Verification, Validation and Credibility of the NASA Integrated Medical Model Sleep Disruption-Medical Intervention Forecasting Tool
Exploration Medicine Capabilities Project
Human Research Program

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Focus on the future, Informed with the past

- ## Questions for NASA Human Research Program
  - How do we best inform decision makers and mission planners on what is needed to allow humans to visit Moon, Mars, and other celestial bodies?
  - How do we optimize medical needs for astronauts with limited Mass, Volume and Power?
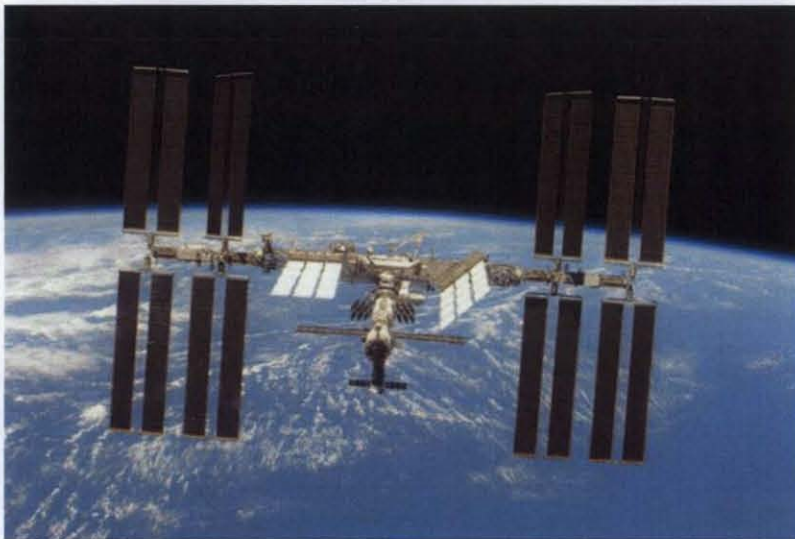
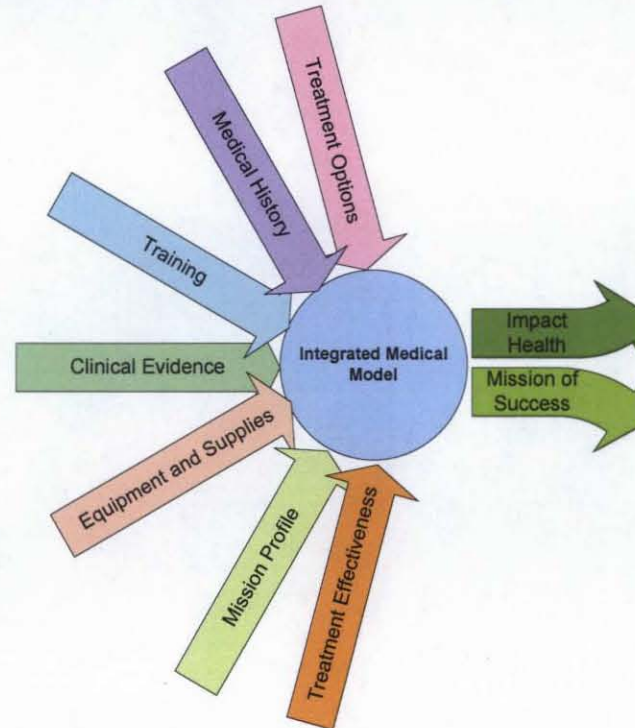S119E009765

Integrated Medical Model (IMM)

"The most important questions of life are indeed, for the most part, really only problems of probability." ~Pierre Simon Laplace

Potential Medical Condition

Evaluate with IMM

Treatment Options

Medical History

Training

Clinical Evidence

Equipment and Supplies

Mission Profile

Treatment Effectiveness

Integrated Medical Model

Impact Health

Mission of Success

**Likelihood of occurrence, probable severity of occurrence, and optimization of treatment and resources.**

- Integrate best available evidence to quantify the probability and consequences of medical risks
- Identify medical resources and inform operational decisions which optimize health and mission success
- "Data hungry" process

