The Integrated Medical Model

Eric Kerstman M.D., MPH

Advanced Projects

Wyle Integrated Science and Engineering Group

The Aerospace Medical Association
81st Annual Scientific Meeting
Phoenix, Arizona
May 12, 2010

The Integrated Medical Model

A Risk Assessment and Decision Support Tool for Space Flight Medical Systems

Eric Kerstman, MD, MPH[1], Charles Minard, PhD[2], Lynn Saile, RN, MS[2], Mary Freiere de Carvalho, PhD[2], Jerry Myers, PhD[3], Marlei Walton, PhD[2], Douglas Butler, MBA[2], Sriram Iyengar, PhD[4], Kathy Johnson-Throop, PhD[5], David Baumann[5]

[1]University of Texas Medical Branch, Galveston, TX; [2]Wyle, Houston, TX; [3]NASA Glenn Research Center, Cleveland, OH, [4]University of Texas Health Science Center, Houston, TX, [5]NASA Johnson Space Center, Houston, TX

IMM Project Goals

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

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

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 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

Who can benefit from IMM capabilities?

- Flight Surgeons
  - What in-flight medical threats are greatest for reference mission A?
- Risk Managers
  - What is the risk of evacuation - due to a medical event - for a 6-person, 180-day mission assuming the current in-flight medical capability?
- Vehicle Designers
  - What is the optimum medical mass allocation for given level of risk?
- Health Care System Designers
  - What medical items do we fly for a given mass/volume allocation?
- Trainers
  - How do I prioritize limited crew training hours?
- Requirement Managers
  - What is the rationale for this crew health requirement?

"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?

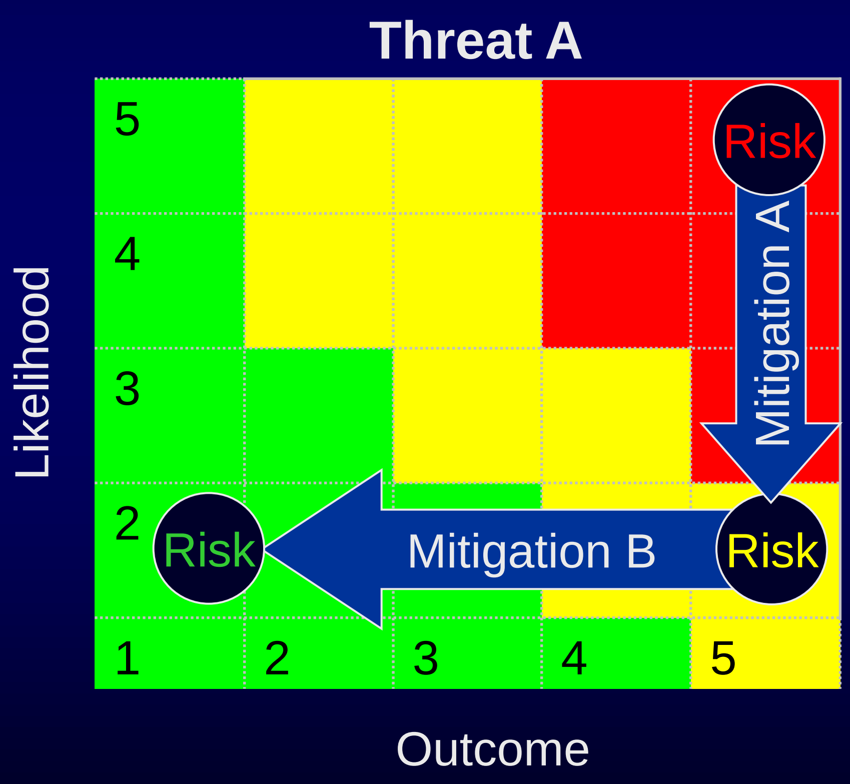
Use History

- ISS medical system redesign rationale
- Storage Capacity Requirements of Vomitus and Diarrhea for Constellation
- ExMC List of Prioritized Medical Conditions
- ExMC Technology Watch
- Orion medical kit design support
- ISS Probabilistic Risk Assessment Updates

