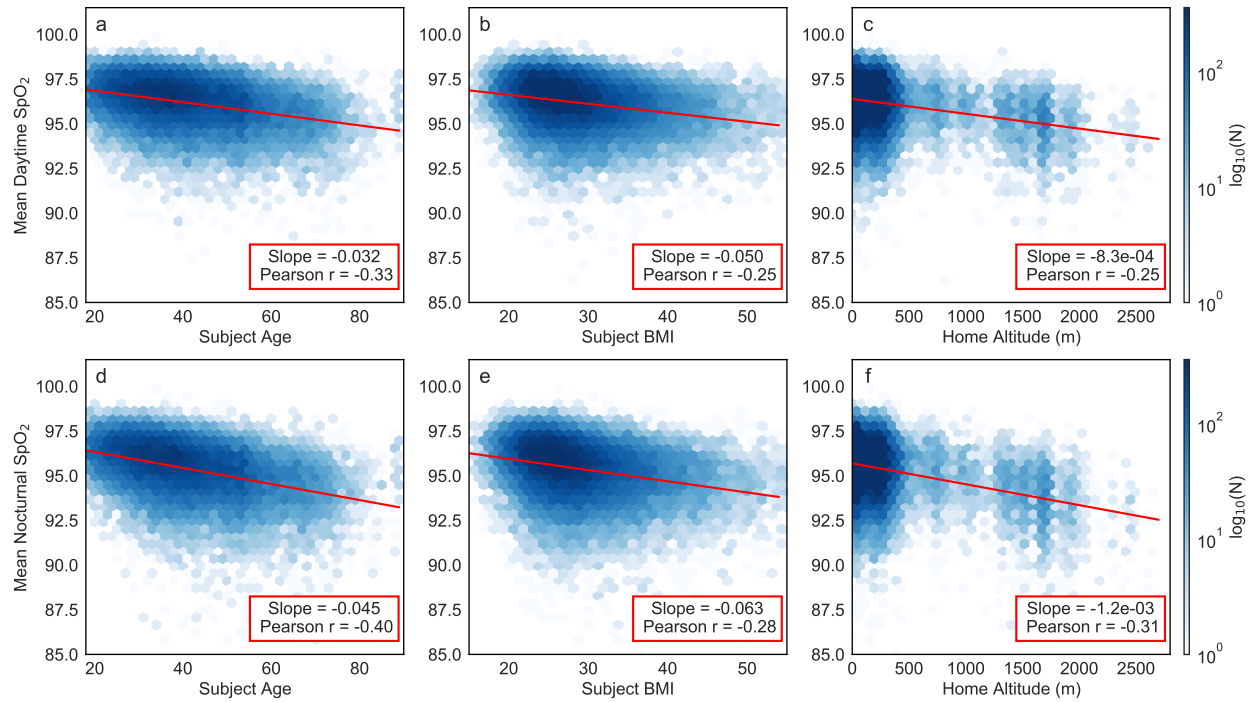


Figure 7: Linear relationships between mean daytime SpO₂ (a-c, top row), mean nocturnal SpO₂ (d-f, bottom row) and the three independent variables exhibiting the strongest correlation with these metrics. Each plot presents a 2-dimensional histogram of values from all 33,080 subjects in evenly-spaced hexagonal bins, with the color density corresponding to log-scaled bin counts for clarity. In each plot, the overlaid red line represents the simple univariate linear regression fit using the independent variable shown on the x-axis. The listed slope and Pearson correlation coefficient correspond to the same univariate linear fit.