Houston, we have a problem

- **Forecasting rare medical events confounded by space travel**
  - Insufficient data
    - Few or no occurrences
  - No clear correlation to terrestrial analog
  - Multiple influencing conditions
    - Mission details
    - Vehicle limitations (environment)
    - Physiological adaptations
    - Interaction of the contributing factors
- **How do we verify and validate?**
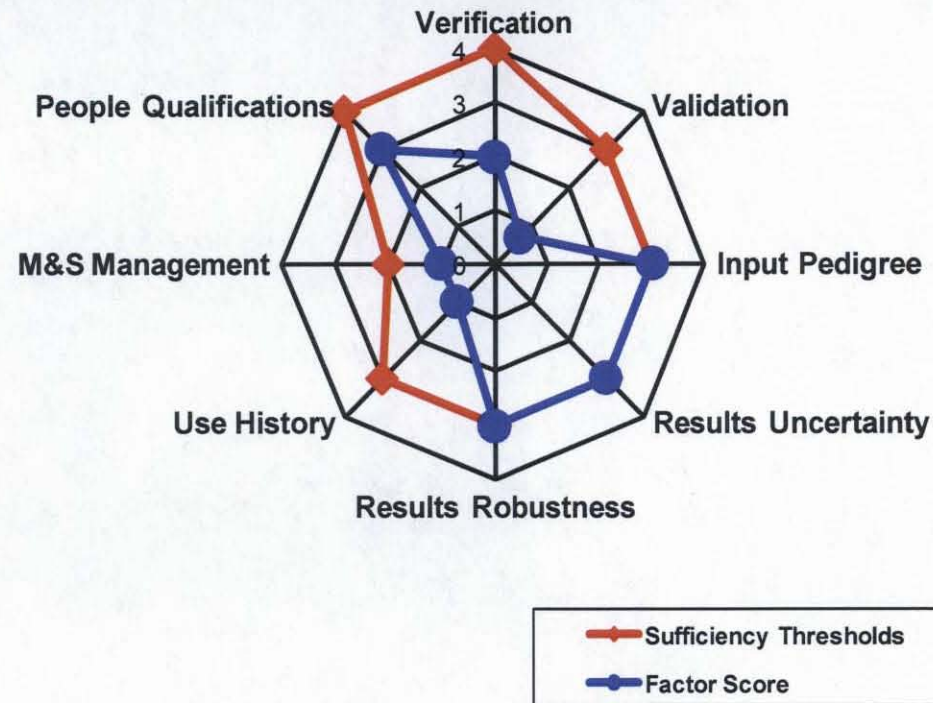 - When we are data "starved"
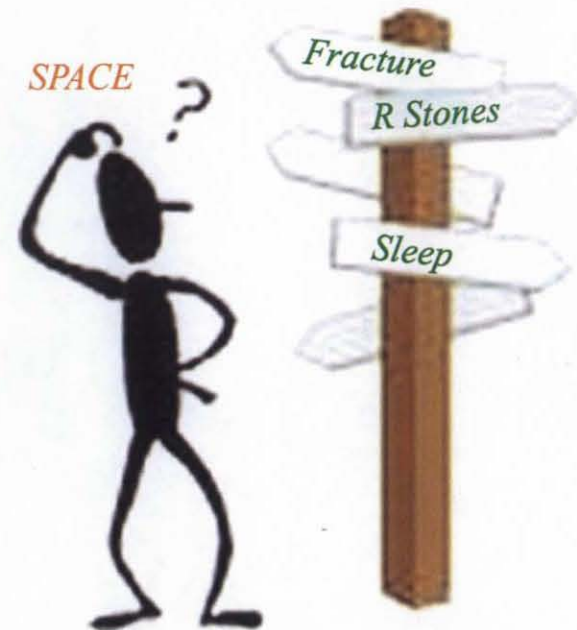
Its Really About Model *Credibility*!

Achieving a high level of belief or trust in the model

- ## NASA-STD-7009
  - Standard for Models and Simulations (M&S)
- ## M&S Development
  - Verification
  - Validation
- ## M&S Operations
  - Input Pedigree
  - Results Uncertainty
  - Results Robustness
- ## Supporting Evidence
  - Use History
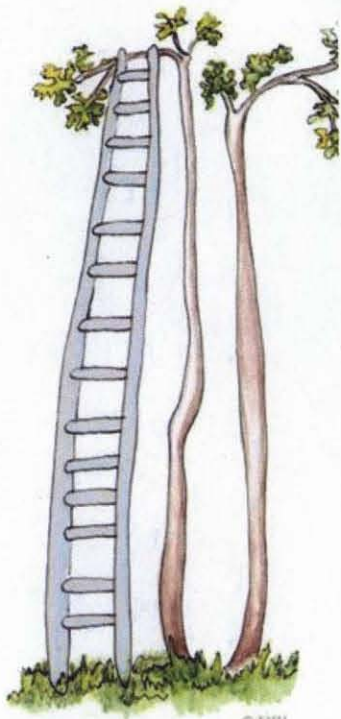 - M&S Management
  - People Qualifications

