

STrengthening Altitude Knowledge (STAK): a Delphi study to define minimum knowledge of altitude illness for laypersons traveling to high altitude

Short title: Strengthening Altitude Knowledge

Remco R. Berendsen¹, Peter Bärtsch², Buddha Basnyat³, Marc Moritz Berger⁴, Peter Hackett⁵, Andrew M. Luks⁶, Jean-Paul Richalet⁷, Ken Zafren⁸, Bengt Kayser⁹, and the STAK plenary group¹

Correspondence:

Remco Berendsen

Leids Universitair Medisch Centrum

Postzone P5-Q

Postbus 9600

2300 RC Leiden

r.r.berendsen@lumc.nl

<https://orcid.org/0000-0002-2848-8699>

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¹ STAK (STrengthening Altitude Knowledge) panel members, excluding the moderators and core experts: J Anholm³, PS Auerbach^{3†}, BA Beidleman², KE Bloch¹, M Brodmann², H Brugger³, M Burtscher³, C Dehnert³, L Dumont³, M Faulhaber³, R Fischer³, H Gatterer³, F Gekeler¹, CK Grissom³, MPW Grocott³, D Hillebrandt³, B Honigman³, C Imray¹, MS Koehle³, GS Lipman², JA Loeppky³, M Maggiorini², LG Moore³, SR Muza¹, M Pun³, RC Roach¹, C Sartori³, U Scherrer³, G Sikri³, AW Subudhi³, ER Swenson³, AA Thompson³, S Verges³ and DR Woods³ (¹: participated in the first round only; ²: participated to two rounds; ³: participated to all three rounds; †passed away after submitting his comments on the final round).

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Authors copy of published manuscript

Affiliations

1. Department of Anesthesiology, Leiden University Medical Centre, Leiden, The Netherlands
2. Department of Internal Medicine, University Hospital, Heidelberg, Germany
3. Oxford University Clinical Research Unit-Nepal, Kathmandu, Nepal
4. Department of Anesthesiology and Intensive Care Medicine, Essen University Hospital, University Duisburg-Essen, Germany
5. Department of Medicine, Altitude Research Center, Division of Pulmonary and Critical Care Medicine, University of Colorado, Aurora, Colorado.
6. Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine. University of Washington, Seattle, Washington
7. INSERM U1272, Hypoxie et Poumon. Université Sorbonne Paris Nord, Bobigny, France
8. Department of Emergency Medicine, Stanford University Medical Center, Stanford, California.
9. Institute of Sport Sciences (ISSUL), University of Lausanne, Switzerland. <https://orcid.org/0000-0002-9776-7501>

Abstract

Introduction. A lack of knowledge among laypersons about the hazards of high-altitude exposure contributes to morbidity and mortality from acute mountain sickness (AMS), high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE) among high altitude travelers. There are guidelines regarding the recognition, prevention, and treatment of acute altitude illness for experts, but essential knowledge for laypersons traveling to high altitudes has not been defined. We sought expert consensus on the essential knowledge required for people planning to travel to high altitudes.

Methods: The Delphi method was used. The panel consisted of two moderators: a core expert group and a plenary expert group. The moderators made a preliminary list of statements defining the desired minimum knowledge for laypersons traveling to high altitudes, based on the relevant literature. These preliminary statements were then reviewed, supplemented, and modified by a core expert group. A list of 33 statements was then presented to a plenary group of experts in successive rounds.

Results: It took 3 rounds to reach a consensus. Of the 10 core experts invited, seven completed all the rounds. Of the 76 plenary experts, 41 (54%) participated in round 1, and of these 41 a total of 32 (78%) experts completed all three rounds. The final list contained 28 statements in five categories (altitude physiology, sleeping at altitude, AMS, HACE, and HAPE). This list represents an expert consensus on the desired minimum knowledge for laypersons planning high altitude travel.

Conclusion: Using the Delphi method, the STAK initiative yielded a set of 28 statements representing essential learning objectives for laypersons who plan to travel to high altitudes. This list could be used to develop educational interventions.

Introduction

Millions of people travel for work or leisure to altitudes greater than 2,400 m each year (Luks et al. , 2021) where they are at risk of developing several forms of acute altitude illness (Bärtsch and Swenson ER, 2013b), including the relatively common and unpleasant, but benign, acute mountain sickness (AMS), as well as potentially life-threatening high altitude cerebral edema (HACE) and high altitude pulmonary edema (HAPE). (Bärtsch and Swenson ER, 2013a; Hackett and Rennie D, 2002; Hackett and Roach RC, 2001, 2004; Luks et al. , 2017)

Traveling to high altitude triggers a series of physiological responses, in most cases allowing individuals to acclimatize to lower ambient oxygen levels over several days to weeks, but occasionally leading to maladaptive responses predisposing to acute altitude illness. The most common altitude illness is AMS, a syndrome characterized by non-specific symptoms. Although some experts disagree on the deletion of the sleep disorder item in the 2018 consensus (Chen et al. , 2021; Richalet, Julia, et al. , 2021; Roach et al. , 2018), headache is still considered to be the cardinal symptom (Roach et al. , 2011), accompanied by one or more other symptoms, including gastrointestinal symptoms, dizziness, and/or fatigue. The most important risk factor for AMS is rapid ascent ($\geq 400\text{--}500 \text{ m} \cdot \text{d}^{-1}$) above 2,800 m without any rest days. (Luks et al. , 2019; Richalet, Pillard, et al. , 2021)

Despite the importance of rapid ascent as a significant risk factor for altitude illness, the reasons for this have received little attention. The choice of ascent profiles for trekking is driven by intrinsic factors, such as motivation and performance expectations, and extrinsic factors, such as peer pressure, time constraints and environmental characteristics, terrain steepness, and availability of overnight accommodation. Behavior is also a function of knowledge. Lack of knowledge can lead to behavior that increases the risk of altitude illness and can lead to poor management. Epidemiological studies have

shown that poor knowledge is accompanied by an increased risk of altitude illness, while greater knowledge is associated with a lower incidence of altitude illness.(Crouchs et al. , 2022; Gaillard et al. , 2004; Hackett et al. , 1976; Kayser, 1991; McDevitt et al. , 2014; Shlim and Gallie J, 1992)

Although a lack of knowledge may affect the risk of developing acute altitude illness, no resources have defined the appropriate baseline level of knowledge about high-altitude physiology and medicine for laypersons traveling to high altitude. The overwhelming majority of consensus statements and guidelines are intended for healthcare professionals, trekking or expedition leaders, or mountain guides (Kupper, 2020; Kupper et al. , 2012) and do not specifically target laypersons. The purpose of this study was to fill this gap and establish a minimum set of essential knowledge items about the recognition and management of acute altitude illness for laypersons planning to travel to high altitude to reduce altitude illness related symptoms.

Methods

We used the Delphi method to develop an expert consensus definition of the essential knowledge for safe travel to high altitude. The Delphi method is based on successive rounds of surveys among experts, who anonymously rate and adapt a series of statements so that consensus is eventually reached.(Hasson et al. , 2000)

Definition of "altitude traveler."