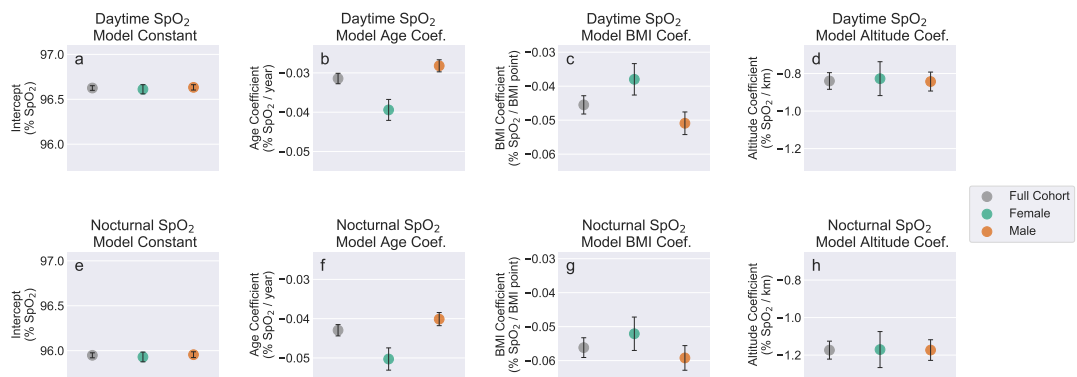


Figure 8: Comparison of fit coefficients for M_1 models fit to the full cohort and $M_{1,sex}$ models fit independently to female and male subjects, for daytime SpO_2 (a-d, top row) and nocturnal SpO_2 (e-h, bottom row). Error bars represent 99.5% confidence intervals for the fitted coefficients. Race/Ethnicity variables are omitted for clarity. Plotted coefficients and confidence intervals are identical to the values listed in Supplementary Table S.1.

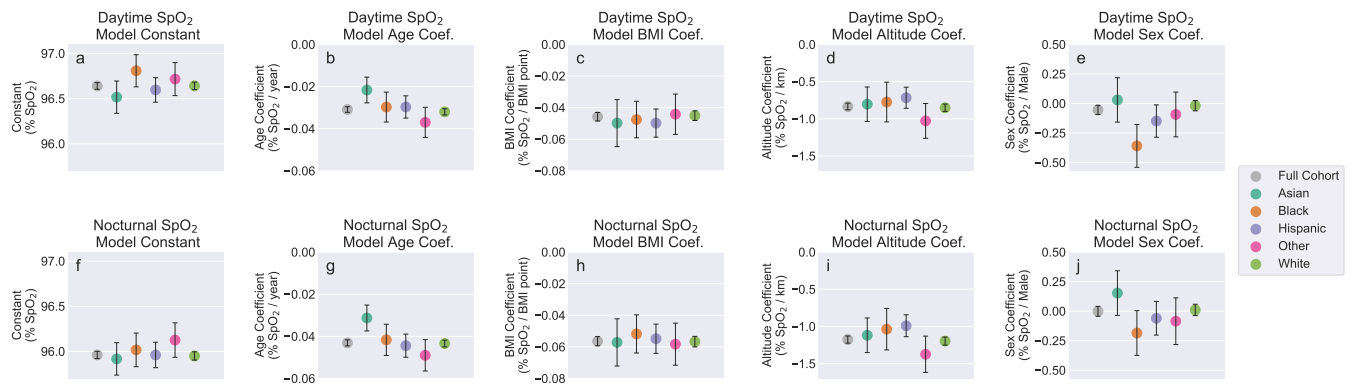


Figure 9: Comparison of model coefficients for for M_1 models fit to the full cohort, and for $M_{1,race-ethn.}$ models fit independently to each race/ethnicity group, for daytime SpO₂ (top row) and nocturnal SpO₂ (bottom row). Error bars represent 99.5% confidence intervals for the fitted coefficients. Plotted coefficients and confidence intervals are identical to the values listed in Supplementary Table S.2.

Model Name	Covariates	Model Usage
M_{Age}	Age (yr)	Comparison with low-altitude univariate SaO ₂ model (R. Crapo, <i>et al.</i> [3])
M_{Ref}	Age (yr) Height (cm) Weight (kg) Barometric pressure (mmHg) Sex (categorical)	Comparison with reference SaO ₂ model (R. Crapo, <i>et al.</i> [3])
M_1	Age - 40 (yr) BMI - 25 (kg/m ²) Home altitude (km) Sex (categorical) Race/Ethnicity (categorical)	Proposed full-cohort SpO ₂ linear model.
$M_{1,sex}$	Age - 40 (yr) BMI - 25 (kg/m ²) Home altitude (km) Race/Ethnicity (categorical)	Sex subgroup analysis.
$M_{1,race-ethn.}$	Age - 40 (yr) BMI - 25 (kg/m ²) Home altitude (km) Sex (categorical)	Race/ethnicity subgroup analysis.

