

Issue 170

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This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

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Drug treatment

Am J Ophthalmol. 2014 Feb 18. pii: S0002-9394(14)00099-3. doi: 10.1016/j.ajo.2014.02.035. [Epub ahead of print]

Long-Term Effects of Multiple Intravitreal Anti- Vascular Endothelial Growth Factor Injections on Intraocular Pressure.

Kim YJ, Sung KR, Lee KS, Joe SG, Lee JY, Kim JG, Yoon YH.

PURPOSE: To evaluate long-term effects of multiple intravitreal anti- vascular endothelial growth factor (VEGF) injections on intraocular pressure (IOP) in eyes with neovascular age-related macular degeneration (AMD) or retinal vein occlusion (RVO).

DESIGN: Retrospective cohort study.

METHODS: This study enrolled patients who underwent multiple (more than three) intravitreal anti-VEGF injections and who were followed for more than 12 months after their last injection. IOP elevation was defined as an increase of 5 mmHg over the baseline measurement on two consecutive visits. The frequency of IOP elevation was determined. A hazard ratio of each putative risk factor for IOP elevation was calculated using the Cox proportional hazard model for the total participants, incorporating underlying disease as a covariate, as well as for each cohort.

RESULTS: Six-hundred and twenty-nine eyes with neovascular AMD and 95 eyes with RVO were included in the analysis. Twenty eyes with neovascular AMD (3.0%) and 7 eyes with RVO (7.4%) experienced IOP elevation after multiple anti-VEGF injections, with an overall incidence of 3.7%. In the Cox proportional hazard analysis of total participants, a diagnosis of RVO (3.424, $P = 0.005$), a history of glaucoma (8.441, $P = 0.001$), and low baseline IOP (0.865, $P = 0.040$) were all significant risk factors for IOP elevation after multiple anti-VEGF injections.

CONCLUSION: A history of multiple intravitreal anti-VEGF injections was not a significant risk factor for IOP elevation in our study. IOP elevation was more common in eyes with RVO than with AMD after anti-VEGF injection.

PMID: 24561173 [PubMed - as supplied by publisher]

Korean J Intern Med. 2014 Jan;29(1):1-11. Epub 2014 Jan 2.

Antiangiogenesis therapy: an update after the first decade.

De Falco S.

Abstract: Angiogenesis is a complex biological phenomenon that forms new blood vessels from the pre-existing vasculature. Aberrant angiogenesis has been implicated in a variety of diseases such as cancer, atherosclerosis, arthritis, obesity, pulmonary hypertension, diabetic retinopathy, and age-related macular degeneration. These conditions collectively affect nearly 10% of the global population. Much effort has focused on identifying new therapeutic agents that inhibit pathological angiogenesis since 1971, when Judah Folkman published the hypothesis that tumor growth is angiogenesis-dependent and that its inhibition may be therapeutic. In 2004, the U.S. Food and Drug Administration approved the first antiangiogenic drug for the treatment of metastatic colon cancer, bevacizumab (Avastin, Genentech). This drug is a humanized monoclonal antibody that neutralizes the vascular endothelial growth factor. It is used in combination with chemotherapy, and its use began the era of antiangiogenesis therapy. Several new therapeutic agents have been added to the list of approved drugs, and clinical trials of new therapeutic options and antiangiogenic agents are ongoing. This review describes the progress made in the first decade of antiangiogenesis therapy, and addresses both validated and possible targets for future drug development.

PMID: 24574826 [PubMed - as supplied by publisher]

Ann Intern Med. 2014 Jan 7;160(1). doi: 10.7326/M13-0768.

Cost-effectiveness of treatment of diabetic macular edema.

Pershing S, Enns EA, Matesic B, Owens DK, Goldhaber-Fiebert JD.

BACKGROUND: Macular edema is the most common cause of vision loss among patients with diabetes.

OBJECTIVE: To determine the cost-effectiveness of different treatments of diabetic macular edema (DME).

