The Integrated Medical Model
A Risk Assessment and Decision Support Tool for Human Space Flight Missions

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Integrated Medical Model (IMM)

A Risk Assessment and Decision Support Tool for Human Space Flight Missions

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Outline

- IMM Overview
- International Space Station Probabilistic Risk Assessment Update
- Validation
- Optimization

IMM Project Goals

- To develop an integrated, quantified, evidence-based decision support tool useful to NASA crew health and mission planners.

- To help align science, technology, and operational activities intended to optimize crew health, safety, and mission success.

What is IMM?

- A software-based decision support tool
  - Forecasts the impact of medical events on space flight missions
  - Optimizes the medical system within the constraints of the space flight environment during simulations.

Scope and Approach

IMM addresses in-flight risk using ISS data as a stepping stone

- Scope
  - Forecast medical outcomes for in-flight operations only
  - Forecast medical impacts to mission
  - Does not assess long-term or chronic post-mission medical consequences

- Approach
  - Use ISS data as stepping stone to Exploration Program
  - Employ best-evidence clinical research methods
  - Employ Probability Risk Assessment (PRA) techniques
  - Collaborate with other NASA Centers and Organizations

"What if…?" Questions

IMM is designed to help answer specific in-flight questions

Questions

- Is the current ISS medical kit adequate for a crew of 6 on a 6-month mission?
- Does a 33-day lunar sortie mission require a different Level of Care than a 24-day lunar sortie mission?
- Are we carrying enough Ibuprofen for a crew of six on a 12-month mission?
- How does risk change if the ventilator fails at the start of a 3-year mission?

Questions

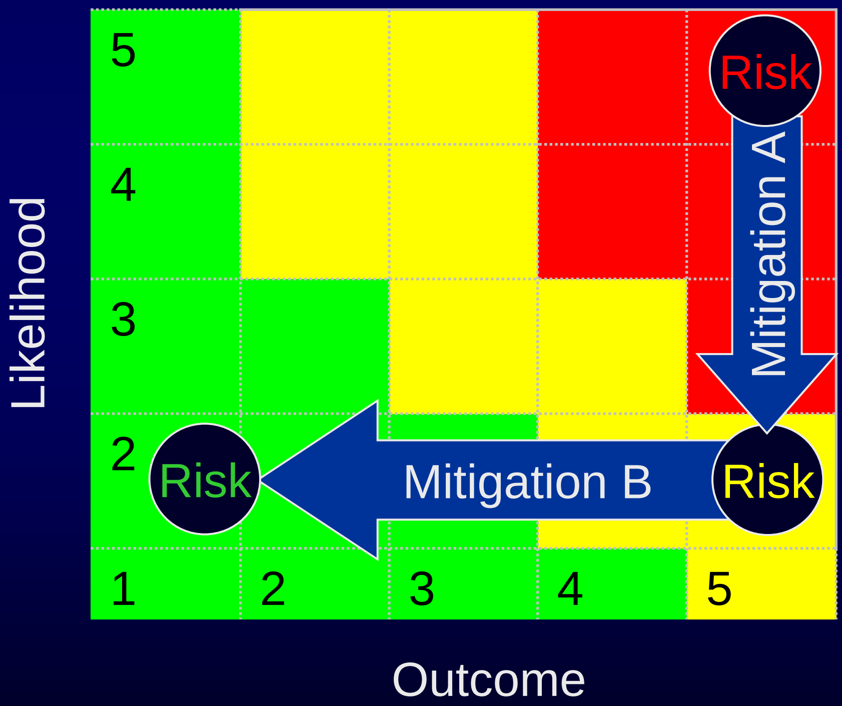
- What is the probability of a bone fracture occurring 10 years **after** a 6-month mission?
- What is the probability of renal stone formation **after** a 12-month mission?

Risk and Risk Components

"Risk" is what is left over after you have accounted for likelihood, outcome, and the mitigation associated with the threat.

