Multiple studies have established the role anti-VEGF therapy plays in treating neovascular age-related macular degeneration (AMD). Debate exists about the optimal spacing of injections, but researchers agree that compliance with follow-up is essential for long-term VA maintenance. Little research has been done in the United States to evaluate loss to follow-up (LTFU) rates and risk factors. Data from European studies have identified several risk factors for high LTFU rates, but the risk factors may be different in the United States.

We conducted a study to determine LTFU rates and risk factors within a large retina practice that has offices in Pennsylvania, Delaware, and New Jersey.

**STUDY DESIGN**

Patients receiving anti-VEGF injections for neovascular AMD from April 2012 to January 2017 were identified, and data from their treatment were analyzed. The intervals between injections and visits were measured. LTFU was defined as at least one interval that exceeded a duration of 12 months to be considered LTFU. Baseline characteristics included age, race, regional adjusted gross income based on home zip code, distance to clinic, and VA.

**SUMMARY OF FINDINGS**

A total of 9,007 patients were included in the final analysis, of whom 2,003 (22.2%) were LTFU. This LTFU rate surprised us, as most physicians, including us, surmise that patients with neovascular AMD adhere to recommendations. The high rate of LTFU underscores the importance of identifying key risk factors and encouraging return visits. Some of these risk factors were identified in our analysis. Patient sex was not a significant factor in LTFU rate.

Age was a statistically significant risk factor associated with LTFU, and increased incidence of LTFU was observed in older patients ($P < .01$ for all ages vs. youngest group; Table 1). This is expected given the increasing number of comorbidities with aging. The rise in comorbidities may prevent individuals from functioning independently. This is particularly damaging to these patients, as neovascular AMD treatment typically requires multiple visits per year.

Race was also found to be a statistically significant risk factor in LTFU rates. Patients who were African American, Asian, Hispanic/Native American/Pacific Islander, or refused to identify a race showed a higher...

**AT A GLANCE**

- Limited research has been performed in the United States on patients with AMD who were receiving anti-VEGF therapy and were lost to follow-up.
- A study examining rates of patients lost to follow-up assessed risk factors including age, income, and distance from care.
- The study results identify populations of patients who are at highest risk for not returning for anti-VEGF treatment.
incidence of LTFU status compared with white patients (*P* < .01 for all groups; Table 2). Disparities in compliance with follow-up by race have been previously described, and the results appear equivocal. Distrust in the health care system may be one of the reasons LTFU differences exist among races, which may be relevant in explaining the high LTFU rate in patients with an unreported race. Further study, however, will be required to elucidate the underlying differences in LTFU among different races.

Regional adjusted gross income was a significant risk factor in LTFU rates (Figure). As we initially expected, rates of LTFU increased as regional adjusted gross income decreased, with rates ranging from about 26% for patients with incomes less than $50,000 to 18% for patients with incomes more than $100,000. Although not necessarily reflective of an individual’s income, regional socioeconomic status has been associated with increased mortality after adjusting for personal income. This may be helpful when designing future interventions that target susceptible populations.

Distance is another factor to consider when evaluating patients LTFU. In our analysis, patients living more than 20 miles from a clinic had a significant (5-7%; *P* < .01) increase in LTFU rate. However, the population living more than 20 miles from a clinic composed only about 11% of the total study population, which suggests that distance may not play as large a role in LTFU rates in our geographic location as we initially assumed. The relatively narrow distribution may suggest that distance acts as more of a barrier to initiating treatment than to compliance with follow-up.

Evaluation of VA provided varied results. Worse VA at first and final injection was associated with increased odds of LTFU. Patients who had no change in vision from first to final injection had the highest odds of LTFU, with risk of LTFU being 50% higher when compared with patients who experienced improvement of more than 2 lines. This is important when one considers that anti-VEGF therapy plays a

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### TABLE 1. AGE OF PATIENTS AND FOLLOW-UP STATUS

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Total Patients</th>
<th>Not Lost to Follow-Up</th>
<th>Lost to Follow-Up</th>
<th>Percentage Lost to Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80</td>
<td>3,687</td>
<td>3,104</td>
<td>583</td>
<td>16%</td>
</tr>
<tr>
<td>81-85</td>
<td>2,171</td>
<td>1,713</td>
<td>458</td>
<td>21%</td>
</tr>
<tr>
<td>86-90</td>
<td>2,042</td>
<td>1,475</td>
<td>567</td>
<td>28%</td>
</tr>
<tr>
<td>&gt; 90</td>
<td>1,107</td>
<td>712</td>
<td>395</td>
<td>36%</td>
</tr>
</tbody>
</table>


### TABLE 2. RACE OF PATIENTS AND FOLLOW-UP STATUS

<table>
<thead>
<tr>
<th>Race</th>
<th>Total Patients</th>
<th>Not Lost to Follow-Up</th>
<th>Lost to Follow-Up</th>
<th>Percentage Lost to Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>7,905</td>
<td>6,299</td>
<td>1,606</td>
<td>20%</td>
</tr>
<tr>
<td>African American</td>
<td>143</td>
<td>104</td>
<td>39</td>
<td>27%</td>
</tr>
<tr>
<td>Asian</td>
<td>101</td>
<td>67</td>
<td>34</td>
<td>34%</td>
</tr>
<tr>
<td>Unreported</td>
<td>832</td>
<td>519</td>
<td>313</td>
<td>38%</td>
</tr>
<tr>
<td>Hispanic, Native American, and Pacific Islander</td>
<td>26</td>
<td>15</td>
<td>11</td>
<td>42%</td>
</tr>
</tbody>
</table>


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Figure. Regional adjusted gross income was a statistically significant risk factor seen in the study, with lower rates of LTFU status seen in wealthier brackets.
pivotal role in maintaining vision. If patients are unaware of the consequences of interrupted therapy, then they may be more likely to discontinue treatment after experiencing no improvement. Therefore, it may be necessary to consistently reinforce the role of anti-VEGF therapy in vision maintenance.

**FINAL THOUGHTS**

Our study demonstrates a clear problem with follow-up compliance in patients with neovascular AMD, with more than one in five patients LTFU after at least one treatment session. These findings are alarming, particularly given the risk of further vision loss after discontinued treatment. Previous studies have focused on optimal spacing of injections with the hope of reducing treatment burden and improving patient adherence. Unfortunately, these patients still require multiple visits per year for examination and evaluation. This reinforces the need to address key risk factors of LTFU and to identify alternative treatment modalities that provide sustained anti-VEGF release. A combination of both approaches may help reduce LTFU rates and improve outcomes of neovascular AMD treatment.


JASON HSU, MD
- Codirector of Retina Research and Faculty Member of the Retina Service, Wills Eye Hospital; Partner, Mid Atlantic Retina; and Associate Professor of Ophthalmology, Thomas Jefferson University; all in Philadelphia
- jhsu@midatlanticretina.com
- Financial disclosure: Grants (Ophthotech, Roche/Genentech, Santen); Personal Fees (Ophthotech)

ANTHONY OBEID, MD, MPH
- Postdoctoral Research Fellow, Wills Eye Hospital, Philadelphia
- aobeid@midatlanticretina.com
- Financial disclosure: None