

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Effect of Commercial Aircraft Cabin Altitude on Passenger Discomfort

Supplementary Appendix

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Test Conditions

The study was conducted in a hypobaric chamber manufactured by C.G.S. Scientific Corporation which had an airlock that allowed ingress and egress of personnel and supplies without affecting the altitude in the main chamber. Twelve coach-class airplane seats spaced 34 inches from seat back to seat back (typical United States domestic commercial aircraft seat spacing is 28 - 35 inches, with most at 31 inches.), 2 video monitors and an exercise treadmill were installed in the 8 feet wide x 7 feet high x 20 feet long (2.4 m x 2.1 m x 6.1 m) main section of the chamber. The airplane seats served as sleeping space. Toilet facilities were provided. Ventilation was maintained at 10 cubic feet / minute / occupant (0.283 cubic meters / minute / occupant) at all altitudes using conditioned air from the building housing the chamber.

Point Prevalence and Cumulative Prevalence

Criterion scores have been established to assist in interpreting the results of the computed ESQ-IV factor scores of a volunteer (see below). We considered a volunteer to have experienced the factor at hour t if the factor score for that factor was larger than its corresponding criterion score at hour t . The **point prevalence** for the symptom at hour t is the proportion of volunteers who experienced the symptom *at* hour t . The **cumulative prevalence** for the symptom at hour t is the proportion of volunteers who had experienced the symptom *by* hour t . Once a volunteer had a score greater than the criterion score for a factor, he was considered a "case" in the determination of cumulative prevalence at all subsequent hours even if his score dropped below the criterion score for the subsequent hours.

Time Dependent Criterion Scores

The Environmental Symptom Questionnaire IV (ESQ-IV) is a validated survey consisting of 68 symptoms, (Table MII).¹⁹ Each symptom was scored 0 if the respondent did not have the symptom and on a scale of 1 to 5 if the symptom was present, with 1 = Slight, 2 = Somewhat, 3 = Moderate, 4 = Quite a bit, and 5 = Extreme. Factor scores were calculated using published symptom weights (Table MIII).¹⁹ Note that for the Alert factor, symptoms 56, 57, 58, 59 and 65 were placed on a reverse scale by subtracting the symptom score from 5. These new variables are called 56r, 57r, 58r, 59r and 65r.

Sampson *et. al.* published criterion scores for AMS-C or AMS-R, specifically $AMS-C > 0.7$ and $AMS-R > 0.6$, which are used to separate "noise" from "signal" in the factor scores calculated from responses to the ESQ-IV.¹⁹ These criterion scores are independent of the number of hours of exposure to altitude the volunteers had experienced.

Figures M2 and M3 of Supplementary Appendix: Methods display the distributions of the AMS-C and AMS-R scores at different times during the simulated 20-hour flight at ground level (650 feet). From these figures and the summary statistics in Supplementary Appendix: Methods Table MIV it appears that both the mean and the variance of factor scores increase over time. Thus the distributions of AMS-C or AMS-R scores appeared to depend on the number of hours of the 20-hour simulated flight that the volunteers had experienced.

Similar patterns were observed for the distributions of scores for AMS-C and AMS-R at the other altitudes, suggesting that the assumption that AMS-C and AMS-R criterion scores are independent of time might not be valid for the altitudes and exposure time investigated. This observation suggests the need for developing factor criterion scores that are time-dependent.

Since altitude-related symptoms occur only when a volunteer is exposed to an altitude to which she/he is not acclimatized, it is reasonable to classify the factor scores from volunteers at the altitude at which they reside, which in this study was 650 feet above sea level, as being due to noise. In our data, there are two sets of these scores: those calculated from all 502 volunteers prior to depressurizing the chamber; and those calculated from the 103 passengers at the ground level altitude group (650 feet) during the 20-hour simulated flight.

The following rules were used to define the time-dependent criterion for all ESQ-IV factors at each hour of exposure.

- i. Determine the 97.5th percentile of the factor scores prior to depressurizing the chamber as follows:
 - a. Calculate the 502 scores for each factor from the ESQ-IV administered prior to depressurizing the chamber.
 - b. Exclude from this set of scores any volunteer with outlier responses (AMS-C > 1.5, AMS-R > 1.5).
 - c. Determine the 97.5th percentile of the remaining factor scores.
- ii. Determine the 97.5th percentile of the factor scores for hour t ($t = 1, 3, 5, 7, 9, 11, 13, 19, 20, 21$) as follows:
 - a. Calculate the 103 scores for each factor from the ESQ-IV administered at ground level altitude (650 feet) at hour t .
 - b. Exclude from this set of scores any volunteer with outlier responses (AMS-C > 1.5, AMS-R > 1.5)
 - c. For each hour t , determine the 97.5th percentile of the factor scores
- iii. Define the criterion score at hour t to be the larger of the 97.5th percentile from hour 0 and the 97.5th percentile from the t^{th} hour.

Defining criterion scores in this way introduces a time-dependency that improves our ability to distinguish the effects of exposure to altitude from those of unidentified time-related stressors associated with being in the chamber. The outlier exclusion criteria resulted in the exclusion of a single factor score in hour 5 and in hour 19.

Supplementary Appendix: Methods Tables MIV gives relevant statistics for AMS-C, and MV the resulting time-dependent criterion scores for AMS-C and all other ESQ-IV factors. We see that the 97.5th percentile of the 502 scores from hour 0 is 0.432. Up to and including hour 7, the 97.5th percentile at 650 feet for the t^{th} hour is less than 0.432 and so, up to and including hour 7 the time-dependent criterion for AMS-C is 0.432. Beyond hour 7, the 97.5th percentile at 650 feet for the t^{th} hour is greater than 0.432 and so beyond hour 7 the time-dependent criterion is 97.5th percentile at 650 feet for hour t .

We considered alternative noise exclusion levels to that of 97.5% described above. A rationale for using the 97.5% noise exclusion level as opposed to some other noise exclusion level is that at the mid-flight period (hours 9 and 11) the criteria for AMS-C and AMS-R are similar to the published criteria of Sampson *et. al.*¹⁹

To illustrate the calculation of cumulative prevalence, suppose that we have the AMS-R factor scores for four hypothetical volunteers in Supplementary Appendix: Methods Table MVI. The data, including the time-dependent criterion are plotted in Supplementary Appendix: Methods Figure M4. We see that at hour 3, volunteer B's factor score exceeded the criterion of 0.402. At hours 5 and 7, the factor scores for both A and B exceeded the appropriate time-dependent criterion. At hour 9 the factor score for volunteer B no longer exceeded the hour 9 criterion. So at hour 9, the point prevalence is based on only one volunteer since only one volunteer (A) exceeds the hour 9 criterion, but the cumulative prevalence is based on two volunteers since two volunteers (A and B) had exceeded a time-dependent criterion by hour 9. The point and the cumulative prevalence by hour are given in the last two columns of Supplementary Appendix: Methods Table MVII. Over the course of the 20-hour exposure three of the volunteers exceeded at least one time-dependent criterion and so the cumulative prevalence is based on three volunteers.

Post-hoc Symptom-by-Symptom Analysis

A post-hoc analysis of the symptom scores was conducted to look at the effect of altitude on the scores of the individual symptoms. The objective of this analysis was to examine which symptoms might be the important contributors to any observed significant effect that altitude has on factor scores. The weights in Table MIII were used to combine individual symptoms to obtain an overall factor score. Consequently a symptom that is significantly affected by altitude might have a small effect on the factor score because the symptom has a low weight.

Ordered categorical data are frequently analyzed by fitting a standard regression-type model to scores that are applied to the categories. In this appendix we describe a method using a proportional odds model. This modeling approach depends on less restrictive assumptions.²⁰

A separate proportional odds model was fit for each of the 68 ESQ symptoms and for each hour (hour=1, 3, 5, 7, 9, 11, 13, 19, 20). All models included terms for activity (sedentary vs. exercise), gender, age (young, middle-age, older) and altitude. Altitude was considered either a continuous covariate, in which case a test for slope was conducted, or a categorical covariate, in which case tests involving altitude contrasts of interest were conducted.

A crude measure of the contribution of each symptom to discomfort was developed by counting the number of times during the test session that the slope of the symptom or selected contrasts were significantly related to altitude and multiplying that number by the factor-specific weights of the symptom. These products were then summed over all the altitude-related factors to assess the contribution of that symptom to discomfort. The symptoms were then ranked from high to low by this sum of products and the highest ranked symptoms were considered to be important contributors. (Supplementary Appendix Methods: Table RIX)

Table MI Disqualifying Conditions

Chronic Conditions†	<ul style="list-style-type: none"> • COPD* • Asthma* • Restrictive Lung Diseases* • Coronary Artery Disease* • Arrhythmia* • Congestive Heart Failure* • Cerebrovascular accident • Lower Extremity DVT • Diabetes mellitus, poorly controlled (change in medication doseage/ frequency in past month) 	<ul style="list-style-type: none"> • Seizure within past 6 months. • Claustrophobia that would impair chamber participation • Musculoskeletal disorder that impairs self care and self locomotion. • Current anemia of any cause • Sickle Cell Trait • Other conditions, which, in the opinion of the Principal Investigator, might result in excessive risk upon exposure to a hypobaric environment.
Acute Conditions‡	<ul style="list-style-type: none"> • Contagious disease (including upper respiratory illness) • Pregnancy • Within 4 weeks of a major surgical procedure. • Dental abscesses 	<ul style="list-style-type: none"> • Scuba diving within 24 hours of test • Donated blood within 24 hours of test • Under the influence of drugs or alcohol

* If AMS Disability Class III or worse

† Screening was conducted during orientation session days to weeks before study session.

