How to Interpret and Present a Journal Club: Using 2019 Beers Criteria® References

Presented by PGY-2 Geriatric Residents

Coordinated by Dawn Gerber, PharmD, BCGP, FASCP
PGY-2 Geriatric Residency Program Coordinator
Midwestern University College of Pharmacy, Glendale, Arizona
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Please access www.ascp.com/qa and find the session title to submit your questions.
LEARNING OBJECTIVES

At the conclusion of this activity, the learner should be able to:

1. Identify the different approaches and formats in presenting a journal club.
2. Demonstrate journal club methods using a variety of publications.
3. Interpret the findings of various articles which lead to the updated AGS Beers Criteria
Disclosures

• Dawn Gerber
• Taylor Naberhaus
• Sarah Visintainer
• Chris Blum & Emily Weigand
• Nicole Cheung
• Micaela Leblanc
• Shannon Riggins

have no actual or potentially relevant conflict of interest in relation to this activity.
<table>
<thead>
<tr>
<th>Journal Club</th>
<th>Corresponding 2019 Beers Criteria® statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, Van den brink W. Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case-control study. PLoS Med. 2017;14(10):e1002396.</td>
<td>“Avoid; exceptions are when transitioning from opioid therapy to gabapentin or pregabalin, or when using gabapentinoids to reduce opioid dose, although caution should be used in all circumstances.”</td>
</tr>
<tr>
<td>Cummings, J, Isaacson S, Mills R, et al. Pimavanserin for Patients with Parkinson’s Disease Psychosis: A Randomized, Placebo-Controlled Phase 3 trial. Lancet. 2014; 383(9916):533-540.</td>
<td>&quot;After reviewing and discussing the evidence on antipsychotics to treat psychosis in patients with Parkinson disease, the panel decided to remove aripiprazole as preferred...”</td>
</tr>
<tr>
<td>Thorlund K, Druyts E, Wu P, Balijepalli C, Keohan D, Mills E. Comparative Efficacy and Safety of Selective Serotonin Reuptake Inhibitors and Serotonin-Norepinephrine Reuptake Inhibitors in Older Adults: A Network Meta-Analysis. Journal of the American Geriatrics Society. 2015;63(5):1002-1009.</td>
<td>&quot;The serotonin-norepinephrine reuptake inhibitors (SNRIs) have been added to the list of drugs to avoid in patients with a history of falls or fractures (Table 3).&quot;</td>
</tr>
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Gabapentin, Opioids, and the Risk of Opioid-Related Death: A population-based nested case-control study

Taylor Naberhaus, PharmD
PGY2 Geriatric Pharmacy Resident
Midwestern University, Glendale, Arizona
tnaber@midwestern.edu
PIES Method

Patient Population  Intervention  Endpoints  Statistics

Baroletti S. Crit Pathw Cardiol. 2004;3(4):205-8
Inclusion:

- Ontario Drug Benefit individuals 15-105 years-old
- Use of ≥1 oral or transdermal opioid prescription from 1997-2013
- Cases: Those who died from opioid-related cause

Exclusion:

- Rarely used opioids, parenteral or intranasal, and methadone
- Diagnosis of cancer or evidence of palliative care
- Cases: Opioid overdose identified as suicide or homicide from coroner

Generalizability:

- Those being treated with opioid analgesics for non-cancer related chronic pain
### Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n=1256)</th>
<th>Controls (n=4619)</th>
<th>Standardized Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid dose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 MME daily</td>
<td>141 (11.2%)</td>
<td>1,162 (25.2%)</td>
<td>0.37</td>
</tr>
<tr>
<td>20-49 MME daily</td>
<td>228 (18.2%)</td>
<td>1,340 (29%)</td>
<td>0.26</td>
</tr>
<tr>
<td>&gt;200 MME daily</td>
<td>496 (39.5%)</td>
<td>949 (20.5%)</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>Median number of drugs (IQR)</strong></td>
<td>11 (7-15)</td>
<td>9 (6-13)</td>
<td>0.3</td>
</tr>
<tr>
<td>SSRI use</td>
<td>556 (45.1%)</td>
<td>1,690 (36.6%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Other antidepressant use</td>
<td>622 (49.5%)</td>
<td>1,736 (37.6%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Benzodiazepine use</td>
<td>971 (77.3%)</td>
<td>2,604 (56.4%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Long-acting opioid</td>
<td>784 (62.4%)</td>
<td>1,828 (39.6%)</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Table adapted from Gomes T, et al. *PLoS Med. 2017;14(10):e1002396*
Significant risk of adverse events with no benefit for gabapentinoids in chronic back pain

