

ORIGINAL ARTICLE

Effect of Aircraft-Cabin Altitude on Passenger Discomfort

J. Michael Muhm, M.D., M.P.H., Paul B. Rock, D.O., Ph.D.,
Dianne L. McMullin, Ph.D., Stephen P. Jones, Ph.D., I.L. Lu, Ph.D.,
Kyle D. Eilers, David R. Space, and Aleksandra McMullen, M.S.

ABSTRACT

BACKGROUND

Acute mountain sickness occurs in some unacclimatized persons who travel to terrestrial altitudes at which barometric pressures are the same as those in commercial aircraft during flight. Whether the effects are similar in air travelers is unknown.

METHODS

We conducted a prospective, single-blind, controlled hypobaric-chamber study of adult volunteers to determine the effect of barometric pressures equivalent to terrestrial altitudes of 650, 4000, 6000, 7000, and 8000 ft (198, 1219, 1829, 2134, and 2438 m, respectively) above sea level on arterial oxygen saturation and the occurrence of acute mountain sickness and discomfort as measured by responses to the Environmental Symptoms Questionnaire IV during a 20-hour simulated flight.

RESULTS

Among the 502 study participants, the mean oxygen saturation decreased with increasing altitude, with a maximum decrease of 4.4 percentage points (95% confidence interval, 3.9 to 4.9) at 8000 ft. Overall, acute mountain sickness occurred in 7.4% of the participants, but its frequency did not vary significantly among the altitudes studied. The frequency of reported discomfort increased with increasing altitude and decreasing oxygen saturation and was greater at 7000 to 8000 ft than at all the lower altitudes combined. Differences became apparent after 3 to 9 hours of exposure. Persons older than 60 years of age were less likely than younger persons and men were less likely than women to report discomfort. Four serious adverse events, 1 of which may have been related to the study exposures, and 15 adverse events, 9 of which were related to study exposures, were reported.

CONCLUSIONS

Ascent from ground level to the conditions of 7000 to 8000 ft lowered oxygen saturation by approximately 4 percentage points. This level of hypoxemia was insufficient to affect the occurrence of acute mountain sickness but did contribute to the increased frequency of reports of discomfort in unacclimatized participants after 3 to 9 hours. (ClinicalTrials.gov number, NCT00326703.)

From the Shared Services Group (J.M.M.), Boeing Commercial Airplanes (D.L.M., K.D.E., D.R.S., A.M.), and Phantom Works (S.P.J., I.L.L.), Boeing Company, Seattle; and the Center for Aerospace and Hyperbaric Medicine, Oklahoma State University Center for Health Sciences, Tulsa (P.B.R.). Address reprint requests to Dr. Muhm at Boeing Medical, P.O. Box 3707 MC 7H-90, Boeing Company, Seattle, WA 98124-2207, or at mike.muham@boeing.com.

N Engl J Med 2007;357:18-27.
Copyright © 2007 Massachusetts Medical Society.

A COMMONLY ENCOUNTERED BUT GENERALLY unrecognized exposure to moderate altitude (6500 to 8000 ft [1981 to 2438 m]) occurs during commercial flight. Although the cabins of commercial aircraft are pressurized to protect occupants from the very low barometric pressures at flight altitudes, sea-level pressure (760 mm Hg) is not maintained. Instead, aircraft are designed to maintain cabin pressure at a level no lower than 565 mm Hg (equivalent to an altitude of 8000 ft) when the airplane is at its maximum operating altitude.¹ Higher levels of pressurization decrease the energy available for other aircraft systems, reduce the operational lifetime of aluminum airframes, and necessitate increased structural weight, resulting in decreased fuel efficiency.

Some unacclimatized persons who travel to terrestrial altitudes above 6500 ft experience acute mountain sickness, a self-limited syndrome characterized by symptoms of headache, nausea, vomiting, anorexia, lassitude, and sleep disturbance.² The prevalence of acute mountain sickness increases with the altitude attained, the rate of ascent, and the presence or absence of a history of acute mountain sickness.²⁻⁸ Although the pathophysiology of acute mountain sickness is not completely understood, hypobaric hypoxia is thought to play a predominant role,⁹ and the severity of symptoms is inversely related to arterial oxygen saturation.^{4,10}

Some passengers on long commercial flights experience discomfort characterized by symptoms similar to those of acute mountain sickness.^{11,12} The symptoms are often attributed to factors such as jet lag, prolonged sitting, dehydration, or contamination of cabin air.¹³ However, because barometric pressures in aircraft cabins are similar to those at the terrestrial altitudes at which acute mountain sickness occurs, it is possible that some of the symptoms are related to the decreased partial pressure of oxygen and are manifestations of acute mountain sickness.¹⁴

Although immobility may contribute to passengers' discomfort,¹⁵ exercise may not be beneficial. Exercise reduces arterial oxygenation,¹⁶ which can increase the frequency and severity of acute mountain sickness¹⁷ and affect sensory perception and psychomotor performance.¹⁸

We conducted a prospective, single-blind, controlled study to determine the effect of baromet-

ric pressures equivalent to terrestrial altitudes of up to 8000 ft on oxygen saturation and the occurrence of acute mountain sickness and discomfort in volunteers selected to represent commercial airline passengers during a simulated 20-hour flight. Secondary objectives were to determine the effect of exercise at these altitudes on discomfort and the effect of altitude on sensory and psychomotor performance.

METHODS

The study protocol was approved by the institutional review boards of Oklahoma State University and the Boeing Company before the recruitment of volunteers began. All volunteers gave written consent to participate after being informed of the study's purpose, procedures, and inherent risks and benefits. Data collection began on October 26, 2002, and ended on April 22, 2003. The study was funded by the Boeing Company. The data were held jointly by the Boeing Company and Oklahoma State University under a data-confidentiality agreement. Two of the authors, both employees of Boeing, performed the statistical analysis. All authors contributed to the design, interpretation, and preparation of the manuscript and attest to the accuracy and completeness of the information reported.

