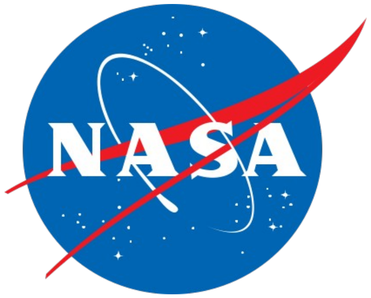

Medical Care during Contingency Suited Return for Orion Artemis Missions

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Disclosure Statement

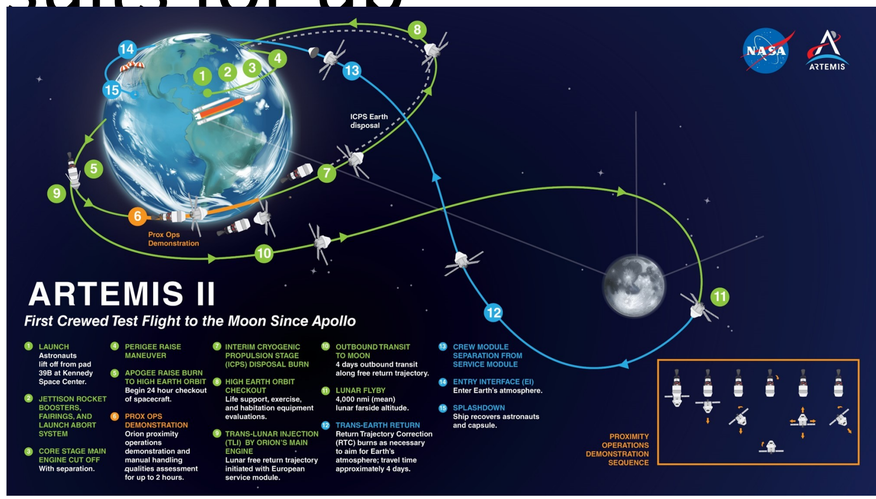
92nd Annual Scientific Meeting

- We have no financial relationships to disclose
- We will not discuss off-label and/or investigational uses

Orion Depress Scenario

If the Orion spacecraft were to suffer an unrecoverable cabin depressurization, the capsule would be uninhabitable

- Crew would be required to wear pressure suits for up to 6 days (144 hours) for return to Earth
- Requires in-suit fecal & urine management
- Need in-suit nutrition & water delivery



https://www.nasa.gov/sites/default/files/thumbnails/image/artemis_2_map_october_2021.jpg

The medical team needs to predict and manage impacts to crew health during this scenario.

Objective for Medical Operations

Orion shall sustain life of the suited crew without permanent disability in an unpressurized cabin for at least 144 hours for Lunar Missions.

The moment crew enters the suits, we are clearly dealing with a medical management crisis, and we need the tools to manage it.

Methods

- The Orion Medical Operations team developed a list of indications that could occur in this suited return scenario and then listed the result for the crew if that indication were to be left untreated.
- The indications and consequences were then ranked and grouped into 2 major categories
  - loss of crew/permeant disability
  - performance

Infection Risk

- Astronauts have decrements noted in immune system function during spaceflight
- Bacteria have been shown to have increased resistance and virulence in microgravity
- Bacterial sensitivity to antibiotics varies and changes over time
  - No antibiotic is effective for all bacteria.
  - Changes in sensitivity may require future formulary changes

Infection Risk

- Prolonged contact with fecal matter and urine in the suit
  = high likelihood of significant medical issues

- Difficult to find analogous terrestrial population
  - Invasive catheters ⎵ 5% bacteriuria risk/person/day (Trautner 2004)
  - 56% probability of infection in at least 1 crew member after 3 days (4-member crew)

- Serious infection carries a risk of permanent disability or death <u>despite the best possible terrestrial medical care</u>
  - 20-40% mortality rate once patient is in Urosepsis
  - We want to avoid sepsis by early and appropriate use of antibiotics

Just getting crew home alive is not enough to avoid all risk of death/permanent disability.

