

Supplementary Online Content

Vitale S, Clemons TE, Agrón E, et al; Age-Related Eye Disease Study 2 (AREDS2) Research Group. Evaluating the validity of the Age-Related Eye Disease Study grading scale for age-related macular degeneration: AREDS2 report 10. *JAMA Ophthalmol*. Published online July 21, 2016. doi:10.1001/jamaophthalmol.2016.2383.

eAppendix. The Age-Related Eye Disease Study 2 (AREDS2) Research Group

eTable 1. Baseline Characteristics of AREDS and AREDS2 Participants Free of Late AMD in Both Eyes at Baseline

eTable 2. Percent Developing Late AMD in 5 Years in the AREDS and AREDS2, Both Eyes Free of Late AMD at Baseline

eTable 3. 5-Year Rates of Late AMD and (for Eyes That Did Not Progress to Late AMD) Rates of Progression From Scale Steps 1 to 6 to Step 7 or 8 or to Step 9, Right and Left Eyes Combined, of AREDS2 Participants Free of Late AMD in Both Eyes at Baseline

eTable 4. 5-Year Rates of Late AMD (and for Eyes That Did Not Progress to Late AMD) Rates of Progression From Scale Steps 1 to 6 to Step 7 or 8 or to Step 9, Right and Left Eyes Combined, of AREDS2 Participants With Neovascular AMD in the Fellow Eye at Baseline

eTable 5. Combined Data From AREDS and AREDS2 (Based on Table 2 of the Article)

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. The Age-Related Eye Disease Study 2 (AREDS2) Research Group

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(048) Northwestern University, Ophthalmology

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(049) Ophthalmic Consultants of Boston

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(050) Pacific Eye Associates

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(051) Penn State M.S. Hershey Medical Center

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(052) Palmetto Retina Center

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Megan Rakes (Ophthalmic Technician)
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(054) Retina Consultants, PLLC

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(055) University of Iowa

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(056) Wills Eye Hospital/Mid Atlantic Retina

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(057) Doheny Eye Institute USC

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(058) The Retina Group of Washington

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Robert Murphy, MD, (Ophthalmologist)
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(060) The Medical College of Wisconsin

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David V. Weinberg, MD, (Ophthalmologist)
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Krissa Packard (Clinic Coordinator)
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(061) John Moran Eye Center

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(064) Baylor College of Medicine

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(066) Carolina Retina Center

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(067) Case Western Reserve University

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Kathleen Carlton (Ophthalmic Technician)
Claudia Clow (Ophthalmic Technician)
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(069) Eye Foundation of Kansas City

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(070) Jones Eye Institute - UAMS

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(071) Kresge Eye Institute

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(072) Colorado Retina Associates PC

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(075) University Health Care - Mason Eye Institute

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(076) University of Tennessee HSC

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(077) Fletcher Allen Health Care

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(078) Mayo Clinic

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(079) The Retina Institute

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(082) UMDNJ

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(084) The University of Illinois

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(085) Jules Stein Eye Institute

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(086) Univ. of Alabama at Birmingham

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(089) Duke University

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(093) Shiley Eye Center - UCSD

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eTable 1. Baseline Characteristics of AREDS and AREDS2 Participants Free of Late AMD in Both Eyes at Baseline