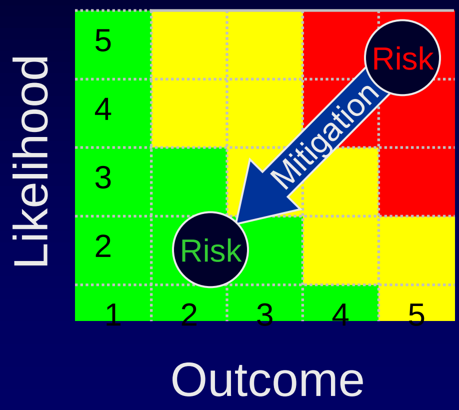
5 x 5 Risk Matrix

Threat A



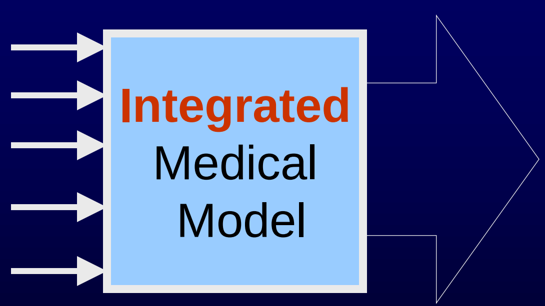
5x5 Matrix	IMM
Likelihood (Score 1-5)	Medical Condition Incidence
Mitigation?	In-flight Medical Capabilities
Outcome (Score 1-5)	Crew Functional Impairment
Risk Score (2x1) for a single "risk"	Impact to mission due to all medical conditions for the crew compliment

Comparison – 5x5 Risk Matrix vs. IMM



5x5 Matrix	IMM
Qualitative	Quantitative
Categorical	Probabilistic, Stochastic
Subjective	Evidence-based
Single Risk	Integrated Risks
No Uncertainty	Uncertainty
No Confidence Interval	Confidence Interval
Limited context	In context

- Medical Conditions & Incidence Data
- Crew Profile
- Mission Profile & Constraints
- Crew Functional Impairments
- In-flight Medical Resources

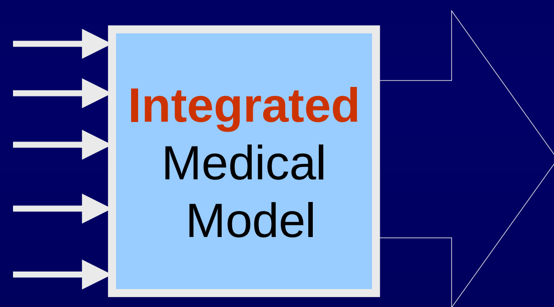


- Medical Condition Occurrences
- Crew Impairment
- Clinical/Mission End States
- Resource Utilization
- Optimization of Vehicle Constraints and Medical System Capabilities

IMM Conceptual Model

INPUTS

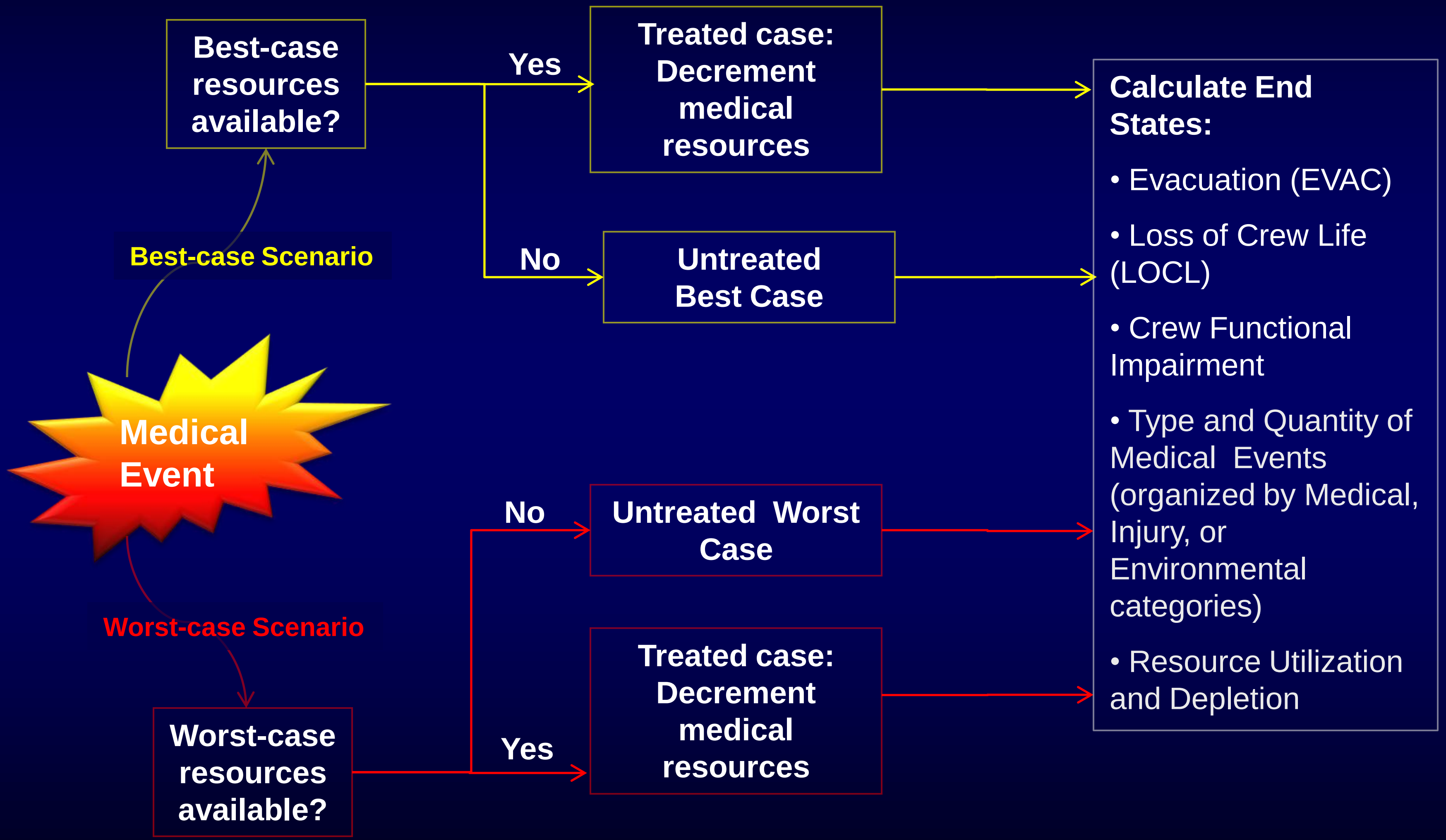
- Medical Conditions & Incidence Data
- Crew Profile
- Mission Profile & Constraints
- Potential Crew Impairments
- Potential Mission End states
- In-flight Medical Resources