Table 2: Summary of models employed in linear regression analysis. $M_{1,sex}$ differs from M_1 only by the omission of the categorical variable encoding sex. $M_{1,race-ethn.}$ differs from M_1 only by the omission of the categorical variables encoding race/ethnicity.

Univariate Regression Results for Blood Oxygen Saturation (Low-Altitude Subjects Only)				
Model	R ²	SEE	Constant	Age (yr)
Reference univariate SaO ₂ (R. Crapo, <i>et al.</i> [3])	0.32	0.85	97.66	-0.0296
Daytime SpO ₂ (low-alt. subjects)	0.12	1.14	97.65 (97.57,97.74)) [p < 1.0e-10]	-0.0322 (-0.0341,-0.0303)) [p < 1.0e-10]

Table 3: Tabulated comparison of reference SaO₂ linear model coefficients (top row; adapted from reference 3) with results obtained from equivalent fits to daytime mean SpO₂ (middle row) using only low-altitude subjects (estimated home altitude <155m) from our data set. Values in parentheses indicate 99.5% confidence intervals for fit coefficients. Values in brackets are coefficient p-values determined as described in Methods. R² = coefficient of determination. SEE = standard error of the estimate.

Linear Regression Results for Blood Oxygen Saturation: Fit Coefficients for Reference Model (M_{Ref})								
Model	R^2	SEE	Constant	Age (yr)	Baro. Press. (mm Hg)	Weight (kg)	Sex (m=1, f=0)	Height (cm)
Reference SaO ₂ (R. Crapo, <i>et al.</i> [3])	0.56	0.85	89.41	-0.0362	0.0128	-0.0159	n.s.	n.s.
Daytime SpO ₂	0.23	1.13	89.25 (88.68,89.83) [p < 1.0e-10]	-0.0309 (-0.0322,-0.0296) [p < 1.0e-10]	0.0100 (0.0094,0.0105) [p < 1.0e-10]	-0.0149 (-0.0157,-0.0140) [p < 1.0e-10]	-0.0168 (-0.0686,0.0351) [p = 0.36]	0.0123 (0.0098,0.0149) [p < 1.0e-10]
Nocturnal SpO ₂	0.32	1.21	87.12 (86.50,87.74) [p < 1.0e-10]	-0.0431 (-0.0445,-0.0417) [p < 1.0e-10]	0.0140 (0.0134,0.0146) [p < 1.0e-10]	-0.0182 (-0.0192,-0.0173) [p < 1.0e-10]	0.1629 (0.1071,0.2187) [p < 1.0e-10]	0.0069 (0.0042,0.0097) [p < 1.0e-10]

Table 4: Tabulated comparison of reference SaO₂ linear model coefficients (top row; adapted from reference 3) with linear model coefficients obtained from equivalent fits to daytime mean SpO₂ (middle row) and overnight SpO₂ (bottom row) using our data. Values in parentheses indicate 99.5% confidence intervals for fit coefficients. Values in brackets are coefficient p-values determined as described in Methods. R^2 = coefficient of determination. SEE = standard error of the estimate.