For this study, laypersons were defined as travelers who had never previously been to high altitude and those who had traveled to high altitude but remained ill-informed about the risks of high-altitude travel.

Selection of experts

The group consisted of two moderators: a core group of experts and a plenary group of experts. Moderators and core experts were also part of a plenary group of experts. Individuals were deemed eligible to serve as core experts if they had published a minimum of nine articles identified in the Medline database with the phrase “acute mountain sickness’ [All Fields] by May 2019. Further, experts were identified by screening the references of the articles by the moderators. The moderators personally selected the core experts based on their qualifications. The moderators approached the experts through automatically generated emails, followed by direct personal emails to limit attrition. (Hsu and Sandford BA, 2007)

Delphi process

Using their experience in teaching the principles of mountain medicine, the two moderators first formulated a preliminary version of the desired minimum knowledge in the form of a list of 36 statements. These statements were based on the current literature and grouped into five themes: 1) high-altitude physiology (n=3), 2) sleep at high altitude (n=3), 3) acute mountain sickness (n=18), 4) high altitude cerebral edema (n=6), and 5) high altitude pulmonary edema (n=6). The preliminary list of statements was then presented to core experts for revision and additional statements. Using feedback from core experts, the moderators compiled a revised list of statements for the first Delphi round. This list of statements was subsequently presented to the plenary group to rate the suitability of each statement for inclusion using a Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree, and 5 = strongly agree). The experts were required to comment on a statement if their rating was ≤ 3 , and could also comment on any other statement. In the subsequent rounds, the members of the plenary group were presented with the anonymized comments of the others on the

prior versions of the statements, together with their own ratings and comments, and a quantitative breakdown of how many experts agreed or disagreed on retaining the statement for inclusion in the final list. Members of the plenary group were allowed to change or maintain their ratings during the new round and provide further comments. Between rounds, the moderators reviewed the comments of the plenary group and revised the statements for consideration by the plenary group in the next round.

Data security

A secure online survey system was used. NET core 3.1 (.NET Foundation, Redmond, WA, USA). Each participant received a personal invitation with a nonpublic URL and a password. The Delphi survey was protected by unique identifiers to reference the data and create encrypted connections for users to modify the data. Each new survey had a unique identifier in the system. A link was created for the survey owner by using this identifier, which was then encrypted with a timestamp. Through this unique encrypted link, the survey owner can create Delphi statements and invite users to participate in the survey. Users were added with their email addresses, and optionally with their names. A Delphi identity is created for each user using a unique identifier. Rijndael 256-bit cryptography was used for the encryption.

Delphi rounds

In Round 1, the first list of statements was presented to the plenary group without accompanying comments, except for general instructions. In round 2, using the ratings and comments on the statements on which agreement had not been reached, a list of modified statements was presented to the plenary group. This list consisted of the revised statements and an explanation of each statement based on the results of the previous round to guide further review and comments. Some statements

were retained in their original form, with an explanation of why they were shown again. In round 3, all remaining statements that were still under consideration were presented after incorporating the comments from the previous round(s). In this final round, the plenary members had to accept or reject each statement but also had an escape option: no opinion. Experts who did not respond to the invitation in the first round were not invited to participate in further rounds. Experts who completed the first round but did not respond to the second round were sent multiple reminders, including personal emails asking them to provide their input.

Criteria for inclusion of statements

We defined the level of agreement in rounds 1 and 2 as the percentage of positive responses (“agree” or “strongly agree”). Reaching agreement was defined *a priori* as 65-79% agreement, indicating moderate consensus, and $\geq 80\%$ agreement, indicating strong consensus. The score for each statement was calculated using the mean Likert score. For a statement to be included in the consensus, at least 75% of the experts had to agree and the average score had to be ≥ 3.5 . Since Round 3 consisted of three choices, with “no opinion” as 1 of the choices, the agreement percentage in Round 3 was defined as the fraction of positive answers (“accept”). Again, there had to be $\geq 75\%$ agreement with the statement to be included in the final list.

Data analysis and presentation

We entered the data into a database (FileMaker Pro, version 18, Santa Clara, CA, USA) and analyzed it using Microsoft Excel for macOS (Microsoft®, version 16.56, Seattle, WA USA) and GraphPad Prism for macOS (GraphPad Software, version 9.3.1, San Diego, CA USA). We present the results descriptively

(numbers, ratios, and mean \pm SD). We performed a Wilcoxon signed-rank test to gauge the effect of attrition (IBM SPSS Statistics for Macintosh, version 25.0. IBM Corp., Armonk, NY, USA).

Results

We submitted an initial list of 36 statements prepared by the moderators for comments to 10 core experts, all of whom agreed to participate. Nine core experts completed the preliminary round. These nine experts rejected four statements: one because of similarity to another statement, one for irrelevance, and two for excess specificity. Based on the comments of the nine core experts, 1 new statement was added. The initial list for the first Delphi round contained 33 statements scored by the plenary group (Supplementary table S1).

Results of Rounds 1-3

In Round 1, we presented 33 statements to the plenary group (including core experts). Of these, 41 completed the first round (response rate: 54%) (Figure 2 and Supplementary table S2). Three statements were rejected (average score 3.1 ± 0.4 ; agreement 50 ± 16 %, red dots in figure 2). Of the remaining statements, 10 were accepted (average score 4.0 ± 0.4 ; agreement 80 ± 13 %). Of these statements, 3 statements had not strictly met the a priori acceptance requirements but were nevertheless accepted (see supplementary document S4 for a comprehensive explanation). In Round 2, we presented 21 statements. Twelve statements (average score 4.2 ± 0.2 ; agreement rate 88 ± 5.1 %) were accepted by 36 experts (88% response rate). In Round 3, three of the remaining nine statements (average score 4.0 ± 0.1 ; agreement rate 69 ± 3.1 %) were rejected by 32 experts (78% response rate). After the third and final Delphi round, there was a list of 28 statements on which 32 experts had reached consensus for

their appropriateness as minimum desired knowledge for laypersons planning travel to altitude (Table 1 and figure 3).

Assessment for bias

To assess for bias related to attrition from rounds 1 to 3, a Wilcoxon matched-pairs signed-rank test was performed to compare the results with and without the experts who had dropped out. There were no statistically significant differences between the median scores of the statements with and without experts who dropped out for rounds 2 and 3.

Discussion

The objective of this study was to reach a consensus among experts in mountain medicine and physiology on a minimum level of knowledge desirable for laypersons planning to travel to altitudes at which there is a risk of acute altitude illness. Three Delphi rounds were sufficient to reach consensus among 32 experts on a final set of 28 statements. This list of statements (Table 1) can now be used to formulate learning objectives for educational interventions and provide a common basis for information and education strategies aimed at laypersons planning to travel to altitude.

Learning objectives on altitude illness for lay travelers to high altitude, when accompanied by educational guidelines and, ideally, evaluation of core competencies, would be expected to reduce the incidence of altitude illness and its complications. A recent survey among a representative panel of Dutch Mountain and Climbing Federation (NKBV) members about reasons why they could not continue

their trekking found that 25% mentioned AMS as the cause, and 30% said that they were interested in learning more about AMS (RB, unpublished data).

