Research Prioritization Topic Brief

Topic 15: “Macular Degeneration”

Comparative effectiveness of treatment for patients with age-related macular degeneration (AMD).

PCORI Scientific Program Area: Assessment of Prevention, Diagnosis and Treatment Options

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### Overview/definition of topic

**DESCRIPTION OF CONDITION**
- Macular degeneration is a degenerative disease of the central portion of the retina (macula).
- Age-related macular degeneration (AMD) is the most common form.
- Two types of AMD:
  - Dry (atrophic) is chronic.
  - Wet (neurovascular or exudative) is an abrupt onset that can rapidly progress to blindness if untreated.
- Dry AMD is a risk factor or precursor state for wet AMD, with early dry phase converting to more severe wet form in 10-20% of patients.
- Early stage of dry AMD is asymptomatic.

### Relevance to patient-centered outcomes

**SYMPTOMS**
- With AMD, there is progressive visual loss, primarily of the central (rather than peripheral) vision.
- Central vision is needed for reading and driving.
- Central vision loss is associated with increased falls and hip fractures.

### Burden on Society

**PREVALENCE**
- 10-15 million people in the United States are living with AMD, two million of whom have advanced disease.
- Prevalence is increasing (by 2020, three times as many people will have AMD than in 1995).
- Prevalence increases with age, with 2% of people at age 40 to 25% at age 80.
- Risk factors include age, smoking, family history, cardiovascular disease, lightly pigmented skin, and female sex.

**INCIDENCE**
- 15-year cumulative incidence is 14% for early AMD and 3% for late AMD.

**QUALITY OF LIFE (QOL)**
- AMD is the leading cause of blindness in the United States.
- AMD is associated with impairment in driving, ambulation, reading, recognizing faces, and all activities of daily living.

**PRODUCTIVITY**
- Condition can result in loss of independent living.

**FUNCTIONAL CAPACITY**
- Leads to vision impairment or blindness.

**USE OF HEALTH CARE SERVICES**
- Among Medicare beneficiaries diagnosed with wet AMD between 2004 and 2008, the mean cost per case for the year after diagnosis was $12,422 ($4,884 higher than the year before diagnosis).

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How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?

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<tr>
<th>Options for Addressing the Issue</th>
<th>TREATMENT OPTIONS</th>
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<td>Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?</td>
<td>There are no proven effective treatments for dry AMD, which is asymptomatic in the early stages.</td>
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<td>For wet AMD, treatment options include:</td>
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<td>o <strong>Laser photocoagulation</strong> prevents further vision loss by destroying the new vessels that develop in AMD. Introduced in the 1980s and less commonly used now, in part because it is generally not indicated for disease at the center of the macula.</td>
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<td>o <strong>Photodynamic therapy</strong> uses a combination of laser and injected medicine. Requires evaluation by a retina specialist to determine eligibility.</td>
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<td>o <strong>Macular translocation surgery</strong> involves moving the macula to a different part of the retina to restore central vision. Still largely experimental.</td>
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<td>o <strong>Intravitreal injections</strong> with vascular endothelial growth factor (VEGF) inhibitors (prevent or inhibit VEGF; which are proteins that stimulate the creation of new blood vessels) such as ranibizumab, pegaptanib, bevacizumab, or aflibercept. In the past six years, VEGF inhibitors have largely replaced laser photocoagulation and photodynamic therapy. Ranibizumab has been shown in a randomized sham-controlled study to be effective in the treatment of AMD. Bevacizumab has been used off-label to treat AMD, despite the absence of similar supporting data. A recent comparison of AMD treatments trials (CATT study) showed that ranibizumab and bevacizumab did not differ in effects on visual acuity for wet AMD when administered according to the same schedule, and suggests that modification of monthly dosing regimens is feasible. Uncertainties include:</td>
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<td>▪ <strong>Dosing regimen</strong></td>
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<td>▪ <strong>Cost</strong></td>
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<td>▪ Safety concerns, including possible increased risk of systemic vascular events</td>
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<td>o <strong>Diet and supplements</strong> such as omega-3 fatty acids and/or high doses of antioxidants and minerals such as vitamins C and E, beta-carotene, and zinc. A meta-analysis suggests that foods rich in omega-3 fatty acids may be associated with a lower risk of AMD, there is insufficient evidence (few prospective studies and no randomized controlled trials [RCTs]), to support their consumption for AMD prevention.</td>
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<td>o <strong>Visual rehabilitation</strong> using visual aids can be effective in managing vision loss.</td>
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What could new research contribute to achieving better patient-centered outcomes?

