Table 2 The odds ratios adjusted for age, smoking, and body mass index and stratified by the daily linoleic acid intake

	Any AMD		Early AMD		Late AMD	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
All participants:						
International classification AMD						
Daily linoleic acid intake ≥ 7.17 g	0.70 (0.44 to 1.13)	0.142	0.77 (0.47 to 1.25)	0.296	0.15 (0.03 to 0.69)	0.014
Crude daily LZ intake (mg) (DLAI < 7.17 g)	1.02 (0.66 to 1.57)	0.944	1.09 (0.70 to 1.69)	0.713	0.27 (0.04 to 1.70)	0.163
Crude daily LZ intake (mg) (DLAI ≥ 7.17 g)	1.42 (1.03 to 1.94)	0.030	1.34 (0.97 to 1.86)	0.075	3.16 (1.28 to 7.79)	0.013
Wisconsin AMD						
Daily linoleic acid intake ≥ 7.17 g	0.41 (0.20 to 0.80)	0.010	0.48 (0.23 to 1.02)	0.057	0.15 (0.04 to 0.65)	0.011
Crude daily LZ intake (mg) (DLAI < 7.17 g)	0.54 (0.26 to 1.09)	0.087	0.60 (0.28 to 1.28)	0.191	0.26 (0.04 to 1.55)	0.140
Crude daily LZ intake (mg) (DLAI ≥ 7.17 g)	1.60 (1.03 to 2.47)	0.037	1.41 (0.86 to 2.31)	0.168	2.83 (1.24 to 6.45)	0.013
International classification AMD						
Daily linoleic acid intake ≥ 7.17 g	0.62 (0.38 to 1.04)	0.069	0.70 (0.42 to 1.18)	0.185	0.10 (0.02 to 0.54)	0.007
Adjusted daily LZ intake (mg) (DLAI < 7.17 g)	1.04 (0.68 to 1.57)	0.870	1.11 (0.73 to 1.69)	0.636	0.30 (0.06 to 1.66)	0.170
Adjusted daily LZ intake (mg) (DLAI ≥ 7.17 g)	1.74 (1.18 to 2.57)	0.005	1.61 (1.08 to 2.40)	0.020	5.50 (1.70 to 17.8)	0.005
Wisconsin AMD						
Daily linoleic acid intake ≥ 7.17 g	0.35 (0.17 to 0.73)	0.005	0.44 (0.20 to 0.97)	0.041	0.11 (0.02 to 0.51)	0.005
Adjusted daily LZ intake (mg) (DLAI < 7.17 g)	0.71 (0.37 to 1.35)	0.298	0.82 (0.42 to 1.62)	0.571	0.29 (0.06 to 1.51)	0.142
Adjusted daily LZ intake (mg) (DLAI ≥ 7.17 g)	2.44 (1.43 to 4.17)	0.001	2.13 (1.19 to 3.83)	0.011	4.72 (1.60 to 13.9)	0.005
Excluding those who took supplements:						
International classification AMD						
Daily linoleic acid intake ≥ 7.17 g	0.56 (0.33 to 0.96)	0.037	0.64 (0.37 to 1.12)	0.117	0.12 (0.02 to 0.58)	0.009
Crude daily LZ intake (mg) (DLAI < 7.17 g)	0.94 (0.56 to 1.58)	0.817	1.03 (0.61 to 1.75)	0.906	0.27 (0.04 to 1.91)	0.190
Crude daily LZ intake (mg) (DLAI ≥ 7.17 g)	1.68 (1.18 to 2.39)	0.004	1.59 (1.10 to 2.28)	0.013	3.65 (1.37 to 9.76)	0.010
Wisconsin AMD						
Daily linoleic acid intake ≥ 7.17 g	0.35 (0.16 to 0.78)	0.010	0.46 (0.19 to 1.11)	0.083	0.12 (0.03 to 0.56)	0.007
Crude daily LZ intake (mg) (DLAI < 7.17 g)	0.61 (0.27 to 1.40)	0.244	0.75 (0.31 to 1.82)	0.526	0.26 (0.04 to 1.71)	0.160
Crude daily LZ intake (mg) (DLAI ≥ 7.17 g)	2.04 (1.26 to 3.30)	0.004	1.85 (1.08 to 3.15)	0.025	3.15 (1.30 to 7.59)	0.011
International classification AMD						
Daily linoleic acid intake ≥ 7.17 g	0.50 (0.28 to 0.89)	0.018	0.58 (0.32 to 1.05)	0.070	0.08 (0.01 to 0.49)	0.006
Adjusted daily LZ intake (mg) (DLAI < 7.17 g)	1.04 (0.64 to 1.68)	0.870	1.14 (0.70 to 1.86)	0.604	0.32 (0.05 to 1.97)	0.219
Adjusted daily LZ intake (mg) (DLAI ≥ 7.17 g)	2.27 (1.46 to 3.53)	< 0.001	2.11 (1.35 to 3.32)	0.001	6.39 (1.71 to 23.9)	0.006
Wisconsin AMD						
Daily linoleic acid intake ≥ 7.17 g	0.32 (0.14 to 0.75)	0.009	0.44 (0.17 to 1.12)	0.085	0.09 (0.02 to 0.47)	0.005
Adjusted daily LZ intake (mg) (DLAI < 7.17 g)	0.86 (0.41 to 1.79)	0.684	1.08 (0.5 to 2.36)	0.842	0.30 (0.05 to 1.73)	0.179
Adjusted daily LZ intake (mg) (DLAI ≥ 7.17 g)	3.17 (1.74 to 5.77)	< 0.001	2.88 (1.5 to 5.54)	0.002	5.18 (1.59 to 16.9)	0.007

