Executive Summary

This request utilized 3 different crew profiles for 7 DRMs. The 14 day DRM crew profile has 7 crewmembers, the 180 day DRM crew profile has 6 crewmembers, and the remaining DRMs have 4 crewmembers and varying mission lengths from 21 to 1195 days. The 14 and 180 day DRMs have scheduled EVAs and the other DRMs do not. The Total Medical Events (TME) shows an upward trend as the length of the mission increases with the exception of the 14 day (7 crew) and 21 day (4 crew) DRMs. When there is not an overlap between the confidence intervals, the CHI tends to decrease as the mission duration increases. The probability of EVAC and LOCL increases as the length of the mission increases. The TME, CHI, EVAC, and LOCL results are presented in tables and figures in the results section.

Background

The IMM is a stochastic model that uses Monte Carlo methodology to simulate medical outcomes during spaceflight missions. The IMM consists of a three-step process. First, mission and crew member characteristics are specified to define a particular mission profile, or design reference mission (DRM). Next, medical events and outcomes during the space flight mission are randomly generated based on pre-defined incidence values and probability distributions. Finally, total crew health and mission impact outcomes are summarized. For this report, the primary outcomes of interest are crew health index (CHI), need for evacuation (EVAC) and loss of crew life (LOCL).

The IMM is most useful for comparing risks across multiple mission profiles based on probable events and resource availability. Biased results may be incurred due to limitations of the model, but the bias will be consistent across mission profiles within the same service request.

Methods

Crew and Mission Parameters

The DRMs were configured using the crew profiles shown in Tables 1-3. The outcomes of certain IMM medical conditions are influenced by pre-existing medical history including: coronary artery calcium score (CAC), dental crowns, contact lenses, and history of prior abdominal surgery. Pre-existing conditions, as defined here, are consistent with historical U.S. crew data.

Table 1: 14 day DRM crew profile

	Sex	CAC	Crowns	Contacts	Prior Abdominal Surgery	EVA
Crew 1	Male	No	Yes	No	No	No
Crew 2	Male	Yes	No	No	Yes	Yes (3)
Crew 3	Female	No	No	Yes	No	Yes (3)
Crew 4	Female	No	No	No	Yes	No
Crew 5	Male	No	No	Yes	No	No
Crew 6	Male	No	Yes	No	No	No
Crew 7	Female	No	No	Yes	No	No

Table 2: 21 day DRM, 42 day DRM, 365 day DRM, 730 day DRM, and 1195 day DRM crew profile

	Sex	CAC	Crowns	Contacts	Prior Abdominal Surgery	EVA
Crew 1	Male	No	Yes	No	No	No
Crew 2	Male	Yes	No	No	No	No
Crew 3	Female	No	No	Yes	No	No
Crew 4	Female	No	No	No	Yes	No

Table 3: 180 day DRM crew profile

	Sex	CAC	Crowns	Contacts	Prior Abdominal Surgery	EVA
Crew 1	Male	No	No	Yes	No	No
Crew 2	Male	Yes	No	No	No	Yes (3)
Crew 3	Female	No	No	Yes	No	Yes (3)
Crew 4	Female	No	Yes	No	Yes	No
Crew 5	Male	No	No	Yes	No	No
Crew 6	Male	No	Yes	No	No	No

Medical Conditions and Resources

The one hundred medical conditions currently included in the IMM are shown in Appendix A. The incidence of IMM medical events occurring during simulated missions are based on historical mission and cohort data contained within the iMED. For each condition the percentage of "best case" and "worst case" scenarios are specified, as well as a defined set of medical resources that are used to treat the condition. The iMED entry for each condition details the specific medical resources and quantity necessary for treatment in both the best and worst-case scenarios. In-flight medical treatment is assumed to follow a specified protocol [5] or clinical practice guidelines for each medical condition and is constrained by resource availability on the ISS (i.e. the ISS medical capabilities (MedCap)). Model outcomes can be given for the all-treated (continuous resupply, e.g. ISS in low earth orbit), all-untreated (no Medkit) and baseline MedCap (ISS Medkit without resupply). For longer duration missions, the MedCap state should most closely resemble a real world deep space mission where resupply is not possible but where utilization of partial and alternative treatment can occur.

Main Outcomes

The IMM primary medical outcomes include: total medical events (TME), crew health index (CHI), probability of Evacuation (EVAC), probability of Loss of Crew Life (LOCL), and required resources.

CHI is a calculated percentage using the quality-adjusted mission time lost (QAMTL) due to in-flight medical events and resources available to treat those conditions [2].

CHI = (1- (QAMTL ÷ Mission Length)) x 100

For a given condition, QAMTL is determined by summing the product of functional impairment and duration for all three clinical phases of that condition: i) diagnosis and initial treatment, ii) ongoing treatment, and iii) end-state. CHI percent values range from 0-100, where zero represents complete crew impairment and one hundred represents a completely functional crew.

EVAC in the context of IMM means that medical evacuation from the ISS would be considered for definitive treatment of the afflicted crew member(s). EVAC is considered an end state result if any of the following criteria are met: 1) potential LOCL; 2) potential significant permanent impairment; or 3) potential intractable pain. When EVAC is calculated by the IMM, no consideration has been given to the availability of a return vehicle or the likelihood of a successful clinical outcome should a return vehicle be available.