2016 CDC Guideline for Chronic Pain

- Nonpharmacologic and nonopioid pharmacologic therapy preferred for chronic pain
- Gabapentin and pregabalin preferred for diabetic neuropathy and post-herpetic neuralgia

Gabapentin use has increased for chronic back pain

Significant risk of adverse events with no benefit for gabapentinoids in chronic back pain

<table>
<thead>
<tr>
<th>Patients Exposed to Gabapentin</th>
<th>Cases Opioid-related Death (n=1256)</th>
<th>Controls No Opioid-related Death (n=4619)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Not Exposed to Gabapentin</td>
<td>1,101</td>
<td>4,306</td>
</tr>
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</table>

Self-Calculated Odds Ratio = 1.94
Primary endpoint: Gabapentin use

- 12.3% of cases and 6.8% of controls, p<0.001
- Odds of death is 49% higher in those exposed to gabapentin, p=0.005

Secondary endpoint: Gabapentin dose

- Moderate (900 to 1,799 mg daily) or high dose (1,800 mg daily or more) associated with ~60% increased odds of opioid-related death, p=0.024

Sensitivity analysis: Recent NSAID use

- No significant association between recent exposure to concomitant NSAIDs and opioid-related death, p=0.083
Conditional logistic regression

• Adjusted all models for important covariates

Odds ratios

• “Adjusted OR=1.49”
• Calculated OR=1.94
References


Renal Insufficiency in Concert with Renin-angiotensin-aldosterone Inhibition Is a Major Risk Factor for Hyperkalemia Associated with Low-dose Trimethoprim-sulfamethoxazole in Adults

Sarah Visintainer PharmD
PGY-2 Geriatrics Pharmacy Resident
Texas Tech University Health Sciences Center School of Pharmacy
Dallas, Texas
RAAMbo Method

- **Representation**
  - Patient enrollment & recruitment
- **Allocation/Adjustment/Accountability**
  - Stratification into subgroups
  - Matching enrollment to outcomes
- **Measured/Maintained**
  - Outcome measurement and maintenance of groups
- **Blinding/objective**
  - How patients are blinded
  - Subjective or objective outcomes
**Inclusion**

- > 20 years old
- 1st time prophylaxis for PCP with TMP-SMX (dose < 80mg TMP and < 400mg SMX per day)
- January 2014 - January 2015
- Secondary referral hospital in Ehime, Japan

**Exclusion**

- Previously prescribed TMP-SMX
- Therapeutic TMP-SMX dose
- No K data within 30 days of treatment
- Serum K ≥ 5mEq/L when starting treatment
- Hemodialysis patients
- At least weekly blood data unavailable

PCP = pneumocystis pneumonia, K = potassium, TMP-SMX = trimethoprim-sulfamethoxazole
## Baseline Characteristics

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<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>Total patients, n</td>
<td>186</td>
</tr>
<tr>
<td>Age (years), median (range)</td>
<td>66 (20-94)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>95 (51.1)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²), mean (SD)</td>
<td>72.5 (29.9)</td>
</tr>
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</table>

## Concomitant drugs, n (%)

<table>
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<th>Drug</th>
<th>n (%)</th>
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<tr>
<td>ACEi/ARB</td>
<td>44 (23.7)</td>
</tr>
<tr>
<td>B-blockers</td>
<td>22 (11.8)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>16 (8.6)</td>
</tr>
<tr>
<td>K-sparing diuretic</td>
<td>6 (3.2)</td>
</tr>
</tbody>
</table>
A Retrospective cohort study

