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Systemic Medication Use with the Incidence and Growth of Geographic Atrophy

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Financial disclosures:

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My role in this research:

- Conception and design of the work/project
- Analysis and interpretation of data
- Creation and/or critical review of the presentation

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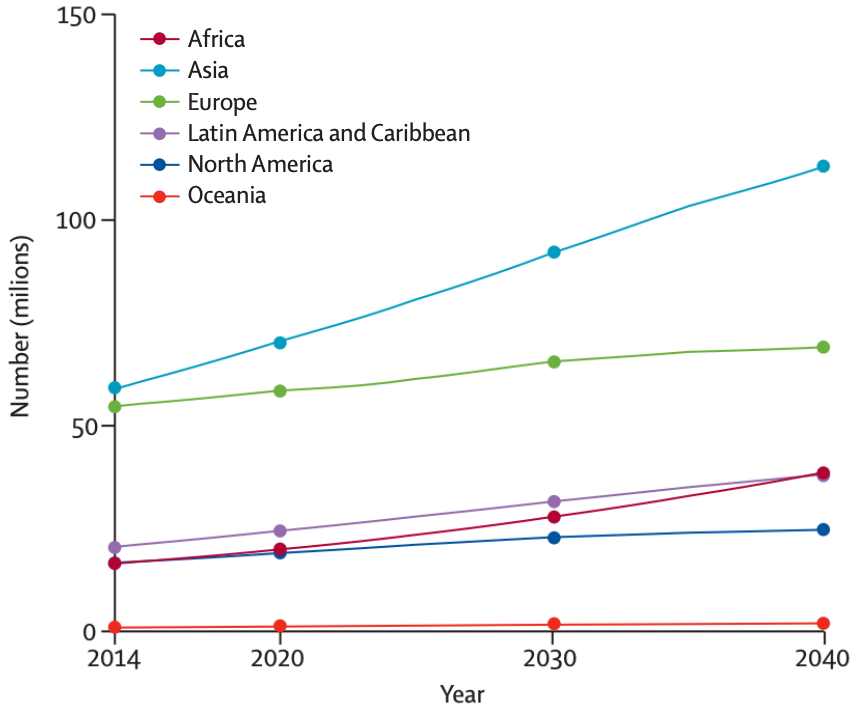
Background

The projected number of people with age-related macular degeneration (AMD) in 2020 is 196 million, increasing to 288 million in 2040*.



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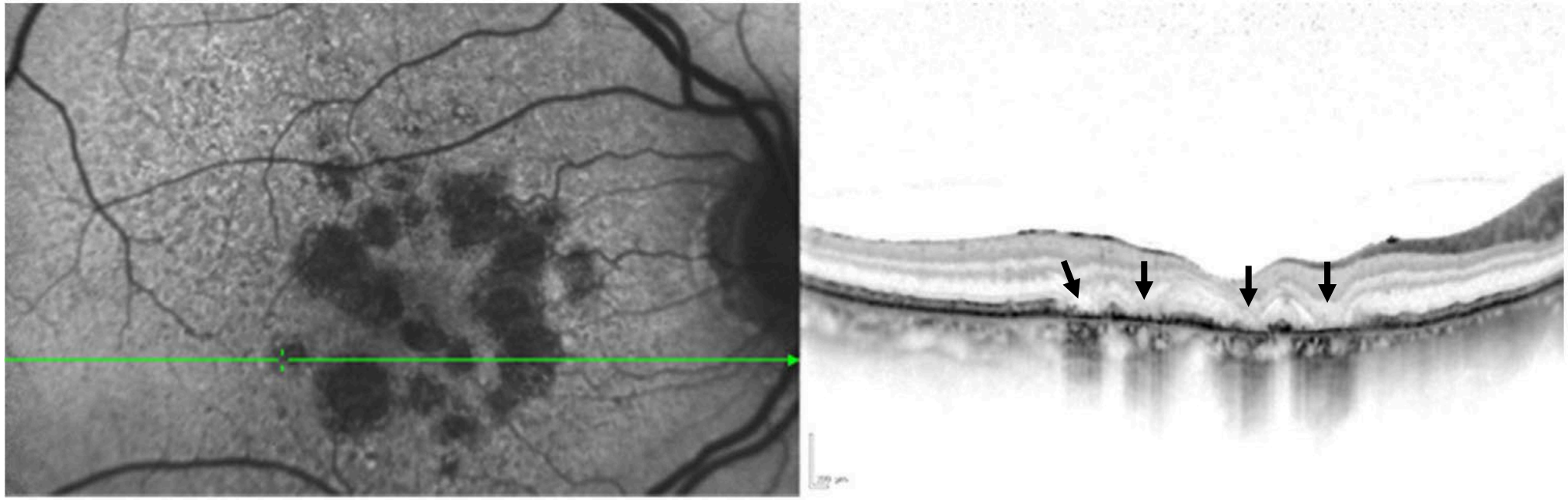
*Lancet Glob Health. 2014;2(2):e106-116.

