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# **Wet Age-Related Macular Degeneration in the Asia-Pacific: Critical Pathways Forward**

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A Report Based on an Asia-Pacific  
Wet Age-Related Macular Degeneration Coalition Expert Summit  
Convened in Hong Kong, February 2013



# KEY POINTS

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1. Age-related macular degeneration (AMD), which primarily strikes people over the age of 50, is the second-leading cause of irreversible blindness in the world.
2. The prevalence of early and late AMD among Asia-Pacific populations aged 40 to 79 is estimated at 6.8%. The number of people affected is expected to increase dramatically during the coming decades as those populations age. According to United Nation projections, almost 24% of Asians will be aged 60 years or older by 2050.
3. During the past decade, new therapies and diagnostic techniques, in the form of VEGF-targeted anti-angiogenesis therapy and spectral domain optical coherence tomography (SD-OCT), have produced a true paradigm shift in the diagnosis and treatment of wet AMD, the most serious form of the disease. Patients now have effective treatment options that can help keep them from going blind, and in some cases, even restore vision. This paradigm shift can have a major impact on eye care programs in Asia-Pacific countries.
4. Research has found, however, that Asians are more likely than non-Asians to develop a poorly understood variant of AMD, polypoidal choroidal vasculopathy (PCV). The pathogenesis, genetic and environmental risk factors, natural history, and treatment response of PCV is not as well established as it is for classic AMD.
5. The majority of patients with wet AMD living in the Asia-Pacific region are not receiving the optimal evidence-based care that is needed to maintain vision and prevent progressive vision loss. The treatment window for wet AMD is relatively short, and access to immediate, continuing care is essential. Any delay or interruption in care can mean the difference between retaining vision and blindness.
6. The barriers in the Asia-Pacific region to receiving timely and optimal care are many. They include:
  - A lack of awareness by both the public and policymakers about AMD, especially about the need for early diagnosis and treatment;
  - Limited patient access to diagnostic screening, including SD-OCT, and treatment;
  - The high financial cost of anti-VEGF treatment;
  - Limited access to continuing care, particularly for patient follow-up for anti-VEGF treatment;
  - Fragmented delivery-of-care systems; and
  - A limited scientific understanding of the pathogenesis and differences in treatment of AMD and PCV.
7. As a result of these and other barriers, many patients
  - Do not seek treatment at all;
  - Are delaying seeking diagnosis and treatment; and
  - Are not receiving optimal treatment.
8. All these factors increase the likelihood of potentially catastrophic outcomes for patients with wet AMD in the Asia-Pacific region. Overcoming these current challenges to the early diagnosis and effective treatment of wet AMD will require the concerted efforts of stakeholders in the Asia-Pacific and the global community, including patients, family caregivers, physicians, researchers, scientists, industry leaders, regulators, policymakers, funders, the media, and society-at-large.



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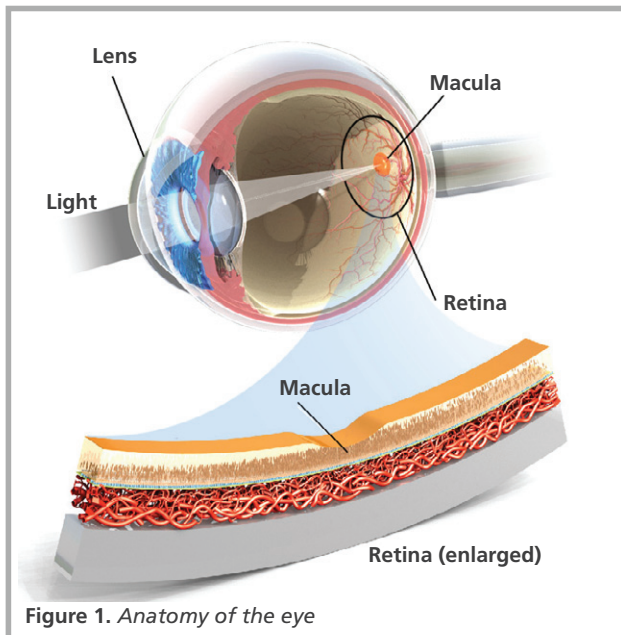


# Introduction

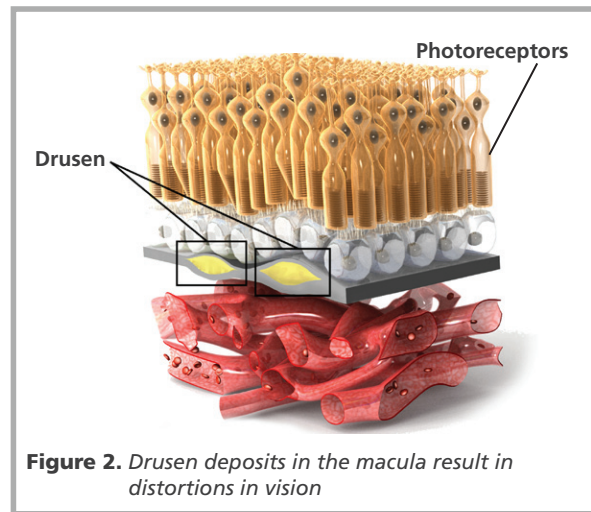
## What Is AMD?

Age-related macular degeneration (AMD) is a disease associated with aging that gradually destroys sharp, central vision needed to read, recognize faces, drive, and in general, to see most things clearly. As its name implies, AMD affects the macula, which is located in the centre of the retina, the light-sensitive tissue at the back of the eye. The macula is the part of the eye needed to see fine details.

There are two main types of AMD: early (with no or minimal vision loss) and late (with vision loss). Late can be further split into dry, or atrophic, AMD (also known as geographic atrophy) and wet AMD. Both the dry and wet forms can occur in one or both eyes, although the development of AMD in one eye appears to increase the risk that AMD will develop in the second eye. Neither form of AMD is painful. As a result, the disease may not be diagnosed until it produces marked loss in vision. When AMD affects one eye, it often goes undetected because the brain uses visual information from the second eye to compensate for any loss of vision in the first eye.



Early AMD, the more common form of macular degeneration, is characterized by the accumulation of drusen, small yellowish deposits that build up beneath the macula. As the number of drusen or their size increases, cells in the retina may become damaged, producing distortions in vision that are most apparent when reading. Early AMD generally develops slowly, but can progress to late-stage dry AMD, which can impose significant vision loss.



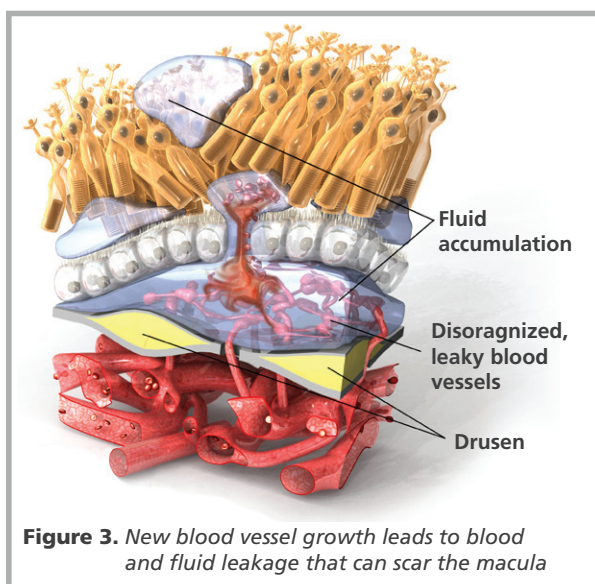
Wet AMD is the more serious form of the disease. For reasons that are as yet unclear, 10% to 15% of adults with early or dry AMD will suddenly progress to wet AMD and experience abnormal blood vessel growth under the macula. The growth of new blood vessels, known as angiogenesis or neovascularization, leads to blood and fluid leakage that can scar the macula and retina, producing rapid and permanent loss of central vision in as little as three months.<sup>1</sup> An example of an early symptom of wet AMD is that straight lines appear wavy.