186 patients enrolled and evaluated
Start TMP-SMX
Baseline serum K

Serum K at least once weekly

Serum K
Serum K

Last serum K drawn

Day 1 of therapy
Day 30 of therapy
B/O

Gender

Identify risk factors for hyperkalemia associated with low-dose TMP-SMX

Age

eGFR

Concomitant medications

2019 ASCP Annual Meeting & Exhibition
Aged to Perfection
#ASCP50
<table>
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<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
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<tr>
<td>Age ≥ 65 years</td>
<td>2.36 (0.82-4.71)</td>
<td>0.10</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>1.97 (0.82-4.71)</td>
<td>0.13</td>
</tr>
<tr>
<td>eGFR &lt;60 (mL/min/1.73m2)</td>
<td>4.62 (1.93-11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>2.24 (0.93-5.37)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Potassium (K) changes after TMP-SMX Initiation

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<th>Duration reaching maximal serum K, median (range)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max serum K (mEq/L), median (range)</td>
<td>4.4 (3.3-6.2)</td>
</tr>
<tr>
<td>Change in K: baseline to maximal serum K, median (range)</td>
<td>0.4 (-1–2.4)</td>
</tr>
<tr>
<td>Hyperkalemia, n (%)</td>
<td>32 (17.2)</td>
</tr>
</tbody>
</table>
Strengths, Limitations, Application

Strengths

• Median age: 66 years (60.8% > 65 years)
• Evaluated low dose TMP-SMX, addressed gap in evidence

Limitations

• Single centered study in Japan
• 30 day follow up
• “Use with caution in patients on ACEI or ARB and decreased creatinine clearance” – low quality of evidence, strong recommendation
References


Pimavanserin for Patients with Parkinson’s Disease Psychosis: A Randomized, Placebo-Controlled Phase 3 trial

Christopher Blum, PharmD & Emily Weigand, PharmD
PGY-2 Geriatric Pharmacy Residents
VA Northeast Ohio Healthcare System
Cleveland, Ohio
Background

• About 50% of Parkinson’s disease patients will demonstrate psychosis in the form of hallucinations and delusions

• Initial therapy involves mitigating dopaminergic activity with subsequent initiation of antipsychotics, which can ultimately worsen parkinsonism

• Pimavanserin is an atypical antipsychotic indicated for use in Parkinson’s disease psychosis, offering the benefit of controlling psychosis without effecting dopamine signaling

### Objectives/Outcomes

<table>
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<tr>
<th><strong>Primary Objective</strong></th>
<th>Assess efficacy and safety of pimavanserin among patients with Parkinson’s disease psychosis over six weeks.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>Change in total score of Parkinson’s disease-adapted scale for assessment of positive symptoms (SAPS-PD) from baseline to day 43.</td>
</tr>
</tbody>
</table>
| **Secondary Outcomes**| 1. Change in clinical global impression-severity (CGI-S) and improvement (CGI-I) scales  
2. Change in caregiver burden scale (CBS)  
3. Change in Scales for Outcomes in PD for nighttime sleep quality (SCOPA-NS) and daytime wakefulness (SCOPA-DS)  
4. Change in unified Parkinson’s disease rating scale (UPDRS) |

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Study design

- Randomized, double-blind, placebo controlled
- 52 centers in USA and Canada

### Inclusion

- > 40 y/o
- PD psychosis for >1 yr
- Psychosis symptoms severe enough to warrant treatment
- Mini-mental status examination score of at least 21 points out of 30 and no delirium
- Stable dose of anti-PD drugs

### Exclusion

- Psychosis secondary to other cause
- Dementia diagnosed with or before PD
- Stroke or recent MI
- Uncontrolled serious medical illness
- CHF
- QTcB >460ms for men or >470ms for women
- Concomitant antipsychotics, anticholinergics, or drugs with potential to prolong QT interval

Study Design

• Randomly assigned 1:1 to pimavanserin or placebo

NPI: neuropsychiatric inventory items A (delusions) and B (hallucinations)
SAPS: scale for assessment of positive symptoms for hallucinations or delusions
SAPS-PD: Parkinson’s disease adapted SAPS