LOCL in the context of IMM should be interpreted to mean that the clinical scenario resulted in death of the affected crew member(s). In version 4.1 of the IMM, crew members are usually only assigned one end state of EVAC or LOCL. In rare instances a crewmember can get a condition that will go to EVAC

or LOCL, and then develop another condition that will also go to EVAC or LOCL in the time between the onset of first condition and the EVAC or LOCL time. Both events are recorded as EVAC or LOCL outcomes. These assumptions should result in more accurate IMM forecasts for the occurrence of EVAC and LOCL as compared to the prior versions of the model.

Required resources for treatment are tracked for each simulated mission trial. The number of each resource that is used to treat a given condition is decremented from available resources. If more of any particular resource is used than is available, then that resource is considered "depleted" in the MedCap scenario. Events that require a "depleted" resource are considered "partially treated" if only a portion of the required resources are available. If there are sufficient available alternate resources in the MedCap, the event is considered "fully treated." If there are not enough resources available to treat the event, the event is considered "untreated." The initial quantities for medical resources are baselined to a fully stocked ISS medical kit (MedCap). Note that when an event is partially treated, its outcomes are based on a weighted average of the treated and untreated values. For example, if a condition has a 0% chance of going to EVAC in the best case treated scenario and a 0-100% chance of going to EVAC in the best case untreated scenario, then under best case partial treatment, it is possible the condition will go to EVAC.

Modeling Approach

One hundred thousand (100,000) trials were run for each DRM where each trial can be considered an individual "mission". This ensures that the distribution of outcomes meet convergence criteria. Convergence criteria are met when there is less than or equal to a 5% change in the average standard deviation of the CHI, EVAC, and LOCL primary model outcomes in the last 2 - 1,000 mission increments. This last step is performed manually by the modelers using the IMMV4ConvergenceReport.

IMM outcomes were determined for the DRMs using the ISS MedCap scenario where all conditions are treated, partially treated or untreated based on the available resources of the ISS MedCap. CHI is calculated as a percentage, with 95% confidence intervals (CIs) for the associated distributions. EVAC and LOCL are probabilities, with 95% CI for EVAC and LOCL obtained using bootstrap resampling of the simulation output [3]. In this report, TME, CHI, EVAC and LOCL results, as well as pertinent influential conditions, are described. IMM version 4.1 has certain features, assumptions and limitations that impact modeled outcomes. IMM 4.1 represents a significant advance over IMM 3.0. Improvements in IMM 4.1 include inclusion of a timeline, and alternate or partial treatment capability. Features, assumptions and limitations pertinent to this report are described below.

Features, Assumptions and Limitations of IMM Version 4.1 [3]

1. All non-SA and non-extravehicular activity (EVA) related conditions have a uniform likelihood of occurring throughout the mission duration. Space Adaptation Syndrome conditions occur in the first 5 days of the mission, with a peak occurrence at 48 hours.
2. Individuals cannot get the same condition for which they are currently being treated (i.e. during Clinical Phase (CP) I and II).
3. EVAC and LOCL are generated for each medical event, and then the timing of the EVAC or LOCL is generated according to a specified distribution.
4. Individuals are no longer at risk for further conditions once their status changes to either EVAC or LOCL. From the start time of the EVAC or LOCL, the functional impairment of the crew member is assumed to be 100%.
5. When the status of a crew member changes to EVAC, only one crew member is evacuated.
6. The IMM assumes that, per crew member, the first condition requiring a specific therapy utilizes all resources required for treating that condition before a second condition has access to those resources.
7. Most medical conditions, with exceptions including acute radiation syndrome and EVA-linked conditions, occur independently of the occurrence of mission events and other medical conditions. Currently there is no correlation or association within or between crew members for most medical conditions.
8. The model assumes another crew member is available to act as caregiver but does not track the time impact of providing this care.
9. Medical procedures are accurately followed and successful; no mistakes occur in executing medical procedures.
10. Crew medical skill level and preflight/inflight training is not modeled.
11. All diagnoses are 100% accurate.
12. All pharmaceuticals maintain maximum efficacy.
13. All medical events receive the appropriate treatment.
14. All medical events respond to the treatment as expected terrestrially.
15. All medical equipment is 100% reliable.
16. For each of the medical conditions specified in iMED, all crew members with the same characteristics (sex, presence of CAC, crowns, contacts, history of abdominal surgery) have the same likelihood distribution of experiencing the condition.
17. All crew members are assumed to have all intrinsic body parts intact (i.e. appendix, gall bladder, and uterus or prostate, etc.).
18. IMM assumes ISS power, potable water and oxygen resources are always available in unlimited supply.
19. No Russian medical capabilities aboard the ISS are available to US crew members in this model.
20. Medical capabilities do not include the use of personal crew carry-on items contained in the Individual Medical Accessories Kit, (IMAK).
21. If a crew member is undergoing treatment for concurrent medical conditions requiring the same

consumable resource, the crew member will only utilize resources at the level required by the condition that requires the most resources.

22. If the primary resource required for treating a medical condition is unavailable, one or more alternative resources are considered, if appropriate. One example might be using acetaminophen in place of ibuprofen.
23. Total quantities of a consumable medical resource requiring a daily dose will be adjusted if a dosage schedule runs past the end of the mission.
24. If a solar particle event causes acute radiation sickness in one or more crew members, IMM assumes the condition begins identically in all affected crew members at the beginning of the solar particle event.
25. The IMM does not decrement non-consumable items and allows all non-consumable items to be used simultaneously by multiple astronauts (e.g. blood pressure cuff).