Unlike Western societies, AMD is a relatively unappreciated disease in Asia-Pacific countries, in part because it usually affects people over the age of 50 years whereas the Asia-Pacific region has had a relatively young population for a long time. AMD was therefore once believed to be uncommon among Asians, but recent epidemiologic studies have found that the prevalence of the disease in Asian populations is comparable to that in white populations once age is taken into account. A 2010 meta-analysis, for example, found that the pooled prevalence of AMD among the populations of five Asian countries was 6.8%, which compares to 8.8% in similarly aged white populations.<sup>2</sup>

Importantly, research has also indicated that Asians may be more likely than whites to develop what may be a variant of wet AMD, polypoidal choroidal vasculopathy (PCV).<sup>3</sup> PCV and wet AMD resemble each other clinically, but they behave differently in terms of pathogenesis, symptom presentation, disease progression, and response to treatment. The natural history of wet AMD involves progressive scarring, whereas scarring in PCV tends to occur in periodic episodes.<sup>3</sup> The most commonly used treatment for PCV is photodynamic therapy (PDT) in conjunction with the drug verteporfin, although PCV

patients are also sometimes treated with anti-VEGF injections. Wet AMD, on the other hand, is treated primarily with anti-VEGF drugs. PCV is associated with an estimated 8% to 13% of wet AMD diagnoses among Western populations.<sup>3</sup> Studies involving Asian populations, however, have found a higher prevalence. In Korean and Japanese populations, for example, an estimated 22% to 50% of wet AMD diagnoses were associated with PCV.<sup>3</sup> Genetic differences may explain the variations in AMD and PCV prevalence,<sup>4</sup> or it may be that the limitations of current imaging tools have not yet revealed its prevalence in other populations.<sup>4</sup> In addition, few efforts have been made to date to identify PCV in non-Asian populations.

AMD is a serious cause of vision loss and disability in all countries. In 2007, the World Health Organization (WHO) estimated that wet AMD affects 3 million people globally and accounts for 8.7% of all blindness and 50% of blindness in industrialized nations.<sup>5</sup> The WHO projects that these numbers will double by 2020 as populations age in many countries, including those in the Asia-Pacific region. According to United Nation projections, almost 24% of Asians will be aged 60 years or older by 2050.<sup>6</sup>

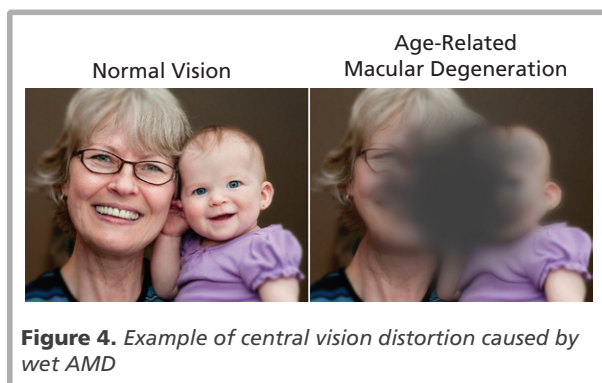


**Figure 3.** New blood vessel growth leads to blood and fluid leakage that can scar the macula

## Paradigm Change

Anti-angiogenesis focused research, which began in the early 1970s, made dramatic advances in the late 1990s.<sup>7</sup> Those advances culminated in the identification of specific anti-angiogenic-related approaches to treating a variety of diseases, ranging from cancer to skin disease to blinding disorders, such as wet AMD. Presently, more than 10,000 laboratories around the world are involved in angiogenesis research, and more than USD\$5 billion has been invested globally in treatment-oriented

research and development. This rapidly developing field has witnessed important advances, particularly in the last decade, that have had a major impact on the lives of patients. Ten years ago, AMD was a significant cause of blindness in the elderly. Today, vision loss and blindness from wet AMD is largely treatable with early, appropriate care.



**Figure 4.** Example of central vision distortion caused by wet AMD

## Anti-Angiogenesis Therapies

In December 2004, the U.S. Food and Drug Administration (FDA) approved pegaptanib (intravitreal injection), the first inhibitor of angiogenesis to be successfully developed for wet AMD. Clinical trials showed that pegaptanib slowed the rate of vision loss caused from wet AMD.<sup>8</sup> This anti-angiogenic therapy, aimed at halting abnormal blood vessel growth, became recognized as an entirely new class of disease treatment.

An even more effective drug, ranibizumab, was approved for the treatment of wet AMD in the United States in late 2006. Ranibizumab, as well as pegaptanib, interferes with a small protein known as vascular endothelial growth factor (VEGF). This growth factor stimulates the angiogenesis that lies at the heart of wet AMD. Clinical trials had demonstrated that 95% of patients treated with a once-monthly intravitreal injection of ranibizumab into the eye maintained their vision as long as the injections continued over the course of the trial.<sup>9,10</sup> "Maintaining vision" meant that their ability to read a vision chart declined by no more than 15 letters, or three lines. In addition, up to 40% of those treated with monthly ranibizumab for a year experienced an improvement of 15 or more letters (3 lines) in visual acuity.

For the first time, physicians could offer their patients the opportunity to save vision, and even reverse lost vision in some individuals. The major drawbacks to this new therapy, however, were its price, about USD\$2,000 per injection, and the burden that receiving a monthly injection places on the patient and caregivers.

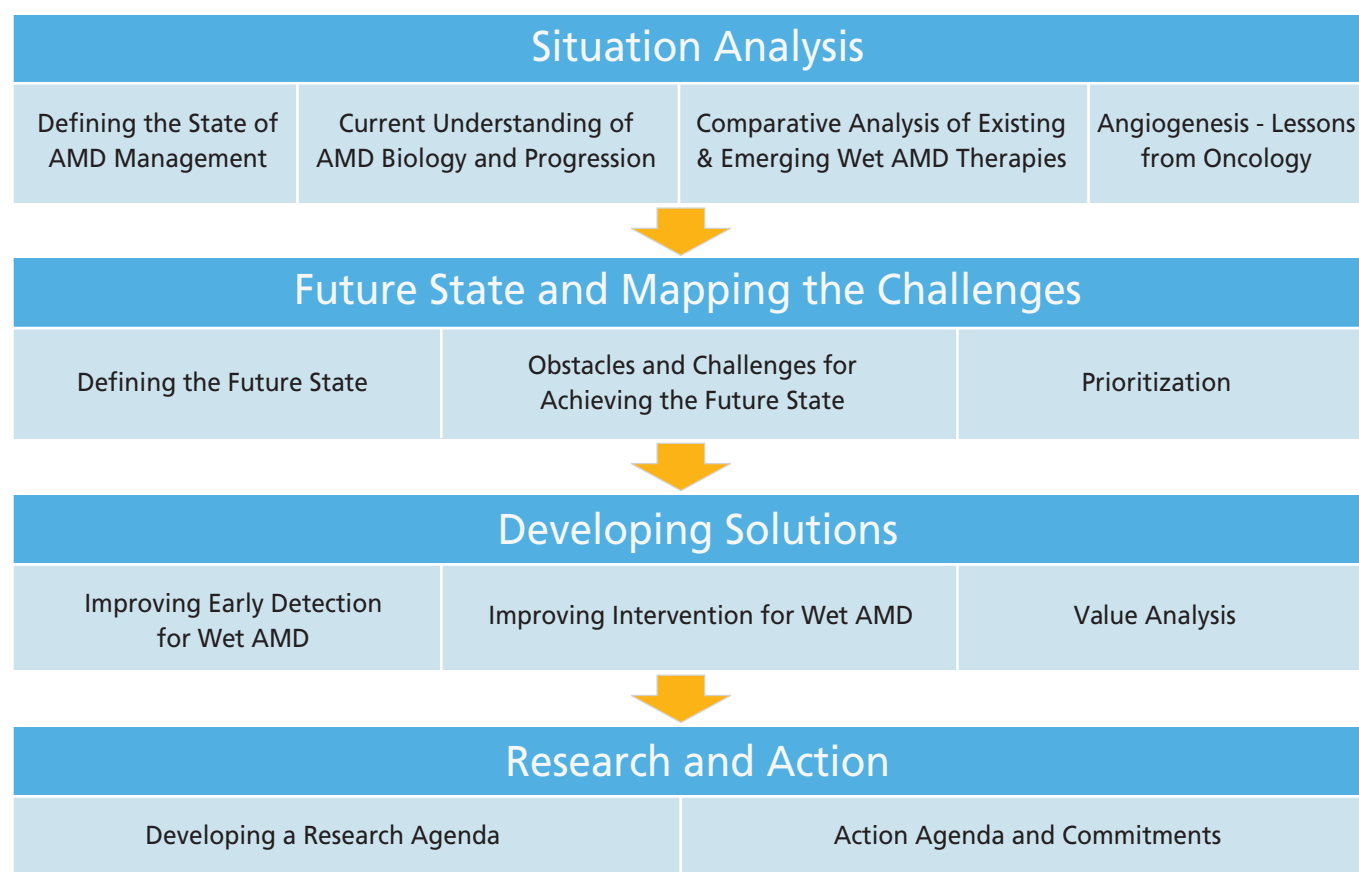


Before ranibizumab was approved, retinal specialists began experimenting with another anti-VEGF agent, bevacizumab. It had been used since 2004 for the treatment of colorectal cancer in many countries, and was later also approved for the treatment of other cancers. Bevacizumab is a larger molecule, known as a monoclonal antibody, from which ranibizumab, a monoclonal antibody fragment, is derived.