‡ Screening was conducted morning of study session

Table MII. ESQ-IV Questionnaire¹⁹

		Not at All	Slight	Some-what	Moderate	Quite a bit	Extreme
1.	I felt lightheaded.....	0	1	2	3	4	5
2.	I had a headache.....	0	1	2	3	4	5
3.	I felt sinus pressure.....	0	1	2	3	4	5
4.	I felt dizzy.....	0	1	2	3	4	5
5.	I felt faint.....	0	1	2	3	4	5
6.	My vision was dim.....	0	1	2	3	4	5
7.	My coordination was off.....	0	1	2	3	4	5
8.	I was short of breath.....	0	1	2	3	4	5
9.	It was hard to breathe.....	0	1	2	3	4	5
10.	It hurt to breathe.....	0	1	2	3	4	5
11.	My heart was beating fast.....	0	1	2	3	4	5
12.	My heart was pounding.....	0	1	2	3	4	5
13.	I had a chest pain.....	0	1	2	3	4	5
14.	I had chest pressure.....	0	1	2	3	4	5
15.	My hands were shaking or trembling.....	0	1	2	3	4	5
16.	I had a muscle cramp.....	0	1	2	3	4	5
17.	I had stomach cramps.....	0	1	2	3	4	5
18.	My muscles felt tight or stiff.....	0	1	2	3	4	5
19.	I felt weak.....	0	1	2	3	4	5
20.	My legs or feet ached.....	0	1	2	3	4	5
21.	My hands, arms, or shoulders ached.....	0	1	2	3	4	5
22.	My back ached.....	0	1	2	3	4	5
23.	I had a stomachache.....	0	1	2	3	4	5
24.	I felt sick to my stomach (nauseous).....	0	1	2	3	4	5
25.	I had gas pressure.....	0	1	2	3	4	5
26.	I had diarrhea.....	0	1	2	3	4	5
27.	I felt constipated.....	0	1	2	3	4	5
28.	I had to urinate more than usual.....	0	1	2	3	4	5
29.	I had to urinate less than usual.....	0	1	2	3	4	5
30.	I felt warm.....	0	1	2	3	4	5
31.	I felt feverish.....	0	1	2	3	4	5
32.	My feet were sweaty.....	0	1	2	3	4	5
33.	I was sweating all over.....	0	1	2	3	4	5
34.	My hands were cold.....	0	1	2	3	4	5

Table MII. ESQ-IV Questionnaire¹⁹

		Not at All	Slight	Some-what	Moderate	Quite a bit	Extreme
35.	My feet were cold.....	0	1	2	3	4	5
36.	I felt chilly.....	0	1	2	3	4	5
37.	I was shivering.....	0	1	2	3	4	5
38.	Parts of my body felt numb.....	0	1	2	3	4	5
39.	My skin was burning or itchy.....	0	1	2	3	4	5
40.	My eyes felt irritated.....	0	1	2	3	4	5
41.	My vision was blurry.....	0	1	2	3	4	5
42.	My ears felt blocked up.....	0	1	2	3	4	5
43.	My ears ached.....	0	1	2	3	4	5
44.	I couldn't hear well.....	0	1	2	3	4	5
45.	My ears were ringing.....	0	1	2	3	4	5
46.	My nose felt stuffed up.....	0	1	2	3	4	5
47.	I had a runny nose.....	0	1	2	3	4	5
48.	I had a nose bleed.....	0	1	2	3	4	5
49.	My mouth was dry.....	0	1	2	3	4	5
50.	My throat was sore.....	0	1	2	3	4	5
51.	I was coughing.....	0	1	2	3	4	5
52.	I lost my appetite.....	0	1	2	3	4	5
53.	I felt sick.....	0	1	2	3	4	5
54.	I felt hungover.....	0	1	2	3	4	5
55.	I was thirsty.....	0	1	2	3	4	5
56.	I felt tired.....	0	1	2	3	4	5
57.	I felt sleepy.....	0	1	2	3	4	5
58.	I felt wide awake (couldn't sleep).....	0	1	2	3	4	5
59.	My concentration was off.....	0	1	2	3	4	5
60.	I was more forgetful than usual.....	0	1	2	3	4	5
61.	I felt worried or nervous.....	0	1	2	3	4	5
62.	I felt irritable.....	0	1	2	3	4	5
63.	I felt restless.....	0	1	2	3	4	5
64.	I was bored.....	0	1	2	3	4	5
65.	I felt depressed.....	0	1	2	3	4	5
66.	I felt alert.....	0	1	2	3	4	5
67.	I felt good.....	0	1	2	3	4	5
68.	I was hungry.....	0	1	2	3	4	5

Table MIII. Symptom Weights for ESQ-IV Factor Score¹⁹

<u>AMS-C</u>			<u>Ear, Nose, Throat</u>		
1	Lightheaded	0.489	3	Sinus	0.302
2	Headache	0.465	39	Burning/itchy	0.367
4	Dizzy	0.466	42	Ears blocked	0.441
5	Faint	0.346	43	Ears ached	0.300
6	Dim vision	0.510	44	Couldn't hear	0.759
7	Coordination	0.519	45	Ears ringing	0.784
19	Weak	0.387	46	Stuffy nose	0.329
24	Nauseated	0.347	49	Dry mouth	0.470
52	Lost appetite	0.413	50	Sore throat	0.555
53	Sick	0.692			
54	Hungover	0.584			
<u>AMS-R</u>			<u>Cold Stress</u>		
2	Headache	0.312	15	Shaking	0.358
8	SOB	0.745	19	Weak	0.331
9	Hard to breathe	0.763	27	Urinate frequently	0.447
10	Hurt to breathe	0.734	31	Feverish	0.364
17	Stomach cramp	0.516	34	Hands cold	0.642
22	Back ache	0.686	35	Feet cold	0.737
23	Stomach ache	0.744	36	Chilly	0.720
24	Nauseated	0.691	37	Shivering	0.580
46	Stuffy nose	0.534	61	Worried	0.520
48	Nose bleed	0.578			
58	Wide-awake	0.355			
65	Depressed	0.480			
<u>Muscular Discomfort</u>			<u>Alert</u>		
16	Muscle cramp	0.402	56r	Tired	0.314
18	Tight stiff	0.594	57r	Sleepy	0.300
19	Weak	0.307	58r	Wide-awake	0.379
20	Legs/feet ache	0.492	59r	Concentration	0.351
21	Hands/arms ache	0.406	65r	Depressed	0.300
22	Back ache	0.303	66	Alert	0.783
25	Gas pressure	0.317	67	Good	0.787
38	Numb	0.315			
55	Thirsty	0.330			
<u>Distress</u>			<u>Exertion</u>		
10	Hurt to breathe	0.315	1	Lightheaded	0.371
13	Chest pain	0.566	8	SOB	0.321
14	Chest pressure	0.540	9	Hard to breathe	0.419
51	Coughing	0.523	10	Hurt to breathe	0.351
53	Sick	0.373	11	Fast Heart	0.573
56	Tired	0.348	12	Pounding heart	0.505
57	Sleepy	0.318	13	Chest pain	0.471
61	Worried	0.379	19	Weak	0.366
62	Irritable	0.546			
63	Restless	0.525			
64	Bored	0.492			
65	Depressed	0.479			
			<u>Fatigue</u>		
			1	Lightheaded	0.384
			4	Dizzy	0.418
			5	Faint	0.416
			19	Weak	0.492
			40	Eyes irritated	0.398
			41	Blurry vision	0.304
			47	Runny nose	0.319
			55	Thirsty	0.371
			56	Tired	0.665
			57	Sleepy	0.579
			58	Wide-awake	0.300
			59	Concentration	0.312

Table MIV. Summary Statistics for AMS-C and AMS-R at 650 feet

Hour	AMS-C					AMS-R			
	N	Mean	Std Dev	Max	97.5 %ile	N	Mean	Std Dev	Max
0	103	0.048	0.121	0.926	0.432	103	0.083	0.124	0.736
1	103	0.030	0.075	0.496	0.255	103	0.080	0.120	0.780
3	103	0.049	0.095	0.478	0.387	103	0.100	0.121	0.775
5	94	0.049	0.180	1.613	0.350	94	0.110	0.161	1.117
7	103	0.047	0.094	0.448	0.343	103	0.115	0.135	0.686
9	103	0.065	0.154	0.942	0.621	103	0.130	0.155	0.775
11	103	0.075	0.156	0.813	0.621	103	0.160	0.182	1.221
13	103	0.088	0.138	0.986	0.496	103	0.169	0.195	1.179
19	102	0.167	0.306	1.881	1.116	101	0.303	0.298	1.498
20	103	0.130	0.226	1.217	0.835	103	0.217	0.232	1.320
21	103	0.134	0.264	1.487	0.801	102	0.195	0.205	1.044

Table MV. Time-dependent Criterion Scores for ESQ-IV Factors*

Hour	Number of Factor Scores	AMS-C	AMS-R	Muscular Discomfort	Exertion	Fatigue	Cold Stress	Distress	ENT	Alert
0	502	0.432	0.402	0.724	0.328	1.067	0.893	0.541	0.554	2.678
1	103	0.432	0.402	0.752	0.328	1.067	1.150	0.541	0.904	2.825
3	103	0.432	0.402	0.992	0.389	1.067	0.893	0.720	0.822	2.678
5	93	0.432	0.402	1.038	0.328	1.067	0.893	0.724	0.900	2.799
7	103	0.432	0.471	1.450	0.328	1.067	0.893	0.885	0.904	2.678
9	103	0.621	0.587	1.686	0.328	1.338	1.200	1.128	1.076	2.678
11	103	0.621	0.593	1.942	0.328	1.410	0.983	1.403	1.081	2.853
13	103	0.496	0.603	1.834	0.328	1.756	0.953	1.435	1.047	3.059
19	101	1.116	1.174	2.928	0.657	2.052	1.170	1.886	1.257	3.665
20	103	0.835	0.912	2.722	0.328	1.985	0.893	1.743	1.065	3.371
21	103	0.801	0.775	3.050	0.328	2.210	1.017	1.277	1.076	3.405

* Time-dependent Criterion Score for factor at tth hour is greater of 97.5th percentile value for factor at Hour 0 and 97.5th percentile value for that factor at Hour t.