Statistics

Power calculation
• Sample size of 200 for 90% power at 5% significance level to detect a 3 point difference in SAPS-PD

Analysis type
• Modified ITT analysis

Superiority or non-inferiority
• Non-inferiority tested using ANCOVA
• Margin of 5 agreed upon by FDA

Key statistical tests used
• All efficacy measures analyzed with mixed model repeated measures

ITT: Intention to treat
ANCOVA: analysis of covariance
FDA: Food and Drug Administration
## Results

<table>
<thead>
<tr>
<th>Primary analysis</th>
<th>Placebo (n=90)</th>
<th>Pimavanserin (n=95)</th>
<th>Treatment Change</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS-PD</td>
<td>−2.73 (0.67)</td>
<td>−5.79 (0.66)</td>
<td>−3.06 (0.94)</td>
<td>−4.91 to −1.20</td>
<td>0.0014</td>
</tr>
</tbody>
</table>

Conclusion

Authors’ conclusion

• Pimavanserin significantly reduced psychotic symptoms in patients with moderate to severe Parkinson’s disease

Clinical significance

• Additional option for PD psychosis is favorable given current limited options
• Novel selective receptor profile may offer advantages compared to antipsychotics
• Further studies warranted to determine place in therapy as compared to antipsychotics and to further assess safety/tolerability compared to other agents

Critique

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ 2 week-lead in may have reduced placebo</td>
<td>X Drug company sponsored, designed, and analyzed study results</td>
</tr>
<tr>
<td>response</td>
<td>X 6 week duration insufficient to make safety/tolerability conclusions</td>
</tr>
<tr>
<td>✓ 6 week duration is consistent with accepted</td>
<td>X First study to utilize SAPS-PD</td>
</tr>
<tr>
<td>precedent for psychosis studies per FDA</td>
<td>X No comparison to standard of care (antipsychotics)</td>
</tr>
</tbody>
</table>

Place in Beer’s Criteria 2019 Update

- Pimavanserin added as an exception to the list of antipsychotics to avoid in PD patients as it was found not to worsen PD symptoms
Proton Pump Inhibitors and Risk of Mild Cognitive Impairment and Dementia

Nicole Cheung, Pharm.D.
PGY-2 Geriatrics Pharmacy Resident
Upstate University Hospital, Syracuse, New York
Cheungn@upstate.edu | 315-492-5254
Theory

- Increased Beta-Amyloid
- Decreased Vitamin B-12

PPI Use

- Formation of plaques
- Disruption of cell function
- Increased homocysteine

↑ Beta-Amyloid

↓ Vitamin B-12

Association ≠ Causality

Alzheimer’s Disease
Proton Pump Inhibitors and Risk of Mild Cognitive Impairment and Dementia


- Observational, longitudinal study
- 33 Alzheimer’s Disease Centers
- September 2005 to September 2015
PIES: Patient Population

• Are the inclusion and exclusion appropriate?

• Are there differences in patient characteristics between groups?

• Is this patient population applicable to my patients and practice site?
Inclusion Criteria

• Normal cognition (n = 7404)
• MCI (n = 3082)
• Information about PPI use at every visit

Exclusion Criteria

• Baseline age < 50 years (n = 240)
• Unstable diagnosis (n = 1523)
• Transition to impaired cognition but not MCI (n = 167)

