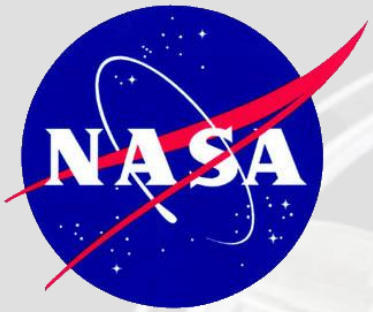

45th International Conference on Environmental Systems

The Integrated Medical Model:

A probabilistic simulation model for predicting in-flight medical risks

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Hilton Bellevue, Bellevue, WA

July 12-16, 2015

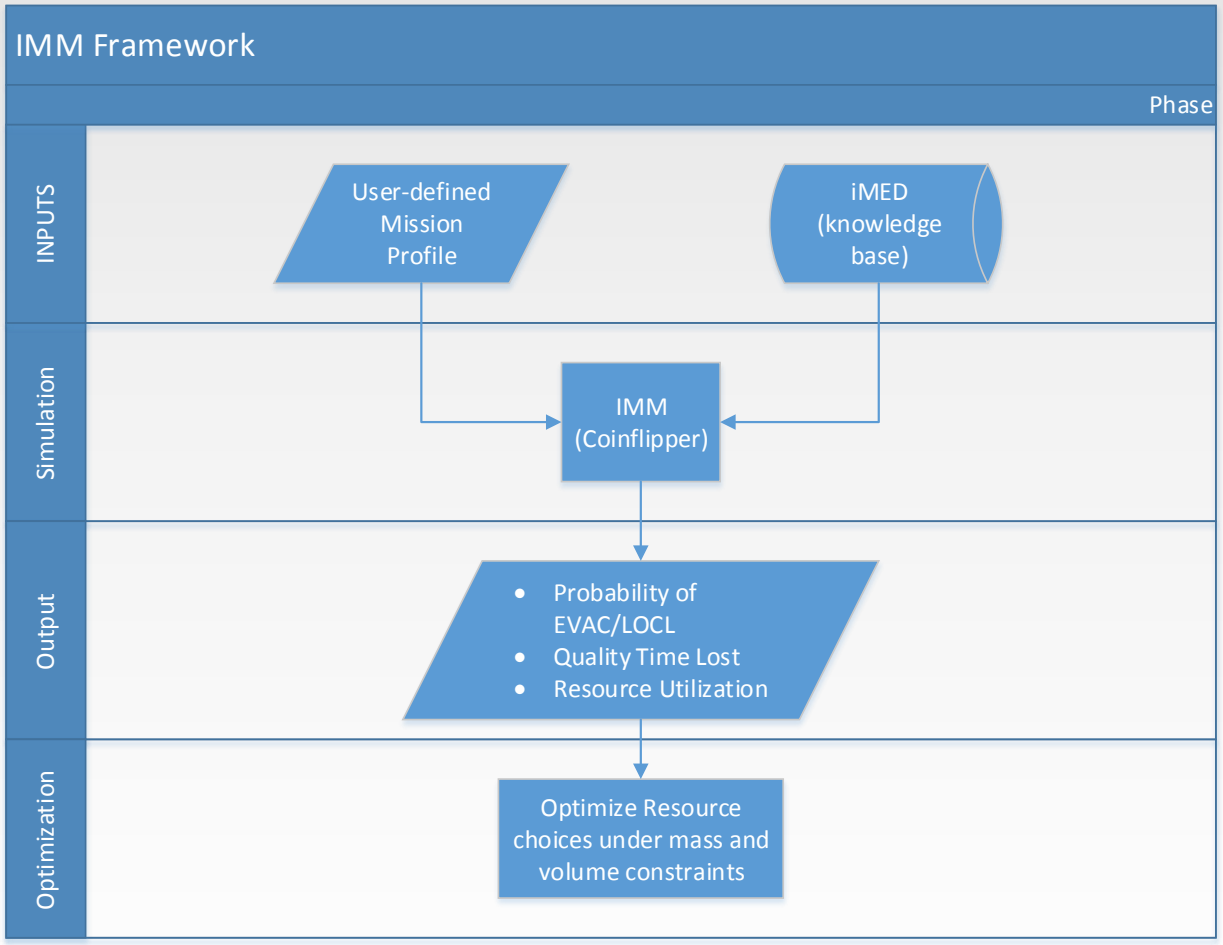
Integrated Medical Model (IMM) Project

- **Conceived in 2005, envisioned development of a simulation model as a means to inform medical resource planning for the International Space Station (ISS) and for future space flight missions**
- Additional applications to quantifying aspects of medical conditions could be elucidated with this approach because of the need to quantify risk metrics
    - Loss of Crew Life (LOCL)
    - Consideration of Evacuation (EVAC)
    - Quality Time Lost (QTL)
- **Intent was to utilize available space flight community knowledge base as an integral part of the simulation environment**
    - Sources: U.S. astronaut data, analog and general population information with appropriate quality and applicability to space flight concepts
- **Not envisioned to be**
    - A diagnosis tool or definitive assessment of medical treatment
    - A means of assessing countermeasure efficacy or performance decrement

