Clinical Finding Form (CliFF)

Branch Baseline

ICL73_Otitis Externa

Otitis Externa (OE), also known as “swimmer’s ear”, is a common condition involving inflammation of the ear canal (Osguthorpe 2006; Schaefer 2012). Risk factors of OE include high humidity, prolonged water exposure such as swimming, warm temperatures, local trauma, and presence of foreign materials in the ear canal (Beers 2004). Most OEs are acute, often presenting as rapid onset of otalgia, itching, otorrhea, canal edema and canal erythema (Schaffer 2012). More than 98% of terrestrial acute OE cases in North America are caused by bacterial infection, with Pseudomonas aeruginosa and Staphylococcus aureus being the most common culprits (Roland 2002). Topical antimicrobials are often used as initial treatment of uncomplicated acute OE. Most patients will experience considerable improvement of symptoms after just one day of treatment. Oral analgesics such as NSAIDs and acetaminophen are also often used to control pain associated with OE (Schaeffer 2012). The chronic form of OE is defined as OE lasting more than three months (Osguthorphe 2006). Chronic OE is more likely in the setting of patients with the following comorbidities: seasonal allergies, fungal infections, chronic dermatologic conditions, or inadequately treated acute OE (Osguthorphe 2006; Schaefer 2012). On rare occasions, OE infection can invade the surrounding soft tissues and temporal bone, resulting in malignant otitis externa (Daneshrad 2002; Al Aaraj 2021). It is mostly seen in diabetic, immunocompromised, and elderly patients (Al Aaraj 2021). Malignant otitis externa is important as it is life-threatening without adequate systemic antibiotics and potentially surgical treatment (Al Aaraj 2021).

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

Current spaceflight data on OE are limited to a case series and evidence reports. NASA case files reported 6 inflight events during the Apollo mission. Antonsen, 2017 also reported 3 events among crew members from missions spanning the Space Shuttle Program, Mir, and ISS. However, incidence is difficult to calculate with unknown denominator. Crucian, 2016 reported 6 events of “ear-related” conditions which includes OE and OM among 46 US astronauts on board the International Space Center. With a total of 20.57 flight years, incidence was 0.3 events/flight year. This data is limited due to the lack of data on OE alone.

ANALOG LITERATURE

Wingelaar, 2017 examined the incidence of OE in military divers during their initial diving training. The population of military divers shares similarities with space crews, generally healthy and young, but the exposure to water accounted for much higher incidence of OE. Rates are also higher after prolonged exposure to water with increased OE incidence in the final weeks of the study compared to the first few weeks of diving. Therefore there is limited generalizability of this population to the spaceflight population.

TERRESTRIAL LITERATURE

Rolands, 2001 conducted a large retrospective chart review of patients in the UK. Females were found to have a slightly higher annual incidence of 1.3% compared to 1.16% in male. This data is helpful in obtaining the terrestrial incidence in the general population but has limited application to spaceflight population given that terrestrial peak prevalence is in late middle age and the elderly, populations older than the crew members on space missions.

OVERALL INCIDENCE SUMMARY

INCIDENCE

mean 0.06589, SD 0.03826

INCIDENCE SUMMARY

Evidence from Antonsen, 2017 and LSAH data. Total 3 cases over 45.49 person-years (up through Exp 40). IR: 6.595E-2 (95%CI: 1.677E-2, 17.95E-2). The Bayesian posterior distribution for the incidence rate given the spaceflight data (3 events over 45.49 person-years) under an uninformative prior is Gamma(shape=2.966, rate=45.012) with mean 0.06589 and SD 0.03826.