Results

The IMM results for TME, CHI, EVAC, LOCL and influential conditions for the simulated DRMs are presented in the tables below. Table 4 and figures 1 and 2 show the average number of total medical events (TME) during the mission across all of the DRMs.

Table 4: Average number of total medical events (TME) for the DRMs

		TME	95% CI	
14 day 7 crew DRM	MedCap	28.97	21	38
	Treated	28.97	21	38
	Untreated	28.66	21	37
21 day 4 crew DRM	MedCap	18.18	12	25
	Treated	18.18	12	25
	Untreated	17.95	11	25
42 day 4 crew DRM	MedCap	25.47	17	34
	Treated	25.47	17	34
	Untreated	24.94	17	34
180 day 6 crew DRM	MedCap	104.18	85	124
	Treated	104.21	85	124
	Untreated	97.14	73	120
365 day 4 crew DRM	MedCap	126.79	103	150
	Treated	126.98	103	150
	Untreated	109.78	69	143
730 day 4 crew DRM	MedCap	237.43	190	273
	Treated	239.62	195	274
	Untreated	180.36	94	253
1195 day 4 crew DRM	MedCap	369.95	285	424
	Treated	381.22	301	429
	Untreated	244.04	106	376

Figure 1: Average number of total medical events (TME) for the DRMS