✓ Inclusion and exclusion criteria are appropriate
<table>
<thead>
<tr>
<th>BASELINE CHARACTERISTICS</th>
<th>Always PPI Users n = 884</th>
<th>Intermittent PPI Users n = 1925</th>
<th>Never PPI Users n = 7677</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>73.5 ± 8.9</td>
<td>73.7 ± 8.4</td>
<td>72.6 ± 9.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>522 (59.0)</td>
<td>1168 (60.7)</td>
<td>4756 (62.0)</td>
<td>0.18</td>
</tr>
<tr>
<td>African American, n (%)</td>
<td>92 (11.1)</td>
<td>249 (13.7)</td>
<td>971 (13.5)</td>
<td>0.14</td>
</tr>
<tr>
<td>High school or above, n (%)</td>
<td>833 (94.4)</td>
<td>1793 (93.4)</td>
<td>7318 (95.7)</td>
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<tr>
<td>Heart disease, n (%)</td>
<td>289 (32.8)</td>
<td>588 (30.8)</td>
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<td>Diabetes mellitus, n (%)</td>
<td>131 (14.8)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>543 (61.7)</td>
<td>1144 (59.6)</td>
<td>3646 (47.6)</td>
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<tr>
<td>Depression, n (%)</td>
<td>239 (27.1)</td>
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<td>Stroke, transient ischemic attack, n (%)</td>
<td>84 (9.6)</td>
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<td>Histamine-2 receptor antagonist , n (%)</td>
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<td>Anticholinergic medication, n (%)</td>
<td>212 (24.0)</td>
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<td>Number of visits, median (IQR)</td>
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<td>519 (27.0)</td>
<td>1586 (20.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke/transient ischemic attack, n (%)</td>
<td>84 (9.6)</td>
<td>190 (9.9)</td>
<td>520 (6.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Histamine-2 receptor antagonist, n (%)</td>
<td>106 (12.0)</td>
<td>440 (22.9)</td>
<td>651 (8.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anticholinergic medication, n (%)</td>
<td>212 (24.0)</td>
<td>491 (25.5)</td>
<td>1034 (13.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of visits, median (IQR)</td>
<td>3.0 (2.0–4.0)</td>
<td>5.0 (3.0–7.0)</td>
<td>4.0 (2.0–6.0)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Baseline characteristics are statistically different**

**Not adjusted as potential confounder**

---

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PIES: Intervention

• Is the intervention based on current practice guidelines?

• Are there previous well-conducted studies on this intervention?
Previous Studies


• 3076 patients – 23% PPI users
  • ≥ 75 years old
• Dementia:
  • HR = 1.38
    • 95% CI = 1.04–1.83, P = 0.02
• Alzheimer’s Disease:
  • HR = 1.44
    • 95% CI = 1.01–2.06
    • P = 0.04


• 73679 patients – 4% PPI users
  • ≥ 75 years old
• Dementia:
  • HR = 1.44
    • 95% CI = 1.36–1.52, P < 0.001
✓ PPI and cognitive impairment
✓ Addressed limitations from previous studies:
  ✓ Diagnoses by experienced clinicians
  ✓ Broad age range of individuals
PPI

- Omeprazole
- Omeprazole-sodium bicarbonate
- Esomeprazole
- Lansoprazole
- Pantoprazole
- Rabeprazole
- Dexlansoprazole

✘ Dose
✘ Frequency
✘ Duration
✘ Self-reported
PIES: Endpoint

• What are the endpoints?

• Is the primary endpoint relevant to purpose of study?

• Is the endpoint clinically significant?
### Primary Endpoint

- Risk of incident MCI, dementia, and AD with PPI use

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cognitive Decline to MCI or Dementia from Any Cause*</th>
<th>Cognitive Decline to MCI or Alzheimer’s Disease*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 10486</td>
<td>0.78 (0.66-0.93), 0.005</td>
<td>0.82 (0.69-0.98), 0.026</td>
</tr>
<tr>
<td>Always vs never PPI user</td>
<td>0.84 (0.76-0.93), 0.001</td>
<td>0.82 (0.74-0.91), &lt; 0.001</td>
</tr>
</tbody>
</table>

* Hazard Ratio (95% Confidence Interval), P-value

- **✓** Hard endpoint
- **✓** Clinically & statistically significant
PIES: Statistics

- Was the sample size for power achieved?