TABLE 1. INCIDENCE MODEL

Incidence Details

Incidence Type
General

Segment
All

Env. Exposure
NA

Sex
Any

Crowns
Any

Contacts
Any

Pregnancy
Any

Incidence Distribution

Occurrence Dist
Poisson

Incidence Dist.
Gamma

Mean
0.0658935

SD
0.0382611

Gamma
(Shape): 2.966
(Rate): 45.012

TABLE 2. INCIDENCE LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Antonsen, 2017	spaceflight	4
Johnston, 1975	spaceflight	4
Crucian, 2016	spaceflight	4
Wingelaar, 2017	analog	2
Rolands, 2001	terrestrial	1

Antonsen, 2017 receives a level 4 value because the population of the study is astronauts during inflight missions and the duration of the study contains missions from the Space Shuttle Program, Mir, and ISS (through Expedition 13 in 2006), representing a wide range of dates and missions. Johnston, 1975 receives a 4 because the population is astronauts during inflight missions and the timeframe is Apollo missions. However, both studies were incidence reports without denominator. Also appears that the Apollo cases did not occur inflight as per the "Biomedical Results of Apollo." Therefore calculated only using Antonsen report and LSAH data requests. Table 2 – 3 cases of otitis externa. Table 1 – 0 cases. This agrees with the IMM assessments. Total 3 cases over 45.49 person-years (up through Exp 40). IR: 6.595E-2 (95%CI: 1.677E-2, 17.95E-2) Crucian, 2016 receives a level 4 value because it is also a population of astronauts. They reported “ear-related” condition (OE and OM) incidence of 0.3 events/flight year among 46 US astronauts onboard ISS. Reported 6 ear-related conditions (pain, congestion, itchiness). ISS through Expedition 37/38. However, since this report contains events more than just Otitis Externa (non-specific) and the reporting overlaps with the Antonsen report, this report was not included to not double count the ISS missions. Wingelaar, 2017 receives a 2 because although the study evaluates the military diving population, with water exposure being a significant risk factor of OE, the difference of being underwater vs in the space shuttle may account for drastic differences in incidence. Rowlands, 2001 receives a 1 because the population of the terrestrial study does not well-represent space crew population as it is in the general public and the majority of cases of OE were in older populations (>65 years old).

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

Hearing assessment test and physical exams of the ear are performed as part of preflight medical requirements.

BEST CASE SCENARIO DEFINITION

Otitis externa resolving with one course of antibiotics. Associated pain is controlled with non-opioid analgesics.

WORSE CASE SCENARIO DEFINITION

Otitis externa that is accompanied by pain that cannot be controlled with non-opioid analgesics, or requires more than one course of antibiotics.

CONDITIONS INCLUDED, BUT NOT EXPLICITLY STATED (CNES)

None

BEST CASE/WORST CASE PROBABILITY COMMENTS

According to literature, up to 73%-98% (Mösges, 2011; Schwartz, 2006; Rahman, 2007;) of non-complicated OE cases resolve with one course of appropriate treatment within 2 weeks. Rowlands, 2001 reported around 1.5% of persistent disease despite treatment. Review by Osguthorpe, 2006 reported worst-case scenario of having life-threatening temporal bone infection to be < 0.5% in the general population. Another review by Chadhary, 2015 also demonstrated incidence of progression to extracranial or intracranial infection among OE to be <1% in the general public. However, most severe forms of infection occur in immunocompromised or elderly patients. For this reason, although the data would estimate that the worst-case probability is 1.5-2%, it is likely much lower than this in our spaceflight population than the terrestrial population given that astronauts will be screened pre-flight and are healthy individuals.

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

Citation	Source	LOC Value
Chadhary, 2015	Terrestrial	1
Osguthorpe, 2006	Terrestrial	1
Schwartz, 2006	Terrestrial	1
Rahman, 2007	Terrestrial	2
Mösges, 2011	Terrestrial	3
van Asperen, 1995	Terrestrial	1

Osguthorpe, 2006 and Chadhary, 2015 are review articles of OE which provided data on incidence of complication from OEs but does not represent the space crew population. 2006 study by Schwartz and colleagues looked at pediatric patients with OE rather than adults. Rahman, 2007 pooled the outcomes of two clinical trials with data including both adults and children. Mösges, 2011 is a meta-analysis of 12 RCTs comparing efficacy of antibiotic treatments for OE. Van Asperen, 1995 is a older retrospective study on risk and outcomes of OEs after swimming.