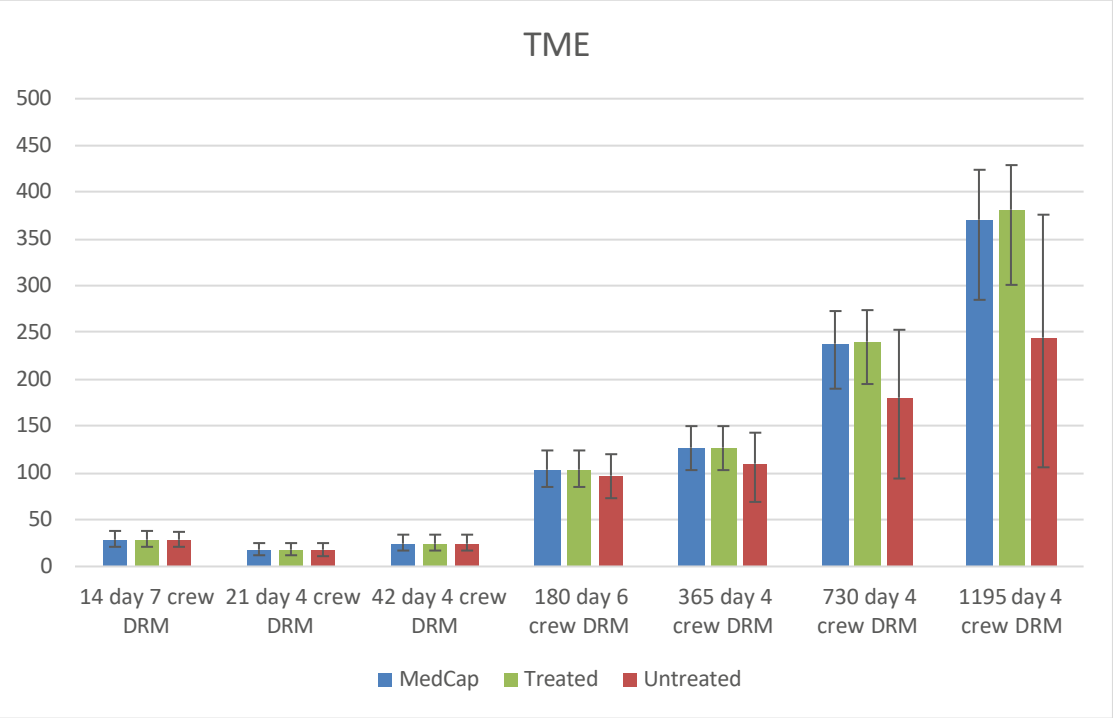


Figure 2: Average number of TME for DRMs by timeline

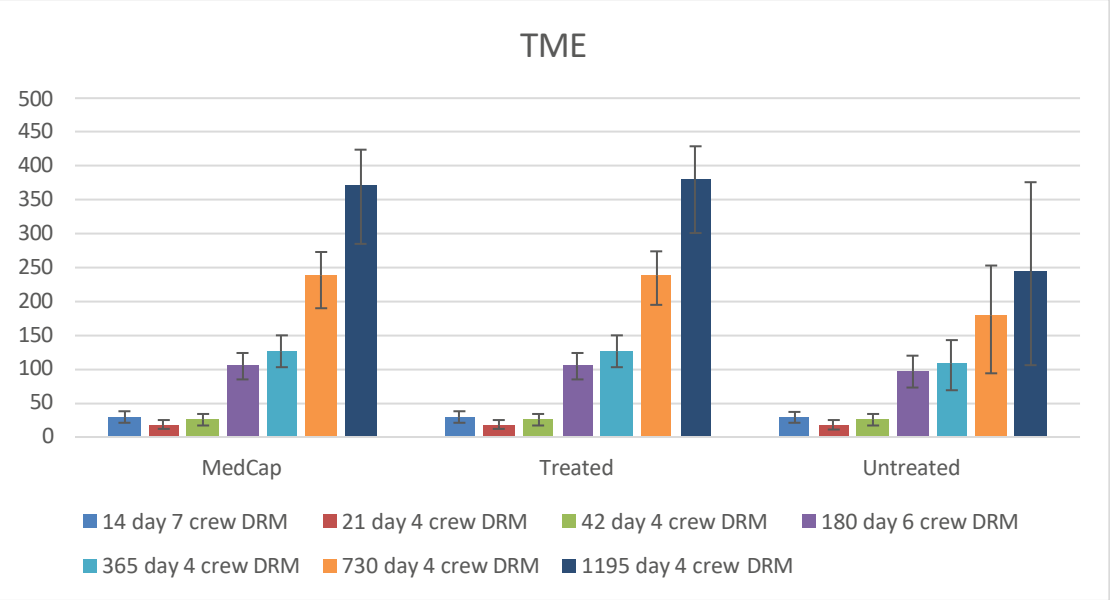


Table 5 and figures 3 and 4 show the average CHI across all of the DRMs.

Table 5: Average Crew Health Index (CHI) for the DRMs

		CHI	95% CI	
14 day 7 crew DRM	MedCap	96.04	92.51	98.16
	Treated	96.03	92.40	98.16
	Untreated	90.58	78.37	95.81

21 day 4 crew DRM	MedCap	96.99	92.99	98.84
	Treated	96.99	92.95	98.84
	Untreated	90.23	69.75	96.89
42 day 4 crew DRM	MedCap	97.36	92.90	98.99
	Treated	97.36	92.87	98.99
	Untreated	86.13	65.24	94.80
180 day 6 crew DRM	MedCap	95.01	84.43	98.49
	Treated	95.05	84.59	98.50
	Untreated	60.72	45.02	72.46
365 day 4 crew DRM	MedCap	93.02	76.17	98.32
	Treated	93.36	76.69	98.43
	Untreated	41.44	25.63	54.39
730 day 4 crew DRM	MedCap	86.00	68.28	94.89
	Treated	90.39	72.11	97.38
	Untreated	23.78	14.00	32.58
1195 day 4 crew DRM	MedCap	72.35	55.04	84.16
	Treated	86.87	67.72	95.75
	Untreated	14.82	8.64	20.52