Geographic atrophy (GA) is characterized by loss of retinal photoreceptors, RPE, and choriocapillaris.



“Will taking a beta-blocker interfere with my AMD?”

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ELSEVIER

Ophthalmology
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Report

β-blockers and Neovascular Age-related Macular Degeneration

Ling Yeung MD [1, 2], Ting-Shuo Huang MD, PhD [3, 4, 5, 6], Yun-Hsuan Lin MD [1], Kuang-Hung Hsu PhD [7, 8], Jerry Chien-Chieh Huang MD [1, 2], Chi-Chin Sun MD, PhD [1, 4, 5]

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Retina. 2019 May ; 39(5): 918–925. doi:10.1097/IAE.0000000000002059.

Systemic Beta-Blockers and Risk of Progression to Neovascular Age-related Macular Degeneration

Anton M. Kolomeyer, MD, PhD[1], **Maureen G. Maguire, PhD**[2,3], **Wei Pan, MS**[2], and **Brian L. VanderBeek, MD, MPH, MSCE**[1,3,4]

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Original Contribution

December 19, 2012

Long-term Use of Aspirin and Age-Related Macular Degeneration

Barbara E. K. Klein, MD, MPH; Kerri P. Howard, MS; Ronald E. Gangnon, PhD; Jennifer O. Dreyer, BS; Kristine E. Lee, MS; Ronald Klein, MD, MPH

AMERICAN ACADEMY OF OPHTHALMOLOGY®

The Association of Aspirin Use with Age-Related Macular Degeneration Progression in the Age-Related Eye Disease Studies

Age-Related Eye Disease Study 2 Report No. 20

Purpose:

To determine associations of systemic medications with the incidence and growth of GA in participants of the Comparison of Age-related Macular Degeneration Treatments Trials (CATT)

