Clinical Finding Form (CliFF)

Branch Baseline

ICL39_Eva Related Decompression Sickness

Decompression Sickness (DCS) is caused by evolved gas bubbles which form when living tissues are subjected to reductions in environmental pressure. Such reductions in pressure can occur during decompression prior to EVA in space. Before decompression, nitrogen (N2) is dissolved in the body tissues and fluids at a partial pressure of the N2 in a normal human breathing mixture. Nitrogen supersaturation occurs in the tissues and fluids during decompression as the environmental pressure is reduced more rapidly than the tissue pressure of N2. When the magnitude and rate of environmental pressure reductions are sufficient, supersaturation with N2 can lead to the transition of N2 from the dissolved phase into the gas phase as gas emboli. Various clinical symptoms of altitude DCS are thought to result mainly from physical interactions of gas bubbles with tissues and fluids. Size and location of these bubbles are thought to have a significant effect on the resulting DCS symptoms. Gas bubbles deform tissues and interact with nerve endings or block microcirculation. In addition, bubbles interacting with lung tissue may release various mediators resulting in systemic symptoms. The resulting symptoms include pain, sensory deprivation, skin manifestations, and respiratory distress. Risk of DCS increases with extended altitude exposure times, very high altitudes, and greater physical activity during the exposure. The risk decreases with preoxygenation, particularly when combined with exercise. (Conkin, 2004). In spaceflight the greatest risk for DCS occurs during EVA due to the decreased pressure used in the EVA suit as compared to the primary vehicle. Symptoms would be expected to occur during the EVA. Terrestrially, DCS is typically broken into 2 categories: Type I or “pain only” DCS and Type II which involves neurologic manifestations and/or cutaneous involvement (Conkin, 2020). In spaceflight 4 Cuff Classes (so named because the criteria reside on the cuff of the EVA suit for ease of access) are used to delineate the symptoms of DCS. Cuff Classes 1 and 2 correlate to Type 1 DCS, Cuff Class 3 could represent either Type 1 or Type 2 depending on symptom involvement, and Cuff Class 4 correlates to Type 2 DCS.

INCIDENCE DATA INCLUDED IN THE MODEL

The model imports the following incidence information from the MEDPRAT Evidence Library Database: incidence data category, space adaption status, EVA status, incidence data type, incidence and occurrence distribution data and incidence data characteristics. Data category defines the type of data available for incidence calculations (i.e. raw data vs. adjusted data). Space adaptation identifies medical events that where onset occurs in the first 5-7 days of flight and does not reoccur. EVA-related incidence values identify medical events that occur only during an EVA. Incidence values types vary by data category and define the number of medical events per person-year (rates) or medical events per person at-risk (proportion) for each medical condition. Incidence values can be modified by crew characteristics such as gender sex and certain crew medical history characteristics. Modifying characteristics are noted below and incidence values are listed individually for each characteristic. Distributions are assigned to medical events incidence values and occurrences in the model. For each crewmember in a given trial, the incidence and number of occurrences of each medical condition are randomly selected from these probability distributions. Detailed descriptions of the distributions are included in the MEDPRAT Technical Description Document.

INCIDENCE DATA

SPACEFLIGHT LITERATURE

There have been no documented cases of DCS during EVA in U.S. Spaceflight (NASA, Decompression Sickness Secondary to Extravehicular Activity CLiFF, 2016). According to Biomedical Results of Apollo the Command Module Pilot revealed in his account of the Apollo Program that he had experienced dysbarism (bends) on his first space flight (Gemini 10) as well as on his second space flight (Apollo 11). He experienced pain in his left knee during cabin pressure change from 14.7 to 5.0 psia. He described symptoms involving the left knee as a sharp, throbbing ache which gradually worsened and leveled off at a moderate, but very uncomfortable level of pain. The symptomatology was less painful on Apollo 11 than it had been on Gemini 10 (NASA, Decompression Sickness Secondary to Extravehicular Activity CLiFF, 2016). However, neither of these events was associated with extravehicular activity (EVA) and thus is not counted as part of the incidence information used for this medical condition, DCS associated with EVA.

ANALOG LITERATURE

Conkin, 2020 was used to inform the incidence distribution for this condition. It describes a probabilistic model used at NASA, JSC to predict the risk of hypobaric decompression sickness (DCS) and venous gas embolism (VGE) (an asymptomatic precursor of bubble formation to DCS). The model is derived from baseline data regarding DCS and VGE from 1,031 hypobaric decompressions from 1983 to 2016. A total of 577 humans participated in 49 hypobaric chamber tests to evaluate denitrogenation procedures used by astronauts in the Space Shuttle and International Space Station programs. Participants were mostly male (80.9%: M, 834 exposures, F, 197 exposures), with a mean age of 32.1 years (SD 7.9 years), and a mean body mass index of 24.2 (SD 2.8). This study specifically looked at the agreed upon Exploration Atmosphere (EA) prebreathe protocol for exploration missions to quantify the risk of DCS and VGE during exploration surface EVAs such as Lunar and Martian EVAs. It reports a risk of 3.1% (1.8% to 5.2 95% confidence interval) of a DCS event occurring. "The EA prebreathe protocol is an engineering solution to eliminate DCS as an operational and medical concern and to free the crew from the overhead of conducting a lengthy in-suit prebreathe. Current prebreathe options require the crew to flawlessly execute the protocol with significant support from Mission Control personnel. Protocols available for the International Space Station are considered “just in time” mitigations in that you complete the minimum prebreathe just in time before the EVA. This approach has more uncertainty as to its efficacy than an alternative approach. A better approach is to live in an environment where tissue N2 tension is reduced to a point where it is very near or even lower than the suit pressure. In this way, you minimize with greater certainty the tissue N2 supersaturation during the EVA. The challenge with this approach is to reduce atmospheric PN2 without increasing atmospheric PO2 to minimize the risk of flammability and medical concerns with hyperoxia. The approach is to reduce ambient pressure in the habitat while increasing the O2 concentration to achieve as low a PN2 while minimizing hypoxia and the risk of fire." (Conkin, 2020). The EA prebreathe protocol involves the