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 0.06589, SD 0.03826	98 - 98	100	1	2.80361	24	336	0	0	0	0	0
Treated Worst Case (TWC)		2 - 2	100	1	14.6293	336	672	0	0	0.5	0	0.095
Untreated Best Case (UTBC)	N/A	N/A	N/A	1	14.5628	24	336	0	0	0	0	0
Untreated Worst Case (UTWC)	N/A	N/A	N/A	1	35.1847	336	672	35.1847	0	1	0	0.6

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

The best case scenario involves OE that is uncomplicated and can either resolve spontaneously or cause minimal disturbance and is treated with one course of antibiotics and does not require opioids for pain management. This is true for the vast majority of OE cases terrestrially. The cornerstones of treatment will likely include symptomatic management of pain. Given a paucity of data regarding spaceflight or analog OE leading to a return to definitive care, OE that was severe enough that it might warrant hospital admission due to refractory malignant OE (MOE, also may be referred to necrotizing otitis externa NOE) was chosen as the surrogate for RTDC. MOE is the most critical complication of OE and was therefore a surrogate for RTDC and provided data for LOCL.

TREATED BEST CASE (TBC) SCENARIO COMMENTS

In summary, with appropriate treatment, patients with OE should expect to have significant symptomatic relief within 24 hours of antibiotic initiation (Schaefer, 2012, Rosenfeld, 2006) The majority of cases resolve within 7 days (Rosenfeld, 2006, Pistorius, 1999) though more severe cases may require 14 days of treatment (Schaefer, 2012). For best-case RTDC and LOCL, based on definition, it is expected that the probabilities will be 0%. Despite adequate treatment, van Asperen, 1995 found around 36% of cases reported inability to participate in certain activities of daily living due to the discomfort of OE.

TREATED WORST CASE SCENARIO (TWC) COMMENTS

OEs unresponsive to a single course of antibiotics may require treatment duration up to four weeks (Tong 1996). Malignant OE (MOE) in the past did incur high rates of morbidity and mortality (~50%), but with highly effective anti-pseudomonal antibiotics and more rapid diagnostic techniques, both morbidity and mortality are much lower. For MOE, median hospitalization = 12 days (Sokołowski, 2019), surgery for diagnosis or debridement = 25- 57% of patients (Le Clerc, 2014, Sokołowski, 2019), average duration of antibiotics= 68 days (Le Clerc, 2014). The rates of recurrent NOE are 9.6%- 17.5% (Le Clerc, 2014, Soudry, 2010, Omran, 2012). Mortality from MOE = 0- 9.5% (Johnson, 2014, Mahdyoun, 2013, Soudry, 2010). With adequate treatment and less than 1% chance of progression to MOE, it can be assumed for LOCL, the minimum would be 0%, and maximum could be conservatively estimated around 0.1% (1%x9.5%).

UNTREATED BEST CASE (UTBC) SCENARIO COMMENTS

There is a paucity of data on bast case scenarios for untreated OEs. Due to the possibility of spontaneously resolving OEs, duration can range from 24 hours to requiring one course of antibiotics (up to 14 days of treatment) in best-case scenarios. RTDC and LOCL incidences would be 0%.

UNTREATED WORST CASE (UTWC) SCENARIO COMMENTS

Less than 1% of OEs progress to MOE (Osguthorpe, 2006), with the majority of patients being elderly and more than 90% of cases in diabetic individuals (Carfrae, 2008). Probability of space crew members developing MOE (surrogate for RTDC) should therefore be much lower than 1%, if not close to 0%. However, in case of development of MOE, without treatment, mortality is high. A range of recurrent MOE was found by Rubin, 1988 and LOCL from MOE was originally described by Chandler, 1968, who coined the phrase "malignant otitis externa" and found mortality to range from 10-50%. Involvement of cranial nerves has been associated with the highest mortality, cited up to 60% (Babiatzki, 1987). In summary, RTDC incidence was estimated as a minimum 0% and maximum of 1%. In case of the development of MOE, with mortality up to 60% without treatment, LOCL incidence was estimated as maximum of 0.6% (1% x 60%).

