Probabilistic Assessment of Sex-Dependent Medical Risk During Spaceflight



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We will not discuss off-label use and/or investigational use in this presentation

Quantifying Risk

- Differences between males and females create different medical risks
- These differences may effect medical outcomes and mission success
- The Integrated Medical Model (IMM) was used to quantify these risks

Sex Differences Examples

| System | Male | Female |
|-----------------|--|--|
| Cardiovascular | Predisposition to cardiovascular events (e.g. stroke ⁶ , MI ¹²) | Higher rates of orthostatic intolerance post flight ³ |
| Genitourinary | Prostatitis ^{2,17} | Urinary tract conditions ^{7,17} |
| Musculoskeletal | Higher rates of musculoskeletal injury on ISS ¹⁹ | Osteoarthritis, joint issues ¹⁵ |
| Behavioral | Higher responses with anger, noncooperation, and conflict in psychosocial isolation ⁷ | Higher rates of depression and anxiety ³ |

Study Objective

- Assess medical risk differences between men and women in a space flight environment
- Assess impact of those differences on mission outcomes
- Determine effect of those risks on different mission types/lengths
- Identify ways to mitigate risks

What is the Integrated Medical Model?

- Probabilistic Risk Assessment (PRA) using Monte Carlo methodology
- Used to assess mission risk due to in-flight medical events
- Considers relevant preexisting medical conditions
- User defined Design Reference Missions (DRM) (e.g. crew, duration, EVA, etc.)
- Considers outcomes for 100 medical conditions that have or may occur in-flight
 Incidence data from spaceflight medical events, and analog and general populations

20 of 100 conditions have sex-dependent outcomes

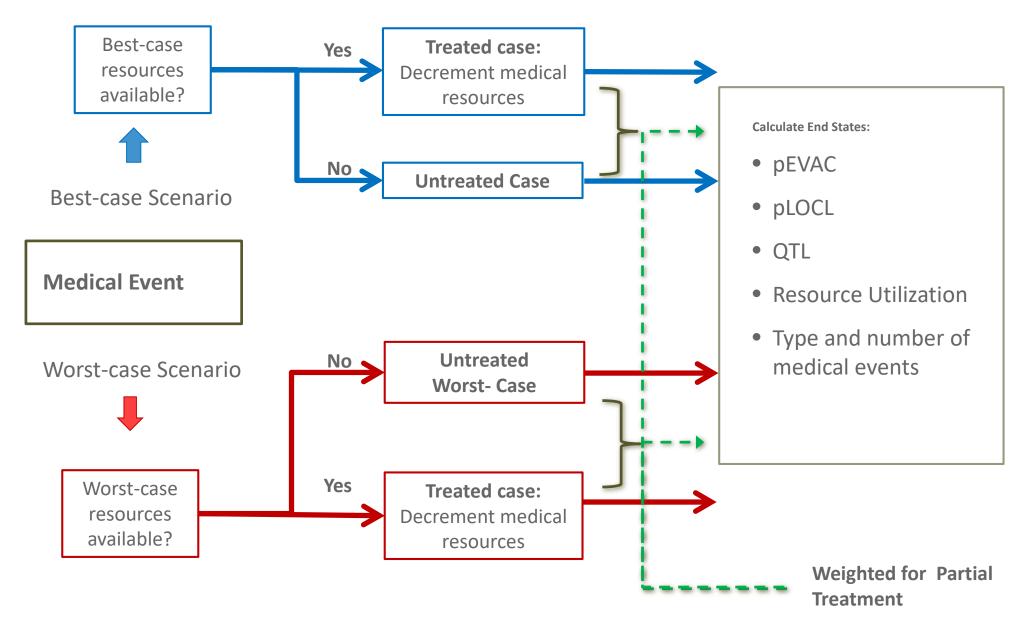
IMM Sex-Dependent Medical Conditions

| Male Predominant | Female Predominant |
|-----------------------------------|---|
| Acute Prostatitis (male only) | Abnormal Uterine Bleeding (female only) |
| Acute Compartment Syndrome | Urinary Incontinence (female only) |
| Angina/MI | Vaginal Yeast Infection (female only) |
| Atrial Fibrillation/Flutter | Acute Arthritis |
| Cardiogenic Shock Secondary to MI | Acute Cholecystitis |
| Hip/Proximal Femur Fracture | Acute Glaucoma |
| Lumbar Spine Fracture | Anxiety |
| Retinal Detachment | Depression |
| Cerebral Vascular Accident | Lower Extremity Stress Fracture |
| | Urinary Retention |
| | Urinary Tract Infection |