following steps: 1) 3 hr prebreathe, depress habitat to 8.2psia/34% O2 2) Equilibrate at 8.2psia/34% O2 for 48 hours (equivalent to being at about 4,000 ft MSL breathing room air) 3) 15 min depress to EVA atmosphere - 4.3 psia/85% O2 for 6 hour EVA 4) Repress to 8.2psia/34% O2 for 41hr 30 min 5) Repeat steps 4 and 5 an additional 4 times (total of 5, 6 hour EVAs) 6) After 15 min at 8.2psia/34% O2, repress to 14.7 psia/RA During the protocol participants perform exercises to simulate a surface EVA. Conkin notes that these exercises are less than the workload in a real EVA, which could result in an underestimation of this risk. However, a limitation of the modeling is that most baseline data is based on 4 hour EVAs (rather than 6 hour EVAs), so extrapolation to 6 hours, as was done in this model, overestimates the DCS risk.

TERRESTRIAL LITERATURE

It was assumed that terrestrial data would be inadequate for providing input that drives the incidence of this spaceflight specific condition. No terrestrial data searches were performed.

OVERALL INCIDENCE SUMMARY

INCIDENCE

Mean: 0.03329
SD: 0.008851

INCIDENCE SUMMARY

Probability of Decompression Sickness and Venous Gas Emboli from 49 NASA Hypobaric Chamber Tests with Reference to Exploration Atmosphere (Conkin, 2020) was used to inform this incidence distribution because it is specific to the exploration atmospheres anticipated for Artemis Missions. It is a probabilistic model used at NASA. The paper states, “We estimate that an exposure to 4.3 psia with simulated extravehicular activity (EVA) that includes ambulation after equilibration to the exploration atmosphere at 8.2 psia with a 34% oxygen atmosphere will result in 3.1% DCS (1.8% to 5.2 95% confidence interval).” Probability 0.031 (95%CI: 0.018, 0.052) matches closely to 16 events out of 516 attempts. IP: 0.031 (95%CI: 0.018, 0.05). In order to fully encompass the range of the 95% CI, we went with 13 events out of 419 attempts. IP: 0.031 (95%CI: 0.017, 0.053). The distribution for the incidence proportion using data approximated from the DCS probabilistic model is Beta(shape1=13.642, shape2=396.15) with mean 0.03329 and SD 0.008851. This probability is per EVA approximated by EVA simulation. Note this distribution shape matches (and slightly exceeds) the uncertainty of the DCS model. The mean is slightly higher than the DCS prediction but matches it exactly at the mode (most-likely) value in the distribution. This was the distribution of best fit as determined by biostatistics. This incidence distribution assumes that one simulated EVA is a good approximation of a true EVA.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
EVA

Segment
EVA All

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Binomial

Incidence Dist.
Beta

Mean
0.0332901

SD
0.00885104

Beta
(Alpha): 13.642
(Beta): 396.15

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Conkin, 2020	Analog	3

Conkin, 2020 describes a probabilistic model used at NASA, JSC to predict the risk of hypobaric decompression sickness (DCS) and venous gas embolism (VGE) (an asymptomatic precursor of bubble formation to DCS). The model is derived from baseline data regarding DCS and VGE from 1,031 hypobaric decompressions from 1983 to 2016. A total of 577 humans participated in 49 hypobaric chamber tests to evaluate denitrogenation procedures used by astronauts in the Space Shuttle and International Space Station programs. This study specifically looked at the agreed upon Exploration Atmosphere (EA) prebreathe protocol for exploration missions to quantify the risk of DCS and VGE. It reports a risk of 3.1% (1.8% to 5.2 95% confidence interval) of a DCS event occurring. During the protocol participants perform exercises to simulate a surface EVA. Conkin notes that these exercises are less than the workload in a real EVA, which could result in an underestimation of this risk. However, a limitation of the modeling is that most baseline data is based on 4 hour EVAs (rather than 6 hour EVAs), so extrapolation to 6 hours, as was done in this model, overestimates the DCS risk.

CREWMEMBER SELECTION/PREVENTION

DISQUALIFYING CONDITIONS

Refer to Medical Evaluation Documents (MED) Volume A, Medical Standards for ISS Crewmembers, International Space Station Program, Rev 3.4 (2016).