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

Citation	Source	LOC Value
Schaefer, 2012	Terrestrial	3
Rosenfeld, 2006	Terrestrial	
Kaushik, 2010	Terrestrial	
Pistorius, 1999	Terrestrial	

Citation	Source	LOC Value
Hajiof, 2015	Terrestrial	
Wright, 2009	Terrestrial	

All papers represent the terrestrial population, and level of evidence is higher for the treated scenarios. Hajiof, 2015 reported few reliable data due to the self-resolving nature of many cases of OE over the course of weeks to months. It is therefore more challenging to find data on minimum and maximum duration for untreated scenarios.

TABLE 6. RTDC LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Mahdyoun, 2013	Terrestrial	
El-Silimy 1992	Terrestrial	
Franco-Vidal, 2007	Terrestrial	
Sokolowski, 2019	Terrestrial	
Le Clerc, 2014	Terrestrial	2
Omran, 2012	Terrestrial	
Soudry, 2010	Terrestrial	
Johnson, 2014	Terrestrial	
Rubin, 1988	Terrestrial	

Most of the publications available evaluated the layperson terrestrial population and therefore have limited generalizability to spaceflight. Mahdyoun, 2013, El-Slimy 1992, Franco-Vidal, 2007, Soudry, 2010, Johnson, 2014, all included populations that were majority diabetic and elderly. Several of the papers also included patients who are immunocompromised. Elderly, immunocompromised and diabetic populations do not well-represent the space crew populations and the complication rate in the populations in the papers is likely far higher than what we will see due to the inclusion of these high-risk patients. Although these papers are not representative of the space crew population, they were helpful in gathering data, hence the grade 2 LOC.

TABLE 7. LOCL LEVEL OF CONFIDENCE (LOC)

Citation	Source	LOC Value
Mahdyoun, 2013	Terrestrial	
Johnson, 2014	Terrestrial	
Soudry, 2010	Terrestrial	3
Loh, 2019	Terrestrial	
Babiatzki, 1987	Terrestrial	

Several of the papers include populations that are not analogous to space crews, Mahdyoun, 2013, El-Slimy 1992, Franco-Vidal, 2007, Soudry, 2010, Johnson, 2014, but they provide helpful data for determining the rate of mortality once a complication of OE occurs. The papers also well-represent what causes the mortality in patients with OE and that is it malignant OE. The older paper, Babiatzki, 1987, provides helpful data for untreated cases of malignant OE because it reported data from a time frame when MOE was more common. Overall, because the condition is well-represented and the overall sample size is robust, the overall grade is a 3, somewhat confident.

CAPABILITY RESOURCE TABLE (CRT) OVERVIEW

Capabilities and Resourcing Scope Overview Worst Case Definition: Otitis externa that is accompanied by pain that cannot be controlled with non-opioid analgesics, or requires more than one course of antibiotics. Best Case Definition: Otitis externa resolving with one course of antibiotics. Associated pain is controlled with non-opioid analgesics. External ear infection associated medical response is to address the pain and discomfort associated with the condition and with antibiotic therapy to mitigate infection risk. Generally this condition is one of discomfort rather than a medical

emergency although some antibiotics may need to be applied to reduce risk. The CRT condition focuses solely on the physical exam in the best case and the prevention of infection and pain management in the worst case. Diagnostic Scope and Resourcing In the best-case scenario, diagnosis is based on history and physical examination. In the worst-case scenario, diagnosis is based on history and physical examination. 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): 1.0 hours This is the longest reasonable time to complete this task for an experienced clinician adjusted for being in the spaceflight environment to do the following: 1 - Take a proper history of the patient 2 - Perform a physical on the patient, including cranial nerve exam CP1 WC (Treated or Untreated): 1.0 hours This is the longest reasonable time to complete this task for an experienced clinician adjusted for being in the spaceflight environment to do the following: 1 - Take a proper history of the patient 2 - Perform a physical on the patient, including cranial nerve exam The highest scope of practice code used in this CRT which includes interpretation of diagnosis, performing diagnostic tests and performing treatment would be a four: this is an intern level. Treatment Scope and Resourcing In the best-case scenario, treatment is addressing mild pain and local antibiotic therapy. Worst case increases the pain management and moves up to more systemic antibiotic therapy. Most mild infections in terrestrial populations (best or worst case) are resolved without management or with only topical antibiotics and NSAIDS. Communications and Support Needs In the best-case scenario, diagnosis and course of treatment is uncomplicated and likely within the scope of care of onboard crew members. In the worst-case condition, ground communications will be helpful given the potentially complicated nature of the condition and the scope of care onboard. REFERENCES