Table MVI. AMS-R Factor Scores for Four Hypothetical Volunteers

Hour	Volunteer				Time-Dependent Criterion	Point Prevalence	Cumulative Prevalence
	A	B	C	D			
1	0.30	0.20	0.25	0.15	0.402	$0/4 = 0\%$	$0/4 = 0\%$
3	0.35	0.45	0.30	0.30	0.402	$1/4 = 25\%$	$1/4 = 25\%$
5	0.65	0.50	0.30	0.35	0.402	$2/4 = 50\%$	$2/4 = 50\%$
7	0.65	0.55	0.35	0.35	0.471	$2/4 = 50\%$	$2/4 = 50\%$
9	0.70	0.55	0.50	0.40	0.587	$1/4 = 25\%$	$2/4 = 50\%$
11	0.80	0.55	0.70	0.45	0.593	$2/4 = 50\%$	$3/4 = 75\%$
13	1.00	0.58	0.70	0.55	0.603	$2/4 = 50\%$	$3/4 = 75\%$
19	1.20	0.70	0.80	0.65	1.174	$1/4 = 25\%$	$3/4 = 75\%$
20	1.20	0.70	0.80	0.70	0.912	$1/4 = 25\%$	$3/4 = 75\%$

Table MVII. Tests of Sensory and Psychomotor Performance

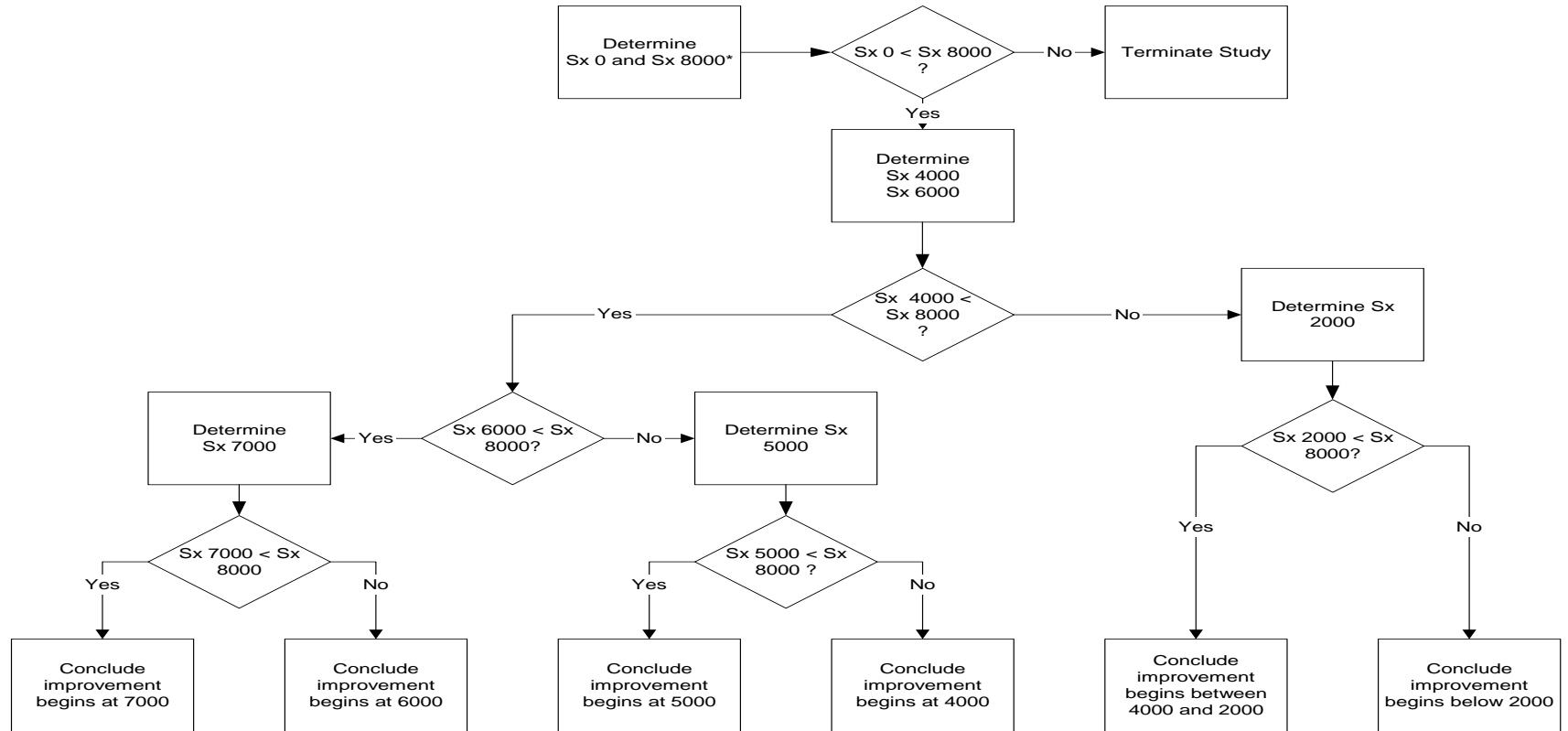
Test of Performance	Description
Purdue Pegboard*	<p>The Purdue Pegboard measures unilateral and bilateral dexterity. The device consists of a board with predrilled holes, pegs, collars, and washers. The pegs are inserted into the holes, and specified combinations of collars and washers in a specified sequence are assembled on the pegs by the test volunteer using the right, left, or both hands. Scoring is based on the number of “assemblies” created in a fixed time period. A higher score is better than a lower score.</p> <p>Normative scores (mean ± 1 SD): 43.6 ± 4.6 assembly job applicants. 39.3 ± 5.9 general factory work applicants 40.7 ± 6.7 production workers</p> <p>Purdue Pegboard Quick Reference Guide, Revised Edition, 1999. Lafayette, IN</p>
Kentucky Comprehensive Listening Test*	<p>The Kentucky Comprehensive Listening Test, published by the Kentucky Listening Research Center, is designed for college students and adults. The most recent version was published in 1985. The test is designed to overcome certain inherent difficulties in listening tests, in which the test measures intelligence rather than listening. The portion of the Test used in this study consisted of a list of 5 numbers presented orally followed by a statement describing one of the numbers. The volunteers were provided an answer sheet that may or may not have included the correct answer. Instructions were to circle the number described by the statement. Scoring was based on number of correct responses. A higher score is better than a lower score.</p> <p>Bostrom RN, Waldhart ES. 1983. The Kentucky Comprehensive Listening Test. Lexington, Kentucky: Kentucky Listening Research Center.</p>
Snellen Visual Acuity†	<p>A standard Snellen Eye Chart was used at a distance of 20 feet. The last row of letters the volunteer could read with less than a 50% error rate determined the measure of visual acuity. For analysis, the denominator of the Snellen "fraction" (20/30) was used as the "score". A lower score is better than a higher score.</p> <p>Norms are incompletely established, but most likely age dependent. Elliott DB, Yang KC, Whitaker D. Visual acuity changes throughout adulthood in normal, healthy eyes: seeing beyond 6/6. Optom Vis Sci, 1995; 72:186-91.</p>
Farnsworth-Munsell 100 Hue Color Discrimination‡	<p>The Farnsworth-Munsell 100 Hue test examines hue discrimination ability. The test kit contains 93 color discs and is conducted on a True Daylight Illuminator, a device that consists of a working surface and an electric light source that provides a standardized illumination environment. The test is performed by mixing a preselected set of disks and having the test volunteer arrange them in order of spectral progression. Scoring was based on number and magnitude of incorrect arrangements. A lower score is better than a higher score.</p> <p>Norms are age dependent. See Kinnear, PR, Sahraie A. New Farnsworth-Munsell 100 hue test norms of normal observers fore each year of age 5-22 and for age decades 30 – 70. Br J. Ophthalmol 2002; 86:1408-11.</p>

* Administered at hours 2, 5, 10, 13, 19, and 21

† Administered at hours 1, 3, 8, 13, 19, and 21

‡ Administered once per volunteer between hours 6 and 12

Altitude Selection Algorithm



* "Sx altitude" means cumulative prevalence of symptoms at that altitude

Figure M1. Logic used to select altitudes to study. Midway thru data collection at 4,000 feet and 6,000 feet it became apparent that 7,000 feet would be selected. To preserve blinding, 4,000 6,000 and 7,000 feet were included in random sequencing.

