A Retrospective Study of Acute Mountain Sickness on Mt. Kilimanjaro Using Trekking Company Data

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Eigenberger P, Faino A, Maltzahn J, Lisk C, Frank E, Frank A, Loomis Z, Schroeder T, Strand M, Irwin D. ***A retrospective study of acute mountain sickness on Mt. Kilimanjaro using trekking company data.*** **Aviat Space Environ Med 2014; 85:1125–9.**

Background: High altitude illnesses (HAI) are a risk factor for any individual who is exposed to a significant increase in altitude. To learn more about the epidemiology of HAI, we sought to determine if health records from a commercial trekking company could provide novel data on the prevalence of HAI, as well as efficacy data regarding common HAI therapeutics. ***Methods:*** Health parameters from 917 tourists ascending Mt. Kilimanjaro over a 10-yr period were analyzed for meaningful data. ***Results:*** Of all subjects, 70% experienced at least one instance of a symptom related to HAI (headache, nausea, vomiting, diarrhea, or loss of appetite) during the trek. Acetazolamide was used at least once by 90% of subjects and, of those who used acetazolamide, 92% began taking it on day 1 of the ascent. Acetazolamide was found to improve oxygen saturation 1.2% above 9842.5 ft (3000 m). Dexamethasone use 12 h prior to ascending above 18,996 ft (5790 m) decreased the probability of a subject exhibiting at least one AMS symptom at that altitude. ***Discussion:*** The prevalence of AMS symptoms was not reduced by taking 2 extra days to reach the summit of Mt. Kilimanjaro. Prophylactic acetazolamide modestly improved oxygen saturation; however, it did not reduce symptoms. Therapeutic dexamethasone, especially at higher altitudes, was effective at reducing symptoms. We conclude that meaningful high altitude physiological data can be obtained from private trekking companies.

Keywords: epidemiology, high altitude, acute mountain sickness, acetazolamide, dexamethasone.

THE PROLIFERATION of global tourism has dramatically increased the number of visitors to the highest and most remote regions of the world. Commercial trekking companies have facilitated this transition by guiding amateur mountaineers to the summits of many 13,123–26,247 ft (4000–8000 m) peaks. As such, there may be a correlation between the increase in populations ascending to high altitude and the prevalence of high altitude illness (HAI). HAI is characterized by several pathological developments such as acute mountain sickness (AMS), high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE) (3,7,8). Mild to moderate AMS has an incidence of 42% at altitudes above 9842.5 ft (3000 m) (2); furthermore, data suggests that 1% of trekkers will develop life-threatening HACE, and up to 15% will develop HAPE above 13,123 ft (4000 m) (3). In response to the health risks posed to their clients, the trekking industry has implemented robust training and stringent protocols so their guides can accurately assess a client's day-to-day health and acclimatization to altitude. These assessments and protocols are used to help determine the rate of ascent for the group as well as the appropriate treatment for individuals developing HAI. The records obtained while monitoring clients for signs of HAI are then archived; consequently, these records may provide vast amounts of data from a unique cohort. This data presents an opportunity for researchers to perform retrospective analysis studies regarding health, acclimatization, and drug efficacy of adventure travelers ascending to high altitudes.

Retrospective cohort studies, a common practice in biomedical research, use archived data such as medical records to assess both the prevalence of disease and efficacy of preventative or therapeutic drugs. However, there are a number of challenges associated with retrospective data analyses that exploit medical records to study HAI. First, hospitals are rarely at an altitude that would be of interest for investigators studying HAI. Second, HAI resolves upon descent; thus, the symptom complex associated with HAI incidences go unreported. Third, there are often administrative challenges associated with obtaining hospital records due to HIPAA regulations, including study justification and ensuring de-identification of data for Institutional Review Board approval. Alternatively, relatively large datasets may be available for researchers investigating the epidemiology of HAI if private trekking companies are willing to collaborate with investigators by providing access to their health records in a de-identified manner.

