

Supplementary Online Content

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eMethods. Rotterdam Study I/II/III Description

eTable 1. Baseline Characteristics of Participants Without and With Eye Examination

eTable 2. Associations of Metformin and Intraocular Pressure

eTable 3. Associations of Separate Diabetes Medications and Age-Related Macular Degeneration

eFigure. Cumulative Lifetime Risk of Development of Age-Related Macular Degeneration

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

eMethods. Rotterdam Study I/II/III Description

The Rotterdam Studies are prospective population-based cohort studies of people living in Ommoord, a district of the city of Rotterdam. The Rotterdam Study consists of three cohorts of which the first started in 1990 and consisted of 7983 participants >55 years (range 55.0 – 99.2)(RS-I, response rate of 78%). The second cohort started recruiting in 2000 and 3011 participants of >55 years were included (range 55.2 – 98.9)(RS-II, response rate of 67.3%). The third cohort also included people aged >45 years (45.7-90.1) and consisted of 3932 participants (RS-III, response rate 64.9%) starting from the year 2006. Follow-up examinations were performed between 1993-1995 (no open-angle glaucoma assessments), 1997-1999, 2002-2004 and 2009-2011, 2004-2005 and 2011-2012 and 2012-2014 for cohort RS-I, RS-II and RS-III, respectively. Participants were extensively examined for presence of diabetes and eye diseases at baseline (prevalence) and were invited for each follow-up round where development of age-related diseases (incidence) was determined. Overall, the age range at the last follow visit was 51.6 – 99.6 years. Participants underwent an extensive physical examination at a research center including blood pressure measurements and questionnaires were used for lifestyle factors. All participants provided written informed consent to participate in the study and to have their information obtained from treating physicians.

eTable 1. Baseline Characteristics of Participants Without and With Eye Examination

	Ophthalmic examination absent (N = 1887)	Ophthalmic examination present (N = 11260)	P- value
Baseline age (mean ± SD)	74.5 ± 12.7	65.1 ± 9.8	<.001
Sex (% female)	69.2	58.7	<.001
Ethnicity (% European)	99.0	98.0	.35
BMI (mean ± SD)	<i>N</i> = 552 26.7 ± 4.8	<i>N</i> = 11144 26.8 ± 4.1	.56
Diabetes	<i>N</i> = 646	<i>N</i> = 8475	
% present	28.0	28.4	.84
Medication ^a			
Metformin (%)	58.0	57.7	
Other diabetes medications (%)	13.8	20.8	

^a In participants with diabetes.

eTable 2. Associations of Metformin and Intraocular Pressure

Medication ^a	IOP			OAG		
	N	Beta (95%CI)	P-value	N	OR (95%CI)	P-value
Metformin	879	0.174 (-0.307 – 0.656)	.48	48	0.17 (0.07 – 0.41)	<.001
Duration	879	0.003 (-0.062 – 0.067)	.94	45	0.75 (0.62 – 0.91)	.003
Cumulative dose	879	0.041 (-0.044 – 0.126)	.34	45	0.59 (0.40 – 0.87)	.008
Other diabetes medication ^b	604	0.501 (-0.128 – 1.130)	.12	49	0.43 (0.18 – 0.99)	.05
Metformin vs. other	603	0.035 (-0.622 – 0.693)	.92	17	0.33 (0.10 – 1.07)	.06

^a Only participants with diabetes

^b OAG (69.1% sulfonylurea derivatives, 24.5% insulin, 6.4% combination)

Abbreviations: OAG, open-angle glaucoma; OR, odds ratio; CI, confidence interval; IOP, intraocular pressure
All analyses are adjusted for age, sex, BMI, use of antihypertensives, use of statins and fasting serum glucose. OAG analyses are additionally adjusted for IOP.

eTable 3. Associations of Separate Diabetes Medications and Age-Related Macular Degeneration

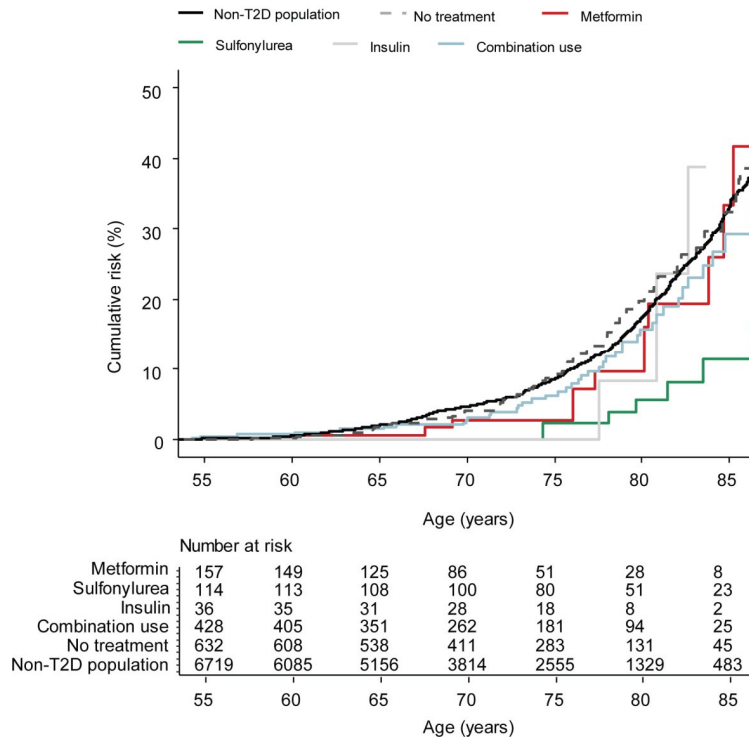
Medication^a	N	AMD	
		OR (95%CI)	P-value
Metformin only	152	0.54 (0.29 – 1.00)	.05
Sulfonylurea only	154	0.32 (0.17 – 0.59)	<.001
Insulin only	145	0.29 (0.10 – 0.88)	.03

^a Only participants with diabetes

Abbreviations: OR, odds ratio; CI, confidence interval; AMD, age-related macular degeneration

All analyses are adjusted for age, sex, BMI, use of antihypertensives, use of statins and fasting serum glucose.

Age-related macular degeneration



eFigure. Cumulative Lifetime Risk of Development of Age-Related Macular Degeneration

Cumulative life-time risk at 85-years of age-related macular degeneration (AMD) as function of age, for participants with diabetes treated with metformin use only (33.3%), sulfonyleurea only (11.5%), insulin only (NA) or a combination of diabetes drugs (29.3%). The number at risk per group shown below plots.