Figure M2. Distributions of AMS-C Scores for the 650 foot Group by Hour

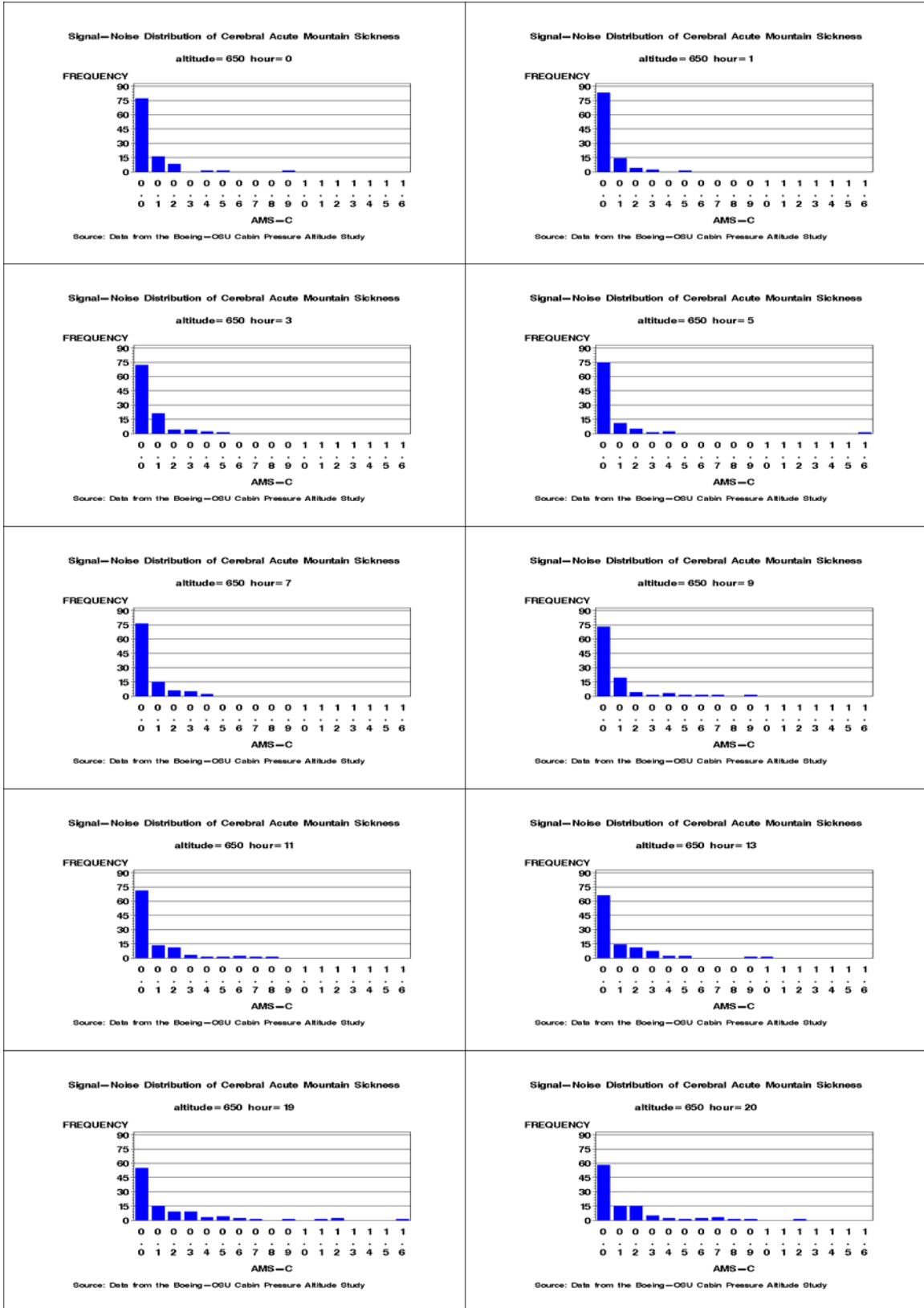
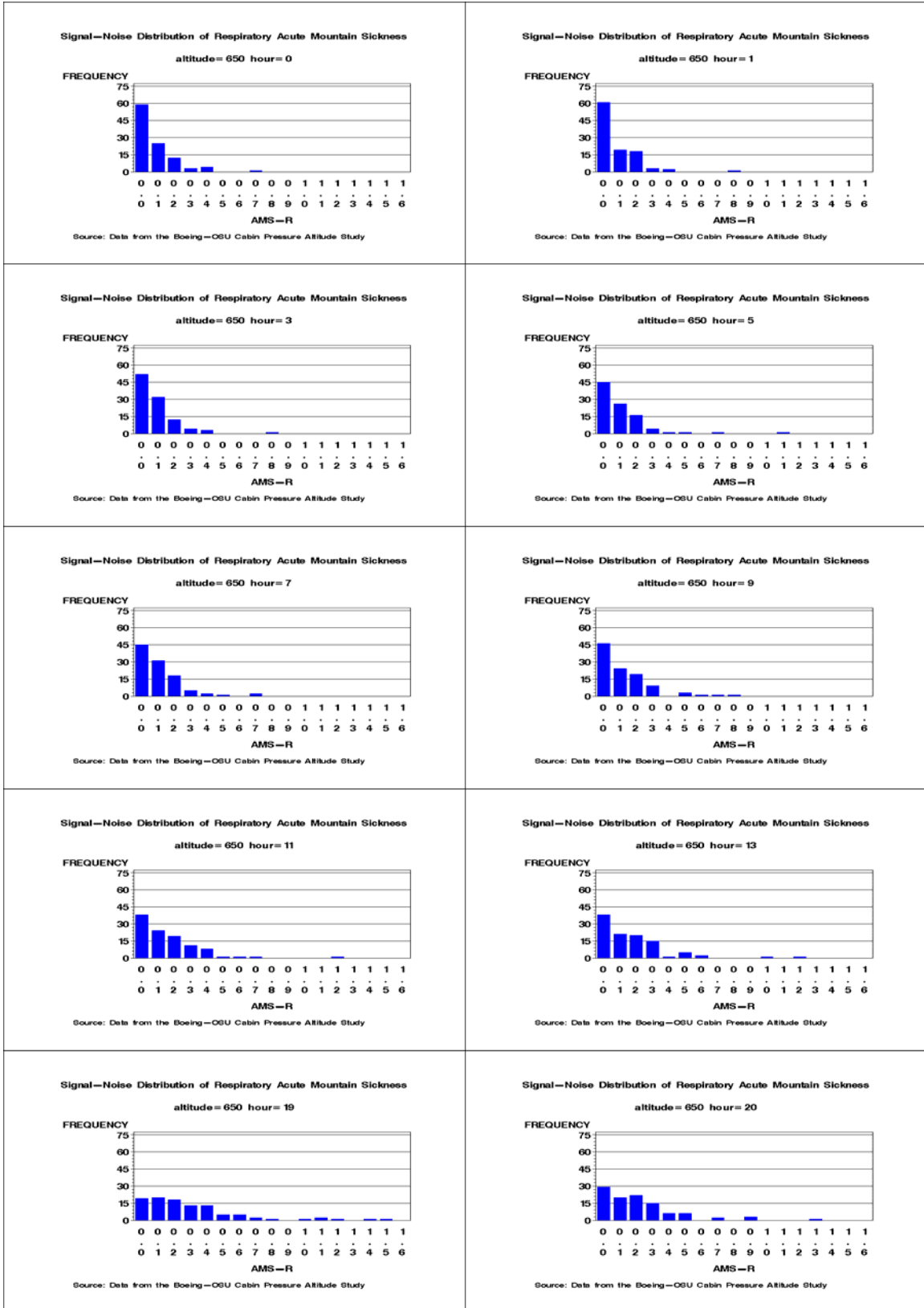


Figure M3. Distributions of AMS-R Scores for the 650 foot Group by Hour



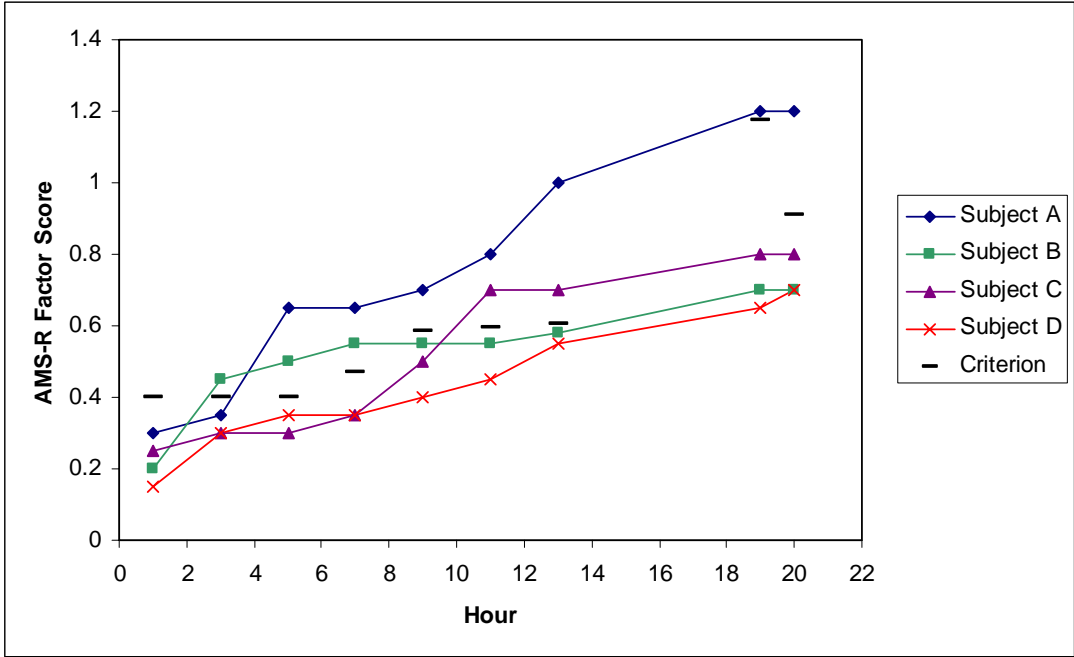


Figure M4. AMS-R Factor Scores for Four Hypothetical Volunteers

Notional Data. Displays AMS-R scores for 4 hypothetical participants and corresponding time-dependent criterion scores. See Table MV for point prevalence and cumulative prevalence calculations.

