THE USE OF PROBABILISTIC RISK ASSESSMENT IN THE MEDICAL CERTIFICATION OF ASTRONAUTS FOR LONG-DURATION MISSIONS

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Beyond the 1% Rule
Risk Matrices and Probabilistic Risk Assessment
New Risk Assessment Tools for Aeromedical Decisions Making

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DISCLOSURE INFORMATION

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We have no financial relationships to disclose

We will not discuss any off-label use of medications
The 1% rule

- First proposed by Tunstall-Pedoe as an acceptable target for the occurrence of cardiovascular events in commercial flight ops
- Similar magnitude as the risk of acceptable mechanical failure
- Based on a series of assumptions
  - Dual pilot operations
  - 1 hour duration flights
  - Take-off and landing flight critical periods
- Considered only the probability of an event
  - Consequences were considered to be total incapacitation
- Assumptions not valid for many aviation and space operations
Objectives

Describe two new tools for aeromedical risk assessment

1. Aeromedical Risk Matrices

2. Probability Risk Assessment (PRA)
Case History
Adhesive Small Bowel Obstruction

50 year old International Space Station (ISS) crewmember (CM) increment-assigned as back-up (8 m) then prime for launch (14 m)

Clinical History
- appendectomy age 15
- Initial episode of small bowel obstruction (SBO) at age 30
  - Treated with midline laparotomy and release of adhesions
- MDC 1 approved for long-duration ISS missions~ age 40
- Developed second episode of small bowel obstruction 10 years later, approximately 14 months before scheduled prime launch
  - Treated with minimally invasive laparoscopy with release of a single adhesion to the previous midline laparotomy scar
  - Surgeon examined the remainder of the small bowel and found no adhesions
  - Emulsified Seprafilm applied to reduce risk of re-adhesion
  - Excellent, rapid recovery, no complications
Aeromedical History

Aeromedical Question:

• Fit or unfit for upcoming six month ISS mission?
MEDICAL EVALUATION DOCUMENTS (MED)
Volume A
Medical Standards for ISS Crewmembers

International Space Station Program
4.9. 11. Intestinal obstruction

a. History of intestinal obstruction due to any chronic or potential recurrent disease

b. Surgery to relieve childhood pyloric stenosis, intussusception or volvulus is not disqualifying if there are no sequelae.

c. History of obstruction due to adhesive disease may be reviewed for certification with Special Consideration by the MSMB after a 10-year observation period.
MED A/Waiver Process

Requirements for MSMB consideration for waiver of a medical standard

1. Evidence-based assessment of the probability of occurrence of a medical event related to the condition
   • Detailed review of the clinical and aeromedical literature
   • Expert opinion inputs
   • Additional imaging/testing as appropriate

2. Assessment of the probable consequences/operational impact of a medical event occurring during the mission

3. Synthesis of the probability of an event occurrence and the consequences of an event into a risk matrix
Several large retrospective and one prospective study of risk of recurrence of adhesive SBO

- Most patients (up to 95%) who undergo abdominal surgery develop adhesions
- Factors which result in adhesions causing SBO are not well understood
  - Type of surgery, underlying pathology, type of adhesion, age of patient
- Risk for a recurrence is highest in the first 2 yrs
  - Approximately 5%/yr
- Risk increases with the number of episodes

The data in these studies was based primarily on adhesive SBO recurrence following laparotomy (which potentially causes further adhesions)
Duron, et al: Prospective study, 286 patients

Recurrence Rate (%) vs Time (months)

- Overall Recurrence
- Surgical Recurrence

5.5% 1 yr
Risk of recurrence of SBO in patients managed with laparoscopic surgery


In 64 patients followed up for an average of 3½ years, only 1/64 developed a recurrence of ASBO

- Low risk of recurrence with laparoscopic management
  - < 0.5%/yr
Expert Opinions

- **Operating Surgeon**
  - Based on clean adhesiolysis of the adhesion to the anterior abdominal wall and application of Seprafilm, the operating surgeon estimated the risk for recurrence as <1% per year.

