This Directed Acyclic Graph and write-up is an excerpt from a larger NASA document.

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Directed Acyclic Graphs: A Tool for Understanding the NASA Spaceflight Human System Risks

Human System Risk Board

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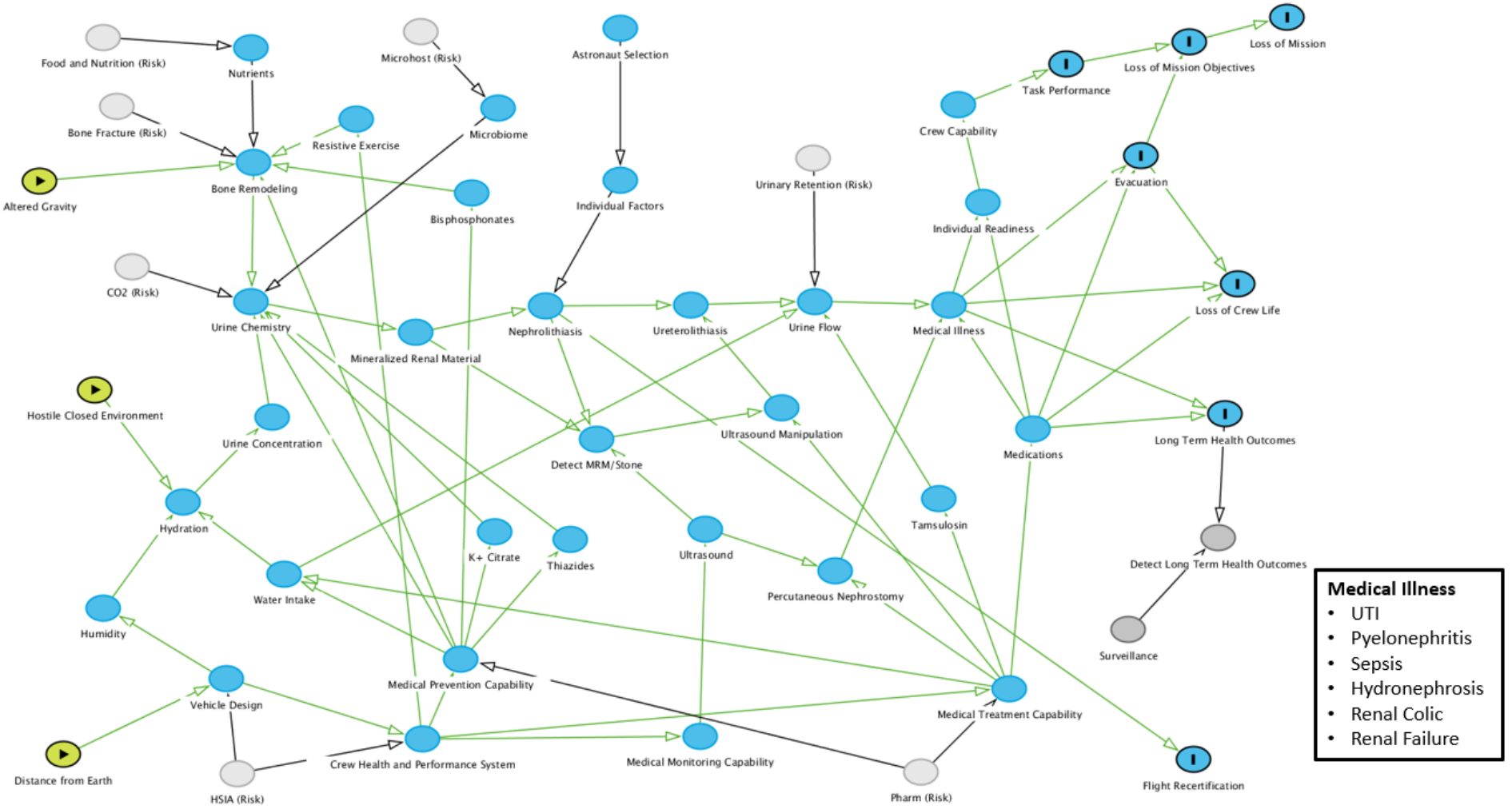
Risk of Renal Stone Formation (Renal Stone Risk)



Renal Stone Risk DAG Narrative

The Risk of Renal Stone Formation (urolithiasis) in spaceflight is predicated on the Hazards influencing **Urine Chemistry. Altered Gravity** may cause increased calcium in the blood and urine due to **Bone Remodeling**, while the **Hostile Closed Environment** may alter the **Hydration Status**.