Table RI. Chamber environmental parameters

	650 feet (742 mm Hg)	4000 feet (656 mm Hg)	6000 feet (609 mm Hg)	7000 feet (586 mm Hg)	8000 feet (565 mm Hg)
Number of Sessions	9*	9	9	9	9†
Equivalent Altitude‡ feet	815 ± 64 (190 - 1400)	4029 ± 66 (620 - 4240)	6033 ± 25 (5930 - 6720)	6993 ± 24 (6740 - 7180)	8085 ± 50 (7936 - 8233)
Barometric Pressure mm Hg§	738 ± 1.8	655 ± 1.8	608 ± 0.7	587 ± 0.7	563 ± 1.4
Temperature degrees F	71.2 ± 2.2 (63.1 - 77.6)	71.5 ± 2.2 (62.1 - 77.2)	71.1 ± 2.3 (63.4 - 79.8)	70.7 ± 1.8 (64.2 - 76.3)	71.1 ± 2.1 (64.1 - 77.9)
Relative Humidity percent	43.3 ± 3.6 (28.3 - 59.5)	33.2 ± 2.7 (16.4 - 71.4)	34.8 ± 3.5 (16.3 - 55.8)	36.9 ± 2.9 (19.7 - 64.7)	36.6 ± 4.5 (17.4 - 71.6)

Results given in mean ± one standard deviation, (range)

* Data not available from 2 sessions

† Data not available from 1 session

‡ Instantaneous readings from hours 2 through 19

§ Pressure calculated from measured equivalent altitude using Standard Atmosphere²¹

Table RII. Preexercise SaO₂ in Exercising and Sedentary Groups

Hour	Young Age (21 – 39 years)				Middle Age (40 – 60 years)				Combined (21 – 60 years)				Old Age (61 – 78 years)
	Exercise		Sedentary	P value*	Exercise		Sedentary	P value*	Exercise		Sedentary	P value*	Sedentary
	Pre	Post			Pre	Post			Pre	Post			
1	96.11	94.90	94.88	<0.001	95.50	94.48	94.71	0.007	95.80	94.69	94.79	<0.001	94.52
3	95.97	94.63	95.23	0.003	95.28	93.82	94.71	0.06	95.62	94.23	94.97	<0.001	94.17
5	95.94	94.47	95.30	0.03	94.57	93.65	94.44	0.71	95.26	94.06	94.87	0.09	93.99
7	95.81	94.44	95.12	0.008	95.31	93.18	94.40	0.004	95.56	93.81	94.76	<0.001	93.51
9	95.86	94.67	95.29	0.03	94.73	93.37	94.35	0.22	95.30	94.02	94.82	0.02	94.03
1 - 9	95.94	94.62	95.16	<0.001	95.08	93.70	94.52	0.02	95.51	94.16	94.84	<0.001	94.04
11	95.05		95.12	0.75	94.27		94.19	0.78	94.66		94.66	0.99	93.62
13	94.97		95.06	0.71	94.24		94.30	0.83	94.61		94.68	0.69	93.59
16	94.50		94.34	0.59	93.05		93.26	0.55	93.77		93.80	0.91	92.51
19	95.43		95.40	0.93	94.61		94.66	0.88	95.02		95.03	0.96	94.08
11 - 19	94.99		94.98	0.98	94.04		94.10	0.79	94.51		94.54	0.85	93.45
Overall	95.52		95.08	0.01	94.62		94.34	0.19	95.07		94.71	0.01	93.78

Exercise hours

* Exerciser (PreExercise) vs Sedentary

Table RIII. Summary of P Values of Log Rank Analyses of Cumulative Prevalence Using Time-Dependent Criterion Scores*

Contrasts	Outcomes					
	AMS†	Altitude-related malaise	Muscular discomfort	Exertion	Fatigue	Cold Stress
All altitudes	0.33	0.02	0.002	0.03	0.10	0.05
8000 ft vs lower	0.17	<0.001	<0.001	0.12	0.05	0.34
7000 ft vs lower	0.70	0.26	0.12	0.004	0.04	0.75

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

† Cumulative prevalence of AMS-C based on published criterion score.

Table RIV. Summary of Analyses of Point Prevalence of ESQ-IV Factors*

Generalized Estimating Equations†							
Outcome	Contrast	P Value	Baseline	Altitude	Age_Activity	Sex	Time
Altitude-related malaise‡	8,000' vs lower	Odds greater at 8,000' P < 0.001	P=0.08	P < 0.001	P < 0.001	P = 0.11	P < 0.001
	7,000' vs lower	P = 0.37					
Altitude-related malaise	8,000' vs lower	Odds greater at 8,000' P < 0.001	P = 0.004	P = 0.01	P < 0.001	P = 0.95	P = 0.02
	7,000' vs lower	P = 0.32					
Muscular Discomfort	8,000' vs lower	Odds greater at 8,000' P < 0.001	P = 0.12	P = 0.02	P = 0.04	P = 0.15	P = 0.49
	7,000' vs lower	P = 0.15					
Distress	8,000' vs lower	P = 0.93	P = 0.02	P = 0.49	P = 0.01	P = 0.38	P = 0.10
	7,000' vs lower	Odds greater at 7,000' P = 0.04					

* **Point Prevalence based on Time-Dependent Criterion Scores except as noted**

† We used Generalized Estimating Equations (GEE) with the within-subject correlation over the flight time modeled as an autoregressive process. Other correlation structures give similar results. The models use the log-odds of the presence of a symptom (AMS, Distress, or Muscular Discomfort) as the response variable and included the following parameters:

Baseline Condition at Hour 0 (1 if symptom present at hour 0, 0 if symptom not present at hour 0),

Altitude (650, 4000, 6000, 7000, 8000),

Sex (Male = 1, Female = 0),

Age_Activity (Young_Exercise, Young_Sedentary, Middle-Age_Exercise, Middle-Age_Sedentary, Old_Sedentary), and

Time (1, 3, 5, 7, 9, 11, 13, 19 hour)

‡ **Point Prevalence based on Published Criterion Scores.**

|| **Direction given only for contrasts where P value < 0.05**

Table RV. Summary of Log Rank and Cox Proportional Hazards Analyses of Cumulative Prevalence Using Published Criterion Scores

Outcome	Contrast	P Value	Model	Altitude Odds Alt+1000 ft / Odds Alt ft	SaO ₂ Odds SaO ₂ +1 % / Odds SaO ₂ %	Exercise Odds Active / Odds Sedentary	Sex Odds Female / Odds Male	Age Odds (Age- 50)/10 + 1 / Odds (Age – 50)/10	Age ² Odds[(Ag e- 50)/10] ² + 1 / Odds [(Age – 50)/10] ²
Altitude-related malaise	All Altitudes	<0.001*	Cox 1†	1.12 (1.02-1.23)	-	0.83 (0.52-1.33)	1.59 (1.04-2.44)	0.71 (0.54-0.92)	0.91 (0.81-1.03)
	8,000' vs lower	<0.001	Cox 2‡	1.03 (0.92-1.15)	0.86 (0.78-0.96)	0.81 (0.51-1.30)	1.83 (1.18-2.84)	0.66 (0.50-0.87)	0.92 (0.81-1.04)
	7,000' vs lower	0.39							
	All Altitudes	0.33	Cox 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)
AMS-C	8,000' vs lower	0.17	Cox 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)
	7,000' vs lower	0.70							
	All Altitudes	<0.001	Cox 1	1.09 (1.00-1.20)	-	0.74 (0.45-1.22)	1.64 (1.04-2.57)	0.67 (0.50-0.90)	0.90 (0.79-1.03)
AMS-R	8,000' vs lower	<0.001	Cox 2	0.99 (0.88-1.11)	0.85 (0.76-0.95)	0.73 (0.44-1.19)	1.92 (1.20-3.06)	0.62 (0.46-0.84)	0.91 (0.79-1.04)
	7,000' vs lower	0.28							

* **Bold font: p < 0.05, or 95% Confidence Interval does not include 1.0**

† **Cox Model 1 includes: Exercise, Sex, Age (centered and in decades), Age², Altitude (in 1000 ft increments)**

‡ **Cox Model 2 includes: Exercise, Sex, Age (centered and in decades), Age², Altitude (in 1000 ft increments), SaO₂**

Criterion scores for only AMS-C and AMS-R have been published.

