NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Diabetic retinopathy: management and monitoring

Draft for consultation, August 2023

This guideline covers diagnosing, managing and monitoring diabetic retinopathy in hospital eye services. This includes care for all people with non-proliferative and proliferative diabetic retinopathy, and diabetic macular oedema.

The guideline does not cover areas that are covered by the NHS diabetic eye screening programme, for example routine annual screening.

Who is it for?

- healthcare professionals in secondary care
- practitioners in ophthalmology and optometry services
- people using these services, their families and carers.

What does it include?

- the recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the recommendations and how they might affect practice.
- the guideline context.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Systemic management for people with diabetic retinopathy and diabetic macular oedema

Effects of rapid blood glucose reduction

1.1.1 All clinicians involved in caring for people with diabetic retinopathy and macular oedema should discuss with patients how good long-term management of their diabetes can have long-term benefits for their vision. Refer to NICE's guidelines on managing type 1 diabetes in adults, managing type 2 diabetes in adults and diagnosing and managing diabetes (type 1 and type 2) in children and young people to support this discussion. **[2023]**

1.1.2 When initiating a diabetes treatment that is likely to result in a rapid, substantial drop in the person's HbA1c, notify the person's ophthalmologist so the person can have an early review. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on effects of rapid blood glucose reduction.

Full details of the evidence and the committee's discussion are in evidence review C: effectiveness of intensive treatments to lower blood glucose levels.

Information that should be available to all people involved in the care of someone who has diabetic retinopathy or diabetic macular oedema

1.1.3 Ophthalmologists should:

- have access to a person's HbA1c and blood pressure results
- discuss them with the person and
- explain to them how lowering these results could reduce the risk of their eye condition progressing to proliferative diabetic retinopathy or diabetic macular oedema. **[2023]**

1.1.4 When making decisions about how often to arrange follow-up appointments, and when deciding on ophthalmic interventions with someone, take into account the person's:

- stage of retinopathy
- HbA1c
- renal function and
- blood pressure. **[2023]**

1.1.5 Provide healthcare professionals involved in diabetes care with information about the severity of a person's diabetic eye disease so it can be taken into account in decisions on their overall diabetes management. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on information for all people involved in the care of someone who has diabetic retinopathy or diabetic macular oedema.

Full details of the evidence and the committee's discussion are in evidence review A: prognostic factors for progression of non-proliferative diabetic retinopathy.

Preventing progression of diabetic retinopathy

Blood pressure management

1.1.6 Refer to NICE's guideline on hypertension for recommendations on blood pressure management for adults with diabetes and hypertension. **[2023]**

1.1.7 Be aware that, for people with hypertension, managing blood pressure can reduce progression of non-proliferative diabetic retinopathy. **[2023]**

1.1.8 Do not offer blood pressure management medicines to people without hypertension for the sole purpose of preventing the progression of non-proliferative diabetic retinopathy. **[2023]**

Statins

1.1.9 Refer to NICE's guideline on cardiovascular disease for recommendations on statins for people with diabetes. **[2023]**

Fibrates

1.1.10 Consider fibrates for people with non-proliferative retinopathy and type 2 diabetes to reduce the progression of diabetic retinopathy. **[2023]**

In July 2023, this was an off-label use of fibrates. See NICE's information on prescribing medicines.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on preventing progression of diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review D: effectiveness of lipid modification therapies and antihypertensive medicines

1.2 Cataract surgery

Cataract surgery for people with diabetic retinopathy and diabetic macular oedema

1.2.1 Before carrying out cataract surgery for a person with diabetes, the surgeon should obtain information about the person's current diabetic eye disease status. This information can then be used by the surgeon to:

- tailor the surgery to the person's eye condition
- give correct post-operation medication
- tailor follow-up to the person's needs. **[2023]**

1.2.2 For guidance on managing cystoid macular oedema as a complication of cataract surgery in people with diabetes, see NICE's guideline on managing cataracts in adults. **[2023]**

Also see recommendation 1.4.6 on anti-VEGF treatment as a temporary solution for people with proliferative diabetic retinopathy who need cataract surgery.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on cataract surgery.

Full details of the evidence and the committee's discussion are in evidence review I: treatments before, during or after cataract surgery.