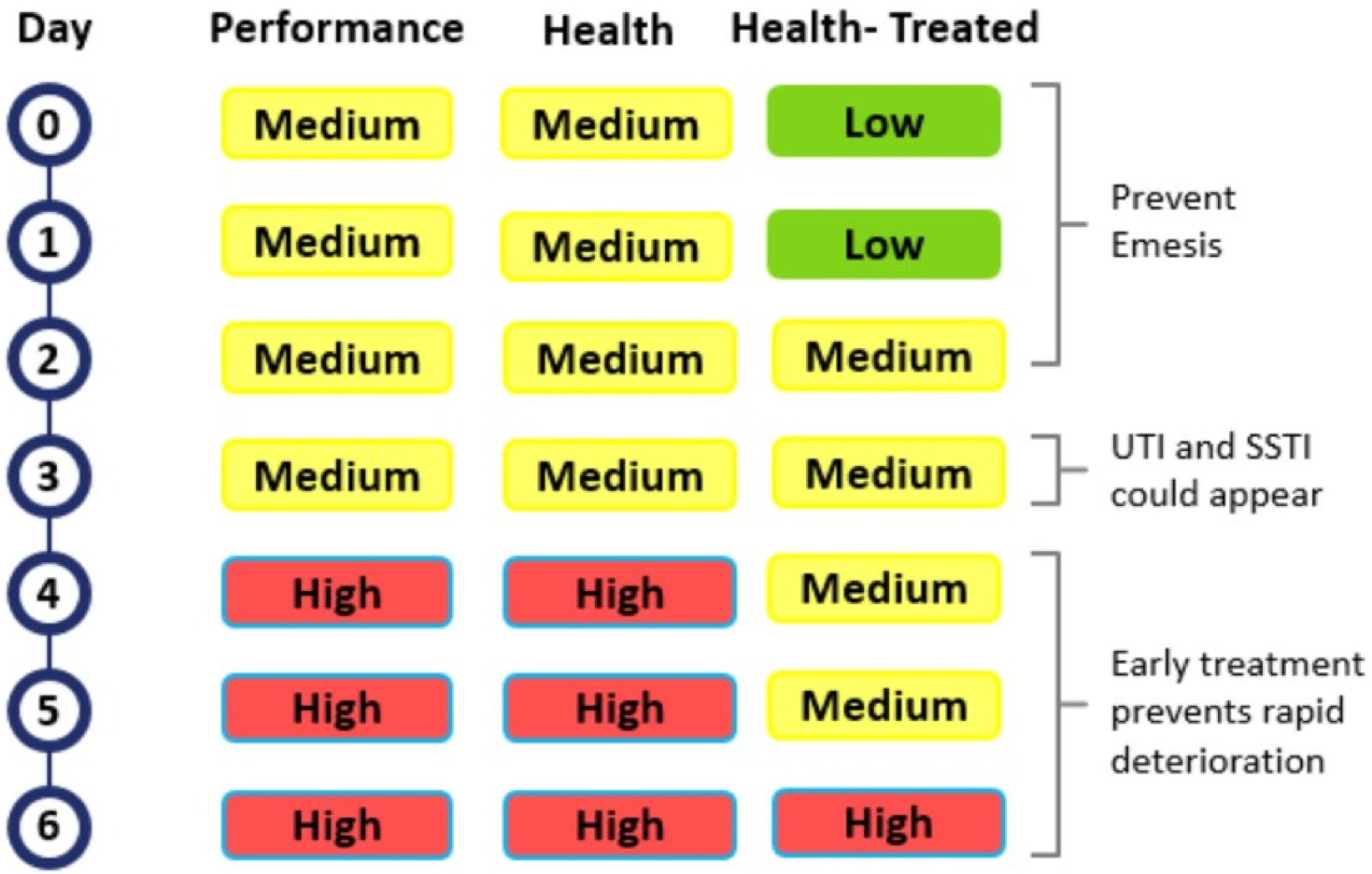
Prioritized Indications

Decreasing Priority

	Indication	Concern if Untreated
Loss of Crew (LOC)/ Permanent Disability	**Skin Infection**	**Severe infection, Sepsis**
	UTI	**Severe infection, Sepsis**
	Nausea / Vomiting	**Choking, aspiration, pneumonia**
Performance	Pain	Increased Anxiety/Stress
	Dermatitis / Rash	Pathway for skin infection
	Insomnia	Decreased immune response
	Diarrhea	Skin breakdown, infection
	Anxiety / Stress	Decreased immune response

