

AREDS Report No. 18 -- APPENDIX

Table 1 appears in the published report and is included here as Appendix Table 1 to facilitate comparisons. Appendix Table 2 is an expansion of Table 2 in the report, to be discussed in conjunction with Appendix Tables 5 and 6.

Some of the cells in Table 1 are made up of several small subgroups. To determine whether these subgroups were appropriately combined, a table of right eye by left eye was constructed using three drusen size categories (small or no drusen, intermediate drusen, large drusen) and two pigment abnormality categories (absent, present) for each eye. Appendix Table 3 presents this information in the format of Table 1. In most cases, the subgroups making up each part of each cell in Table 1 have similar rates; exceptions are described below. In the row 4, column 1 cell, the rates for patients with large drusen in one eye and small or no drusen in the other, and no pigment abnormalities in either eye ($1/71 + 0/46 = 1/117$, 0.9%), appear to increase when the second eye has intermediate drusen ($8/93 + 2/73 = 10/166$, 6.0%). This would be biologically plausible, but in the latter case the difference by presence of the large drusen in the right versus the left eye, which is likely due to chance, also appears substantial, and in both cases numbers are small. Moreover, in the row 4, column 2 cell, the patients with large drusen plus pigment abnormalities in one eye and intermediate drusen in the other ($2/31 + 1/28 = 3/59$, 5.1%) appear to have lower rates than similar patients who have only small or no drusen in the second eye, a biologically implausible finding. From Appendix Table 3 it appears that the combination of subgroups in Table 1 is appropriate.

Alternatives to Table 1 that used the same drusen size categories but different combinations of the three pigmentary abnormalities (each alone and in the three possible pairs of two) are summarized in Appendix Table 4, in which the same information shown in Table 1 is rearranged to form the first section (Any of 3). In the second section (Increased Pigment or Depigmentation), only the three entries that differ from those in the first section are shown. These differences are caused by movement of one patient who developed advanced AMD from 4 to 3 risk factors and two patients who did not develop advanced AMD from 3 to 2 risk factors.

In the remaining sections of Appendix Table 4 data are shown for all drusen size/pigment abnormality categories. The third and fourth sections, increased pigment only and increased pigment or non-central GA, differ very little from the first two sections. The Depigmentation only and Depigmentation or non-central GA sections are almost identical to each other and differ from the preceding four sections mainly by increased rates of advanced AMD in the 3 risk factor row, which average about 39%, versus about 27% in each of the preceding 4 sections. In the final section, in which non-central GA is the only pigment abnormality considered, the rate in the 3 risk factor row increases to about 77%.

Appendix Table 5 is similar to Table 1, but patients with noncentral GA at baseline have been excluded. The principal result of their exclusion is a decrease in the rate for patients with large drusen in both eyes and pigment abnormalities (other than GA) in only one eye, from 27% in Table 1 to 14% in Appendix Table 5, suggesting that addition of pigment abnormalities (other than GA) in one eye of a patient with large drusen in both eyes adds little to the risk of advanced AMD. This observation may be useful if the simplified scale is to be used in planning research studies. When the rates in the cells of this table are combined in the same fashion as those in Table 1, the result is as shown in the second part of Appendix Table 2.

In Appendix Table 6, the pigment abnormality categories are the same as those in Table 1, but in the drusen category, area replaces size. The rates in the two tables are similar, but the risk increases with increasing drusen area to the same degree whether one or both eyes are in the category. For the person, 1 risk factor is assigned if drusen area (in one or both eyes) is “moderate”, and 2 risk factors are assigned if drusen area is “large”. The shaded cells in each risk factor category are combined and shown in the third section of Appendix Table 2. The rates in each risk factor category are similar to those in the first section, but slightly higher.

Appendix Table 7 is similar to Table 1 but considers only patients who had neovascular AMD in one eye at baseline. The 5-year rate of advanced AMD in the second eye was 15% when this eye had neither large drusen nor pigment abnormalities at baseline, 36% when it had either one of these characteristics and 54% when it had both.

Appendix Table 8 provides details by type of advanced AMD for the scale presented in Table 1 and the first section of Table 2. In persons with two or fewer risk factors neovascular AMD was a substantially more common outcome (5 + 15 + 38 persons developed neovascular AMD alone in one eye and 1 + 2 + 7 persons developed neovascular AMD alone in both eyes, vs. 2 + 4 persons who developed central GA in one eye and none who developed it in both eyes). In persons with 4 risk factors, central GA was a slightly more frequent outcome.