Table RVI. Post Hoc Analysis of Items Significantly Related to Altitude

		Frequency * Weight Contribution of Symptom to Factor					
Symptom	Frequency	AMS-C	AMS-R	Exertion	Muscular Discomfort	Fatigue	Total Contribution
Back aches	18	†	12.348		5.454		17.802
Headache	21	9.765	6.552				16.317
Lightheaded	8	3.912		2.968		3.072	9.952
Short of breath	9		6.705	2.889			9.594
Coordination off	16	8.304					8.304
Stuffy nose	15		8.01				8.010
Hard to breathe	6		4.578	2.514			7.092
Feel weak	4	1.548		1.464	1.228	1.968	6.208
Tight/stiff	10				5.94		5.940
Feel numbness	14				4.41		4.410
Eyes irritated	11					4.378	4.378
Legs/feet ached	8				3.936		3.936
Sleepy	6					3.474	3.474
Hands/arms ached	8				3.248		3.248
Dizzy	3	1.338				1.254	2.592
Thirsty	3				0.99	1.113	2.103
Depressed	4		1.92				1.920
Concentration off	6					1.872	1.872
Runny nose	5					1.595	1.595
Blurry vision	5					1.52	1.520
Dim Vision	3	1.503					1.503
Muscle cramp	2					0.804	0.804
Stomach aches	1		0.744				0.744
Tired	1					0.665	0.665
Lost appetite	1	0.413					0.413

* See Table MIII for Symptom weights

† Blank entries indicate Frequency was 0 or Item Weight not published.

Table RVII. Sensory and Psychomotor Performance Measures*

<i>Purdue Peg Board</i>	Hour 2		Hour 5		Hour 10		Hour 13		Hour 19	
	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val
intercept	-30.133	0.94	129.099	0.41	675.231	0.10	433.536	0.06	430.159	0.10
gender	-4.260	<0.001	-3.142	<0.001	-2.682	<0.001	-3.422	<0.001	-3.149	<0.001
exercise	0.910	0.17	-0.004	1.00	1.359	0.03	1.342	0.04	0.357	0.57
age	-0.289	<0.001	-0.293	<0.001	-0.292	<0.001	-0.300	<0.001	-0.277	<0.001
altitude	<0.001	0.26	0.000	0.55	<0.001	0.04	<0.001	0.18	0.000	0.28
altitude ²	0.000	0.56	0.000	0.82	0.000	0.25	0.000	0.60	0.000	0.80
SaO ₂	1.548	0.84	-1.853	0.59	-13.414	0.12	-8.332	0.10	-8.230	0.14
(SaO ₂) ²	-0.007	0.86	0.011	0.55	0.072	0.12	0.045	0.10	0.044	0.14
R²	0.400		0.375		0.409		0.424		0.368	

<i>Kentucky Comprehensive Listening</i>	Hour 2		Hour 5		Hour 10		Hour 13		Hour 19	
	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val
intercept	-60.056	0.60	2.757	0.95	56.412	0.61	-90.817	0.25	42.821	0.55
gender	0.002	0.99	-0.156	0.36	-0.154	0.31	-0.054	0.77	-0.089	0.54
exercise	-0.050	0.81	-0.219	0.27	0.020	0.91	-0.026	0.90	-0.302	0.08
age	-0.035	<0.001	-0.029	<0.001	-0.035	<0.001	-0.044	<0.001	-0.039	<0.001
altitude	0.000	0.31	0.000	0.70	0.000	0.83	0.000	0.34	0.000	0.63
altitude ²	0.000	0.360	0.000	0.57	0.000	0.48	0.000	0.14	0.000	0.35
SaO ₂	1.474	0.54	0.172	0.87	-0.853	0.72	2.247	0.18	-0.602	0.69
(SaO ₂) ²	-0.008	0.54	-0.001	0.86	0.004	0.75	-0.012	0.17	0.003	0.72
R²	0.066		0.039		0.072		0.084		0.082	

<i>Snellen Visual Acuity</i>	Hour 1		Hour 3		Hour 8		Hour 13		Hour 19	
	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val
intercept	-63.772	0.86	494.741	0.14	-269.697	0.41	-285.941	0.27	145.919	0.63
gender	-0.978	0.11	-1.384	0.03	-0.954	0.16	-1.486	0.02	-1.540	0.01
exercise	0.139	0.85	0.115	0.87	0.669	0.39	0.488	0.49	-0.012	0.99
age	0.122	<0.001	0.131	<0.001	0.153	<0.001	0.130	<0.001	0.113	<0.001
altitude	0.000	0.77	<0.001	0.22	0.000	0.60	0.000	0.55	0.000	0.89
altitude ²	0.000	0.72	0.000	0.71	0.000	0.88	0.000	0.96	0.000	0.49
SaO ₂	1.534	0.84	-10.328	0.14	5.885	0.41	6.298	0.26	-2.887	0.66
(SaO ₂) ²	-0.008	0.85	0.055	0.15	-0.031	0.42	-0.033	0.26	0.016	0.65
R²	0.076		0.098		0.081		0.086		0.070	

<i>Farnsworth 100 Hue</i>	Hour 6		Hour 8		Hour 11		Hour 12	
	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val	Est β_i	P-Val
intercept	-45.280	0.99	4948.481	0.57	-1698.788	0.72	2894.907	0.71
gender	6.362	0.41	12.100	0.33	13.765	0.08	-3.196	0.78
exercise	†	†	†	†	-4.641	0.72	†	†
age	1.334	<0.001	2.141	<0.001	1.084	0.01	0.755	0.23
altitude	-0.005	0.37	0.018	0.12	0.000	0.96	0.016	0.11
altitude ²	0.000	0.21	0.000	0.22	0.000	0.61	0.000	0.07
SaO ₂	-1.926	0.98	-114.861	0.54	33.269	0.74	-59.552	0.72
(SaO ₂) ²	0.025	0.96	0.651	0.52	-0.161	0.77	0.308	0.73
R²	0.109		0.262		0.104		0.084	

* The following model was fit separately for each outcome at each of the specified hours using linear regression.

$$\text{Outcome} = \text{intercept} + \beta_1 * \text{gender} + \beta_2 * \text{exercise} + \beta_3 * \text{age} + \beta_4 * \text{altitude} + \beta_5 * \text{altitude}^2 + \beta_6 * \text{O}_2 + \beta_7 * (\text{O}_2)^2$$

Where

gender: male = 1, female = 0

Exercise: active = 1, sedentary = 0

age: continuous in years

altitude: continuous in feet

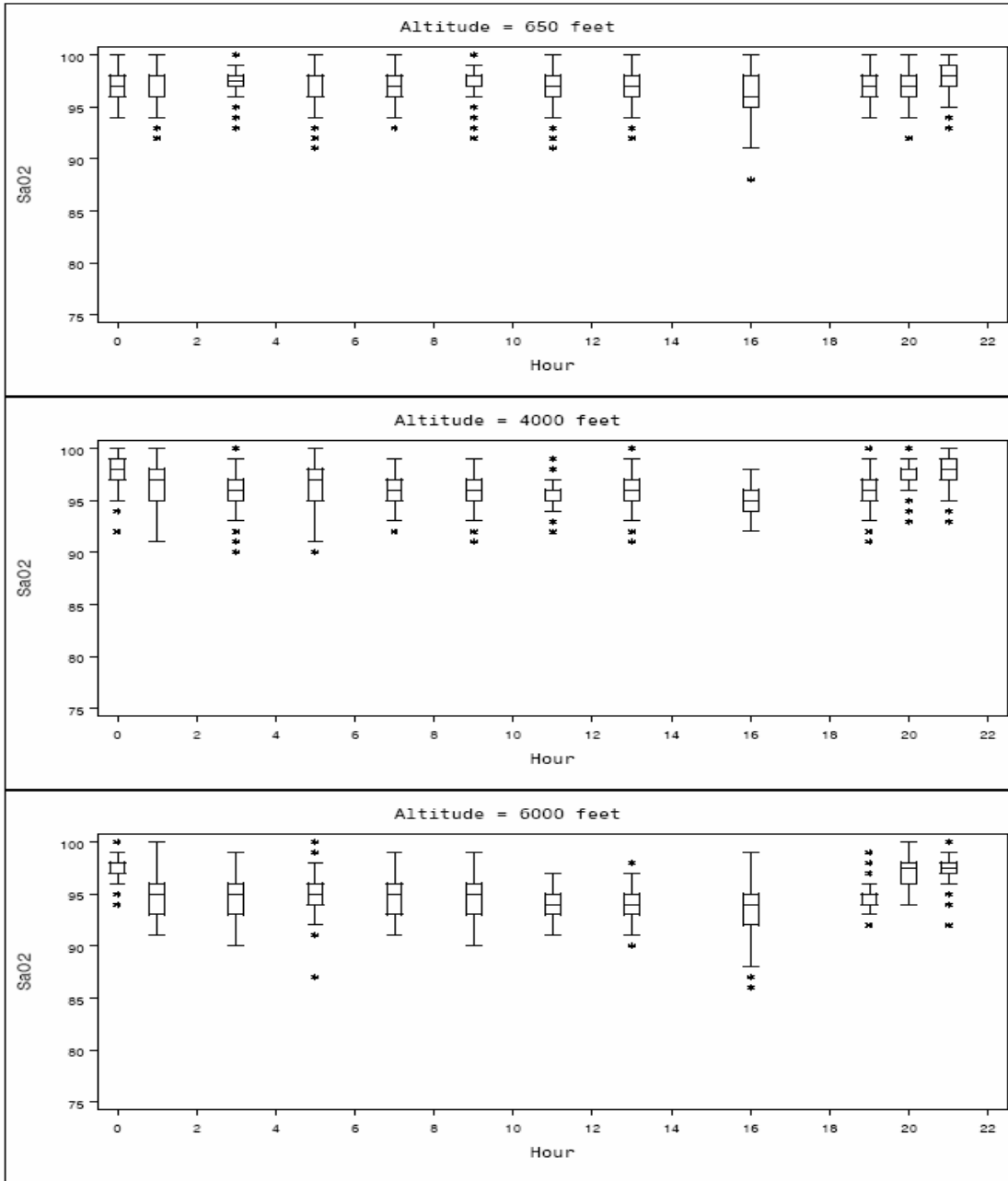
altitude²: continuous in feet²

SaO₂: Oxygen saturation, per cent

(SaO₂)²: continuous in per cent²

† missing data precluded estimation of coefficient

Effect of Commercial Aircraft Cabin Altitude on Passenger Discomfort: Supplementary Appendix



