Validation Of The Integrated Medical Model Using Historical Space Flight Data

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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 has 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

Data Collection

- International Space Station (ISS) missions
  - Increment medical debriefs by ISS crew surgeons
  - ISS Private Medical Conference (PMC) Tool
- Space Shuttle Missions
  - Mission medical debriefs by Shuttle crew surgeons
  - Crew medical debriefs
  - Surgeon logs

Methods

Simulation

- Model was run for seven ISS missions and fourteen Shuttle missions*
- Mission and crew profile was 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 input for the model

Analysis

Qualitative Approach

- Spider Plots
  - Qualitatively assess the accuracy of IMM predictions for the total number of medical events
  - Simultaneously present the predicted and observed data for multiple missions
  - Primarily for face validation
  - Lacks formal statistical testing procedures
  - Useful in identifying potential discrepancies between the IMM and real-world events

Quantitative Approaches

- *Chi-squared Goodness of Fit (GoF)*
  - May be utilized when the expected number of medical events is five or more (*e.g.* skin rashes, headaches)
  - Reasonable test for the total number of medical events, specific medical conditions that occur frequently, and medical resource utilization
  - The test statistic is calculated as: $$X^2_{ts} = \sum_{i=1}^{N} \frac{(E_i - O_i)^2}{E_i} \sim X^2_{df,1-\alpha}$$
  - If the test statistic is greater than the critical value $\left(X^2_{df,1-\alpha}\right)$, then the null hypothesis that the predicted outcomes are statistically equivalent to observed data will be rejected
  - An $\alpha = 0.05$ level of significance was assumed for IMM GoF testing

Quantitative Approaches (Cont'd)

- *Exact Probability Calculations*
  - When expected values for medical events are less than five, *goodness of fit* tests may be done using exact probability calculations
  - The p-value is equal to the proportion of simulated trials where the number of events that occurred is equal to or more than the observed number

Analysis

- Multiple Comparisons
  - The alpha-level for statistical significance was determined using Bonferroni's correction method
  - If *N* statistical tests were performed and the overall alpha was set at 0.05, then the final alpha level for any individual test was 0.05/*N*
- Example
  - A single ISS mission with one crew member and 83 medical conditions
  - The alpha was 0.05/83 (0.0006)
  - Therefore, p-values less than or equal to 0.006 would be statistically significantly different

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

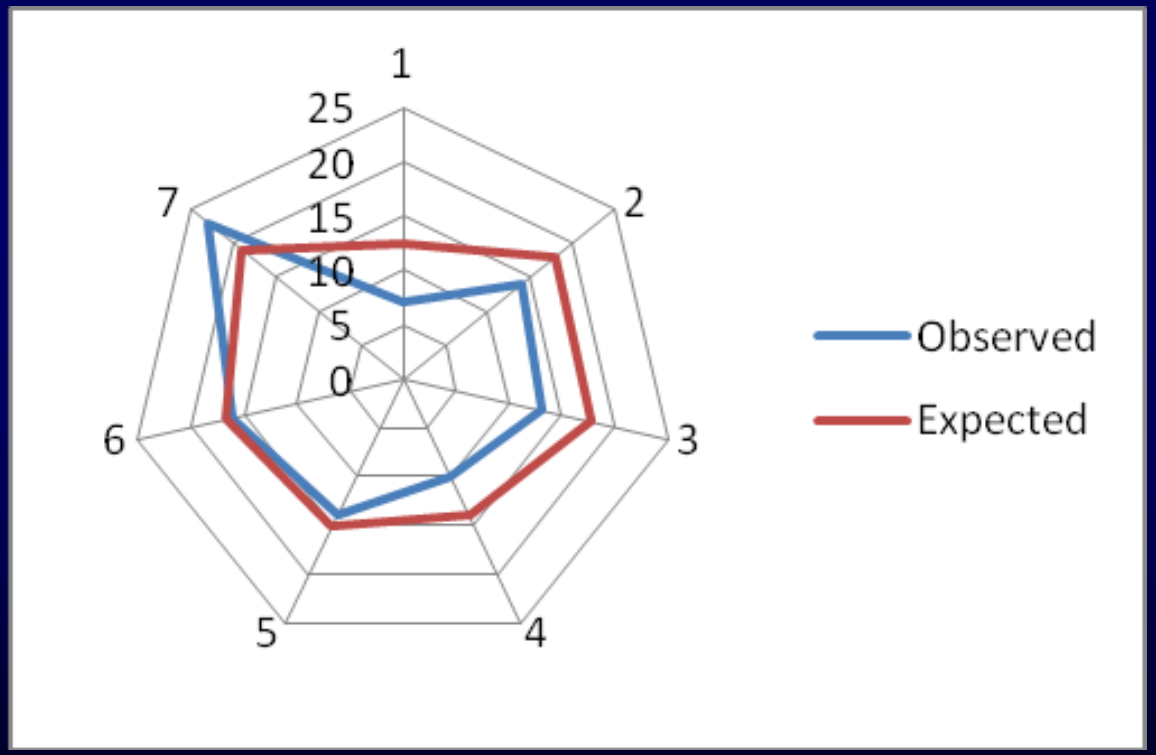
Total Medical Events

- ISS Missions
  - Expected values overestimated the number of medical events for six of the seven missions
  - The difference was not statistically significant ($p = 0.36$)
  - The shape of the expected values is similar to the observed values

