Objective: Define successive bed rest campaigns leading to a potential VIIP countermeasure

To determine if the analog is successful, changes need to occur in following **outcome measures** (dependent variables):

- Intracranial pressure
- Retinal nerve fiber layer
- Choroidal engorgement
- Globe flattening
- Axial biometry
- Optic nerve sheath diameter distention
- Cycloplegic refraction
- Visual acuity

Study parameters (independent variables) to include:

- CO₂
- Sodium
- Exercise (resistive & aerobic)
- Strict tilt angle

What information can the currently defined studies provide?

- Karina/Joerne enVIIP: \( \angle 6°, 12°, 18° + \) eye changes; \( \angle 12° \) w/ 1% CO₂; \( \angle 12° + \) LBNP
- Vascular Compliance: Compares effects of more and less compliance
  - VIIP strongly prefers to add CO₂ to Vascular Compliance
- Vizzeri/Laurie: 1 hour with 1% CO₂ at \( \angle 6° \)
  - VIIP prefers to add 2 compliance groups and longer duration
- Scott: Effects of exercise modalities at \( \angle 15° \)
- NSBRI Pilot – Confirms facility capabilities for CO₂ administration, etc. Defines tilt \( \angle \).
  - VIIP prefers to do multiple tilts \( \angle 6°, 9°, 12° \) with 2 compliance groups (unless another study identifies optimum angle e.g. 9 degrees)
Pilot CO2

<table>
<thead>
<tr>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
<th>FY17</th>
<th>FY18</th>
<th>FY19</th>
<th>FY20</th>
<th>FY21</th>
<th>FY22</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pilot

Expected study parameters:
• 24 hours at $\angle 6^\circ$ Head Down Tilt (HDT)
• CO$_2$ at 0.5% - 1%
• Data collection mirrors ISS Ocular Health
• Prefer 2 Compliance groups
• Sodium levels ??
• N = ??

Assumptions:
• NSBRI sponsored
• Studies completed before this campaign begins:
  • Karina/Joern enVIIP: 5 hrs. at enviHab
  • Location: enviHab
Acute CO₂

Preferred Study parameters:
• 5 - 7 days at ∠12° HDT or 7 - 10 days at ∠9° HDT or 10 - 14 days at ∠6° HDT
  (the tilt angle and duration should be defined by previous studies and what elicits VIIP related change)
• CO₂ at 0.5% - 1% depending on duration and safety
• 2 compliance groups – high (females) and low
• Sodium levels similar to ISS (fixed/constrained)
• N = ?

Assumptions:
• Studies completed before this campaign begins:
  • Karina Bowman / Joern Rittweger 5 hrs. at enviHab
  • NSBRI Pilot 24-hour with CO2 at enviHab
  • Vascular Compliance bedrest at UTMB
  • J. Scott Exercise at JSC
• Location: enviHab
• Year 1 – planning, definition, approvals, pilot.
• Year 2 - Implementation
Chronic CO₂

Study parameters:
- ∠ tbd° Head Down Tilt (HDT) depending on results of Acute study
- Duration: Extended from Acute CO₂ study to ~ 1 month
- CO₂ at 0.5% - 1.0% depending on duration and safety
- 2 compliance groups – high (females) and low
- Sodium levels similar to ISS (fixed/constrained)
- Exercise – resistive (or resistive AND aerobic like ISS)
- N = ?

Assumptions:
- Studies completed before this campaign begins:
  - Acute CO₂ at enviHab
  - Mechanical Countermeasures NRA14
  - J. Scott - Exercise
- Location: enviHab
- Year 1 – planning, definition, approvals, pilot.
- Year 2 - Implementation
Study parameters:
• CO₂ (fixed)
• Tilt (fixed)
• Sodium similar to ISS (fixed)

Countermeasures to be tested
• Mechanical device
• Exercise modalities
• Pharm (only if no mechanical CM has proven effective)

Assumptions:
• Studies completed before this campaign begins:
  • Acute & Chronic CO₂ at enviHab
  • Mechanical Countermeasures NRA14
  • J. Scott – Exercise
  • Location: enviHab