PREFLIGHT PREVENTATIVE MEASURES

Crewmembers receive extensive pre-flight training for EVA pre-breathe protocols on ISS (MR087L). Similar training will be in place for exploration missions. During EVA, crewmembers carry the Cuff Classification for DCS on the sleeve of the EVA suit. This enables real-time assessment of symptoms for reporting to crew surgeons and intervention to prevent progression/treat if necessary.

BEST CASE SCENARIO DEFINITION

Type I DCS with mild to moderate pain in a isolated single joint that resolves spontaneously or with treatment.

WORSE CASE SCENARIO DEFINITION

Severe joint pain, multiple joints with pain, or migrating joint pain, AND/OR Type II DCS with CNS (spotted vision, slurred speech, coordination difficulty, loss of sensation, headache, seizures, unconsciousness) or cardiopulmonary involvement (chest pain, cough, shortness of breath).

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

Conkin, 2020 describes a probabilistic model used at NASA, JSC to predict the risk of hypobaric decompression sickness (DCS) and venous gas embolism (VGE) (an asymptomatic precursor of bubble formation to DCS). The model is derived from baseline data regarding DCS and VGE from 1,031 hypobaric decompressions from 1983 to 2016. In this dataset there have been a total of 125 cases of DCS and 7 have been Type II DCS (worst-case scenario). Therefore the worst-case probability was assigned as 5.6% and the best-case probability was assigned as 94.4%.

TABLE 3.BEST/WORST CASE PROBABILITY LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Conkin, 2020	Analog	4

Conkin, 2020 describes a probabilistic model used at NASA, JSC to predict the risk of hypobaric decompression sickness (DCS) and venous gas embolism (VGE) (an asymptomatic precursor of bubble formation to DCS). The model is derived from baseline data regarding DCS and VGE from 1,031 hypobaric decompressions from 1983 to 2016. A total of 577 humans participated in 49 hypobaric chamber tests to evaluate denitrogenation procedures used by astronauts in the Space Shuttle and International Space Station programs. Participants were mostly male (80.9%: M, 834 exposures, F, 197 exposures), with a mean age of 32.1 years (SD 7.9 years), and a mean body mass index of 24.2 (SD 2.8). In this dataset there have been a total of 125 cases of DCS and 7 have been Type II DCS (worst-case scenario).

TABLE 4. CLIFF TREATMENT & OUTCOME TABLE BY CLINICAL PHASE

Case Scenario	Composite Incidence	Condition Probability %	CP1: Diagnosis		CP2: Treatment			CP3: Condition End State				
			TI%	Duration	TI%	Duration		TI%	RTDC		LOCL	
			Preset	Preset	Preset	Min	Max	Preset	Min%	Max%	Min%	Max%
Treated Best Case (TBC)	Mean: 0.03329 SD: 0.008851	94.4 - 94.4	100	0.5	22.8275	0	24	0	0	0	0	0
Treated Worst Case (TWC)		5.6 - 5.6	100	1.5	52.7239	24	480	5.60723	2.8	20	0	2
Untreated Best Case (UTBC)	N/A	N/A	N/A	0.5	22.8275	0	24	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1.5	100	24	480	100	16.5	52.4	0	50

TABLE 4 KEY

Composite Incidence: The same composite incidence will be used for both TBC and TWC. For EVA conditions: events per EVA (events/EVA). For space adaptation conditions: events per person (events/person). For non-spaceflight conditions: events per person year (events/py).

Condition Probability: The probability that CLiFF condition progresses to a worst case scenario. Best case scenario: 100%-Worst Case.

Clinical Phase General Comments:

- TI% = Task Impairment %. Task Impairment is the % of tasks that the crewmember is incapable of performing without impairment secondary to the medical condition.
- Durations are defined in hours.
- Removal to Definitive Care (RTDC): The probability the entire crew aborts the mission and returns to earth. This is considered as a condition end state result if any of the following criteria are met: 1) the potential for LOCL, 2) potential for significant permanent task impairment, or 3) potential for intractable pain.
- Loss of Crew Life (LOCL): The probability of death of affected crewmember due to medical condition.

Clinical Phase 1: Initial Assessment and Diagnosis:

- Covers only the initial assessment and diagnosis of the affected crewmember to define his or her medical condition. While the affected crewmember is being assessed, he or she is not able to perform any assigned tasks, thus Task Impairment (TI) during this phase is considered 100%. In the untreated case, there is no diagnosis performed, therefore Task Impairment and Duration will always be " not applicable."

Clinical Phase 2: Stabilization, Treatment, and Convalescence:

- The affected crewmember is receiving any appropriate initial or follow-on treatment for his or her medical condition to allow the crewmember to recover as much as he or she is able to recover in the spaceflight environment. Clinical phase 2 also encompasses relapses or recurrences of the same original medical condition in Clinical Phase 1. The duration of Clinical Phase 2 is expressed as minimum and maximum hours.

Clinical Phase 3: Condition End State:

- Reached once the affected crewmember has recovered from the medical condition as much as he or she is able to recover in the spaceflight environment amongst treated and untreated best and worst case scenarios. This may or may not be recovery from the given medical condition to the full extent possible. If this “recovered” state results in Removal to Definitive Care (RTDC) or Loss of Crew Life (LOCL) this will be noted in the condition end state results.