STUDY PARTICIPANTS

Volunteers between 21 and 75 years of age who had not been at altitudes above 4000 ft (1219 m) and had not traveled by commercial airplane for more than 3 hours in the preceding month were recruited from the general population of the greater Tulsa, Oklahoma, area (altitude, 650 ft [198 m]). Equal numbers of men and women were selected so that their age distribution was similar to that of commercial airline passengers (unpublished data). All participants were medically evaluated to exclude those with acute or chronic conditions that could increase the risk of harm from exposure to high altitudes (see Table MI of the Supplementary Appendix, available with the full text of this article at www.nejm.org).

TEST CONDITIONS AND EQUIPMENT

The study was conducted in a hypobaric chamber (C.G.S. Scientific) (see the Methods section of the Supplementary Appendix). Environmental temper-

ature, relative humidity, and altitude were recorded continuously during the test sessions. The altitudes investigated were sequentially selected by means of an algorithm designed to minimize the number of test sessions (see Fig. M1 of the Supplementary Appendix). The altitudes were 650 ft (ground level, 198 m; barometric pressure, 742 mm Hg), 4000 ft (1219 m, 656 mm Hg), 6000 ft (1829 m, 609 mm Hg), 7000 ft (2134 m, 586 mm Hg), and 8000 ft (2438 m, 565 mm Hg).

Each participant took part in only one test session. A maximum of 12 participants, balanced with respect to age and sex, were assigned to each session. We did not consider familial and social relationships when making the assignments. The altitude for each session was randomly selected from those under consideration, and participants were unaware of the selected altitude.

At the beginning of each session, the chamber was depressurized at a rate of 500 ft (152 m) per minute to the target altitude, which was maintained for 20 hours, the maximum anticipated length of nonstop commercial flights. After 20 hours, the chamber was repressurized to ground-level altitude at a rate of 350 ft (107 m) per minute. These are the rates of change in pressure that are commonly used in commercial aviation. To maintain blinding, brief depressurization and repressurization were performed at the beginning and end of the sessions testing ground-level altitude.

Test sessions began at 10 a.m. and ended at 6 a.m. the next day. Meals and snacks were provided, but participants were allowed to bring food and medications. Alcohol consumption and tobacco smoking were prohibited. Participants spent most of the time in assigned coach-class airplane seats but were encouraged to walk or stand when not involved in a particular test activity. They had unrestricted access to toilet facilities within the chamber. Five commercial movies were played in an unvarying sequence and time schedule on in-chamber VCRs, and audio headsets were provided. Viewing was optional. A sleep period extended from 11 p.m. to 5 a.m., during which lights were dimmed and interaction with participants was limited to a single oxygen-saturation measurement.

During hours 1 through 9 of every test session, five randomly selected participants between the ages of 21 and 60 years exercised by walking on a horizontal treadmill at a rate of 3.0 mi (4.8 km) each hour for 10 minutes per hour.

OUTCOME MEASURES

Using a pulse oximeter (Nellcor N-20E), we measured arterial oxygen saturation before depressurization; at 1, 3, 5, 7, 9, 11, 13, 16, and 19 hours after depressurization; and during the first and second hours after repressurization. For participants who exercised during the test session, oxygen saturation was measured immediately before and after each 10-minute exercise period. Oxygen saturation values were not provided to participants during the session.

Symptomatic reactions to the test environment were assessed with the Environmental Symptoms Questionnaire IV (ESQ-IV), in which symptoms are rated on a five-point Likert scale ranging from “not at all” to “extreme” (Table MII of the Supplementary Appendix).¹⁹ The questionnaire was completed independently by each participant according to a standard set of instructions and was administered during the same hours that oxygen saturation was measured, except at hour 16 (during the sleep period). ESQ-IV factor scores were calculated as described by Sampson et al.¹⁹ (Table 1, and Table MIII of the Supplementary Appendix).

Participants were classified as having acute mountain sickness when their score for the factor acute mountain sickness–cerebral (AMS-C) exceeded 0.7, the published criterion score.¹⁹ The proportion of participants classified as having acute mountain sickness at any time was calculated in two ways: the point prevalence (the proportion of participants whose factor score exceeded the criterion score at that time) and the cumulative prevalence (the proportion of participants whose factor score exceeded the criterion score at that time or had exceeded the criterion score at any time since depressurization) (see the Methods section of the Supplementary Appendix).

To assess the occurrence of discomfort, we developed time-dependent criterion scores for all ESQ-IV factors based on the distribution of factor scores when participants were at ground level. The score below which 97.5% of the ground-level scores fell at each administration of the questionnaire was defined as the time-dependent criterion score for that factor at that time. A participant was classified as experiencing specific factor-related discomfort when the participant’s factor score exceeded the corresponding time-dependent criterion score. We combined factors considered a priori to be related to altitude — AMS-C and