Linear Regression Results and Fit Coefficients for Proposed Model (M_1)											
Model	R^2	SEE	Constant	Age (yr)	BMI (kg/m ²)	Altitude (km)	Sex (m=1, f=0)	Asian Race/Ethnicity	Black Race/Ethnicity	Hispanic Race/Ethnicity	Other Race/Ethnicity
Full Cohort Daytime SpO ₂	0.23	1.12	96.66 (96.62,96.70) [p <1e-10]	-0.0314 (-0.0327,-0.0300) [p <1e-10]	-0.0457 (-0.0484,-0.0430) [p <1e-10]	-0.8402 (-0.8845,-0.7959) [p <1e-10]	-0.0490 (-0.0880,-0.0101) [p=4.1e-04]	-0.1004 (-0.1735,-0.0273) [p=1.2e-04]	-0.0648 (-0.1446,0.0150) [p=0.023]	-0.1334 (-0.1936,-0.0733) [p=4.8e-10]	-0.0146 (-0.0986,0.0694) [p=0.63]
Full Cohort Nocturnal SpO ₂	0.32	1.21	95.95 (95.91,95.99) [p <1e-10]	-0.0429 (-0.0444,-0.0415) [p <1e-10]	-0.0562 (-0.0591,-0.0533) [p <1e-10]	-1.1736 (-1.2214,-1.1257) [p <1e-10]	-0.0038 (-0.0459,0.0383) [p=0.80]	0.0775 (-0.0015,0.1564) [p=0.0059]	-0.0068 (-0.0930,0.0794) [p=0.82]	0.0243 (-0.0406,0.0893) [p=0.29]	0.0596 (-0.0311,0.1504) [p=0.065]

Table 5: Linear model M_1 full-cohort fit results for daytime SpO₂ (top row) and nocturnal SpO₂ (bottom row). Sex variables for the full subject cohort are encoded using a value of 1 for Male subjects and 0 for Female subjects. Race/Ethnicity variables for the full cohort and both sex subgroups are encoded using a value of 1 for each listed race/ethnicity group, with White subjects encoded using all zeros. Values listed in parentheses represent 99.5% confidence intervals for the fitted model coefficients. Values in brackets are coefficient p-values determined as described in Methods. R^2 = coefficient of determination. SEE = standard error of the estimate.

11 Supplementary Tables and Figures

Linear Regression Results and Fit Coefficients for Proposed Model (M_1) and Sex Subgroup Analysis Model ($M_{1,sex}$)											
Model	R^2	SEE	Constant	Age (yr)	BMI (kg/m ²)	Altitude (km)	Sex (m=1, f=0)	Asian Race/Ethnicity	Black Race/Ethnicity	Hispanic Race/Ethnicity	Other Race/Ethnicity
Full Cohort Daytime SpO ₂	0.23	1.12	96.66 (96.62,96.70) [p <1e-10]	-0.0314 (-0.0327,-0.0300) [p <1e-10]	-0.0457 (-0.0484,-0.0430) [p <1e-10]	-0.8402 (-0.8845,-0.7959) [p <1e-10]	-0.0490 (-0.0880,-0.0101) [p=4.1e-04]	-0.1004 (-0.1735,-0.0273) [p=1.2e-04]	-0.0648 (-0.1446,0.0150) [p=0.023]	-0.1334 (-0.1936,-0.0733) [p=4.8e-10]	-0.0146 (-0.0986,0.0694) [p=0.63]
Female Daytime SpO ₂	0.24	1.18	96.61 (96.56,96.66) [p <1e-10]	-0.0394 (-0.0421,-0.0368) [p <1e-10]	-0.0380 (-0.0426,-0.0334) [p <1e-10]	-0.8273 (-0.9176,-0.7369) [p <1e-10]	--	-0.1786 (-0.3572,0.0001) [p=0.0050]	0.1435 (0.0071,0.2941) [p=0.0075]	-0.0843 (-0.2121,0.0435) [p=0.064]	0.0160 (-0.1480,0.1799) [p=0.78]
Male Daytime SpO ₂	0.23	1.10	96.63 (96.60,96.66) [p <1e-10]	-0.0282 (-0.0297,-0.0267) [p <1e-10]	-0.0509 (-0.0542,-0.0476) [p <1e-10]	-0.8427 (-0.8932,-0.7922) [p <1e-10]	--	-0.0897 (-0.1688,-0.0106) [p=0.0015]	-0.1506 (-0.2444,-0.0568) [p=6.6e-06]	-0.1439 (-0.2114,-0.0763) [p=2.3e-09]	-0.0260 (-0.1233,0.0713) [p=0.45]
Full Cohort Nocturnal SpO ₂	0.32	1.21	95.95 (95.91,95.99) [p <1e-10]	-0.0429 (-0.0444,-0.0415) [p <1e-10]	-0.0562 (-0.0591,-0.0533) [p <1e-10]	-1.1736 (-1.2214,-1.1257) [p <1e-10]	-0.0038 (-0.0459,0.0383) [p=0.80]	0.0775 (0.0015,0.1564) [p=0.0059]	-0.0068 (0.0930,0.0794) [p=0.82]	0.0243 (0.0406,0.0893) [p=0.29]	0.0596 (-0.0311,0.1504) [p=0.065]
Female Nocturnal SpO ₂	0.34	1.26	95.93 (95.88,95.98) [p <1e-10]	-0.0503 (-0.0531,-0.0474) [p <1e-10]	-0.0521 (-0.0570,-0.0472) [p <1e-10]	-1.1706 (-1.2665,-1.0746) [p <1e-10]	--	-0.0894 (0.2792,0.1005) [p=0.19]	0.1189 (0.0411,0.2790) [p=0.037]	0.0427 (0.0931,0.1785) [p=0.38]	0.1067 (-0.0675,0.2809) [p=0.085]
Male Nocturnal SpO ₂	0.32	1.20	95.96 (95.92,95.99) [p <1e-10]	-0.0401 (-0.0418,-0.0384) [p <1e-10]	-0.0592 (-0.0628,-0.0556) [p <1e-10]	-1.1732 (-1.2282,-1.1182) [p <1e-10]	--	0.1115 (0.0253,0.1977) [p=2.8e-04]	-0.0558 (0.1580,0.0464) [p=0.13]	0.0235 (0.0501,0.0971) [p=0.37]	0.0416 (-0.0644,0.1477) [p=0.27]