Model Outputs

- Total Medical Events (TME)
- Crew Health Index (CHI) 0 to 100%, complete impairment to normal function
- Probability of Evacuation (pEVAC) occurs if...
 - Risk for LOCL (needs advanced care to survive)
 - Risk for significant permanent impairment
 - Risk of intractable pain
- Probability for Loss of Crew Life (LOCL) clinical scenario resulted in death
- Influential Conditions, those that had significant contribution to outcomes
- Medical Resources used

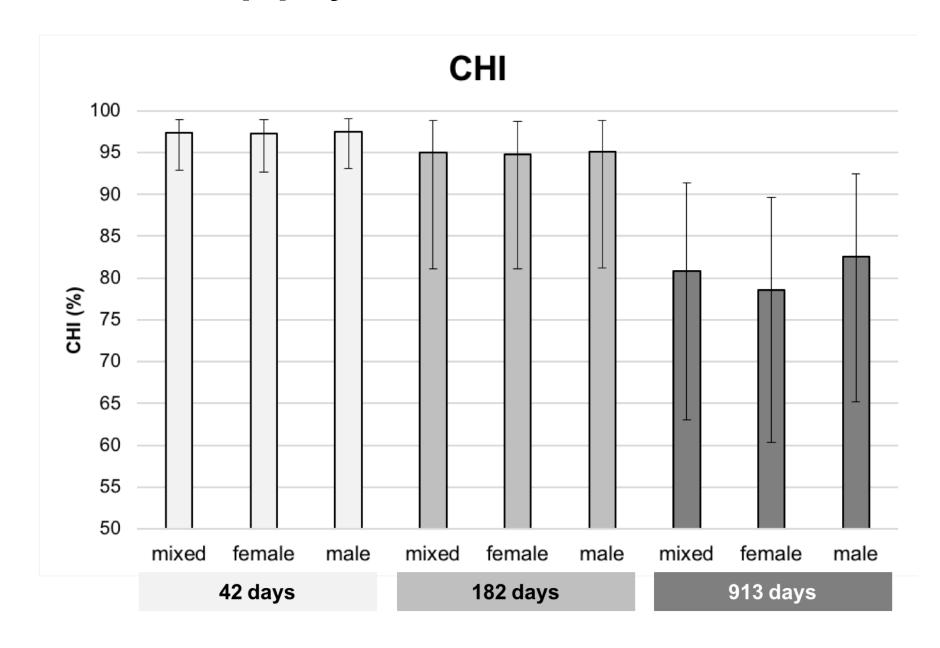
IMM Methodology



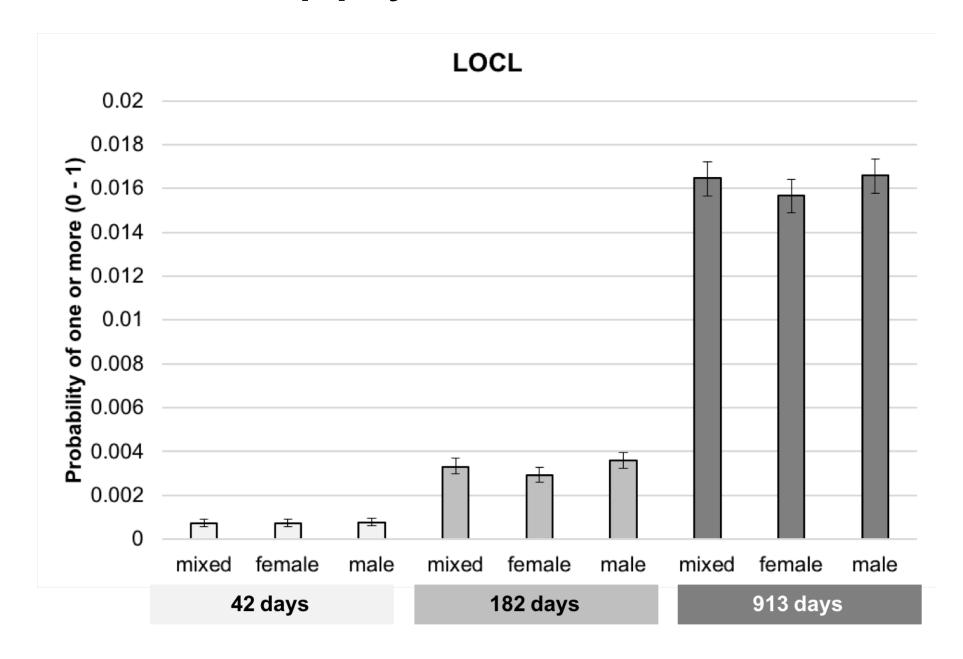
Study Design Reference Missions (DRM)

- 4 crew members in each DRM
- Three different crews → mixed sex, all female, all male,
- Three different mission lengths
 - Lunar sortie (42 days)
 - International Space Station (ISS) mission (182 days)
 - Mars mission (913 days)
- 9 total studies performed
- Inventory of medical supplies from the ISS med kit with and without the possibility of resupply