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

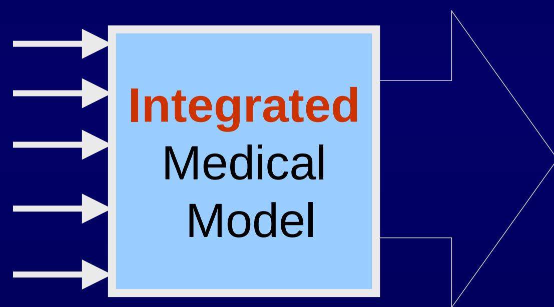


5x5 Matrix	IMM
Likelihood (Score 1-5)	Medical Condition Incidence
Mitigation?	In-flight Medical Capabilities
Outcome (Score 1-5)	Crew Functional Impairment
Risk Score (2x1) for a single "risk"	Impact to mission due to all medical conditions for the crew compliment

IMM Conceptual Model

INPUTS

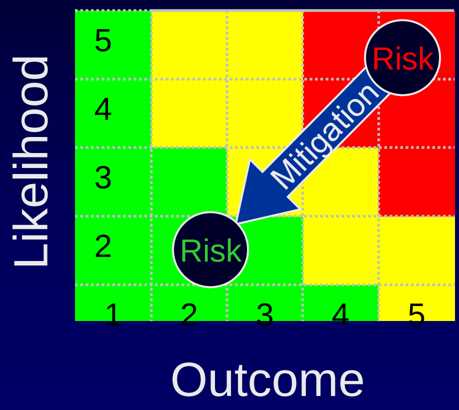
- Medical Conditions & Incidence Data
- Crew Profile
- Mission Profile & Constraints
- Potential Crew Impairments
- Potential Mission End states
- In-flight Medical Resources



OUTPUTS

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

Comparison – 5x5 Risk Matrix vs. IMM



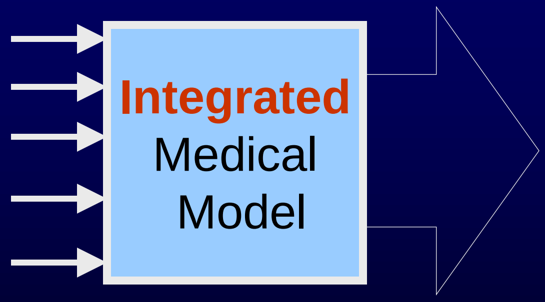
5x5 Matrix

- Qualitative
- Categorical
- Subjective
- Single Risk
- No Uncertainty
- No Confidence Interval
- Limited context