A study among climbers attempting to climb Dhaulagiri explored their knowledge of altitude-related problems. The authors considered the knowledge level of the participants unsatisfactory. Although the number of participants was small (n=17), the authors concluded that high-altitude mountaineers should be better educated about altitude illnesses (Mena et al. , 2018). Another study suggested that more effort is needed to reinforce the message that trekkers should be able to recognize the symptoms and signs of AMS and be made aware of their responsibilities.(Subedi et al. , 2008)

Improved knowledge levels are associated with a reduction in the incidence of altitude illness.(Gaillard et al., 2004; Hackett et al., 1976; Kayser, 1991) One study concluded that physicians, travel companies, and other organizations sponsoring high altitude activities should emphasize pre-trip preparation and education.(McDevitt et al., 2014) The study found that only 42% of trekkers on their way to the Thorong La (5,400 m) had basic awareness of AMS. Awareness of AMS was higher in a previous study in which participants received a lecture on altitude illness before answering questions about symptoms, signs and treatment. (Gaillard et al., 2004)

A structured, expert-supported, international education program for laypersons has not yet been developed. The statements in the list of minimum knowledge for laypersons planning to travel to altitude where there is a risk of altitude illness proposed in this paper can serve as learning objectives for teaching/educational programs and can be used to create information for travel guides and websites. This list of statements may serve as a benchmark for evaluating knowledge of altitude illness. The information and educational materials will have to be specifically tailored for various populations,

ranging from lay but literate people to lay illiterate people, such as Himalayan porters and pilgrims. Our study was not designed to assess the effects of any intervention on knowledge acquisition or retention. Ideally, any intervention should be followed by evaluation of the results. Such studies may yield inputs for adjustments to teaching programs as well as learning objectives. This may be necessary because there are probably too many statements for each to be a separate learning objective.

Limitations

A recurring problem in rounds 1 and 2 was understanding the instructions. We asked the members of the plenary group to give their opinion on what laypersons traveling to altitude *should* know, not what they already know. However, several experts assessed the statements in the former way (e.g., “trekkers in the Himalayas do not know this”). Proficiency in English could have played a role, since 5% of the experts were from Asia, 54% from Europe, and 41% from North America. Comprehension could have played a role (Hoover and Gough PB, 1990), but also haste or disinterest while responding to the survey. The magnitude of this bias cannot be determined.

While the online version of the Delphi method made it possible to involve a large group of international participants while limiting cost, preserving anonymity, and decreasing the risk that a select group of participants would dominate the conversation, it took time to collect the responses, and attrition was frequent, problems that were likely exacerbated by collecting data during the COVID-19 pandemic. The concern of increasing attrition over subsequent rounds is that this could lead to a “false” consensus, as participants with dissenting views start dropping out. (Humphrey-Murto et al. , 2019)

Another important limitation is that the method used to identify the most important learning objectives for laypersons does not identify the most effective teaching methods. However, assuming that what is

learned will be practiced is not necessarily the case. Action is not always consistent with knowledge; a problem referred to as the knowledge-to-action gap.(Kahlke et al. , 2020; Knight et al. , 2008) This may not be an immediate limitation but may become so when implementing the statements

Conclusions

The STAK consensus, developed using the Delphi method, describes 28 learning objectives laypersons should know before traveling to altitude. The list of learning objectives can be used to develop information and teaching materials to increase the knowledge of this target population. Over time, new developments in the field of high-altitude medicine may provide new insights that make these learning objectives subject to modification.

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Author contributions

Study design and methods: RB and BK. Experimental phase: RB, BK, and core experts. Data reduction and analysis: RB and BK. First version of the manuscript: RB and BK. Final version of the manuscript: RB, BK, and core experts.

Conflict of interest

None of the authors has a conflict of interest to report.

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References

- Bärtsch P and Swenson ER. Acute high-altitude illnesses. *N Engl J Med* 2013a; 369(17): 1666-1667
<https://doi.org/10.1056/NEJMc1309747>
- Bärtsch P and Swenson ER. Clinical practice: Acute high-altitude illnesses. *N Engl J Med* 2013b; 368(24): 2294-2302 <https://doi.org/10.1056/NEJMc1214870>
- Chen R, Wang Y, Zhang C, Luo X, Yang J, Liu C and Huang L. Assessment of Acute Mountain Sickness Using 1993 and 2018 Versions of the Lake Louise Score in a Large Chinese Cohort. *High Alt Med Biol* 2021; 22(4): 362-368 <https://doi.org/10.1089/ham.2021.0031>
- Croughs M, Nyakunga GB, Sakita FM, Kilonzo K, Mmbaga BT and Soentjens P. Incidence and predictors of severe altitude illness symptoms in Mt. Kilimanjaro hikers; a prospective cohort study. *J Travel Med* 2022; <https://doi.org/10.1093/jtm/taac044>
- Gaillard S, Dellasanta P, Loutan L and Kayser B. Awareness, prevalence, medication use, and risk factors of acute mountain sickness in tourists trekking around the Annapurnas in Nepal: a 12-year follow-up. *High Alt Med Biol* 2004; 5(4): 410-419 <https://doi.org/10.1089/ham.2004.5.410>
- Hackett P and Rennie D. High-altitude pulmonary edema. *Jama* 2002; 287(17): 2275-2278
<https://doi.org/10.1001/jama.287.17.2275>
- Hackett PH, Rennie D and Levine HD. The incidence, importance, and prophylaxis of acute mountain sickness. *Lancet* 1976; 2(7996): 1149-1155 [https://doi.org/10.1016/s0140-6736\(76\)91677-9](https://doi.org/10.1016/s0140-6736(76)91677-9)
- Hackett PH and Roach RC. High-altitude illness. *N Engl J Med* 2001; 345(2): 107-114
<https://doi.org/10.1056/nejm200107123450206>
- Hackett PH and Roach RC. High altitude cerebral edema. *High Alt Med Biol* 2004; 5(2): 136-146
<https://doi.org/10.1089/1527029041352054>