SCENARIO OVERVIEW COMMENTS

While terrestrially DCS is generally described as Type 1 or Type 2, NASA breaks DCS into 4 “Cuff Class” categories as follows (Norcross et al, 2020): Class 1: Mild pain (single/multiple sites) and/or single extremity numbness/tingling. Difficult to discern from suit pressure points. Symptoms do not interfere with performance. The operational response to Cuff Class 1 DCS is to continue the EVA and report the symptoms post-EVA during the private medical conference (PMC) with the flight surgeon. Class 2: Moderate Class 1 symptoms that interfere with performance or symptoms that resolve upon repress. The operational response to Cuff Class 2 DCS is to perform worksite cleanup, minimize the activity level of the affected crewmember, TERMINATE the EVA, and repressurize. Class 3: Severe Class 1 symptom or migratory, truncal/multiple-site numbness/tingling, unusual headache. The operational response to Cuff Class 3 DCS is to assist the affected crewmember to the control lock, safe the worksite, TERMINATE the EVA, and repressurize. Class 4: Serious symptom –central neurological, cardiopulmonary. The operational response to Cuff 4 is to ABORT the EVA. The affected crewmember must be assisted return of affected crewmember to control lock, where they are repressurized alone while the unaffected crewmember safes worksite, TERMINATE the EVA, and then repressurizes. At the time of the composition of this CLiFF, NASAs plan for Artemis Missions was to have the following atmospheres for different vehicles (Norcross et al, 2020): Gateway Atmosphere: 10.2 psia, 26.5% O2 Lander Atmosphere: 8.2 psia, 34% O2 xEMU suit Atmosphere: Planned operations at 4.3 psia, 85% O2, but the pressure will be variable from 4.3-8.2 psia. (Note, prior suits have not had a variable pressure capability). EVAs are assumed to be 6 hours in length. The RTDC surrogate selected was failure of recompression treatment. The untreated scenarios for this condition are not truly untreated (assuming the crewmember is able to return to the vehicle). The xEMU will nominally operate at 4.3 psia, and the vehicle pressures are planned to be 8.2 psia (lunar) and 10.2 psia (Gateway). Therefore, even in the event of a failure to recompress to 8.2psia in the xEMU, returning to the vehicle would provide 3.9-5.9 psia of recompression (which would comprise partial treatment). This was taken into account whenever possible in determining the duration, RTDC probabilities, and LOCL probabilities. For specific details see individual scenarios below.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

The duration was assigned a range of 0-24 hours based on data that were summarized at the Decompression Sickness HSRB Risk Update in July, 2020 regarding symptom resolution and time to bubble resolution (Conkin et al, 2014; Norcross et al, 2020). Based on hypobaric exposures at NASA and the USAF they were able to predict that a return to an 8.2 psia or 10.2 psia vehicle would resolve symptoms in 52.8-66.7% and 66.7-83.5% of cases. Immediate repressurization of the suit to 8.2 psia with a return to an 8.2 psia vehicle (8.2 + 8.2 = 16.4 psia) resolved symptoms in 88.7-96.2% of cases. Immediate represurrization of the suit with a return to a 10.2 psia vehicle (8.2 +10.2 psia = 18.4 psia) resolved symptoms in 91.3-97.2% of cases. Additionally, they modeled bubble formation occurring at 4.3 psia (simulated EVA) and then documented the time to resolution with immediate recompression of the variable pressure EVA suit to 8.2 psia, followed by return to an 8.2 psia vehicle vs. return to a 10.2 psia vehicle. (Note this was modeled as keeping the suit on, which is effectively 8.2 + 8.2 psia = 16.4 psia total vs. 8.2 + 10.2 psia = 18.4 psia total). They found that immediate recompression of the suit to 8.2 psia arrested the growth of the bubble and return to the vehicle decreased the size of the bubble. Time to resolution in the 8.2 psia vehicle (total 16.4 psia) was 1 hour and 45 minutes and time to resolution in the 10.2 psia vehicle (total 18.4 psia) was 1 hour 39 minutes. (Conkin et al, 2014; Norcross et al, 2020) Although these times to bubble resolution are relatively short (less than 2 hours), a crewmember who experienced DCS would be grounded from duty for 24 hours after the event. Therefore, the duration was assigned a minimum of 0 (symptoms resolved spontaneously) and a maximum duration of 24 hours. Full recovery is anticipated in a best-case treated scenario, thus RTDC was assigned a 0% probability. The LOCL for a best-case treated DCS scenario was assumed to be 0%.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