- Conditions will likely be interlinked
- Regardless of probability, the most highly prioritized conditions have significant risk of permanent disability and death

Health Concerns Risk Timeline



- >50% chance of 1 crew member developing a UTI
- Urosepsis 20-40% mortality with best terrestrial care

Options for In-Suit Medication Delivery

Options for delivering medication to a suited crewmember during a contingency event were derived based on the available forms of the medication:

1. Liquid oral medicine
2. Intramuscular (IM) injections
3. Crushed tablets
4. Unaltered tablets & capsules
5. Compounding medication

Note: Prophylactic medication - Per Space Medicine opinion, medication administered prior to suit donning and provides little to no benefit to crew health during the 144-hour contingency period.

1) Most medications require multiple doses over a period of time
2) Potential side effects (nausea, gastrointestinal upset, etc.)
3) Administering medicine before symptoms present themselves will likely not impede development of the symptoms
4) Insufficient time to administer medicine during the brief suit donning period

Liquid Medicine in a Modified SNHC* Bag

- Liquid medicines are only available in pediatric doses. Additional volume needs to be supplied for adult dosages.
  - Assuming 80 doses/bags (high mass and volume)
- Using a modified SNHC bag will require additional oxygen allocation, which had not been yet determined to be available
- Additional water may be needed to flush/deliver residual medicine from SNHC bag
- Cost and schedule impacts to SNHC and medical system projects

* Suited Nutrition and Hydration for Contingencies

Intramuscular (IM) Injections

- IM Injection to a suited crew member would require:
  - Injection port added to the Orion Suit – location TBD.
  - Novel medication delivery mechanism (i.e. syringe) that can be operated by suited crewmembers and can interface with the suit injection port
- Further investigation would be needed to determine feasibility and impacts of including an injection port on the Orion Suit and developing a delivery mechanism
  - Large cost and schedule impact to suit and medical system projects

Crushing Tablets

- Crushing tablets can affect the kinetics (e.g., absorption, distribution properties in the body) of the desired medications.
- Water & crushed medicine may not mix well, resulting in unknown delivered dosage
- Capsules cannot be crushed, leaving a deficiency in the treatment capability if this option were chosen.
- Two options are presented for the packaging and delivery of crushed medicine:

  a) Preflight: Pills crushed and packaged in SNHC bags*

  b) In-flight: Pills crushed with pill crusher/syringe

  *Since there are no data on the stability of crushed tablets beyond immediate use, there is an unknown risk of using tablets crushed on the ground. Stability study would incur a considerable cost/schedule impact (~$400k+ per medicine).

Tablets Crushed Preflight

- Tablets are crushed pre-flight using standard methods (mortar and pestle, tablet crusher, etc.)
- Crushed medicine is packaged in a smaller SNHC bag (size is TBD)
  - Although different options exist for packaging crushed medicine (e.g. syringe), the SNHC design was considered for a cost/schedule savings.
  - Technical limitations of the SNHC to deliver medication would need to be investigated.
- Anticipated use
  - Fill bag with water from the Portable Water Dispenser (PWD) prior to ingesting medicine

Tablets Crushed In-Flight

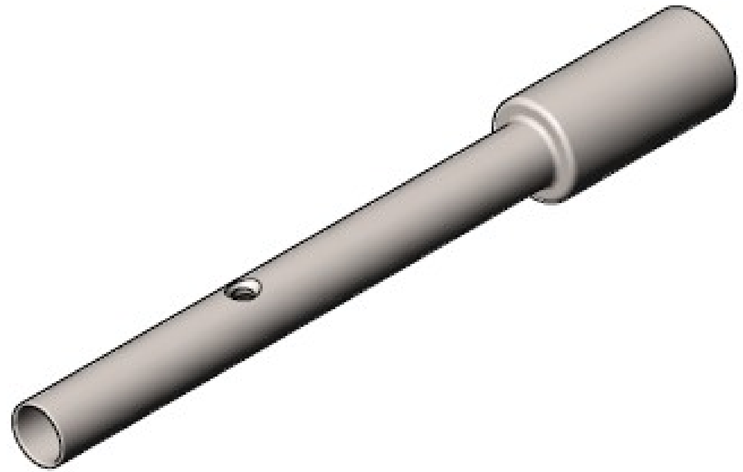
- Option A) In-flight tablet crushing in the existing SNHC bag
  - Would require new crushing mechanism
  - Could compromise the integrity of the bag
- Option B) Crushing in syringe/tablet crusher.