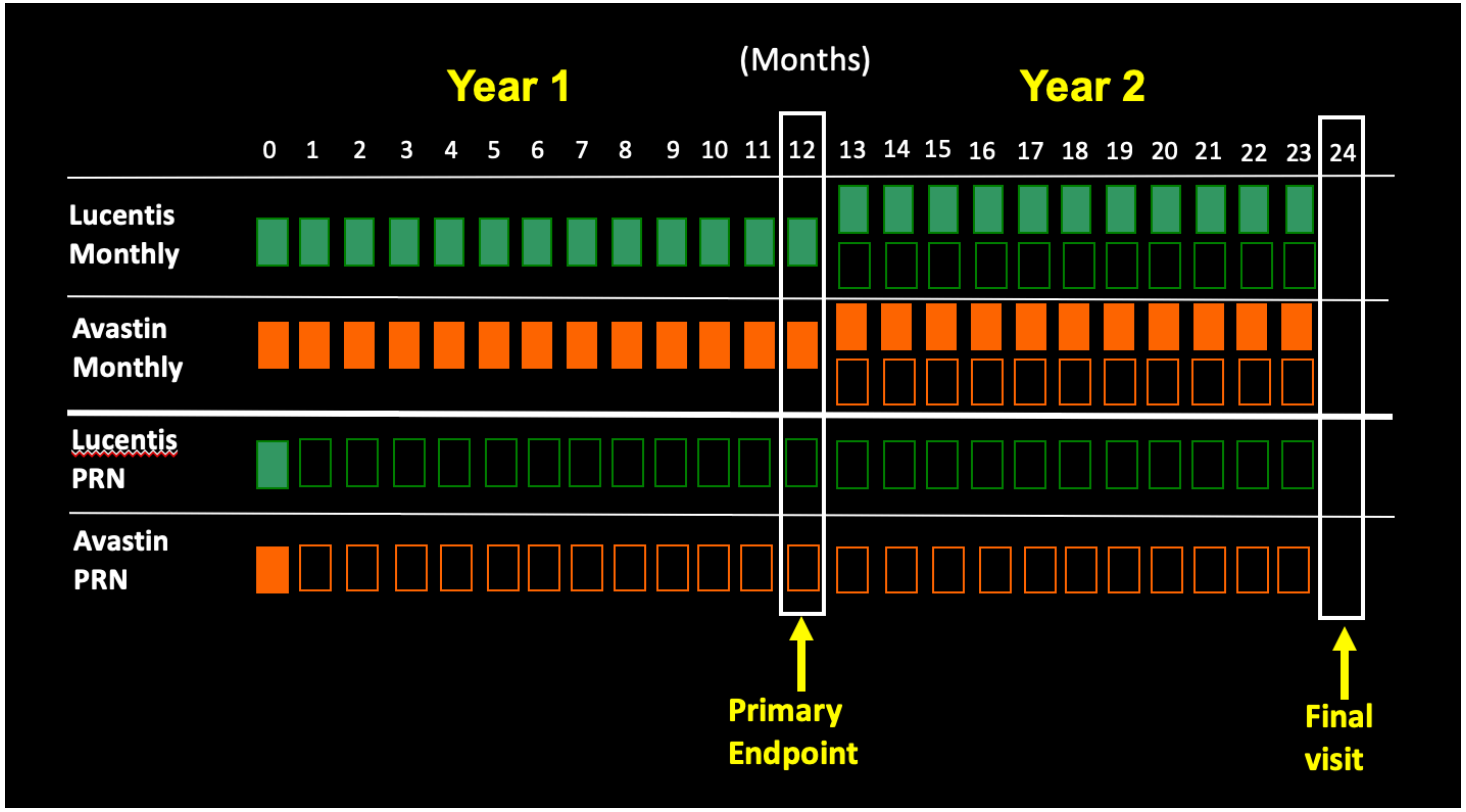
Exposure:

Systemic medications

- Cholinesterase inhibitor
- ACE inhibitors
- Calcium channel blockers
- Beta-blockers
- Diuretics
- Aspirin
- Steroids
- Statins
- Hormone replacement therapy
- Antacids
- Drugs targeting G protein-coupled receptors.

Methods:

- CATT is a multicenter, prospective, noninferiority, clinic trial evaluating the safety and efficacy of ranibizumab or bevacizumab in the treatment of exudative AMD.



Methods:

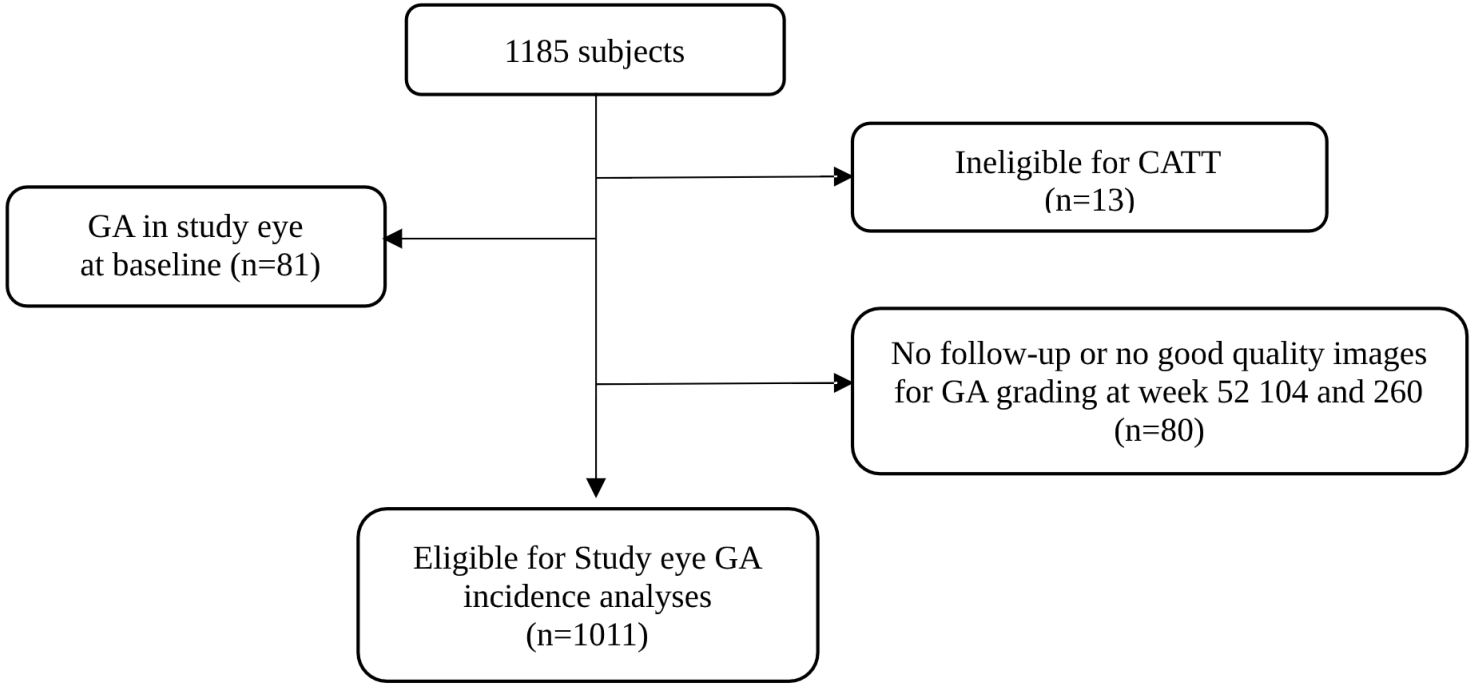
- The GA was defined as a partial or complete depigmentation of one or more patches ≥ 250 μ in longest linear dimension in the macula in the color fundus photos.
- The area of individual GA lesion was measured manually with Image J.

Methods:

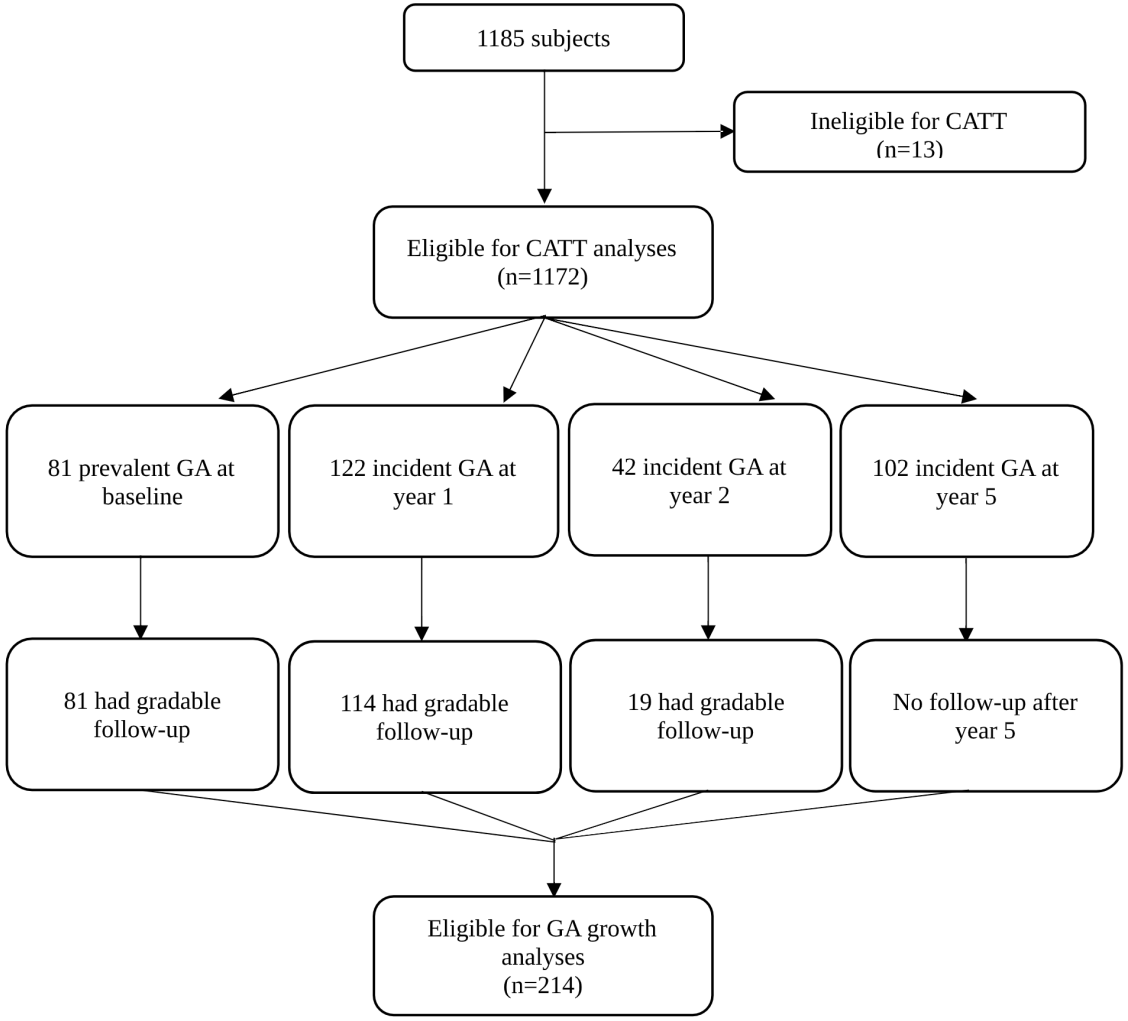
- Univariable and multivariable Cox regression models were used in assessing the association between systemic medication and GA incidence.
- Univariable and multivariable mixed effects models were used in assessing the association between systemic medication and GA growth.

Results:

Flow chart for the study eye GA incidence analysis cohort



Flow chart for the study eye GA growth analysis cohort



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The baseline characteristics of study eye GA incidence cohort and GA growth cohort

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Baseline Characteristics	GA Incidence Cohort (N=1011)	GA Growth Cohort (N=214)
Baseline age: Mean (SD)	78.9 (7.6)	80.6 (6.4)
Gender: Female (%)	623 (61.6%)	136 (63.6%)
Smoking Status		
Never	436 (43.1%)	94 (43.9%)
Former	491 (48.6%)	106 (49.5%)
Current	84 (8.3%)	14 (6.5%)
Randomized Treatment Drug		
Ranibizumab	517 (51.1%)	118 (55.1%)
Bevacizumab	494 (48.9%)	96 (44.9%)
Baseline visual acuity in study eye (letters): Mean (SD)	60.7 (13.4)	59.4 (13.1)
Baseline GA in fellow eye: yes (%)	87 (8.7%)	63 (29.7%)
Baseline study eye CNV area (DA): mean (SD)	2.5 (2.5)	2.5 (2.6)
RAP lesion in study eye: yes (%)	112 (11.2%)	38 (17.8%)
Hemorrhage in study eye: yes (%)	606 (60.4%)	155 (72.4%)
Sub-RPE fluid in study eye: yes (%)	495 (53.0%)	106 (53.8%)

The association between baseline medication use with 5-year incidence of GA (N=1011)