Table S.1: Linear model M_1 fit results for three subject groups (full cohort, female subjects only, and male subjects only), applied to either daytime SpO₂ (top three rows of coefficients) or to nocturnal SpO₂ (bottom three rows of coefficients). Sex variables for the full subject cohort are encoded using a value of 1 for Male subjects and 0 for Female subjects. Race/Ethnicity variables for the full cohort and both sex subgroups are encoded using a value of 1 for each listed race/ethnicity group, with White subjects encoded using all zeros for these variables. Values listed in parentheses represent 99.5% confidence intervals for the fitted model coefficients. Values in brackets are coefficient p-values determined as described in Methods. R^2 = coefficient of determination. SEE = standard error of the estimate.

Linear Regression Results and Fit Coefficients for Race/Ethnicity Subgroup Analysis Models $M_{1,race-ethn}$.							
Model	R^2	SEE	Constant	Age (yr)	BMI (kg/m^2)	Altitude (km)	Sex (m=1, f=0)
Asian R/E Daytime SpO ₂	0.13	1.16	96.52 (96.34,96.69)	-0.0216 (-0.0277,-0.0155)	-0.0498 (-0.0646,-0.0349)	-0.8041 (-1.0358,-0.5724)	0.0303 (-0.1576,0.2183)
Black R/E Daytime SpO ₂	0.18	1.22	96.81 (96.63,96.99)	-0.0297 (-0.0368,-0.0226)	-0.0475 (-0.0591,-0.0360)	-0.7746 (-1.0418,-0.5073)	-0.3590 (-0.5400,-0.1779)
Hispanic R/E Daytime SpO ₂	0.19	1.17	96.60 (96.46,96.73)	-0.0297 (-0.0350,-0.0244)	-0.0498 (-0.0587,-0.0409)	-0.7169 (-0.8588,-0.5751)	-0.1485 (-0.2823,0.0116)
Other R/E Daytime SpO ₂	0.25	1.18	96.72 (96.53,96.90)	-0.0370 (-0.0441,-0.0298)	-0.0442 (-0.0569,-0.0314)	-1.0287 (-1.2627,-0.7946)	-0.0928 (-0.2823,0.0967)
White R/E Daytime SpO ₂	0.25	1.10	96.64 (96.60,96.68)	-0.0320 (-0.0335,-0.0305)	-0.0451 (-0.0481,-0.0420)	-0.8515 (-0.9007,-0.8024)	-0.0183 (-0.0621,0.0254)
Asian R/E Nocturnal SpO ₂	0.21	1.16	95.92 (95.74,96.10)	-0.0313 (-0.0374,-0.0251)	-0.0572 (-0.0721,-0.0422)	-1.1187 (-1.3514,-0.8860)	0.1530 (-0.0357,0.3418)
Black R/E Nocturnal SpO ₂	0.24	1.27	96.02 (95.83,96.20)	-0.0416 (-0.0491,-0.0342)	-0.0518 (-0.0639,-0.0397)	-1.0364 (-1.3156,-0.7572)	-0.1849 (-0.3740,0.0043)
Hispanic R/E Nocturnal SpO ₂	0.28	1.21	95.96 (95.82,96.10)	-0.0444 (-0.0499,-0.0389)	-0.0548 (-0.0641,-0.0456)	-0.9904 (-1.1378,-0.8430)	-0.0600 (-0.2024,0.0823)
Other R/E Nocturnal SpO ₂	0.35	1.23	96.13 (95.93,96.32)	-0.0490 (-0.0564,-0.0415)	-0.0583 (-0.0716,-0.0450)	-1.3740 (-1.6182,-1.1299)	-0.0849 (-0.2825,0.1128)
White R/E Nocturnal SpO ₂	0.33	1.21	95.95 (95.90,96.00)	-0.0434 (-0.0450,-0.0418)	-0.0567 (-0.0600,-0.0533)	-1.1963 (-1.2502,-1.1423)	0.0104 (-0.0376,0.0585)