DESIGN: Markov model. **DATA SOURCES:** Published literature and expert opinion. **TARGET**

POPULATION: Patients with clinically significant DME.

TIME HORIZON: Lifetime. **PERSPECTIVE:** Societal.

INTERVENTION: Laser treatment, intraocular injections of triamcinolone or a vascular endothelial growth factor (VEGF) inhibitor, or a combination of both.

OUTCOME MEASURES: Discounted costs, gains in quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs).

RESULTS OF BASE-CASE ANALYSIS: All treatments except laser monotherapy substantially reduced costs, and all treatments except triamcinolone monotherapy increased QALYs. Laser treatment plus a VEGF inhibitor achieved the greatest benefit, gaining 0.56 QALYs at a cost of \$6975 for an ICER of \$12 410 per QALY compared with laser treatment plus triamcinolone. Monotherapy with a VEGF inhibitor achieved similar outcomes to combination therapy with laser treatment plus a VEGF inhibitor. Laser monotherapy and triamcinolone monotherapy were less effective and more costly than combination therapy.

RESULTS OF SENSITIVITY ANALYSIS: VEGF inhibitor monotherapy was sometimes preferred over laser treatment plus a VEGF inhibitor, depending on the reduction in quality of life with loss of visual acuity. When the VEGF inhibitor bevacizumab was as effective as ranibizumab, it was preferable because of its lower cost.

LIMITATION: Long-term outcome data for treated and untreated diseases are limited.

CONCLUSION: The most effective treatment of DME is VEGF inhibitor injections with or without laser treatment. This therapy compares favorably with cost-effective interventions for other conditions.

PMID: 24573663 [PubMed - in process]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2014 Feb 26;55(2):1191-202. doi: 10.1167/iovs.13-13481.

Developing cellular therapies for retinal degenerative diseases.

Bharti K, Rao M, Hull SC, Stroncek D, Brooks BP, Feigl E, van Meurs JC, Huang CA, Miller SS.

Abstract: Biomedical advances in vision research have been greatly facilitated by the clinical accessibility of the visual system, its ease of experimental manipulation, and its ability to be functionally monitored in real time with noninvasive imaging techniques at the level of single cells and with quantitative end-point measures. A recent example is the development of stem cell-based therapies for degenerative eye diseases including AMD. Two phase I clinical trials using embryonic stem cell-derived RPE are already underway and several others using both pluripotent and multipotent adult stem cells are in earlier stages of development. These clinical trials will use a variety of cell types, including embryonic or induced pluripotent stem cell-derived RPE, bone marrow- or umbilical cord-derived mesenchymal stem cells, fetal neural or retinal progenitor cells, and adult RPE stem cells-derived RPE. Although quite distinct, these approaches, share common principles, concerns and issues across the clinical development pipeline. These considerations were a central part of the discussions at a recent National Eye Institute meeting on the development of cellular therapies for retinal degenerative disease. At this meeting, emphasis was placed on the general value of identifying and sharing information in the so-called "precompetitive space." The utility of this behavior was described in terms of how it could allow us to remove road blocks in the clinical development pipeline, and more efficiently and economically move stem cell-based therapies for retinal degenerative diseases toward the clinic. Many of the ocular stem cell approaches we discuss are also being used more broadly, for nonocular conditions and therefore the model we develop here, using the precompetitive space, should benefit the entire scientific community.

PMID: 24573369 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2014 Feb 25. pii: iovs.13-13048v1. doi: 10.1167/iovs.13-13048. [Epub ahead of print]

Quantifying disrupted outer retina-subretinal layer in SD-OCT images in choroidal neovascularization.

Zhang L, Sonka M, Russell S, Folk J, Abramoff MD.

Purpose: To report a fully automated method to identify and quantify the thickness of the outer retinal-subretinal (ORSR) layer from clinical spectral-domain optical coherence tomography (SD-OCT) scans of choroidal neovascularization (CNV) due to exudative age-related macular degeneration (e-AMD).