Figure 3: Average Crew Health Index (CHI) for the DRMs

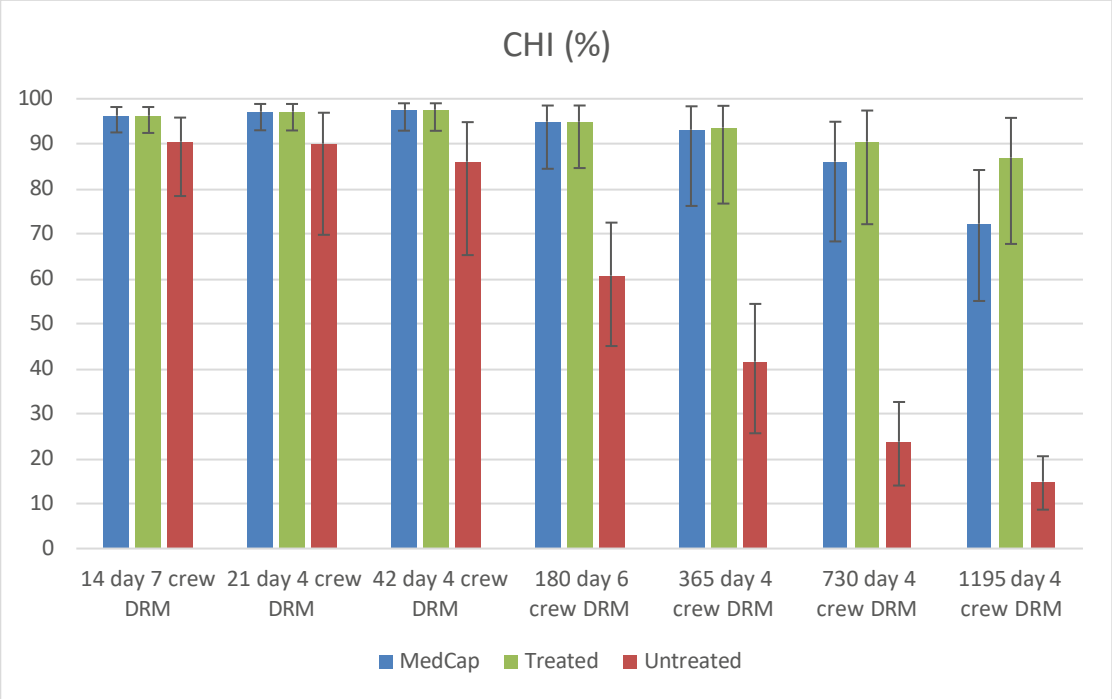


Figure 4: Average Crew Health Index (CHI) for the DRMs by timeline

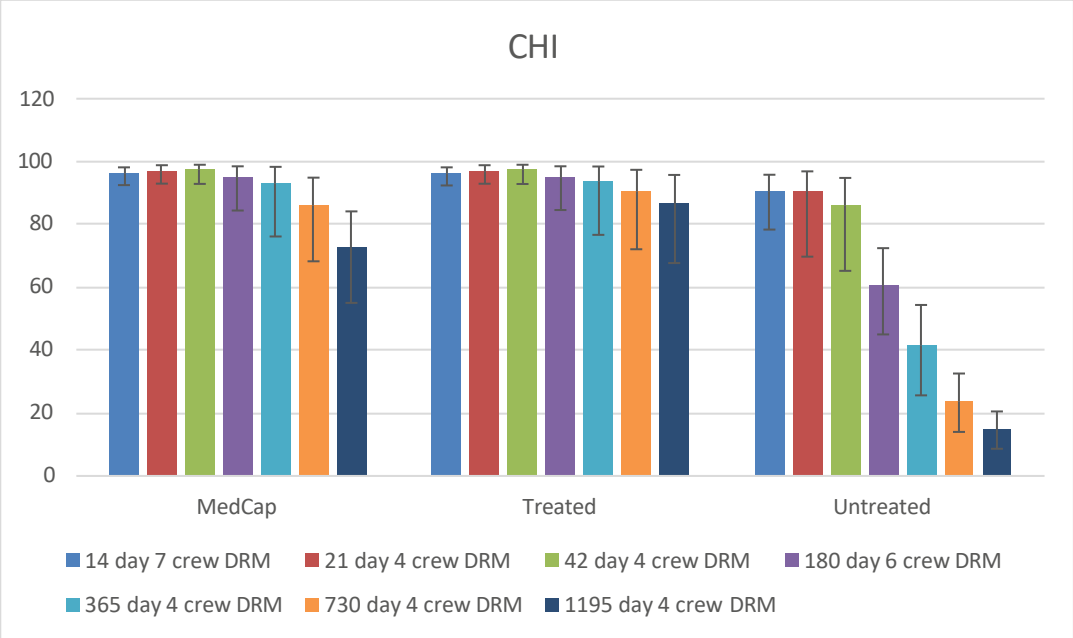


Table 6 along with figures 5-8 show the probability of EVAC and LOCL across all of the DRMs.

Table 6: Probability of EVAC and LOCL for the DRMs

		EVAC			LOCL		
		Probability	95% CI		Probability	95% CI	
14 day 7 crew DRM	MedCap	0.0032	0.0029	0.0036	0.0005	0.0003	0.0006
	Treated	0.0031	0.0028	0.0035	0.0005	0.0004	0.0006
	Untreated	0.2044	0.2017	0.2069	0.0022	0.0019	0.0025
21 day 4 crew DRM	MedCap	0.0027	0.0024	0.0030	0.0003	0.0002	0.0005
	Treated	0.0026	0.0023	0.0029	0.0003	0.0002	0.0005
	Untreated	0.1400	0.1379	0.1421	0.0015	0.0013	0.0018
42 day 4 crew DRM	MedCap	0.0109	0.0102	0.0115	0.0007	0.0006	0.0009
	Treated	0.0106	0.0100	0.0113	0.0007	0.0006	0.0009
	Untreated	0.2035	0.2009	0.2059	0.0033	0.0030	0.0037
180 day 6 crew DRM	MedCap	0.0547	0.0532	0.0560	0.0049	0.0045	0.0054
	Treated	0.0468	0.0454	0.0481	0.0048	0.0044	0.0053
	Untreated	0.6469	0.6439	0.6498	0.0194	0.0185	0.0202
365 day 4 crew DRM	MedCap	0.0755	0.0737	0.0771	0.0059	0.0054	0.0063
	Treated	0.0521	0.0507	0.0535	0.0059	0.0054	0.0063
	Untreated	0.7393	0.7365	0.7420	0.0239	0.0229	0.0248
730 day 4 crew DRM	MedCap	0.2121	0.2096	0.2146	0.0126	0.0119	0.0133
	Treated	0.0951	0.0934	0.0969	0.0124	0.0117	0.0131
	Untreated	0.9243	0.9227	0.9259	0.0425	0.0413	0.0439
1195 day 4 crew DRM	MedCap	0.4330	0.4300	0.4358	0.0214	0.0206	0.0224
	Treated	0.1436	0.1415	0.1458	0.0209	0.0200	0.0217
	Untreated	0.9840	0.9832	0.9848	0.0571	0.0558	0.0585