We sought to determine if the datasets provided by commercial trekking companies would yield important epidemiological information. Mt. Kilimanjaro presents a unique opportunity for study due to the strenuous 16,404.2-ft (5000-m) gain in elevation from Moshi to the summit. The steepest route, Machame, ascends 13,451.4 ft

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This manuscript was received for review in April 2014. It was accepted for publication in August 2014.

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DOI: 10.3357/ASEM.4037.2014

(4100 m) in 4-5 d, while the more common Lemosho route ascends 12,467.2 ft (3800 m) over 6-7 d. Tusker Trail & Safari Co., a commercial trekking company that specializes in trips to the summit of Mt. Kilimanjaro in Tanzania, Africa, were able to provide de-identified health assessments from approximately 1000 trekkers ascending Mt. Kilimanjaro on either the Machame or Lemosho route. From these health records a database was created ($N = 917$) to further investigate the epidemiology of HAI in trekkers as they ascended Kilimanjaro using statistical modeling. This retrospective study demonstrated that a unique source of archived data exists with commercial trekking companies and this data can provide useful information with regard to the study of HAI.

METHODS

Institutional Review and Data Collection

The Colorado Multiple Institutional Review Board (COMIRB) evaluated the medical records provided by Tusker Trail & Safari Co. COMIRB determined there was no identifying information, nor any invasive procedures performed, and approved the study as Not Human Subject Research COMIRB # 11-0597. Trekking guides employed by the private trekking company, Tusker Trail & Safari Co., received training as High Altitude First Responders per the Eddie Frank protocol prior to guiding clients on ascents of Mt. Kilimanjaro. Clients that ascended Mt. Kilimanjaro began in the town of Moshi (average elevation of 2726.4 ft/831 m) and traversed either the Machame (4-5 d to summit) or Lemosho (6-7 d to summit) routes to the Kilimanjaro summit at 19,340.6 ft (5895 m). The Machame route was deemed to be the most strenuous due to an average elevation gain of 2690.3 ft/day (520 m/day), compared to 1778.2 ft/day (542 m/day) on Lemosho.

From Moshi to the summit, Tusker Trail & Safari Co. guides recorded vital statistics, symptoms, and medication use of trekkers twice daily: once in the morning (AM) prior to trekking and again in the evening (PM) after trekking (**Table I**). Recorded data included: time of day; location and elevation of camp; overall well-being (scale of 1-10 with 10 being the highest); oxygen saturation; heart rate; the presence or absence of headache, nausea, vomiting, diarrhea, appetite, difficulty breathing, or coughing; and whether or not acetazolamide and/or dexamethasone (DEX) was administered. Tusker Trail & Safari Co. provided paper photocopies of approximately 1000 unique health assessments of trekkers ascending Mt. Kilimanjaro that spanned a period of approximately 10 yr (1997–2007). Of these, 917 subject records were manually entered into a Microsoft Excel database.

Statistical Methods

Lake Louise scores, the standard to assess AMS, were not recorded, but symptoms indicative of AMS were documented (**Table II**). For the purpose of analysis, an individual was considered symptomatic for AMS (AMS occurrence) if they had one or more of the following five symptoms: headache, nausea, diarrhea, vomiting, and/or loss of appetite (the variable was set to missing for a given subject if three or more symptoms did not have a recorded response). A generalized linear model logit link (i.e., logistic regression) was used to fit the presence of AMS symptoms (one or more versus no symptoms) as a function of DEX use 12 h prior (yes/no), AMS symptoms 12 h prior (yes/no), same day supplemental oxygen use (yes/no), and elevation (modeled as continuous). A quadratic term for elevation was included in the model, plus the following interaction terms: DEX*AMS symptoms, DEX*elevation, DEX*elevation^2,

TABLE I. COUNTS FOR DEMOGRAPHIC VARIABLES.