Methods: 23 Subjects with CNV met eligibility. Volumetric SD-OCT scans of 23 eyes were obtained (Zeiss Cirrus, 200×200×1024 voxels). In a subset of eyes, scans were repeated. OCT volumes were analyzed using our standard parameters and using a 3D graph-search approach with an adaptive cost function. A retinal specialist graded the segmentation as generally accurate, local segmentation inaccuracies, or failure. Reproducibility on repeat scans was analyzed using root mean square coefficient of variation (RMS CV) of the average ORSR thickness.

Results: Using a standard segmentation approach, 1/23 was graded generally accurate, and 22/23 OCT segmentations were failure(s). With the adaptive method 21/23 segmentations were graded generally accurate; 2/23 were local segmentation inaccuracies and none was failure. The inter-method quality of segmentation was significant difference ($p < 0.001$). The average ORSR thickness measured on CNV patients (78.0 μ m, 95% Confidence Interval: 72.5 μ m - 83.4 μ m) is significantly larger ($p < 0.001$) than normal average ORSR layer thickness (51.5 μ m $\pm$ 3.3 μ m). RMS CV was 8.1%.

Conclusion: We have developed a fully automated 3D method for segmenting the ORSR layer in SD-OCT of patients with CNV from eAMD. Our method can quantify the ORSR layer thickness in the presence of fluid, which has the potential to augment management accuracy and efficiency of anti-VEGF treatment.

PMID: 24569576 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 Feb 25. doi: 10.1136/bjophthalmol-2013-303846. [Epub ahead of print]

Pathology detection rate of spectral domain optical coherence tomography devices.

Sharma S, Sayanagi K, Kaiser PK.

BACKGROUND: Spectral domain optical coherence tomography (SDOCT) allows for higher resolution scans and higher scanning speeds compared to time domain OCT (TDOCT). The purpose of this study is to compare the pathology detection rates of various SDOCT devices to the Stratus TDOCT.

METHODS: Patients with neovascular age-related macular degeneration were imaged on the Stratus and one of four SDOCT devices. The images were then analysed in a masked manner evaluating for the presence of epiretinal membrane (ERM), pigment epithelial detachment (PED) and subretinal fluid (SRF). After determining that low scan density with one of the devices was likely the cause of missed PED and SRF compared to the other SDOCT devices the study was repeated with a higher scan density.

RESULTS: 60 eyes from 60 patients with neovascular macular degeneration were imaged on each SDOCT device, for a total of 240 eyes from 240 patients imaged on Stratus. There were no instances where pathology was visible on Stratus but was missed on SDOCT. The highest incidence of missed pathology was with SRF, followed by ERM and PED.

CONCLUSIONS: The increased resolution and image quality of SDOCT devices over TDOCT allows for finer discrimination of retinal structures. The increased speed of SDOCT allows for dense coverage of the macula resulting in the ability to see smaller areas of PED and SRF. There was a critical threshold for the distance between B-scans in the three-dimensional cube scan for detection of pathology.

PMID: 24568868 [PubMed - as supplied by publisher]

J Alzheimers Dis. 2014 Feb 20. [Epub ahead of print]

Choroidal Thinning as a New Finding in Alzheimer's Disease: Evidence from Enhanced Depth Imaging Spectral Domain Optical Coherence Tomography.

Gharbiya M, Trebbastoni A, Parisi F, Manganiello S, Cruciani F, D'Antonio F, De Vico U, Imbriano L, Campanelli A, De Lena C.

Background: The involvement of retina and its vasculature has been recently described in Alzheimer's disease (AD). However, none of the previous works have yet investigated the choroid in vivo.

Objective: Spectral domain optical coherence tomography (SD-OCT) and enhanced depth imaging (EDI) technique is non-invasively used to assess choroidal thickness in patients with AD and to determine whether the peripapillary retinal nerve fiber layer (RNFL) and central retinal thickness are reduced compared to normal subjects.