- Hasson F, Keeney S and McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs* 2000; 32(4): 1008-1015 <https://www.ncbi.nlm.nih.gov/pubmed/11095242>
- Hoover WA and Gough PB. The simple view of reading. *Reading and Writing* 1990; 2(2): 127-160
<https://doi.org/10.1007/BF00401799>
- Hsu C-C and Sandford BA. The Delphi Technique: Making Sense of Consensus. *PARE* 2007; 12
<https://doi.org/https://doi.org/10.7275/pdz9-th90>
- Humphrey-Murto S and de Wit M. The Delphi method-more research please. *J Clin Epidemiol* 2019; 106: 136-139 <https://doi.org/10.1016/j.jclinepi.2018.10.011>
- Kahlke RM, McConnell MM, Wisener KM and Eva KW. The disconnect between knowing and doing in health professions education and practice. *Adv Health Sci Educ Theory Pract* 2020; 25(1): 227-240 <https://doi.org/10.1007/s10459-019-09886-5>
- Kayser B. Acute mountain sickness in western tourists around the Thorong pass (5400 m) in Nepal. *Journal of Wilderness Medicine* 1991; 2(2): 110-117 <https://doi.org/doi.org/10.1580/0953-9859-2.2.110>
- Knight AT, Cowling RM, Rouget M, Balmford A, Lombard AT and Campbell BM. Knowing but not doing: selecting priority conservation areas and the research-implementation gap. *Conserv Biol* 2008; 22(3): 610-617 <https://doi.org/10.1111/j.1523-1739.2008.00914.x>
- Kupper T. Re: "A Review of Medical Problems in Himalayan Porters" by Dawadi et al. *High Alt Med Biol* 2020; 21(4): 437 <https://doi.org/10.1089/ham.2020.0130>
- Kupper T, Gieseler U, Angelini GD, Hillebrandt D and Milledge JS. Consensus Statement of the UIAA Medical Commission vol. 2. Emergency Field Management of Acute Mountain Sickness, High Altitude Pulmonary Edema, and High Altitude Cerebral Edema. 2012; 2: 19
- Luks AM, Ainslie PN, Lawley JS, Roach RC and Simonson TS. (2021). *Ward, Milledge and West's High Altitude Medicine and Physiology* (6th ed.). CRC Press. <https://doi.org/10.1201/9780429444333>

- Luks AM, Auerbach PS, Freer L, Grissom CK, Keyes LE, McIntosh SE, Rodway GW, Schoene RB, Zafren K and Hackett PH. Wilderness Medical Society Clinical Practice Guidelines for the Prevention and Treatment of Acute Altitude Illness: 2019 Update. *Wilderness Environ Med* 2019; 30(4S): S3-S18
<https://doi.org/10.1016/j.wem.2019.04.006>
- Luks AM, Swenson ER and Bärtsch P. Acute high-altitude sickness. *Eur Respir Rev* 2017; 26(143)
<https://doi.org/10.1183/16000617.0096-2016>
- McDevitt M, McIntosh SE, Rodway G, Peelay J, Adams DL and Kayser B. Risk determinants of acute mountain sickness in trekkers in the Nepali Himalaya: a 24-year follow-up. *Wilderness Environ Med* 2014; 25(2): 152-159 <https://doi.org/10.1016/j.wem.2013.12.027>
- Mena N, Muñoz P and Seguel N. 3985 Level of knowledge about mountain medicine in mountaineers who tried to ascend Mt. Dhaulagiri during spring 2018. *High Altitude Medicine & Biology* 2018; 19(4): A-405-A-472 <https://doi.org/10.1089/ham.2018.29015.abstracts>
- Richalet JP, Julia C and Lhuissier FJ. Evaluation of the Lake Louise Score for Acute Mountain Sickness and Its 2018 Version in a Cohort of 484 Trekkers at High Altitude. *High Alt Med Biol* 2021; 22(4): 353-361 <https://doi.org/10.1089/ham.2020.0226>
- Richalet JP, Pillard F, D LEM, Riviere D, Oriol P, Poussel M, Chenuel B, Doutreleau S, Verges S, Demanez S, Vergnion M, Boulet JM, Douard H, Dupre M, Mesland O, Remetter R, Lonsdorfer-Wolf E, Frey A, Vilcoq L, . . . Lhuissier FJ. Validation of a Score for the Detection of Subjects with High Risk for Severe High-Altitude Illness. *Med Sci Sports Exerc* 2021; 53(6): 1294-1302
<https://doi.org/10.1249/MSS.0000000000002586>
- Roach R, Kayser B and Hackett P. Pro: Headache should be a required symptom for the diagnosis of acute mountain sickness. *High Alt Med Biol* 2011; 12(1): 21-22; discussion 29
<https://doi.org/10.1089/ham.2010.1070>

Roach RC, Hackett PH, Oelz O, Bärtsch P, Luks AM, MacInnis MJ and Baillie JK. The 2018 Lake Louise
Acute Mountain Sickness Score. High Alt Med Biol 2018; 19(1): 4-6

<https://doi.org/10.1089/ham.2017.0164>

Shlim DR and Gallie J. The causes of death among trekkers in Nepal. Int J Sports Med 1992; 13 Suppl 1:
S74-76 <https://doi.org/10.1055/s-2007-1024601>

Subedi D, Marahatta R, Sharma S, Bajracharya R, Hillenbrand P and Soon Y. Trekkers' awareness of acute
mountain sickness and acetazolamide. Wilderness Environ Med 2008; 19(4): 321-322

<https://doi.org/10.1580/07-weme-le-179.1>

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Table 1: The final statements.

No.	Final statement
1	The altitude traveler understands that symptoms he/she may experience at altitude are likely due to reduced oxygen levels but is aware that other things such as jet lag or poor sleep may cause similar symptoms.
2	The altitude traveler knows that at altitude the blood oxygen saturation is lower than at sea-level.
3	The altitude traveler knows that he/she will feel different, e.g., increased heart and respiratory rates and increased general fatigue, at altitude even if he/she is otherwise not sick and that this different feeling will generally improve over a few days of stay at the same altitude.
4	The altitude traveler knows that irregular “periodic” breathing during sleep is a common response in many individuals at altitude.
5	The altitude traveler knows that AMS symptoms can develop in previously healthy individuals who ascend rapidly to elevations above 2,500 – 3,000 m and that the altitude at which they appear can vary among individuals.
6	The altitude traveler knows that the most important risk factor of AMS is going too high too fast.
7	The altitude traveler knows that adequate fluid intake is necessary in general but that drinking lots of fluid does not prevent AMS.

8	The altitude traveler knows that acetazolamide can be taken for prevention of AMS if the planned ascent profile and the individual's sensitivity to altitude are of concern. Ideally a knowledgeable physician should be consulted for advice and a prescription.
9	The altitude traveler knows that good physical fitness is not protective against the various forms of altitude illness but that it is a prerequisite for trekking and climbing at altitude.
10	The altitude traveler knows that AMS gradually develops following ascent (usually during the first 48h). It is unusual for AMS to arise after having stayed at the same altitude for several days (i.e. more than 3 days).
11	The altitude traveler knows that pharmacological prevention of AMS with acetazolamide means that the risk of getting AMS is reduced but is not eliminated entirely.
12	The altitude traveler knows there are no characteristic physical examination findings to diagnose acute mountain sickness.
13	The altitude traveler knows the main symptoms of AMS: headache, lightheadedness/dizziness, anorexia/nausea/vomiting, fatigue/lethargy, feeling sick/hungover.
14	The altitude traveler understands that symptoms of AMS are not specific and can be due to other health issues not directly related to altitude, but despite this, any symptoms compatible with AMS at high altitude must be managed as if they are AMS until proven otherwise.