Table 1. ESQ-IV Factors and Participant Symptoms and Sensations.*

Factor	Symptoms and Sensations
AMS-C†	Headache,‡ sick to stomach, feel sick, feel weak, lightheaded,‡ dizzy, faint, vision dim, coordination off,‡ lost appetite, feel hung over
AMS-R†	Headache,‡ sick to stomach, hurts to breathe, depressed, backache,‡ hard to breathe, could not sleep, short of breath,‡ stomach cramps, stomachache, nose stuffed, nosebleeds
Muscular discomfort	Backache,‡ feel weak, thirsty, muscle cramps, muscles tight, legs ache, feet ache, hands ache, arms ache, shoulders ache, gas pressure, numbness
Exertion	Lightheaded,‡ hard to breathe, hurts to breathe, chest pains, feel weak, heartbeat fast, heart pounding, short of breath‡
Fatigue	Feel weak, dizzy, faint, thirsty, feel tired, feel sleepy, could not sleep, concentration off, eyes irritated, vision blurry, runny nose
Cold stress	Feel weak, feel worried, hands shaking, urinate more, feel feverish, hands cold, feet cold, feel chilly, shivering
Distress	Feel sick, hurts to breathe, depressed, chest pains, feel tired, feel sleepy, feel worried, feel irritable, feel restless, bored, chest pressure, cough
Ear, nose, and throat discomfort	Sinus pressure, skin burns and itches, ears blocked, ears ache, cannot hear, ears ringing, nose stuffed, mouth dry, sore throat
Alertness	Feel tired, feel sleepy, could not sleep, concentration off, depressed, feel alert, feel good

* Adapted from Sampson et al.¹⁹

† Both AMS-C (acute mountain sickness–cerebral) and AMS-R (acute mountain sickness–respiratory) are considered a priori to be altitude-related.

‡ In post hoc analysis, this symptom was found to be one of the most important contributors to discomfort.

acute mountain sickness–respiratory (AMS-R) — into a single factor, altitude-related malaise, which was considered to be present when the factor scores for AMS-C, AMS-R, or both exceeded their respective time-dependent criterion scores (see the Methods section of the Supplementary Appendix).

The Purdue Pegboard Dexterity Test, Kentucky Comprehensive Listening Test, Snellen Visual Acuity Test, and Farnsworth–Munsell 100-Hue Test were administered before, after, and intermittently during each session to assess psychomotor and sensory performance (see Table MVII of the Supplementary Appendix).

STATISTICAL ANALYSIS

We estimated that at each altitude, a group of 108 participants would provide 80% power to detect a twofold difference in the expected prevalence of outcomes at a 5% significance level. Values for missing factor scores were imputed by using a value midway between the factor scores immediately before and after the missing score. Mixed models were used to determine the effects of altitude, time since the beginning of the session, exer-

cise, age, and sex on oxygen saturation. Logistic regression was used to analyze the point prevalence of the ESQ-IV factors.²⁰ Log-rank tests and Cox proportional-hazards regression^{21,22} were used with cumulative prevalence, and linear regression was used for measures of performance. Data that were missing because the participant left the study were treated as censored for all subsequent periods in the Cox models. Two-sided Fisher's exact tests were used to compare the hour-by-hour cumulative prevalence of each ESQ-IV factor.²³ P values based on Fisher's exact tests were not corrected for multiple comparisons. A post hoc analysis was conducted to determine the contribution of individual symptoms to the observed effect altitude had on discomfort (see the Methods section of the Supplementary Appendix).

RESULTS

Of 759 applicants, 502 participated in the study (Fig. 1). A total of 209 of the 431 participants who were 60 years of age or younger were randomly assigned to exercise. Testing was stopped at hour 5 (altitude, 8000 ft) in the case of one participant,