- Suggested use:
  1. Fly/launch each medicine (single doses) placed in separate syringes
  2. Crewmember crushes tablets using syringe
  3. Interface syringe to a water bag (requires custom adapter) to draw water
  4. Use a custom adapter/straw connected to the syringe to deliver medicine to the crewmember through the helmet port

Unaltered Medication Delivery Tool Concept

Con Ops:

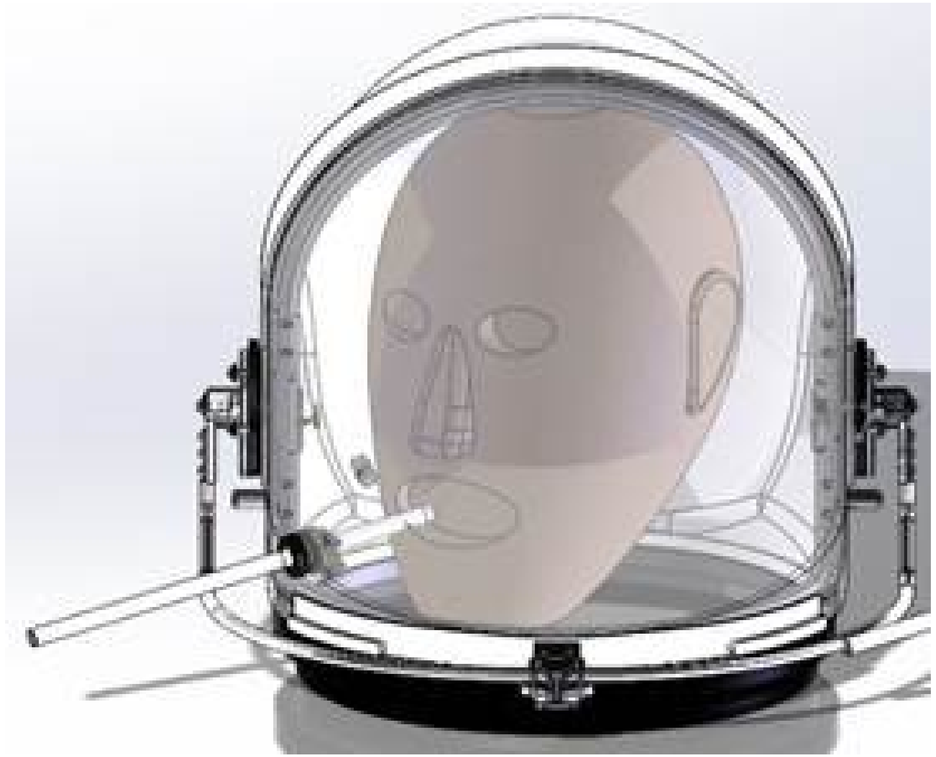
- Install medication into straw tool
- Insert edible “plug” to contain medication within to
- Insert tool through helmet port
- Crew ingests edible “plug” and medication
- Remove tool from helmet port and stow



Notes:

- Crew will require water to ingest the medication. Recommend administering medicine immediately prior to “scheduled” water consumption with water bag
- Ease of crew use is unknown. If crew cannot position helmet port in front of them by swiveling helmet, assistance from second crewmember may be needed
- Capsules may fit in the tool; whereas they cannot be crushed in other delivery options

Suit Interface



Unaltered Medication Tool Concept Test

- Medication is manually inserted into straw by crewmember
- Test demonstrated that subject in pressurized suit can:
  - Insert medication into straw within bag (most effective)
  - Pick up medication from table and insert medication into straw (less effective)

