



Diabetic retinopathy

- Diabetic retinopathy (DR) is the leading cause of vision loss in working-age adults in most developed countries.
- More than 1 in 3 people living with diabetes will develop DR.¹
- The majority of people remain asymptomatic until the late stages of DR, when sight is threatened.
- Symptoms usually result from complications:
 - dark or empty areas in vision
 - floaters (resolution of vitreous bleed)
 - a “curtain falling” (vitreous bleed)
 - reduced vision (acuity) or blindness.

Risk factors

- Hyperglycaemia:
 - The risk of the development and progression of DR increases with HbA_{1c}.
- Type and duration of diabetes:
 - Prevalence of DR is greater in people with type 1 diabetes compared to those with type 2 diabetes, and increases with duration of diabetes.
 - **Maculopathy** is more common in people with type 2 diabetes.
- **Proliferative DR** is more common in people with type 1 diabetes.
- Blood pressure:
 - Systolic BP >140 mmHg is associated with increased risk of DR.
- Dyslipidaemia.
- Smoking.
- Presence of other microvascular complications of diabetes (e.g. nephropathy, neuropathy).
- Pregnancy.
- Genetic predisposition.

Pathophysiology

- Chronic hyperglycaemia leads to a series of changes to retinal vasculature:
 - pericyte loss
 - basement membrane thickening
 - endothelial damage
 - increased retinal blood flow
 - microthrombosis
 - microaneurysms (a pathognomonic sign).
- This triggers a cascade of pathophysiological changes:
 - Retinal ischaemia results in retinal hypoxia, which stimulates vascular endothelial growth factors that cause retinal neovascularisation.
 - Increased vascular permeability and subsequent retinal oedema.
- Chronic hyperglycaemia also results in the accumulation of advanced glycation end-products (AGEs) and increased oxidative stress, again resulting in retinal neovascularisation.

Grading of DR—see *Table 1*.

Screening

- Screening is essential to detect those at risk before visual symptoms occur.
- Treatment can prevent blindness in 90% of those at risk, if applied early and adequately.
- The NHS Diabetic Eye Screening (DES) Programme offers regular retinopathy screening for all people with type 1 and type 2 diabetes aged ≥12 years.
- The current screening interval for all eligible people with diabetes is yearly, but that might change.
- In 2016, the UK National Screening Committee recommended that the DES programme:
 - Extend screening intervals for people with low risk of sight loss* from 1 year to 2 years. (*Two successive clear diabetic eye screenings.)
 - Retain the current screening interval for people with a higher risk of sight loss.

Outcomes in England and Wales

- Between 2009 and 2010, DR/maculopathy stopped being the leading cause of certifiable blindness in working age adults in England and Wales.²
- Between 2007 and 2015, there was an almost 50% reduction in new certifications of sight impairment in Wales.³

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Management

Prevention: management of risk factors

1. Glycaemic management

- An 11 mmol/mol (1%) decrease in HbA_{1c} reduces the incidence and progression of DR by approximately 40% and progression to vision-threatening DR by 25%.
- Target HbA_{1c}:
 - 53 mmol/mol (7.0%) for type 2 diabetes⁴
 - 48 mmol/mol (6.5%) for type 1 diabetes (not at the expense of severe hypoglycaemia).⁵
- In those with elevated blood glucose and existing DR, rapid reduction may result in acceleration of DR.

2. Blood pressure management

- Target BP:
 - 135/85 mmHg for type 1 diabetes⁵
 - 140/90 mmHg for type 2 diabetes aged <80 years; 150/90 mmHg for type 2 diabetes aged >80 years⁶
 - 130/80 mmHg if microalbuminuria present or at risk of cardiovascular disease
 - Not recommended for systolic BP to be below 120 mmHg.

3. Lipid modification

- Combination treatment (simvastatin and fenofibrate) reduces DR progression.⁷

- Fenofibrate reduces the need for laser therapy for DR.⁸
 - If fenofibrate is discontinued, there is no further benefit (no legacy effect).

4. Pregnancy

- Pre-conception care:
 - Offer retinal assessment at the first pre-conception clinic visit (unless an annual retinal assessment has been done in the last 6 months).⁹
- Pregnancy with pre-existing diabetes:
 - For all women with diabetes who become pregnant, the relevant DR screening programme should be notified and the relevant national pathway adopted.
 - Offer retinal assessment at or soon after first antenatal clinic visit (unless a retinal assessment has been done in the last 3 months) and again at 28 weeks.
 - Perform an additional retinal assessment at 16–20 weeks if any DR present at first antenatal clinic visit (or in the prior 3 months).
 - Any women who have DR during pregnancy must receive retinal assessment within 3 months of delivery.
 - Any women who have pre-proliferative DR or any form of referable DR should be under the care of ophthalmology.