Bevacizumab is not indicated for eye diseases, and has not been approved by any regulatory authority for use in the eye. It has been shown, nonetheless, to be clinically effective for the treatment of wet AMD, and is used off label for this purpose at a cost of about USD\$50 per intravitreal injection.<sup>10</sup> (Off-label drugs are ones that are prescribed for a use not approved by a country's regulatory agency.) Because it is produced in a concentrated form in large vials for cancer treatments, bevacizumab must be divided by a compounding pharmacy into the much smaller, diluted quantities needed for treating the eye. Numerous documented cases of infection from bevacizumab's use in the eye have been reported. These cases are likely due to poor pharmacy practice when dividing the product, not the molecule itself. Clinical trials comparing ranibizumab

with bevacizumab have suggested, however, that both drugs are similarly effective at stopping disease progression and restoring visual acuity, at least when dosed monthly during the first two years of treatment.<sup>10,11</sup>

On November 18, 2011, a third anti-angiogenic drug, aflibercept, received its first global approval for the treatment of wet AMD from the U.S. FDA.<sup>12</sup> Based on a novel drug technology that fuses proteins (VEGFR1 and VEGFR2) together to neutralize not only VEGF-A (like ranibizumab and bevacizumab) but also VEGF-B and PlGF. Aflibercept is designed to be administered by intravitreal injection, every other month, following three initial monthly injections. Clinical trials comparing ranibizumab with aflibercept show that both drugs are similarly effective at stopping disease progression and restoring visual acuity with fewer injections for aflibercept.<sup>13</sup> In 2012, aflibercept was approved for the treatment of wet AMD in the European Union, Switzerland, Australia, Brazil, and Colombia. In September 2012, Japan became the first country in the Asia-Pacific region to approve aflibercept for the treatment of wet AMD.<sup>14</sup>



**Figure 5.** Schematic Flow of the Asia-Pacific Expert Summit

## Current Status of AMD Therapies in the Asia-Pacific Region

While these paradigm shifts have ameliorated the effects of AMD for Western populations, their impact in Asia-Pacific has yet to be fully realized.<sup>16</sup> In Denmark, for example, national level statistics show a 50% reduction in the incidence of blindness attributable to AMD from 2000 to 2010.<sup>17</sup>

The Asia-Pacific region has highly diverse health systems; each offers a different mix of public/private financing and delivery of medical services. This diversity can be seen in the financing and delivery of approved treatments for wet AMD and for its possible variant, PCV.

In Hong Kong, for example, treatments for both wet AMD and PCV are paid for by the patient, except for 250 patients who receive free ranibizumab treatments for wet AMD under a special government program. In Taiwan, ranibizumab treatments for wet AMD are covered by government insurance, but only up to three injections per year; PCV treatments are not covered. In Thailand, bevacizumab, but not ranibizumab, is covered by government insurance; up to 12 injections per eye are permitted throughout a patient's lifetime. Ranibizumab is also approved for the treatment of wet AMD in Thailand, but patients must cover the cost of this drug themselves. PDT treatments for PCV are generally not covered.

Under South Korea's universal government health insurance plan, wet AMD patients can receive up to 10 injections per lifetime of ranibizumab. The government pays 90% of the cost of the exam and drug, and the

patient pays for the remaining 10%. If the patient does not respond to the treatment after three months of consecutive injections, however, the treatment may be terminated; patients who wish to continue with the injections must then cover the costs themselves. PDT treatments—5 times per eye per patient lifetime—are also covered by government insurance.

In Malaysia, about 60 percent of residents are covered by a government-run universal healthcare system; the other 40 percent have private insurance. Private insurance places an annual monetary cap on medical costs; many patients, therefore, must pay out-of-pocket for all or part of their wet AMD treatments. Ranibizumab is the only drug currently approved by the Malaysian ministry of health for the treatment of wet AMD, although bevacizumab is sometimes used off-label in the private sector. Under the government health plan, patients can receive up to five PDT treatments each year.

In Singapore, where government healthcare is self-funded, both ranibizumab and PDT treatments have been approved for the treatment of wet AMD and PCV. The high cost of the treatments, particularly ranibizumab, makes it difficult, however, for most patients to afford them. In some cases, bevacizumab is used off-label as a less expensive alternative to ranibizumab. In the Philippines, most patients with wet AMD must self-pay for ranibizumab treatments, although a few private insurance companies have begun to cover some of the costs of the drug. The country's national health insurance program, PhilHealth, is currently considering covering the treatment. Because of its lower costs, bevacizumab is frequently used off-label in the Philippines for the treatment of wet AMD.



**Figure 6.** Expert Summit, Hong Kong, February 19, 2013

None of the above countries has approved aflibercept for the treatment of wet AMD, but all are in the process of doing so.

### **The Need for Improvement**

The globally expanding use of anti-VEGF therapies is dramatically improving the quality of life for countless numbers of individuals with wet AMD in the Asia-Pacific region and around the world. Many more people are now able to retain their vision and, consequently, their independence. Yet, much more can be done. Innovative research into both wet AMD and PCV is needed, for example, as are enhancements to existing healthcare systems. Such actions will help ensure that these diseases are diagnosed and treated early enough to save the sight of hundreds of thousands of people throughout the Asia-Pacific region alone over the next decade.

## **The Asia-Pacific Wet AMD Coalition Expert Summit**

Given the changes that have come with the advent of multiple effective therapies, and the fact that these therapies have revolutionized the field of ophthalmology, the Angiogenesis Foundation determined in 2009 that it was an opportune time for the AMD stakeholder community to take a step back and review the progress it had made, the challenges it faced, and the questions that needed to be answered to best meet the needs of those with wet AMD.

As a scientific nonprofit organization whose mission is to conquer disease through the control of neovascularization, the Angiogenesis Foundation recognized that it was well positioned to play the role of a neutral facilitator of such a review. The Angiogenesis Foundation immersed itself in the field of macular degeneration and began looking at how it could apply the lessons it learned from its interactions within the oncology and wound healing communities to this new area of clinical opportunity.

As its first major global step, it decided to assemble an interdisciplinary group of international leaders in AMD treatment and translational science. The International Expert Summit for Age-Related Macular Degeneration was convened in Berlin, Germany, on November 14-15, 2011. Its success led to a second event, the Latin American Wet AMD Coalition Expert Summit, which was held in Bogota, Colombia, on March 10, 2012, in

partnership with the Pan-American Retina & Vitreous Society. This was followed by a third meeting, the Australian Wet Age-Related Macular Degeneration Coalition Expert Summit, which was held in Sydney on July 12, 2012, in partnership with the Macular Disease Foundation Australia (then called the Macular Degeneration Foundation of Australia). Experts at all these meetings identified, discussed, and achieved agreement on the rationale for anti-angiogenic therapy to treat wet AMD; the role of early intervention in preventing wet AMD-associated blindness; the safety of repeated, long-term therapy; and the role of chronic suppressive anti-angiogenic therapy for wet AMD. Each meeting resulted in a white paper that provided an overview of the group's discussions and presented the key steps needed to advance the treatment of wet AMD using anti-VEGF therapies to impact the greatest number of individuals possible.