15	The altitude traveler knows that acetazolamide is the main pharmacological prophylaxis against AMS. The typical effective dose is 125 mg twice daily and ideally a knowledgeable physician should be consulted for advice and prescription.
16	The altitude traveler knows that persons with mild altitude illness must stop ascending and may stay at the same altitude, while in case of severe disease, descent is mandatory.
17	The altitude traveler knows that someone with severe AMS must not be left alone but should be treated with immediate accompanied descent and given supplemental oxygen if available.
18	The altitude traveler knows that individuals with AMS who fail to improve or worsen over time, should descend until symptoms resolve.
19	The altitude traveler can recognize a patient with suspected HACE in the setting of a recent gain in altitude, the presence of a change in mental status and/or difficulties maintaining balance (ataxia).
20	The altitude traveler knows that HACE is a serious form of altitude illness and that the person affected can die rapidly within a day from HACE.
21	The altitude traveler knows that difficulties maintaining balance (ataxia) also includes not being able to walk in a straight line (perform the heel-to-toe test).
22	The altitude traveler knows that a change in mental status means that the affected person behaves differently than normally or is overly sleepy or acting confused.
23	The altitude traveler knows that in case of HACE descent is the most important treatment.

24	The altitude traveler knows in case of HACE that immediate accompanied descent can be lifesaving. If available, supplemental oxygen and dexamethasone should be administered.
25	The altitude traveler knows that, in case of HACE or HAPE, when evacuation is not possible, a hyperbaric bag (Gamow [®] bag, Certec [®] bag or PAC [®]) can be used but (s)he needs training to be able to use it properly and safely.
26	The altitude traveler knows that inappropriate loss of performance, poor recovery from exercise, shortness of breath at rest, coughing, and feeling very weak may indicate HAPE after a recent gain in altitude.
27	The altitude traveler knows that in case of HAPE descent is the most important treatment.
28	The altitude traveler knows in case of HAPE supplemental oxygen should be used, if available, during the descent and that the patient needs to be accompanied during the descent.

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Pubmed search: "acute mountain sickness"
[All Fields]
(n = 5068)

Authors with < 9 publications
(n = 4978)

Moderator
(n = 1)

Extra authors identified by screening
with < 9 publications
(n = 11)

No e-mail address found
(n = 19)

Deceased / severely ill
(n = 3)

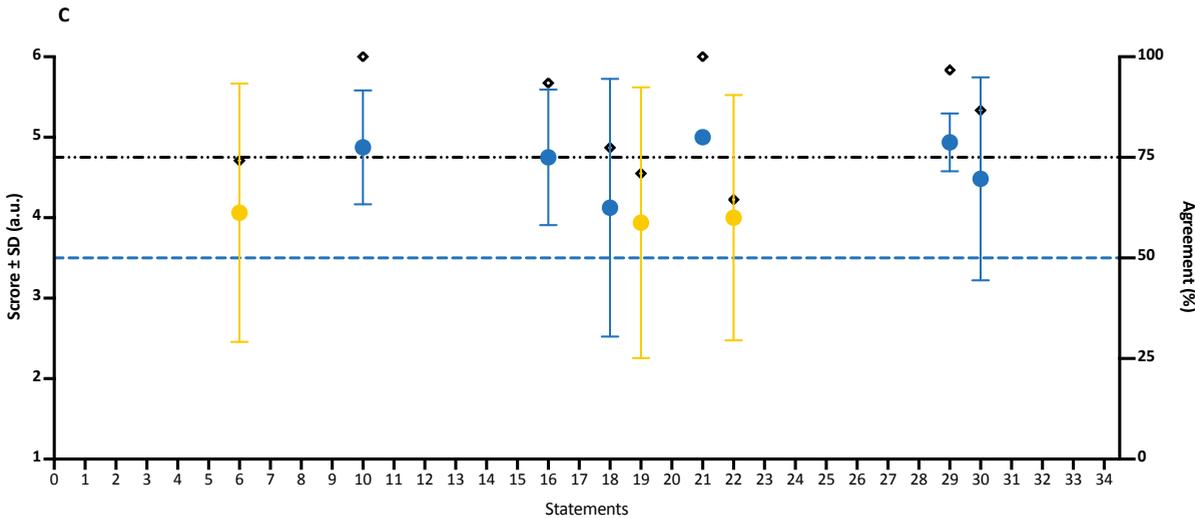
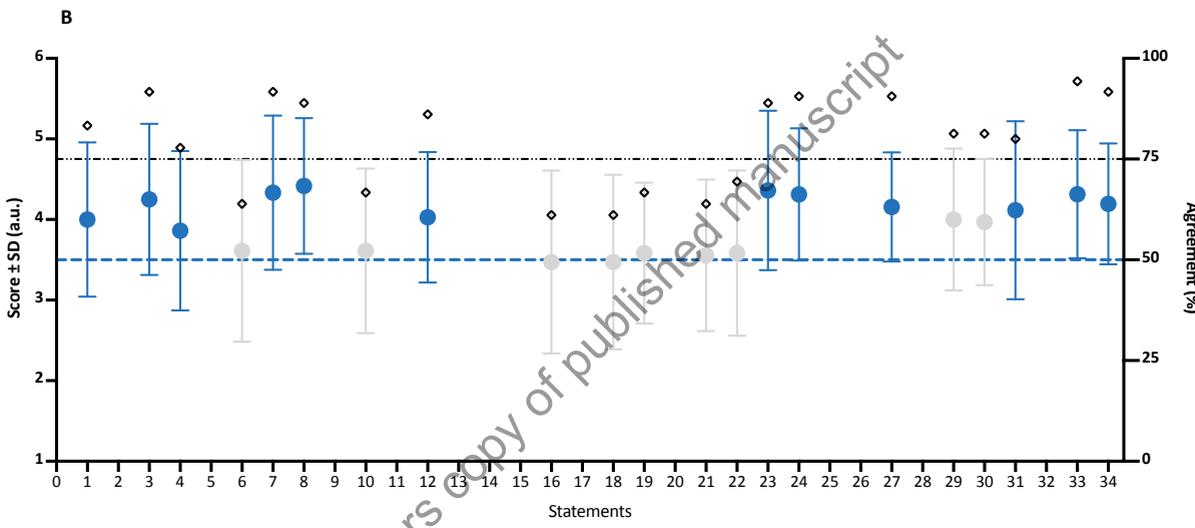
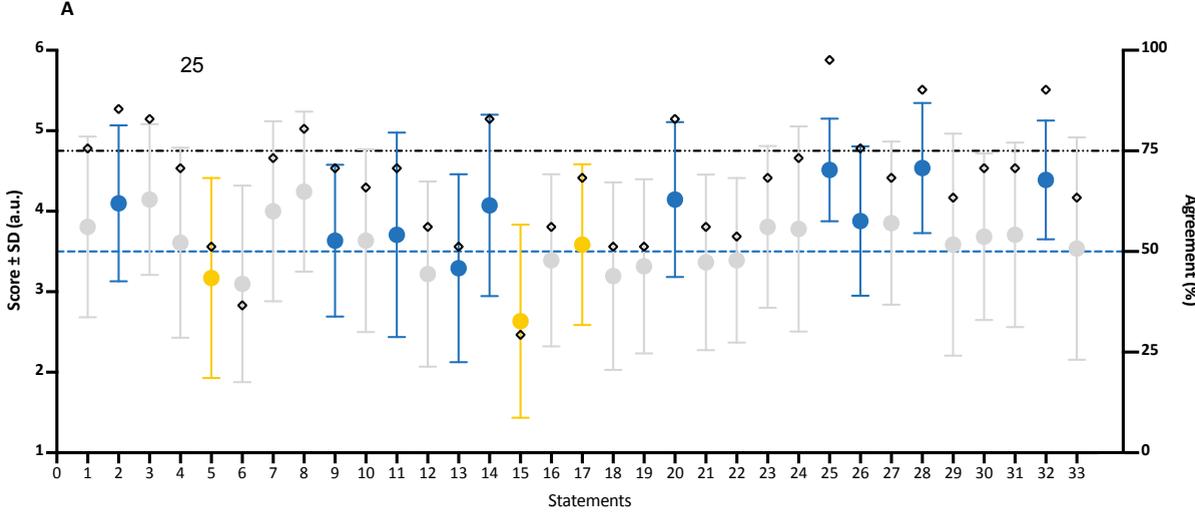
Invited by e-mail to participate
(n = 78)