1.3 People with non-proliferative diabetic retinopathy

Monitoring frequencies for non-proliferative diabetic retinopathy

1.3.1 For monitoring diabetic retinopathy during pregnancy, refer to the section on retinal assessment during pregnancy in NICE's guideline on diabetes in pregnancy. **[2023]**

1.3.2 Hospital eye services should monitor disease progression in people with moderate, severe or very severe non-proliferative retinopathy who are not

being currently treated and have not been previously treated. Consider seeing them:

- every 6 to 12 months if they have moderate non-proliferative diabetic retinopathy.
- every 3 to 6 months if they have severe or very severe non-proliferative retinopathy. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on monitoring frequencies.

Full details of the evidence and the committee's discussion are in evidence review J: effectiveness of different monitoring frequencies.

1.4 People with proliferative diabetic retinopathy

Treatment strategies for proliferative diabetic retinopathy

1.4.1 Discuss with the person with proliferative diabetic retinopathy the benefits and potential side effects of each option:

- panretinal photocoagulation
- anti–vascular endothelial growth factor medicines (anti-VEGFs)
- no treatment (observation).

As part of this discussion, tell them which treatment is likely to work best for them.

Follow the recommendations on communication and information in NICE's guideline on patient experience in adult NHS services and NICE's guideline on shared decision making. **[2023]**

1.4.2 Offer panretinal photocoagulation to all patients when they are first diagnosed with proliferative diabetic retinopathy. **[2023]**

1.4.3 Start panretinal photocoagulation within 2 weeks of offering it and complete it within 4 weeks of starting treatment. **[2023]**

1.4.4 For people with high-risk characteristics or who have difficulty attending appointments, offer to start panretinal photocoagulation on the same day. For example, offer this to people who have neovascularisation which meets the criteria for high-risk characteristics, or those who have difficulty accessing transport to be able to attend hospital appointments. **[2023]**

1.4.5 Offer additional anti-VEGF treatment for people whose proliferative diabetic retinopathy remains active after complete panretinal photocoagulation. If more than one anti-VEGF is available, use the cheapest. **[2023]**

1.4.6 Consider anti-VEGF treatment as a temporary solution for people with proliferative diabetic retinopathy who cannot have panretinal photocoagulation at present because they:

- have vitreous haemorrhage secondary to proliferative diabetic retinopathy (see recommendations 1.4.13 to 1.4.15)
- need cataract surgery (see recommendations 1.2.1 to 1.2.2).

If more than one anti-VEGF is available, use the cheapest**. [2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact sections on treatment strategies for non-proliferative and proliferative diabetic retinopathy and on effectiveness of different thresholds or criteria for starting treatment.

Full details of the evidence and the committee's discussion are in:

- evidence review E: Effectiveness and acceptability of anti-VEGFs and laser photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy

- evidence review B: Effectiveness of different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema.

Monitoring proliferative diabetic retinopathy

1.4.7 In the eye clinic, consider using ultrawide-field fundus imaging alongside clinical examination when assessing the eyes of patients for the presence of proliferative diabetic retinopathy. **[2023]**

1.4.8 In a diagnostic clinic, between appointments at the eye clinic, consider using ultrawide-field fundus imaging alongside other techniques when assessing the eyes of patients for the presence of proliferative diabetic retinopathy. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on monitoring diabetic retinopathy and diabetic macular oedema.

Full details of the evidence and the committee's discussion are in evidence review K: diagnostic accuracy of ultrawide-field fundus photography and optical coherence tomography.

Monitoring frequencies for proliferative diabetic retinopathy

1.4.9 For monitoring proliferative diabetic retinopathy during pregnancy, refer to the section on retinal assessment during pregnancy in NICE's guideline on diabetes in pregnancy. **[2023]**

1.4.10 Assess disease regression in people who have received treatment for proliferative diabetic retinopathy. Conduct this assessment 2 to 3 months after treatment has ended (see recommendations 1.4.7 and 1.4.8 on monitoring for proliferative diabetic retinopathy). **[2023]**

1.4.11 For people whose disease has regressed after treatment for proliferative diabetic retinopathy:

- For the first 12 months after the end of treatment, monitor under the care of hospital eye services using an individualised monitoring frequency.
- After the first 12 months, discharge to the diabetic screening programme. If the person's retina has features that make them ineligible for the screening programme, monitor under the care of hospital eye services, and consider seeing the person every 12 months (see recommendations 1.4.7 and 1.4.8 on monitoring for proliferative diabetic retinopathy). **[2023]**

1.4.12 For people whose disease has not regressed after treatment for proliferative diabetic retinopathy, see recommendations 1.4.1 to 1.4.6 on treatment strategies for proliferative diabetic retinopathy. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on monitoring frequencies.