Building on the success of those earlier meetings, the Angiogenesis Foundation convened the Asia-Pacific Expert Summit on Wet Age-Related Macular Degeneration in Hong Kong on February 19, 2013. The Asia-Pacific summit, like the three earlier ones, was not a traditional scientific meeting, but rather an interactive, professionally moderated set of short presentations and roundtable discussions that aimed to establish a dialog and agreement among the participants.

The summit opened with two short presentations. One recapped what is currently known about the epidemiology, risk factors, clinical characteristics, natural history, and management of wet AMD among Asia-Pacific populations. The other offered angiogenesis lessons from the field of oncology. Under the direction of the moderator, the assembled experts then spent the rest of the morning engaging in a series of discussions that defined where the field wants to be in terms of detecting and treating wet AMD and outlined the barriers that lie in the path of achieving that goal. A graphic recorder captured key points of the discussion, enabling the participants to visually review the content of their conversations as they worked through the tasks at hand. During the summit's afternoon session, the experts focused on developing solutions to overcoming the barriers identified earlier in the day. Working off the basis laid by these discussions, the experts then developed a research agenda specific to the Asia-Pacific region that could move the field toward the desired future state of AMD prevention, diagnosis, and treatment. As the meeting progressed, the participants identified a list of desired future actions. This white paper provides an overview of the group's discussions.



## The Role of the Angiogenesis Foundation

Founded in 1994 and headquartered in Cambridge, Massachusetts, the Angiogenesis Foundation is the world's first 501(c)(3) nonprofit organization dedicated to conquering disease with approaches based on angiogenesis, the growth of new blood vessels in the body. Its global mission is to help people benefit from the full promise of angiogenesis-based medicine, and to make life-, limb-, and vision-saving treatments available to everyone in need.

As a scientific organization, the Angiogenesis Foundation is independent of any individual, institution, or commercial entity, and as such, it takes a unique approach to achieving its mission to help people lead longer, better, and healthier lives. It has helped propel innovative research involving both angiogenesis inhibitors and stimulators. Although much of this research has been pharmacological, promising studies involving nutrition and biomarkers are also being actively pursued. In addition, the Angiogenesis Foundation is constantly looking for ways to innovate patient-centered care pathways.

Angiogenesis-related research is being conducted across a remarkably wide variety of disease states. In recent years, for example, profound angiogenesis-treatment breakthroughs have been discovered in oncology, wound care, and cardiovascular disease. But nowhere has the promise of angiogenesis-related research become more apparent than in the field of ophthalmology, most notably with treatments for retinal diseases such as wet AMD, diabetic macular edema, and retinal vein occlusions.

The Angiogenesis Foundation recognizes the challenges of optimizing patient care and outcomes with such paradigm-shifting discoveries as angiogenesis-based treatments for retinal diseases. It also deeply understands that to meet the goal of improving global health through angiogenesis-based medicine, the complex needs of all the stakeholder groups involved, including patients, caregivers, patient-support organizations, physicians, researchers, scientists, industry leaders, regulators, policymakers, and funders, must be aligned and met. The Angiogenesis Foundation is committed to helping those groups work together to make sure that all people benefit from current and future advances in angiogenesis-based medicine.



**Figure 7.** Moderated discussion at Expert Summit, Hong Kong, February 19, 2013

# The Asia-Pacific Summit

The Asia-Pacific summit opened with two 15-minute background presentations by the event's co-chairs, Dr. Tien Yin Wong, director of the Singapore Eye Research Institute and professor and chairman of the department of ophthalmology at the National University of Singapore, and Dr. William W. Li, president and medical director of the Angiogenesis Foundation. Dr. Wong's presentation recapped what is currently known about the epidemiology, risk factors, clinical characteristics, natural history, and management of wet AMD among Asia-Pacific populations. Dr. Li's presentation provided an overview of how angiogenesis research is transforming the field of oncology and a discussion of the lessons that transformation offers AMD researchers, patients, and healthcare professionals.

## The State of AMD in the Asia-Pacific Region

### Epidemiology and Risk Factors

Although the epidemiology and risk factors of AMD in Western populations have been well described, less is known about the eye disease in Asia-Pacific populations. In recent years, however, epidemiologists have uncovered an increasing amount of population-based data on the prevalence, risk factors, and treatment responses of AMD among people living in the Asia-Pacific region. That emerging research has revealed both similarities and differences with Western populations. A 2010 meta-analysis, for example, found that the prevalence of AMD among Japanese, Korean, Chinese, Malay, and Indian populations was comparable to that reported in white populations, although the presentation of small drusen was less common among Asians. In that study, the pooled prevalence of early and late AMD in the Asian populations (aged 40 to 79 years) was 6.8%, which compares to 8.8% in similarly aged white populations.<sup>2</sup>

Other research suggests that Asian and white populations also share the same key AMD risk factors: age, cigarette smoking, obesity, sunlight exposure, and cardiovascular disease.<sup>4,15</sup> Some of the genetic variants associated with AMD appear to be different in Asian and white populations, while others appear to be similar.<sup>18</sup> One example of the latter is the complement factor H (CFH) Y402H gene, which is associated with the development of AMD among populations of both European and Asian ancestry. Among European-ancestry populations, the CFH CC and CT alleles have been found to be 6.35 and 2.5 times more likely, respectively, to

develop wet AMD than those with the non-risk CFH TT allele.<sup>19</sup> Among Asian populations, possession of at least one copy of the C allele has been found to increase the risk of the disease almost two-fold.<sup>20</sup> C alleles appear to be less prevalent among Asians with wet AMD, however. The CT allele, for example, is found almost five times less often among Chinese<sup>21</sup> and Japanese<sup>22,23</sup> patients with AMD than among whites with the disease. This finding suggests that other genetic factors are more likely contributing to increased risk among Asian populations. Recently, a consortium of researchers across the Asia-Pacific region has begun an in-depth investigation of the genetic variants among Asia-Pacific populations with AMD.

### Polypoidal Choroidal Vasculopathy

It has been estimated that more than half of all cases of AMD in Asians may have the variant PCV. In China alone, there is an estimated 900,000 cases of PCV.<sup>24</sup>

Genetics may also explain why Asians are more likely than whites to develop PCV. It is not yet certain whether PCV is a different disease than AMD, partly because the criteria for the diagnosis of PCV are not well established. Patients with classic PCV, unlike those with AMD, lack drusen, a factor that suggests that the underlying pathogenesis of PCV differs from that of AMD. During a funduscopy exam, PCV lesions often appear as reddish-orange polyp-like dilations, and are associated with hemorrhagic and/or serous detachment of the layer of cells known as the retinal pigment epithelium (RPE).<sup>3</sup> Yet, there is no agreement on the defining characteristic of PCV lesions, including their appearance and size. A more precise classification of PCV is needed in order to attain widespread acceptance of the disease. There is also no current consensus on the best way to image PCV. Experts are mixed on whether scanning laser ophthalmoscope (Heidelberg retina angiogram) (SLO [HRA]) is a more effective imaging technique for PCV than flash indocyanine green angiography (ICGA). Although used routinely in the Asia-Pacific region for identifying the presence of PCV, ICGA is not used very often in Western countries. The lack of general ICGA screening in the West may indicate that PCV is underdiagnosed among its populations.

Treatment strategies for PCV are also not well defined, primarily because of the natural history of the disease. Whereas AMD scarring progresses very rapidly without treatment, PCV's scarring has a more variable progression. For many years, ophthalmologists believed PCV self-resolved; thus, it was seldom treated. Today, PCV is often treated with PDT and/or anti-VEGF injections, but very little data are available about the

effectiveness of those approaches. To date, only one randomized clinical trial, which followed only 61 patients for six months, has been published on anti-VEGF treatments for PCV. It found that PDT alone or combined with ranibizumab was superior to ranibizumab monotherapy in achieving complete polyp regression in Asian patients with PCV, while the visual acuity gain was similar in all three groups.<sup>25</sup> Additional trials are now underway with larger populations and longer durations. It is hoped that these and other new trials will provide appropriate guidelines for the management of both PCV and AMD in Asian populations.

