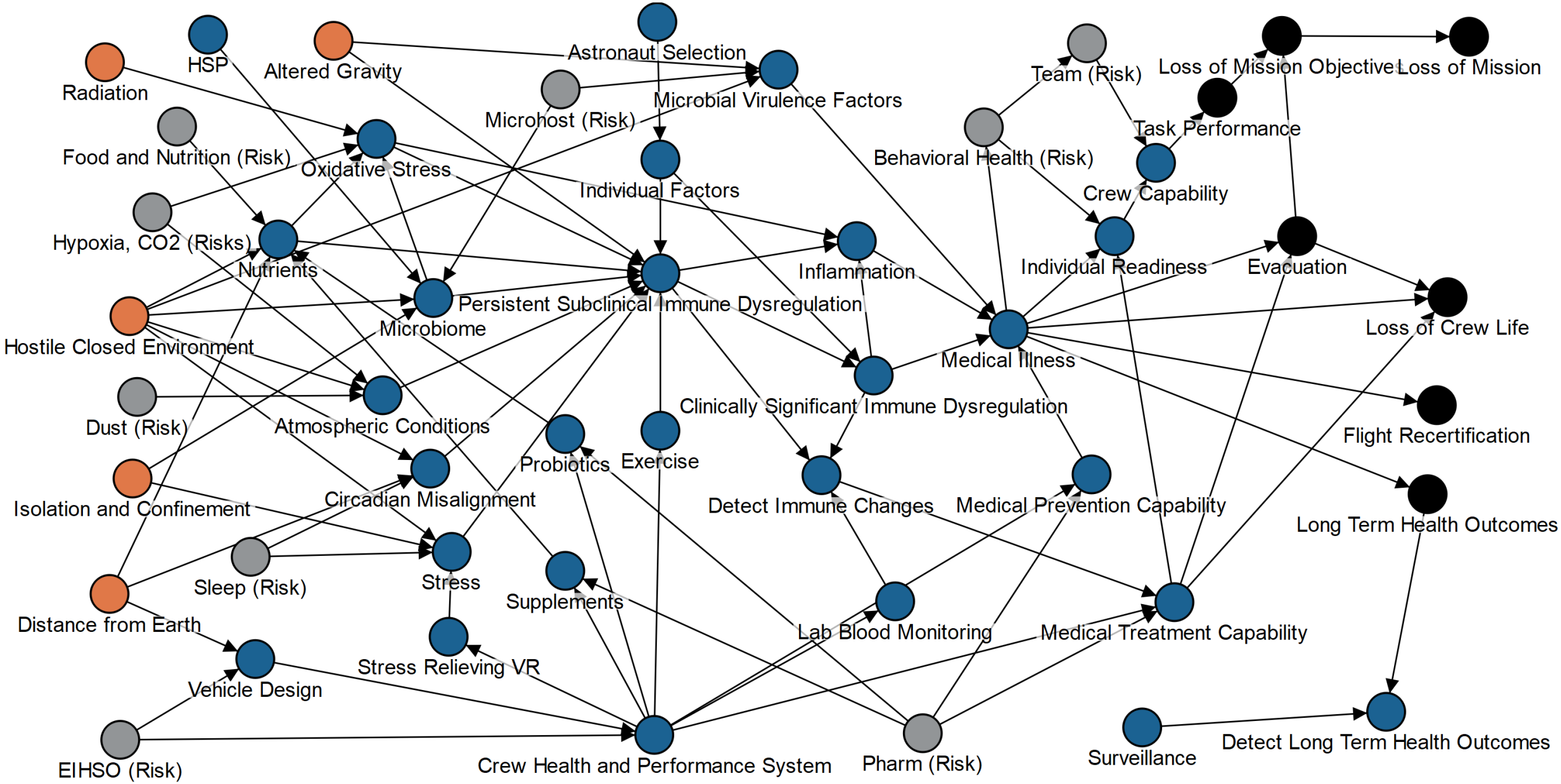
Immune Risk Directed Acyclic Graph Narrative

- The central issue in the Immune risk is the progression from **Persistent Subclinical Immune Dysregulation** -> **Clinically significant Immune Dysregulation** -> **Medical Illness**. **Oxidative Stress**, **Persistent Subclinical Immune Dysregulation** and **Clinically Significant Immune Dysregulation** can affect **Inflammation** levels in the body that contribute to **Medical Illness**.