Full details of the evidence and the committee's discussion are in evidence review J: effectiveness of different monitoring frequencies.

Vitrectomy for people with proliferative diabetic retinopathy

1.4.13 Consider vitrectomy for people with proliferative diabetic retinopathy and vitreous haemorrhage that has not cleared within 3 months (often called 'non-clearing vitreous haemorrhage' in clinical practice). Perform the vitrectomy within 3 months of offering it. **[2023]**

1.4.14 Offer vitrectomy to people with proliferative diabetic retinopathy and macular-involving or macular-threatening retinal detachment. **[2023]**

1.4.15 Consider vitrectomy for people with non-macular-involving or non-macular-threatening retinal detachment who, despite complete panretinal photocoagulation, have:

- proliferative diabetic retinopathy that is active, or
- recurring vitreous haemorrhages related to active proliferative diabetic retinopathy. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on vitrectomy and the rationale and impact section on effectiveness of different thresholds or criteria for starting treatment.

Full details of the evidence and the committee's discussion are in:

- evidence review F: Vitrectomy
- evidence review B: Effectiveness of different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema.

1.5 People with diabetic macular oedema

Treatment strategies for diabetic macular oedema

People with clinically significant diabetic macular oedema

1.5.1 Offer treatment to people with clinically significant macular oedema (centre-involving and non-centre-involving). **[2023]**

1.5.2 Discuss with the person with macular oedema the benefits and potential side effects of:

- anti-VEGF treatment
- macular laser treatment
- steroid treatment
- observation.

As part of this discussion, tell them:

- if they have centre-involving or non-centre-involving macular oedema
- which treatment is likely to work best for their particular condition.

Follow the recommendations on communication and information in NICE's guidelines on patient experience in adult NHS services and shared decision making. **[2023]**

People with non-centre-involving diabetic macular oedema

1.5.3 Offer macular laser treatment to people with non-centre-involving clinically significant macular oedema. **[2023]**

People with centre-involving diabetic macular oedema

1.5.4 When people have centre-involving diabetic macular oedema and good vision (that is, 79 letters or better) consider either observation or macular laser. Discuss these 2 options with the person with macular oedema. **[2023]**

1.5.5 When people have centre-involving diabetic macular oedema, central retinal thickness of less than 400 micrometres and visual impairment, consider anti–vascular endothelial growth factor (anti-VEGF) treatment or macular laser. If more than one anti-VEGF is available, use the cheapest. **[2023]**

In July 2023, this was an off-label use for one anti-VEGF, bevacizumab. See NICE's information on prescribing medicines.

1.5.6 When people have centre-involving diabetic macular oedema, central retinal thickness of 400 micrometres or more and visual impairment, offer them anti-VEGF treatment. If more than one anti-VEGF is available, use the cheapest. **[2023]**

In July 2023, this was an off-label use for one anti-VEGF, bevacizumab. See NICE's information on prescribing medicines.

1.5.7 For guidance on the use of specific anti-VEGFs for people with diabetic macular oedema, see NICE's technology appraisal guidance on ranibizumab, aflibercept, faricimab and brolucizumab for treating diabetic macular oedema. **[2023]**

1.5.8 After the loading phase, assess the effectiveness of anti-VEGF treatment for the person, based on their visual acuity and the reduction of oedema. **[2023]**

1.5.9 If anti-VEGF treatment alone does not stabilise or improve the person's vision after the loading phase, consider:

- using macular laser as rescue treatment **or**
- changing anti-VEGF treatment. **[2023]**

1.5.10 Assess response to treatments after 12 months. Consider switching to a dexamethasone intravitreal implant if the response is suboptimal. **[2023]**