- **Board Consultant Surgeons**
  - Estimated risk as very low
    - Two surgeons made estimate contingent on absence of re-adhesion following the recent laparoscopic adhesiolysis.
Additional diagnostic procedure

- Specialized abdominal ultrasound to assess for adhesion
- No evidence of recurrence of midline adhesion on ultrasound
Risk for recurrence of adhesive SBO event

- Older literature indicates a potential high recurrence rate, up to 5%/yr short-term, based primarily on adhesive SBO recurrence following laparotomy
- More recent laparoscopic literature suggests a much lower recurrence rate, <0.5%/yr
- No evidence of recurrence of midline adhesion on ultrasound

Based on synthesis of literature and expert opinion, the Board estimated recurrence rate

- ~1% per year risk overall for adhesive SBO recurrence during mission
- ~0.5%/yr risk for recurrence requiring surgical intervention (i.e. medical evacuation from ISS)
- Wide confidence intervals in estimates
# Medical Risk Matrix – Long-Duration Missions

## MDC-1

<table>
<thead>
<tr>
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### MSMB Risk-based Decision Analysis

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<tr>
<th>Likely ≥2%&lt;5%</th>
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<tr>
<td>Low risk – acceptable for MDC 1 disposition (long duration)</td>
<td>Moderate risk – Further consideration required for an MDC 1 disposition</td>
<td>Surgical SBO</td>
<td></td>
</tr>
</tbody>
</table>
Risk estimates indicate potentially acceptable levels of risk, but wide confidence intervals.

Risk assessment further can be further refined by means of a probabilistic risk assessment (PRA).
PRA using the Integrated Medical Model (IMM)

Risk = Likelihood x Consequence

PRA Triplet

1. What can go wrong? -----------» Medical Event
2. How likely is it to occur? ------» Probability of Occurrence
3. What is the consequence? ---» Functional Impairment
   - Loss of Crew Life (LOCL)
   - Evacuation (EVAC)
What is the 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
Risk and Risk Components

5 x 5 Risk Matrix
Medical Condition

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Outcome</th>
<th>Risk</th>
<th>Mitigation A</th>
<th>Mitigation B</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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<td>3</td>
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<tr>
<td>2</td>
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<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5x5 Matrix

<table>
<thead>
<tr>
<th>5x5 Matrix</th>
<th>IMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likelihood (Score 1-5)</td>
<td>Medical Condition Incidence</td>
</tr>
<tr>
<td>Outcome (Score 1-5)</td>
<td>Crew Functional Impairment</td>
</tr>
<tr>
<td>Mitigation?</td>
<td>In-flight Medical Capabilities</td>
</tr>
<tr>
<td>Risk Score (2x1) for a single “risk”</td>
<td>Impact to mission due to all medical conditions for the crew compliment</td>
</tr>
</tbody>
</table>
Comparison – 5x5 Risk Matrix vs. IMM

5x5 Matrix
- Qualitative
- Categorical
- Subjective
- Single Risk
- No Uncertainty
- No Confidence Interval
- Limited Context

IMM
- Quantitative
- 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 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 State (LOCL)
- Mission End State (EVAC)
- Resource Utilization
- Optimized Medical System
IMM Logic - Event Sequence Diagram

Best-case Scenario:
- Best-case resources available?
  - Yes: Treated case: Decrement medical resources
  - No: Untreated Best-Case

Worst-case Scenario:
- Worst-case resources available?
  - Yes: Treated case: Decrement medical resources
  - No: Untreated Worst-Case

Calculate End States:
- Evacuation (EVAC)
- Loss of Crew Life (LOCL)
- Crew Functional Impairment
- Type and Quantity of Medical Events (organized by Medical, Injury, or Environmental categories)
- Resource Utilization and Depletion

Medical Event
Methodology

- Compare simulated ISS missions (100k trials) with and without the CM in question

Reference Mission (No Appendectomy)
- 6 Crew/6 Month ISS Mission
- No crewmembers with history of abdominal surgery
- ISS Medical Capability

CM Mission (Appendectomy)
- 6 Crew/6 Month ISS Mission
- One crewmember with history of appendectomy and recurrent adhesive SBO
- ISS Medical Capability
IMM Inputs for CM Mission (Appendectomy)

- Incidence of SBO (beta pert distribution)
  - Prime Mission
    - 0.014 events/person-yr (most likely)
    - 0.005 to 0.039 events/person-yr (range)
  - Back-up Mission
    - 0.018 events/person-yr (most likely)
    - 0.005 to 0.044 events/person-yr (range)

- Incidence of Appendicitis = 0 for CM in question

- Best Case/Worst Case Percentages for SBO
  - 73% to 91% / 9% to 27%
  - Best case = responds to conservative treatment
  - Worst case = requires surgical treatment
IMM Inputs (cont’d)