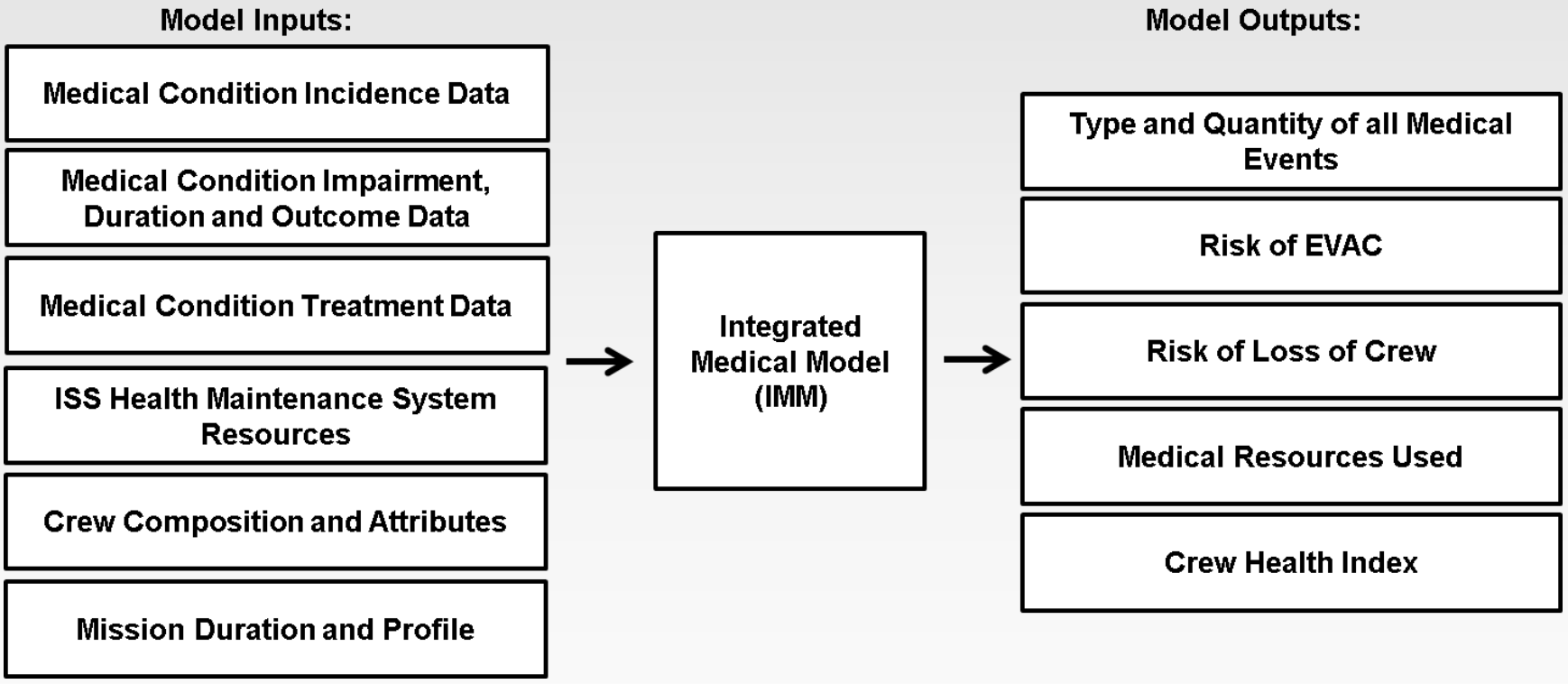
Integrated Medical Model (IMM)

Stochastic simulation model used to predict in-flight medical events, the resources required to treat, and impacts to the spaceflight mission.

IMM Project Flow



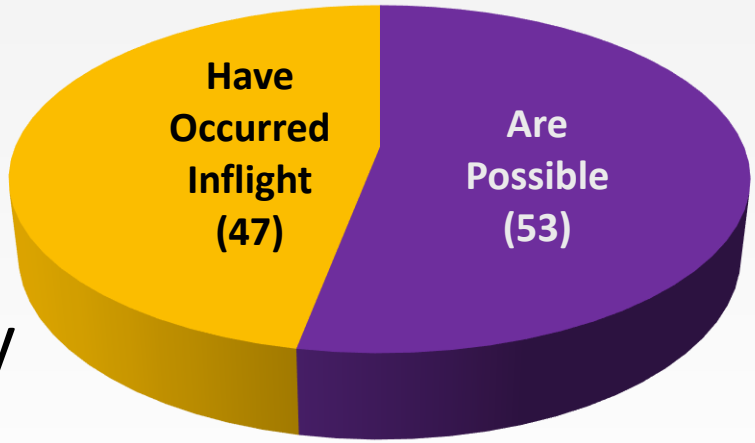
IMM Data Flow



IMM Evidence Database (iMED)

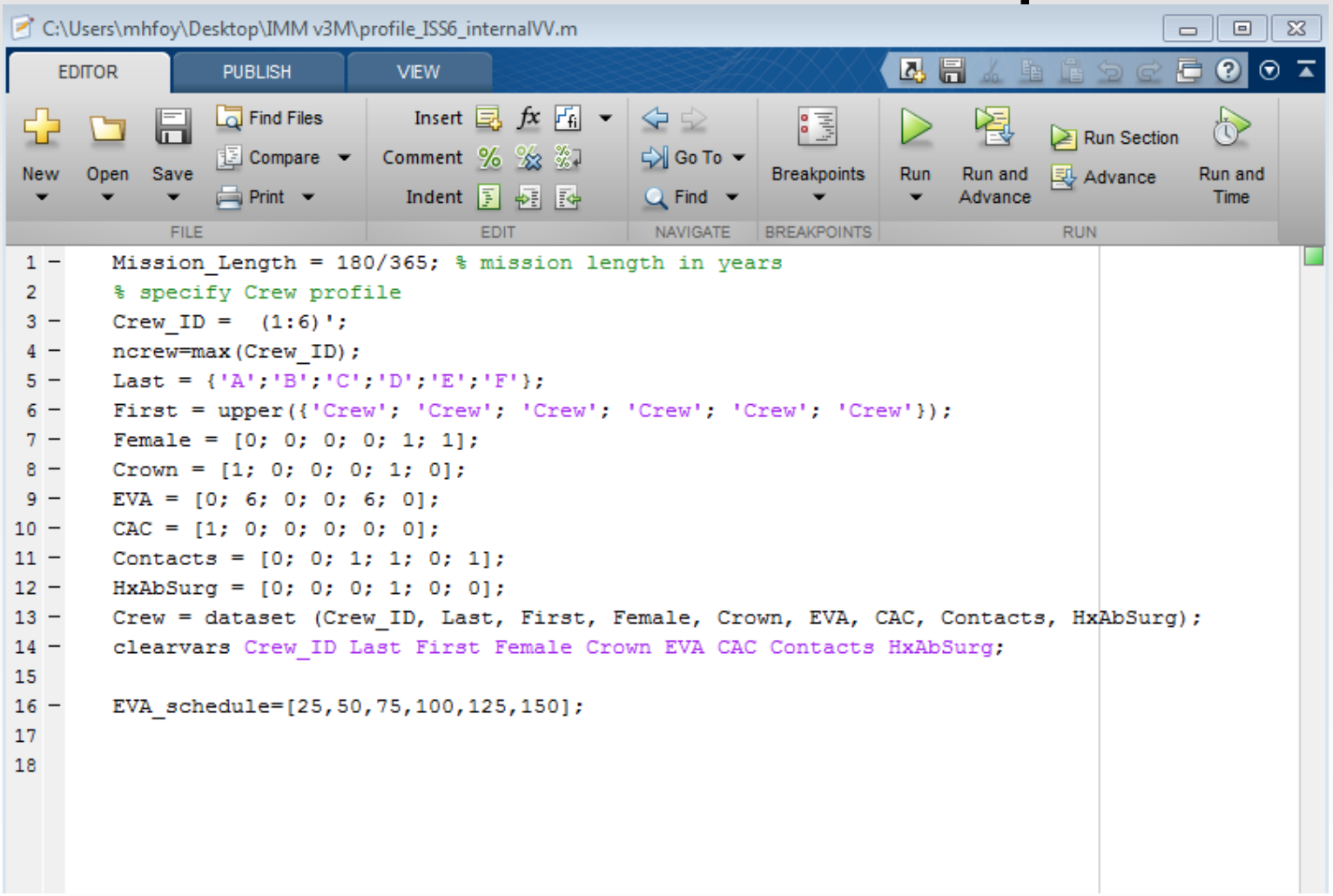
- Lifetime Surveillance of Astronaut Health (LSAH)
  - ISS Expeditions thru 13 (2006)*
  - STS Missions thru STS-114 (2005)
  - Apollo, Skylab, Mir (U.S. crew)
- Bayesian Analysis
- Predictive Models
- Analog, Terrestrial Data
- Flight Surgeon Delphi Study