IMM CLIFF RECONCILATION COMMENTS

The best case scenario definition slightly differs from IMM CLiFF. Best case scenario definition has changed from mild OE resolving in 48-72 hours from the start of treatment to OE resolving with one course of antibiotics. Not requiring opioid for pain management as part of best case scenario criteria remains the same for both CLiFFs. Treatment duration is therefore altered for each scenario due to this change of definition. However, with most mild cases of OE resolving within two days of initiating treatment, reported percentage of best case scenario is similar. For worst case scenario, IMM CLiFF excluded the possibility of developing malignant otitis externa among crew members. Although unlikely, the development of this severe complication is not impossible. Therefore, in this CLiFF, with refractory MOE as a surrogate for RTDC, we report a maximum of 1% chance of RTDC.

LIMITATIONS SUMMARY

Most available studies examining OE reflect terrestrial and elderly populations, which are not generalizable to the spaceflight population. Also, there was no available data regarding number of cases that required opioid analgesia versus non-opioid analgesics. This is a subjective point of quantification, and likely the necessity of opioid analgesia for OE would be provider and patient dependent if any studies did exist. Therefore it was difficult to discern the likelihood of the BC and WC in spaceflight. Similarly, given that a course of antibiotic therapy for OE may vary in duration, the definition of requiring a second course of antibiotics could be better defined (i.e. if only 3 days is given at first, and then a further 3 days prescribed - would this still qualify as a second course and that patient would meet definition for worst case while another patient prescribed 14 days initially would not?). We may consider re-wording the definition of worst case scenario to state "remains symptomatic after more than 14 days of antibiotic treatment."

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)												
Untreated Best Case (UTBC)		664		89								
Treated Worst Case (TWC)		664		89				5				
Untreated Worst Case (UTWC)	223	664		89				5				
	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)								211	211	3763	0.0560723	5.60723
Untreated Best Case (UTBC)	132							211	1096	3763	0.291257	29.1257
Treated Worst Case (TWC)	132							211	1101	3763	0.292586	29.2586
Untreated Worst Case (UTWC)	132							211	1324	3763	0.351847	35.1847

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		89				5				
	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)									0	3763	0	0
Untreated Worst Case (UTWC)	132							211	1324	3763	0.351847	35.1847

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.