Results

Spider Plot for ISS Missions

Total Number of Medical Events by Mission



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

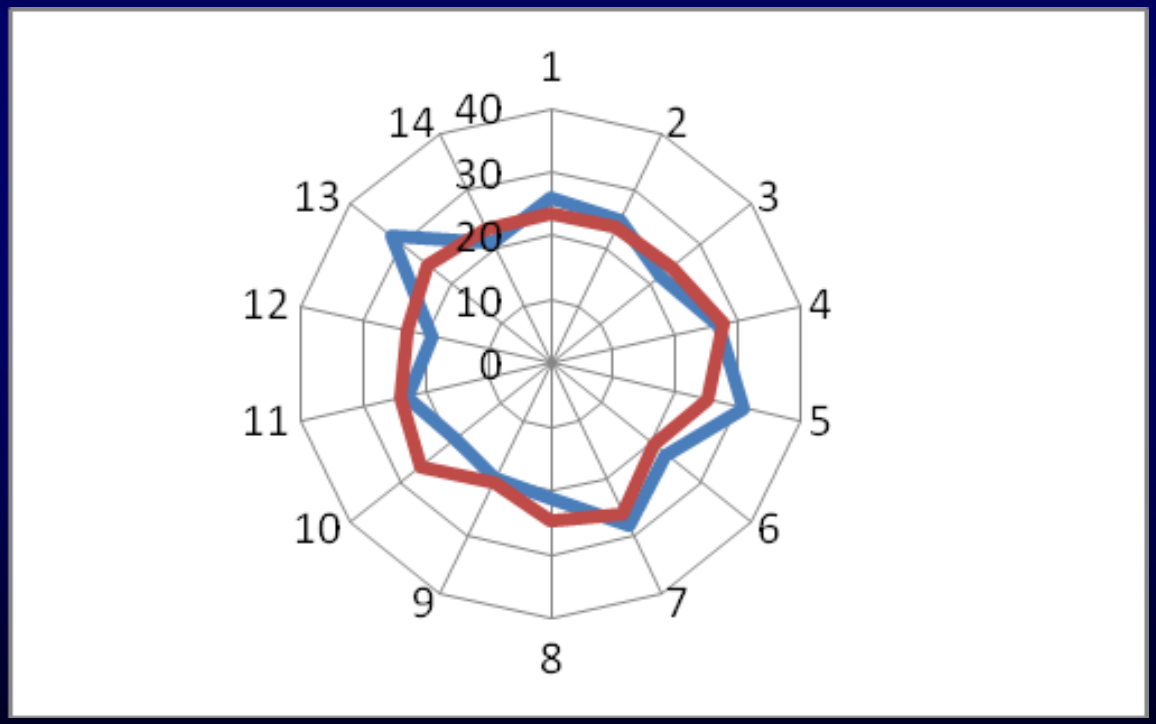
Total Medical Events

- Shuttle Missions
  - Expected values overestimated the number of medical events for eight missions
  - Expected values underestimated the number of medical events for six missions
  - The difference was not statistically different ($p = 0.83$)
  - The shape of the expected values is similar to the observed values

Results

Spider Plot for Shuttle Missions

Total Number of Medical Events by Mission



Results

- Specific Medical Events
  - 83 Medical conditions in the model
  - GoF testing performed for all conditions individually
  - Alpha level set at 0.0006 (0.05/83)

Results

Specific Medical Events

- ISS Missions
  - One medical condition was underestimated by the model (skin abrasion/laceration)
  - Three medical conditions were overestimated by the model (hip sprain/strain, paresthesias, and CO_2 headache)

Results

Specific Medical Events

- Shuttle Missions
  - Five medical conditions were underestimated by the model (nasal congestion, hip sprain/strain, constipation, early insomnia, and CO_2 headache)
  - One condition was overestimated by the model (space motion sickness)
  - Space adaptation headache and paresthesias were underestimated in some missions and overestimated in others

Results

- Resource Utilization
  - Only available for Shuttle missions
  - Only pharmaceutical usage on Shuttle missions was reliably tracked
  - There are 204 resources in the model
  - The alpha level was set at 0.0002 (0.05/204)
  - Ten pharmaceutical resources were underestimated by the model
  - Eleven pharmaceutical resources were overestimated by the model

Results – Resource Utilization

Pharmaceutical Resources Underestimated on one or more simulations

Resource	Overall p-value
Afrin	0
Ambien	0
Double Antibiotic Ointment	0
Dulcolax Suppository	0
Sonata	0
Bacitracin	1.51E-08
Triamcinolone Cream	4.5E-08
Aspirin	8.75E-07
Dulcolax Tablet	7.8E-06
Claritin	2.01E05

Results – Resource Utilization

Pharmaceutical Resources Overestimated on one or more simulations

Resource	Overall p-value
Phenergan Tablet	1E-44
Tylenol	5.69E-32
Sudafed	7.43E-23
Phenergan Injectable	4.76E-21
Afrin	1.95E-17
Ibuprofen	2.17E-13
Milk of Magnesia	7.49E-07
Ambien	7.49E-07
Dulcolax Tablet	1.01E-05
Benadryl Capsule	1.42E-05
Povidone Iodine Swabs	1.71E-05

Discussion

- For both ISS and Shuttle missions, the total number of medical events expected was accurately predicted by the model
- For both ISS and Shuttle missions, specific medical events were forecast well by the model
- Shuttle medical resource utilization was well predicted by the model

Limitations

- Limited number of ISS missions
- Missing or incomplete historical mission data
- Model baselined to ISS medical resources when analyzing Shuttle pharmaceutical utilization

Conclusions

- This analysis provides strong evidence for the validity of the IMM in predicting medical event occurrences and resource utilization for ISS and Shuttle missions
- The model results were validated by historical mission data that have not been used in the model
- A small percentage of medical conditions and medical resource utilization were under or over predicted by the model
- These differences between model output and historical mission data can be used to improve model input data and the accuracy of predicted outcomes

Questions?