Benefits

- Medication can be flown in Ziploc bags (nominal Med Kit design), eliminating need for individual tablet & capsule modules that were proposed in an earlier concept
- Simplifies medication delivery tool design (reduced cost)

Case Study in Medication Measurement: Vicodin

- Medication sizes change frequently and unpredictably when JSC pharmacy supplier changes
  - Size changes can happen each time there is a new manufacturer, a patent expires, a company buys another, there is a market shortage, etc.
- Vicodin
  - Routinely flown on ISS for pain management
  - Vicodin was measured in July and again in November 2018. In July measurements indicated that Vicodin fit the 5/16” port hole.
  - By November, the previously measured Vicodin was not available. Measurement of the new version found Vicodin no longer fits in 5/16” port.
  - JSC Pharmacy Team has not previously had to monitor changes in medication sizes.
    - Further investigation in this case revealed 3 different manufacturers of vicodin as a result of market availability over the course of this project in 2018.

This is an example of one drug changing manufactures 3 times in 2018 due to market availability.

Risk: the medications that fit in the helmet port today may not fit in the future.

Compounding Medications

- Any manipulation of a medication that is not from the manufacturer falls under the category of “compounding” in pharmacy practice.
- Medications that come in tablet form cannot be crushed into a powder and put into capsules or pressed into different pill shapes.
- Compounding of medications requires an onerous certification process; Compounding pharmacy regulations have become much stricter as a result of patient safety concerns.
- Shelf life of crushed or compounded medication is extremely limited and can’t be sustained in the spaceflight environment; medication will not last the entire mission.
  - NASA Space Medicine Decision Memo: do not plan to use expired medications in a contingency.

Compounding has been considered in the past, and the JSC Pharmacy has found it to be cost prohibitive and expiration date limitations are a showstopper.

Medication Delivery Assessment Results

Options Assessed:

- IM injection, liquids, crushed tablets (pre-flight & in-flight), unaltered tablets & capsules, compounded medication

Space Medicine preferred method: IM injection

Selected method: unaltered medication through helmet port

- Space Medicine & Human Systems Engineering & Integration conducted a study of oral medication sizes
- SD recommended: Unaltered medication delivery with larger suit helmet port size since
  - current port size did not accommodate all primary medications
  - future pharmaceutical industry changes could impact our limited medication options and may eliminate our ability to treat the crew

End Result

- Program had to trade modifying/enlarging the existing helmet port that had an unknown risk for introducing an air leak.
  - A risk that could affect the nominal case of wearing the helmet for launch. landing, and throughout the 144-hour contingency scenario.

- While the Program chose not to enlarge the port size and accepted the risks associated with the current helmet port, the Program at least ensured that limited <u>medication treatment capability was provided:</u>
  - Authorized development and certification of the contingency medication delivery tool
  - Accommodated mass and volume for the delivery tool and associated medications