Appendix Table 1. Number and Percent of Patients Developing Advanced AMD in One or Both Eyes At or Before the 5-year Follow-up Visit for 3211 Patients Free of Advanced AMD in Both Eyes at Baseline

Drusen Size and Number of eyes	Pigment Abnormalities					
	None		1 Eye		Both Eyes	
	n/N	%	n/N	%	n/N	%
Small, only one or both eyes (or none)	4/1017	0.4	0/64	0.0	1/8	12.5
Intermediate, one eye (no large)	2/449	0.5	5/101	5.0	4/31	12.9
Intermediate, both eyes (no large)	4/187	2.1	6/50	12.0	7/35	20.0
Large, one eye	11/283	3.9	17/168	10.1	30/117	25.6
Large, both eyes	27/208	13.0	48/176	27.3	150/317	47.3

n = number of events; N = number at risk



0 1 2 3 4
Number of Risk Factors

Appendix Table 2. Five-year rates of advanced AMD (in one or both eyes for patients with both eyes at risk)

	Patients without advanced AMD in either eye at baseline						Patients with neovascular AMD in fellow eye at baseline					
	Drusen size and pigment abnormalities			Patients with noncentral GA excluded			Drusen area and pigment abnormalities			Drusen size and pigment abnormalities *		
Risk Factors	No. At Risk	No.	%	No. At Risk	No.	%	No. At Risk	No.	%	No. At Risk	No.	%
0	1466	6	0.4	1466	6	0.4	1772	10	0.6			
1	635	20	3.1	635	20	3.1	497	24	4.8			
2	465	55	11.8	451	48	10.6	381	56	14.7	145	22	15.2
3	328	85	25.9	289	55	19.0	259	78	30.1	165	59	35.8
4	317	150	47.3	148	314	47.1	302	148	49.0	233	125	53.6

* Two risk factors assigned for presence of neovascular AMD in fellow eye.

Appendix Table 3. Five-year rates of advanced AMD in one or both eyes for 3211 patients free of advanced AMD in both eyes at baseline

Drusen Size Category	Pigment Abnormality Category								
	1. None			2. 1 Eye			3. Both Eyes		
	Subgroup	n/N	%	Subgroup	n/N	%	Subgroup	n/N	%
1. Small/none, one or both eyes	All	4/1017	0.4	RE s/n, LE s/n+p	0/33		RE s/n+p, LE s/n+p	1/8	12.5
				LE s/n, RE s/n+p	0/31				
				Total	0/64 0.0				
2. Intermediate, one eye	RE	1/213		RE int, LE s/n+p	1/11		RE s/n+p, LE int+p	1/14	
	LE	1/236		LE int, RE s/n+p	0/18		LE s/n+p, RE int+p	3/17	
				RE int+p, LE s/n	3/35				
				LE int+p, RE s/n	1/37				
	Total	2/449	0.5	Total	5/101	5.0	Total	4/31	12.9
3. Intermediate, both eyes	RE int, LE int	4/187	2.1	RE int+p, LE int	1/31		RE int+p, LE int+p	7/35	20.0
				LE int+p, RE int	5/19				
				Total	6/50 12.0				
4. Large, one eye	RE large, LE s/n	1/71		RE large, LE s/n+p	0/4		RE large+p, LE s/n+p	6/15	
	LE large, RE s/n	0/46		LE large, RE s/n+p	0/8		LE large+p, RE s/n+p	3/13	
	RE large, LE int	8/93		RE large, LE int+p	4/16		RE large+p, LE int+p	12/48	
	LE large, RE int	2/73		LE large, RE int+p	2/23		LE large+p, RE int+p	9/41	
				RE large+p, LE s/n	2/24				
				LE large+p, RE s/n	6/34				
				RE large+p, LE int	2/31				
				LE large+p, RE int	1/28				
	Total	11/283	3.9	Total	17/168	10.1	Total	30/117	25.6
	5. Large, both eyes	RE large, LE large	27/208	13.0	RE large, LE large+p	23/86		RE large+p, LE large+p	150/317
LE large, RE large+p					25/90				
Total					48/176 27.3				

Appendix Table 4. Five-year rates of advanced AMD in one or both eyes for 3211 patients free of advanced AMD in both eyes at baseline