Treatment

The aims of treatment are to: prevent blindness; restore impaired vision loss (where possible); prevent further vision loss; and improve visual function.

1. Laser therapy

- Aims to protect vision and prevent further vision loss, rather than to improve vision.
- Adverse effects: pain during treatment; transient rise in intraocular pressure; corneal abrasions; retinal fibrosis; choroidal scarring; macular oedema; visual acuity loss; visual field loss; and loss of dark adaptation.

2. Medical therapy

- Anti-vascular endothelial

growth factor (anti-VEGF) for treatment of diabetic macular oedema (DMO) and proliferative DR.

- Anti-VEGF agents: ranibizumab, bevacizumab, aflibercept.
- For resistant DMO, intravitreal corticosteroid therapy is an option.
- Corticosteroid/vitreous inserts (sustained delivery) include: triamcinolone acetonide, dexamethasone, fluocinolone acetonide.
- Polytherapy with laser plus anti-VEGF plus intravitreal steroid may be required.

Practical tips

- Assess the severity of DR before initiating stringent glycaemic control.
- Avoid a huge reduction in HbA_{1c} >22 mmol/mol (>2%) in those with pre-existing severe DR.
- Exercise caution with the introduction of GLP-1 receptor agonist therapies in the following situations because of a risk of worsening DR:¹⁰
 - Proliferative DR or maculopathy requiring active follow-up
 - HbA_{1c} >91 mmol/mol (10.5%)
 - Current insulin treatment.
- Pioglitazone should be used with caution in people with maculopathy as it can increase the rate of fluid retention and thus DMO.

Communication and education

- Ensure the person with diabetes understands the benefits of good diabetes management so they are suitably empowered.
- Regular screening will help to ensure that vision is protected.

Table 1. Staging of diabetic retinopathy.¹¹

Grading level	Retinopathy level	Features
R0	No DR	
R1	Background DR (Figure 1)	<ul style="list-style-type: none"> • Microaneurysms • Blot haemorrhages • Cotton-wool spots • Hard exudates (outside 1 disc-diameter of fovea) • Venous loop
R2	Pre-proliferative DR (Figure 2)	<ul style="list-style-type: none"> • Multiple blot haemorrhages • Intraretinal microvascular anomalies (IRMA) • Venous beading • Venous duplication
R3A	Active proliferative DR (Figure 3)	<ul style="list-style-type: none"> • New vessels on disc • New vessels elsewhere • New vitreous or pre-retinal haemorrhage • New retinal detachment • New retinal fibrosis
R3S	Stable treated proliferative DR	<p>One of the following features, with evidence of peripheral retinal laser treatment:</p> <ul style="list-style-type: none"> • Stable pre-retinal fibrosis • Stable fibrous proliferation • Stable R2 features • R1 features
P1	Evidence of laser photocoagulation	
U	Unassessable	
M0	No maculopathy	
M1	Maculopathy (Figure 4)	<p>Clinically significant macular oedema:</p> <ul style="list-style-type: none"> • Retinal thickening within 500 microns of the fovea • Hard exudates within 500 microns of the fovea if associated with adjacent retinal thickening, or • One or more areas of retinal thickening at least 1500 microns in diameter that is within one disc-diameter (1500 microns) of the fovea

R=retinopathy; P=photocoagulation; M=maculopathy.



Figure 1: Background DR.



Figure 2: Pre-proliferative DR.



Figure 3: Proliferative DR.



Figure 4: Maculopathy.

References

- ¹Thomas RL et al (2019) *Diabetes Res Clin Pract* **157**: 107840
- ²Liew G et al (2014) *BMJ Open* **12**: e004015
- ³Thomas RL et al (2017) *BMJ Open* **18**: e015024
- ⁴NICE (2019) *Type 2 diabetes in adults: management* (NG28). NICE, London; <https://www.nice.org.uk/guidance/ng28>
- ⁵NICE (2016) *Type 1 diabetes in adults: diagnosis and management* (NG17). NICE, London; <https://www.nice.org.uk/guidance/ng17>
- ⁶NICE (2019) *Hypertension in adults: diagnosis and management* (NG136). NICE, London; <https://www.nice.org.uk/guidance/ng136>
- ⁷Chew EY et al (2014) *Ophthalmology* **121**: 2443–51
- ⁸Keech A et al (2005) *Lancet* **366**: 1849–61
- ⁹NICE (2015) *Diabetes in pregnancy: management from preconception to postnatal period* (NG3). NICE, London; <https://www.nice.org.uk/guidance/ng3>
- ¹⁰Bain SC et al (2019) *Diabetes Obes Metab* **21**: 454–66
- ¹¹Harding S et al (2003) *Diabet Med* **20**: 965–71