OUTPUTS

- Medical Condition Occurrences
- Crew Impairments
- Clinical End States
- Mission End States
- Resource Utilization
- Optimized Medical System

IMM Logic - Event Sequence Diagram



IMM Logic

For each comparative assessment, the identical questions are asked 10,000+ times to develop outcome distributions

- Did the medical condition happen?
- How many times?
- Best- or worst-case scenario?
- Were resources available?
- What was the outcome?

Clinical Findings Form (CliFF)

Standardized Format for IMM Clinical Inputs

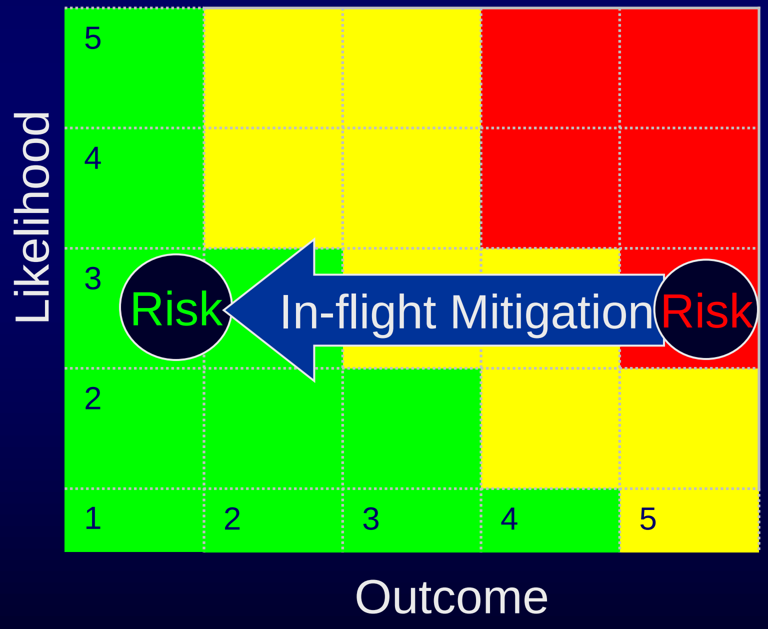
- The likelihood of occurrence of the medical condition
  - Incidence proportion or incidence rate
- The clinical outcomes of the medical condition
  - Considers ISS-based best-case, worst-case, and untreated case scenarios
  - Specifies functional impairments and duration times
  - Specifies potential end states (evacuation, loss of crew life)
  - Specifies levels of evidence for input data
  - References sources of data
- Medical Resource Tables
  - Specifies the resources required to diagnose and treat best- and worst-case scenarios