1.5.11 For guidance on the use of dexamethasone intravitreal implant, see NICE's technology appraisal guidance on dexamethasone intravitreal implant for treating diabetic macular oedema. **[2023]**

1.5.12 For guidance on the use of fluocinolone acetonide intravitreal implant for people with diabetic macular oedema in eyes that have previously had cataract surgery, see NICE's technology appraisal guidance on fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy. **[2023]**

1.5.13 If a person does not want to continue with regular anti-VEGF injections, consider switching treatment to a dexamethasone intravitreal implant. **[2023]**

1.5.14 When people with centre-involving diabetic macular oedema have visual impairment and cannot have non-corticosteroid therapy, consider a dexamethasone intravitreal implant. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on treatment strategies for diabetic macular oedema and on effectiveness of different thresholds or criteria for starting treatment.

Full details of the evidence and the committee's discussion are in:

- evidence review G: Effectiveness and acceptability of intravitreal steroids, laser photocoagulation and anti-VEGFs for treating diabetic macular oedema
- evidence review B: Different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema.
- evidence review C: Clinical features for switching or stopping treatment.

Monitoring diabetic macular oedema

1.5.15 Use optical coherence tomography (OCT) imaging when assessing the eyes of patients for the presence of diabetic macular oedema. **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on monitoring diabetic retinopathy and diabetic macular oedema.

Full details of the evidence and the committee's discussion are in evidence review K: Diagnostic accuracy of ultrawide-field fundus photography and optical coherence tomography.

Monitoring frequencies for diabetic macular oedema

1.5.16 For people whose disease has resolved after treatment for diabetic macular oedema:

- For the first 12 months after the end of treatment, monitor under the care of hospital eye services using an individualised monitoring frequency.
- After the first 12 months, discharge to the diabetic screening programme. If the person's retina has features that make them ineligible for the screening programme, monitor under the care of hospital eye services, and consider seeing the person every 12 months. **[2023]**

1.5.17 For people whose disease has not resolved after treatment for diabetic macular oedema, see recommendations 1.5.1 to 1.5.14 on treatment strategies for diabetic macular oedema. **[2023]**

> For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on monitoring frequencies.
>
> Full details of the evidence and the committee's discussion are in evidence review J: Effectiveness of different monitoring frequencies.

Vitrectomy for people with diabetic macular oedema

1.5.18 Consider vitrectomy for people with diabetic macular oedema that does not respond to anti-VEGF treatment and also have either:

- vitreomacular traction or
- epiretinal membrane.

Consider this before any permanent damage occurs. **[2023]**

> For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on vitrectomy.
>
> Full details of the evidence and the committee's discussion are in evidence review F: Vitrectomy.

Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline. For other definitions see the NICE glossary and the Think Local, Act Personal Care and Support Jargon Buster.

Early worsening

Progression of diabetic retinopathy as a result of a sudden drop in blood glucose levels from intensive blood glucose lowering treatments or other causes, such as pancreas transplant.

Disease regression (proliferative diabetic retinopathy)

Proliferative diabetic retinopathy regression is defined by:

- regression or disappearance of new vessels as seen on fundus examination or fundus imaging, or fluorescein angiography
- fibrosis developing in areas of new vessels
- absence of new vitreous or preretinal haemorrhages.

Complete panretinal photocoagulation

Panretinal photocoagulation is complete when all of the midperipheral retina and peripheral retina (from 2 disc diameters away from the fovea to the equator) has been treated with panretinal photocoagulation, leaving one-size burn space in between burns.

High-risk characteristics

High-risk proliferative diabetic retinopathy as defined by the Early Treatment Diabetic Retinopathy Studies (ETDRS studies) is characterised by:

- either on or within one disc diameter of the optic disc, neovascularisation greater than one-fourth to one-third disc area in size
- elsewhere in the retina, neovascularisation greater than one-half a disc area in size with a preretinal haemorrhage or vitreous haemorrhage
- any optic disc with a vitreous or preretinal haemorrhage.

Clinically significant diabetic macular oedema

Diabetic macular oedema is clinically significant when any of the following signs are present, based on slit-lamp biomicroscopy with stereopsis:

- retinal thickening at or within 500 micrometres of the centre of the fovea
- hard exudation at or within 500 micrometres of the centre of the fovea with adjacent retinal thickening

- retinal thickening of 1 disc area or more within 1 disc area of the centre of the fovea.