The duration was assigned a range of 24-480 hours. The minimum duration is based on bubble resolution simulations from Conkin et al, 2014 (Conkin et al, 2014; Norcross et al, 2020) and a current grounding time of 24 hours after a DCS event. The maximum duration is informed by Vann et al, 2010. This is a terrestrial review, primarily of hyperbaric exposures (diving). It states that if DCS symptoms persist, the terrestrial treatment standard of care is daily hypobaric oxygen treatment. Most patients with residual neurologic manifestations will reach a clinical plateau in 2-3 treatments, but severe cases require 15-20 repetitive treatments to reach a clinical plateau. Thus 20 days (480 hours) was assigned as the maximum duration. The RTDC probability was assigned a range of 2.8-20%. The minimum probability was informed by Conkin et al, 2014 (summarized in the HSRB update Norcross et al, 2020) in which they report a 2.8-11.3% failure rate for symptom resolution with repressurization (xEMU repressurized to 8.2 and vehicle 10.2, total of 18.4 psia). Note, these data include Type I and Type II DCS. It is unclear whether repeat treatments will be feasible in exploration missions, but if the crewmember came out of the suit the ambient pressure of the vehicle is still higher than that of an EVA. With time, symptoms may continue to improve. The maximum probability was informed by Butler et al, 2000; a USAF review of 1153 cases of altitude DCS (both chamber and operational) spanning 58 years report an overall failure rate of recompression of 2-5%. However, when these data are restricted to Treatment Table 6 and Treatment Table 8 protocols (used for Type 2 DCS) the range of failure is 0-20%. The LOCL probability was assigned 0-2% based on approximately 17 fatalities in 743 cases of "serious" DCS in a USAF review of 1153 cases of altitude DCS between 1941-1999 (Butler et al, 2000).

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

The duration was assigned a range of 0-24 hours based on data presented at the Decompression Sickness HSRB Risk Update in July, 2020 regarding symptom resolution and time to bubble resolution (Conkin et al, 2014; Norcross et al, 2020). This is the same as the duration assigned to the treated best-case scenario for multiple reasons: 1) In a case that resolves spontaneously, the minimum duration is unchanged. 2) Per Vann et al, the outcome in minor cases of DCS is likely to be similar in untreated and treated patients (Vann et al, 2010). 3) As long a crewmember with DCS on an EVA could get back to the vehicle, this condition would not have a truly "untreated" scenario because repressurization from EVA (4.3 psia) to the pressure of the vehicle (either 8.2 or 10.2 psia) in itself is partial treatment. Based on hypobaric exposures at NASA and the USAF Conkin et al were able to predict that a return to an 8.2 psia or 10.2 psia vehicle would resolve symptoms in 52.8-66.7% and 66.7-83.5% of cases (Conkin et al, 2014; Norcross et al, 2020). A crewmember who experienced DCS would be grounded from duty for 24 hours after the event. Therefore, the duration was assigned a minimum of 0 (symptoms resolved spontaneously) and a maximum duration of 24 hours. The RTDC probability was

assigned 0% for this scenario based on the assumption that a best-case scenario DCS outcome would be unlikely to be significantly worse in the untreated scenario (Vann et al, 2010). This is especially true given (assuming the crewmember is able to return to the vehicle), "lack of treatment" would consist of recompression to at least 8.2 psia (a differential of 3.9 psia above the xEMU pressure). The LOCL probability was assigned 0% for this scenario based on the assumption that a best-case scenario DCS outcome would be unlikely to be significantly worse in the untreated scenario (Vann et al, 2010). This is especially true given (assuming the crewmember is able to return to the vehicle), "lack of treatment" would consist of recompression to at least 8.2 psia (a differential of 3.9 psia above the xEMU pressure). It is assumed that Type I DCS is not associated with fatality.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

There is a paucity of data regarding untreated type 2 DCS. Therefore, the duration is repeated from the worst-case treated scenario. As long a crewmember with DCS on an EVA could get back to the vehicle, this condition would not have a truly "untreated" scenario because repressurization from EVA (4.3 psia) to the pressure of the vehicle (either 8.2 or 10.2 psia) in itself is partial treatment. Based on hypobaric exposures at NASA and the USAF Conkin et al were able to predict that a return to an 8.2 psia or 10.2 psia vehicle would resolve symptoms in 52.8-66.7% and 66.7-83.5% of cases (Conkin et al, 2014; Norcross et al, 2020). The minimum duration is based current duty grounding time of 24 hours after a DCS event. The maximum duration is informed by Vann et al, 2010. This is a terrestrial review, primarily of hyperbaric exposures (diving). It states that if DCS symptoms persist, the terrestrial treatment standard of care is daily hypobaric oxygen treatment. Most patients with residual neurologic manifestations will reach a clinical plateau in 2-3 treatments, but severe cases require 15-20 repetitive treatments to reach a clinical plateau. Thus 20 days (480 hours) was assigned as the maximum duration. The RTDC probability was assigned a range of 16.5-52.4%. This probability was informed by Conkin et al, 2014 (summarized in the HSRB update Norcross et al, 2020) in which they report a symptom recovery rate of 47.6-66.7% with only return to 8.2psia and a symptom recovery rate of 66.7-83.5% with return to 10.2 psia. This corresponds to a 16.5-52.4% failure rate for symptom resolution with repressurization (to 8.2 psia or 10.2 psia). This would represent returning to the vehicle, but not having the capability to repressurize the xEMU suit above ambient pressure. Assuming the crewmember was able to return to the vehicle, this is the "untreated" scenario. Note, these data include Type I and Type II DCS. There is a paucity of data to inform LOCL for untreated Type II DCS. Therefore the LOCL probability of an untreated, Type II DCS was assigned a range of 0-50% to account for this uncertainty based on subject matter expert opinion.