## Angiogenesis: Lessons from Oncology

An important aspect of angiogenesis is microcirculation (the transportation of blood within an organ's tissue by small blood vessels). Microcirculation is remarkably adaptive and varies according to the organ involved. As a result, angiogenesis in the colon is very different than in, say, the breast or the brain. Microcirculation varies at different times in a person's life cycle, and even from organ to organ within the same person. Indeed, within the same organ, angiogenesis will form differently in scar tissue than in healthy tissue. Scientists do not currently understand what drives these differences. Some answers may emerge from the Human Vascular Mapping Project, which is currently underway at the University of Texas MD Anderson Cancer Center in Houston, Texas.<sup>26</sup> For that project, researchers are subjecting endothelial cells harvested from diseased cancer tissue to genomics and proteomics studies and examining the results for context-specific differences between healthy and disease tissue.

Many of the factors involved with the progression of wet AMD are also commonly seen in cancer. As in wet AMD, VEGF helps drive tumor angiogenesis and leads to disease progression. Many other characteristics of the progression of wet AMD, such as leaky, abnormal vessels, fibrosis, scarring, and inflammation, are also seen with tumor angiogenesis. In tumors, as in the eye, VEGF induces vascular permeability,<sup>27</sup> and studies have shown that treating tumors with anti-VEGF therapies can markedly decrease interstitial fluid leakage<sup>28</sup>—again, as it does in the eye.

Since 2004, more than a dozen anti-VEGF therapies have been approved for the treatment of a variety of cancers, including those involving the colon, lung, breast, brain, kidney, pancreas, and liver. This compares with three anti-angiogenesis drugs (pegaptanib, ranibizumab, and aflibercept) approved in ophthalmology. Oncologists have begun to expand their focus, however, to other angiogenesis targets. More than 30 additional targets have already been identified, and each has become the subject of developmental therapeutics by biopharmaceutical companies. Where we are today with anti-VEGF cancer therapy may soon be eclipsed by these other drugs if they are shown to be more effective. Some may find uses in ophthalmology as well.

Although the ability of anti-VEGF drugs to reduce neovascularization and its related edema and hemorrhage is essential for the treatment of AMD and possibly of PCV, long-term, chronic VEGF inhibition may have undesirable effects. In the eye, VEGF is also neuroprotective and promotes retinal cell survival. Extended VEGF blockade may detrimentally affect retinal cells. While such a detrimental effect remains to be shown in patients who are treated with anti-angiogenic drugs, it may eventually turn out that the goal of long-term treatment may need to include maintaining VEGF at a physiological balance instead of a sustained and complete depletion.<sup>29</sup>

## **The research-to-date in oncology offers five broad take-away lessons about anti-VEGF therapies:**

### **1. Different anti-VEGF agents have different effects.**

As comparative-effectiveness testing in animal models has shown,<sup>30</sup> different anti-VEGF therapies target different members of the VEGF family of growth factors. Ranibizumab, for example, blocks only VEGF-A, while aflibercept has a broader mechanism of action, targeting VEGF-A, VEGF-B and PlGF (placental growth factor). Neither drug, however, blocks other members of the VEGF family (VEGF-C, and VEGF-D).<sup>31</sup>

### **2. Ongoing maintenance therapy is important.**

After anti-VEGF treatment is initiated, the blood vessels of a tumor that has rapidly vascularized can regress quite dramatically. When the treatment is stopped, however, the blood vessels grow right back—and in the same empty sleeves of the basement membranes (the thin sheet of fibers that underlie the epithelium) of the vessels that had regressed.<sup>32</sup> Thus, the chemotherapy treatment model of “drug holidays” does not seem to be beneficial with anti-VEGF therapies. How to influence those “ghost vessels” so they do not grow back after anti-VEGF therapy is halted is currently under study.

### **3. Targeting multiple pathways improves outcomes.**

New blood vessel growth is most likely initiated by the activation of more than one pro-angiogenic pathway. Blocking one pathway with an anti-VEGF drug, therefore, may eventually cause other pathways to increase their pro-angiogenic efforts, limiting the effectiveness of the drug. Making anti-VEGF therapies more effective may require giving the drugs in combination rather than alone. Indeed, treatment of renal cell carcinoma patients with a combination of bevacizumab plus interferon alfa-2a (IFN), another powerful angiogenesis inhibitor, results in significantly greater improvement in progression-free survival than IFN treatment alone.<sup>33</sup> In addition, a 2012 phase II clinical trial reported that combining an anti-PDGF (platelet-derived growth factor) drug (aptamer) with an anti-VEGF drug (ranibizumab) was more effective than anti-VEGF monotherapy in the treatment of AMD.<sup>34</sup>

### **4. Responses to anti-VEGF therapies are not homogeneous.**

Not everybody responds the same way to the same anti-VEGF drug, and response changes over time. Anti-VEGF therapy has, for example, transformed the treatment of kidney cancer, but even in that indication, patient response to anti-VEGF treatment differs significantly. There are good responders, non-responders, and intermediate responders. Even among patients who are initially good responders, their response can vary over time. Some respond quickly, but then their disease recurs after a short time, while others have a sustained response over a considerable period of time. Sometimes the best response is stable disease, when the tumor does not grow, but remains the same size. Also, a patient may not respond to one anti-VEGF therapy but may still respond well to a different, subsequent anti-VEGF therapy. Differences in responses are also seen in patients with AMD. An AMD patient may never respond to anti-VEGF therapy, or may initially respond and then stop responding over time. In addition, patients with PCV seem to respond more poorly to anti-VEGF therapy than those with AMD. Treatment outcomes need to be captured and studied to better understand these response differences—and to develop more effective “personalized” therapies.

### **5. Sequential therapy can improve disease control.**

Sequential anti-VEGF therapy (sunitinib followed by sorafenib) has been shown to improve disease control in kidney-cancer patients.<sup>35</sup> Research also suggests that some patients with kidney cancer respond to a later re-challenge by their initial anti-VEGF therapy.<sup>36,37</sup> Sequential anti-VEGF therapy (e.g., ranibizumab, followed by bevacizumab; or bevacizumab and/or ranibizumab, followed by aflibercept) may therefore prove beneficial for AMD patients who are non- or poor-responders, or who become resistant to the initial anti-VEGF drug with which they are treated.<sup>38, 39, 40</sup>



# Where We Want to Be

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Anti-VEGF therapy is undoubtedly making a remarkable difference in the lives of people with wet AMD, and will significantly impact millions living in the Asia-Pacific region. Still, there is considerable room for improvement in terms of how patients are brought into the treatment system and how they are treated once their condition is diagnosed.

## The Desired Future State of AMD Treatment in the Asia-Pacific Region

The moderator opened this segment of the summit by asking participants to discuss a key question: As leading practitioners in this field who treat or interact with AMD patients every day, what would a patient-centered system of AMD treatment and care look like in the Asia-Pacific region if that system could become completely successful?

### From the Perspective of the Patient

The summit participants agreed that the most desired patient-centered outcome would be the maintenance of functional vision so that patients could fully enjoy a high quality of life. The participants also agreed that the definition of “high quality of life” has changed among older Asians in recent years; many now expect to work into their 60s and 70s and to be able to live independently and continue to read, drive, and use their smartphones and computers. Because of these changing expectations, a successful system of wet AMD treatment and care in the Asia-Pacific region must include a high standard for functional vision.

Summit participants also agreed that a completely successful AMD care system would include earlier access to diagnostic and treatment services. The earlier AMD is detected in the disease’s progression, the greater the likelihood of a good treatment outcome. Yet too many AMD patients in the Asia-Pacific region do not have their vision screened until they have already lost vision in one eye. These treatment delays are partly the result of a lack of a uniform screening system and partly because the public remains generally uninformed about early symptoms of the disease. In some instances, patients may realize they are having vision problems, but don’t seek a diagnosis because they must pay out-of-pocket for both the screening and the treatment. The summit participants agreed that in a successful AMD care system, AMD eye exams would be part of regular medical checkups for people aged 50 and older. In addition, patients would know when to seek diagnosis, and out-of-pocket screening and treatment costs would be lowered to a level that all patients could afford.