Human research program:
a) Scoring subject to SME review
b) Results used to balance project derived evidence

Facts are Stubborn Things
Credibility Levels of Evidence

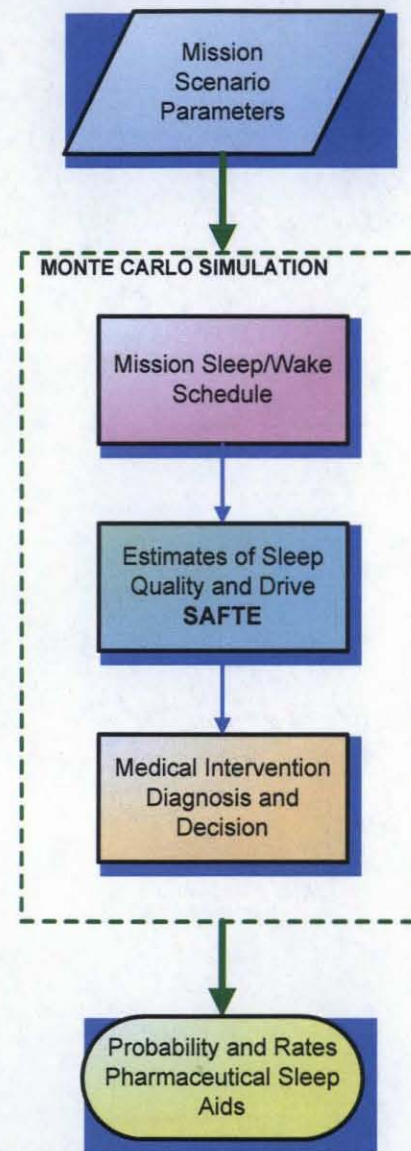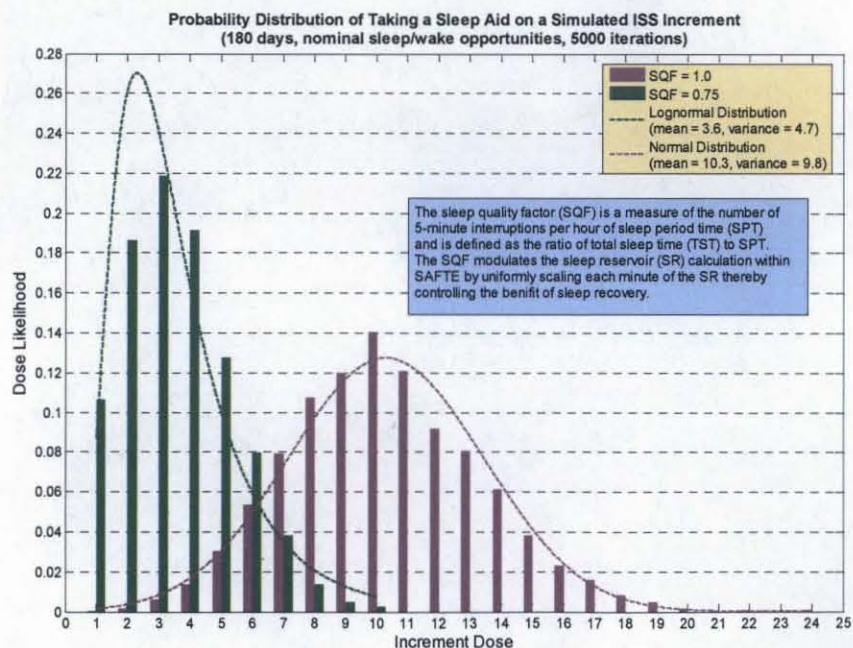| Level	Verification	Validation	Input Pedigree	Results Uncertainty	Results Robustness	Use History	M&S Management	People Qualifications
4	Numerical errors small for all important features.	Results agree with real-world data.	Input data agree with real-world data.	Non-deterministic & numerical analysis.	Sensitivity known for most parameters; key sensitivities identified.	De facto standard.	Continual process improvement.	Extensive experience in and use of recommended practices for this particular M&S.
3	Formal numerical error estimation.	Results agree with experimental data for problems of interest.	Input data agree with experimental data for problems of interest.	Non-deterministic analysis.	Sensitivity known for many parameters.	Previous predictions were later validated by mission data.	Predictable process.	Advanced degree or extensive M&S experience, and recommended practice knowledge.
2	Unit and regression testing of key features.	Results agree with experimental data or other M&S on unit problems.	Input data traceable to formal documentation.	Deterministic analysis or expert opinion.	Sensitivity known for a few parameters.	Used before for critical decisions.	Established process.	Formal M&S training and experience, and recommended practice training.
1	Conceptual and mathematical models verified.	Conceptual and mathematical models agree with simple referents.	Input data traceable to informal documentation.	Qualitative estimates.	Qualitative estimates.	Passes simple tests.	Managed process.	Engineering or science degree.
0	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.
	M&S Development			M&S Operations			Supporting Evidence	