Table S.2: Linear regression results for participants in each race/ethnicity group, fit to $M_{1,race-ethn}$. (identical to model M_1 , except for the omission of variables encoding race/ethnicity). Models are fit using either daytime SpO₂ as the dependent variable (top five rows of coefficients) or nocturnal SpO₂ as the dependent variable (bottom five rows of coefficients). Sex variables for all subgroups are encoded using a value of 1 for Male subjects and 0 for Female subjects. Values listed in parentheses represent 99.5% confidence intervals for the fitted model coefficients. R^2 = coefficient of determination. SEE = standard error of the estimate.

Linear Model Fit Coefficients for Hourly Mean SpO₂ Values

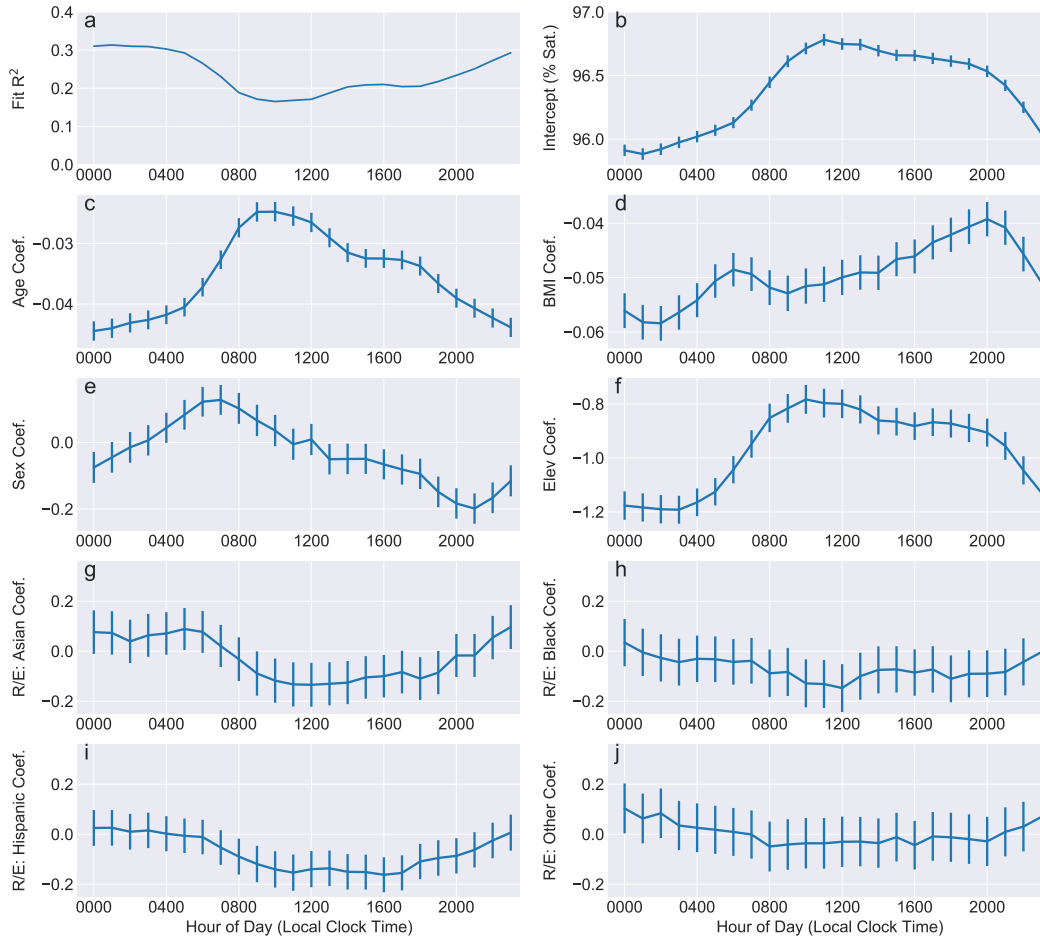


Figure S.1: Linear regression R^2 and model coefficients produced by fitting M_1 using subject-mean SpO₂ aggregated for each individual hour of the day: (a) Fitted R^2 is highest during typical sleep hours (approx 22:00–06:00) compared with daytime hours. Age (c), BMI (d) and altitude (f) coefficients