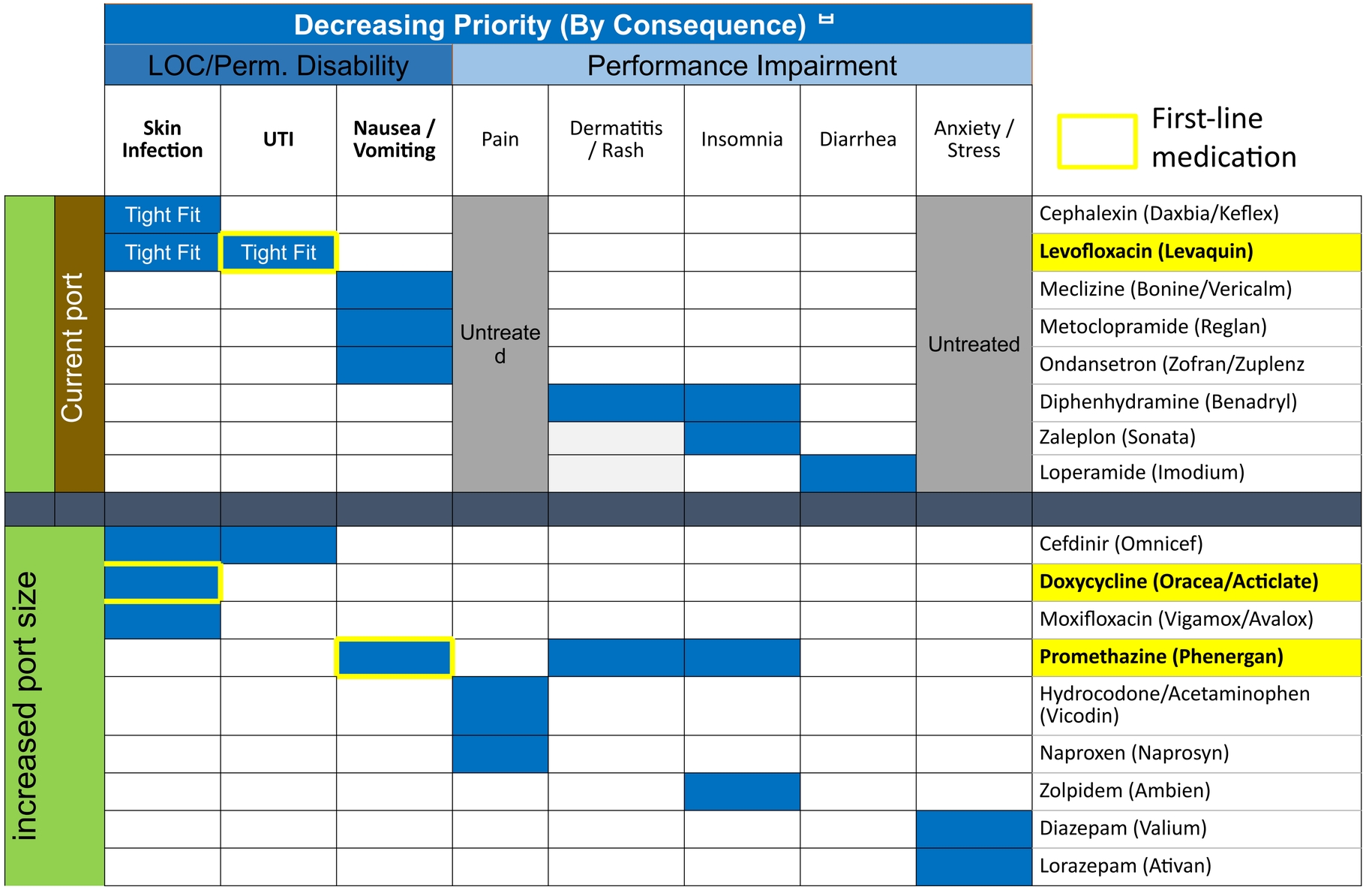
- The process used to determine the components of care in this scenario demonstrate the interplay between
  - Medical

Designing medical capabilities for extreme survival situations in austere environments is complicated

Questions?

Orion Spacecraft Medical Kit
https://www.flickr.com/photos/nasaorion/23128844405/in/album-72157633479431041/

Backup


Decreasing Priority (By Consequence)
LOC/Perm. Disability
Performance Impairment
Skin Infection
UTI
Nausea / Vomiting
Pain
Dermatitis / Rash
Insomnia
Diarrhea
Anxiety / Stress
First-line medication
Current port
increased port size
Tight Fit
Tight Fit
Tight Fit
Untreated
Untreated
Cephalexin (Daxbia/Keflex)
Levofloxacin (Levaquin)
Meclizine (Bonine/Vericalm)
Metoclopramide (Reglan)
Ondansetron (Zofran/Zuplenz
Diphenhydramine (Benadryl)
Zaleplon (Sonata)
Loperamide (Imodium)
Cefdinir (Omnicef)
Doxycycline (Oracea/Acticlate)
Moxifloxacin (Vigamox/Avalox)
Promethazine (Phenergan)
Hydrocodone/Acetaminophen (Vicodin)
Naproxen (Naprosyn)
Zolpidem (Ambien)
Diazepam (Valium)
Lorazepam (Ativan)