Climb the Ladder

Sleep Disruption- Medical Intervention Forecasting (SDMIF) Tool

- ## Predict the sleep inducing medication use during a space mission
  - Resulting from circadian rhythm disruption, insomnia, and environmental disruptions

Probability Distribution of Taking a Sleep Aid on a Simulated ISS Increment
(180 days, nominal sleep/wake opportunities, 5000 iterations)

Legend:
- SQF = 1.0
- SQF = 0.75
- Lognormal Distribution (mean = 3.6, variance = 4.7)
- Normal Distribution (mean = 10.3, variance = 9.8)

The sleep quality factor (SQF) is a measure of the number of 5-minute interruptions per hour of sleep period time (SPT) and is defined as the ratio of total sleep time (TST) to SPT. The SQF modulates the sleep reservoir (SR) calculation within SAFTE by uniformly scaling each minute of the SR thereby controlling the benifit of sleep recovery.

Axis labels: Dose Likelihood (y), Increment Dose (x)

Flow chart:
- Mission Scenario Parameters
- MONTE CARLO SIMULATION
  - Mission Sleep/Wake Schedule
  - Estimates of Sleep Quality and Drive **SAFTE**
  - Medical Intervention Diagnosis and Decision
- Probability and Rates Pharmaceutical Sleep Aids

SDMIF: Verification and Validation

- Limited space flight data most likely used in the development of the model
- Verification exercises
  - Fixed and Extreme value testing of all PDFs
  - Estimates of numerical error
- Validation of individual components
  - Validate conceptual structure by SME review
    - Schedulers verify mission schedule component
    - Medical Ops validate the diagnosis component
- Validation of Module Performance
  - Face validation as V&V tool
    - Turing or Schruben tests with operational and flight medical experts
  - Direct comparison to observed incidence
    - Historical testing – Select data used for validation
    - Prospective validation – Future missions observations

Model Data, Robustness and Uncertainty

- **Model Data**
  - Desired: Assure data are appropriate for the intended model use
  - Achieved: Highest quality of the data correlated to the scenario

- **Model Robustness**
  - Desired: percentage of the contribution of an independent variable to the variation of the outcome
  - Achieved : Rank order correlation sensitivity analysis

- **Model Uncertainty**
  - Desired: magnitude and confidence of estimate
  - Achieved: quantified based on non-deterministic analysis

Use History, Management and Qualifications

- Use History
  - Desired: Model use extended to address similar questions
  - Achieved:
    - Similar outputs to other tools in limited scenarios
    - When Model is used to inform real world decisions

- Management: Continuous Improvement
  - Desired and Achieved: Document all activity, management processes and decisions affecting code development, input changes, and V&V efforts.

- Qualifications
  - Desired: Staff can interpret and use the results
  - Achieved: Development staff maintains expertise levels required to develop, maintain, update and operate the model environment.

Implementation in Global IMM

- **Implementation requires that modules**
  - Undergo subject matter review
    - SDMIF – Conceptual model, Input data, validation process reviewed by National Space Biomedical Research Institute
  - Undergo integration team review
    - IMM team review of module performance and evidence
      - Credibility MUST be at least that of the rest of the IMM
  - New IMM model undergoes V&V and credibility assessment
- **All evidence meticulously documented**
  - "We can lick gravity, but sometimes the paperwork is overwhelming." ~Wernher von Braun

CHECKLIST

Let's Review

- Models related to medical events used to inform Space Flight Operations and Planning
  - Must exhibit a high level of *Credibility* for the intended use
  - Must have their *Credibility* assessed over multiple factors
- Chief factor is an acceptable V&V process
  - Complicated by limited in-flight data
  - Relies on systematic use of SME's and Face Validation to balance limits in direct comparative evidence

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