Clinically significant non-centre-involving diabetic macular oedema

Clinically significant diabetic macular oedema that does not involve the central 1 mm of the macula.

Centre-involving diabetic macular oedema

Diabetic macular oedema that involves the central 1 mm of the macula. Centre-involving diabetic macular oedema is always clinically significant.

Stabilising vision

Visual acuity remaining within 5 letters of what it was before treatment.

Suboptimal treatment response for diabetic macular oedema

Treatment response for diabetic macular oedema is suboptimal if after the loading dose, there is either:

- reduced vision as a result of diabetic macular oedema
- increased diabetic macular oedema
- no change, or increase, in retinal thickness.

Resolved macular oedema

Presence of isolated or sparse, small, intraretinal cysts with no other features as seen from OCT scans.

Visual impairment

78 ETDRS letters or less, or a Snellen acuity of 6/9 or worse.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Effectiveness of clinical features or factors that suggest treatment should be switched or stopped

What are the clinical features or factors that suggest treatment should be switched or stopped for people with diabetic macular oedema?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on clinical features for switching or stopping treatment.

Full details of the evidence and the committee's discussion are in evidence review H: Clinical features or factors that suggest treatment should be switched or stopped for people diagnosed with proliferative diabetic retinopathy or diabetic macular oedema.

2 Prognostic factors for the progression of non-proliferative diabetic retinopathy to proliferative diabetic retinopathy, diabetic macular oedema or macular ischemia

What are the prognostic factors for the progression of non-proliferative diabetic retinopathy to proliferative diabetic retinopathy, diabetic macular oedema and macular ischemia?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on risk factors for the progression of diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review A: Prognostic factors for progression of non-proliferative diabetic retinopathy.

3 Effectiveness of different treatment strategies for non-proliferative diabetic retinopathy

What is the effectiveness and acceptability of observation, anti–vascular endothelial growth factor agents and laser photocoagulation (alone or in combination) for the treatment of severe non-proliferative diabetic retinopathy?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review E: Effectiveness and acceptability of anti-VEGFs and laser photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy.

4 Rapid blood glucose reduction interventions

In people experiencing a rapid substantial reduction in HbA1c, what is the risk of short-term progression of diabetic retinopathy or diabetic macular oedema, and is there a risk of long-term visual loss?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on effects of rapid blood glucose reduction.

Full details of the evidence and the committee's discussion are in evidence review C: Effectiveness of intensive treatments to lower blood glucose levels.

5 Effectiveness of different treatment strategies for proliferative diabetic retinopathy

What is the effectiveness and acceptability of combination treatments for proliferative diabetic retinopathy?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review E: Effectiveness and acceptability of anti-VEGFs and laser photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy.

Other recommendations for research

Effectiveness of different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy

What is the effectiveness of different thresholds or criteria for starting treatment for people with non-proliferative diabetic retinopathy?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on different thresholds or criteria for starting treatment .

Full details of the evidence and the committee's discussion are in evidence review B: Different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema.

Statins for the prevention of progression of diabetic macular oedema

What is the effectiveness of intensive statin treatment compared with standard statin treatment for people with non-proliferative diabetic retinopathy and diabetic macular oedema?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on preventing progression of diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review D: Effectiveness of lipid modification therapies and antihypertensive medicines.

Fibrates for the prevention of progression of diabetic retinopathy

What is the effectiveness of fibrates for the prevention of progression of diabetic retinopathy in people with different ethnicities?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on preventing progression of diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review D: Effectiveness of lipid modification therapies and antihypertensive medicines.

Effectiveness of different treatment strategies for proliferative diabetic retinopathy

What is the most effective and acceptable method of delivering panretinal photocoagulation for people with proliferative diabetic retinopathy?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.

Full details of the evidence and the committee's discussion are in evidence review E: Effectiveness and acceptability of anti-VEGFs and laser photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy.