Participants	AREDS		AREDS2	
	n	%	n	%
Age*	N= 2506		N=2723	
<55	0	0%	69	2.5%
55-64	548	21.9%	471	17.3%
65-69	888	35.4%	499	18.3%
70-79	1070	42.7%	1236	45.4%
80+	0	0%	448	16.4%
Right eyes	N=3212		N=2720	
Drusen area*†				
None, Questionable (Q), <C-0, <C-1	1522	47.4	38	1.4
≥C-1, <C-2	463	14.4	57	2.1
≥C-2, <I-2	315	9.8	86	3.2
≥I-2, <O-2	259	8.1	266	9.8
≥O-2, <0.5DA	186	5.8	446	16.4
≥0.5DA, <1.0DA	164	5.1	677	24.9
≥1.0DA	303	9.4	1150	42.3
Maximum drusen size*				
None	155	4.8	13	0.5
Questionable (Q)	91	2.8	5	0.2
<C-0 (<63 um)	1249	38.9	16	0.6
≥C-0, <C-1 (≥63, <124 um)	713	22.2	121	4.4
≥C-1, <C-2 (≥125, <249 um)	603	18.8	1145	42.1
≥C-2 (≥250um)	401	12.5	1420	52.2
Predominance of soft indistinct drusen*				
Absent	2003	62.4	61	2.2
Questionable			205	7.5
Present, not predominant	136	4.2	839	30.8
Predominant in 1 of 3 zones	430	13.4	123	4.5
Predominant in 2 of 3 zones	335	10.4	242	8.9
Predominant in 3 of 3 zones	308	9.6	1250	46.0
Area of increased pigmentation*				
None	2464	76.7	821	30.2
Q	66	2.0	87	3.2
>Q, <C-2	484	15.1	1084	39.8
≥C-2	198	6.2	728	26.8
Area of depigmentation/presence of GA*				
Depigmentation				
None	2793	87.0	1878	69.0
Questionable (Q)	117	3.6	101	3.7
>Q, <I-2	88	2.7	233	8.6
≥I-2, <0.5DA	131	4.1	285	10.5
≥0.5DA	48	1.5	87	3.2

GA	35	1.1	136	5.0
Area of increased/decreased pigment or presence of GA*				
None	2412	75.1	795	29.2
Increased pigmentation \geq Q and/or depigmentation $<$ I-2	586	18.2	1324	48.7
Depigmentation \geq I-2, $<$ 0.5DA	131	4.1	300	11.0
Depigmentation \geq 0.5DA	48	1.5	95	3.5
GA	35	10.9	106	3.9

* $p < .0001$, comparing the AREDS2 and AREDS distributions

† C-0, C-1, C-2, I-2, and O-2 are standard circles used in fundus photograph gradings. They have diameters of 63, 125, 250, 354, and 650 μm , respectively. DA: disc area.

eTable 2. Percent Developing Late AMD in 5 Years in the AREDS and AREDS2, Both Eyes Free of Late AMD at Baseline

	AREDS		AREDS2	
Right eyes	x/n	%	x/n	%
Total	200/3212	6.2	616/2720	22.6
Drusen area				
None, Q, <C-0, <C1	9/1522	0.6	2/38	5.3
≥C-1, <C-2	11/463	2.4	6/57	10.5
≥C-2, <I-2	13/315	4.1	11/86	12.8
≥I-2, <O-2	19/259	7.3	43/266	16.2
≥O-2, <0.5DA	26/186	14.0	66/446	14.8
≥0.5DA, <1.0DA	42/164	25.6	145/677	21.4
≥1.0DA	80/303	26.4	343/1150	29.8
Maximum drusen size				
None	0/155	0	1/13	7.7
Q	1/91	1.1	1/5	20
<C-0 (<63 um)	5/1249	0.4	0/16	0
≥C-0, <C-1 (≥63, <124 um)	27/713	3.8	19/121	15.7
≥C-1, <C-2 (≥125, <249 um)	65/603	10.8	197/1145	17.2
≥C-2 (≥250um)	102/401	25.4	398/1420	28.0
Predominance of soft indistinct drusen				
Absent	28/2003	1.4	5/61	8.2
Questionable			23/205	11.2
Present, not predominant	9/136	6.6	184/839	21.9
Predominant in 1 of 3 zones	38/430	8.8	38/123	30.9
Predominant in 2 of 3 zones	48/335	14.3	64/242	26.4
Predominant in 3 of 3 zones	77/308	25.0	302/1250	24.2
Area of increased pigmentation				
None	48/2464	1.9	73/821	8.9
Q	10/66	15.2	12/87	13.8
>Q, <C-2	79/484	16.3	215/1084	19.8
≥C-2	63/198	31.8	316/728	43.4
Area of depigmentation/presence of GA				
Depigmentation				
None	105/2793	3.8	287/1878	15.3
Q	10/117	8.5	26/101	25.7
>Q, <I-2	11/88	12.5	65/233	27.9
≥I-2, <0.5DA	32/131	24.4	102/285	35.8
≥0.5DA	25/48	52.1	47/87	54.0
GA	17/35	48.6	89/136	65.4
Area of increased/decreased pigment or presence of GA				
None	38/2412	1.6	63/795	7.9
Increased pigmentation ≥Q and/or depigmentation <I-2	88/586	15.0	319/1324	22.4