IMM

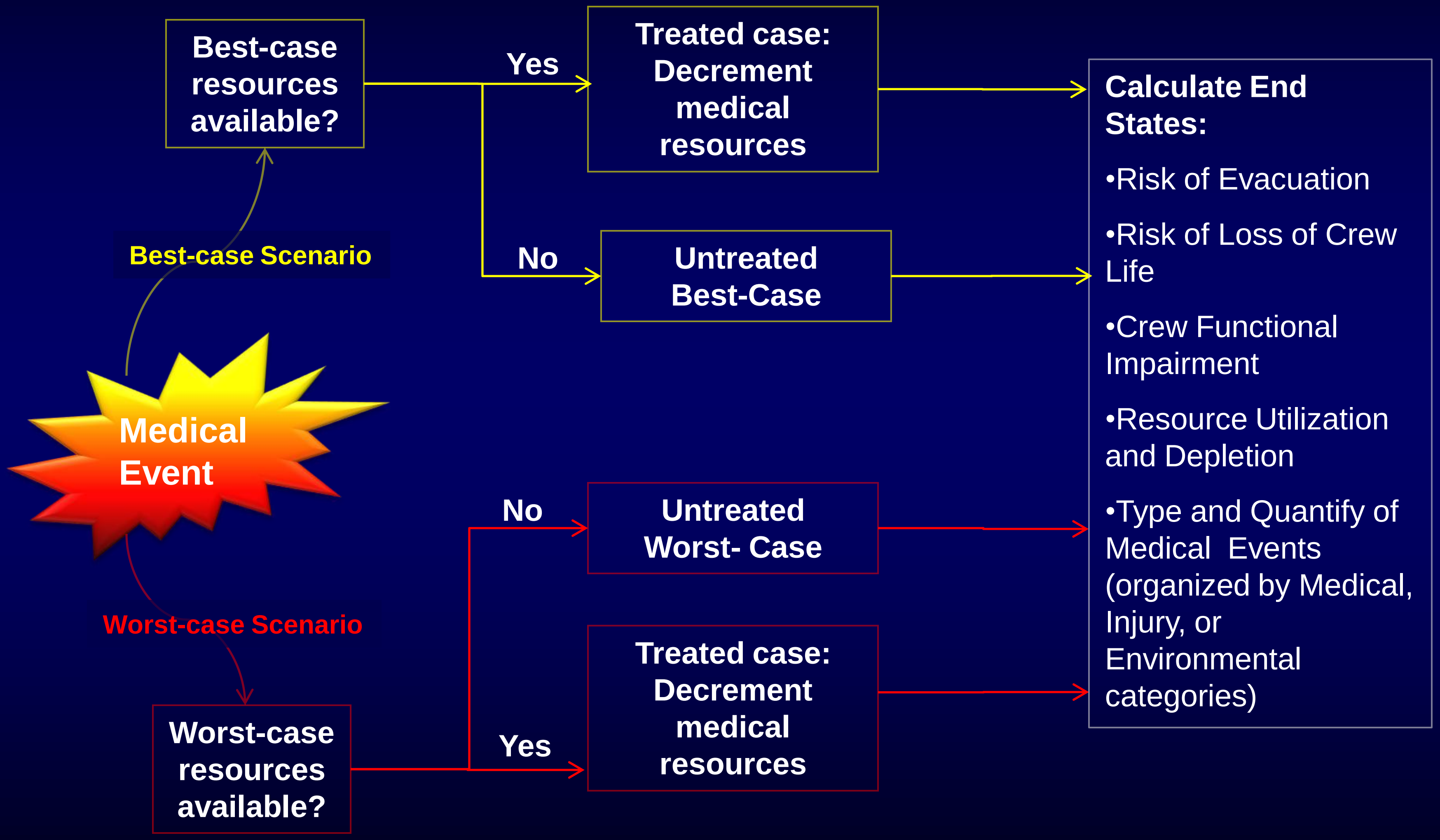
- Quantitative
- Probabilistic, Stochastic
- Evidence-based
- Integrated Risks
- Uncertainty
- Confidence Interval
- In context

- 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 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?

Key Development Steps

Each step is critical in the development process

- Develop and Validate a Conceptual Model
- Create initial list of relevant medical conditions
- Characterize incidence data
- Quantify crew impairment and clinical end states
- Quantify resources needed to diagnose and treat
- Develop a quantified Crew Health Index
- Understand implications of assumptions
- Verify & Validate
- Refine & Maintain Data

IMM Clinical Inputs

- Medical Conditions
- Incidence Rates
- Functional Impairments
- Potential End States (EVAC, LOCL)
- Required Resources

Medical Condition List

Purpose

- To provide a list of medical conditions relevant to in-flight operations

Relevant Medical Conditions

- Have occurred in flight or has the potential to occur in flight
- Require mitigation and/or result in functional impairment

Current Status

- Consists of 83 medical conditions (47 have occurred in flight)

Longitudinal Study of Astronaut Health

In-flight Medical Condition Occurrences

- Includes Apollo, Skylab, Mir, Shuttle, and ISS
- STS-1 through STS-114 in 2005
- Expedition 1 through Expedition 13 in 2006
- 47 relevant medical conditions

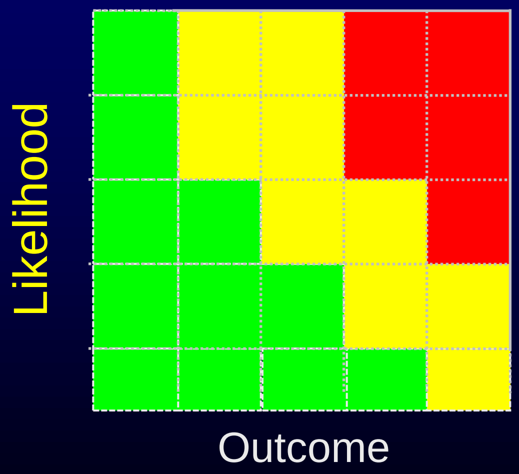
IMM Evidence Base

- Longitudinal Study of Astronaut Health
- Review of crew medical debriefs
- Analog population data
- General terrestrial population data
- Flight Surgeon Delphi Study