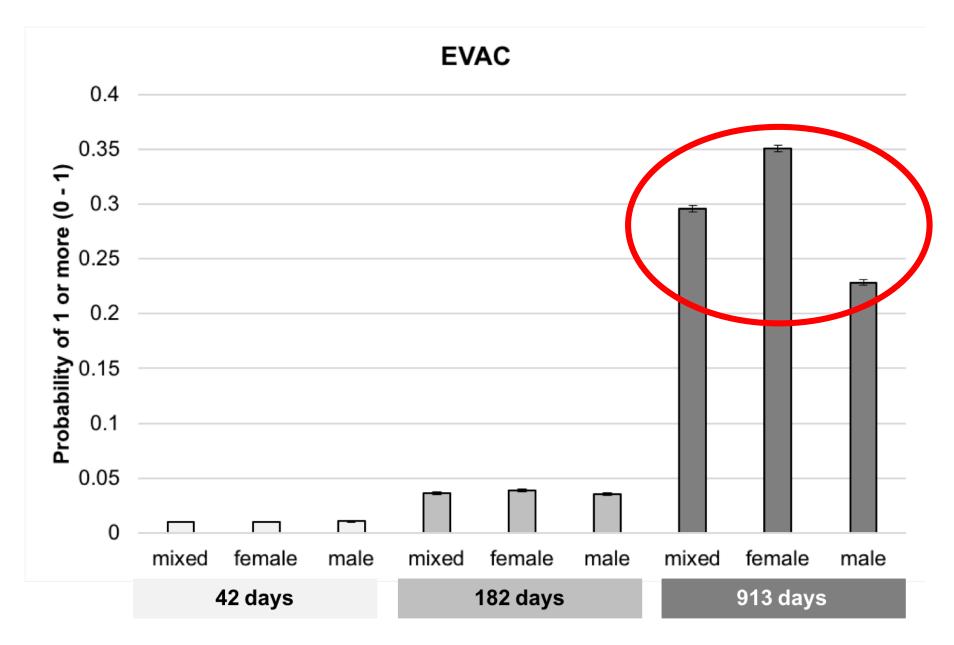
CHI - No resupply



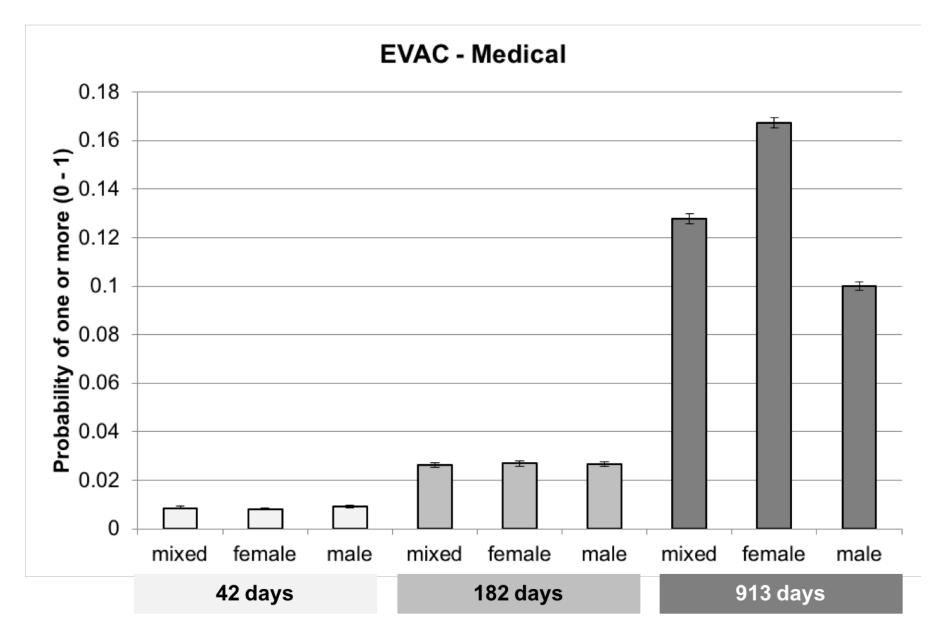
pLOCL - No resupply



pEVAC - No Resupply



pEVAC Medical - No Resupply



pEVAC (No Resupply): Female Influential Conditions

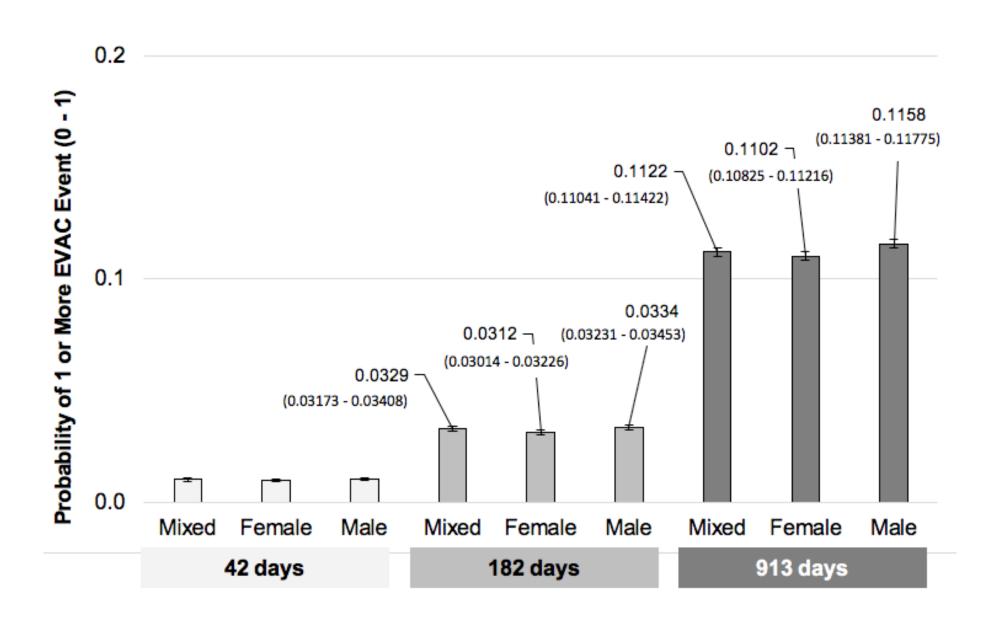
| All Female | | | | | | |
|------------|-------|---------|-------------------------|--------|------------------|----------------|
| Rank | Case | Treated | Condition | Events | Contribution (%) | Cumulative (%) |
| 1 | BEST | PARTIAL | EYE CHEMICAL BURN | 11702 | 28.45 | 28.45 |
| 2 | WORST | PARTIAL | URINARY TRACT INFECTION | 7710 | 18.74 | 47.19 |
| 3 | WORST | PARTIAL | BACK SPRAIN/STRAIN | 2088 | 5.08 | 52.27 |
| 4 | WORST | PARTIAL | EYE CHEMICAL BURN | 1877 | 4.56 | 56.83 |
| 5 | BEST | PARTIAL | FINGER DISLOCATION | 1527 | 3.71 | 60.54 |
| 6 | WORST | PARTIAL | NEPHROLITHIASIS | 1124 | 2.73 | 63.28 |
| 7 | WORST | TREATED | SANS | 1026 | 2.49 | 65.77 |
| 8 | WORST | TREATED | SMOKE INHALATION | 668 | 1.62 | 67.39 |
| 9 | WORST | PARTIAL | EYE INFECTION | 617 | 1.50 | 68.89 |
| 10 | WORST | PARTIAL | LE STRESS FRACTURE | 534 | 1.30 | 70.19 |