Methods: Forty-two eyes of 21 patients (mean age, 73.1 ± 6.9 years) with a diagnosis of mild to moderate AD and 42 eyes of 21 age-matched control subjects (mean age, 70.3 ± 7.3 years) were included in this prospective, cross-sectional study. All the subjects underwent neuropsychological (MMSE, ADAS-Cog, and CDR) and ophthalmological evaluation. The SD-OCT images of the choroid were obtained by EDI modality. Choroidal thickness was measured by manual segmentation. The following parameters, measured

automatically by the OCT software, were also analyzed for each eye: 1-mm central subfield (CSF) retinal thickness, peripapillary RNFL thickness.

Results: Choroidal thickness was significantly thinner in AD than in control eyes ($p < 0.05$). No difference in CSF retinal thickness was found between groups ($p > 0.05$). Mean peripapillary RNFL thickness in all four quadrants was similar between groups ($p > 0.05$). OCT measurements were not correlated with any of the tested psychometric parameters ($p > 0.05$).

Conclusion: Compared with healthy subjects, patients with AD showed a significant reduction in choroidal thickness. Choroidal thinning may represent an adjunctive biomarker for the diagnosis and follow-up of this disease.

PMID: 24577467 [PubMed - as supplied by publisher]

Pathogenesis

BMC Ophthalmol. 2014 Feb 27;14(1):22. [Epub ahead of print]

Blood expression levels of chemokine receptor CCR3 and chemokine CCL11 in age-related macular degeneration: a case-control study.

Falk MK, Singh A, Faber C, Nissen MH, Hviid T, Sørensen TL.

BACKGROUND: Dysregulation of the CCR3/CCL11 pathway has been implicated in the pathogenesis of choroidal neovascularisation, a common feature of late age-related macular degeneration (AMD). The aim of this study was to investigate the expression of CCR3 and its ligand CCL11 in peripheral blood in patients with neovascular AMD.

METHODS: Patients with neovascular AMD and healthy controls were included. Blood samples were obtained and prepared for flow cytometry to investigate the expression of CCR3. Levels of CCL11 were measured in plasma using Cytometric Bead Array. Differences between the groups were tested using Kruskal-Wallis test and Mann-Whitney U test.

RESULTS: Patients ($n = 83$) with neovascular AMD and healthy control persons ($n = 114$) were included in the study. No significant difference in the expression of CCR3 was found on CD9+ granulocytes when comparing patients suffering from neovascular AMD with any of the control groups. We did not find any alteration in CCL11 levels in patients among the age matched groups. There was no correlation between expression of CCR3/CCL11 and clinical response to treatment with anti-vascular endothelial growth factor (VEGF) CONCLUSION: Our results do not suggest a systemic alteration of the CCR3/CCL11 receptor/ligand complex in patients with neovascular AMD.

PMID: 24575855 [PubMed - as supplied by publisher]

Biochimie. 2014 Feb 21. pii: S0300-9084(14)00059-5. doi: 10.1016/j.biochi.2014.02.007. [Epub ahead of print]

Functional expression of electron transport chain complexes in mouse rod outer segments.

Calzia D, Garbarino G, Caicci F, Manni L, Candiani S, Ravera S, Morelli A, Traverso CE, Panfoli I.

Abstract: Rod photoreceptors efficiently carry out phototransduction cascade, an energetically costly process. Our recent data in bovine rod outer segment (OS) demonstrated that ATP for phototransduction is produced by an extramitochondrial oxidative phosphorylation, thanks to the expression of the Electron Transport Chain (ETC) complexes and of F1Fo ATP synthase in disks. Here we have focused on mouse retinas, reporting the activity of ETC complexes I, II, IV assayed directly on unfixed mouse eye sections, as