Variable	*N*	%[†]
Gender		
Male	226	24.6
Female	393	42.8
Unlisted	298	32.5
Route		
Machame	208	22.7
Lemosho	709	77.3
AMS Positive	646	70.4
Headache	537	58.6
Nausea	192	21.0
Vomiting	63	6.9
Diarrhea	144	19.6
Loss of Appetite	197	29.4
Oxygen Supplementation	53	5.8
Acetazolamide*		
Ever taken	827	90.2
AMS positive	594	71.8
AMS negative	233	28.2
Never taken	89	9.7
AMS positive	63	70.8
AMS negative	26	29.2
Dexamethasone**		
Ever taken	221	56.2
AMS positive	212	95.9
AMS negative	9	4.1
Never taken	172	43.8
AMS positive	101	58.7
AMS negative	71	41.3

* 1 subject with no information recorded.
** 523 subjects with no information recorded.
[†] Percentages are relative to total sample size ($N = 917$) for main categories and relative to category total for subcategories.

TABLE II. COUNTS FOR AMS POSITIVE STATUS BY ROUTE.

	Machame *N** (%)	Lemosho *N* (%)	Overall *N* (%)
AMS at least once	139 (66.8)	507 (71.5)	646 (70.4)
AMS by day			
Days 1-2	53 (25.7)	123 (17.6)	176 (19.4)
Days 3-4	96 (46.6)	267 (37.9)	363 (39.8)
Days 5-6	74 (40.0)	222 (31.9)	296 (33.6)
Days 7-8	#	308 (45.5)	311 (43.7)
Days 9-10	#	52 (20.8)	53 (21.1)
AMS by elevation (m)			
1300	12 (13.8)	13 (4.3)	25 (6.5)
2650	#	71 (10.1)	71 (10.1)
3000–3963	118 (56.7)	241 (34.3)	359 (39.5)
4200–4600	75 (38.7)	336 (47.7)	411 (45.7)
5700–5790	#	200 (56.5)	200 (56.2)

[#] Little or no data available
* Note that *N* (%) data refers to AMS positive status based on completed records for given days or altitudes.

AMS symptoms*elevation, AMS symptoms*elevation^2, DEX*AMS symptoms*elevation, and DEX*AMS symptoms*elevation^2. This final model was arrived at based on QIC goodness-of-fit statistics. Generalized estimating equations were employed to account for the repeated measures in the data (daily AM and PM measurements) using a first-order autoregressive (1) working covariance structure. Records showed that DEX therapy was rarely used during the first 3 d of the ascent and was discontinued during the last day (descent) of the trek. Thus, data used to model the effects of DEX therapy were limited to days 4 through 8 of the ascent.

A linear mixed model was used to fit oxygen saturation as a quadratic function of altitude, with acetazolamide use (ever/never) and interaction terms to allow separate quadratic effects for acetazolamide groups. Random intercept and slopes for linear and quadratic altitude terms were included for each subject to allow their own individual quadratic trajectories. Further, repeated measures within subjects were modeled using an autoregressive (1) covariance structure. Estimates and comparisons between groups were then derived from this model. All analyses were conducted using SAS version 9.3 and plotted using SAS or R version 3.0.2.