pEVAC (No Resupply): Male Influential Conditions

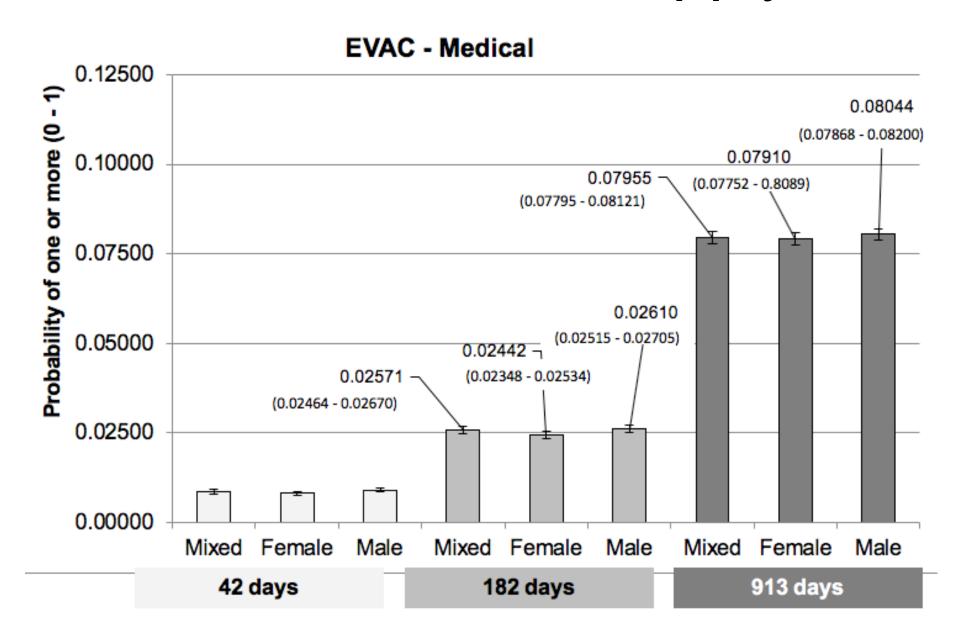
| All Male | | | | | | |
|----------|-------|---------|--------------------|--------|------------------|----------------|
| Rank | Case | Treated | Condition | Events | Contribution (%) | Cumulative (%) |
| 1 | BEST | PARTIAL | EYE CHEMICAL BURN | 4072 | 16.08 | 16.08 |
| 2 | WORST | PARTIAL | BACK SPRAIN/STRAIN | 2033 | 8.03 | 24.10 |
| 3 | BEST | PARTIAL | FINGER DISLOCATION | 1603 | 6.33 | 30.43 |
| 4 | WORST | TREATED | SANS | 1022 | 4.03 | 34.47 |
| 5 | WORST | PARTIAL | EYE CHEMICAL BURN | 925 | 3.65 | 38.12 |
| 6 | WORST | PARTIAL | NEPHROLITHIASIS | 811 | 3.20 | 41.32 |
| 7 | WORST | TREATED | NEPHROLITHIASIS | 689 | 2.72 | 44.04 |
| 8 | WORST | TREATED | SMOKE INHALATION | 674 | 2.66 | 46.70 |
| 9 | WORST | PARTIAL | EYE INFECTION | 659 | 2.60 | 49.30 |
| 10 | WORST | PARTIAL | DENTAL ABSCESS | 482 | 1.90 | 51.21 |

But...