Invalid e-mail address
(n = 2)

Total successful invitations
(n = 76)

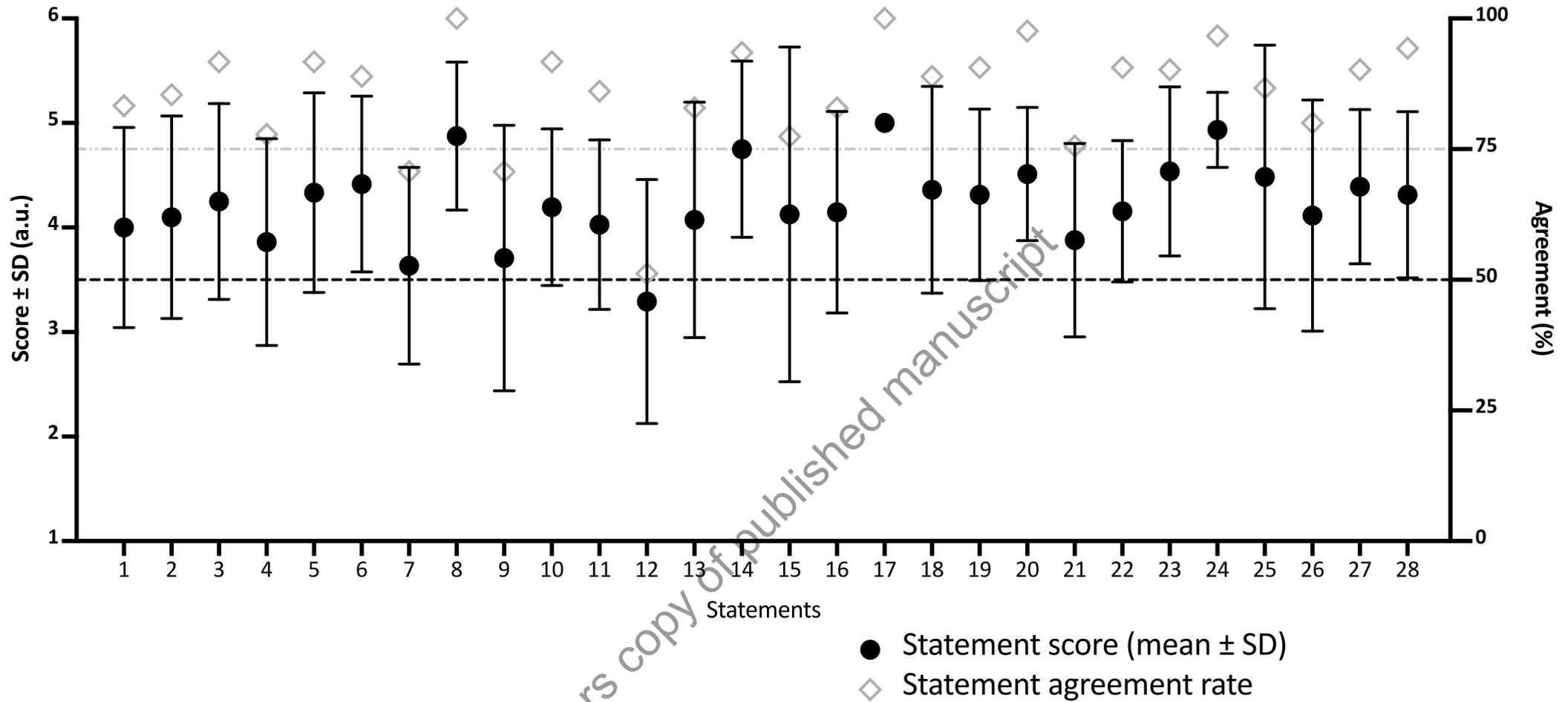
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- ◆ Agreement rate
- Re-evaluation
- Accepted
- Rejected



	1	2	3	4	5 (7)	6 (8)	7 (9)	8 (10)	9 (11)	10 (34)	11 (12)	12 (13)	13 (14)	14 (16)	15 (18)	16 (20)	17 (21)	18 (23)	19 (24)	20 (25)	21 (26)	22 (27)	23 (28)	24 (29)	25 (30)	26 (31)	27 (32)	28 (33)
●	4.0	4.1	4.3	3.9	4.3	4.4	3.6	4.9	3.7	4.2	4.0	3.3	4.1	4.8	4.1	4.1	5.0	4.4	4.3	4.5	3.9	4.2	4.5	4.9	4.5	4.1	4.4	4.3
T	1.0	1.0	0.9	1.0	1.0	0.8	0.9	0.7	1.3	0.7	0.8	1.2	1.1	0.8	1.6	1.0	0.0	1.0	0.8	0.6	0.9	0.7	0.8	0.4	1.3	1.1	0.7	0.8
◇	83	85	92	78	92	89	71	100	71	92	86	51	83	94	77	83	100	89	91	98	76	91	90	97	87	80	90	94

Legends

Figure 1: Schematic representation of expert selection (n=number of identified experts).

Figure 2: Mean scores and the agreement rates (%) of all statements. Red represents the rejected statements, green represents the accepted statements, and gray represents the statements to be re-evaluated. The x-axis shows that in Round 2, 1 new statement was added. The black diamond represents the agreement rate.

Figure 3: Mean final scores and the agreement rates (%) of the accepted statements. The black dotted line indicates the cutoff value for the score. The gray dotted line indicates the cutoff value for the agreement rate. The table below the graph shows the data associated with the figure and indicates which original statement corresponds to which newly numbered statement.

Table 1: List of the final statements and their corresponding numbers.

Supplements for online publication only

Supplementary Table S1: The original statements from Round 1.

Supplementary Table S2: The mean scores and the agreement rates for Round 1.

Supplementary Table S3: The list of the statements in round 3, including the 3 rejected statements with their results. The cells highlighted in gray represent the rejected statements. Below the statement numbers from round 3 are the statement numbers (in parentheses) from the final list of statements.

Supplementary document S4: A detailed description of the rounds in the Delphi process.