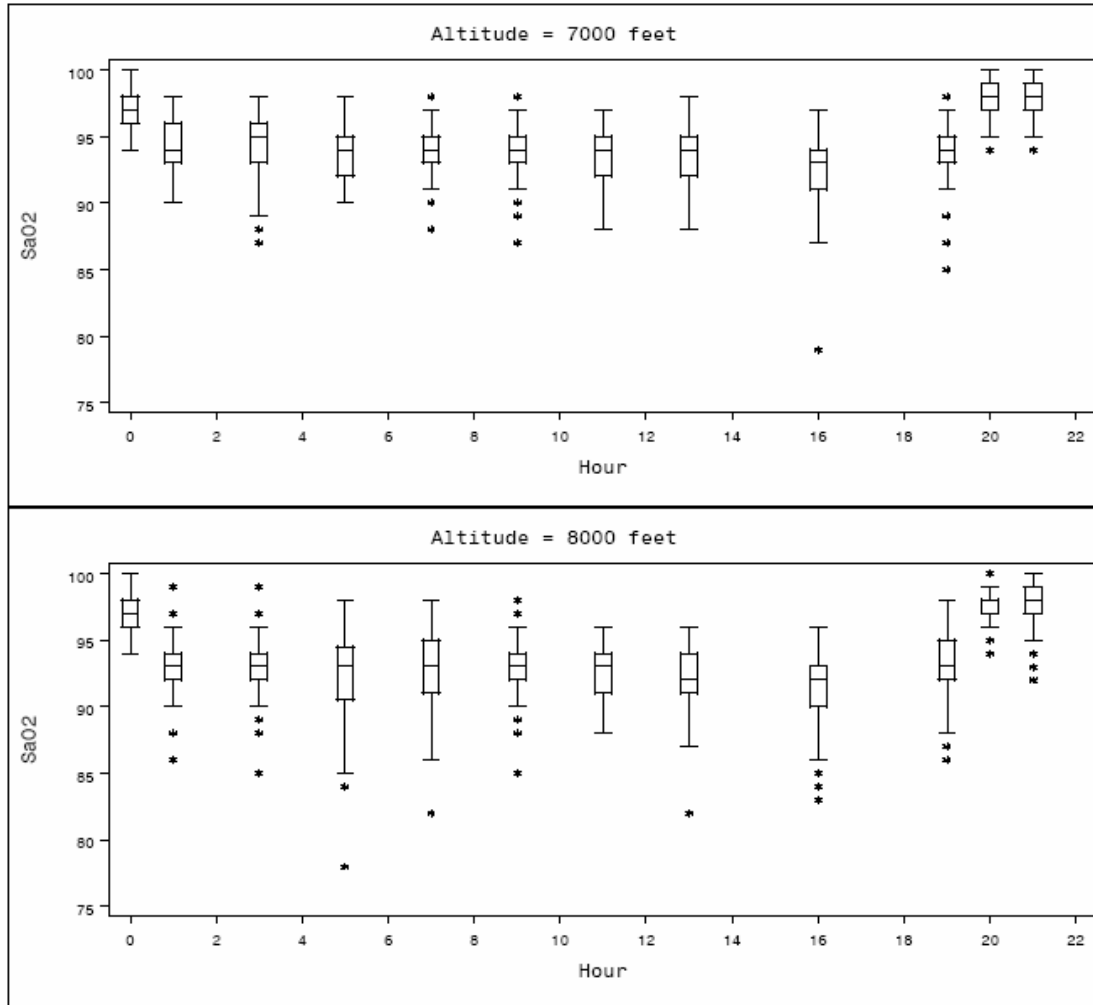


Figure R1. SaO₂ vs Time. Box and Whisker Plot

The bottom and top of the box are located at the 25th and the 75th percentiles. The center line in the box indicates the median. The whiskers are drawn from the box to the most extreme point within 1.5 quartile ranges from the median. Any values more extreme are marked with a star.

Mean SaO₂ decreases and range of values increases with altitude.

Note: in Figures R2 through R5, the label "AMS-D" refers to the factor called "altitude-related malaise" in text.