- Determine clinical significance
  - Evaluate absolute values
  - Calculate number needed to treat or number needed to harm
  - Misleading: Odds Ratio, Relative Risk Ratio

- Are the statistical tests appropriate?
Statistics

- No calculations for sample size
- Only provided hazards ratio
- Multivariable Cox Regression Analyses
  - Association between PPI use and annual conversion
  - Controlled for:
    - Demographic characteristics
    - Vascular comorbidities
    - Mood
    - Use of anticholinergics
    - Use of H2RA

- Appropriate statistical analyses
- Addressed majority of confounding factors
- Family history, head injury

? Missing power, but n = 10,486
? No absolute values, but HR < 1
References


Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly

Micaela Leblanc, PharmD
PGY-2 Geriatric Pharmacy Resident
VA Connecticut Healthcare System
West Haven, CT

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GATE Frame

GATE = Graphical Appraisal Tool for Epidemiological studies

• Attracts visual learners

• Incorporates five sections:
  • Study participation
  • Intervention
  • Comparison
  • Outcome
  • Study time

Research Question

Over a 5 year period, does the daily use of 100mg of enteric-coated aspirin have an effect on cardiovascular disease or bleeding events in healthy older adults?

Methods: Population

12 centers in Australia
28 centers in United States
83,163 patients screened
19,114 patients randomized
Eligibility

**Inclusion**

- Generally healthy individuals aged 65 years and older (African American) or 70 years and older (all other groups)
- Able to give informed consent
- Able to attend a study visit

**Exclusion**

- Past medical history with established CVD or atrial fibrillation
- Pill compliance less than 80% during 4 week run-in phase
- Anemia or other condition with high risk of bleeding
- Condition likely to cause death within 5 years
- Current use of aspirin for secondary prevention

Methods

Overall Design:
- Double-blind, randomized, placebo-controlled trial with an average follow-up of 5 years
- Four week run-in phase to assess compliance before randomization

Randomization:
- Remotely randomized via ASPREE web portal in a ratio of 1:1
- Stratified according to trial center and age (65 to 79 years or ≥ 80 years)

Primary Outcome: Cardiovascular Events

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No Event</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>448</td>
<td>9077</td>
</tr>
<tr>
<td>N=9525</td>
<td>(4.7%)</td>
<td>(95.3%)</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>474</td>
<td>9115</td>
</tr>
<tr>
<td>N=9589</td>
<td>(4.9%)</td>
<td>(95.1%)</td>
</tr>
</tbody>
</table>

HR (95% CI): 0.95 (0.83-1.08)

Median of 4.7 years

Primary Outcome: Hemorrhagic Events

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No Event</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=9525</td>
<td>361</td>
<td>9164</td>
</tr>
<tr>
<td>(3.8%)</td>
<td>(96.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=9589</td>
<td>265</td>
<td>9324</td>
</tr>
<tr>
<td>(2.8%)</td>
<td>(97.2%)</td>
<td></td>
</tr>
</tbody>
</table>

HR (95% CI): 1.38 (1.18-1.62)

Median of 4.7 years

Prevalence vs. Incidence

Hazard ratio, 1.38 (95% CI, 1.18-1.62) P<0.001

Aspirin
Placebo

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The use of low-dose aspirin as primary prevention in older adults resulted in significantly higher risk of major hemorrhage and did not result in significantly lower risk of cardiovascular disease than placebo.

No relevant policy considerations, however, 2019 Beers criteria has changed their recommendations in response to this evidence.

Consider bleeding and cardiovascular risk, drug interactions, past medical history.

Willingness to discontinue aspirin.
References


Comparative Efficacy and Safety of Selective Serotonin Reuptake Inhibitors and Serotonin-Norepinephrine Reuptake Inhibitors in Older Adults: A Network Meta-Analysis

Shannon Riggins, PharmD
PGY2 Geriatric Resident
University of Maryland School of Pharmacy

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Disclosure

• I have no personal or financial interests to disclose
### PIES Method of Critique

<table>
<thead>
<tr>
<th>P</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Intervention</td>
</tr>
<tr>
<td>E</td>
<td>Endpoints</td>
</tr>
<tr>
<td>S</td>
<td>Statistics</td>
</tr>
</tbody>
</table>
Research Question:

What is the efficacy and safety comparison of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) in older adults?
# Population