Figure 5: Probability of EVAC for the DRMs

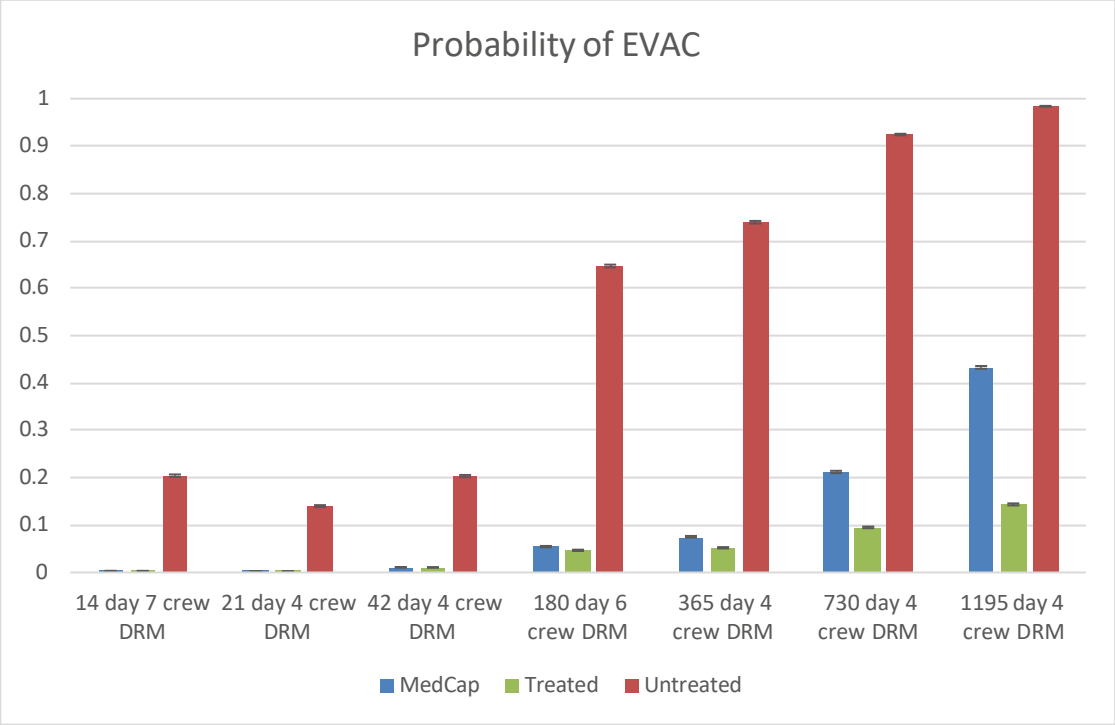


Figure 6: Probability of EVAC for the DRMs by timeline

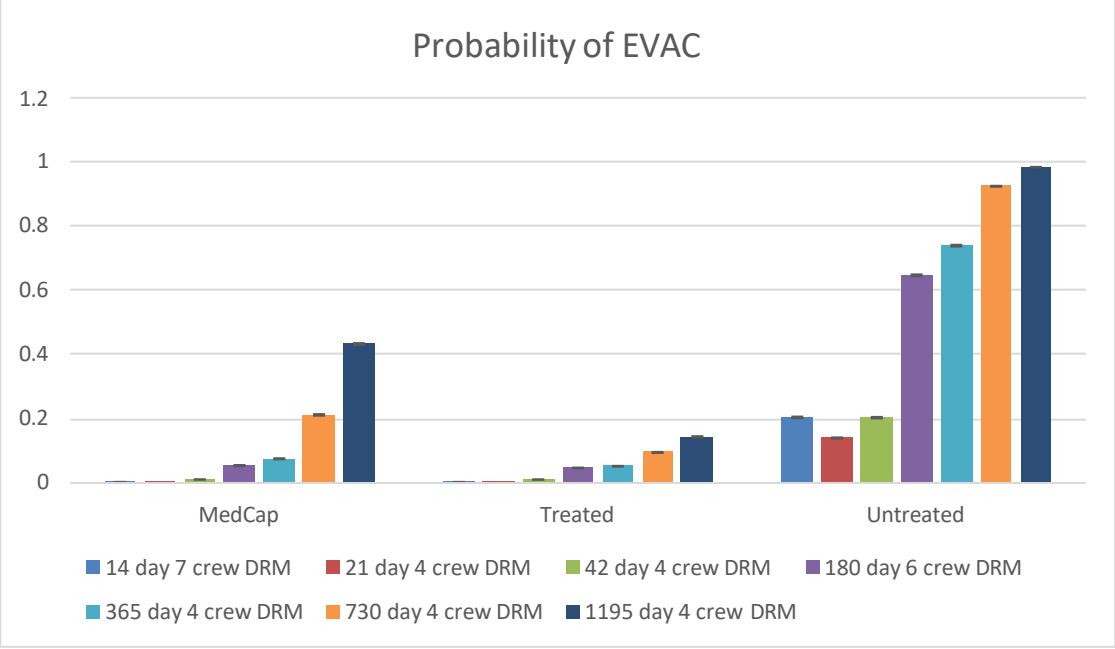


Figure 7: Probability of LOCL for the DRMs

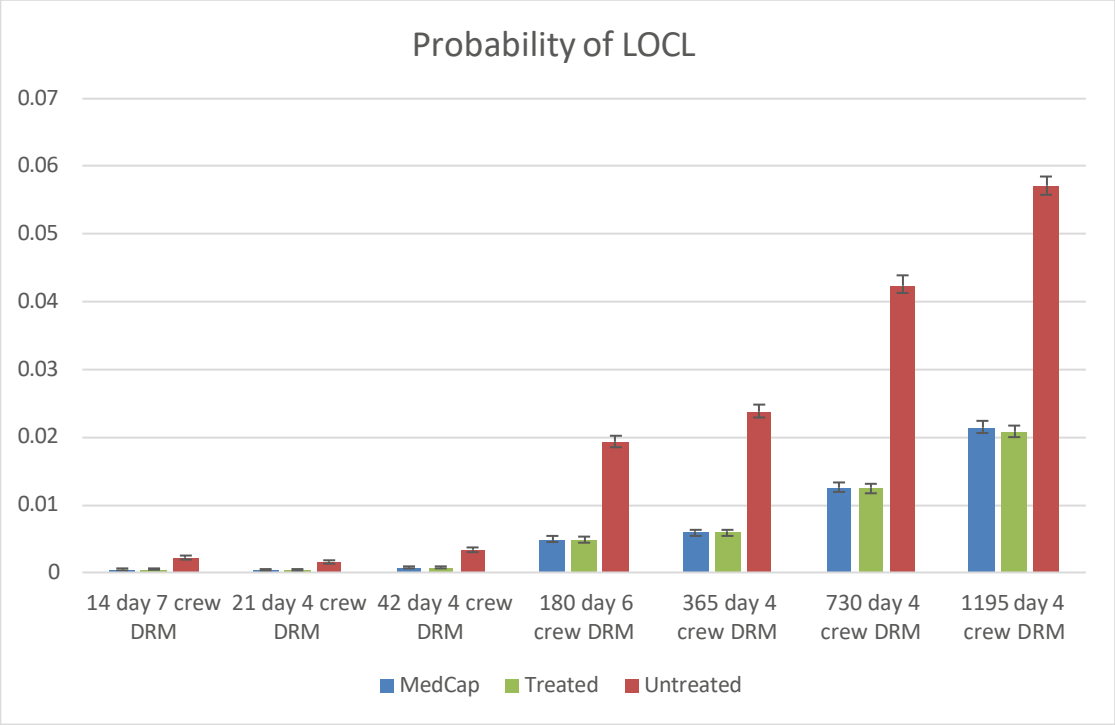
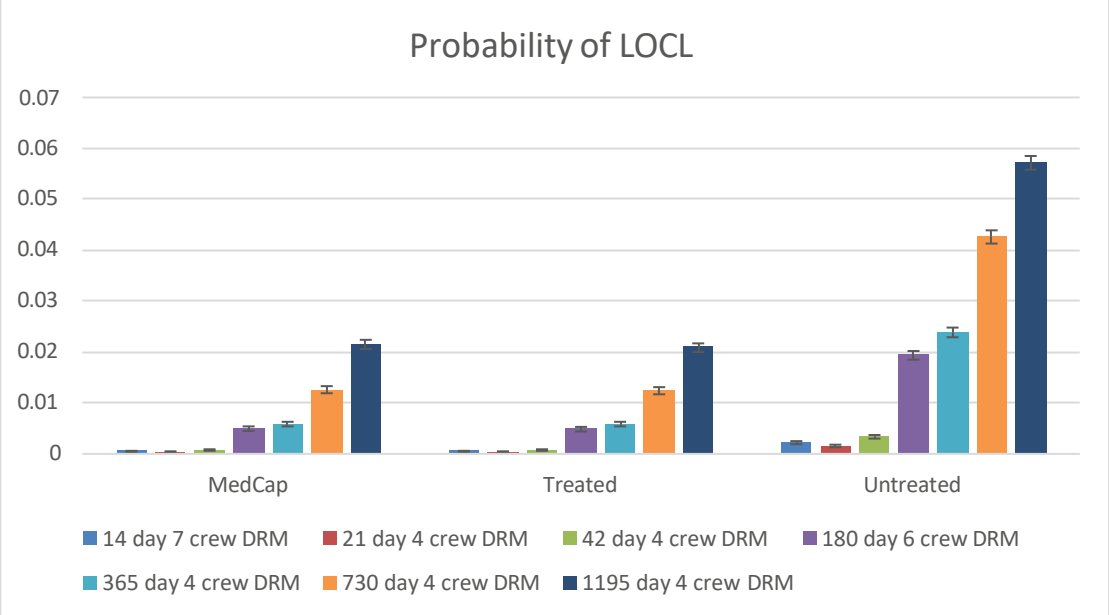


Figure 8: Probability of LOCL for the DRMs by timeline



References

1. Integrated Medical Model Project. Integrated Medical Model Operations Plan. JSC-66114. 2011. Houston, TX, NASA, Johnson Space Center. *Ref Type: Report*

