Retinopathy

The ACCORDION Eye Study: What can we learn from it?

Deborah Broadbent
Honorary Senior Lecturer, Royal Liverpool University Hospital, Liverpool

The ACCORD (Action to Control Cardiovascular Risk in Diabetes) Eye Follow-On Study (ACCORDION Eye; summarised alongside) investigated two effects. The first was whether, as in the DCCT (Diabetes Control and Complications Trial) in patients with type 1 diabetes, there was a "metabolic memory" or legacy effect from intensive glycaemic control on the progression of retinopathy in patients with type 2 diabetes. The second was whether there was also a legacy effect from fenofibrate treatment of dyslipidaemia, which in the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) study demonstrated a reduced retinopathy progression and need for laser treatment, particularly in patients with pre-existing retinopathy. The ACCORD Eye Study confirmed the beneficial effect of intensive glycaemic control and of combined simvastatin and fenofibrate therapy on progression of retinopathy, as noted in the FIELD study.

The ACCORDION Eye Study demonstrated that intensive glycaemic control did indeed confer enduring protection from progression of retinopathy. This effect suggests that, even relatively late in the course of diabetes (the average duration at baseline was 9.9 years), improved glycaemic control can have a beneficial effect.

The ACCORD Eye and FIELD studies showed that fenofibrate reduced the progression of retinopathy, need for laser treatment and need for vitrectomy, particularly in patients with pre-existing retinopathy. However, the ACCORDION Eye study did not demonstrate a "legacy" effect. This suggests that patients need to continue on long-term treatment with fenofibrate.

Unfortunately, fenofibrate did not demonstrate an effect on cardiovascular events in the ACCORD and FIELD studies, and some concerns have been raised regarding its safety. It is, therefore, not routinely prescribed for the management of dyslipidaemia by either general practitioners or diabetologists.

Historically, ophthalmologists have not intervened in the medical management of diabetes, although medical retina specialists are becoming more confident in the assessment of risk factors for development and progression of diabetic retinopathy, and in referring their patients for improved diabetes care. There exists a niche specialty in the UK – medical ophthalmology. Medical ophthalmologists are qualified in both medicine and ophthalmology. They are able to directly intervene in the medical management of diabetes, but there are relatively few posts, mainly in centres of excellence.

Good collaborative management of patients with diabetes between ophthalmologists, diabetologists and general practitioners in the UK is patchy, despite the evidence from a paper on reduction of blindness in Sweden that clearly attributed success to a combination of good ascertainment of diabetes, effective screening for diabetic retinopathy and collaboration between ophthalmologists, diabetes physicians and primary care providers (Olafsdottir et al, 2007). The same lead author has demonstrated in another paper (summarised on the following page) that early detection of type 2 diabetes combined with screening for diabetic retinopathy reduced the prevalence and severity of retinopathy. This highlighted the need for ophthalmologists and general practitioners to work together.

In conclusion, the ACCORDION Eye Study suggests that the role of fenofibrate for the treatment of diabetic retinopathy, regardless of its lack of effect on cardiovascular events, needs to be considered by providers of diabetes care across the UK. ■

Olafsdottir E, Andersson DK, Stefánsson E (2007) Visual acuity in a population with regular screening for type 2 diabetes mellitus and eye disease. *Acta Ophthalmol Scand* **85**: 40–5

Diabetes Care

Persistent effects of glycaemic control on retinopathy in T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The ACCORD (Action to Control Cardiovascular Risk in Diabetes) Eye Study, a subset of participants in the ACCORD study, established that intensive glycaemic control and treatment with fenofibrate (a cholesterol-lowering drug) both reduced retinopathy progression in people with established T2D and additional cardiovascular (CV) risk factors.

2 In the follow-on study, a subset of 2856 participants who underwent eye examination throughout the original study were re-examined 4 years after its close-out.

3 This re-examination revealed that intensive glycaemic control reduced the risk of diabetic retinopathy progression compared with standard treatment (5.8% vs 12.7%; adjusted odds ratio, 0.42; $P<0.001$). This was despite HbA_{1c} levels having equalised between the groups since the close of the original study.

4 This is the first study in people with T2D of 10 years' duration and established CV disease to demonstrate this legacy effect. The findings suggest that the progression of retinal disease can be reduced by glucose lowering relatively late in the course of diabetes and that the retina responds to relatively short-term changes in glucose levels.

5 The benefit of fenofibrate seen during the original trial did not persist once its use was discontinued. This suggests that treatment needs to be ongoing to maintain benefit, although further study is required to confirm this.