The IMM Conditions



* More current data used for select conditions

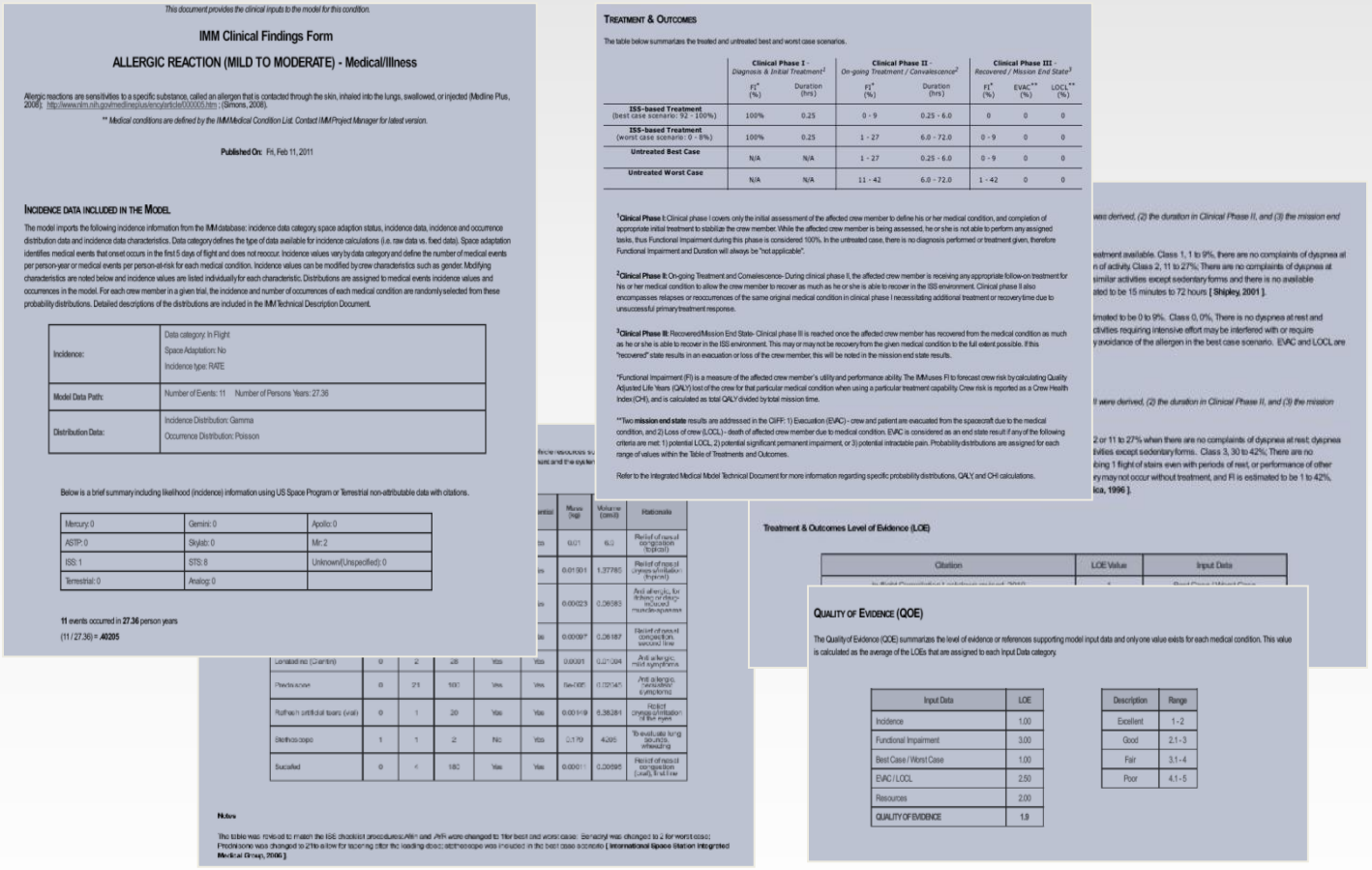
IMM: User-defined Inputs



IMM Conditions

1. Abdominal Injury
2. Abdominal Wall Hernia
3. Abnormal Uterine Bleeding
4. Acute Arthritis
5. Acute Cholecystitis / Biliary Colic
6. Acute Compartment Syndrome
7. Acute Diverticulitis
8. Acute Glaucoma
9. Acute Pancreatitis
10. Acute Prostatitis
11. Acute Radiation Syndrome
12. Acute Sinusitis
13. Allergic Reaction (mild to moderate)
14. Altitude Sickness
15. Angina/ Myocardial Infarction
16. Anaphylaxis
17. Ankle Sprain/Strain
18. Anxiety
19. Appendicitis
20. Atrial Fibrillation/ Flutter
21. Back Injury
22. Back Pain (SA)
23. Barotrauma (sinus block)
24. Behavioral Emergency
25. Burns secondary to Fire
26. Cardiogenic Shock secondary to Infarction
27. Chest Injury
28. Choking/Obstructed Airway
29. Constipation (SA)
30. Decompression Sickness Secondary to EVA
31. Dental : Exposed Pulp
32. Dental Caries
33. Dental: Abscess
34. Dental: Avulsion (Tooth Loss)
35. Dental: Crown Loss
36. Dental: Filling Loss
37. Dental: Toothache
38. Depression
39. Diarrhea
40. Elbow Dislocation
41. Elbow Sprain/Strain
42. Eye Abrasion (foreign body)
43. Eye Chemical Burn
44. Eye Corneal Ulcer
45. Eye Infection
46. Eye Penetration (foreign body)
47. Finger Dislocation
48. Fingernail Delamination (EVA)
49. Gastroenteritis
50. Head Injury
51. Headache (CO_2 induced)
52. Headache (Late)
53. Headache (SA)
54. Hearing Loss
55. Hemorrhoids
56. Herpes Zoster
57. Hip Sprain/Strain
58. Hip/Proximal Femur Fracture
59. Hypertension
60. Indigestion
61. Influenza
62. Insomnia (SA)
63. Knee Sprain/Strain
64. Late Insomnia
65. Lower Extremity Stress Fracture
66. Lumbar Spine Fracture
67. Medication Overdose / Reaction
68. Mouth Ulcer
69. Nasal Congestion (SA)
70. Nephrolithiasis
71. Neurogenic Shock
72. Nose bleed (SA)
73. Otitis Externa
74. Otitis Media
75. Paresthesias
76. Pharyngitis
77. Respiratory Infection
78. Retinal Detachment
79. Seizures
80. Sepsis
81. Shoulder Dislocation
82. Shoulder Sprain/Strain
83. Skin Abrasion
84. Skin Infection
85. Skin Laceration
86. Skin Rash
87. Small Bowel Obstruction
88. Smoke Inhalation
89. Space Motion Sickness (SA)
90. Stroke (CVA)
91. Sudden Cardiac Arrest
92. Toxic Exposure: Ammonia
93. Traumatic Hypovolemic Shock
94. Urinary Incontinence (SA)
95. Urinary Retention (SA)
96. Urinary Tract Infection
97. Vaginal Yeast Infection
98. VIIIP – Visual Impairment/ Increased Intracranial Pressure (SA)
99. Wrist Fracture
100. Wrist Sprain/Strain

iMED Clinical Findings Form (CliFF)



This document provides the clinical inputs to the model for this condition.

IMM Clinical Findings Form

ALLERGIC REACTION (MILD TO MODERATE) - Medical/Illness