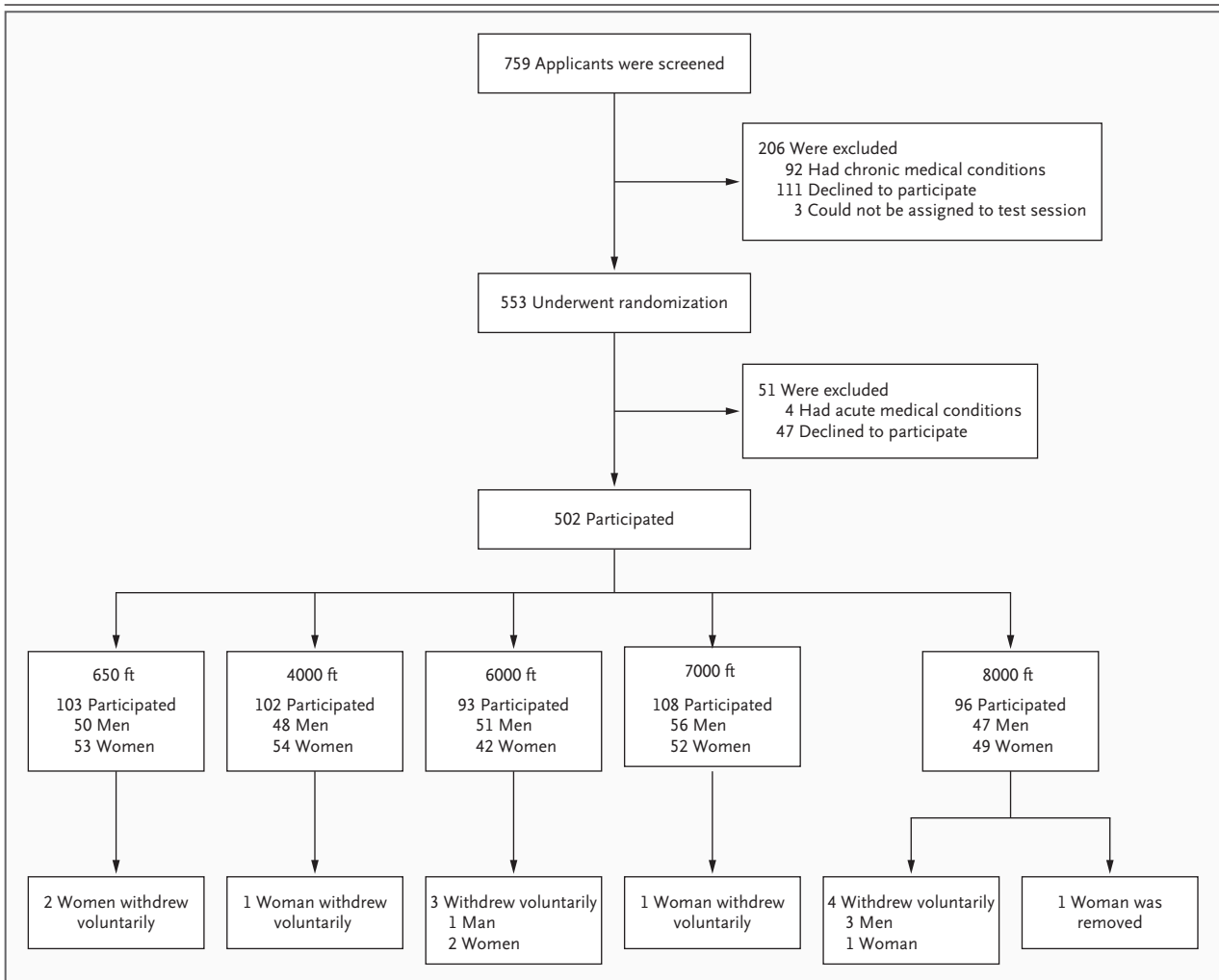


Figure 1. Enrollment and Randomization of Study Participants.

Eleven participants withdrew from the study voluntarily. During the 650-ft session, a 21-year-old woman withdrew at hour 13 because of headache and a 53-year-old woman at hour 1 because of anxiety. During the 4000-ft session, a 21-year-old woman withdrew at hour 19 for personal reasons. During the 6000-ft session, a 55-year-old man withdrew at hour 7 because of headache, a 27-year-old woman at hour 13 because of headache and nausea, and a 71-year-old woman at hour 13 because of diarrhea. During the 7000-ft session, a 31-year-old woman withdrew at hour 13 because of headache and nausea. During the 8000-ft session, a 29-year-old woman withdrew at hour 9 for personal reasons, and three men withdrew — a 22-year-old at hour 9 for personal reasons, a 25-year-old at hour 9 because of back pain, and a 24-year-old at hour 5 because of nasal congestion. In addition, a 75-year-old asymptomatic woman was removed from the 8000-ft session at hour 5 by an investigator because of falling oxygen saturation (95% initial saturation, 78% at hour 5, and 95% immediately after repressurization).

a 75-year-old asymptomatic woman, because her oxygen saturation had decreased to 78%. Immediately after repressurization, it rose to 95%, her pre-exposure value. Eleven other participants withdrew voluntarily during the study: eight because of symptoms of discomfort and three for personal reasons (Fig. 1).

Barometric pressure and the corresponding altitude were the only environmental variables that

varied systematically among the test sessions. Mean relative humidity was higher at ground level than at the other altitudes (see Table RI of the Supplementary Appendix).

OXYGEN SATURATION

Mean oxygen saturation decreased as altitude increased, with a maximum decrease of 4.4 percentage points (95% confidence interval [CI], 3.9 to 4.9)

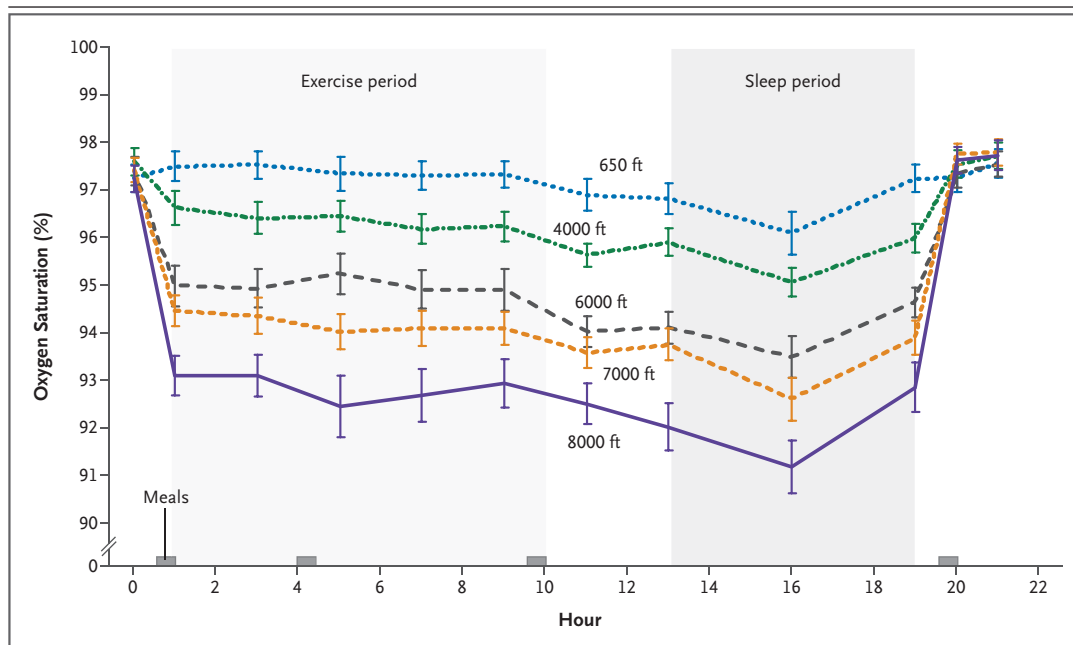


Figure 2. Mean Oxygen Saturation during Test Session.