  - **Subclinical Immune Dysregulation** refers to changes in cellular proliferation and function that does not have a known clinical issue directly following it.
  - **Clinically Significant Immune Dysregulation** refers to the threshold at which those cellular issues have a known prognostic indication for impending disease.
  - The **Medical Illnesses** that can result are a function of both hypoactive and hyperactive immune dysregulation
  - Hypoactive dysregulation predisposes astronauts to increased probability of infections
  - Hyperactive dysregulation predisposes astronauts to increased probably of hypersensitivity reactions like rashes and autoimmune disease
- Increasing probability of **Medical Illnesses** contributes to deterioration of **Individual Readiness** and **Crew Capability** which affects **Task Performance**, likelihood of **Evacuation** for medical reasons, and in severe cases can contribute to **Loss of Crew Life**. Persistent medical issues post flight and post career may affect **Flight Recertification** and **Long-Term Health Outcomes**.
- Contributors to the start of this chain of events include:
  - **Radiation** exposure leads to **Oxidative Stress** that can contribute to immune dysregulation**.**
  - **Nutrients** are dependent on the safe and acceptable **Food and Nutrition (Risk)**.
  - The **Microbiome** which is dependent on the status of the **Microhost (Risk)**.
  - **Health Stabilization Program (HSP)** may reduce the risk of harmful microorganisms entering the crew Microbiome.
  - **Atmospheric Conditions** including airborne content affected by the **Hypoxia, CO2, Dust (Risks).**
  - **Circadian Misalignment** associated with the **Sleep (Risk)** is known to affect immune function.
  - **Stress** associated with the **Behavioral (Risk)** is known to affect immune function.
- Countermeasures that affect immune system function must be included in the **Crew Health and Performance System** and accommodated in **Vehicle Design**. These are affected by the **EIHSO (Risk)** and include:
  - Countermeasures that may prevent Persistent Subclinical Immune Dysregulation
    - **Probiotics** and **Supplements** which are dependent on the Pharm (Risk) and may require different storage modalities.
    - Other stress relieving techniques such as **Stress relieving** Virtual Reality **(VR)**.
  - **Exercise** has been shown to improve Subclinical changes in the immune system.
  - **Lab Blood Monitoring** (2x baseline, monthly during flight, R+0, R+45) enables the ability to Detect Immune Changes that are either subclinical or clinically significant. When detected, these can enable further interventions including
    - **Medical Treatment Capability** that responds to the infections or hypersensitivity reactions that occur and seek to minimize the consequences of those medical conditions.
    - This is dependent on the Pharm (Risk) as medications used are subject to stability and pharmacokinetic (PK)/pharmacodynamic (PD) issues.
- The likelihood of infectious diseases (**Medical Illness**) in a mission is also affected by **Microbial Virulence Factors** which have been shown to change in spaceflight.
- **Long Term Health Outcomes** that may occur as a result of immune dysregulation must be included in **Surveillance** post flight and post-career in order to effectively **Detect Long Term Health Outcomes** and characterize the magnitude of this risk in the Long-Term Health domain. These can include hypersensitivity conditions, autoimmune disorders, and cancer.


Radiation
HSP
Altered Gravity
Astronaut Selection
Microhost (Risk)
Microbial Virulence Factors
Food and Nutrition (Risk)
Oxidative Stress
Individual Factors
Hypoxia, CO2 (Risks)
Nutrients
Inflammation
Persistent Subclinical Immune Dysregulation
Microbiome
Hostile Closed Environment
Dust (Risk)
Atmospheric Conditions
Clinically Significant Immune Dysregulation
Probiotics
Exercise
Isolation and Confinement
Circadian Misalignment
Detect Immune Changes
Medical Prevention Capability
Sleep (Risk)
Stress
Supplements
Distance from Earth
Lab Blood Monitoring
Medical Treatment Capability
Stress Relieving VR
Vehicle Design
ElHSO (Risk)
Crew Health and Performance System
Pharm (Risk)
Surveillance
Detect Long Term Health Outcomes
Team (Risk)
Loss of Mission Objective
Loss of Mission
Task Performance
Behavioral Health (Risk)
Crew Capability
Individual Readiness
Evacuation
Loss of Crew Life
Medical Illness
Flight Recertification
Long Term Health Outcomes