Allergic reactions are sensitivities to a specific substance, called an allergen that is contacted through the skin, inhaled into the lungs, swallowed, or injected (Medline Plus, 2008); http://www.nlm.nih.gov/medlineplus/encyclopedia/000005.htm ; (Simons, 2008).

*** Medical conditions are defined by the IMM Medical Condition List. Contact IMM Project Manager for latest version.*

Published On: Fri, Feb 11, 2011

INCIDENCE DATA INCLUDED IN THE MODEL

The model imports the following incidence information from the IMM database: incidence data category, space adaption status, incidence data, 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. fixed data). Space adaptation identifies medical events that onset occurs in the first 5 days of flight and does not reoccur. Incidence values vary by data category and define the number of medical events per person-year or medical events per person-at-risk for each medical condition. Incidence values can be modified by crew characteristics such as gender. 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 crew member 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 IMM Technical Description Document.

Incidence:	Data category: In Flight Space Adaptation: No Incidence type: RATE
Model Data Path:	Number of Events: 11 Number of Persons Years: 27.36
Distribution Data:	Incidence Distribution: Gamma Occurrence Distribution: Poisson

Below is a brief summary including likelihood (incidence) information using US Space Program or Terrestrial non-attributable data with citations.

Mercury: 0	Gemini: 0	Apollo: 0
ASTP: 0	Skylab: 0	Mir: 2
ISS: 1	STS: 8	Unknown(Unspecified): 0
Terrestrial: 0	Analog: 0	

11 events occurred in **27.36** person years

(11 / 27.36) = **.40205**

TREATMENT & OUTCOMES

The table below summarizes the treated and untreated best and worst case scenarios.

	Clinical Phase I - *Diagnosis & Initial Treatment*[1]		Clinical Phase II - *On-going Treatment / Convalescence*[2]		Clinical Phase III - *Recovered / Mission End State*[3]		
	FI* (%)	Duration (hrs)	FI* (%)	Duration (hrs)	FI* (%)	EVAC** (%)	LOCL** (%)
ISS-based Treatment (best case scenario: 92 - 100%)	100%	0.25	0 - 9	0.25 - 6.0	0	0	0
ISS-based Treatment (worst case scenario: 0 - 8%)	100%	0.25	1 - 27	6.0 - 72.0	0 - 9	0	0
Untreated Best Case	N/A	N/A	1 - 27	0.25 - 6.0	0 - 9	0	0
Untreated Worst Case	N/A	N/A	11 - 42	6.0 - 72.0	1 - 42	0	0

[1]**Clinical Phase I:** Clinical phase I covers only the initial assessment of the affected crew member to define his or her medical condition, and completion of appropriate initial treatment to stabilize the crew member. While the affected crew member is being assessed, he or she is not able to perform any assigned tasks, thus Functional Impairment during this phase is considered 100%. In the untreated case, there is no diagnosis performed or treatment given, therefore Functional Impairment and Duration will always be "not applicable".