During the exercise period, 209 of 431 participants 60 years of age or less were randomly assigned to exercise, which consisted of walking on a horizontal treadmill at a rate of 3.0 mi (4.8 km) per hour for 10 minutes of every hour during 9 hours of the test session. Oxygen saturation values in the sedentary group and pre-exercise values in the exercise group were used to calculate mean oxygen saturation during exercise hours. During the sleep period, with participants sleeping in coach-class airplane seats, lights were dimmed and interaction with participants was limited to a single measurement of oxygen saturation. I bars indicate 95% CIs.

at 8000 ft as compared with 650 ft (Fig. 2, and Fig. R1 of the Supplementary Appendix). At all times during the sessions, all interaltitude comparisons were significant. Mean oxygen saturation fell by 0.9 percentage point (95% CI, 0.7 to 1.1) during sleep, and it was lower in the older participants: 95.3% (95% CI, 95.1 to 95.5) in those less than 40 years of age, 94.5% (95% CI, 94.3 to 94.7) in those 40 to 60, and 93.8% (95% CI, 93.5 to 94.1) in those older than 60 years. Women had a higher mean oxygen saturation level than men (95.1% [95% CI, 94.9 to 95.2] vs. 94.3% [95% CI, 94.1 to 94.4]).

In the exercise group, the mean oxygen saturation after exercise was 1.3 percentage points lower than the value before exercise (95% CI, 1.1 to 1.6). During the exercise period (hours 1 to 9 of the study session), the mean pre-exercise oxygen saturation was 0.7 percentage point (95% CI, 0.4 to 1.0) higher in the exercise group than in the group of participants who did not exercise. There was no significant difference in mean oxygen saturation between the two groups after the exercise period (0.0 percentage point; 95% CI, -0.3 to 0.3) (see Table RII of the Supplementary Appendix).

ACUTE MOUNTAIN SICKNESS AND DISCOMFORT

Only 0.17% of the responses to the questionnaire (634 of 375,496) were missing; most missing responses (614 of 634) were due to failure to administer the test during hour 5 in one test session. The cumulative prevalence of acute mountain sickness (AMS-C factor score, >0.7) was 7.4% (with symptoms reported by 37 of 502 participants) and did not vary significantly among the altitudes studied (Table 2, Fig. 3, and Table RIII of the Supplementary Appendix). The results of the analyses of ESQ-IV factor scores were consistent whether published criterion scores for AMS-C and AMS-R (0.7 and 0.6, respectively) or time-dependent criterion scores for all factors were used to determine point or cumulative prevalences. We report hereafter only the results of the analysis of cumulative prevalence based on published criterion scores (AMS-C >0.7) to assess acute mountain sickness and the cumulative prevalence based on time-dependent criterion scores for other ESQ-IV factors to assess discomfort. For other results, see Tables RIV and RV and Figures R2, R3, and R4 of the Supplementary Appendix.

Table 2. Results of the Cox Proportional-Hazards Analyses.*

Outcome	Odds Ratios for Independent Variables†					
	Altitude	Oxygen Saturation	Exercise	Sex	Age	Age ²
Acute mountain sickness‡						
Cox model 1§	1.11 (0.96–1.28)	—	1.05 (0.48–2.27)	1.66 (0.83–3.32)	0.80 (0.53–1.19)	0.94 (0.78–1.13)
Cox model 2¶	1.06 (0.88–1.27)	0.92 (0.77–1.10)	1.04 (0.48–2.25)	1.78 (0.87–3.62)	0.77 (0.51–1.17)	0.95 (0.79–1.15)
Altitude-related malaise						
Cox model 1	1.13 (1.02–1.25)	—	0.77 (0.45–1.32)	1.48 (0.91–2.40)	0.64 (0.46–0.90)	0.86 (0.74–1.00)
Cox model 2	1.04 (0.91–1.18)	0.87 (0.77–0.98)	0.80 (0.47–1.36)	1.69 (1.03–2.78)	0.60 (0.43–0.85)	0.86 (0.74–1.00)
Muscular discomfort						
Cox model 1	1.25 (1.06–1.47)	—	0.38 (0.18–0.82)	2.20 (1.11–4.39)	0.56 (0.34–0.90)	0.84 (0.68–1.04)
Cox model 2	1.07 (0.89–1.29)	0.80 (0.69–0.92)	0.41 (0.19–0.86)	2.88 (1.41–5.89)	0.48 (0.29–0.79)	0.84 (0.68–1.04)
Exertion						
Cox model 1	1.11 (0.98–1.27)	—	0.74 (0.37–1.50)	1.28 (0.69–2.38)	0.69 (0.45–1.04)	0.83 (0.68–1.00)
Cox model 2	1.00 (0.85–1.18)	0.84 (0.73–0.98)	0.80 (0.39–1.61)	1.51 (0.80–2.84)	0.64 (0.42–0.98)	0.84 (0.69–1.02)
Fatigue						
Cox model 1	1.14 (1.01–1.29)	—	0.63 (0.34–1.16)	2.31 (1.27–4.21)	0.53 (0.33–0.84)	0.93 (0.77–1.12)
Cox model 2	1.03 (0.88–1.19)	0.84 (0.73–0.96)	0.64 (0.35–1.19)	2.79 (1.50–5.19)	0.48 (0.30–0.77)	0.93 (0.77–1.12)
Cold stress						
Cox model 1	1.11 (1.02–1.21)	—	1.21 (0.74–1.97)	2.79 (1.77–4.41)	0.91 (0.72–1.13)	0.92 (0.82–1.03)
Cox model 2	1.16 (1.03–1.29)	1.06 (0.95–1.19)	1.16 (0.70–1.89)	2.66 (1.67–4.24)	0.93 (0.73–1.17)	0.92 (0.83–1.03)

* Cumulative prevalence is based on time-dependent criterion scores except as noted.