Effectiveness of treatments before, during or after cataract surgery for managing non-proliferative diabetic retinopathy

In people with moderate to severe non-proliferative diabetic retinopathy who are about to undergo or who have undergone cataract surgery, what is the effectiveness and acceptability of different treatments for diabetic retinopathy (before, during or after surgery)?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on cataract surgery.

Full details of the evidence and the committee's discussion are in evidence review I: Treatments before, during or after cataract surgery.

Effectiveness of treatments before, during or after cataract surgery for managing diabetic macular oedema

In people with diabetic macular oedema who are about to undergo, or who have undergone cataract surgery, what is the effectiveness and acceptability of different treatments for diabetic macular oedema (before, during or after surgery)?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on cataract surgery.

Full details of the evidence and the committee's discussion are in evidence review I: Treatments before, during or after cataract surgery.

Monitoring frequencies for people with non-proliferative diabetic retinopathy

What is the most effective monitoring frequency for people with non-proliferative diabetic retinopathy who are cared for under hospital eye services and are not receiving treatment?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on monitoring frequencies.

Full details of the evidence and the committee's discussion are in evidence review J: Effectiveness of different monitoring frequencies.

Monitoring frequencies for people with proliferative diabetic retinopathy or diabetic macular oedema

What is the most effective monitoring frequency for people with proliferative diabetic retinopathy or diabetic macular oedema who have received treatment?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on monitoring frequencies.

Full details of the evidence and the committee's discussion are in evidence review J: Effectiveness of different monitoring frequencies.

Diagnostic test accuracy for monitoring disease progression

For people who are under the care of hospital eye services, what is the diagnostic test accuracy of ultrawide-field fundus imaging for diagnosing the progression of diabetic retinopathy to proliferative diabetic retinopathy?

For a short explanation of why the committee made this recommendation for research, see the rationale and impact section on monitoring diabetic retinopathy and diabetic macular oedema.

Full details of the evidence and the committee's discussion are in evidence review K: Diagnostic accuracy of ultrawide-field fundus photography and optical coherence tomography.

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

Effects of rapid blood glucose reduction

Recommendations 1.1.1 to 1.1.2

Why the committee made the recommendations

Evidence from several randomised controlled trials showed that, for people with non-proliferative retinopathy, intensive blood glucose management brings long-term benefits. The studies showed that intensive therapy slows rates of retinopathy progression.

One randomised controlled trial showed that people with type 1 diabetes who kept their blood glucose levels as close to normal as possible and had intensive diabetes treatment early in their overall diabetes disease also had fewer diabetes-related health problems (including progression of retinopathy and incidence of macular oedema after 9 years) than those who had standard, non-intensive treatment.

The committee thought it was important for clinicians to highlight to patients the benefits that good blood glucose management can have for their vision, as this may reduce their risk of vision loss. Sustained good blood glucose management could also avoid the need for intensive treatments at a later stage, thereby avoiding potential complications of intensive treatment, including early worsening of diabetic retinopathy.

The committee noted that NICE's guidelines on managing type 1 diabetes in adult, managing type 2 diabetes in adults and diagnosing and managing diabetes (type 1 and type 2) in children and young people include recommendations on blood glucose management. They therefore decided that those recommendations should be taken into account in discussions with patients about diabetes and vision.

Although no studies evaluated the effects of rapid glucose lowering for people with proliferative retinopathy or macular oedema, the committee thought that the recommendations were still important for these groups, to ensure that all patients are aware of the long-term benefits of good diabetes management and that no one misses out on monitoring.

Short-term outcomes

Some of the studies included both short- and long-term follow-up. The committee were interested in these short-term outcomes to see if they showed evidence of early

worsening. However, there were a number of limitations to this evidence base, including:

- small sample sizes
- the use of treatments that do not fully reflect current practice and
- the fact studies were not designed to detect early worsening.

It was therefore difficult to determine what the effects of treatments currently used to lower blood glucose may be on both early worsening and long-term retinopathy and macular oedema outcomes. This made it difficult to make strong recommendations on these effects, or to identify whether some intensive interventions are more likely to result in early worsening. The committee therefore decided to include a research recommendation designed to evaluate the short-term effects from current treatments on early worsening and whether any effects are sustained long-term.