- 15 Randomized Control Trials (RCTs)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Countries</strong></td>
<td>US, Canada, UK, Australia, Germany, Italy</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td><strong>Inclusion criteria:</strong> $\geq$ 60 years old w/dx of MDD 67-80</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Mostly community</td>
</tr>
<tr>
<td></td>
<td>1 trial – community &amp; hospital</td>
</tr>
<tr>
<td></td>
<td>1 trial – hospital</td>
</tr>
<tr>
<td><strong>Depression Scale</strong></td>
<td>HDRS or MADRS*</td>
</tr>
<tr>
<td><strong>Length of Therapy</strong></td>
<td><strong>Inclusion Criteria:</strong> minimum of 6 weeks. 6 - 12 weeks; 11/15 were 8 weeks or longer.</td>
</tr>
</tbody>
</table>

*HDRS - Hamilton Depression Rating Scale
MADRS - Montgomery–Asberg Depression Rating Scale
Intervention: Methods

• Systematic Review and network meta-analysis
  • Search Strategy: Comprehensive literature search conducted in numerous databases utilizing terms related to each intervention of interest
  • Study Selection: Two investigators reviewed all abstracts and proceedings with a third investigator providing arbitration for any study discrepancies

• Randomized controlled trials (RCTs) comparing SSRIs or SNRIs with placebo or another active antidepressant were included:
  • citalopram, escitalopram, paroxetine, fluoxetine, sertraline, duloxetine, venlafaxine
  • trazodone and amitriptyline were included to strengthen network evidence
Outcome: Efficacy

Primary Endpoint:

- Efficacy: 50% reduction in depression score from baseline utilizing the HDRS or MADRS scale
Outcome: Dizziness

Primary Endpoint:

- Safety: dizziness, vertigo, syncope, falls, loss of consciousness
### Outcome:
Falls, Syncope, Vertigo, Loss of Consciousness

#### Falls

<table>
<thead>
<tr>
<th>Trial</th>
<th>Medication</th>
<th>No. of Falls</th>
<th>No. of Patients in Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Paroxetine</td>
<td>2 (0.7%)</td>
<td>334</td>
</tr>
<tr>
<td>b.</td>
<td>Duloxetine</td>
<td>1 (0.5%)</td>
<td>201</td>
</tr>
<tr>
<td>c.</td>
<td>Sertraline</td>
<td>1 (0.3%)</td>
<td>360</td>
</tr>
</tbody>
</table>

#### Syncope

<table>
<thead>
<tr>
<th>Trial</th>
<th>Medication</th>
<th>Episodes of Syncope</th>
<th>No. of Patients in Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Escitalopram</td>
<td>1 (0.8%)</td>
<td>129</td>
</tr>
<tr>
<td>a.</td>
<td>Placebo</td>
<td>1 (0.8%)</td>
<td>134</td>
</tr>
<tr>
<td>c.</td>
<td>Sertraline</td>
<td>1 (0.3%)</td>
<td>360</td>
</tr>
</tbody>
</table>

- No data was available on episodes of vertigo or loss of consciousness
- Adverse events were likely underreported due to inadequate capture at the time of the trials
Statistical Analysis

• **Geometric networks** were plotted for each outcome

• The **Bucher test** evaluated the differences in estimates between two sets of evidence for inconsistencies

• Appropriate use of **Bayesian network meta-analysis**
  • Comparative odds ratio and 95% credible intervals (CrIs) were obtained from a logistic regression group
    • **Markov Chain Monte Carlo sampling** converted the comparative odds ratio into relative risk (RRs) with 95% (CrIs)
2019 Updated American Geriatrics Society Beers Criteria for Potentially Inappropriate Medications states SNRIs should be used in caution for adults with a history of falls or fractures.
References


How to Interpret and Present a Journal Club:
Using 2019 Beers Criteria® References

Presented by PGY-2 Geriatric Residents:
Taylor Naberhaus, Sarah Visintainer, Chris Blum & Emily Weigand, Nicole Cheung, Micaela Leblanc, Shannon Riggins

Coordinated by:
Dawn Gerber, PharmD, BCGP, FASCP

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