Resource Tables

The resource tables specify the required in-flight medical resources

- Specify resources required for diagnosis and treatment

- Consider the best-case and worst-case scenarios



Best and Worst Cases

Best-Case Scenario

Consumable	Disorder: Musculoskeletal	Description	Quantity	Mass Kg	Mass GM	Volume cc3	Volume mm3	Power (W)	Cost Estimates	COTS	Flight Certify	Sustaining Eng
1	Sprain/Strain Extremities	Ace Bandage	1	0.03875	38.75	442.5	442500			$ 3.08		
		SAM splint	1	0.1134	113.4	1336.3575	1336357.5			$ 12.00		
1		Acetaminophen	2	0.00036	0.36	0.02632	26.32			$ 0.10		
1		Ibuprofen	1-9	0.00066	0.66	0.04202	42.02			$ 0.14		

Worst-Case Scenario

Consumable	Disorder	Description	Quantity	Mass Kg	Mass Gm	Volume cc^3	Volume mm^3	Power	Cost Estimates	COTS	Flight Certify	Sustaining Eng
	Sprain/Strain Extremities	Ace Bandage	1	0.03875	38.75	442.5000	442500			$ 3.08		
		SAM splint	1	0.1134	113.4	1336.3575	1336357.5			$ 12.00		
1		acetaminophen (2 tabs*4-6hr)	8	0.00036	0.36	0.0263	26.32			$ 0.10		
1		ibuprofen (1-2 tabs*8hr)	10	0.00066	0.66	0.0420	42.02			$ 0.14		
1		Vicodin (1-2 tabs *4-6 hr)	2	0.00064	0.64	0.0483	48.30			$ 0.50		
1		Gauze Pads	4	0.00504	5.04	7.6000	7600.00			$ 0.16		
1		Nonsterile Gloves pr	1	0.014	14	3.1000	3100			$ 0.10		
		Sharps container	1	0.59553	595.53	2909.1250	2909125.00		$ 817.06			
1		20 G catheter	2	0.00622	18.51	7.5000	7500			$ 0.15		
1		10cc syringe	1	0.01123	11.23	4.1700	4170			$ 0.15		
1		Y-type catheter	1	0.00868	8.68	0.1000	100.00			$ 0.50		
1		Tegaderm Dressing	1	0.00252	2.52	108.2000	108200			$ 0.38		
1		Saline, 500mL	1	0.48929	489.29	750.8390	750839.00			$ 10.81		
1		Iodine Pads	1	0.00108	1.08	0.1500	150.00			$ 0.04		
1		Alcohol Pads	12	0.00108	1.08	0.1500	150.00			$ 0.02		
1		Tourniquet	1	0.00603	6.03	5.0000	5000			$ 0.24		
1		Tape	0.1	0.00906	9.06	6.4220	6422.00			$ 0.11		
1		Morphine	1-10ml	0.00795	7.95	6.8855	6885.53			$ 21.50		
1		carpuject	1	0.01524	15.24	5.6267	5626.67			$ 5.01		

Crew Health Index (CHI)

- Quality-Adjusted Mission Time
- Modification of quality-adjusted life years (QALY)
  - Standard epidemiologic measure
- Single, weighted measure of the net change in quality time

Example of QALY

- Consider the following individual:
  - 35 years old
  - 75-year life expectancy
- Medical event results in 30% functional impairment
  - Below knee amputation
- What is the QALY?

$$QALY = 40 - 40(0.3) = 40 - 12 = 28\ \text{yrs}$$

$$PQALY = \frac{28}{40} \cdot 100\% = 70\%$$

Crew Health Index (CHI)

- With respect to IMM, “life years” is mission time

Crew Health Index (CHI)

Measure of crew health based on functional impairment

- Ranges from 0 to 100%
- 0% - completely impaired due to medical conditions for duration of mission
- 100% - no impairment due to medical conditions

Summary

- IMM is an evidence-based decision support tool that can be used for risk assessment and mission planning
- IMM forecasts the impact of in-flight medical events on space flight missions
- IMM inputs include 83 medical conditions, incidence values, functional impairments, potential end-states (EVAC, LOCL) and required medical resources
- IMM outputs include EVAC, LOCL, CHI, and resource utilization
- IMM can be used to optimize the medical system within the constraints of the space flight environment