well as immunogold TEM analysis of fixed mouse eye sections to verify the presence of ND4L subunit of ETC complex I and subunit IV of ETC complex IV in rod OS. Data suggest the presence of functional ETC in mouse rod OS, like their bovine counterpart. The protocol here developed for in situ assay of the ETC complexes activity represents a reliable method for the detection of ETC dysfunction in mice models of retinal pathologies. In fact, the ETC is a major source of reactive oxygen intermediates, and oxidative stress, especially when ectopically expressed in the OS. In turn, oxidative stress contributes to many retinal pathologies, such as diabetic retinopathy, age related macular degeneration, photoreceptor death after retinal detachment and some forms of retinitis pigmentosa.

PMID: 24565809 [PubMed - as supplied by publisher]

Neuron. 2014 Feb 19;81(4):800-13. doi: 10.1016/j.neuron.2014.01.003.

Restoring Visual Function to Blind Mice with a Photoswitch that Exploits Electrophysiological Remodeling of Retinal Ganglion Cells.

Tochitsky I, Polosukhina A, Degtyar VE, Gallerani N, Smith CM, Friedman A, Van Gelder RN, Trauner D, Kaufer D, Kramer RH.

Abstract: Retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are blinding diseases caused by the degeneration of rods and cones, leaving the remainder of the visual system unable to respond to light. Here, we report a chemical photoswitch named DENAQ that restores retinal responses to white light of intensity similar to ordinary daylight. A single intraocular injection of DENAQ photosensitizes the blind retina for days, restoring electrophysiological and behavioral responses with no toxicity. Experiments on mouse strains with functional, nonfunctional, or degenerated rods and cones show that DENAQ is effective only in retinas with degenerated photoreceptors. DENAQ confers light sensitivity on a hyperpolarization-activated inward current that is enhanced in degenerated retina, enabling optical control of retinal ganglion cell firing. The acceptable light sensitivity, favorable spectral sensitivity, and selective targeting to diseased tissue make DENAQ a prime drug candidate for vision restoration in patients with end-stage RP and AMD.

PMID: 24559673 [PubMed - in process] PMCID: PMC3933823

Curr Eye Res. 2014 Feb 21. [Epub ahead of print]

Pharmacokinetics of HM-3 After Intravitreal Administration in Mice.

Yuan D, Shen H, Yuan S, Liu X, Xia X, Xie P, Li W, Hu J, Liu Q, Xu H.

Abstract Purpose: HM-3, an RGD-modified endostatin-derived polypeptide, is a potent angiogenesis inhibitor synthesized in our laboratory. This study investigated the HM-3 pharmacokinetics of intravitreally administered in mice eyes as an anti-angiogenesis drug for age-related macular degeneration.

Materials and methods: A total of 288 C57BL/6J mice were evaluated and divided into four groups. Each mouse in different groups received single bilateral intravitreal injection with HM-3. The concentrations of HM-3 in choroid/sclera, retina and serum were determined by indirect competitive enzyme-linked immunosorbent assay.

Results: After intravitreal administration of doses of 0, 10, 20 and 40 µg/eye HM-3, the observed maximum concentration (C_{max}) was 12.98 ± 1.42, 27.87 ± 3.64 and 55.96 ± 11.94 ng/mg, respectively; and the total area under the curve (AUC_{tot}) was 739.23 ± 190.32, 1171.74 ± 528.75 and 1777.71 ± 511.64 h ng/mg; the elimination half-life (T_{1/2}) in retina was 104.85 ± 36.90, 107.42 ± 35.25 and 101.12 ± 15.82 h; the mean residence time (MRT) was 172.46 ± 63.80, 164.70 ± 52.72 and 181.32 ± 26.01 h, respectively. In choroid/sclera, the C_{max} was 5.29 ± 0.34, 6.29 ± 1.87 and 8.14 ± 0.71 ng/mg, respectively; AUC_{tot} was 579.03 ±