TABLE 5. CLINICAL PHASE II DURATION LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Norcross et al, 2020	Analog	3
Conkin et al, 2014	Analog	
Vann et al, 2010	Analog	

Durations were informed by altitude DCS analog data from NASA and the USAF. When possible, data specific to the atmospheres of the xEMU suit and the vehicles that will be used in Artemis were used to inform the durations.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Butler et al, 2000	Analog	3
Norcross et al, 2020	Analog	
Conkin et al, 2014	Analog	
Vann et al, 2010	Analog	

RTDC probabilities were informed by altitude DCS analog data from NASA and the USAF. When possible, data specific to the atmospheres of the xEMU suit and the vehicles that will be used in Artemis were used to inform these probabilities. The assumption was made that in a best-case scenario, RTDC probability would be 0%.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Butler et al, 2000	Analog	
Norcross et al, 2020	Analog	

Citation	Source	LOC Value 2
Conkin et al, 2014	Analog	
Vann et al, 2010	Analog	

LOCL probabilities were informed by altitude DCS analog data from NASA and the USAF. When possible, data specific to the atmospheres of the xEMU suit and the vehicles that will be used in Artemis were used to inform these probabilities. The assumption was made that in a best-case scenario, LOCL probabilty would be 0%. There is a paucity of data to inform a worst-case scenario, untreated, probability of LOCL. Therefore the range of 0-50% was assigned to this scenario based on subject matter expert opinion.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope

Overview

Decompression sickness occurs when intravascular dissolved gas compressed under pressure dissolves into tissue and rapidly reexpand into bubbles when pressure is reduced. Paramount of these gases is nitrogen which is not buffered by hemoglobin and instead reaches equilibrium between tissue and inspired partial pressure. Bubble formation has mechanical effects on local tissue, directly obstructs blood flow, or induces clot formation causing the constellation of symptoms that defines this syndrome. DCS has been effectively mitigated in spaceflight thus far operationally with oxygen prebreathing protocols. However, for future lunar missions there are likely to be substantially more EVA's per mission and varied pressure environments from transport to space station to lunar module to xEMU.
Type I DCS is considered mild and includes only pain symptoms and typically presents as musculoskeletal, joint, or skin pain (the 'bends') and may have some cutaneous erythema. Type II DCS typically presents as neurologic symptoms and/or gas embolism and is considered more severe. The definition used for the best case scenario in this condition was Type I DCS with mild to moderate pain in a isolated single joint that resolves spontaneously or with treatment. The definition used for worst case scenario in this condition was "severe joint pain, multiple joints with pain, or migrating joint pain, AND/OR Type II DCS with CNS (spotted vision, slurred speech, coordination difficulty, loss of sensation, headache, seizures, unconsciousness) or cardiopulmonary involvement (chest pain, cough, shortness of breath)."

Diagnostic Scope and Resourcing
In the best-case scenario, diagnosis is based on history and physical alone. It is assumed that in this case the crew member has mild joint pain during or post EVA that is clearly related to pressure changes and DCS without a broad differential diagnosis

In the worst-case scenario, diagnosis is based on history, physical, EKG, and ultrasound. Type II DCS includes more severe cardiopulmonary and neurologic features which may limit the utility of H&P alone and thus consideration of a larger differential diagnosis is included. Ultrasound would be preferred for differential diagnosis consideration but is not necessary.

Clinical Phase 1 Duration and Rationale
This version of IMPACT presumes physician level knowledge, skill, and ability will be present on the mission. The CRT working group SME consensus duration is as follows:

CP1 BC (Treated or Untreated): 0.5 hours
CP1 WC (Treated or Untreated): 1.5 hours

Scope of practice for this condition with regards to both the best-case and worst-case scenario was determined to be level 5 (attending level physician). This is due to the possible complexity of diagnosis in type II DCS (WC scenario) and broad differential diagnosis. From a treatment side, it was determined that in both the WC and BC scenario the immediate initiation of hyperbarics would lead to the greatest possible outcome. The skill necessary to manage this patient would be level 5 at minimum and only if a streamlined operational protocol was in place.

Treatment Scope and Resourcing
Treatment of a best-case scenario involving crew member DCS includes minor supportive care and hyperbaric oxygen therapy

Treatment of a worst-case scenario involving severe/type II DCS includes more aggressive supportive care and hyperbaric oxygen therapy

With regards to supportive care this includes non-invasive oxygenation with 100% O2, crystalloid fluid resuscitation, and passive external rewarming which is standard treatment. Hyperbaric oxygen was included due to the significant improvement in outcomes with regards to symptoms, functional outcomes, RTDC, and LOCL. To date, the ship and habitat designs for lunar missions have not been decided and may include the capability to hyperpressurize an airlock but this is not a standard requirement. The alternative treatment would be over pressurization the xEMU above ambient pressure for several hours. Both approaches are likely to be effective but create a number of logistical challenges for the management of the patient. ISS EVA protocols appear to also include aspirin administration before and during EVA however there does not appear to be adequate evidence for any anti-platelet or anti-thrombotic treatment and so these were excluded from this CRT.