ACCORDION Eye Study Group, ACCORDION Study Group (2016) Persistent effects of intensive glycemic control on retinopathy in type 2 diabetes in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Follow-On Study. *Diabetes Care* **39**: 1089–100

Acta Ophthalmol

Prevalence and severity of retinopathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Shortening the delay in the diagnosis of diabetes provides scope for therapeutic measures to be taken against risk factors for complications, such as retinopathy.

2 This study explored whether the prevalence and severity of retinopathy, evaluated by an ophthalmologist from fundus photography, differed between two cohorts of adults with T2D. One cohort (n=151) was diagnosed through screening for retinopathy; the other (n=106) was diagnosed through conventional care.

3 Of those in the screening-detected group, 22% had retinopathy compared to 51% of those clinically detected (P<0.0001).

4 Multivariate analysis revealed that individuals with retinopathy were more likely to have increased average fasting blood glucose and peripheral neuropathy, but less likely to have screening-detected diabetes. Similar results were found using increasing severity grade of retinopathy as an outcome.

5 After 10 years of follow-up, significantly lower cumulative retinopathy prevalence emerged among the screening-detected cohort compared with those in the clinically diagnosed cohort (P=0.0002), even when other risk factors for retinopathy were considered.

6 The investigators conclude that the early detection and treatment of diabetes in combination with screening for retinopathy may reduce the prevalence and severity of retinopathy. They advise that general practitioners and eye specialists work together to reduce retinopathy among individuals with T2D.

Olafsdottir E, Andersson DKG, Dedorsson I et al (2016) Early detection of type 2 diabetes mellitus and screening for retinopathy are associated with reduced prevalence and severity of retinopathy. *Acta Ophthalmol* **94**: 232–9

J Diabetes Complic

Novel device for retinopathy testing

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The RETeval handheld device tests for diabetic retinopathy by measuring the eye's electrical and pupillary responses.

2 In this study, 468 participants were randomised to two groups. Results from a calibration phase were used to formulate an equation correlating with the presence of vision-threatening diabetic retinopathy (VTDR). A validation phase was used to validate the equation.

3 Analysis suggests that for 100 individuals with diabetes tested with this device, 76 will have a negative result and, of those, 75 (99%) will not have VTDR.

4 The authors conclude that the benefits of this device include its ease of use, no requirement to dilate pupils and the short testing time.

Maa AY, Feuer WJ, Davis Q et al (2016) A novel device for accurate and efficient testing for vision-threatening diabetic retinopathy. *J Diabetes Complications* **30**: 524–32

Acta Ophthalmol

Retinal changes with pump therapy

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Two groups of adults with T1D and similar baseline characteristics were followed in this prospective, controlled, observational study.

2 One group (n=31) was initiated on continuous subcutaneous insulin infusion (CSII); the control group (n=20) continued with multiple daily insulin (MDI) injections.

3 After 1 year, the CSII group showed a 17.8 mmol/mol (1.6%) improvement in HbA_{1c} compared to 3.1 mmol/mol (0.3%) in the MDI group (P<0.0001).

4 A small increase in retinal thickness was found in the CSII group, but there was no worsening of retinopathy, macular oedema or other retinal parameters.

5 Longer observation may reveal additional differences, and the investigators will study the 2-year effects in the same individuals.

Klefter ON, Hommel E, Munch IC (2016) Retinal characteristics during 1 year of insulin pump therapy in type 1 diabetes: a prospective, controlled, observational study. *Acta Ophthalmol* **94**: 540–7

JAMA Ophthalmol

Povidone-iodine and antibiotic elimination

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 During eight clinical trials conducted by the US Diabetic Retinopathy Clinical Research Network (DRCR.net) between 2006 and 2015, 28 786 intravitreous injections were administered.

2 The DRCR.net protocol required the use of topical povidone-iodine prior to injection. After injections performed with povidone-iodine (n=11 565), endophthalmitis occurred in 0.05% of cases (approximately 1 in 2000) with topical antibiotic use. This compared to 0.02% of cases (approximately 1 in 5700) without topical antibiotics (n=17 208; P=0.17).

3 Among 13 injections without povidone-iodine pretreatment (against protocol), there was a 15% risk of endophthalmitis.

4 A low rate of endophthalmitis can be achieved without topical antibiotics when the injection procedure includes topical povidone-iodine.

Bhavsar AR, Glassman AR, Stockdale CR et al (2016) Elimination of topical antibiotics for intravitreous injections and the importance of using povidone-iodine: update from the Diabetic Retinopathy Clinical Research Network. *JAMA Ophthalmol* **134**: 1181–3

"The early detection and treatment of diabetes in combination with screening for retinopathy may reduce the prevalence and severity of retinopathy."