† For each outcome, the displayed odds ratios (and 95% confidence intervals) are the ratios of the odds of designated outcome at the following levels of the independent variable: altitude=[(altitude in feet ÷ 1000) + 1] ÷ [altitude in feet ÷ 1000]; oxygen saturation=(SaO₂ + 1%) ÷ SaO₂; exercise=active ÷ sedentary; sex=women ÷ men; age=[(age in years – 50) ÷ 10 + 1] ÷ [(age in years – 50) ÷ 10]; age²=[(age in years – 50) ÷ 10 + 1]² ÷ [(age in years – 50) ÷ 10]².

‡ Acute mountain sickness is defined as the cumulative prevalence of acute mountain sickness–cerebral (AMS-C) based on the published criterion score.

§ Cox model 1 included altitude (in 1000-ft increments), exercise, sex, age, and age².

¶ Cox model 2 included oxygen saturation in addition to all the variables included in Cox model 1.

The cumulative prevalence of some measures of discomfort — the ESQ-IV factors for altitude-related malaise, muscular discomfort, and fatigue (Table 1) — were directly related to altitude and inversely related to oxygen saturation. The cumulative prevalences of altitude-related malaise and muscular discomfort at 8000 ft were significantly greater than the prevalences at the lower altitudes combined. At both 7000 ft and 8000 ft, the cumulative prevalence of the ESQ-IV factor for fatigue exceeded that at the combined lower altitudes. The exertion factor was inversely related to oxygen saturation, and its cumulative prevalence at 7000 ft differed from that at the combined lower altitudes. These differences in measures of discomfort became apparent after 3 to 9 hours of exposure to altitude. The cold-stress factor was not related to

altitude in the log-rank test but was related to altitude, although not to oxygen saturation, in the Cox proportional-hazards models. The cumulative prevalence of cold stress at 650 ft was less than that at the higher altitudes. The cumulative prevalences of the factors distress, alertness, and ear, nose, and throat discomfort through the 19th hour (the last hour of measurements before repressurization) were not significantly affected by altitude or oxygen saturation (Table 2 and Fig. 3).

Exercise was associated with a reduced overall cumulative prevalence of muscular discomfort but did not affect other outcomes. Women were more likely than men to report discomfort (Table 2). Participants in the oldest age group were less likely than those in the other age groups to report discomfort, and those in the middle age group

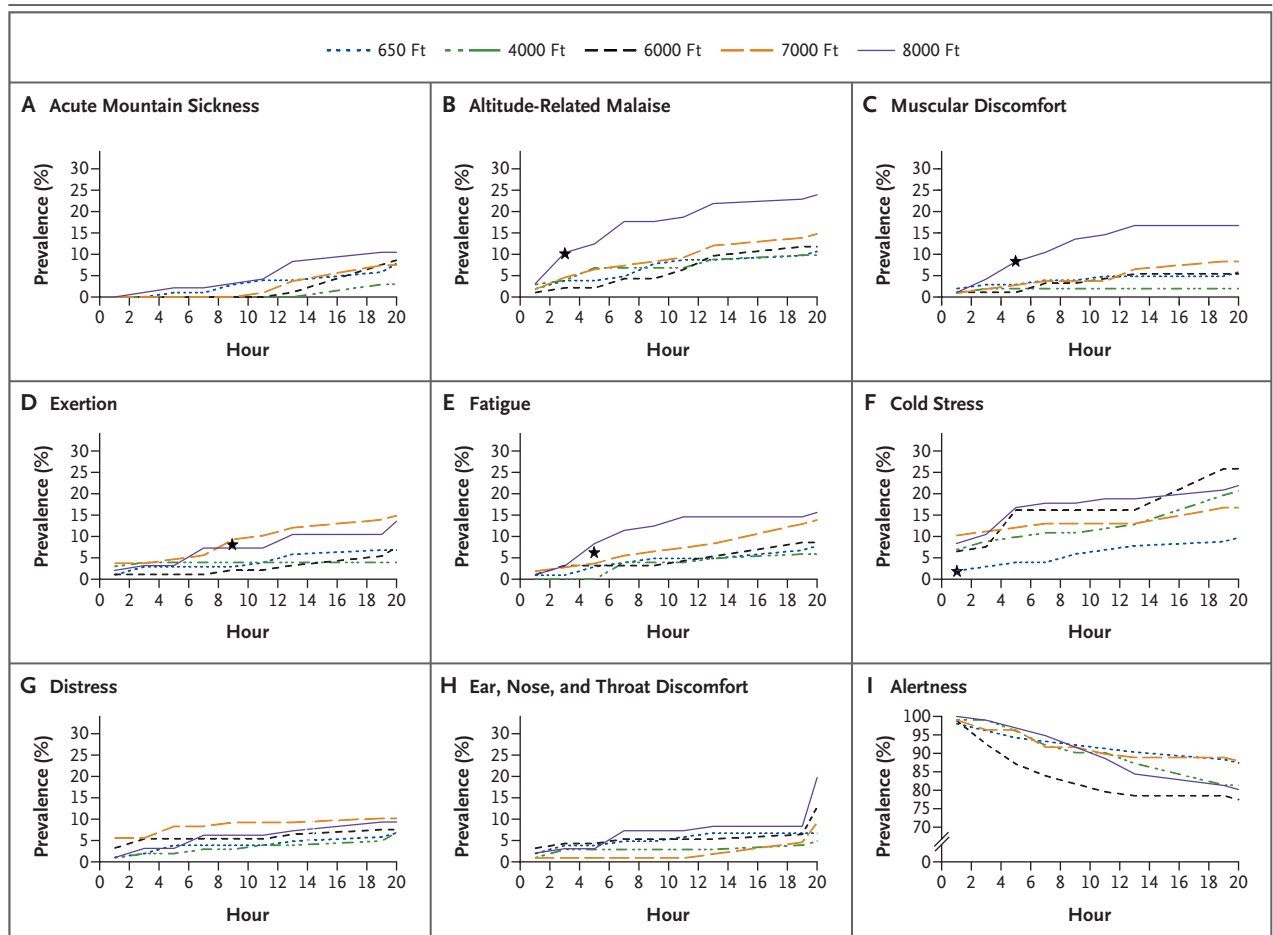


Figure 3. Cumulative Prevalence of ESQ-IV Factors.