Russian medical data not included

The Use of Incidence

- Incidence is a measure of the likelihood of developing a medical condition
- IMM uses incidence to quantify the likelihood of occurrence of medical conditions in flight



Incidence Definitions

The number of new medical events that occur within a specified time period

Incidence Proportion (Cumulative Incidence)

- The proportion of a population who develop a medical condition within a specified period of time (events/person)

Incidence Rate (Incidence Density)

- The number of new medical events that occur within a population divided by the total time the population was at risk (events/person-year)
- Accounts for the different times that each individual was at risk

IMM Classification of Medical Conditions

- Space Adaptation Syndrome (SAS)
- Non-Space Adaptation Syndrome

SAS Medical Conditions

1) Back Pain
2) Constipation
3) Headache
4) Insomnia
5) Nasal Congestion
6) Nosebleed
7) Space Motion Sickness
8) Urinary Incontinence
9) Urinary Retention

Space Adaptation Syndrome Medical Conditions

- Likelihood of occurrence is not related to mission duration
- Condition does not recur
- Incidence proportions (events/person) are determined from LSAH in flight occurrence data

Example: Nasal Congestion

405 events among 660 persons = 0.614 events/person

Non-SAS Medical Conditions

- The likelihood of occurrence is related to mission duration
- Condition may recur
- Incidence rates (events/person-year) are determined from LSAH in-flight occurrence data or other sources

Example: Skin Rash

90 events within 27.34 person-years = 3.29 events/person-year

Incidence Rate Determinations

Conditions that have occurred in flight

- LSAH in-flight occurrence data

Conditions that have not occurred in flight

- External models (fractures)
- Environmental engineering data (altitude sickness)
- Terrestrial general/analog population data (appendicitis)
- Bayesian statistics for rare events (kidney stones)

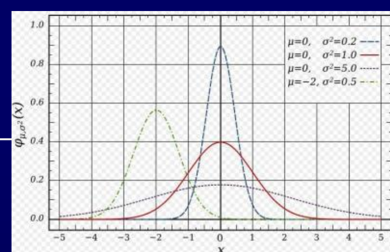
Independent Risk Models & IMM

Risk Drivers

Independent Model (Renal Stone)

Independent Model (Bone Fracture)

Independent Model (Insomnia)



Integrated Medical Model

Risk of EVAC

Risk of LOCL

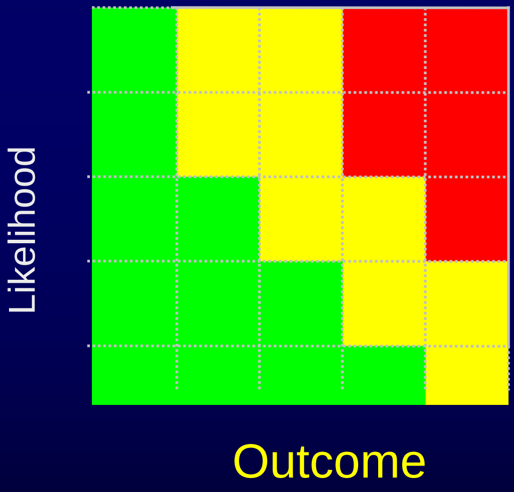
For a specified mission scenario, the output from independent models can provide distributions of incidence data.

The Use of Functional Impairments

IMM uses the concept of functional impairments to quantify the severity of medical condition outcomes

Impairment

- A loss or loss of use of a body part, organ system, or organ function
- Considers both anatomic and functional loss
- Can develop from an illness or injury



American Medical Association Guides to the Evaluation of Permanent Impairment

Impairments

- Percentages that reflect the severity of the medical condition
- No impairment = 0 percent
- Fully dependant/approaching death = 100 percent

Examples

Skin Infection = 10 to 24 percent impairment

Shoulder Dislocation = 36 to 74 percent impairment

Clinical Findings Form (CliFF)