2. Integrated Medical Model Project. Integrated Medical Model Software Requirements Specification.

IMM-SFTWR-008. 2017. Houston, Texas, KBRwyle IntegratedScience, Technology and Engineering.*Ref Type: Report*

3. Integrated Medical Model Project. Integrated Medical Model version 4 Assumptions and Limitations. IMM-GEN-300. 2017. Houston, Texas, KBRwyle Integrated Science and Engineering Space Medicine Information Technology. *Ref Type: Report*

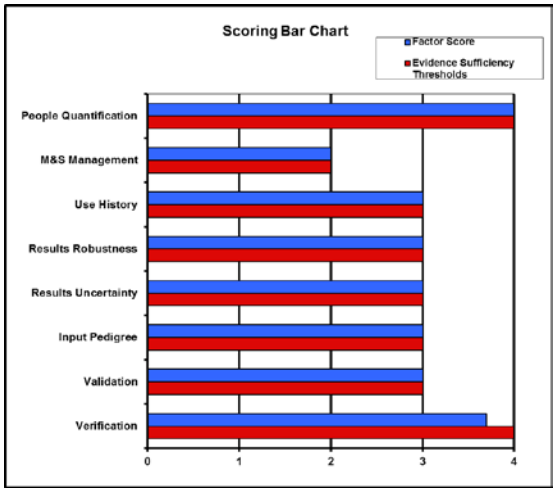
4. NASA-STD-7009: Standard for Models and Simulations (2008). NASA: Washington, DC.