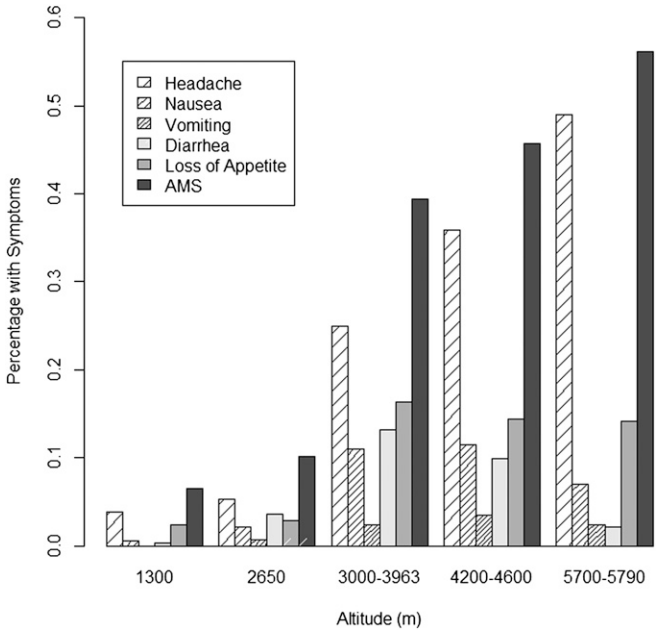

Fig. 1. AMS symptoms by elevation. Data does not discriminate between Machame and Lemosho routes. The data labeled AMS represents the occurrence of one or more of the following variables: headache, nausea, vomiting, diarrhea, or loss of appetite.

RESULTS

Of all subjects (N = 917), 393 (43%) were identified as men, 226 (25%) as women, and 298 (32%) were unreported. Of the trekkers, 23% ascended via the Machame route (7 d to summit; N = 208) and 77% ascended via the Lemosho route (10 d to summit; N = 709). Of all subjects, 70% (N = 646) experienced at least one instance of AMS over the duration of the trip. Of the trekkers, 8% presented with one or more AMS symptoms at Moshi (4265.1 ft/1300 m; **Fig. 1**). The most common AMS symptoms at all elevations were headache followed by loss of appetite; the least common symptoms at all altitudes were nausea and vomiting (Fig. 1). Day-by-day there was an 8.3% (SD = 0.3%) greater incidence of AMS on the Machame route vs. the Lemosho route. However, we found no statistical difference in the total percent of individuals that experienced at least one instance of AMS between the Machame and Lemosho routes [χ^2 (1) = 0.23, P = 0.63]. The Machame route was used by 208 (23%) trekkers, of which 69% (139 of 208) experienced an AMS symptom at least once. Of the 709 (77%) of individuals who ascended the Lemosho route, 72% (507 of 709) experienced an AMS occurrence. Of the subjects, 56% exhibited AMS symptoms during days 2 through 4 of the ascent (N = 359) and 89.4% of these first occurrences happened at elevations of 13,779.5 ft (4200 m) or less. As a whole, the percent of individuals symptomatic for AMS was positively associated with altitude (Table II). The overall summit success rate was 29.4% based on 670 subjects for whom data was available.

Tusker Trail & Safari Co. administered acetazolamide as a preventative therapy for their clients. The dataset supported this practice as acetazolamide use was documented at both AM and PM health checks for all 917 subjects, and 90% of subjects used acetazolamide at least once during the ascent. The use of acetazolamide did not significantly differ by route [χ^2 (1) = 0.01, P = 0.92]. The majority of subjects that used acetazolamide began use on the first day of ascent (N = 761, 92%), and 82% of acetazolamide users took the drug for 5 or more days (1 d includes use at both AM and PM). Of the 89 subjects that never took acetazolamide, 63 individuals (70%) experienced an AMS occurrence, and of the 827 individuals that took acetazolamide, 594 (72%) experienced an AMS occurrence. Data analyses did not reveal a positive or negative association between acetazolamide use and documented headache or overall well-being score (data not shown). As expected, oxygen saturation was negatively associated with elevation (**Fig. 2**) and a small but significant difference in mean oxygen saturation was noted between those that used acetazolamide versus those that did not. As altitude increased, based on quadratic fits, acetazolamide use was associated with a mean improvement in estimated mean oxygen saturation. Specifically, analyses of the quadratic fit (Fig. 2) between acetazolamide users and nonusers revealed no difference in the oxygen saturation curves at altitudes less than 9842.5 ft (3000 m), a 0.5% difference at an altitude of 3000 m [t(10,621) = 2.11, P = 0.03], and a 1.2% difference at an altitude of 16,404.2 ft (5000 m) [82.0% users, 80.8% for nonusers; t(10,621) = 2.44, P = 0.01].