[2]**Clinical Phase II:** On-going Treatment and Convalescence- During clinical phase II, the affected crew member is receiving any appropriate follow-on treatment for his or her medical condition to allow the crew member to recover as much as he or she is able to recover in the ISS environment. Clinical phase II also encompasses relapses or reoccurrences of the same original medical condition in clinical phase I necessitating additional treatment or recovery time due to unsuccessful primary treatment response.

[3]**Clinical Phase III:** Recovered/Mission End State- Clinical phase III is reached once the affected crew member has recovered from the medical condition as much as he or she is able to recover in the ISS environment. This may or may not be recovery from the given medical condition to the full extent possible. If this "recovered" state results in an evacuation or loss of the crew member, this will be noted in the mission end state results.

*Functional Impairment (FI) is a measure of the affected crew member's utility and performance ability. The IMMuses FI to forecast crew risk by calculating Quality Adjusted Life Years (QALY) lost of the crew for that particular medical condition when using a particular treatment capability. Crew risk is reported as a Crew Health Index (CHI), and is calculated as total QALY divided by total mission time.

Two **mission end state results are addressed in the CliFF: 1) Evacuation (EVAC) - crew and patient are evacuated from the spacecraft due to the medical condition, and 2) Loss of crew (LOCL) - death of affected crew member due to medical condition. EVAC is considered as 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. Probability distributions are assigned for each range of values within the Table of Treatments and Outcomes.

Refer to the Integrated Medical Model Technical Document for more information regarding specific probability distributions, QALY and CHI calculations.

was derived, (2) the duration in Clinical Phase II, and (3) the mission end

eatment available. Class 1, 1 to 9%, there are no complaints of dyspnea at n of activity. Class 2, 11 to 27%, There are no complaints of dyspnea at similar activities except sedentary forms and there is no available sted to be 15 minutes to 72 hours **[Shipley, 2001].**

imated to be 0 to 9%. Class 0, 0%, There is no dyspnea at rest and ctivities requiring intensive effort may be interfered with or require y avoidance of the allergen in the best case scenario. EVAC and LOCL are

ll were derived, (2) the duration in Clinical Phase II, and (3) the mission

2 or 11 to 27% when there are no complaints of dyspnea at rest; dyspnea ivities except sedentary forms. Class 3, 30 to 42%, There are no oing 1 flight of stairs even with periods of rest, or performance of other ey may not occur without treatment, and FI is estimated to be 1 to 42%, **ica, 1996].**

Treatment & Outcomes Level of Evidence (LOE)

Citation	LOE Value	Input Data

QUALITY OF EVIDENCE (QOE)

The Quality of Evidence (QOE) summarizes the level of evidence or references supporting model input data and only one value exists for each medical condition. This value is calculated as the average of the LOEs that are assigned to each Input Data category.

Input Data	LOE
Incidence	1.00
Functional Impairment	3.00
Best Case / Worst Case	1.00
EVAC / LOCL	2.50
Resources	2.00
QUALITY OF EVIDENCE	1.9

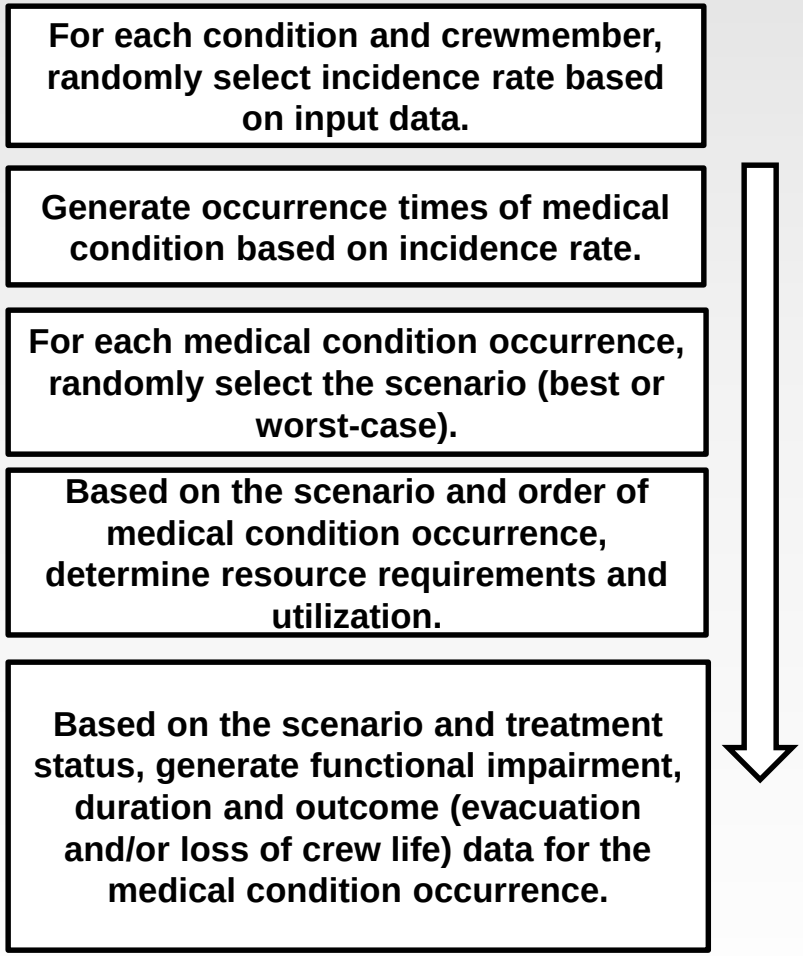
Description	Range
Excellent	1 - 2
Good	2.1 - 3
Fair	3.1 - 4
Poor	4.1 - 5