Depigmentation \geq -2, <0.5DA	32/131	24.4	114/300	38.0
Depigmentation \geq 0.5DA	25/48	52.1	52/95	54.7
GA	17/35	48.6	68/106	64.2

eTable 3. 5-Year Rates of Late AMD and (for Eyes That Did Not Progress to Late AMD) Rates of Progression From Scale Steps 1 to 6 to Step 7 or 8 or to Step 9, Right and Left Eyes Combined, of AREDS2 Participants Free of Late AMD in Both Eyes at Baseline

Step	No. at risk	Step 7 or 8		Step 9		Neovascular AMD (only)		Central GA (only)		Neovascular AMD, central GA, or both*	
		No.	%	No.	%	No.	%	No.	%	No.	%
1, 2, 3	206	12	5.8	0	0	4	1.9	1	0.5	5	2.4
4	323	66	20.4	6	1.8	11	3.4	5	1.5	21	6.5
5	591	324	54.8	13	2.2	29	4.9	6	1.0	47	8.0
6	1354	1117	82.5	63	4.6	100	7.4	47	3.5	174	12.8
7	2145	N.A.	-	293	13.6	298	13.9	226	10.5	563	26.2
8	554	N.A.	-	184	33.2	88	15.9	157	28.3	257	46.4
9	219	N.A.	-	N.A.	-	32	14.6	104	47.5	134	61.2
Total	5392	1519	61.4	559	10.8	562	10.4	546	10.1	1201	22.3

*Includes those with neovascular AMD who had missing information for central GA, and also those with central GA who had missing information for neovascular AMD.

eTable 4. 5-Year Rates of Late AMD (and for Eyes That Did Not Progress to Late AMD) Rates of Progression From Scale Steps 1 to 6 to Step 7 or 8 or to Step 9, Right and Left Eyes Combined, of AREDS2 Participants With Neovascular AMD in the Fellow Eye at Baseline

		No.	%	No.	%	No.	%	No.	%
Step	No. at risk	Step 7 or 8		Step 9		Neovascular AMD (only)		Central GA (only)	
1, 2, 3	65	3	4.6	1	1.5	9	13.8	0	0
4	93	16	17.2	3	3.2	16	17.2	0	0
5	147	77	52.4	4	2.7	46	31.3	5	3.4
6	306	214	69.9	23	7.5	100	32.7	10	3.3
7	522	N.A.	-	68	13.0	210	40.2	45	8.6
8	226	N.A.	-	33	14.6	70	31.0	60	26.5
9	131	N.A.	-	N.A.	-	26	19.8	72	55.0
Total	1490	310	50.7	132	9.7	477	32.0	192	12.9

eTable 5. Combined Data From AREDS and AREDS2 (Based on Table 2 of the Article)

AREDS detailed severity scale score	No. at risk	No. developing late AMD in 5 yrs	% developing late AMD in 5 yrs	Lower 95% CL	Upper 95% CL
1-3	2836	18	0.63	0.34	0.93
4	830	46	5.54	3.98	7.10
5	863	63	7.30	5.56	9.04
6	1729	228	13.19	11.59	14.78
7	2512	673	26.79	25.06	28.52
8	702	326	46.44	42.75	50.13
9 (non-central GA)	270	163	60.37	54.54	66.20