In contrast to acetazolamide, records for DEX use were documented in only 393 of the 917 subjects and data from these records show that 56% of these subjects used DEX at least once (N = 221). Of the individuals that used DEX, 87% (192 of 221) also had used acetazolamide at least once during the trek. Nearly half of the subjects began DEX usage on days 6 or 7 of the ascent (N = 108,

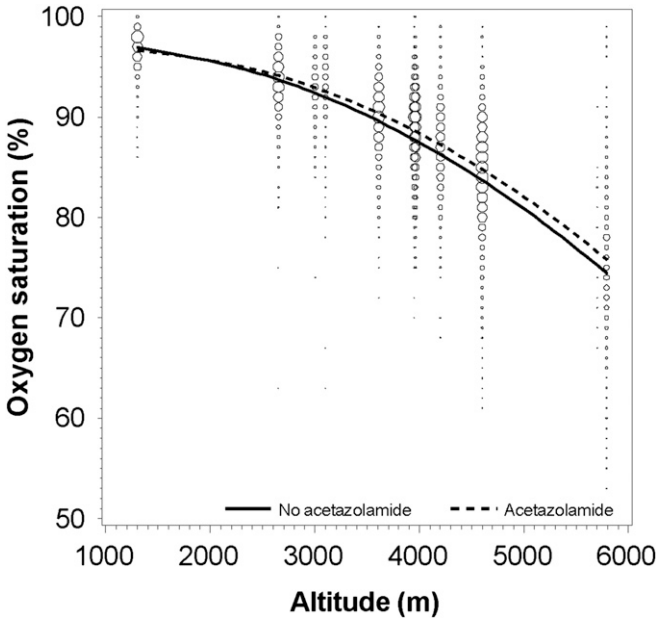

Fig. 2. Predicted oxygen saturation level as a function of altitude, by ever-takers (dashed) and never-takers (solid) of acetazolamide during the expedition. Predicted values were derived from linear mixed model fits as described in the text. Circles represent observed values of oxygen saturation with the size of the bubble indicating how many values occurred at that point (the larger the circle, the more values). There were a total of 13,369 records for 916 subjects used in the analysis.

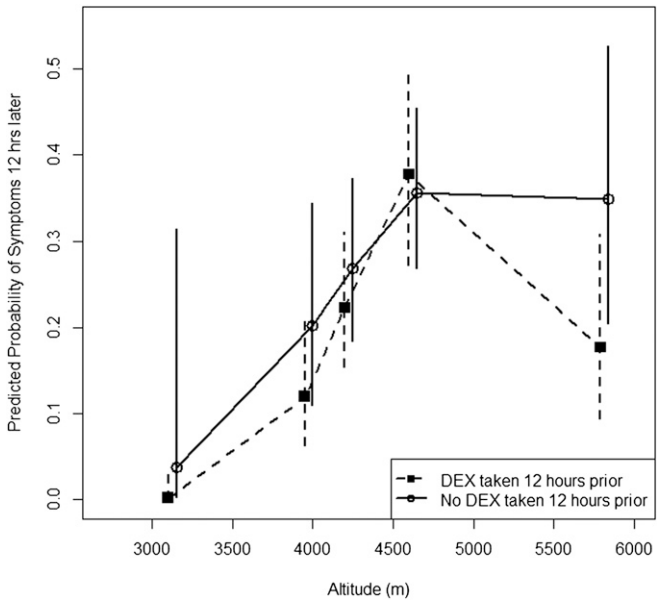

Fig. 3. Predicted probability of remaining symptomatic 12 h later for subjects who did or did not take dexamethasone (DEX). Plot corresponds to subjects who were symptomatic 12 h prior and were not taking supplemental oxygen 12 h later. Plotted circles (solid line) correspond to subjects who did not take DEX and plotted squares (dotted line) correspond to subjects who did take DEX. Elevation was modeled as a continuous variable; however, plotted points correspond to elevations of camps where recordings were taken.