Communications and Support Needs

In the best and worst-case scenario, real-time audio and video would be helpful from a diagnosis and management standpoint given the severity of illness and the logistical challenges of hyperbaric

IMM CLIFF RECONCILATION COMMENTS

The best and worst-case scenario definitions are essentially unchanged from the prior IMM CLiFF. The IMM CLiFF, however, is specific to ISS. Thus all data used to inform the IMM CLiFF is related to the EMU suit and ISS atmospheres. Artemis missions are planned to use a new suit, the xEMU. The xEMU will be the first suit that has the capability of varying pressure (4.3-8.2psia). Further, the atmospheres of Gateway and the Lander

will be unique. This was taken into account when creating this CLiFF. Therefore, the duration, RTDC probabilities, and LOCL probabilities are unique as compared to the IMM CLiFF.

LIMITATIONS SUMMARY

• The incidence Note this distribution shape matches (and slightly exceeds) the uncertainty of the DCS model. The mean is slightly higher than the DCS prediction but matches it exactly at the mode (most-likely) value in the distribution. This was the distribution of best fit as determined by biostatistics. • RTDC and LOCL probabilities for the best-case scenarios were assumed to be 0%. • The untreated scenarios (assuming that the crewmember can make it back to the vehicle) are not truly “untreated” since the change in pressure from the xEMU suit to the vehicle pressure would comprise partial treatment. This was taken into consideration for the various scenarios. • Artemis Mission atmospheres are planned at the time of composition of this CLiFF but may change. Should that occur, the durations, RTDCs, and LOCLs would need to be reconsidered.

TABLE 8. TASK IMPAIRMENT CALCULATION BASED ON AFFECTED HUMAN SYSTEMS TASK CATEGORIES (HSTC)

Clinical Phase 2: Treatment												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)							145					
Untreated Best Case (UTBC)							145					
Treated Worst Case (TWC)	223	664	113	89	854	44	145	5	13			
Untreated Worst Case (UTWC)	223	664	113	89	854	44	145	5	13	6		
	Affected HSTCs (Continued)								TI Calculation			TI Score
	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)	132	564	414	22	196		34	211	1718	3763	0.456551	45.6551
Untreated Best Case (UTBC)	132	564	414	22	196		34	211	1718	3763	0.456551	45.6551
Treated Worst Case (TWC)	132	564	414	22	196	34	34	211	3757	3763	0.998406	99.8406
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3763	3763	1	100

Clinical Phase 3: Condition End State												
	Affected HSTCs											
	Cognitive - Simple	Cognitive - Complex	Communications	Inter-personal Skills	Vision	Hearing	Cardio-pulmonary	Dentition	GI	GU		
Treated Best Case (TBC)												
Untreated Best Case (UTBC)												
Treated Worst Case (TWC)												
Untreated Worst Case (UTWC)	223	664	113	89	854	44	145	5	13	6		
	Affected HSTCs (Continued)								TI Calculation			TI Score

	Hand (Dom)	Hand (Any)	Upper Extremity	Lower Extremity	Ambul & Standing (g)	Translation & Stabilization (microgravity)	Don/Doff Equipment	Pressure Ops	Total Tasks Impaired By Condition	Total Human System Category Tasks Full Mission	TI Decimal	TI %
Treated Best Case (TBC)									0	3763	0	0
Untreated Best Case (UTBC)									0	3763	0	0
Treated Worst Case (TWC)								211	211	3763	0.0560723	5.60723
Untreated Worst Case (UTWC)	132	564	414	22	196	34	34	211	3763	3763	1	100

TABLE 8 KEY
Human System Task Category (HSTC) Definitions: Cognitive-Simple: Tasks requiring simple cognitive involvement (low levels of attention, following simple checklists, and not requiring extensive decision making) in conjunction with inputs from other systems. Cognitive-Complex: Tasks requiring complex cognitive involvement (requiring constant attention, frequent interpretation of outside stimuli to inform real-time situations) in conjunction with inputs from other systems. Communication: Tasks requiring primarily communication, via hearing and speaking. Interpersonal Skills: Tasks requiring interpersonal, social interaction between crew including complex technical tasks that require extended crew interaction. Vision: Tasks in which visual information is required. Hearing: Tasks in which primarily auditory information is required, excluding communication, e.g. hearing alarms, medical auscultation, OOHAs. Cardiopulmonary: Tasks requiring greater-than-baseline cardiopulmonary effort, e.g. physically strenuous activities. Dentition: Tasks requiring use of teeth for mastication. GI (Gastrointestinal): Tasks requring use of the alimentary sytem, e.g. solids/liquids consumption and solids excretion. GU (Genitourinary): Tasks requiring use of the male/female genitourinary systems. Hand (Dominant): Tasks performed using primarily the hand, requiring use of the dominant hand (piloting, medical procedures, dental procedures). Hand (Any): Tasks performed using primarily the hand(s), with no preference for dominance, with equivalent bilateral effectiveness. Upper Extremity: Tasks requiring specific use of the upper extremities, excluding hands. Lower Extremity: Tasks requiring specific use of the lower extremities (excluding ambulation and standing in the presence of gravity), e.g. using exercise equipment. Ambulation and Standing (g): Tasks requiring use of both lower extremities to accomplish ambulation or standing in the presence of gravity. Translation and Stabilization (microgravity): Tasks requiring use of either the upper or lower extremities to accomplish translational movement and stabilization (securing oneself to remain stationary) in the setting of microgravity. Don/Doff Equipment: Tasks requiring the donning of personal equipment (including pressure suit, exercise harness, EVA equipment, etc). Pressure Ops: EVA/contingency tasks performed while pressurized in a suit.