Supplementary table S1: Statements Round 1

1	The altitude traveler is able to correlate the perceived and/or experienced disabilities at altitude to the reduction in oxygen availability in the air.
2	The altitude traveler knows that at altitude the blood oxygen saturation is lower than at sea-level.
3	The altitude traveler knows that they will feel different, e.g. an increased heart rate and respiratory rate, at altitude even if they are otherwise not sick.
4	The altitude traveler knows that irregular breathing during sleep is a common response at altitude in most subjects above 5,000 m.
5	The altitude traveler knows that irregular breathing during sleep is not a sign of AMS.
6	The altitude traveler knows that low dose acetazolamide can improve sleep at altitude by reducing irregular breathing and that a (mountain medicine) physician can be consulted for advice on this medication.
7	The altitude traveler knows that AMS is a self-limiting condition, that the altitude at which symptoms start varies between individuals and locations in the world and that it appears in previously healthy individuals who ascend rapidly above 2,500 m.
8	The altitude traveler knows that there is an interaction between the rate of ascent and the ultimate altitude achieved and that the most important risk factor is going too fast too high.
9	The altitude traveler knows that adequate fluid intake is necessary in general but that drinking lots of fluid does not prevent AMS.

10	The altitude traveler knows that acetazolamide can be taken for prevention of AMS starting the day before or the day of ascent and that a (mountain medicine) physician can be consulted for advice on this medication.
11	The altitude traveler knows that good physical fitness is not protective against the various forms of altitude illness but is a prerequisite for trekking and climbing at altitude.
12	The altitude traveler knows that AMS gradually develops after 4-12 hours following ascent to a given elevation and rarely after 24 hours after arriving at that altitude.
13	The altitude traveler knows there are no characteristic physical examination findings to diagnose acute mountain sickness.
14	The altitude traveler knows the main symptoms of AMS: headache, lightheadness/dizziness, anorexia/nausea/vomiting, fatigue/lethargy, feeling sick/hungover.
15	The altitude traveler is able to use the modified functional score* in order to diagnose and determine the severity of AMS. *Modified AMS Clinical Functional Score. Overall, if you have AMS symptoms, how do they affect your activities? 0—Not at all; 1—Symptoms present, but do not force any change in activity or itinerary; 2—My symptoms force me to stop the ascent; 3—My symptoms force me to go down on my own power; 4—I have to be evacuated to a lower altitude
16	The altitude traveler understands that symptoms of AMS are not specific and can also indicate dehydration, viral infection, migraine, hangover or carbon monoxide poisoning, and even acetazolamide side effects.
17	First time altitude travelers should adhere to the recommended ascent rates and may be able to go faster or have to go slower on a subsequent trip.

18	The altitude traveler knows that acetazolamide is the main pharmacologic prophylaxis against AMS in a dose of 125 mg every 12 hours and that a (mountain medicine) physician can be consulted for advice on this medication.
19	The altitude traveler knows that acetazolamide does not mask AMS, it is helping the body to acclimatize.
20	The altitude traveler knows that persons with mild altitude illness can stop ascending and stay at the same altitude, while in case of severe disease, descent is mandatory.
21	The altitude traveler knows that in severe AMS descent can be supplemented with taking dexamethasone (4 mg every 6 hours).
22	The altitude traveler knows that those individuals whose symptoms resolve with appropriate treatment can continue their ascent to higher elevation and may use prophylactic acetazolamide (125 mg every 12 hours) during this time.
23	The altitude traveler knows that individuals with mild AMS who fail to improve after appropriate therapy or worsen at any time, should descend until symptoms resolve.
24	The altitude traveler is able to recognize a patient with HACE: In the setting of a recent gain in altitude, the presence of change in mental status or acting drunk in a person with AMS, or the presence of both mental status change and acting drunk in a person without AMS.
25	The altitude traveler knows that HACE is a serious form of altitude illness and that the person affected can die from this illness.
26	The altitude traveler knows that acting drunk means, not able to walk in a straight line (perform the heel-to-toe test).

27	The altitude traveler knows that a mental status change means, a change in the level of alertness or consciousness and or alterations in cognitive function.
28	The altitude traveler needs to know that in case of HACE descent is the primary treatment.
29	The altitude traveler knows in case of HACE to add dexamethasone to the treatment (4 mg every 6 hours with a starting dose of 8 mg), and oxygen when present, but that this should not delay the descent, and that the patient should be supported down preferably by a medically knowledgeable person.
30	The altitude traveler knows, in case of HACE, that when evacuation is not possible a hyperbaric bag can be used.
31	The altitude traveler is able to recognize a patient with HAPE: In the setting of a recent gain in altitude, and the presence of shortness of breath at rest, cough, weakness or decreased exercise performance and poor recovery from exercise.
32	The altitude traveler knows that in case of HAPE, descent is the primary treatment.
33	The altitude traveler knows in case of HAPE to add nifedipine to the primary treatment (30 mg slow release every 12 hours) and that oxygen should be used when present but that this should not delay the descent and that the patient should be supported down.

Supplementary table S2: Mean \pm SD score per statement for Round 1 and the agreement rate.

Statement	Mean \pm SD	Agreement (%)
1	3.8 \pm 1.1	76
2	4.1 \pm 1.0	85
3	4.1 \pm 0.9	83
4	3.6 \pm 1.2	71
5	3.2 \pm 1.2	51
6	3.1 \pm 1.2	37
7	4.0 \pm 1.1	73
8	4.2 \pm 1.0	80
9	3.6 \pm 0.9	71
10	3.6 \pm 1.1	66
11	3.7 \pm 1.3	71
12	3.2 \pm 1.2	56
13	3.3 \pm 1.2	51
14	4.1 \pm 1.1	83
15	2.6 \pm 1.2	29
16	3.4 \pm 1.1	56
17	3.6 \pm 1.0	68
18	3.2 \pm 1.2	51
19	3.3 \pm 1.1	51

20	4.1 ± 1.0	83
21	3.4 ± 1.1	56
22	3.4 ± 1.0	54
23	3.8 ± 1.0	68
24	3.8 ± 1.3	73
25	4.5 ± 0.6	98
26	3.9 ± 0.9	76
27	3.9 ± 1.0	68
28	4.5 ± 0.8	90
29	3.6 ± 1.4	63
30	3.7 ± 1.0	71
31	3.7 ± 1.1	71
32	4.4 ± 0.7	90
33	3.5 ± 1.4	63

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Supplementary table S3. The list of the statements in Round 3