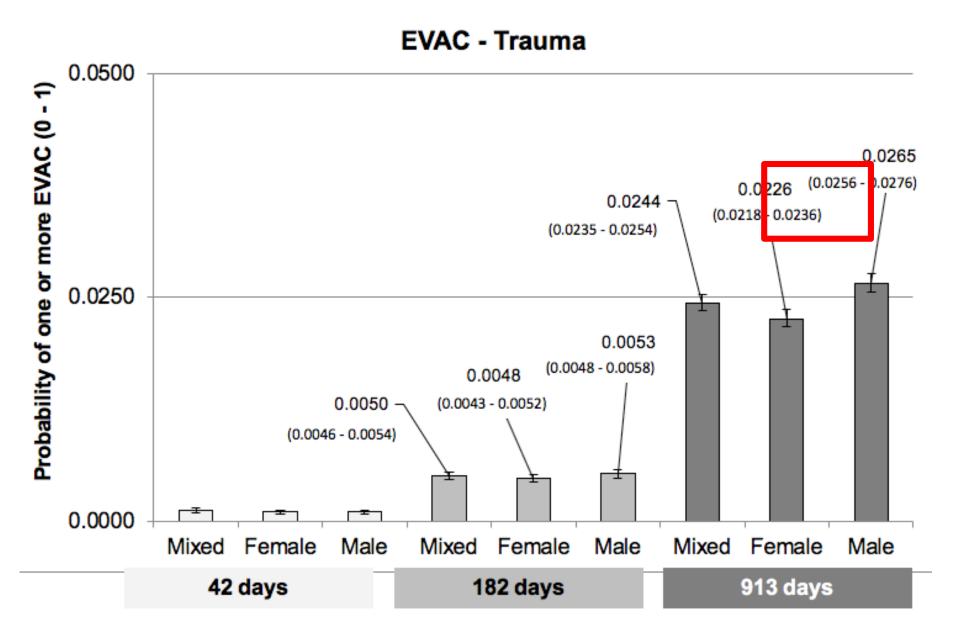
pEVAC - With Resupply



pEVAC Medical – With Resupply



pEVAC Trauma – With Resupply



pEVAC (With Resupply): Female Influential Conditions

| All Female | | | | | | |
|------------|----------|---------|------------------------------|---------------|--------------|------------|
| | | | | | Contribution | Cumulative |
| Rank | Scenario | Treated | Condition | Events | (%) | (%) |
| 1 | WORST | TREATED | NEPHROLITHIASIS | 1490 | 12.95 | 12.95 |
| 2 | WORST | TREATED | SANS | 1074 | 9.33 | 22.28 |
| 3 | WORST | TREATED | DENTAL ABSCESS | 924 | 8.03 | 30.31 |
| 4 | WORST | TREATED | SEPSIS | 770 | 6.69 | 37.00 |
| 5 | WORST | TREATED | SMOKE INHALATION | 726 | 6.31 | 43.31 |
| 6 | BEST | TREATED | SMALL BOWEL OBSTRUCTION | 519 | 4.51 | 47.82 |
| 7 | WORST | TREATED | WRIST FRACTURE | 441 | 3.83 | 51.66 |
| 8 | WORST | TREATED | BACK SPRAIN/STRAIN | 336 | 2.92 | 54.58 |
| 9 | WORST | TREATED | URINARY TRACT INFECTION | 305 | 2.65 | 57.23 |
| 10 | WORST | TREATED | HEAD INJURY | 249 | 2.16 | 59.39 |
| 11 | BEST | TREATED | CEREBROVASCULAR ACCIDENT | 245 | 2.13 | 61.52 |
| 12 | WORST | TREATED | TRAUMATIC HYPOVOLEMIC SHOCK | 236 | 2.05 | 63.57 |
| 13 | BEST | TREATED | SEIZURES | 236 | 2.05 | 65.62 |
| 14 | WORST | TREATED | CEREBROVASCULAR ACCIDENT | 221 | 1.92 | 67.54 |
| 15 | BEST | TREATED | ANGINA/MYOCARDIAL INFARCTION | 190 | 1.65 | 69.19 |