- New research on comparative effectiveness, safety, and cost of management options could inform providers and patients. Research on prevention of AMD as well as management of vision loss might also improve patient-centered outcomes.
- A technology assessment published in 2009 by the Canadian National Institutes for Health Research evaluated cost-effectiveness associated with different dosing regimens of VEGF inhibitors; additional research in this area could help inform dosing decisions.

Have recent innovations made research on this topic especially compelling?

The most recent innovation has been the approval of VEGF inhibitors for the treatment of AMD. Current uncertainties regarding comparative effectiveness, safety, and cost of different VEGF inhibitors, as well as unanswered questions about optimal dosing regimens, may make this topic compelling for new CER. Advances in retinal imaging represent another innovation that could lead to improved screening and management.

How widely does care now vary?

Management of AMD in the United States is generally provided by ophthalmologists with appropriate expertise. There is evidence that black patients are less likely than white patients to receive VEGF inhibitor therapy.11

What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?

**Medline search from 1/1/2008 to 12/31/2013:**
- Total: 2,341 citations
  - Labeled as RCTs: 333 citations
  - Systematic Reviews: 159 citations

**Search on ‘clinicaltrials.gov’:**
- Ongoing trials: 420*
- Completed trials: 398

*The AREDS2 trial is an ongoing RCT designed to evaluate whether the vitamin supplements lutein, zeaxanthin, or omega-3 fatty acids affect the course of dry AMD.

How likely is it that new CER on this topic would provide better information to guide clinical decision making?

- New CER that provides compelling information about screening or prevention measures could inform clinical decision making by patients and providers.
- More information about different responses to treatment by patient subgroups may also guide clinical decision making.
- Primary care providers might encourage routine eye exams to more patients (eg, patients older than 50, relatives of affected individuals) if new findings supported that approach.
- If patients knew that they should be screened based on age or risk factors, they might be willing to get their eyes examined more often.
- If people knew, they could prevent AMD by engaging in lifestyle changes (like changing their diet or taking vitamins)

### Potential for New Information to Improve Care and Patient-Centered Outcomes

**FACILITATORS**
- Most care is provided by ophthalmologists, so rapid dissemination of new findings to the target audience is feasible with a targeted audience of one type of health care provider.
- Active patient advocacy groups (AMD Alliance, Macular Degeneration Foundation, and Macular Degeneration International) could assist with dissemination to patients

**BARRIERS**
- New findings would likely need to be strongly compelling to result in changes in decision making by ophthalmologists.
How likely is it that the results of new research on this topic would be implemented in practice right away?

- There are certainly knowledge gaps, but there may not be a strong sense among ophthalmologists with expertise in AMD that current treatment practice needs to change (unless there is compelling research showing new and improved screening and treatments).
- Also, if new research findings support that lifestyle changes or taking vitamins or omega-3 supplements would prevent or reduce worsening of AMD, then research findings might be implemented quickly by patients.

Would new information from CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?

- This is a relatively active area of research, with 424 ongoing trials identified in clinicaltrials.gov and identified by the search terms “macular degeneration.”
- New information about the most effective prevention and treatment therapies, including optimal dose and timing of treatments, may remain current for several years.

REFERENCES

10. www.cadth.ca/media/pdf/htis/L0026%20Pharmacological%20Management%20in%20AMD%20final.pdf

APPENDIX: Topic Questions
1) What is the optimal treatment and dosing schedule as a patient with AMD? Does it vary based on age, gender, ethnicity, etc.?

   **Population:** Typically, these are older white patients.
   **Importance:** This is an important question because of the significant impact that age-related macular degeneration has on the United States’ population, and the implication for patients (number of visits, out-of-pocket costs) and for third-party payers.