Criteria for Assignment of Conditions to HSTCs (any of the following):
1) Is affected crew member physically incapable of performing the human system task category, without impairment, with the condition?
2) Would the treatment (e.g. medications) impair the crewmember's ability to perform the human system task category? (Does not apply to UTx)
3) Does the condition have a high likelihood of causing a significant aeromedical contraindication with an associated human system task category
4) Would performing tasks in an associated task category worsen the condition? (If so, it is affected).
5) Does pain associated with the condition impair any further human system categories?

TASK IMPAIRMENT COMMENTS

CP2: No comment. CP3: No comment.

EVIDENCE COLLECTION PROCESS

Mesh terms that most closely resembled the best-case and worst-case scenarios, and associated Conditions Included but Not Explicitly Stated (CNES), were utilized to build incidence, duration, RTDC, and LOCL searches by best- and worst-case.

Incidence:
Databases searched for spaceflight and analog incidence data included: PubMed, Google Scholar, NASA Technical Reports Server (NTRS) public search, Defense Technical Information Center (DTIC), and Barratt MR, Baker E, Pool SL. Principles of Clinical Medicine for Space Flight. New York, NY: Springer; 2019. 2nd Edition. Databases searched for terrestrial incidence included: DynaMed, PubMed, and Google Scholar.

Duration, RTDC, LOCL:
Databases searched for duration, RTDC, and LOCL included: Dynamed, Cochrane, PubMed, and Google Scholar. Note, that if duration, RTDC, or LOCL data was found in a DynaMed search, the other search engines were not included. Relevant articles were selected and reviewed. If applicable, the article was included in the CLiFF.

LEVEL OF CONFIDENCE (LOC) SCORING

Articles obtained to update the evidence behind this CLiFF were scored by ExMC editors, based on their applicability to the Exploration Spaceflight environment using the following grading scale:

4 – Confident
3 – Somewhat confident
2 – Neutral
1 – Somewhat unconfident
0 – Not confident

The following considerations factor into the grading scale above:

• How closely does the paper describe the medical condition as defined by the IMPACT 1.0 Condiltion List (relevance)?
• How closely does the population included resemble the astronaut population?
• Quality of the paper (number of subjects, methods, etc.)
• How much does the editor trust the source of the evidence?
• How closely does the editor think that the data represents the exploration spaceflight environment?
• Other considerations, at the discretion of the editor, supported in the comments for LOE scoring.

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ACRONYMS

ACRONYM	PHRASE
AAOMS	American Association of Oral and Maxillofacial Surgeons
AMA	American Medical Association
ARCL	All Remaining Conditions List
ARS	Acute Radiation Sickness
BHP	Behavioral Health and Performance
CAC	Coronary Artery Calcium
CHS	Crew Health and Safety
CL	Condition List
CliFF	Clinical Finding Form
CMO	Crew Medical Officer
COMFORT	Clinical Outcome Metrics for Optimization of Robust Training
CP1	Clinical Phase 1
CP2	Clinical Phase 2
CP3	Clinical Phase 3
CRL	Clinical Resource Level
CRT	Capability Resource Table
CST	Clinical Science Team
DCS	Decompression Syndrome
DRM	Design Reference Mission
ED	Emergency Medicine Doctor

EL	Evidence Library
EMCL	Exploration Medical Condition List
EMT	Emergency Medical Technician
EVA	Extravehicular Activity
EXMC	Exploration Medical Capability
HRP	Human Research Program
ICD	International Classification of Disease
ICL 1.0	IMPACT 1.0 Medical Conditions List
ICU	Intensive Care Unit
IMCL	iMED Condition List
iMED	Integrated Medical Evidence Database
IMM	Integrated Medical Model
IMPACT-MD	Impact Medical Database
IP	Incidence Proportion
IR	Incidence Rate
ISS	International Space Station
IV	Intravenous
JSC	Johnson Space Center
LEO	Low-Earth orbit
LEVA	Lunar Extravehicular Activity
LOCL	Loss of Crew Life
LOM	Loss of Mission
LSAH	Lifetime Surveillance of Astronaut Health
LSO	Lunar Surface Operations
MCL	Master Condition List
MEVA	Medical Extravehicular Activity
NASA	National Aeronautics and Space Administration
N/A	Not Applicable
NP	Nurse Practitioner
OBGYN	Obstetrics and Gynecology
OR	Occurrence Rate
PA	Physician Assistant
PDQ	Pain Disability Questionnaire
PFCL	Proposed Future Conditions List
PPE	Personal Protective Equipment
PTRS	Project Technical Requirements Specification
PRL	Pharmaceutical Resource Level
QTL	Quality Time Lost
RCL	Removed Conditions List
REP	Rochester Epidemiology Study
RTDC	Removal to Definitive Care
SANS	Spaceflight-Associated Neuro-ocular Syndrome
SAS	Space Adaptation Syndrome

SEVA	Spaceflight Extravehicular Activity
SME	Subject Matter Expert
SoP	Standard Operating Procedure
SPE	Solar Particle Event
TBD	To Be Determined
TI	Task Impairment