48.9%); these days corresponded to elevations of 15,091.9 ft (4600 m) and 18,996.1 ft (5790 m), respectively, and the majority of subjects only used DEX once (either AM or PM, $N = 118$, 53%). Subjects who used DEX 12 h prior to ascending to 5790 m (**Fig. 3**) were less likely to remain symptomatic for AMS compared to subjects who refrained from taking DEX [χ^2 (1) = 3.26, $P = 0.07$]. At all lower elevations apart from 4600 m (Fig. 3), subjects who used DEX were less likely to be symptomatic 12 h later compared to subjects who did not take DEX; however, these differences were not significant.

DISCUSSION

The goal of the study was to determine if archived health records of trekkers obtained from a commercial trekking company (ascending to an altitude of 13,123.4 ft/4000 m or greater) would be a unique source of data which could provide new insights into acclimatization and HAI. The Tusker Trail & Safari Co. provided records of trekkers who ascended Mt. Kilimanjaro, from which a database of $N = 917$ was created for analysis. The data demonstrated: 1) 70% of subjects experienced at least one episode of headache, nausea, vomiting, diarrhea, or loss of appetite over the duration of the trip; 2) acetazolamide therapy was used by 90% of trekkers and was associated with a small but significant improvement in oxygen saturation which increased with elevation; and 3) at 18,996.1 ft (5790 m), individuals reported an improvement in AMS symptoms 12 h after dexamethasone treatment. This study suggests that commercial trekking companies are a promising source of data for investigators interested in assessing health risks associated with high altitude, as well as the benefits of the drugs used by a tourist population ascending to high altitudes.

This dataset revealed an overall 70% incidence of AMS symptoms while climbing Mt. Kilimanjaro, which is comparable to what has been reported from prospective studies that demonstrate an incidence of AMS on Mt. Kilimanjaro between 50–86% (1,4,6). Interestingly, one study reported that trekkers who modified their ascent profile and slept at lower altitude on the third day of the Machame route had a delayed onset of AMS, but were not protected from AMS symptoms (6), similar to our findings. Compared to the Machame route, the Lemosho route ascends Mt. Kilimanjaro more slowly, taking 3 extra days to reach the summit. On a day-by-day basis, the steeper Machame route experienced the highest incidence of AMS. Subjects on the Machame route were also three times more likely to report onset of AMS-type symptoms on the first day of ascent compared to subjects on the Lemosho route (21.6% versus 8.5%, respectively, Chi-squared $P = 0.0003$). However, the overall percentage of climbers who experienced at least one occurrence of an AMS symptom was not significantly different between routes (Chi-squared $P = 0.63$). Thus, it appears that on Mt. Kilimanjaro, a modified ascent profile from 7 to 10 d (~50% slower) is still not sufficient to protect individuals from AMS symptoms.

Acetazolamide is considered the standard of care drug for prophylaxis of AMS. It is a carbon anhydrase inhibitor and promotes acclimatization to high altitudes by increasing bicarbonate secretion from the kidneys, inducing metabolic acidosis, which subsequently stimulates ventilation and increases blood oxygen saturation