- The central story of the Renal Stone Risk focuses on the pathway from **Urine Chemistry** to **Medical Illness**. The steps included are:
  - **Urine Chemistry** is affected by a variety of factors including the **Microbiome**. The calcium, potassium, citrate, oxalate and other chemical concentrations in the urine determine the probability that **Mineralized Renal Material** will precipitate out of the urine and adhere to the wall of the nephron or calyx.
  - The growth of this **Mineralized Renal Material** in part determines the likelihood that it will break off and become a kidney stone also called **Nephrolithiasis**. When this occurs, the stone exists in the kidney but does not cause pain or infection.
  - There is some probability that the stone in the kidney will progress and enter the ureter. This is called **Ureterolithiasis** and at this point the stone can cause pain and other symptoms. This includes affecting **Urine Flow** which can predispose to several types of **Medical Illness** including **Hydronephrosis**, **UTI**, **Pyelonephritis**, and possibly **Sepsis** if untreated.
  - All of these things can affect **Crew Capability** because the pain, nausea, and infections can cause functional incapacitation for some time, typically less than 14 days unless the stone fails to pass. With failure to pass and progression to other **Medical Illnesses**, there is a chance that **Evacuation** or **Loss of Crew Life** could occur. Effects on **Individual Readiness**, **Crew Capability** or **Evacuation** can lead to problems with **Task Performance** that can lead to **Loss of Mission Objectives** or **Loss of Mission** if severe.
- There are several contributing factors that can modify the likelihood of each of the above steps occurring. Those include:
  - **Urine Chemistry** is affected by:
    - Excess calcium in the blood that can occur as a result of **Bone Remodeling** which is affected by the **Bone Fracture (Risk).**
    - Changes in Urine Concentration that are affected by Hydration Status
    - And the **CO2 (Risk)** that affects the acid-base balance in the body.
  - **Nephrolithiasis** is affected by **Individual Factors** such as genetic predispositions as well as by **Astronaut Selection** as those individuals with a high risk of renal stones would not be selected into the Astronaut Corps.
  - Urine Flow is also affected by the Urinary Retention (Risk).
- To counteract the progress of this process, multiple **Crew Health and Performance System** Capabilities must be considered in **Vehicle Design.** These are affected by the **HSIA (Risk).**
- **Medical Prevention Capabilities** can affect several steps in this process:
  - **Water Intake** requirements for crew affect the **Hydration Status** and has been shown to be effective at preventing stone formation.

  - **Potassium Citrate** and **Thiazide** medications directly affect the **Urine Chemistry** and can help prevent stone formation.
  - **Exercise** and **Bisphosphonate** medications directly affect **Bone Remodeling** including the calcium released into the bloodstream.
  - **Nutrients** affect **Urine Chemistry** through the intake of various substances such as oxalate, calcium, magnesium, etc. and must be considered in the **Food and Nutrition (Risk).**
  - Medical Monitoring Capabilities:
    - **Ultrasound Diagnosis** is a key monitoring capability for several reasons. It allows diagnosis and monitoring of **Mineralized Renal Material** and **Nephrolithiasis** before they become significant clinical issues. **Ultrasound** may also detect stones within the ureter.
- It also enables several treatment options discussed below:
  - Medical Treatment Capabilities:
    - Recent progress has been made in focused ultrasound applications that enable non-invasive **Ultrasound Manipulation** of stones in the kidney before they enter the Ureter. It also may enable **Ultrasound Manipulation** of stones in the Ureter including the capability to remove some stones from the proximal or distal Ureter and decreasing the time that crew are symptomatic.
    - In the case of **Hydronephrosis** or **Pyelonephritis**, **Ultrasound** can be used to guide insertion of a **Percutaneous Nephrostomy** Tube that can alleviate symptoms and help stabilize an otherwise sick astronaut.
    - **Tamsulosin** is a medication that relaxes the smooth muscle in the Ureter and can help allow **Ureterolithiasis** to pass faster.
    - **Medications** can include pain medications like NSAIDs and Opioids as well as anti-emetic medications such as Ondansetron that can control the symptoms of the **Medical Illnesses** caused by renal stones. This can also include antibiotics in the cases of **UTI** and **Pyelonephritis**. Effectiveness of all medications is in part affected by the **Pharm (Risk).**
- Failure to diagnose and treat renal stones can lead to **Long Term Health Outcomes** including chronic kidney disease and other issues. **Surveillance** post-mission and post career enables us to **Detect Long Term Health Outcomes** and better characterize the long term risk.