pEVAC (With Resupply): Male Influential Conditions

| All Male | | | | | | |
|----------|----------|---------|------------------------------|---------------|--------------|------------|
| | | | | | Contribution | Cumulative |
| Rank | Scenario | Treated | Condition | Events | (%) | (%) |
| 1 | WORST | TREATED | NEPHROLITHIASIS | 1507 | 12.45 | 12.45 |
| 2 | WORST | TREATED | SANS | 1058 | 8.74 | 21.18 |
| 3 | WORST | TREATED | DENTAL ABSCESS | 803 | 6.63 | 27.82 |
| 4 | WORST | TREATED | SEPSIS | 794 | 6.56 | 34.37 |
| 5 | WORST | TREATED | SMOKE INHALATION | 734 | 6.06 | 40.44 |
| 6 | BEST | TREATED | SMALL BOWEL OBSTRUCTION | 497 | 4.10 | 44.54 |
| 7 | WORST | TREATED | WRIST FRACTURE | 463 | 3.82 | 48.36 |
| 8 | WORST | TREATED | HIP/PROXIMAL FEMUR FRACTURE | 383 | 3.16 | 51.53 |
| 9 | WORST | TREATED | CEREBROVASCULAR ACCIDENT | 340 | 2.81 | 54.34 |
| 10 | WORST | TREATED | BACK SPRAIN/STRAIN | 326 | 2.69 | 57.03 |
| 11 | BEST | TREATED | CEREBROVASCULAR ACCIDENT | 323 | 2.67 | 59.70 |
| 12 | BEST | TREATED | ANGINA/MYOCARDIAL INFARCTION | 290 | 2.40 | 62.09 |
| 13 | WORST | TREATED | TRAUMATIC HYPOVOLEMIC SHOCK | 264 | 2.18 | 64.27 |
| 14 | BEST | TREATED | ATRIAL FIBRILLATION/ FLUTTER | 263 | 2.17 | 66.44 |
| 15 | BEST | TREATED | SEIZURES | 240 | 1.98 | 68.43 |

Discussion

- No differences in CHI or LOCL between sexes
- Partially-treated UTI drives higher female EVAC using the base ISS med kit
- Coronary and trauma risks for males are important for long missions
- Appropriate med kit design and prevention can mitigate sex-dependent risks
- Other conditions have sex-dependent risks which are not represented
- PRA is a useful tool to ask "what if..."!

Disclaimer

These results are subject to the biases inherent in the model and should only be used by subject matter experts as one point of information among many.

Thank you!

"All models are wrong. Some are useful."

- George Box (1919 – 2013)

Back Up

Other Considerations: Landing/Postflight

- Orthostatic intolerance
- Landing impact trauma
- Neurosensory
 - Men: higher incidence of post-flight motion sickness
 - Women: higher incidence of post-flight vestibular instability symptoms

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- Landing impact trauma
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 - Men: higher incidence of post-flight motion sickness
 - Women: higher incidence of post-flight vestibular instability symptoms

Other Considerations: Behavioral/Social

- Response to stress due to psychosocial isolation⁷
 - Women: more likely to be interpersonally supportive
 - Men: more often respond with anger, noncooperation and conflict
- Inconclusive studies in spaceflight and Antarctic groups as to ideal crew composition^{7,8,10,28}

Other Considerations: Malignancy

- Women have increased susceptibility to radiation induced cancer 9
- Antarctic winter-overs as analogue: multiple instances of cancer
- Large induction period for many cancers, but still possible for cancer to surface
 - Breast, lung, testicular carcinoma^{1,2}
- Evacuation unlikely

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