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	Medications No	Medication Yes	Multivariable Analysis*	
Systemic medications taken at baseline	Crude GA incidence in study eye (%)	Crude GA incidence in study eye (%)	Adjusted HR (95% CI)	p-value
Cholinesterase inhibitor	257/994 (25.9%)	8/17 (47.1%)	1.65 (0.80, 3.43)	0.18
ACE inhibitors	142/542 (26.2%)	123/469 (26.2%)	1.12 (0.87, 1.45)	0.38
Calcium channel blockers	189/736 (25.7%)	76/275 (27.6%)	1.17 (0.89, 1.54)	0.27
Beta-blocker	176/674 (26.1%)	89/337 (26.4%)	1.01 (0.78, 1.32)	0.93
Diuretics	158/593 (26.6%)	107/418 (25.6%)	1.00 (0.77, 1.29)	0.98
Aspirin	163/584 (27.9%)	102/427 (23.9%)	0.91 (0.70, 1.18)	0.48
Steroids	232/885 (26.2%)	33/126 (26.2%)	1.29 (0.87, 1.90)	0.21

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* Using no mediation as reference group, adjusted by age, smoking status, drug, treatment regimen, baseline visual acuity in study eye, baseline CNV area, RPA lesion, GA in fellow eye, subretinal tissue complex, intraretinal fluid, subretinal fluid, and AREDS severity scale.

The association between baseline medication use with 5-year incidence of GA (N=1011)

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	Medications No	Medication Yes	Multivariable Analysis*	
Systemic medications taken at baseline	Crude GA incidence in study eye (%)	Crude GA incidence in study eye (%)	Adjusted HR (95% CI)	p-value
Statin	130/515 (25.2%)	135/496 (27.2%)	1.19 (0.92, 1.53)	0.18
Iron medication (all doses)	259/996 (26.0%)	6/15 (40.0%)	1.52 (0.68, 3.42)	0.31
Iron medication (50mg or more)	261/1001 (26.1%)	4/10 (40.0%)	1.86 (0.69, 4.99)	0.22
Iron supplements	228/868 (26.3%)	37/143 (25.9%)	1.15 (0.80, 1.65)	0.46
Hormone replacement (females only)	253/977 (25.9%)	12/34 (35.3%)	1.35 (0.76, 2.41)	0.31
Drug targeting G protein coupled receptors	239/906 (26.4%)	26/105 (24.8%)	0.98 (0.64, 1.51)	0.94
Antacid	247/954 (25.9%)	18/57 (31.6%)	1.20 (0.74, 1.93)	0.47

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* Using no mediation as reference group, adjusted by age, smoking status, drug, treatment regimen, baseline visual acuity in study eye, baseline CNV area, RPA lesion, GA in fellow eye, subretinal tissue complex, intraretinal fluid, subretinal fluid, and AREDS severity scale.

The association between baseline medication with GA growth during 5-year CATT (N=214)

			Univariable Analyses		Multivariable Analyses*	
Systemic medications taken at baseline		Frequency (%)	Mean GA Growth Rate mm/year (SE)	p-value	Mean Growth Rate mm/year (SE)[1]	p-value
Calcium channel blockers	Yes	58 (27.1%)	0.38 (0.05)	0.06	0.40 (0.05)	0.02
	No	156 (72.9%)	0.31 (0.02)		0.30 (0.02)	
Steroids (Oral)	Yes	5 (2.3%)	0.57 (0.12)	0.04	NA	NA
	No	209 (97.7%)	0.32 (0.02)		NA	

*Adjusted by drug, treatment regimen, baseline GA in fellow eye, hemorrhage, and sub-RPE fluid.

Conclusions:

- In the eyes treated with anti-VEGF for exudative AMD, no significant association between GA development with cholinesterase inhibitor, ACE inhibitors, calcium channel blockers, beta-blockers, diuretics, aspirin, steroids, statins, hormone replacement therapy, antacids, and drugs targeting G protein-coupled receptors.

- Calcium channel blockers were associated with higher growth rate of GA, which requires validation in future studies.

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- Dr. Maureen Maguire
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- Center for Preventive Ophthalmology and Biostatistics at Penn
- CATT study group

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