DLAI, daily linoleic acid intake.

were similar to that of only 4.9 g in another US study of 261 AMD patients.^{2,4}

The main strengths of our study are the relatively large, population based sample, two different definitions of AMD, the use of a comprehensive ophthalmological examination, and the FFQ validated by the Cancer Council Victoria. The daily LZ intake mean was 914 μ g in the BMES while it was 803 μ g in the MVIP.⁹ Furthermore, our quintile medians (μ g/4.18 MJ) were from 29% to 36% lower than the population based BDES (table 1).¹⁰ The LZ intakes in other volunteer case-control studies that were from three to five times higher in each quintile than the population based intakes clearly show a "healthy volunteer bias".^{2,3} Limitations of this study include cross sectional data, a possibility of selection bias because of loss of follow up, and the problem of 24% cumulative missing data.

In our study there was a harmful effect of higher LZ intake on AMD among those with high level of linoleic acid intake. Based on these data LZ supplementation could not be recommended.

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Corneal ectasia associated with Cohen syndrome: a role for COH1 in corneal development and maintenance?

Cohen syndrome¹ is a rare autosomal recessive condition with a pleiotropic phenotype. Ocular findings of high myopia and early

onset retinochoroidal dystrophy are almost universal. The extraocular manifestations include developmental delay, a typical facial gestalt, and granulocytopenia. Elsewhere, we have described the identification of the *COH1* gene which is mutated in this condition² and have reported an extensive genotype-phenotype screen.³

We report a case of corneal ectasia in a patient with confirmed Cohen syndrome, who is now 50 years of age. She presented at age 17 with high myopia, astigmatism, and retinochoroidal dystrophy; refractive error was $-11.50/+3.50@90$ in the right eye and $-13.00/+3.00@80$ in the left. By the age of 30 she had developed posterior subcapsular cataracts associated with a mild progression of myopia ($-16.00/+4.00@90$ in the right eye and $-17.00/+2.50@80$ in the left). Early keratoconus was noted in the left cornea (fig 1), along with subluxation of both the lenses. The corneal ectasia has subsequently worsened in the left eye and has been repeatedly confirmed on slit lamp examination. Further details of the ectasia could not be established as accurate topography and pachymetry have not been possible because of poor cooperation. For the same reason, subtle signs of ectasia cannot be excluded in the right eye. At age 42 her corrected visual acuities were 6/24 right eye, hand movement in the left eye. She underwent bilateral lensectomy with pars plana vitrectomy, for lens subluxation and progression of the lenticular opacities. The reduced visual acuity in the left eye was caused by the combination of retinochoroidal dystrophy, cataract and corneal ectasia.