ISS PRA Update using IMM

- **Purpose**
  - To update medical risk forecasts of evacuation (EVAC) and loss of crew life (LOCL) for ISS
- **Justification**
  - Current medical risk data and approach were developed over 12 years ago, use broad assumptions, and only address a subset of medical conditions relevant to the current mission profile
  - Risk of EVAC and LOC due to medical events will be underreported
  - Updated crew health risk estimates help prioritize medical system capabilities

Background - ISS Risk Model

- Probability Risk Assessment (PRA) methods required by ISS Program (per NPR 8705.5)

- Current Approach for Medical Risk
  - Based on pre-ISS operations evidence (1997)
  - Medical conditions organized by 9 categories
  - Only ‘severe’ medical conditions addressed
  - Assumes medical resources available > 98%
  - Assumes positive clinical outcomes > 75%

IMM Evidence Base

- Astronaut Health Database
- ISS Expeditions 1 thru 13 (2006)
- STS-01 thru STS-114 (2005)
- Apollo, Skylab, Mir (U.S. crew only)
- Analog, terrestrial data
- Review of crew medical charts
- Flight Surgeon Subject Matter Expertise
- Russian medical data not used

ISS PRA Update - Methods

- Reference Mission (as defined by ISS PRA Group)
  - 6-person crew (1 female, 5 males)
  - 6-month mission
  - 3 EVAs total for mission
- 83 medical conditions
- Industry standard statistical software, SAS 9.1
- SQL Database manages all clinical inputs
- Monte Carlo Simulations
- Fully treated medical with ISS medical system
- In-flight ISS Resource Utilization

Results

ISS Reference Mission - Fully Treated

Category	EVAC	EVAC (%)	95% CI
Medical Illness	**1 in 32**	3.14	2.97-3.32
Injury/Trauma	**1 in 169**	0.59	0.52-0.67
Environmental	**1 in 135**	0.74	0.65-0.81
All Conditions	1 in 23	**4.43**	**4.25-4.61**

Category	LOC	LOC (%)	95% CI
Medical Illness	**1 in 270**	0.37	0.31-0.43
Injury/Trauma	**1 in 769**	0.13	0.10-0.16
Environmental	**1 in 172**	0.58	0.49-0.65
All Conditions	1 in 94	**1.06**	**0.97-1.16**

Conversion of % EVAC to events/person-yr

- IMM forecasts a 4.43% probability of EVAC for a 6-crew/6-month ISS mission
  - 6 crew x 0.5 years (6 months) = 3 person-yrs
  - 0.0443 events/3 person-yrs = 0.015 events/person-yr
- IMM forecasts a 1.06% probability of LOCL for a 6-crew/6-month ISS mission
  - 6 crew x 0.5 years (6 months) = 3 person-yrs
  - 0.0106 events/3 person-yrs = 0.0035 events/person-yr

Comparison of *Risk of EVAC* Rates

IMM forecasted *Risk of EVAC* rates compare favorably with literature review EVAC rates (0.010 to 0.072)

Source	Low (events/person-yr)	Max (events/person-yr)
IMM (mean)	0.015	-
ISS PRA (mean)	0.001	-
ISS Independent Safety Task Force (February 2007)	0.028	0.042
Terrestrial General Population	0.060	-
Antarctic Population	0.036	-
U.S. Submarine Population	0.023	0.028
Russian Historical Space Flight Data	0.032	0.072
LSAH (Astronaut Health) Data	0.010	0.020
SSF Clinical Experts Seminar Proceedings (1990)	0.010	0.030

Validation - Risk of EVAC

IMM Simulation Data

Medical illness (71%)

1. Dental Abscess
2. Sepsis
3. Kidney Stones
4. Stroke
5. Atrial Fibrillation
6. Acute Chest Pain/Angina

Injury/Trauma (13%)

1. Hypovolemic Shock
2. Wrist Fracture

Environmental (16%)

1. Smoke Inhalation
2. Toxic Exposure

Actual Russian Flight Data

Three EVACs

1. Urosepsis
2. Cardiac Arrhythmia
3. Smoke Inhalation

Three Close Call EVACs

1. Kidney Stone
2. Dental Abscess
3. Toxic Exposure

NOTE: No Russian data are in the IMM

Validation – *Risk of LOCL* forecast

IMM forecasted *Risk of LOC* rates compare favorably with literature review results for LOC rates (0.0028 to 0.0081)