5. ISS Medical Checklist (Med CL), 04 June 2014, NASA Johnson Space Center, Medical Operations Group.

Appendix A: IMM Status at Time of Service Request Report

Validation status for IMM

IMM V&V Matrix: The following bar chart shows the IMM v4.1 MATLAB status of IMM validation for each IMM element listed.



Compliance with NASA-Standard-7009 requirements

IMM Compliance Matrix: The IMM has no waivers to any of the requirements in the NASA-Standard-7009 for Models and Simulations (6); however there are certain requirements that are not applicable to the IMM and other requirements where IMM compliance has not yet been fully attained.

Compliant	Compliance Incomplete	Not applicable
36	5	5

Current NASA-Standard-7009 credibility assessment score

IMM Credibility Matrix: The following table shows the overall IMM v4.1 MATLAB credibility assessment score (CAS), individual factor CAS, customer-specified sufficiency thresholds, and weighted scores. Legend depicts CAS score designated range and color assignments from NASA-Standard-7009.

Factor	Sufficiency Thresholds	Factor Score	Weighted Scores	Overall Score
Verification	**4**	**3.7**	0.28	
Validation	**3**	**3**	0.45	
Input Pedigree	**3**	**3**	0.53	
Results Uncertainty	**3**	**3**	0.60	**3.06**
Results Robustness	**3**	**3**	0.45	
Use History	**3**	**3**	0.45	
M&S Management	**2**	**2**	0.10	
People Qualification	**4**	**4**	0.20	

Legend from NASA-STD-7009	
	CAS Score > Threshold ***Exceeds credibility requirements***
	Threshold ≥ CAS Score ≥ (Threshold-0.5) ***Ready for use***
	Threshold-0.5 > CAS Score ≥ Threshold-1.0 ***Use with caution***
	CAS Score < Threshold - 1.0 ***Use not recommended or to be used with EXTREME CAUTION by subject matter experts only***

Additional verification and validation information applicable to this analysis

none

Integrated Medical Evidence Database (iMED) code version and date accessed

iMED Lockdown ID: (26), created on (2/21/2017)

IMM version and code version

Data analysis for this report was generated using IMM v4.1 with release 2016a of MATLAB software. MATLAB and all other MathWorks product or service names are registered trademarks or trademarks of MathWorks, Natick, MA, USA.

Modifications made to the code for analysis

None

Appendix B: Medical Conditions in iMED by Category (iMED_20170221)

ENVIRONMENTAL
Acute Radiation Syndrome
Altitude Sickness
Barotrauma (ear/sinus block)
Burns secondary to Fire
Decompression Sickness Secondary to EVA
Eye Chemical Burn
Headache (CO_2 induced)
Smoke Inhalation
Toxic Exposure: Ammonia

INJURY/TRAUMA
Abdominal Injury
Acute Compartment Syndrome
Ankle Sprain/Strain
Back Sprain/Strain
Chest Injury
Dental: Avulsion (tooth loss)
Elbow Dislocation
Elbow Sprain/Strain
Eye Irritation/Abrasion
Eye Penetration (foreign body)
Finger Dislocation
Fingernail Delamination Secondary to EVA
Head Injury
Hip Sprain/Strain
Hip/Proximal Femur Fracture
Knee Sprain/Strain
Lower Extremity Stress Fracture
Lumbar Spine Fracture
Neck Sprain/Strain
Neurogenic Shock
Paresthesias Secondary to EVA
Shoulder Dislocation
Shoulder Sprain/Strain
Skin Abrasion
Skin Laceration
Traumatic Hypovolemic Shock
Wrist Fracture
Wrist Sprain/Strain

MEDICAL ILLNESS
Abdominal Wall Hernia
Abnormal Uterine Bleeding
Acute Angle-Closure Glaucoma
Acute Arthritis
Acute Cholecystitis/Biliary Colic
Acute Diverticulitis
Acute Pancreatitis
Acute Prostatitis
Acute Sinusitis
Allergic Reaction (mild to moderate)
Anaphylaxis
Angina/Myocardial Infarction

MEDICAL ILLNESS (continued)
Anxiety
Appendicitis
Atrial Fibrillation/Atrial Flutter
Back Pain (space adaptation)
Behavioral Emergency
Cardiogenic Shock Secondary to Myocardial infarction
Choking/Obstructed Airway
Constipation (space adaptation)
Dental: Exposed Pulp
Dental Caries
Dental: Abscess
Dental: Crown Loss
Dental: Filling Loss
Depression
Diarrhea
Eye Corneal Ulcer
Eye Infection
Gastroenteritis
Headache (Late)
Headache (space adaptation)
Hearing Loss
Hemorrhoids
Herpes Zoster Reactivation (shingles)
Hypertension
Indigestion
Influenza
Insomnia (space adaptation)
Medication Overdose/Adverse Reaction
Mouth Ulcer
Nasal Congestion (space adaptation)
Nephrolithiasis
Nose bleed (space adaptation)
Otitis Externa
Otitis Media
Pharyngitis
Respiratory Infection
Retinal Detachment
Seizures
Sepsis
Skin Infection
Skin Rash
Sleep Disorder
Small Bowel Obstruction
Space Motion Sickness (space adaptation)
Stroke (Cerebrovascular Accident)
Sudden Cardiac Arrest
Urinary Incontinence (space adaption)
Urinary Retention (space adaptation)
Urinary Tract Infection
Vaginal Yeast Infection
Visual Impairment and Increased Intracranial Pressure (VIIP) (space adaptation)