



# ISS Real World System Validation for IMM 4.0

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## Background

- Purpose
  - To perform a qualitative assessment of the predictive performance of IMM 4.0 with respect to ISS Real World System (RWS) referent data
  - Qualitative assessment based on the ability of IMM to predict total medical events (TME), specific medical condition incidence, and medical resource utilization
  - IMM 4.0 functionalities of timeline, partial treatment capability, and alternative medication capability



## Methods

- Data Acquisition
  - Formal request from IMM project to Lifetime Surveillance of Astronaut Health (LSAH) to obtain in-flight medical data for ISS missions
  - Data requested
    - Crew member health history including medical waivers for spaceflight
    - Mission duration and number of Extravehicular Activities (EVAs)
    - All medical events captured for each crew member
    - Flight days and duration of medical events
    - Medications used to treat each medical event
    - Crew member response to medication treatment
    - Additional information regarding medical events, including severity and comments from crew members, crew medical officers, and flight surgeons
  - Data obtained from 31 ISS missions encompassing ISS Expeditions 14 through 39/40.



## Methods

- Data Organization of ISS Medical Events
  - Data sorted by crew member
  - Each crew member assigned a unique identification number
  - Medical events characterized by type
  - Additional medical event information included mission day of occurrence, duration, medications utilized for treatment, and additional notes
  - Each medical event was mapped to an IMM medical condition if possible
  - If the medical event could not be mapped to a current IMM medical condition, it was captured as a potential future IMM medical condition



## Methods

- Data Organization of ISS Medication Utilization
  - Medications grouped by categories
    1. Antacid
    2. Antibiotic
    3. Antidiarrheal
    4. Antiemetic
    5. Antifungal
    6. Antihistamine
    7. Antiviral
    8. Decongestant
    9. Hypnotic
    10. Laxative
    11. Non-opioid Analgesic
    12. Ophthalmic
    13. Opioid Analgesic
    14. Steroid



## Methods

- Preparation for Validation Analysis
  - All medical events per mission summed by condition
  - Total number of medications reported as utilized summed by category
  - Medication category sums ranked numerically from most frequently to least frequently utilized
  - Mission duration for each crew member converted from days to years
  - Number of EVAs per mission summed to obtain total EVAs
  - Crew members with no reported medical data were excluded from analysis



## Methods

- IMM Simulation
  - IMM 4.0 was used to simulate each of the 31 RWS ISS missions
  - An IMM simulation was performed for each ISS mission based on the corresponding mission profiles
    - Mission length
    - Number of crew
    - Sex of each crew member
    - Number of EVAs
    - Presence of eye contacts
    - Presence of dental crowns
    - CAC score
    - History of abdominal surgery

# Qualitative Validation of IMM 4.0



## Methods

### Qualitative Comparison

#### Performance Characterization of Qualitative Parameters

Parameter	Visualization	Performance Characterization
Total Medical Events	Spider Plots/Linear Plots	IMM TME should be reasonable estimate of RWS TME
Medical Conditions: Incidence	Bar Charts	IMM incidence values should be of similar magnitude as RWS incidence values
Medical Resources	Tabulation of resource rankings	IMM resource utilization ranking should be consistent with RWS resource utilization ranking



## Methods

### Qualitative Comparison

- Total Medical Events
  - RWS TME compared to IMM forecasted TME per ISS mission
  - Observed values of TME were compared to predicated means and 90% confidence limits for each ISS mission
  - IMM forecasted TME classified as in-range or out-of-range for each ISS mission based on 90% confidence limits
  - Out-range- forecasts further classified as overestimates or underestimates of TME



## Methods – Qualitative Comparison

### Medical Conditions: Incidence

- Incidence values were expressed as either a rate (events/person-year) or as a proportion (events/person)
- If IMM incidence values differ significantly from RWS incidence values, IMM predictions of medical events and associated end-states (EVAC and LOCL) would be expected to differ
- Qualitative Evaluation Criteria
  1. The ratio of IMM vs RWS incidence values assessed by order of magnitude [less than 0.1(low) or greater than 10 (high)]
  2. The ratio of IMM vs RWS incidence values assessed by ratio difference [less than 50% (low) or greater than 150% (high)]
- Zero-event Data
  - For rare medical events in IMM that have not occurred on RWS ISS missions, an estimation of the upper bound for the incidence was used  $(1/2.5n)^*$