Source	LOC (events/person-yr)
IMM (6-crew/6-month mission)	0.0035
ISS PRA (3-crew/6-month mission)	0.0006
Terrestrial Mortality Rate	0.0081 (2006)
48-year old male	0.0047 (2006)
48-year old female	0.0028 (2006)
Antarctic	0.0054 (1904-1964)
LSAH Data	0.0054 (1959-1991)

Summary of Validation

Risk of Evacuation (EVAC) Estimates

Source	Low (events/person-year)	Max (events/person-year)
IMM (mean)	0.015	-
ISS PRA (mean)	0.001	-
Evidence-based Literature	0.010	0.072

Risk of Loss of Crew Life (LOCL) Estimates

Source	Low (events/person-year)	Max (events/person-year)
IMM (mean)	0.0035	-
ISS PRA (mean)	0.0006	-
Evidence-based Literature	0.0028	0.0081

Comparison of Data – IMM vs. ISS PRA

Source Model	Risk of EVAC*	Risk of LOC*
IMM (mean)	0.015 (4.43%)	0.0035 (1.06%)
ISS PRA (mean)	0.001 (0.35%)	0.0006 (0.17%)
Difference	**x15 factor**	**x5.8 factor**

*** Shown as events/person-year, and percent during mission**

Summary of ISS PRA Update

- Medical events will be lead contributor to “Risk of EVAC/LOC”, surpassing ISS PRA estimates of “Risk of EVAC/LOC” from MMOD
- A comprehensive evidence review forms the basis for updating the ISS PRA Risk Model
- Presented to and accepted by the ISS Program Office in December, 2010

IMM Validation - Background

- The IMM is expected to be a significant contributor to medical decision making in operational and planning processes for space flight missions

- NASA Standard 7009 requires that real world events be accurately represented by the model results to reach sufficient levels of validation

- For the IMM, this requirement is partially fulfilled by comparing the model's predicted outcomes with observed mission data that have not been included in the model

Validation

- Model Validation
  - "Substantiation that a computerized model within its domain of applicability possesses a satisfactory range of accuracy consistent with the intended application of the model"
    - Schlesinger et al. Terminology for model credibility. *Simulation.* 32 (3): 103-104
- Historical Data Validation
  - "If historical data exist, part of the data is used to build the model and the remaining data are used to determine (test) whether the model behaves as the system does"
    - Sargent. Verification and Validation of Simulation Models. *Proceedings of the 2007 Winter Simulation Conference*

Data Analysis

- Data on historical space flight missions were collected from mission medical records

- Data available for comparison included
  - Total number of medical events
  - The number of occurrences of each medical event
  - Medical resource utilization

Validation Approach

- Qualitative and quantitative approaches were used to compare historical data to model output
- Qualitative Approach
  - Plots were created to visualize the differences between the model and historical data
- Quantitative Approach
  - Goodness of Fit (GoF) testing was chosen to test the null hypothesis that the predicted outcomes are statistically equivalent to the observed data

Methods

Simulation

- Model was run for seven ISS missions and fourteen Shuttle missions *
- Mission and crew profile were matched to historical mission data [# of crew, sex, mission length, and number of extravehicular activities (EVAs)]
- Each simulation was executed for 20,000 trials