REFERENCES

Reference
Al Aaraj MS, Kelley C. Malignant Otitis Externa. 2020 Dec 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 32310598.
Antonsen, Erik, et al. Risk of Adverse Health Outcomes and Decrements in Performance due to In-Flight Medical Conditions - Human Research Program Exploration Medical Capabilities Element - 2017
Babiatzki A, Sadé J. Malignant external otitis. J Laryngol Otol. 1987 Mar;101(3):205-10. doi: 10.1017/s0022215100101549. PMID: 3106545.
Beers SL, Abramo TJ. Otitis externa review. Pediatr Emerg Care. 2004;20:250–6
Johnston 1975– Biomedical Results of Apollo. Apollo era 1 report of otitis media over Apollo missions. Berry, Charles A, Richard S. Johnston, Lawrence F . Dietlein, M.D - 1975
Carfrae M.J. & Kesser B.W. (2008) Malignant otitis externa. Otolaryngol. Clin. North Am., 41, 537–549, viii – ix
Chawdhary G, Liow N, Democratis J, Whiteside O. Necrotizing (malignant) otitis externa in the UK: a growing problem. Review of five cases and analysis of national Hospital Episode Statistics trends. J Laryngol Otol. 2015 Jun;129(6):600-3. doi: 10.1017/S002221511500105X. Epub 2015 May 20. PMID: 25990028.
Clerc, N.L., Verillaud, B., Duet, M., Guichard, J.-P., Herman, P. and Kania, R. (2014), Skull base osteomyelitis: Incidence of resistance, morbidity, and treatment strategy. The Laryngoscope, 124: 2013-2016.
Crucian B, Babiak-Vazquez A, Johnston S, Pierson DL, Ott CM, Sams C. Incidence of clinical symptoms during long-duration orbital spaceflight. Int J Gen Med. 2016;9:383-391. Published 2016 Nov 3. doi:10.2147/IJGM.S114188
Daneshrad D, Kim JC, Amedee RG. Acute otitis externa. J La State Med Soc. 2002;154:226–8
el-Silimy O, Sharnuby M. Malignant external otitis: management policy. J Laryngol Otol. 1992 Jan;106(1):5-6. doi: 10.1017/s0022215100118456. PMID: 1541892.
Franco-Vidal V, Blanchet H, Bebear C, Dutronc H, Darrouzet V. Necrotizing external otitis: a report of 46 cases. Otol Neurotol. 2007 Sep;28(6):771-3. doi: 10.1097/MAO.0b013e31805153bd. PMID: 17721365.
Hajioff D, MacKeith S. Otitis externa. BMJ Clin Evid. 2015 Jun 15;2015:0510. PMID: 26074134; PMCID: PMC4466798.
Johnson AK, Batra PS. Central skull base osteomyelitis: an emerging clinical entity. Laryngoscope. 2014 May;124(5):1083-7. doi: 10.1002/lary.24440. Epub 2013 Nov 7. PMID: 24115113.
Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD004740. doi: 10.1002/14651858.CD004740.pub2. PMID: 20091565.
Loh TL, Renger L, Latis S, Patel H. Malignant otitis externa in Australian Aboriginal patients: A 9-year retrospective analysis from the Northern Territory. Aust J Rural Health. 2019 Feb;27(1):78-82. doi: 10.1111/ajr.12468. Epub 2019 Jan 30. PMID: 30698313.
Mahdyoun P, Pulcini C, Gahide I, Raffaelli C, Savoldelli C, Castillo L, Guevara N. Necrotizing otitis externa: a systematic review. Otol Neurotol. 2013 Jun;34(4):620-9. doi: 10.1097/MAO.0b013e3182804aee. PMID: 23598690.
Mösges R, Nematian-Samani M, Hellmich M, Shah-Hosseini K. A meta-analysis of the efficacy of quinolone containing otics in comparison to antibiotic-steroid combination drugs in the local treatment of otitis externa. Curr Med Res Opin. 2011 Oct;27(10):2053-60. doi: 10.1185/03007995.2011.616192. Epub 2011 Sep 15. PMID: 21919557.
Omran AA, El Garem HF, Al Alem RK. Recurrent malignant otitis externa: management and outcome. Eur Arch Otorhinolaryngol. 2012 Mar;269(3):807-11. doi: 10.1007/s00405-011-1736-2. Epub 2011 Aug 11. PMID: 21833561.
Osguthorpe JD, Nielsen DR. Otitis externa: Review and clinical update. Am Fam Physician. 2006 Nov 1;74(9):1510-6. PMID: 17111889.
Rahman A, Rizwan S, Waycaster C, Wall GM. Pooled analysis of two clinical trials comparing the clinical outcomes of topical ciprofloxacin/dexamethasone otic suspension and polymyxin B/neomycin/hydrocortisone otic suspension for the treatment of acute otitis externa in adults and children. Clin Ther. 2007 Sep;29(9):1950-6. doi: 10.1016/j.clinthera.2007.09.005. PMID: 18035194.
Pistorius, Bruce1; Westberry, Karen2; Drehobl, Margaret3; Williams, David4; Bock, Thomas5; Lucente, Frank E.6; Shan, Michael7; Perroncel, Renee7; Heyd, Allen7 Otitis Externa Study Group Prospective, Randomized, Comparative Trial of Ciprofloxacin Otic Drops, with or Without Hydrocortisone Otic Suspension in the Treatment of Acute Diffuse Otitis Externa, Infectious Diseases in Clinical Practice: November 1999 - Volume 8 - Issue 8 - p 387-395
Rahman A, Rizwan S, Waycaster C, Wall GM. Pooled analysis of two clinical trials comparing the clinical outcomes of topical ciprofloxacin/dexamethasone otic suspension and polymyxin B/neomycin/hydrocortisone otic suspension for the treatment of acute otitis externa in adults and children. Clin Ther. 2007 Sep;29(9):1950-6. doi: 10.1016/j.clinthera.2007.09.005. PMID: 18035194.
Richard H. Schwartz & for the Study Investigators (2006) Once-daily ofloxacin otic solution versus neomycin sulfate/polymyxin B sulfate/hydrocortisone otic suspension four times a day: a multicenter, randomized, evaluator-blinded trial to compare the efficacy, safety, and pain relief in pediatric patients with otitis externa, Current Medical Research and Opinion, 22:9, 1725-1736, DOI: 10.1185/030079906X121057
Roland PS, Stroman DW. Microbiology of acute otitis externa. Laryngoscope. 2002;112(7 pt 1):1166–1177.