56.50, 762.20 ± 201.09 and 720.91 ± 243.87 h ng/mg; T1/2 was 54.04 ± 25.99, 59.33 ± 24.46 and 47.10 ± 10.00 h, respectively; MRT was 139.98 ± 23.93, 155.43 ± 17.81 and 136.45 ± 18.17 h, respectively. But in serum, the Cmax was 482.00 ± 38.97, 493.94 ± 97.64 and 1033.10 ± 276.33 ng/ml, respectively; AUCtot was 21128.55 ± 4683.68, 53444.57 ± 16963.99 and 53164.84 ± 1535.06 h ng/ml; T1/2 was 48.39 ± 14.89, 47.96 ± 12.97 and 49.98 ± 30.07 h, respectively; MRT was 108.6 ± 47.17, 159.76 ± 18.82 and 125.33 ± 21.41 h, respectively.

Conclusions: The pharmacokinetic profiles of intravitreal administration HM-3 provide the basis for the development of reasonable dosing regimens of clinical choroidal neovascularization (CNV) treatment. However, the vitreous and blood retinal barrier might be barriers to drug distribution and diffusion. In addition, fluid flow for the anterior transport and choroidal blood circulation might play important roles for multiple peaking. Carrying out the research into pharmacokinetics of HM-3 provides the information for laying down drug delivery scheme in mice model of CNV.

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Epidemiology

Graefes Arch Clin Exp Ophthalmol. 2014 Feb 25. [Epub ahead of print]

Prevalence of age-related macular degeneration in a large European cohort: Results from the population-based Gutenberg Health Study.

Korb CA, Kottler UB, Wolfram C, Hoehn R, Schulz A, Zwiener I, Wild PS, Pfeiffer N, Mirshahi A.

BACKGROUND: The aim of this study was to describe the sex- and age-specific prevalence of age-related macular degeneration (AMD) and its correlation with urban or rural residence in a large and relatively young European cohort.

METHODS: We evaluated fundus photographs from participants in the Gutenberg Health Study (GHS), a population-based, prospective, observational, single-centre study in the Rhineland-Palatine region in midwestern Germany. The participants were 35-74 years of age at enrolment. The fundus images were classified as described in the Rotterdam Study and were graded independently by two experienced ophthalmologists (CK and UBK) based on the presence of hard and soft drusen, retinal pigmentary abnormalities, and signs of atrophic or neovascular age-related macular generation (AMD).

RESULTS: Photographs from 4,340 participants were available for grading. Small, hard drusen (<63 µm, stages 0b and 0c) were present in 37.4 % of participants (95 % confidence interval [CI], stage 0b, 31.6 % [30.3-33.7]; stage 0c, 5.8 % [5.1-6.5]). Early AMD (soft drusen, pigmentary abnormalities, stages 1-3) was present in 3.8 % of individuals in the youngest age group (35-44 years) (95 % CI, stage 1a, 0.4 % [0.3-0.5 %]; stage 1b, 3.2 % [2.9-3.5 %]; stage 2a, 0.1 % [0.1-0.2 %]; stage 2b, 0 % [0-0.0 %]; stage 3, 0.1 % [0.1-0.2 %]), whereas late AMD (stages 4a and 4b) did not appear in the youngest age group. In all age groups, signs of early AMD were detected in 11.9 % of individuals (stage 1a, 2.1 % [1.7-2.6]; stage 1b, 8.0 % [7.2-8.8]; stage 2a, 1.0 % [0.7-1.3]; stage 2b, 0.5 % [0.3-0.7]; stage 3, 0.3 % [0.2-0.6]). Late AMD (geographic atrophy or neovascular AMD) was found in 0.2 % of individuals (stage 4a, 0.1 % [0.0-0.2]; stage 4b, 0.1 % [0.0-0.2]). AMD increased significantly with age (odds ratio [OR], 1.09; 95 % CI, 1.08-1.10). Sex, iris colour, and residence (rural vs. urban) were not associated with different rates of AMD.