exhibit clear circadian variation and have greatest absolute magnitude during typical sleep hours. (e) Biological sex and race/ethnicity group (g-j) also exhibit a small degree of diurnal variation. In all plots, error whiskers correspond to 99.5% confidence intervals.

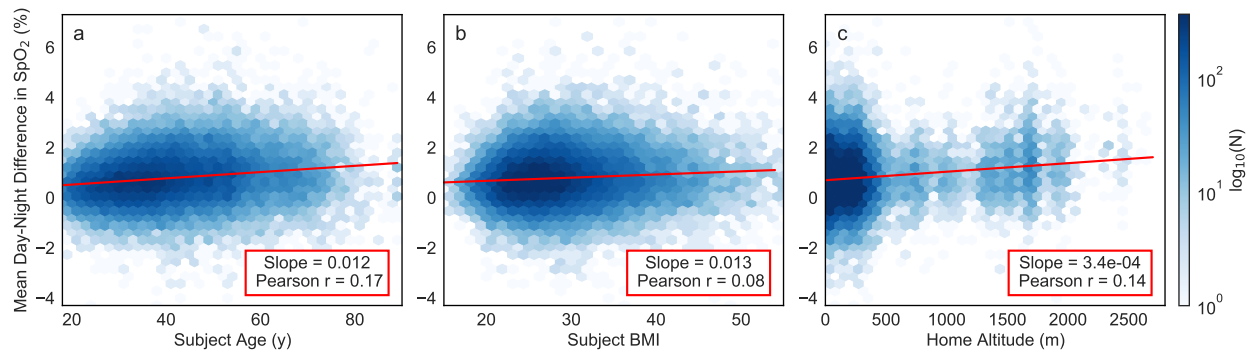


Figure S.2: Linear relationships between mean day-night SpO₂ difference ($dn\Delta SpO_2$) and the three independent variables exhibiting the strongest correlation with these metrics: age (a), BMI (b) and estimated home altitude (c). Each plot presents a 2-dimensional histogram of values from all 33,080 subjects in evenly-spaced hexagonal bins, with the color density corresponding to log-scaled bin counts for clarity. Positive values for $dn\Delta SpO_2$ correspond to an overnight drop in measured SpO₂. In each plot, the overlaid red line represents the simple univariate linear regression fit using the independent variable shown on the x-axis. The listed slope and Pearson correlation coefficient correspond to the same univariate linear fit.

