Prevention of Serious Adverse Events Following Angiography (PRESERVE) Study
• 2x2 Factorial Design
• Interventions:
  ◦ Isotonic sodium bicarbonate vs isotonic saline
  ◦ N-Acetylcysteine vs placebo
- **Fluid administration protocol**
  - Pre-procedure: 3-12 ml/kg/hr over 1-12 hours
    - Inpatient: 1 ml/kg/hr for 6-12 hours
    - Outpatient: 3 ml/kg over 1 hour
  - Post-procedure: 6-12 ml/kg/hr over 4-12 hours
    - Inpatient: 1 ml/kg/hr for 6-12 hours
    - Outpatient: 1.5 ml/kg/hr for 4 hours

- **N-Acetylcysteine/Placebo**
  - 1200 mg po 1 hour pre-angiography
  - 1200 mg po 1 hour post-angiography
  - 1200 mg po bid on subsequent 4 days
- Primary endpoint (MAKE-D)
  - Death within 90 days
  - Need for RRT within 90 days
  - Persistent decline in kidney function at day 90
    - Defined as a 50% increase in serum creatinine, verified on repeat measurement 7-14 days later
Secondary Endpoints

- CIAKI
- Death within 90 days
- Renal components of the primary endpoint
  - Need for RRT within 90 days
  - Persistent decline in kidney function at day 90
- Hospitalization for ACS, heart failure of CVA within 90 days
- All-cause hospitalization within 90 days
Tertiary outcomes
- Development of ESRD within 1 year
- 1-year all-cause mortality
• **Sample Size**
  ◦ Postulated event rates:

<table>
<thead>
<tr>
<th></th>
<th>Bicarbonate</th>
<th>Saline</th>
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</thead>
<tbody>
<tr>
<td><strong>NAC</strong></td>
<td>5.59%</td>
<td>7.46%</td>
<td>6.52%</td>
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<tr>
<td><strong>Placebo</strong></td>
<td>7.46%</td>
<td>9.95%</td>
<td>8.70%</td>
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<tr>
<td></td>
<td>6.52%</td>
<td>8.70%</td>
<td>7.6%</td>
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◦ $\alpha = 0.025$
◦ $\beta = 0.10$ (power 90%)
◦ 3% loss to follow-up
◦ Projected sample size – 7,680 subjects
- **Study sites**
  - 33 VA Medical Centers
    - 7,860 patients
  - 10 Australian centers
    - 1,000 patients

- **Study Duration**
  - 30 months for subject enrollment
Proposed ancillary studies

- Biomarker repository
  - Urine and serum samples at
    - Baseline
    - 2-4 hours post-angiography
    - 96 hours
    - 90 days

- Long-term follow-up