\* Quigley and Revie, 2011

# Qualitative Validation of IMM 4.0



## Methods – Qualitative Comparison

### Medical Resources

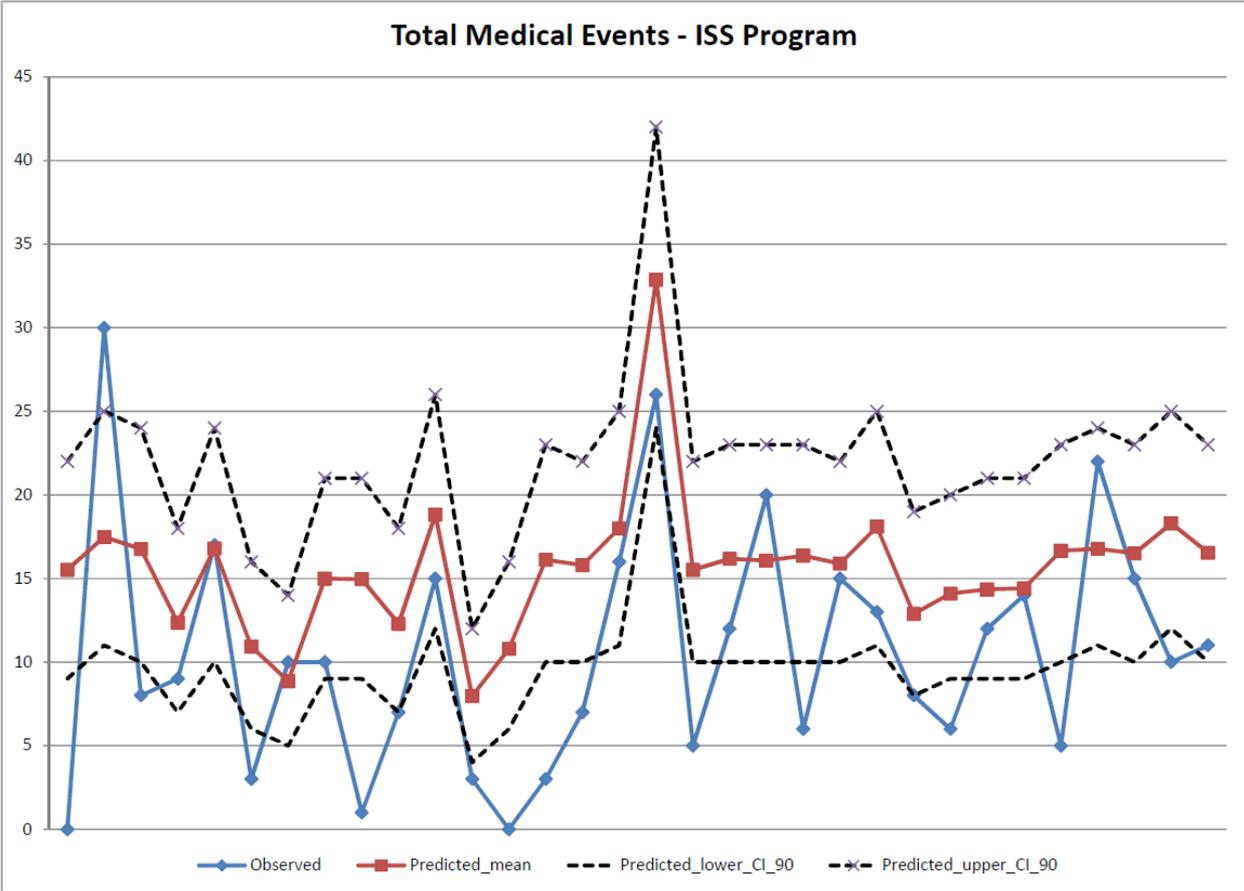
- Only medications were considered for analysis
  - RWS data for non-medication resources are very limited
  - Medications were grouped by category
- Ranked IMM forecasted medication utilization was compared to ranked RWS ISS medication utilization
  - Excellent ( $\leq 2$  difference in relative ranking positions)
  - Fair (3-5 difference in relative ranking positions)
  - Poor ( $\geq 5$  difference in relative ranking positions)

# Qualitative Validation of IMM 4.0



## Results

### Total Medical Events





## Results

### Total Medical Events

- IMM estimated TME were **in-range for 58%** (18 out of 31) of the RWS ISS missions
- IMM **overestimated** TME for **39%** (12 out of 31) of the RWS ISS missions
- IMM **underestimated** TME for **3%** (1 out of 31) of the RWS ISS missions



## Results

### Incidence Values

- IMM incidence values were **in-range** for **70%** (82 out of 118) of the RWS ISS medical conditions
- IMM incidence values were **out-of-range high** for **26%** (31 out of 118) of the RWS ISS medical events
- IMM incidence values were **out-or-range low** for **4%** (5 out of 118) of the RWS ISS medical events

# Qualitative Validation of IMM 4.0



## Results – Medical Resource Utilization

### RWS Rankings

1. Non-opioid Analgesic
2. Hypnotic
3. Decongestant
4. Antihistamine
5. Antiemetic
6. Antifungal
7. Ophthalmic
8. Laxative
9. Steroid
10. Antibiotic
11. Antiviral
12. Antacid
13. Opioid Analgesic
14. Antidiarrheal

### IMM Rankings

- Non-opioid Analgesic
- Hypnotic
- Antibiotic
- Antihistamine
- Ophthalmic
- Antiemetic
- Decongestant
- Antidiarrheal
- Antifungal
- Laxative
- Opioid Analgesic
- Antacid
- Steroid
- Antiviral

### Quality of Match

- Excellent
- Excellent
- Poor
- Excellent
- Excellent
- Excellent
- Fair
- Fair
- Fair
- Excellent
- Excellent
- Excellent
- Fair
- Fair

# Qualitative Validation of IMM 4.0



## Results - Medical Resource Utilization

- Excellent Consistency [58%] (8 out of 14 medication categories)
  - Analgesic
  - Antacid
  - Antiemetic
  - Antihistamine
  - Hypnotic
  - Non-opioid Analgesic
  - Ophthalmic
  - Opioid
- Fair Consistency [36%] (5 out of 14 medication categories)
  - Antidiarrheal
  - Antifungal
  - Antiviral
  - Decongestant
  - Steroid
- Poor [7%] (1 out of 14 medication categories)
  - Antibiotic

# Qualitative Validation of IMM 4.0



## Summary of Results

### TME

- The IMM forecasted TME were consistent with the TME for ISS
- When inconsistent, the IMM tended to overestimate the TME for ISS

### Incidence Values

- IMM incidence values were consistent with the ISS incidence values
- When inconsistent, the IMM incidence values were generally higher than ISS incidence values

### Medical Resource Utilization

- IMM forecasted medication utilization was generally consistent with medication utilization on ISS
- IMM overestimated the use of antibiotics on ISS



## Conclusions

- IMM 4.0 forecasts of TME, Incidence Values, and Medication Utilization are overall consistent with the ISS RWS
- Inconsistencies found between the IMM and the RWS may be used to adjust model inputs and improve the ability of the IMM to accurately simulate the RWS