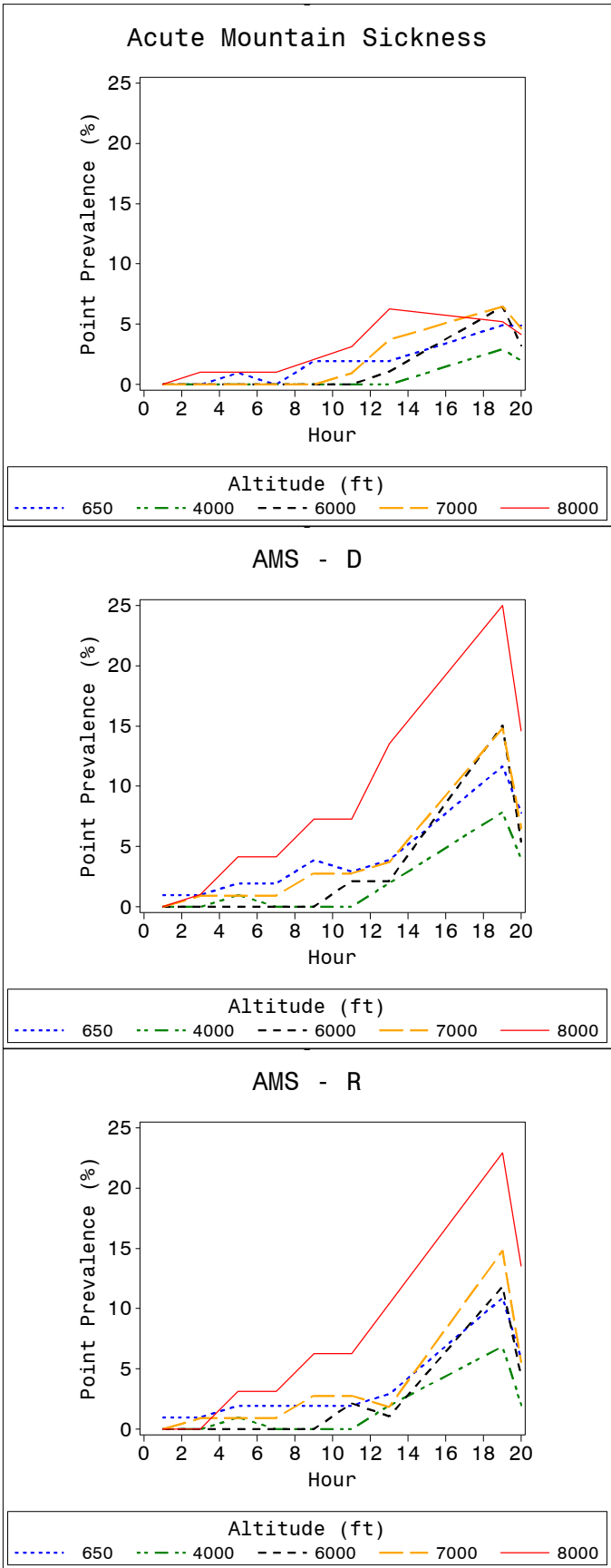


Figure R2: Point Prevalence, Published Criterion Scores

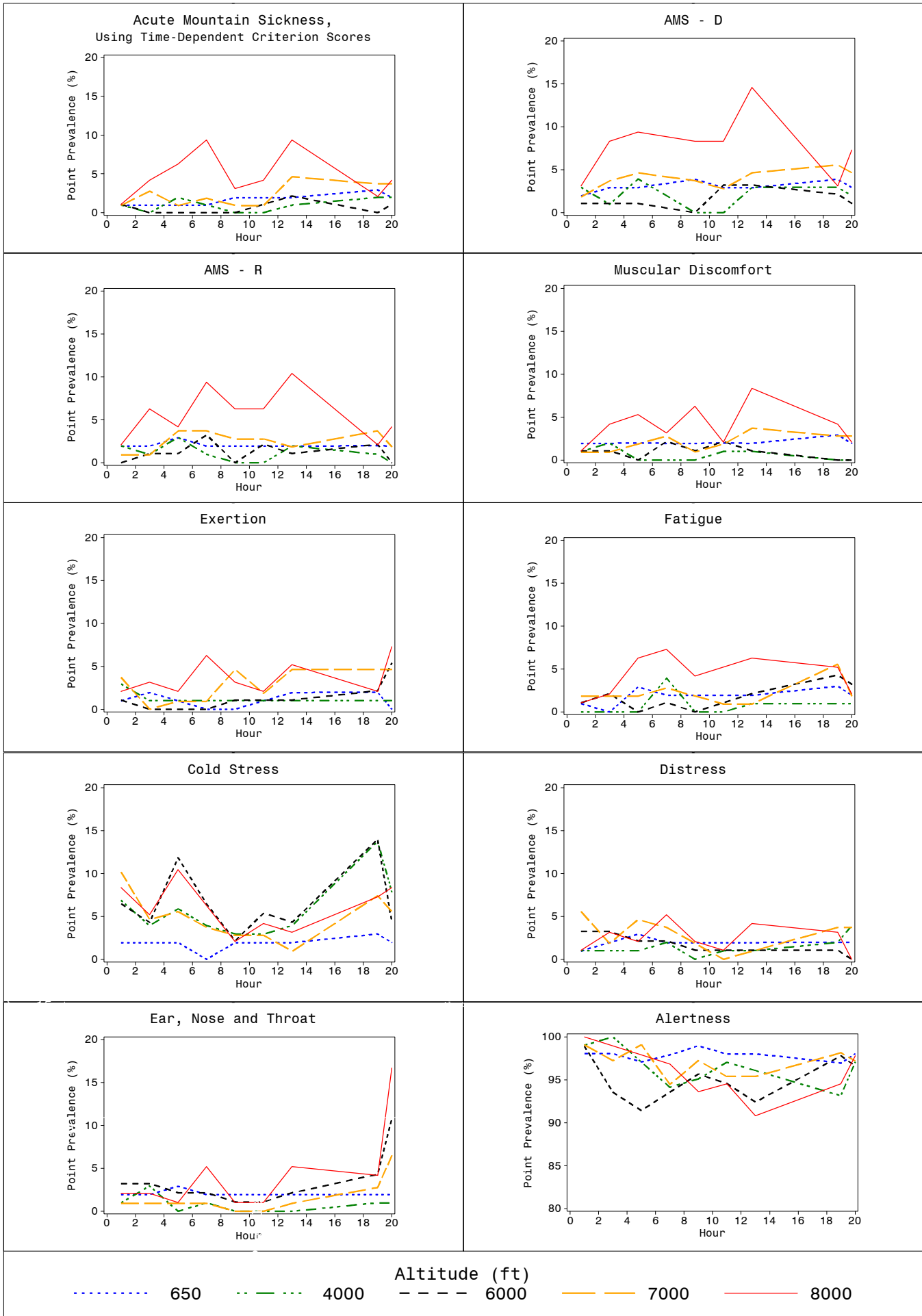


Figure R3: Point Prevalence, Time Dependent Criterion Scores 28

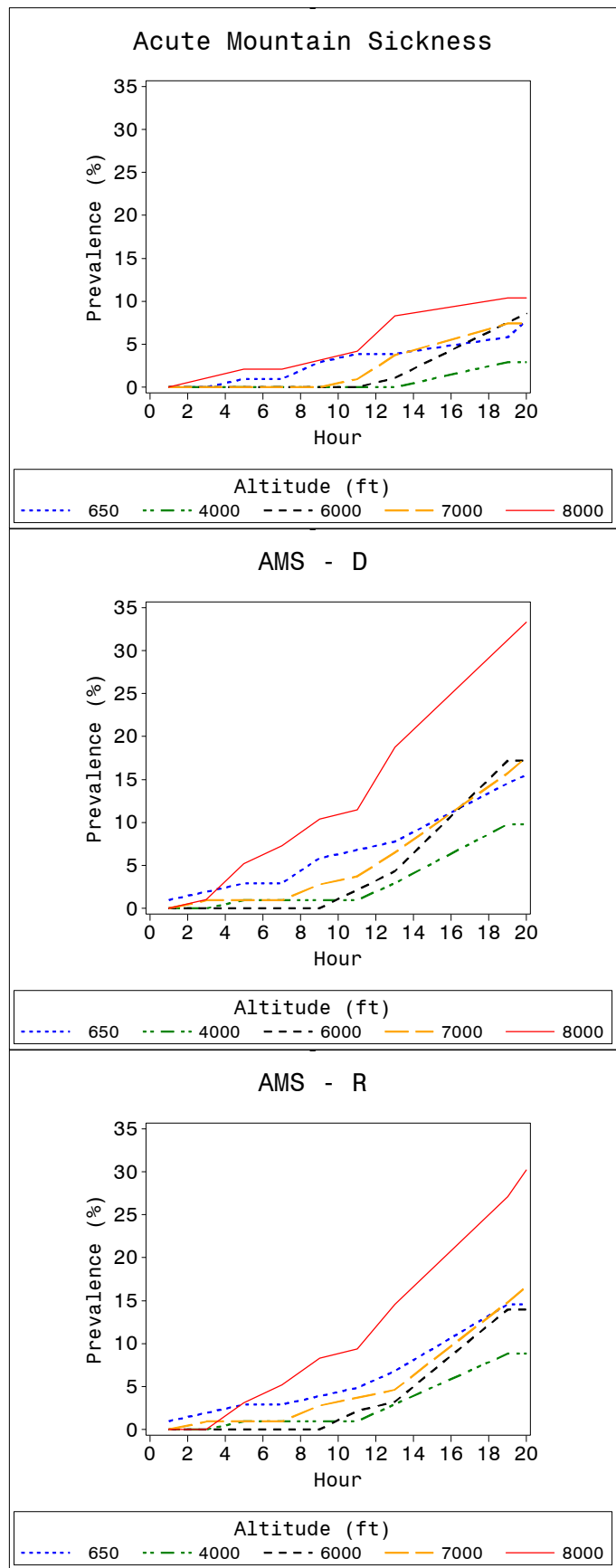


Figure R4: Cumulative Prevalence, Published Criterion Scores

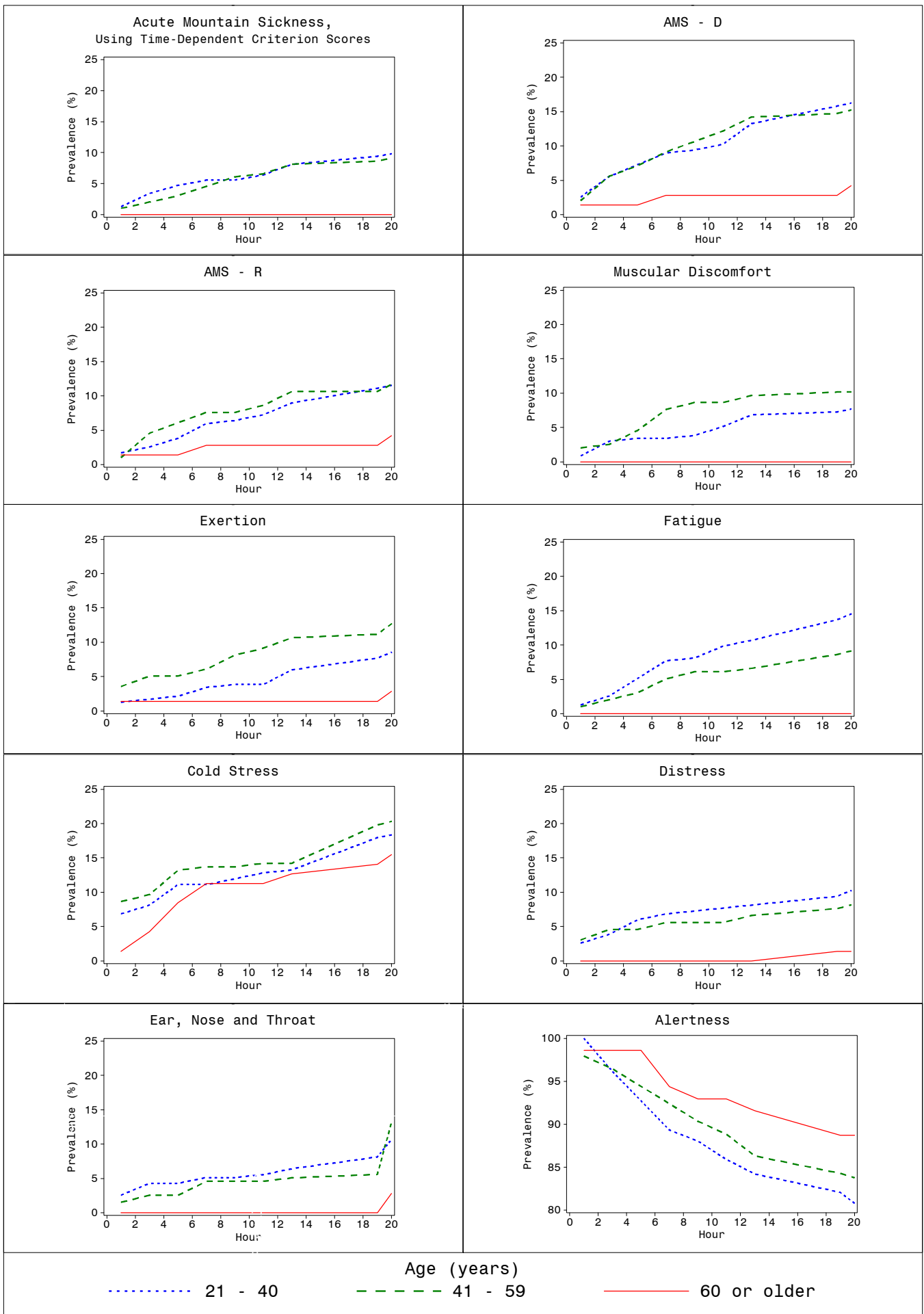


Figure R5: Cumulative Prevalence, Time Dependent Criterion Scores by Age Group