### From the Perspective of the Patient’s Family

Family support of the elderly has been traditionally very strong in the Asia-Pacific region, but that situation has been changing in recent years. An increasing number of older Asians now find themselves without a reliable family support system. Yet without such support, AMD treatments, which can be costly and require frequent visits to a retinal specialist, become out of reach to many older patients. Even for patients with strong family support, the financial and other burdens associated with AMD treatments are often too great for the family to take on. Family members must give up a half or full day of work each time they accompany their elderly relative to a treatment session, for example. That time-off from work is even greater for rural families, who must often travel very long distances to bring a relative to see a retinal specialist. Even if families can get their loved one to a specialist, the cost of anti-VEGF drugs often makes treatment prohibitive.

Summit participants agreed that a completely successful AMD care system would reduce the physical and financial burden on the patient’s family. First, the Asia-Pacific region would have a broader network of retinal specialists, making it easier for patients to receive care no matter where they lived. Second, research would create new treatments—such as eye drops—that require less frequent doctor visits. And, third, governments would initiate policies that would make AMD screening and treatments less expensive for patients and their families.

### From the Perspective of Healthcare Professionals and Institutions

The summit participants then discussed what a successful AMD care system would look like from the point of view of healthcare professionals and institutions. They agreed that currently there is no clear and consistent pathway of care for the treatment of AMD patients in Asia-Pacific countries. The ideal situation would be to have primary care physicians and general ophthalmologists screening patients for AMD and then referring those with suspected disease to retinal specialists for diagnostic confirmation and treatment. Such referrals are not always made, however. In some cases, the physicians and general ophthalmologists give the treatment injections to patients themselves rather than referring patients to specialists. They do this because patients usually self-pay AMD-related treatment costs, and the competition among clinicians for self-pay healthcare dollars is fierce. It’s not clear, however, that general practitioners have the training or skill necessary to provide optimal AMD treatment. A successful AMD care



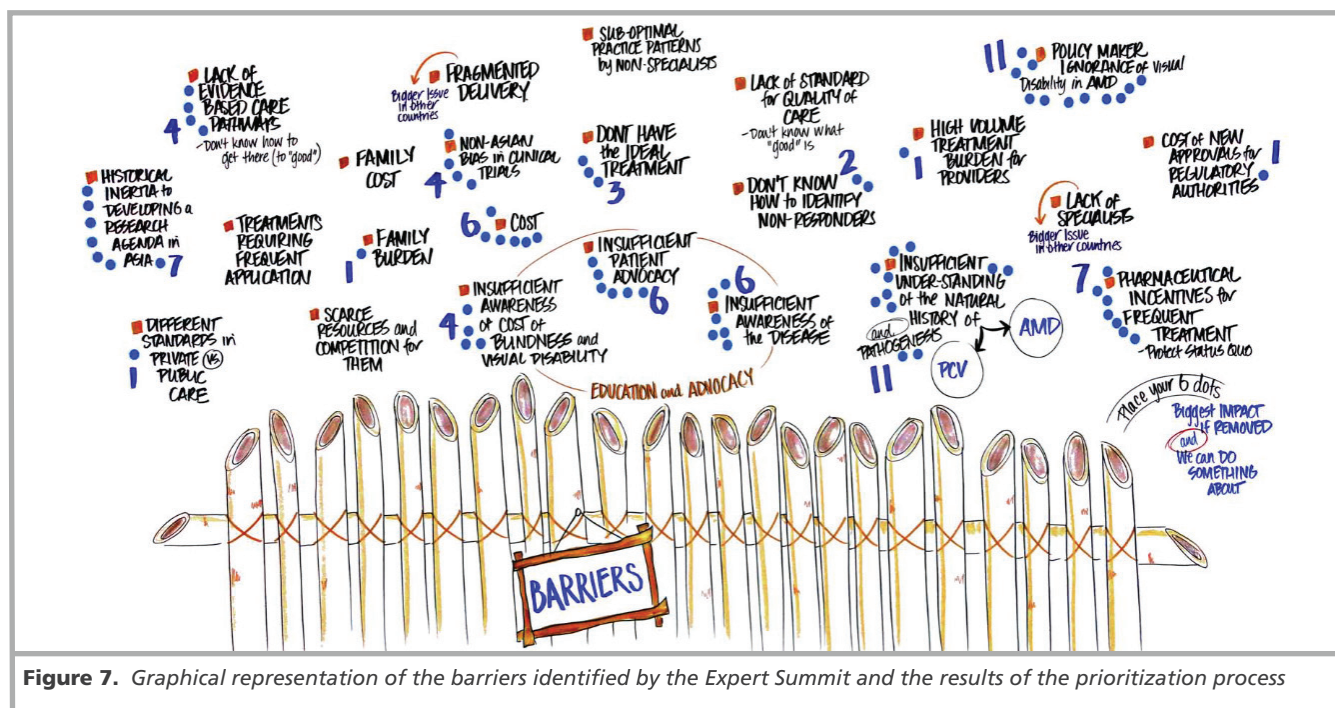
system, stressed the summit participants, would establish clear practice guidelines for the treatment of the disease and ensure that all clinicians who provide treatment are fully qualified to do so.

In regard to healthcare institutions, the summit participants agreed that many in the Asia-Pacific region need additional and more effective resources to handle the growing number of AMD patients. A number of hospitals and clinics lack SD-OCT technology, for example, which is necessary for an accurate diagnosis of AMD. Others lack the necessary staff to treat a sufficient number of AMD patients weekly. Institutions have also established widely varying requirements for treatment, with some even insisting that all injections be performed in an operating room. Such requirements not only raise the cost of the treatment, but also limit the number of patients who can be treated in a single day, thus lengthening the time that new patients must wait to receive treatment. Such a wait can threaten patient care. After AMD is diagnosed, the window of opportunity for successfully treating the disease is relatively short, and any delay can mean the difference between patients retaining their sight and becoming blind. In a successful AMD care system, the summit participants agreed, healthcare institutions would have in place the necessary equipment, staff, and treatment processes to enable timely and optimal diagnosis and treatment of the disease.

## From the Perspective of Government Officials and Policymakers

Most people in the Asia-Pacific region are unaware of AMD. Those who have heard of AMD seldom understand that blindness from the disease can often be prevented with early diagnosis and treatment. Nor are they aware that dietary modification and supplementation may help prevent the disease in high-risk groups. Given the public's widespread lack of knowledge, summit participants agreed that a successful AMD care system would include high-profile AMD-awareness campaigns. These campaigns would provide clear, simple messages that would resonate with all of the region's diverse ethnic and cultural groups.

The summit participants also discussed what a successful AMD care system would look like from the viewpoint of government and health-policy officials in the Asia-Pacific region. They agreed that it would lower the burden of blindness on the region's healthcare and social systems—a burden that is currently projected to significantly increase in the coming decades as the Asia-Pacific population ages. Societies need to recognize the value of ensuring that their elderly populations retain good vision, the summit's participants stressed. Older Asians who lose their sight cannot, for example, help care for their grandchildren. Indeed, they must be cared for themselves. Yet individual families are becoming increasingly unable to take on that responsibility. Thus, when an elderly person loses his or her vision—and independence—the entire society, not just the individual family, is affected.