								Rationale
						0.01	6.0	Relief of nasal congestion (topical)
						0.01301	1.37785	Relief of nasal congestion/allergy (topical)
						0.00023	0.09383	Anti allergic, for asthma or drug-induced musculoskeletal
						0.00097	0.26187	Relief of nasal congestion, second line
Loratadine (Claritin)	0	2	28	Yes	Yes	0.0001	0.21304	Anti allergic, mild symptoms
Prednisone	0	21	100	Yes	Yes	5e-005	0.03147	Anti allergic, sensitized symptoms
Refresh artificial tears (vial)	0	1	20	Yes	Yes	0.00149	6.38281	Relief of severe irritation of the eyes
Stethoscope	1	1	2	No	Yes	0.179	4.205	To evaluate lung sounds, wheezing
Sudafed	0	4	180	Yes	Yes	0.0001	0.00995	Relief of nasal congestion (oral), first line

Notes

The table was revised to match the ISS checklist procedures:Albh and AtR were changed to 1for best and worst case; Benadryl was changed to 2 for worst case; Prednisone was changed to 21to allow for tapering after the loading dose; stethoscope was included in the best case scenario **[International Space Station Integrated Medical Group, 2006].**

Mission Simulation



IMM Medical Event Simulation

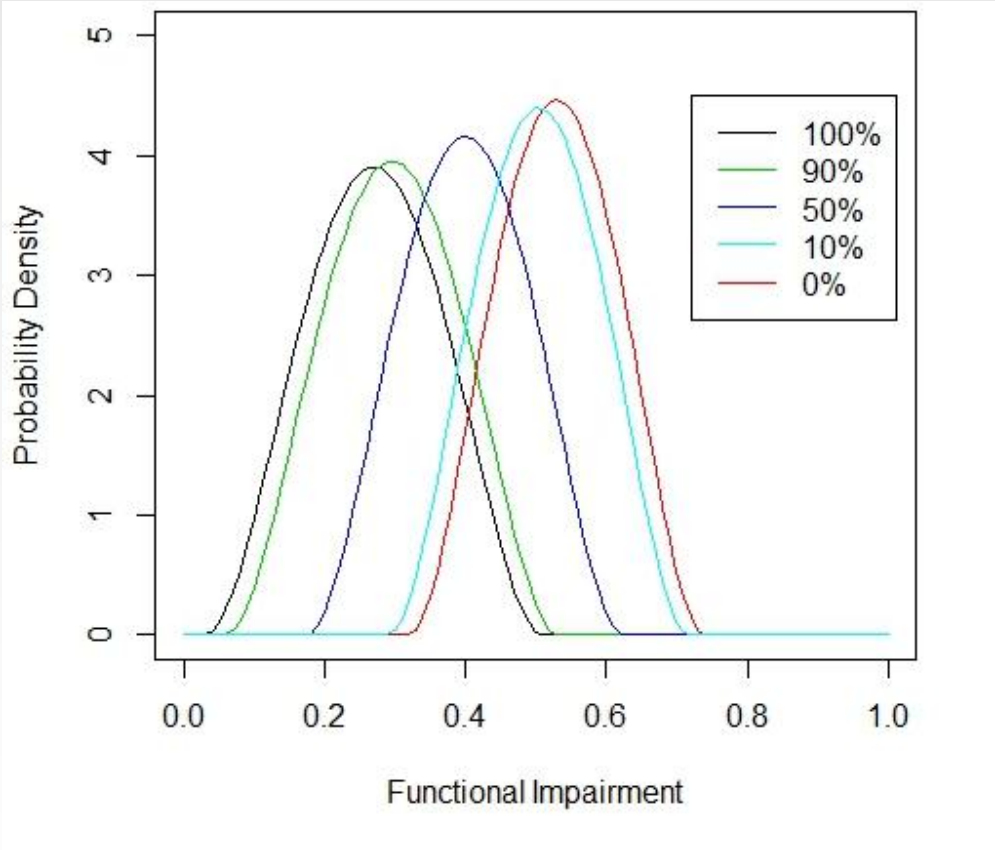
- All possible conditions are matched with crewmembers defined in the profiles
- For each simulated mission, the time of onset of each condition is generated
- Conditions fall under 4 distinct categories when it comes to the simulation:
  - **Space Adaptation Syndromes** are simulated as yes/no events based on an incidence proportion. If yes, then the onset time is generated from a specified distribution
  - **EVA-related conditions** are simulated as yes/no events based on an incidence proportion. If yes, the onset time is set at the pre-specified EVA time
  - **General condition** onset times are simulated with exponential waiting times based on an incidence rate
  - **Acute Radiation Syndrome (ARS)** is simulated separately under 2 steps
    1. The timing of Solar Particle Events (SPE) is generated using exponential waiting times based on an incidence rate
    2. For each generated SPE, ARS is generated as a yes/no event for each crewmember based on an incidence proportion. If yes, the time of onset is set as the time of the SPE

IMM Condition Severity

- Each medical condition is defined based on a dichotomized level of severity (best/worst-case scenarios)
- For each generated event, whether the condition goes best-case or worst-case is assigned according to pre-specified probability ranges in the simulation
- Each best-case or worst-case medical condition defines the treatment required

IMM Medical Condition Outcome Distributions

- Outcome distributions are defined based on the two extremes
  - Full treatment available
  - No treatment available
- The outcome distributions are shifted between the extremes, when some but not all the essential required resources are available at the time the condition occurs (Partial Treatment)



IMM Medical Condition Outcomes

Functional Impairment (FI) and Durations

- Each condition is divided into 3 stages (Clinical Phases)
  - Initial diagnosis and treatment
  - Ongoing treatment
  - Recovery/mission end state (remainder of the mission)
- Each stage is assigned an FI
  - Functional impairment is adapted from a standardized guidelines used in the Insurance industry. To adjust for the temporary nature of the impairment, the IMM FI algorithm calculates based on general principals and rules of the American Medical Association (AMA) “Guides to the Evaluation of Permanent* Impairment”.