Acute mountain sickness is the cumulative prevalence of acute mountain sickness–cerebral (AMS-C) based on the published criterion score. The cumulative prevalence of acute mountain sickness at 8000 ft was significantly different from the prevalence at the lower altitudes combined only at hour 13. Discomfort was evaluated with the use of all other factors based on time-dependent criterion scores. Altitude-related malaise, muscular discomfort, exertion, fatigue, and cold stress were significantly related to altitude. A star on a line indicates the time at which the difference between the altitude represented by that line and all other altitudes combined became significant and remained significant for the balance of the test session. A star between two lines indicates that the comparison was between the altitudes represented by those two lines combined with all other altitudes combined.

were most likely to do so (Table 2, and Fig. R5 of the Supplementary Appendix).

The post hoc analysis showed that the five ESQ-IV symptoms that most contributed to discomfort were backache, headache, light-headedness, shortness of breath, and impaired coordination (Table RVI of the Supplementary Appendix).

SENSORY AND PSYCHOMOTOR PERFORMANCE

None of the tests of sensory perception or psychomotor performance were significantly affected by altitude over the range of altitudes investigated (see Table RVII of the Supplementary Appendix).

ADVERSE EVENTS

No serious adverse events were identified during the test sessions, but in four participants, serious medical conditions were detected 1 to 30 days later. One participant was empirically treated for pneumonia at an acute care clinic 1 day after exposure to an altitude of 6000 ft. The relationship of this event to the study conditions was classified as unknown. The remaining three serious adverse events (acute myelogenous leukemia diagnosed 2 weeks after exposure to 650 ft, lung and prostate cancer diagnosed several days after exposure to 6000 ft, and sarcoidosis diagnosed 4 weeks

after exposure to 8000 ft) were considered to be unrelated to study exposures. Fifteen nonserious adverse events occurred during the chamber exposure, some of which (four instances of pain in four participants from failure to equilibrate middle-ear pressure during recompression, insect bites in two persons during the same session, a panic attack, and low oxygen saturation in an asymptomatic elderly woman at 8000 ft) were classified as related to study conditions.

DISCUSSION

We found that ascent from ground level to 8000 ft by healthy unacclimatized adults lowered oxygen saturation by approximately 4 percentage points. This degree of hypoxemia did not affect the occurrence of acute mountain sickness, other adverse health outcomes, or impairment of sensory or psychomotor performance, but it was associated with an increased prevalence of discomfort after 3 to 9 hours. Exercise reduced muscular discomfort but did not significantly affect other ESQ-IV factors.

Our study was performed under controlled, highly replicable conditions in a hypobaric chamber where the barometric pressure was the only environmental factor that varied systematically. The results of this randomized, controlled study of the effects of simulated altitude exposure on the occurrence of discomfort cannot be explained by other flight-related factors commonly postulated to cause symptoms in commercial-airline passengers. Two studies conducted in commercial aircraft reported oxygen saturation levels lower than those found in our study, raising the possibility that our findings may underestimate the prevalence of discomfort experienced by passengers.^{24,25}

The ESQ-IV is considered a valid and reliable instrument for detecting acute mountain sickness.²⁶ Although we used the traditional methods of ESQ-IV analysis to measure acute mountain sickness, we did not use those methods to evaluate discomfort. Instead, we used time-dependent criterion scores based on frequency distributions of factor scores reported at ground level to differentiate the effects of prolonged confinement from the effects of hypobaric hypoxia. Although this

modification increased the specificity of our analysis, the results based on it are not directly comparable to those of other studies based on ESQ-IV factors. Nevertheless, our results for altitude-related discomfort are generally consistent with reports of acute mountain sickness at similar terrestrial altitudes.^{2-7,27} We found that reports of discomfort were least frequent in the oldest age group and that the timing of the onset of discomfort was in close agreement with the range of 6 to 10 hours reported for acute mountain sickness.² Although the medical literature is inconsistent concerning the distribution of cases of acute mountain sickness according to sex,^{2,4,28} we found that men were less likely than women to report discomfort. The discomfort reported by our participants may represent subclinical acute mountain sickness.

There are few reports of the effects of exposure to altitudes below 10,000 ft (3048 m) in unacclimatized people. In 1971, McFarland summarized studies of hypoxia in normobaric conditions, hypobaric chambers, aircraft, and mountain environments that explored the effects of hypoxia relevant to commercial and military flight.²⁹ His review, which focused on physiological and psychological performance measures, coupled with the experience of military aviators during World War II, led to a general consensus that hypobaric hypoxia associated with barometric pressure equivalent to 8000 ft is not harmful to healthy people.³⁰ Our findings support this conclusion. However, we did find evidence that the level of hypoxemia manifested at 7000 to 8000 ft played an important role in the development of discomfort. On the basis of our findings, we conclude that maintaining a cabin altitude of 6000 ft or lower (equivalent to a barometric pressure of 609 mm Hg or higher) on long-duration commercial flights will reduce the occurrence of discomfort among passengers.

Supported by the Boeing Company.

No potential conflict of interest relevant to this article was reported.