### Key Components of the Desired Future State

In summary, the ideal future state of a patient-centred AMD care system in the Asia-Pacific region would have the following features:

- Effective treatments that enable patients to maintain a high level of functional vision
- Effective treatments that require fewer office visits
- Easy and affordable patient access to diagnostic and treatment services
- A broader and more geographically distributed network of retinal specialists
- Consistent guidelines for the definition, diagnosis, and treatment of AMD and PCV that reflect the accepted evidence for best practice
- A “pathway of care” that includes coordination among all of the patient’s healthcare providers
- Comprehensive training of all clinicians who provide AMD treatment
- Sufficient AMD screening technology and trained staff at medical institutions to ensure timely and optimal diagnosis and treatment of the disease
- On-going, high-profile AMD-awareness campaigns that reach all ethnic and cultural groups
- A society-wide recognition of the high value attached to ensuring that elderly populations retain their vision

## Existing Barriers

With the desired future state of AMD in the Asia-Pacific region defined, the moderator asked participants to list barriers that stand in the way of the region attaining it. Here are the key barriers and underutilized resources that were identified:

- Public unawareness of the disease and especially of the need for early diagnosis and treatment
- The high cost and invasiveness of anti-VEGF treatments
- The lack of universally effective treatments, particularly treatments that are effective for dry AMD
- The high out-of-pocket costs (scanning, consultations, treatments) incurred by patients and their families
- The lack of government and social programs to help patients get access to care when they lack family support
- A lack of evidence-based care pathways for the treatment of AMD and PCV
- Different AMD treatment standards for private and public care-delivery systems
- Fragmented delivery-of-care systems
- An insufficient number of retinal specialists, particularly in rural areas
- Sub-optimal AMD practice patterns by non-retinal specialists
- A lack of understanding of the natural history and pathogenesis of both AMD and PCV
- Few Asian-specific clinical trials
- A lack of validated biomarkers to identify treatment responders and non-responders
- The competition among advocates for various chronic diseases for scarce government resources
- A lack of urgency among many policymakers and public health officials about developing an AMD/PCV research agenda in the Asia-Pacific region
- The aging of Asia-Pacific populations and the concurrent rise in the number of people developing AMD
- Insufficient recognition of the social and financial burden that blindness places on society

# Developing Solutions in the Asia-Pacific Region

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With key barriers defined, the summit participants engaged in a discussion about their findings. They talked about how these barriers might be overcome with improvements to current practices regarding the detection and treatment of wet AMD. They then discussed how to define success regarding treatment outcomes and what research needs to be undertaken to help reach outcomes that would be valued by all stakeholders.

## Improving Early Detection of Wet AMD

Summit participants focused their discussion about improving early detection on 1) the need for greater awareness of early symptoms by the public and first-line clinicians (primarily optometrists and general ophthalmologists), and 2) the need to enlist top governmental officials' support in making AMD a medical priority.

### Early Symptom Recognition

The summit participants agreed that a major barrier to improving early detection of wet AMD is a lack of symptom recognition among people who have developed the disease. Public awareness campaigns are needed, but these initiatives should start at the ministerial level by educating top governmental officials about the importance of AMD screening and early detection as well as about the social and financial impact that AMD has on Asia-Pacific societies. Any broad public awareness campaign will require the full support of health ministers and other leading policymakers if it is to be successful. Some high-level public health officials have already recognized the need for greater awareness about AMD and have committed to making this chronic disease a public health priority.

Although less common in the Asia-Pacific region than in other parts of the world, patient-advocacy groups should also be consulted when public awareness campaigns are being developed. In addition, well-known Asian individuals in the sports and entertainment fields should be asked to participate in publicizing the campaigns, although eliciting support from prominent individuals with the disease may be difficult because of the stigma associated with it. Simple messages (e.g., describing AMD as "an eye attack") would be most effective with the public, and should include the fact that early AMD symptoms are monocular (occurring in

one eye) and therefore may not be apparent unless a person covers one eye while trying to read or perform some other visual task. The development of a smartphone app for this purpose might be useful. It might also be helpful to learn how the Macular Disease Foundation Australia conducted its highly successful AMD awareness campaign. Any awareness campaign launched in the Asia-Pacific region must, however, recognize the region's wide ethnic and cultural diversity.

## The Role of Optometrists, General Ophthalmologists, and Other Clinicians

In most countries in the Asia-Pacific region, optometrists do not screen for eye diseases, nor do they provide treatment. If they suspect a patient has a retinal disease, such as AMD or PCV, they are expected to refer the patient to an ophthalmologist for diagnostic screening. Many general ophthalmologists, however, have not received specialized AMD-related training. Nor do they all have access to up-to-date screening technology. So many patients do not receive a timely diagnosis. In some rural areas where ophthalmologists are scarce, such as in Thailand, nurses are being trained to do the screening and read retinal images. Summit participants discussed the need for more AMD-related training for general ophthalmologists and other clinicians. Standardized practice guidelines for AMD-related screening and a wider distribution of SD-OCT technology would greatly help this effort. It was pointed out that some countries in the region, such as South Korea, have very good early detection systems, which might serve as models for other countries.

## Future Action Steps

Based on their discussion, summit participants concluded that the following actions could be taken to improve the early detection of wet AMD in the Asia-Pacific region:

- Launch an initiative to educate top governmental officials about the crucial need for AMD screening and early detection
- Develop public awareness campaigns that have the full support of health ministers and other leading policymakers
- Create simple messages and tools to support the awareness campaigns
- Develop standardized AMD-related screening guidelines for all healthcare practitioners

- Incentivize general ophthalmologists to refer patients to retinal specialists rather than treat the patients themselves
- Ensure a wider distribution of SD-OCT and ICGA technologies for the screening of both AMD and PCV

## Improving Access to Effective Interventions for Wet AMD

Early diagnosis and prompt and aggressive treatment of wet AMD, particularly within the first year of disease, are essential for improving visual outcomes for patients. Gaps in access to timely interventions exist throughout the Asia-Pacific region, however. In this segment of the summit, the experts discussed the interventions that need to be expanded or added to the region's various healthcare systems to improve access to AMD-related care.

### Easier Accessibility to Retinal Specialists

Too many Asia-Pacific patients with wet AMD do not seek care until the disease is in its late stages, when it is most difficult to treat. Part of the problem is that patients don't know how to recognize the early symptoms of AMD, but an additional obstacle to timely diagnosis and treatment is that patients don't always know where to go to receive specialized care. People understand that if they have a heart problem, they should see a heart specialist (cardiologist); but most are unaware that for AMD, they should see an ophthalmologist who is a retinal specialist. Unfortunately, by the time many AMD patients see a retinal specialist, they have already irreversibly lost most of their vision.

Summit participants talked about the need to move retinal specialists from a passive to an active role in educating the public about when and how to access optimal AMD care. Such education could be conducted through a variety of respected venues, including public lectures and media interviews. They also discussed the need for standardized diagnostic and treatment guidelines that would clearly delineate the roles that different clinicians would perform in the delivery of AMD-related care.

### Greater Affordability of Care

Patient access to retinal specialists is also driven by cost. Most governments want high-level evidence that an AMD treatment works before covering it under their insurance plans, but even with that evidence they may balk at the high cost of the treatments. Indeed, some health ministries will pay for only a fraction of the anti-VEGF injections that are recommended for optimal treatment. In addition, many people in the Asia-Pacific region have self-pay health insurance, which can make AMD treatments prohibitive. The cost issue is also holding back the development of standardized treatment pathways for AMD; governments worry that they will not be able to afford treatments called for in the guidelines.

The ultimate solution for the cost problem would be for the price of anti-VEGF drugs and SD-OCT technology to come down. This would require that pharmaceutical and medical device companies cooperate with governments in lowering those costs. Australia has been somewhat successful in negotiating down the cost of anti-VEGF drugs; countries in the Asia-Pacific region may want to use similar negotiating strategies.

### More Effective, Accessible and Specific PCV Interventions

The summit participants also discussed the need for more effective and accessible interventions for PCV. Laser devices were used initially for the treatment of PCV, but PDT therapy is now considered a safer and more effective option. It was pointed out that medical device manufacturers are no longer making laser devices for the treatment of PCV, and their interest in manufacturing PDT machines is also waning because of the limitations of the therapy's effectiveness. As a result, access to treatments for PCV is often difficult to obtain.

Summit participants agreed that more research into PCV as a possible Asian subtype of AMD is urgently needed to encourage the continued accessibility to existing treatments and the development of new and more effective ones. To date, most of the PCV research has been done on Western populations and thus has a non-Asian focus and bias. The participants stressed that governments in the Asia-Pacific region should take a leading role in PCV research, for economic as well as medical reasons. PCV is an as-yet poorly understood retinal disease that appears to affect a significant percentage of Asians. Basic and clinical research into the disease has the potential, therefore, of not only



improving the lives of millions of Asians, but also of attracting significant business interest and capital to the region for research and development.