Risk Factors	Drusen Size / Pigment Category	Pigment Abnormalities													
		Any of 3		Inc Pg or Depg		Inc Pg Only		Inc Pg or GA		Depg Only		Depg or GA		GA Only	
		n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
0	Small or none/None	4/1017	0.4			4/1029	0.4	4/1029	0.4	4/1046	0.4	4/1045	0.4	5/1088	0.5
	Inter 1 eye/None	2/449	0.5			4/457	0.9	3/456	0.7	5/510	1.0	5/510	1.0	10/580	1.7
1	Inter both/None	4/187	2.1			4/188	2.1	4/188	2.1	11/229	4.8	11/228	4.8	15/267	5.6
	Large 1 eye/None	11/283	3.9			12/307	3.9	12/307	3.9	22/383	5.7	22/383	5.7	53/560	9.5
	Small or none/1 eye	0/64	0.0			0/54	0.0	0/54	0.0	0/39	0.0	0/39	0.0	0/0	
	Inter 1 eye/1 eye	5/101	5.0			5/98	5.1	5/98	5.1	3/61	4.9	3/61	4.9	0/0	
2	Large both/None	27/208	13.0	27/210	12.9	31/230	13.5	29/226	12.8	87/412	21.1	84/407	20.6	194/660	29.4
	Inter both /1 eye	6/50	12.0			7/53	13.2	7/53	13.2	5/29	17.2	4/28	14.3	2/5	40.0
	Large 1 eye/1 eye	17/168	10.1			21/153	13.7	20/152	13.2	20/138	14.5	20/137	14.6	4/7	57.1
	Small or none/Both	1/8	12.5			1/6	16.7	1/6	16.7	1/4	25.0	1/5	20.0	0/1	0.0
	Inter 1 eye/Both	4/31	12.9			2/26	7.7	3/27	11.1	3/10	31.0	3/10	30.0	1/1	100.0
3	Large both/1 eye	48/176	27.3	49/175	28.0	55/173	31.8	52/172	30.2	82/188	43.6	81/188	43.1	29/38	76.3
	Inter both/Both	7/35	20.0			6/31	19.4	6/31	19.4	1/14	7.1	2/16	12.5	0/0	
	Large 1 eye/Both	30/117	25.6			25/108	23.1	26/109	23.9	16/47	34.0	16/48	33.3	1/1	100.0
4	Large both/Both	150/317	47.3	149/316	47.2	139/298	46.6	144/303	47.5	56/101	55.4	60/106	56.6	2/3	66.7

Appendix Table 5. Five-year rates of advanced AMD in one or both eyes for 3155 patients free of advanced AMD and of non-central GA in both eyes at baseline

Drusen Size/Eyes	Pigment Abnormalities					
	None		1 Eye		Both Eyes	
	n/N	%	n/N	%	n/N	%
Small, one or both eyes (or none)	4/1017	0.4	0/64	0.0	1/7	14.3
Intermediate, one eye	2/449	0.5	5/101	5.0	3/30	10.0
Intermediate, both eyes	4/187	2.1	4/45	8.9	7/35	20.0
Large, one eye	11/283	3.9	13/161	8.1	29/116	25.0
Large, both eyes	27/208	13.0	19/138	13.8	148/314	47.1

Appendix Table 6. Five-year rates of advanced AMD in one or both eyes for 3211 patients free of advanced AMD in both eyes at baseline

Drusen Area and Number of Eyes	Pigment Abnormalities					
	None		1 Eye		Both Eyes	
	n/N	%	n/N	%	n/N	%
< moderate * in both eyes (or none)	10/1772	0.6	10/264	3.8	11/89	12.4
moderate, one eye	11/171	6.4	17/125	13.6	27/94	28.7
moderate, both eyes	3/62	4.8	4/28	14.3	6/23	26.1
large †, one eye	11/70	15.7	20/60	33.3	38/95	40.0
large, both eyes	13/69	18.8	25/82	30.5	110/207	53.1

*Area of a circle with diameter approximately one-fourth that of the average optic disk

† Area of a circle with diameter approximately three-fourths that of the average optic disk.

Appendix Table 7. Five-year rates of advanced AMD in the second eye for 543 patients with neovascular AMD in the first eye at baseline

Drusen Size	Pigment Abnormalities			
	None		Present	
	n/N	%	n/N	%
Small or intermediate (or none)	22/145	15.2	21/58	36.2
Large	38/107	35.5	125/233	53.6

Appendix Table 8. Five-year rates of advanced AMD in one or both eyes for 3211 patients free of advanced AMD in both eyes at baseline

Risk Factors	No. at Risk	Advanced AMD							
		1 Eye			Both Eyes			Total	
		Neo No.	GA No.	Both No.	Neo/Neo No.	GA/GA No.	Both No.	No.	%
0	1466	5			1			6	0.4
1	635	15	2	1	2			20	3.1
2	465	38	4	4	7		2	55	11.8
3	328	45	18	4	9	3	6	85	25.9
4	317	47	46	3	10	24	20	150	47.3
Total	3211	150	70	12	29	27	28	316	9.8