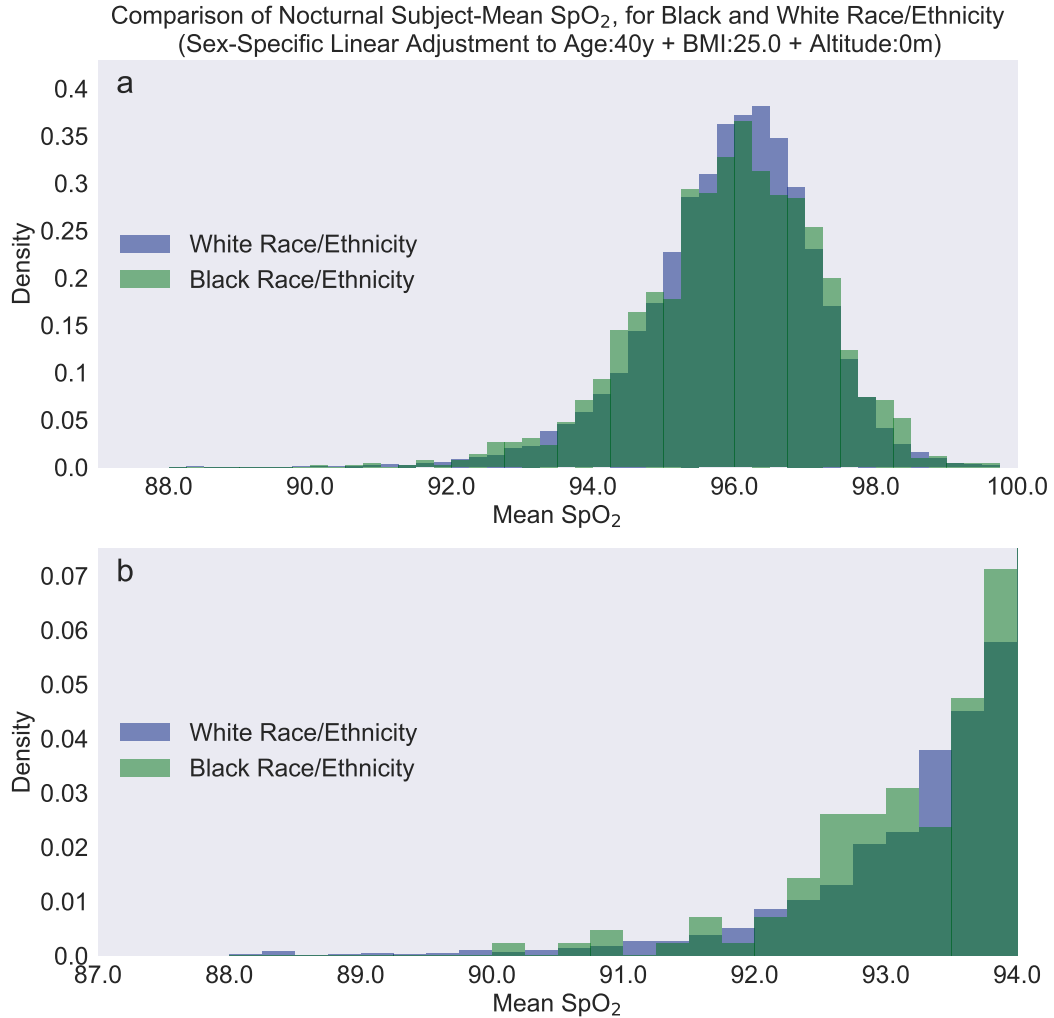


Figure S.3: Histograms of nocturnal SpO₂ for Black and White subjects, after linear adjustment of age to a target of 40 years, BMI to a target of 25.0 kg/m², and home altitude to zero elevation. Distributions are shown for the full range of nocturnal SpO₂ (a) and for the low-saturation range (b). Data for both plots is identical, with only the axes limits differing. The distributions do not differ with statistical significance ($p > .05$) based on two-sample Kolmogorov-Smirnov test using two-sided alternative hypothesis, either over the full range of SpO₂ or if the distributions are clipped at 94% saturation to emphasize the hypoxic tail.