No.	Statement	Mean \pm SD	Agreement (%)
6	The altitude traveler knows that acetazolamide can improve sleep at altitude and that ideally a knowledgeable physician should be consulted for advice on this medication.	4.1 \pm 1.6	72
10 (8)	The altitude traveler knows that acetazolamide can be taken for prevention of AMS if the planned ascent profile and the individual's sensitivity to altitude are of concern. Ideally a knowledgeable physician should be consulted for advice and a prescription.	4.9 \pm 0.7	97
16 (14)	The altitude traveler understands that symptoms of AMS are not specific and can be due to other health issues not directly related to altitude, but despite this, any symptoms compatible with AMS at high altitude must be managed as if they are AMS until proven otherwise.	4.8 \pm 0.8	91
18 (15)	The high altitude traveler knows that acetazolamide is the main pharmacological prophylaxis against AMS. The typical effective dose is 125 mg twice daily and ideally a	4.1 \pm 1.6	75

	knowledgeable physician should be consulted for advice and prescription.		
19	The altitude traveler knows that acetazolamide does not mask AMS symptoms but actually helps the body adapt to the altitude.	3.9 ± 1.7	69
21 (17)	The altitude traveler knows that someone with severe AMS must not be left alone but should be treated with immediate accompanied descent and given supplemental oxygen if available.	5.0 ± 0.0	100
22	The altitude traveler knows that those individuals whose AMS symptoms fully resolve with appropriate treatment can continue their ascent to higher elevation and may use prophylactic acetazolamide at this time.	4 ± 1.5	66
29 (24)	The altitude traveler knows in case of HACE that immediate accompanied descent can be lifesaving. If available, supplemental oxygen and dexamethasone should be administered.	4.9 ± 0.4	97
30 (25)	The altitude traveler knows that in cases of HACE or HAPE, when evacuation is not possible, a hyperbaric bag (e.g. Gamow® bag) can be used but (s)he needs training to be able to use it properly and safely.	4.5 ± 1.3	84

Supplementary document S4: Detailed description of the rounds in the Delphi process.

In Round 1, we presented the 33 statements to the plenary group. The recruitment strategy resulted in 76 experts (including the 10 core experts and the moderators) being invited to participate in the study (Figure 1). Of those, 41 completed the first round (response rate 54%) (Figure 2 and supplementary table S2). Ten statements (5, 6, 12, 13, 15, 16, 18, 19, 21, and 22) reached less than moderate agreement but were not rejected in this round. Of these 10 statements, 1 statement (13) was accepted. Two statements (5 and 15) were rejected based on their scores (2.9 ± 0.4), agreement rate ($40 \pm 16\%$), and comments. The other 7 statements were advanced to the next round. One of these statements (12) was accepted in Round 2. Three were rejected in Round 3 (6, 19, and 22), and 6 (10, 16, 18, 21, 29, and 30) were added to the final minimum set of knowledge for laypersons. The mean score of these final 6 statements was initially 3.5 ± 0.2 with an agreement rate of $61\% \pm 7\%$, while in their final form these statements were accepted with a score of 4.7 ± 0.3 and an agreement rate of $90\% \pm 9\%$. In Round 1 a total of 3 statements were rejected (average score 3.1 ± 0.4 ; agreement $50 \pm 16\%$, red dots in figure 2). One statement was rejected because it was judged redundant and confusing concerning a different statement. A second statement was discarded because of disagreement among the plenary members. It proposed that altitude travelers in non-research settings would use the modified functional score of the Lake Louise score to diagnose and determine the severity of AMS. Similarly, the full Lake Louise AMS score had been proposed in the pre-round but was rejected by the core experts. The reason advanced for these rejections was that in the current Lake Louise consensus it is stated that: "This Lake Louise AMS score is for use by investigators studying AMS".{Roach, 2018 #34} It is not intended for use by clinicians, guides, or laypersons to diagnose or manage AMS outside research settings. The third rejected statement concerned ascent rate recommendations. The applicable guideline distinguishes

between risk categories for developing AMS depending on the ascent rate. {Luks, 2019 #44} An adaptation of this guideline based on personal previous altitude experience of the altitude traveler was rejected by the experts (supplementary table S1). Of the remaining statements, 10 were accepted (average score 4.0 ± 0.4 ; agreement $80 \pm 13\%$). Of these statements, 3 statements had not strictly met the a priori acceptance requirements but were accepted, nevertheless. These are statements 9, 11, and 13.

Statement 9

Statement 9 stated: "The altitude traveler knows that adequate fluid intake is necessary in general, but that drinking lots of fluid does not prevent AMS." Although the score reached 3.6 ± 0.9 , the agreement percentage was 71%. This statement consisted of 2 parts, with the first deemed to be correct, but "necessary in general" was considered too vague. The second part provoked discussion because of current misconceptions among laypersons surrounding fluid intake at altitude. The second part of this statement was formulated by 1 of the core experts. Since the plenary group agreed on the educational importance of this statement, the moderators and core experts decided to accept it.

Statement 11

Statement 11 stated: "The altitude traveler knows that good physical fitness is not protective against the various forms of altitude illness but is a prerequisite for trekking and climbing at altitude." It was intended to clarify that good physical condition does not necessarily protect against altitude illness. While there is no clear evidence that good physical fitness is necessary for comfortably traveling to altitude, the moderators and core experts had proposed this statement. Some plenary members again commented on the current knowledge among laypersons on this topic. Since most plenary members

agreed with the statement, which reached a score of 3.7 ± 1.3 and an agreement rate of 71%, the moderators decided to accept it, keeping in mind that the agreement among the core experts in the pre-round was 89% with a score of 4.4 ± 0.5 .

Statement 13

Statement 13 stated: "The altitude traveler knows there are no characteristic physical examination findings to diagnose acute mountain sickness." This had a score of 3.3 ± 1.2 and an agreement rate of 51%. The plenary experts indicated that medically trained personnel should know this but disagreed on whether laypersons should also know it. Some experts felt that the focus should be on symptoms of altitude illness, while others suggested including clinical signs. Based on their field and teaching experience, the moderators decided to keep the statement.

The remaining 20 statements (average score 3.6 ± 0.3 ; agreement rate $64 \pm 11\%$) were then modified according to the comments from the plenary group in preparation for the next round. Although statements 1, 3, and 8 had already met the acceptance requirements, they were included for the second round because they were conceptually modified based on the comments from the plenary group. Finally, based on the feedback from the plenary group, 1 new statement was added to the list for Round 2.

Round 2

The list submitted to the plenary group in the second round consisted of 21 statements. Thirty-six of the 41 experts (88%) who completed Round 1 also completed Round 2. In the second round, no statements were rejected. Twelve further statements (average score 4.2 ± 0.2 ; agreement rate $88 \pm 5\%$) were accepted by reaching the a priori acceptance requirements. The wording of 10 statements was slightly

reformulated with the help of a native English-speaking plenary member. At the end of this round, 9 statements (average score 3.3 ± 1.2 ; agreement rate $68 \pm 8\%$) needed further consideration and progressed to Round 3.

Round 3

Thirty-two experts participated in the third round, 78% of the initial 41 who participated in the first round. The experts rejected 3 of the remaining 9 statements under consideration (average score 4.0 ± 0.1 ; agreement rate $69 \pm 3\%$). The first rejected statement in this round concerned the use of acetazolamide to improve sleep at high altitude. The general conclusion of the experts was that this is beyond the scope of desired minimum knowledge of the target group. The second statement that was rejected stated that acetazolamide does not mask symptoms of altitude illness but helps with acclimatization. A large fraction of the plenary group expressed concern that this statement would be difficult for laypersons to understand and might encourage excessive use of acetazolamide. The last statement rejected in this round concerned continuing to ascend after recovery from AMS and whether to use acetazolamide to continue the ascent at the traveler's discretion. The proposal to continue ascending after recovery from AMS was not accepted by the plenary group (Supplementary table S3).