### **Future Action Steps**

Based on their discussion, summit participants concluded that the following actions could be taken to improve access to effective interventions for wet AMD and PCV in the Asia-Pacific region:

- Educate the public about the need to see a retinal specialist for AMD treatments
- Advocate for the expansion of insurance coverage for AMD and PCV treatments
- Encourage governments to negotiate with pharmaceutical companies to lower the cost of anti-VEGF drugs and SD-OCT technology
- Develop more efficient systems for ensuring early diagnosis and referral and for delivering AMD-related care.
- Develop an Asia-Pacific-led research program into the development of effective alternative treatments for PCV

## **Value Analysis: Defining Successful Outcomes**

After discussing possible solutions for improving the early detection and treatment of wet AMD, the summit's participants turned their focus to how they would define success regarding the outcomes of such efforts. What are the desired patient-centered outcomes for wet AMD treatment, and how are they measured? The summit participants considered value from the perspectives of patients and policymakers.

### **Value from the Patient's Perspective**

From the perspective of AMD patients, the primary endpoint of effective early detection and treatment is improvement in visual acuity, especially "real-life" functional vision. They value treatments that will help them maintain their independence and enjoy life.

Functional vision is also essential for patients who must manage co-morbidities, such as arthritis, diabetes, or cardiovascular disease. Patients also value treatments that are affordable and that require few doctor visits and, ideally, no injections. They also value support, either from their families or from others in their communities, to help them obtain treatment and, if necessary, to adjust to life with lower vision.

### **Value from the Policymaker's Perspective**

For some policymakers and others in the Asia-Pacific public sector, the value of effective early wet AMD detection and treatment programs begins with lower economic costs. The productivity cost of blindness is high. That cost includes not only the lost productivity of the AMD patient, but also of the person's caregiver, for often a secondary family member is removed from the workforce to care for the blind individual. Countries with social welfare programs must also bear the increasing burden of helping to care for older blind individuals who have no family support. The value of successful AMD detection and treatment programs can also be measured in lower political costs for policymakers. As Asia-Pacific populations age, an increasing number of families are going to become burdened with caring for blind relatives. They are going to expect their governments to assist in easing that burden by offering more effective and innovative AMD-related treatments and services.

For policymakers, there is also high value in turning the AMD research focus to Asia-Pacific populations. That focus has been missing from epidemiological and clinical trial research until recently. As a result, very little is known or understood about AMD in Asia-Pacific populations, and even less is known about the characteristics and pathogenesis of its possible subtype, PCV, which appears to be much more prevalent among Asians than among whites. Summit participants strongly supported the launching of a cooperative initiative among Asia-Pacific governments that would lead the world in Asian-focused AMD and PCV research and development efforts.

## Developing a Strong Research Agenda

One of the themes voiced throughout the summit was the need for more data collection and research for both AMD and PCV in Asia-Pacific populations. As a final item of business, the summit participants listed AMD/PCV knowledge gaps and research priorities, particularly as they relate to improving outcomes for people with the disease in the Asia-Pacific region.

- **Basic research:** A more detailed understanding of the pathogenesis of AMD and PCV is needed. Given that 70% of the pathogenesis of these conditions appears driven by genetic factors, there should be greater investment in the study of genotype and phenotype correlations, including in Asia-Pacific populations. For this basic research to be successful, an animal model for PCV is needed, and AMD animal models need to be improved. Better animal models might lead to the identification of intraocular and circulating biomarkers, which could then be used to determine an individual's risk profile for AMD and PCV and, if the individual goes on to develop the disease, which therapies might be most effective. Such biomarkers hold the promise for the development of more individualized therapies. In addition, a human tissue bank of choroidal tissue needs to be established for the study of PCV.
- **Epidemiological research:** A clearer understanding of AMD and PCV prevalence in Asian populations is needed. In addition, ICGA studies should be conducted to determine if PCV has been underdetected among white populations.
- **Treatment-effectiveness research:** More research is needed on how current AMD and PCV treatments work, including their comparative effectiveness among different ethnic groups. Research into treatment effectiveness should include investigations into how the healthy retina repairs itself. In addition, a study that compares AMD treatment outcomes of generalists and retinal specialists should be undertaken.
- **New-drug discovery research:** A drug-discovery program that looks beyond VEGF as a target is urgently needed. Funding support should also be given to efforts to develop new and less expensive screening instruments, including portable ones, that could be used effectively by a greater numbers of clinicians in the Asia-Pacific region.
- **Risk-factor research:** The role of concomitant disease as a risk factor for AMD and PCV among Asia-Pacific populations needs to be studied. For example: Are Asians with type 2 diabetes at greater risk for developing PCV? Behavioral habits that are associated with an increased risk of AMD and PCV, such as smoking and diet, also need to be investigated to determine if their impact on the diseases within Asia-Pacific populations differs from that within other populations.
- **Quality-of-life research:** Quality-of-life measurements that specifically address the values of older Asia-Pacific populations need to be developed. Many of today's older Asians have redefined what "quality-of-life" means after age 60 to include much more independence. Collecting data on those quality-of-life endpoints is essential to developing effective AMD and PCV care systems.
- **Economic research:** The socio-economic burden of AMD and PCV on Asia-Pacific populations needs to be investigated and quantified. Such research would help all stakeholders—patients, family caregivers, physicians, researchers, scientists, industry leaders, regulators, policymakers, funders, the media, and society-at-large—better understand the importance of improving the access and affordability of early diagnosis and treatment of these potentially devastating diseases.

The summit participants agreed that resolving these and other AMD- and PCV-related knowledge gaps will require a unified effort of all interested stakeholders.

# Summary of Desired Actions

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During the course of the daylong summit, summit participants identified the following key actions that should be taken to improve the care and quality-of-life of the growing number of people in the Asia-Pacific region who will be diagnosed with wet AMD and PCV in the coming years. These desired actions included the following:

## 1. Improve awareness and early detection

- Launch an initiative to educate top governmental officials about the need to make AMD a medical priority.
- Develop AMD public-awareness campaigns that have the full support of health ministers and other leading policymakers.
- Consult with the Angiogenesis Foundation and the Macular Disease Foundation Australia to create simple messages and tools for those campaigns.
- Work with general ophthalmologists and other clinicians to improve early detection of wet AMD and increase referrals to retinal specialists for follow-up exams and treatment.
- Make AMD eye exams part of regular medical checkups for people aged 50 and older.
- Develop comprehensive programs for diagnostic training that will reach a wider range of clinicians beyond ophthalmologists specializing in retinal diseases.
- Increase access to diagnostic technologies for all patients throughout the Asia-Pacific region.

## 2. Improve access to effective interventions

- Advocate for the expansion of insurance coverage for AMD and PCV treatments.
- Develop more efficient care systems for ensuring early diagnosis and referral and for delivering AMD-related care.
- Educate the public and general clinicians about the need for AMD patients to see a retinal specialist for treatment.
- Develop standardized AMD screening and practice guidelines to ensure that all patients receive the same efficient, effective, and high quality care.
- Improve the coordination of healthcare clinicians to better manage co-morbidities associated with wet AMD.
- Increase the number of retinal specialists, particularly in less-populated areas.
- Encourage governments to negotiate with pharmaceutical companies to lower the cost of anti-VEGF drugs and SD-OCT technology.

# Summary of Desired Actions

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## 3. Improve outcome value for stakeholders.

- Advocate for the development of vision-oriented quality-of-life measurement tools that capture the values of the current generation of older Asians.
- Provide services to families to enable them to provide better support and care to older relatives with AMD.
- Investigate and quantify the socio-economic burden of AMD and PCV on Asia-Pacific populations and countries.

## 4. Improve translational research.

- Develop an animal model for PCV and better animal models for AMD.
- Conduct research on the epidemiological studies of the prevalence of AMD and PCV in Asia-Pacific populations.
- Conduct research into the genotype and phenotype correlations of AMD and PCV, particularly in Asia-Pacific populations.
- Conduct research on behavioral and concomitant-disease risk factors for AMD and PCV among Asia-Pacific populations.
- Promote research efforts to develop less invasive and less frequent treatments.
- Promote research efforts to develop less expensive and more portable screening technology.
- Promote research on AMD-related biomarkers.
- Launch a cooperative initiative among Asia-Pacific governments that would lead the world in Asian-focused AMD and PCV research and development.



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# Acknowledgements

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This report was made possible by the support of the  
Terry Collingwood Memorial Fund, the Significance Foundation,  
and Bayer Healthcare Pharmaceuticals