We thank G.W. Tatum (technical director); D.S. Moyers, J.E. Jones, and J.R. Catrett (crew chiefs); Ranae Williams (administrator); and the research assistants from the Center for Aerospace and Hyperbaric Medicine at Oklahoma State University Center for Health Sciences; the study participants; and the people of the greater Tulsa area.

REFERENCES

1. Pressurized cabins, 14 C.F.R. § 25.841 (2006).
2. Hackett PH, Roach RC. High-altitude illness. *N Engl J Med* 2001;345:107-14.
3. Pigman EC, Karakla DW. Acute mountain sickness at intermediate altitude: military mountainous training. *Am J Emerg Med* 1990;8:7-10.
4. Honigman B, Theis MK, Koziol-McLain HJ, et al. Acute mountain sickness in a general tourist population at moderate altitudes. *Ann Intern Med* 1993;118:587-92. [Erratum, *Ann Intern Med* 1994;120:698.]
5. Roach RC, Houston CS, Honigman B, et al. How well do older persons tolerate moderate altitudes? *West J Med* 1995; 162:32-6.
6. Houston CS. Incidence of acute mountain sickness: a study of winter visitors to six Colorado resorts. *Am Alpine J* 1985; 27:162-5.
7. Montgomery AB, Millis J, Luce JM. Incidence of acute mountain sickness at intermediate altitude. *JAMA* 1989;261:732-4.
8. Schneider M, Bernasch D, Weymann J, Holle R, Bartsch P. Acute mountain sickness: influence of susceptibility, preexposure, and ascent rate. *Med Sci Sports Exerc* 2002;34:1886-91.
9. West JB. The physiologic basis of high-altitude diseases. *Ann Intern Med* 2004; 141:789-800.
10. Roach RC, Green ER, Schoene RB, Hackett PH. Arterial oxygen saturation for prediction of acute mountain sickness. *Aviat Space Environ Med* 1998;69:1182-5.
11. Air Transport Medicine Committee, Aerospace Medical Association. The very large airplane: safety, health, and comfort considerations. *Aviat Space Environ Med* 1997;68:943-6.
12. Brown TP, Shuker LK, Rushton L, Warren F, Stevens J. The possible effects on health, comfort and safety of aircraft cabin environments. *J R Soc Health* 2001; 121:177-84.
13. Committee on Air Quality in Passenger Cabins of Commercial Aircraft, Board on Environmental Studies and Toxicology, Division on Earth and Life Sciences, National Research Council. The airliner cabin environment and the health of passengers and crew. Washington, DC: National Academy Press, 2002.
14. Brundrett G. Comfort and health in commercial aircraft: a literature review. *J R Soc Health* 2001;121:29-37.
15. Rayman RB. Passenger safety, health, and comfort: a review. *Aviat Space Environ Med* 1997;68:432-40.
16. Wagner PD, Gale GE, Moon RE, Torre-Bueno JR, Stolp BW, Saltzman HA. Pulmonary gas exchange in humans exercising at sea level and simulated altitude. *J Appl Physiol* 1986;61:260-70.
17. Roach RC, Maes D, Sandoval D, et al. Exercise exacerbates acute mountain sickness at simulated high altitude. *J Appl Physiol* 2000;88:581-5.
18. Banderet LE, Shukitt-Hale B. Cognitive performance, mood, and neurological status at high terrestrial elevation. In: Lounsbury DE, Bellamy RF, Zajtchuk R, eds. Medical aspects of harsh environments. Washington, DC: Office of the Surgeon General, 2002:729-63.
19. Sampson JB, Cymerman A, Burse RL, Maher JT, Rock PB. Procedures for the measurement of acute mountain sickness. *Aviat Space Environ Med* 1983;54:1063-73.
20. Agresti A. Categorical data analysis. New York: Wiley, 1990.
21. Lawless JF. Statistical models and methods for lifetime data. New York: Wiley, 1982.
22. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
23. Bishop YMM, Fienberg SE, Holland PW. Discrete multivariate analysis: theory and practice. Cambridge, MA: MIT Press, 1982.
24. Cottrell JJ, Lebovitz BL, Fennell RG, Kohn GM. Inflight arterial saturation: continuous monitoring by pulse oximetry. *Aviat Space Environ Med* 1995;66:126-30.
25. Kelly PT, Swanney MP, Frampton C, Seccombe LM, Peters MJ, Beckert LE. Normobaric hypoxia inhalation test vs. response to airline flight in healthy passengers. *Aviat Space Environ Med* 2006; 77:1143-7.
26. Savourey G, Guinet A, Besnard Y, Garcia N, Hanniquet AM, Bittel J. Evaluation of the Lake Louise acute mountain sickness scoring system in a hypobaric chamber. *Aviat Space Environ Med* 1995;66: 963-7.
27. Dean AG, Yip R, Hoffmann RE. High incidence of mild acute mountain sickness in conference attendees at 10000 foot altitude. *J Wilderness Med* 1990;1:86-92.
28. Johnson TS, Rock PB. Acute mountain sickness. *N Engl J Med* 1988;319:841-5.
29. McFarland RA. Human factors in relation to the development of pressurized cabins. *Aerosp Med* 1971;42:1303-18.
30. Committee on Airliner Cabin Air Quality, Board on Environmental Studies and Toxicology, Commission on Life Sciences, National Resource Council. The airliner cabin environment: air quality and safety. Washington, DC: National Academy Press; 1986.

Copyright © 2007 Massachusetts Medical Society.

POWERPOINT SLIDES OF JOURNAL FIGURES AND TABLES

At the *Journal's* Web site, subscribers can automatically create PowerPoint slides. In a figure or table in the full-text version of any article at www.nejm.org, click on Get PowerPoint Slide. A PowerPoint slide containing the image, with its title and reference citation, can then be downloaded and saved.