Standardized Format for IMM Clinical Inputs

The likelihood of occurrence of the medical condition

- Incidence proportion or incidence rate

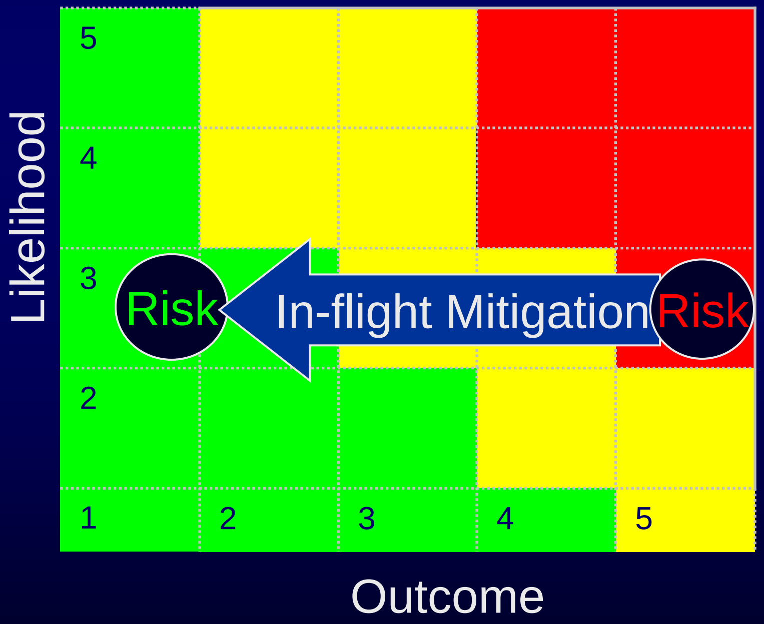
The clinical outcomes of the medical condition

- 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

Resource Tables

The Resource Tables specify the required in-flight medical resources

- Specifies resources required for diagnosis and treatment
- Considers 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

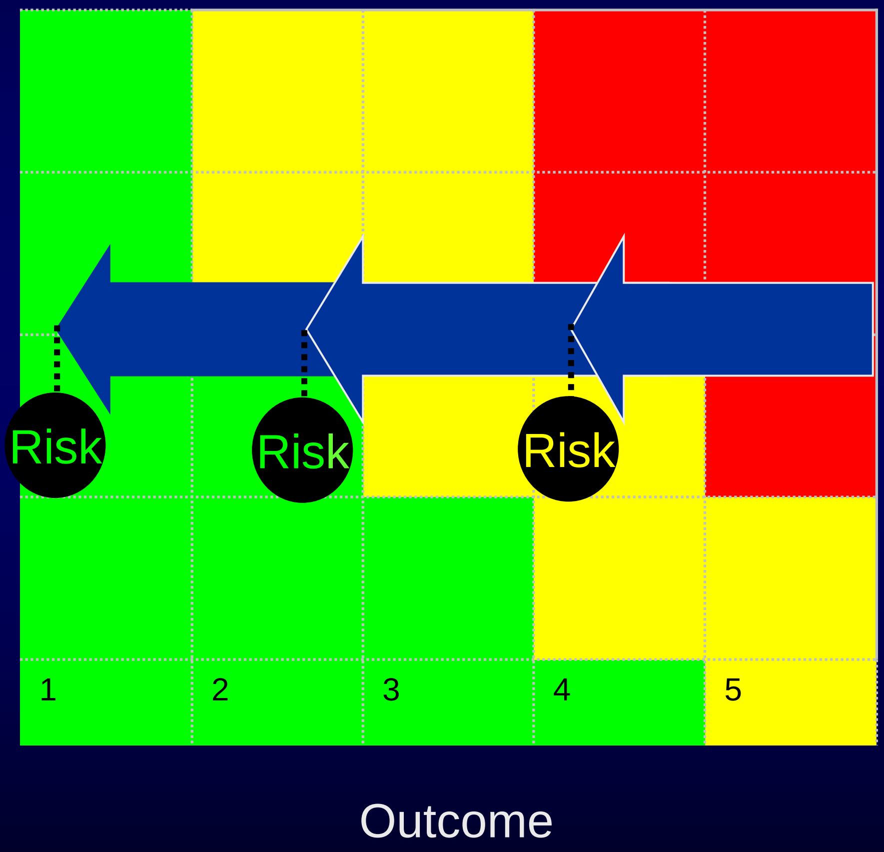
Consumable	Disorder	Description	Quantity	Mass Kg	Mass Gm	Volume cc^3	Volume mm^3	Power	Cost Estimates	COTS	Flight Certify	Sustaining Eng
	Sprain/Strain Extremities	Ace Bandage	1	0.03875	38.75	442.5000	442500			$ 3.08		
		SAM splint	1	0.1134	113.4	1336.3575	1336357.5			$ 12.00		
1		acetaminophen (2 tabs*4-6hr)	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		