Quality Time Lost (QTL)

- Sum of the FI*duration over the 3 Clinical Phases of the condition

EVAC and LOCL are generated from specified probability distributions

* IMM uses same classes as AMA but adjusts for mission time

Additional Condition Assumptions

- Crewmembers cannot get the same condition for which they are already being treated (no identical conditions during CP1-CP2) with the exception of DCS secondary to EVA
- Crewmembers can get no further conditions after EVAC or LOCL, and FI = 1 for the remainder of the mission
- Crewmembers that require the same resource for multiple conditions during a time interval will use the maximum required quantity for each condition to treat both simultaneously

IMM Predictions (Mission-level Outputs)

- Probability (Consideration) of EVAC
  - Proportion of simulated missions with at least one EVAC
  - Confidence limits estimated by bootstrap resampling
- Probability of LOCL
  - Proportion of simulated missions with at least one LOCL
  - Confidence limits estimated by bootstrap resampling
- Quality Time Lost (QTL)
  - Sum of FI x Duration over the mission
  - FIs are adjusted for overlapping (in time) impairments within crewmembers
  - Defined on [0, mission length]

Crew Health Index (CHI)

Definition: Proportion of mission time not lost to medical events

$$1 - \frac{\sum QTL}{L * n} = CHI$$

n = # crew,

L = mission length,

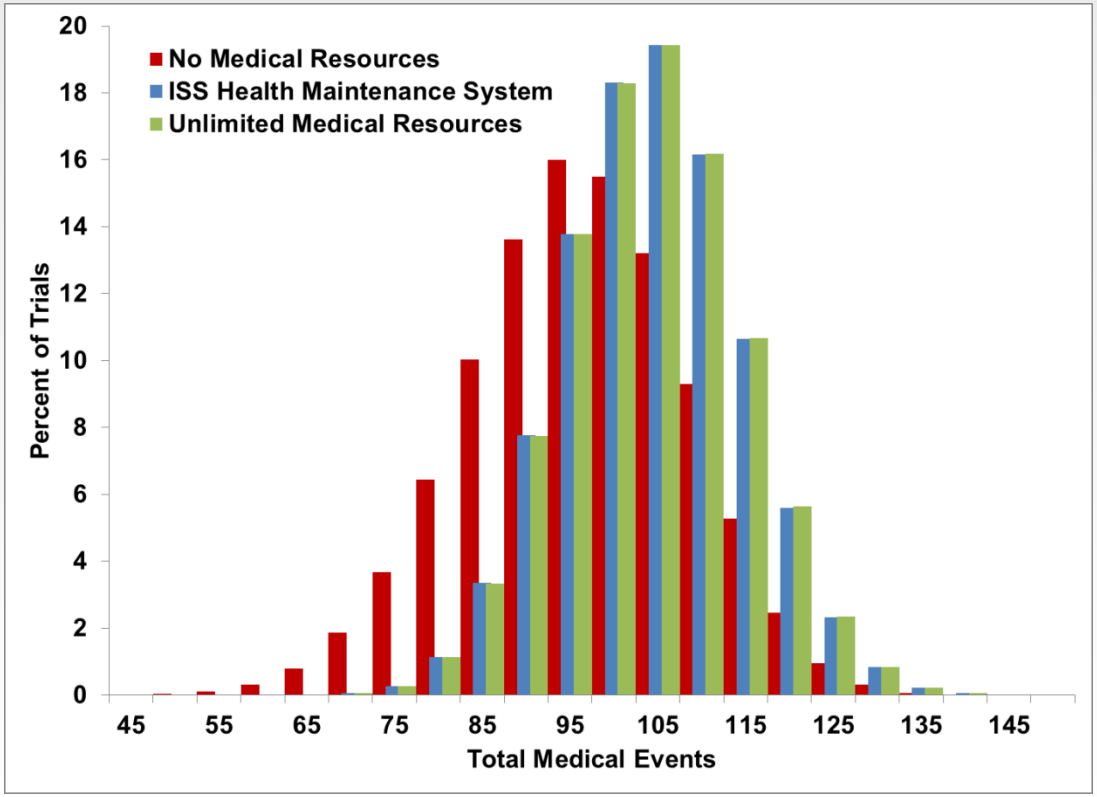
QTL = quality time lost for each condition

- CHI is a normalized calculation of Quality Time Lost. Can be a useful metric when comparing two or more mission profiles.