The patient has clinical features typical of classic Cohen syndrome. These include moderate to severe learning difficulties associated with microcephaly, characteristic facial dysmorphism, truncal obesity with slender extremities, and a neutropenia leading to frequent episodes of cellulitis. Mutation screening of *COH1* was carried out by sequencing the full length cDNA which revealed the proband had compound heterozygous mutations (c.5613_5614insA, p.Lys1872fsX10; and c.11169_11172dupGGAC, p.Arg3725fsX7). The protein for Cohen syndrome is of unknown function. This case suggests that it may be involved in corneal development or collagen metabolism.

Elsewhere we have described the ophthalmic findings associated with Cohen syndrome.⁴ These are mainly early in onset and most patients develop high myopia (often severe) and a progressive retinal dystrophy. Myopia in Cohen syndrome has been attributed to high corneal and lenticular refractive

power in the presence of a normal axial length.⁵ This is indicative of a specific abnormality of emmetropisation, largely as a result of a defect of corneal development. In view of our finding of unilateral corneal ectasia in an older patient with Cohen syndrome it is possible that these findings indicate early or subtle forms of keratoconus.

Three keratoconus loci have been mapped.⁶⁻⁸ The condition can be associated with connective tissue disorders such as Marfan and Ehlers-Danlos syndromes. Other features of Cohen syndrome including hypermobility of joints, skeletal abnormalities, and postural abnormalities also suggest a generalised disorder of connective tissue.

Analysis of the visual problems associated with Cohen syndrome emphasises their importance in a condition associated with developmental delay. This report highlights that progressive visual deterioration may result from corneal ectasia as well as retinal dystrophy. When considering cataract extraction in patients with Cohen syndrome it is important to recognise that refractive error (in particular myopia) usually results from corneal and lenticular abnormalities. Lastly, as patients with Cohen syndrome have evidence of a generalised connective tissue disorder, the *COH1* protein may have a role in extracellular matrix metabolism and suggests that its study may shed light on pathways important in the maintenance of corneal integrity and the development of corneal ectasia.

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Sulphation patterns of keratan sulphate proteoglycan in sclerocornea resemble cornea rather than sclera

Sclerocornea is one of the most frequent causes of congenital blindness,¹ in which the cornea is opaque and resembles sclera at birth.² The stromal matrix in sclera and in cornea is composed of collagen fibrils, with proteoglycans (PGs) in the interfibrillar space fulfilling important roles in relation to tissue structure and function. Sclera and cornea contain distinct PG populations. Whereas the predominant corneal PG carries highly sulphated keratan sulphate (KS) glycosaminoglycans (GAGs), sulphated KSPGs are not major scleral components.³ Here, we investigate if sclerocornea is more like sclera or cornea in terms of its KSPG molecular profile.

Case report

An 8 month old girl, born at 39 weeks after an uncomplicated pregnancy and delivery, had bilateral corneal opacification and was referred to Kyoto Prefectural University of Medicine. There was no family history of eye disease. Slit lamp examination disclosed diffuse, full thickness opacification, which was more severe in her left eye (fig 1A), preventing examination of the anterior chamber. Ultrasound biomicroscopy detected synechiae between the iris and peripheral cornea which histology later showed to be attributable to absence of corneal endothelium and Descemet's membrane. We diagnosed sclerocornea, and this was treated with a penetrating keratoplasty, lensectomy, and anterior vitrectomy. Postoperative medication was 1% methylprednisolone eye drops eight times daily, levofloxacin eye drops four times daily and oral prednisolone (5 mg/day for 3 months). Six months postoperatively the corneal graft was clear without any sign of rejection or infection (fig 1B).

Figure 1 Corneal ectasia in patient with Cohen syndrome with *COH1* mutations confirmed on molecular analysis.