Resource Table Assumptions

- The Resource Tables reflect the current ISS medical equipment, supplies, drugs, etc.
- Conditions go “untreated” when an “essential” item is not available (due to depletion or omission from the health care system)
- Cost information only includes Commercial off-the-shelf (COTS)
- Spacecraft resources (e.g. oxygen, water, power, bandwidth) are not constrained

In-flight Mitigation

- Resource Tables identify the resources required to mitigate risk by providing the in-flight capability to diagnose and treat medical conditions
- Medical resources can be optimized for specific mission and crew profiles



Summary of IMM Inputs

- Relevant list of medical conditions established
- Incidence data established for each medical conditions
- Crew functional impairments and end states (evacuation and loss of crew life) used to characterize impact due to medical events
- Standardized tool (CliFF) established for clinical inputs of likelihood and outcomes for each medical condition
- Resource Tables specify essential and non-essential resources required to diagnose and treat each medical condition

IMM Outputs

"Essentially, all models are wrong, but some are useful."

George Box (1987)

Professor Emeritus of Statistics at the University of Wisconsin

Statistical Methods

- IMM uses Monte Carlo simulation
  - SAS software
  - Distribution of outcomes

- Probability distributions
  - Beta, Beta-PERT, Poisson, Bernoulli, Binomial, Lognormal, Uniform, Discrete uniform
- Crew Health Index (CHI)
  - Quality-adjusted mission time

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” 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

Key Model Assumptions

- 83 medical conditions
- ISS Health Maintenance System (HMS)
- Conservative estimate of Crew Health Index (CHI)
  - Medical events assumed to occur on the first day of the mission

Case Study - Orion Medical Kit Design

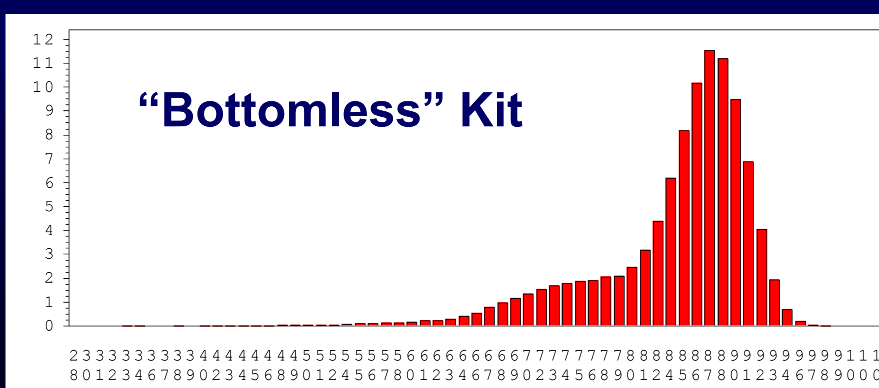
- Goal
  - Identify a medical kit that maximizes the CHI while meeting mass and volume constraints
  - Mass < 4.30 kg
  - Volume < 6421.68 cm^3
- Mission Scenario
  - Crew of four
  - 3-day Orion transfer mission
- Success Criterion
  - The optimized medical kit approaches a risk profile of a medical kit with unlimited resources