* Data from these missions have not been used as inputs for the model

Results

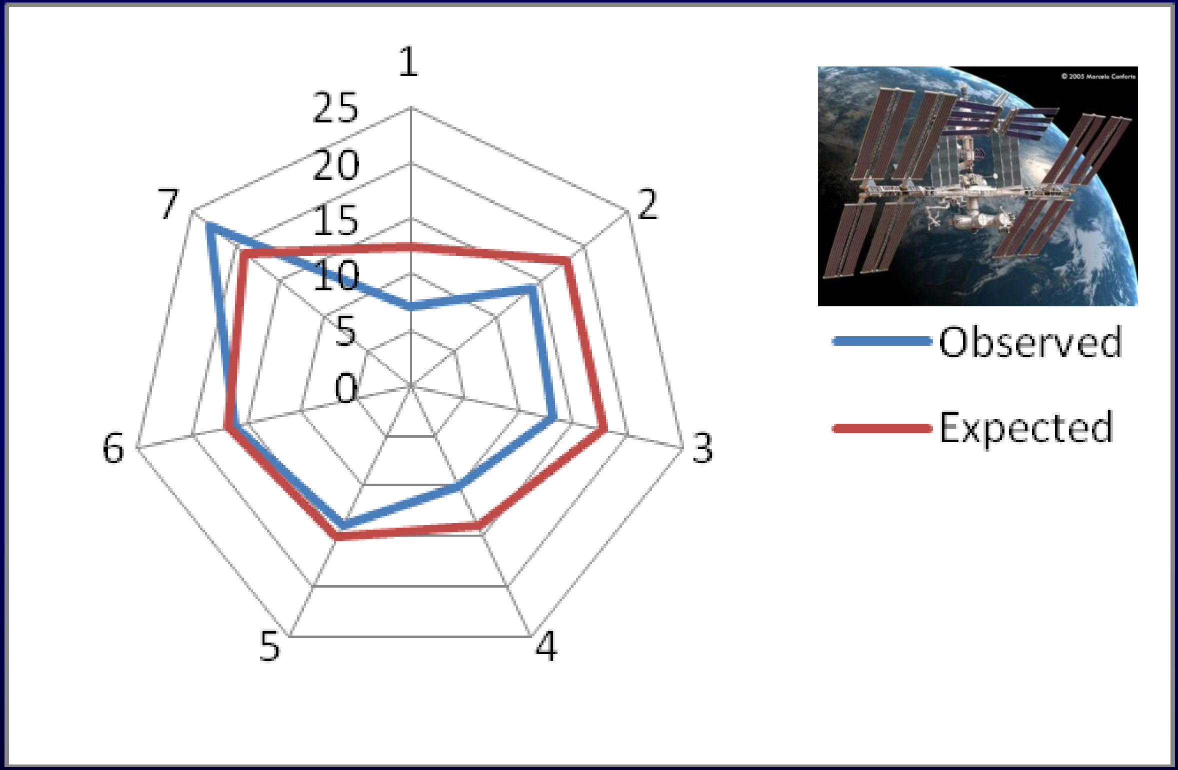
Total Medical Events - ISS Missions

Mission	Expected	Observed	Difference
1	12	7	5
2	18	14	4
3	18	13	5
4	14	10	4
5	15	14	1
6	17	16	1
7	19	23	-4
Average	16	14	2

Results

Spider Plot for ISS Missions

Total Number of Medical Events by Crewmember



p = 0.36

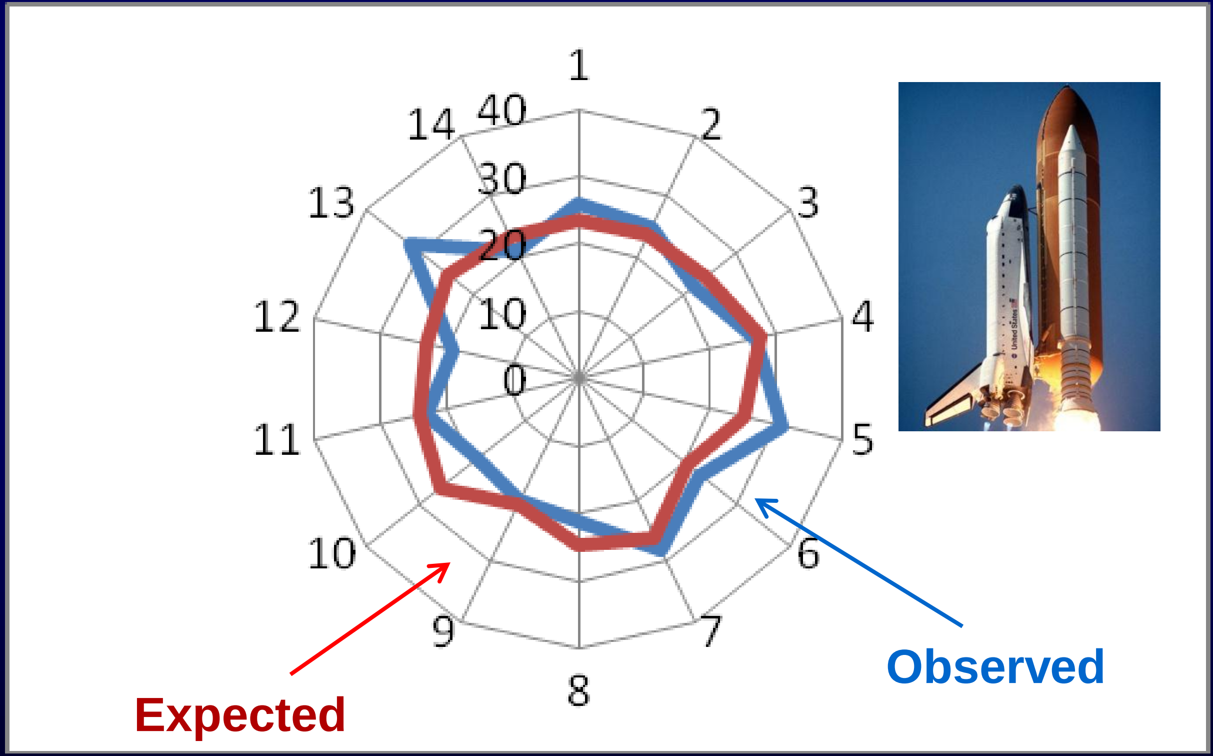
Results – Total Medical Events – Shuttle Missions