Reference
Rosenfeld RM, Brown L, Cannon CR, Dolor RJ, Ganiats TG, Hannley M, Kokemueller P, Marcy SM, Roland PS, Shiffman RN, Stinnett SS, Witsell DL; American Academy of Otolaryngology--Head and Neck Surgery Foundation. Clinical practice guideline: acute otitis externa. Otolaryngol Head Neck Surg. 2006 Apr;134(4 Suppl):S4-23. doi: 10.1016/j.otohns.2006.02.014. PMID: 16638473.
Rowlands S, Devalia H, Smith C, Hubbard R, Dean A. Otitis externa in UK general practice: a survey using the UK General Practice Research Database. Br J Gen Pract. 2001;51(468):533-538.
Rubin J, Yu VL. Malignant external otitis: insights into pathogenesis, clinical manifestations, diagnosis, and therapy. Am J Med. 1988 Sep;85(3):391-8. doi: 10.1016/0002-9343(88)90592-x. PMID: 3046354.
Sander R. Otitis externa: a practical guide to treatment and prevention. Am Fam Physician. 2001 Mar 1;63(5):927-36, 941-2. PMID: 11261868.
Schaefer P, Baugh RF. Acute otitis externa: an update. Am Fam Physician. 2012 Dec 1;86(11):1055-61. PMID: 23198673.
Sokołowski J, Lachowska M, Karchier E, Bartoszewicz R, Niemczyk K. Skull base osteomyelitis: factors implicating clinical outcome. Acta Neurol Belg. 2019 Sep;119(3):431-437. doi: 10.1007/s13760-019-01110-w. Epub 2019 Mar 6. PMID: 30840222; PMCID: PMC6710213.
Soudry E, Hamzany Y, Preis M, Joshua B, Hadar T, Nageris BI. Malignant external otitis: analysis of severe cases. Otolaryngol Head Neck Surg. 2011 May;144(5):758-62. doi: 10.1177/0194599810396132. PMID: 21493363.
Tong MC, Woo JK, van Hasselt CA. A double-blind comparative study of ofloxacin otic drops versus neomycin-polymyxin B-hydrocortisone otic drops in the medical treatment of chronic suppurative otitis media. J Laryngol Otol. 1996 Apr;110(4):309-14. doi: 10.1017/s0022215100133523. PMID: 8733449.
van Asperen IA, de Rover CM, Schijven JF, Oetomo SB, Schellekens JF, van Leeuwen NJ, et al. Risk of otitis externa after swimming in recreational fresh water lakes containing Pseudomonas aeruginosa. BMJ. 1995;311:1407–10.
Wingelaar TT, van Ooij PA, van Hulst RA. Otitis externa in military divers: more frequent and less harmful than reported. Diving Hyperb Med. 2017 Mar;47(1):4-8. doi: 10.28920/dhm47.1.4-8. PMID: 28357818; PMCID: PMC6147244.
Wright A, Hawkins CH, Anggård EE, Harper DR. A controlled clinical trial of a therapeutic bacteriophage preparation in chronic otitis due to antibiotic-resistant Pseudomonas aeruginosa; a preliminary report of efficacy. Clin Otolaryngol. 2009 Aug;34(4):349-57. doi: 10.1111/j.1749-4486.2009.01973.x. PMID: 19673983.

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