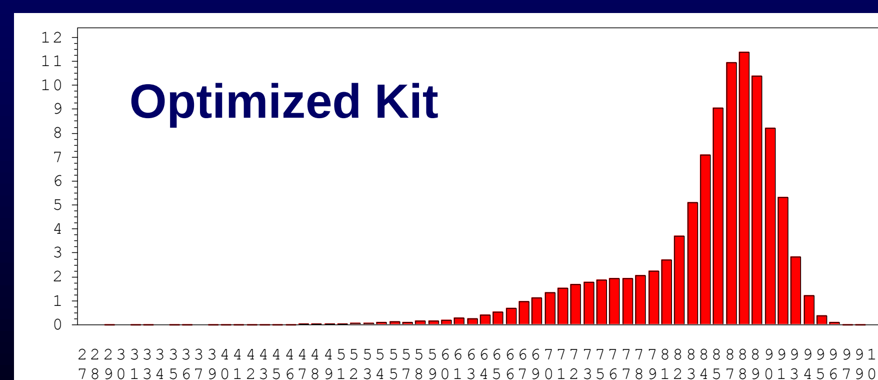
Orion Medical Kit Design - Results

Attribute	Constraint	Optimized Kit	“Bottomless” Kit
Mass (kg)	4.30	4.24*	43.60
Volume (cm^3)	6421.68	6421.68*	144684
CHI (95% C.I.)	**---**	**84.34 (66-93)**	**84.55 (67-93)**
Risk of EVAC	**---**	**1.07%**	**0.07%**
Risk of LOCL	**---**	**0.02%**	**0.01%**

***Includes 30% packing factor**

Crew Health Index (CHI)





Orion Medical Kit Design - Conclusions

- A shoebox-sized kit can be designed
  - Treats medical conditions with a high probability of occurrence during a 3-day mission
  - Does so without a reduction in CHI from the fully treated scenario.
- The Trade-off
  - Does not include resources to treat low probability, worst-case scenario conditions
  - Increases the probability of EAVC and LOCL respective to the fully treated scenario.

Validation – ISS EVAC Rates

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

Source	Low (events/person-yr)	Max (events/person-yr)
IMM	0.018	0.027*
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 Data	0.010	0.020
Space Station Freedom Clinical Experts Seminar Proceedings (1990)	0.010	0.030

* Reference Mission 2: 6 crew, 6 month mission

Validation – ISS LOCL Rates

IMM forecasted LOCL rates compare favorably with literature review results for LOCL rates (0.0029 to 0.0081)

Source	LOCL (events/person-yr)
IMM (3 crew/6-month mission)	0.0042
IMM (6 crew/6-month mission)	0.0043
Terrestrial Mortality Rate	0.0081 (2006)
48-year old male	0.0048 (2005)
48-year old female	0.0029 (2005)
Antarctic	0.0054 (1904-1964)
LSAH Data	0.0054 (1959-1991)

Validation - Sensitivity Analysis

IMM Simulation Data

Medical (59%)

1. Kidney Stone
2. Exposed Dental Pulp
3. Skin Infection
4. Urinary Tract Infection
5. Sepsis
6. Atrial fibrillation

Injury (21%)

1. Chest Injury
2. Wrist Fracture

Environmental (20%)