(1). Thus, it was not surprising to find that 90% of trekkers had documented use of acetazolamide. However, our data does challenge the notion that there is a benefit of using acetazolamide while trekking on Mt. Kilimanjaro. This is based on our evidence demonstrating acetazolamide increased oxygen saturation only 1.2%, which is unlikely to be considered clinically significant with regard to high altitude acclimatization. While the data seemed reasonable and conformed to physiological expectations, it should be noted that cold and hyperventilation are known cofounders of digital pulse oximetry. Although unlikely, we also cannot rule out that climbers who took acetazolamide did so because they were aware of a predisposition toward AMS. For a relatively large sample size, acetazolamide failed to reduce the incidence of being symptomatic for AMS. This data is congruent with others reporting that acetazolamide at 500 $mg \cdot d^{-1}$ may not be sufficient to reduce AMS symptom intensity (5). However, in this dataset, it should be noted that we could not exclude whether acetazolamide reduced the severity of AMS or if trekkers were re-dosing properly to gain the full therapeutic benefit since Lake Louise Scores and exact dosing of acetazolamide were not recorded.

Dexamethasone is a glucocorticoid and its ability to reduce AMS symptoms prophylactically or after onset of AMS is well known (8). Thus, it was not surprising that a predictive model from our dataset demonstrated trekkers were less likely to be symptomatic 12 h after DEX administration at 18,996.1 ft (5790 m). However, it is notable that this effect was greatest only at 5790 m. It is unclear why DEX treatment did not have a greater benefit at lower altitudes, but it is likely that a more robust effect at these lower altitudes would have emerged if either Lake Louise Scores or a more rigorous assessment of the quality of headache (i.e., mild, moderate, severe, or a 1-10 type of score) had been recorded. Interestingly, the data illustrate that 64% of trekkers delayed or refrained from DEX use until they were at the highest elevations (day 6 or later), and often DEX was only taken once. This suggests that trekkers were not necessarily using DEX as a prophylactic to prevent AMS, but rather as therapy after AMS onset.

Although this type of retrospective study yielded some interesting epidemiological and statistical modeling data on HAI, it was ultimately limited in scope by the field data collection practices. The foremost issue was that the health sheets were designed to be an aide to increase the margin of safety and improve the overall trip success rate for the clients of Tusker Trail & Safari Co. Thus, the health record sheets were optimized for the ease of mountain guides to record and interpret trends in client acclimation, not for a rigorous investigation on HAI. This is highlighted by the data that show 8% of individuals presented with AMS symptoms in Moshi at 4265.1 ft (1300 m). It is unlikely trekkers were suffering from AMS in Moshi. Jetlag, change of diet, and flu/cold symptoms have considerable overlap with the types of AMS symptoms recorded by Tusker personnel; thus it is more likely trekkers were suffering from one of these ailments than from AMS. Consequently, more detailed information important to the study of HAI, such as Lake Louise Scores, severity of headaches, or specific drug doses, is lacking in this dataset. Nevertheless, close collaboration between trekking companies and experts in the field of high-altitude physiology could optimize protocols that would be mutually beneficial to both the trekking company and high altitude investigators.

In conclusion, we show that archived health records owned by trekking companies can be used as a source of data for insights into acclimatization and HAI. Specifically, statistical analysis of datasets collected by guides for Tusker Trail & Safari Co. on Mt. Kilimanjaro confirmed an overall incidence of trekkers experiencing AMS to be around 70%. Further, this analysis also revealed: 1) a slower ascent profile by 2 d did not reduce the incidence of AMS; 2) acetazolamide therapy improved oxygen saturation by 1.2% at 16,404.2 ft (5000 m), yet did not show any benefit at reducing AMS symptoms at any elevation; and 3) though this relationship was just outside of the threshold for statistical significance (at the $P = 0.05$ level), DEX proved to be an effective therapeutic, especially at higher altitudes. Finally, in the future, a partnership between trekking companies leading ascents to the world's highest peaks and biomedical investigators may yield an economical and feasible means to gain large volumes of data for new insights into a variety of health issues faced by trekkers.

ACKNOWLEDGMENTS

This study was supported by Defense Advanced Research Projects Agency (DARPA) Rapid Altitude and Hypoxia Acclimation Contract N66001-10c-2134. We would also like to thank the volunteers from the University of Colorado, Denver, whose efforts greatly accelerated the pace of this project.

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