- Best Case Evacuation
  - 5% to 93%

- Worst Case Evacuation
  - 100%

- Best Case Loss of Crew Life
  - 0%

- Worst Case Loss of Crew Life
  - 0% to 9%
### IMM Outputs

#### Summary statistics by mission and crew-profile

<table>
<thead>
<tr>
<th>Measure</th>
<th>PRIME MISSION</th>
<th>BACK-UP MISSION</th>
<th>Summary Statistic</th>
<th>95% CI</th>
<th>Summary Statistic</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evacuation</td>
<td></td>
<td></td>
<td>Appendectomy</td>
<td>4.31, 4.44</td>
<td>No Appendectomy</td>
<td>3.88, 4.13</td>
</tr>
<tr>
<td></td>
<td>4.19, 4.44</td>
<td>3.88, 4.13</td>
<td>Appendectomy</td>
<td>4.47, 4.73</td>
<td>No Appendectomy</td>
<td>4.00, 4.25</td>
</tr>
<tr>
<td>Loss of Crew Life</td>
<td></td>
<td></td>
<td>Probability (%)</td>
<td>0.66, 0.71</td>
<td>No Appendectomy</td>
<td>0.62, 0.72</td>
</tr>
<tr>
<td></td>
<td>0.61, 0.71</td>
<td>0.59, 0.69</td>
<td>Probability (%)</td>
<td>0.62, 0.72</td>
<td>No Appendectomy</td>
<td>0.66, 0.76</td>
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<tr>
<td>SBO</td>
<td></td>
<td></td>
<td>Probability (%)</td>
<td>0.81</td>
<td>No Appendectomy</td>
<td>0.96</td>
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<tr>
<td></td>
<td>0.76, 0.87</td>
<td>-</td>
<td>Probability (%)</td>
<td>0.90, 1.03</td>
<td>No Appendectomy</td>
<td>-</td>
</tr>
<tr>
<td>SBO Evacuation</td>
<td></td>
<td></td>
<td>Probability (%)</td>
<td>0.47</td>
<td>No Appendectomy</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>0.43, 0.51</td>
<td>-</td>
<td>Probability (%)</td>
<td>0.53, 0.62</td>
<td>No Appendectomy</td>
<td>-</td>
</tr>
<tr>
<td>SBO Loss of Crew Life</td>
<td></td>
<td></td>
<td>Probability (%)</td>
<td>2x10^-5</td>
<td>No Appendectomy</td>
<td>9x10^-5</td>
</tr>
<tr>
<td></td>
<td>0.00, 0.0001</td>
<td>-</td>
<td>Probability (%)</td>
<td>0.00, 0.0002</td>
<td>No Appendectomy</td>
<td>-</td>
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### Medical Risk Matrix – Prime Mission

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**MSMB Risk-based Decision Analysis**

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- **High risk** – unsuitable for MDC 1 disposition
# Medical Risk Matrix – Back-up Mission

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<tr>
<td>Overall SBO (1.92%)</td>
<td>Surgical SBO (1.14%)</td>
<td></td>
<td></td>
</tr>
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</table>
Estimated probability of evacuation by mission profile with 95% CI
Quantitative PRA

Relative Risk of Evacuation and Loss of Crew Life

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<tr>
<th>Outcome</th>
<th>Prime Mission Relative Risk</th>
<th>Back-up Mission Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evacuation</td>
<td>1.08 (1.01,1.14)</td>
<td>1.11 (1.05,1.18)</td>
</tr>
<tr>
<td>Loss of Crew Life</td>
<td>1.05 (0.88,1.20)</td>
<td>0.94 (0.82,1.09)</td>
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The above analysis was used to support the aeromedical decision to certify the crewmember for an upcoming six-month ISS mission.
Summary/Conclusions

Summary

- Crewmember with episode of recurrent adhesive SBO 14 months before prime launch for six month ISS mission
- Initial aeromedical review indicates moderate risk for ISS mission
- PRA is used to quantify risk and associated uncertainty
- Medical certification is granted to the crewmember

Conclusions

- Probabilistic Risk Assessment (PRA) can be used as a decision support tool in the ISS Aeromedical Review Process
- PRA provides objective quantified evidence-based data that may be used to inform aeromedical certification decisions when initial risk estimates indicate potentially acceptable, but uncertain levels of risk