1. Toxic Exposure
2. Smoke Inhalation

Actual Russian Flight Data

Three EVACs

1. Urosepsis
2. Cardiac Arrhythmia
3. Toxic Exposure

Three Close Call EVACs

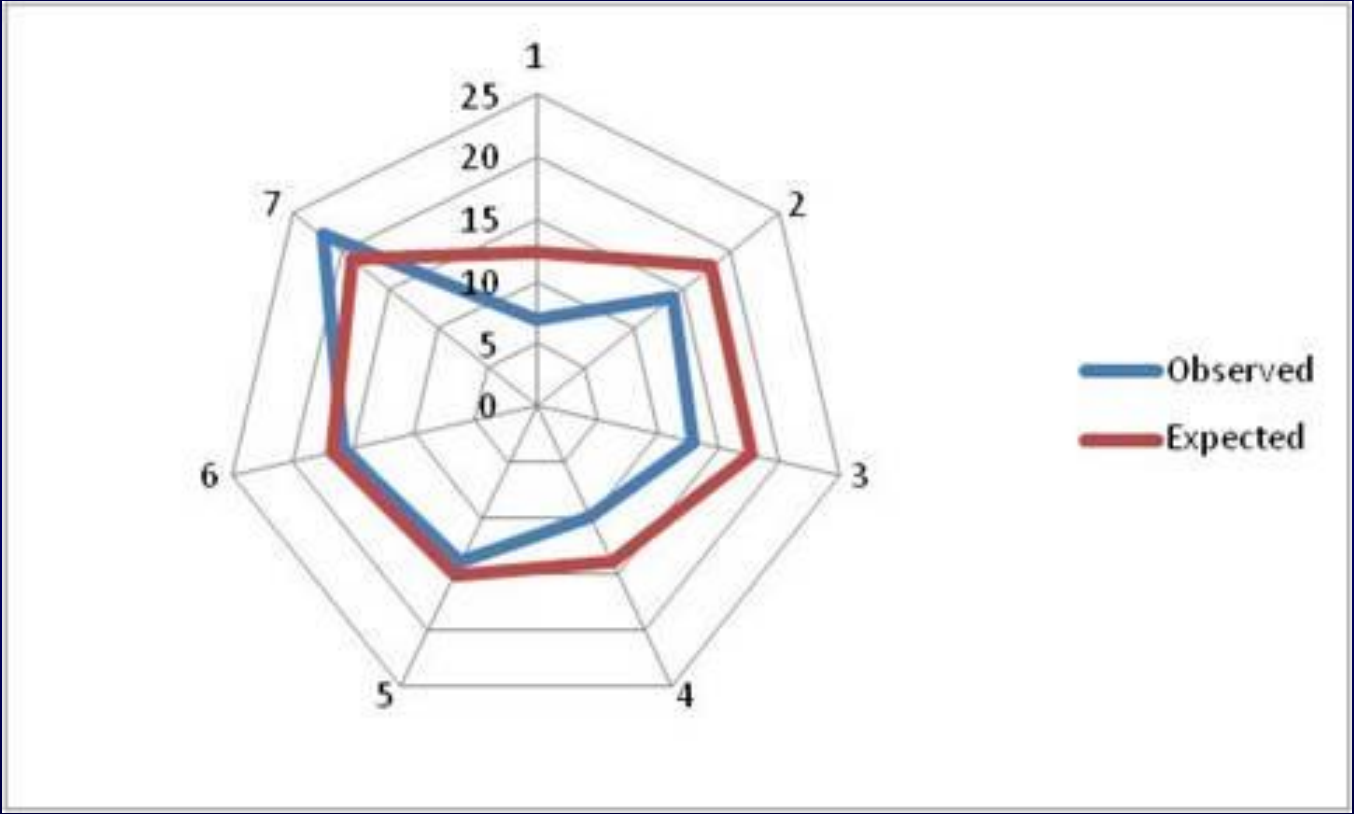
1. Kidney Stone
2. Dental Abscess
3. Toxic Exposure

NOTE: No Russian input data is in IMM

Validation – ISS Total Medical Events

Mission #	ISS Medical Events (Observed)	IMM Medical Events (Expected)	IMM 95% Confidence Interval
1	**7**	**12**	6 - 19
2	**14**	**18**	10 - 26
3	**13**	**18**	10 - 26
4	**10**	**14**	8 - 21
5	**14**	**15**	8 - 23
6	**16**	**17**	9 - 25
7	**22**	**19**	11 - 28

Validation – ISS Total Medical Events



Capability Status

- IMM 2.1/3.0
  - Locked down and undergoing clinical validation
  - Available for risk assessments, trade studies
- 83 medical conditions represented (47 of 83 medical conditions have been recorded to occur in flight)
- In-flight medical resources identified per medical condition
- “Medical”, “injury”, or “environmental” classification of risk drivers
- Established database; build out continues
- Integrated citation management software

Next Steps through Sept 2010

- Validation of IMM 3.0 per plan (Jan-July)
- IMM Database 3.0 Development (Jan-July)
- Complete Ops Documentation (July)
- Operational Acceptance Review (Aug)
- Delivery of IMM 3.0 (Sept)
- Delivery of Database 3.0 (Sept)
- IMM 4.0 Development (Feb-Sept)
- Transition to Operations (1 October 2010)

Summary

- 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

Closing

IMM addresses the observations documented by the RTF Task Group

…experience and instinct are poor substitutes for careful analysis of uncertainty…

…This requires that analytical models be used appropriately to inform decisions…*

* Source: *NASA Return to Flight Task Group Final Report: Annex A.2 Individual Member Observations* by Dr. Dan L. Crippen, Dr. Charles C. Daniel, Dr. Amy K. Donahue, Col. Susan J. Helms, Ms. Susan Morrisey Livingstone, Dr. Rosemary O'Leary, and Mr. William Wegner.

Questions?