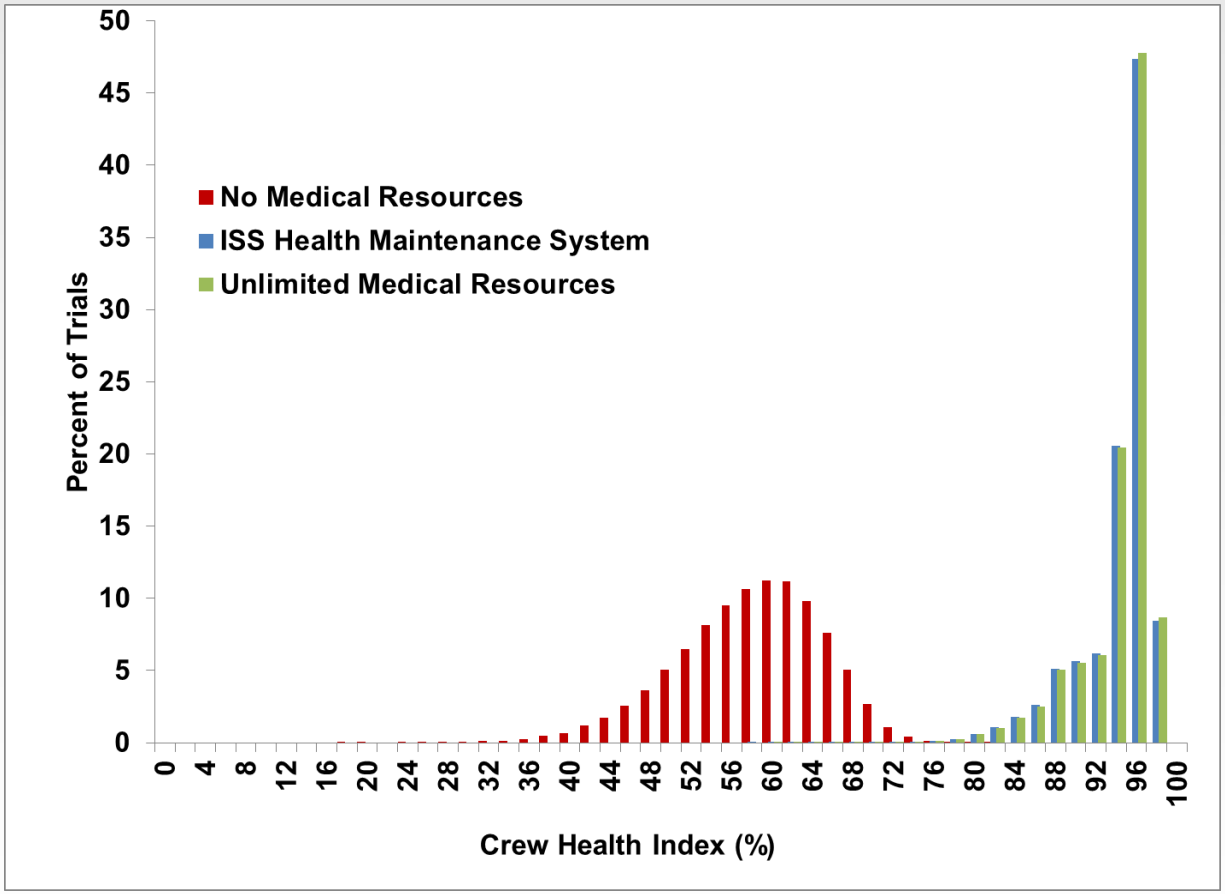
Example Results ISS6 (6 crew, 6 months, 6 two-crew EVAs)

	No Medical Resources			ISS Health Maintenance System			Unlimited Medical Resources		
	Mean	95% Confidence Interval		Mean	95% Confidence Interval		Mean	95% Confidence Interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound		Lower Bound	Upper Bound
TME	98.3	73	122	106	87	126	106	87	126
CHI	59.2	43.36	71.25	94.93	84.32	98.46	94.98	84.44	98.47
pEVAC	66.9	66.57	67.14	5.57	5.43	5.72	4.93	4.8	5.07
pLOCL	2.89	2.78	2.99	0.44	0.4	0.49	0.45	0.41	0.49

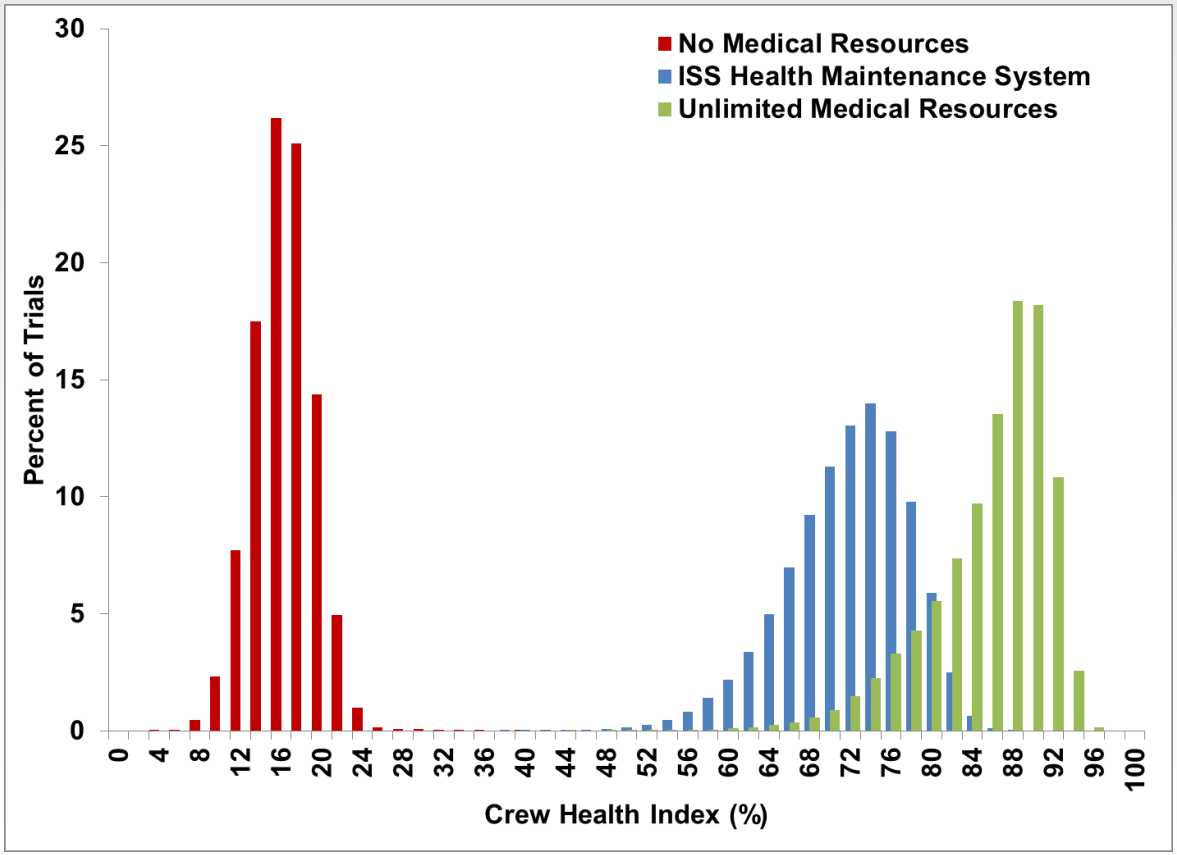
Example Results ISS6 (6 crew, 6 months, 6 two-crew EVAs) Total Medical Events



Example Results ISS6 (6 crew, 6 months, 6 two-crew EVAs) Crew Health Index



Example Results Exploration (6 crew, 2.5 years, 231 two-crew EVAs) Crew Health Index



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