CONCLUSIONS: In this study, the prevalence of AMD increased dramatically with age; however, although AMD is usually thought to occur after age 50, signs of early AMD were found in 3.8 % of individuals in the youngest age group (younger than 45 years). This population-based sample is the first to provide substantial epidemiologic data from a large German cohort, including data on macular degeneration in younger age groups and incidence data after recall.

PMID: 24566902 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 Feb 27. pii: iovs.13-13420v1. doi: 10.1167/iovs.13-13420. [Epub ahead of print]

Genetic and environmental risk factors for age-related macular degeneration in persons 90 years and older.

Ersoy L, Ristau T, Hahn M, Karlstetter M, Langmann T, Dröge K, Caramoy A, den Hollander AI, Fauser S.

Purpose: To study associations of genetic polymorphisms in age related maculopathy susceptibility 2 (ARMS2) and complement factor H (CFH) in nonagenarians with age-related macular degeneration (AMD).

Methods: This case-control study comprised 2737 persons (1204 controls, 1433 AMD-cases) including 166 nonagenarians (52 controls, 114 AMD-cases). Single nucleotide polymorphisms (SNPs) in the genes ARMS2 and CFH were determined. Risk scores were computed by multiple logistic regression analysis, including genetic and environmental risk factors (smoking, hypertension, body mass index, diabetes) for different age groups (<70y (years), 70-79y, 80-89y, ≥90y (nonagenarians)).

Results: In nonagenarians, ARMS2 showed the weakest associations with AMD (Odds ratio (OR)=1.52, $p=0.127$) compared to the other groups (OR 70y=2.23, $p=1.03 \times 10^{-13}$, OR 70-79y=2.70, $p=1.00 \times 10^{-13}$; OR 80-89y=3.11, $p=6.56 \times 10^{-8}$). For CFH, odds ratios for AMD increased with age (<70y: OR=1.96, $p=1.80 \times 10^{-11}$; 70-79y: OR=1.89, $p=4.48 \times 10^{-13}$, 80-89y: OR=2.71, $p=1.28 \times 10^{-7}$) but decreased again in the nonagenarians (OR=2.21, $p=0.005$). Compared to the group <70y, reduced minor allele frequencies (MAF) for AMD patients were observed in the nonagenarians (CFH: 0.54 vs. 0.43, $p=0.009$; ARMS2: 0.44 vs. 0.29, $p=2.97 \times 10^{-5}$) while the MAF in controls were not significantly different. The genetic risk score revealed the lowest discriminative power in the nonagenarians with an area-under-curve (AUC) of 0.658 for receiver-operating characteristics (AUC 80-89y=0.768, 70-79y=0.704, <70y=0.682) while no significant difference was seen for the environmental risk score (AUC <70y=0.579, 70-79y=0.567, 80-89y=0.600, ≥90y=0.608).

Conclusion: Risk alleles in CFH and ARMS2 have a significantly smaller effect on AMD development in nonagenarians while environmental factors retain a similar effect.

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Br J Ophthalmol. 2014 Feb 25. doi: 10.1136/bjophthalmol-2013-304081. [Epub ahead of print]

Prevalence and causes of vision loss in sub-Saharan Africa: 1990-2010.

Naidoo K, Gichuhi S, Basáñez MG, Flaxman SR, Jonas JB, Keeffe J, Leasher JL, Pesudovs K, Price H, Smith JL, Turner HC, White RA, Wong TY, Resnikoff S, Taylor HR, Bourne RR; on behalf of the Vision Loss Expert Group of the Global Burden of Disease Study.

AIM: To estimate the magnitude, temporal trends and subregional variation in the prevalence of blindness, and moderate/severe vision impairment (MSVI) in sub-Saharan Africa.

METHODS: A systematic review was conducted of published and unpublished population-based surveys as part of the Global Burden of Disease, Risk Factors and Injuries Study 2010. The prevalence of blindness and vision impairment by country and subregion was estimated.