Mission	# of Crew	Expected	Observed	Difference
1	6	24	26	-2
2	6	24	25	-1
3	6	24	22	2
4	7	28	27	1
5	6	25	31	-6
6	5	20	23	-3
7	6	26	28	-2
8	6	25	21	4
9	5	21	20	1
10	6	26	19	7
11	6	24	23	1
12	6	23	19	4
13	6	25	32	-8
14	6	24	21	3
Average	6	24	24	0

Results

Spider Plot for Shuttle Missions

Total Number of Medical Events by Mission



p = 0.83

Summary of Results

- Total Medical Events
  - There was no significant difference between the total number of medical events forecasted by IMM and the total number of medical events observed on missions

Optimization

- Optimize medical kit using IMM results
  - Specific mission and crew profile

http://spaceflight.nasa.gov/gallery/images/shuttle/sts-133/html/sts133-s-002.html

- Approaches
  1) Maximize outcome given resource constraints
  2) Minimize resources given desired outcome(s)

Approaches

1) Maximize (or Minimize) outcomes

- What can we fit in the box?
- Resource constraints must be satisfied

2) Minimize resources

- How big of a box do you need?
- Outcome constraints must be satisfied

Resource Constraints

- Multiple constraints on medical resources
  - Mass
  - Volume
  - Cost
  - Packaging
  - Bandwidth
  - Power
  - Etc.

Define Constraints and Outcomes

- Define resource constraints
  - Maximum mass
  - Maximum volume

- Decide which outcome(s) are of interest
  - Maximize CHI
  - Minimize Pr(EVAC)
- Fill medical kit with the most efficient set of medical resources

Example

- Number of crew members
  - 4 (2M, 2F)
- Mission Length
  - 24 days
- Maximize CHI
- Resource constraints
  - 4.3 kg
  - 6421.7 cm3

http://www.nasa.gov/multimedia/imagegallery/iotd.html#

Results (24 days, 4 crew)

- Resource constraints
  - 4.3 kg
  - 6421.7 cm3

	Medical Kit	
Parameter	Optimum	Maximum
Mass (kg)	4.11	67.3
Volume (cm3)	6421.7	188602.8
Mean CHI (%)	**94.7**	**95.2**
EVAC (%)	6.41	0.43
LOCL (%)	0.19	0.10

Minimizing Resources

- Define outcome(s), constraints
  - Pr(EVAC) $\leq$ 2%
  - Mean CHI $\geq$ 90%
- Identify sets of conditions that should be treated to satisfy the constraints
- Identify the minimum such set

Example

- Number of crew members
  - 4 (2M, 2F)
- Mission Length
  - 24 days
- Minimize Mass and Volume
- Evacuation constraints
  - Pr(EVAC) < 2%
  - Mean CHI > 90%

Results (24 days, 4 crew)

- Constraints
  - Pr (EVAC) < 2%
  - Mean CHI > 90%

	Medical Kit	
Parameter	Optimum	Maximum
Mass (kg)	38.66	81.86
Volume (cm3)	94,527.73	201,669.01
Mean CHI (%)	**91.38**	95.21
Evacuation Probability(%)	**1.94**	0.37

Summary

- Two alternative optimization modules
  - Answer different questions
  - Multi-objectives
  - Multiple constrains
- Results provide suggestions
- Compromises must be made
- Results demonstrate effectiveness of these optimization routines

Conclusions

- IMM provides an evidence-based analysis of likely medical events and outcomes during space flight missions
- IMM provides the capability to assess risk
- IMM provides the capability to optimize medical systems
- IMM is a tool to assist in the decision making process
    - It does not make decisions

Questions?