RESULTS: In sub-Saharan Africa, 52 studies satisfied the inclusion criteria. The estimated age-standardised prevalence of blindness decreased by 32% from 1.9% (95% CI 1.5% to 2.2%) in 1990 to 1.3% (95% CI 1.1% to 1.5%) in 2010 and MSVI by 25% from 5.3% (95% CI 0.2% to 0.3%) to 4.0% (95% CI 0.2% to 0.3%) over that time. However, there was a 16% increase in the absolute numbers with blindness and a 28% increase in those with MSVI. The major causes of blindness in 2010 were; cataract 35%, other/unidentified causes 33.1%, refractive error 13.2%, macular degeneration 6.3%, trachoma 5.2%, glaucoma 4.4% and diabetic retinopathy 2.8%. In 2010, age-standardised prevalence of MSVI in Africa was 3.8% (95% CI 3.1% to 4.7%) for men and 4.2% (95% CI 3.6% to 5.3%) for women with subregional variations

from 4.1% (95% CI 3.3% to 5.4%) in West Africa to 2.0% (95% CI 1.5% to 3.3%) in southern Africa for men; and 4.7% (95% CI 3.9% to 6.0%) in West Africa to 2.3% (95% CI 1.7% to 3.8%) in southern Africa for women.

CONCLUSIONS: The age-standardised prevalence of blindness and MSVI decreased substantially from 1990 to 2010, although there was a moderate increase in the absolute numbers with blindness or MSVI. Significant subregional and gender disparities exist.

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Diet & lifestyle

Ophthalmology. 2014 Feb 20. pii: S0161-6420(14)00009-8. doi: 10.1016/j.ophtha.2014.01.002. [Epub ahead of print]

Dietary Patterns and Their Associations with Age-Related Macular Degeneration: The Melbourne Collaborative Cohort Study.

Amirul Islam FM, Chong EW, Hodge AM, Guymer RH, Aung KZ, Makeyeva GA, Baird PN, Hopper JL, English DR, Giles GG, Robman LD.

OBJECTIVE: To evaluate the association between dietary patterns and age-related macular degeneration (AMD).

DESIGN: Food frequency data were collected from Melbourne Collaborative Cohort Study (MCCS) participants at the baseline study in 1990-1994. During follow-up in 2003-2007, retinal photographs were taken and evaluated for AMD.

PARTICIPANTS: At baseline, 41 514 participants aged 40 to 70 years and born in Australia or New Zealand (69%), or who had migrated from the United Kingdom, Italy, Greece, or Malta (31%) were recruited. Of these, 21 132 were assessed for AMD prevalence at follow-up.

METHODS: Principal component analysis was used to identify dietary patterns (Factors F1-6) among the food items. Logistic regression was used to assess associations of dietary patterns with AMD.

MAIN OUTCOME MEASURES: Odds ratios (ORs) for early stages and advanced AMD in association with dietary patterns.

RESULTS: A total of 2508 participants (12.8%) had early stages of AMD, and 108 participants (0.6%) had advanced AMD. Six factors characterized by predominant intakes of fruits (F1); vegetables (F2); grains, fish, steamed or boiled chicken, vegetables, and nuts (F3); red meat (F4); processed foods comprising cakes, sweet biscuits, and desserts (F5); and salad (F6) were identified. Higher F3 scores were associated with a lower prevalence of advanced AMD (fourth vs. first quartile) (OR, 0.49; 95% confidence interval [CI], 0.28-0.87), whereas F4 scores greater than the median were associated with a higher prevalence of advanced AMD (OR, 1.46; 95% CI, 1.0-2.17).

CONCLUSIONS: Rather than specific individual food items, these factors represent a broader picture of food consumption. A dietary pattern high in fruits, vegetables, chicken, and nuts and a pattern low in red meat seems to be associated with a lower prevalence of advanced AMD. No particular food pattern seemed to be associated with the prevalence of the earliest stages of AMD.

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