The committee agreed that, in their experience, the most important risk factor for early worsening is higher HbA1c levels at screening. In their clinics, they regularly see people with very high HbA1c levels (greater than 97 mmol/mol [11%]), who are likely to go through intensive treatment. But there is currently no evidence that evaluates the risk of early worsening for these people. People with very high HbA1c levels were therefore included as a potential subgroup in the research recommendation.

Despite the limited evidence, the committee were concerned about the potential risks of early worsening from treatments for rapid blood glucose reduction, as this is a recognised concept among clinicians. They decided that it is important to be cautious before starting intensive therapies for people with poor glucose management. So they recommended that, before intensive glycaemic treatment is started, an ophthalmologist should review the person's condition. This will allow them to assess the person's current eye disease status and identify any changes once they begin treatment.

How the recommendations might affect practice

The recommendations on blood glucose management will not have a significant resource impact because they are consistent with current practice.

Return to recommendations

Information for all people involved in the care of someone who has diabetic retinopathy or diabetic macular oedema

Recommendations 1.1.3 to 1.1.5

Why the committee made the recommendations

Progression of non-proliferative diabetic retinopathy to proliferative diabetic retinopathy or diabetic macular oedema

Severity of retinopathy, HbA1c levels and blood pressure

Moderate to low quality evidence showed that:

- severity of retinopathy and HbA1c levels can be used to predict how likely it is that non-proliferative diabetic retinopathy will progress to proliferative diabetic retinopathy and
- blood pressure can predict how likely it is that non-proliferative diabetic retinopathy will progress to diabetic macular oedema.

Given the importance of reducing the risk of someone progressing to either of these stages of disease, the committee recommended that ophthalmologists should have access to both a person's HbA1c and blood pressure results so that:

- they are aware that these factors have a role in disease progression to proliferative diabetic retinopathy and diabetic macular oedema
- they encourage people with non-proliferative diabetic retinopathy to take steps to normalise their blood pressure and HbA1c.

The committee highlighted that, in their experience, communication is not always clear between different healthcare professionals. They agreed that it is important to share information about a person's risk factors and retinopathy grading with clinicians who are involved in the person's overall diabetes management. This can help the person get the most effective and appropriate care and reduce the risks of disease progression.

Other prognostic factors

There was evidence on a range of progression prognostic factors, other than severity of retinopathy, HbA1c levels and blood pressure. This evidence ranged from moderate- to very low-quality, and reported on a wide range of different factors, meaning that most of the results were based on single study analysis. Given the limitations of the evidence base, the committee found it difficult to confidently identify many other indicators as clear risk factors for progression. However, they noted that the evidence for renal disease, while low-quality, supported their clinical experience that renal disease can influence progression. They decided that this should also be highlighted in the recommendation.

The committee thought it was important to identify such factors. Identifying people who are at risk of progression will mean their condition can be closely monitored and they can receive early treatment to avoid or reduce the complications associated with progression. The committee therefore made a research recommendation aimed at identifying other prognostic factors.

Progression of non-proliferative diabetic retinopathy to diabetic macular ischemia

There was no evidence on factors that can be used to predict how likely it is that non-proliferative diabetic retinopathy could progress to diabetic macular ischemia. Therefore, the committee could not make recommendations on this and included progression to macular ischemia in a research recommendation.

How the recommendations might affect practice

The recommendations are not expected to have a major impact on practice or increase resource use. The recommendations highlight the importance of regular assessments and access to patient information, and this is something that should already be taking place. In places where patient information is not routinely shared, systems may need to be implemented to allow clinicians to record and access this information.

Return to recommendations

Preventing progression of diabetic retinopathy

Recommendations 1.1.6 to 1.1.10

Why the committee made the recommendations

Blood pressure management

NICE's guideline on diagnosing and managing hypertension in adults includes recommendations on blood pressure management for people with diabetes and hypertension. The committee thought it was important to follow these recommendations for people with hypertension and diabetic retinopathy.

Evidence from one randomised controlled trial for people with non-proliferative diabetic retinopathy showed that, for people with hypertension at baseline:

- intensive blood pressure management can reduce progression of non-proliferative retinopathy, and
- this effect was maintained in the long term.

The committee thought that it was important that clinicians and people with diabetic retinopathy were aware of this information when deciding on management options for hypertension. They also thought a recommendation was important to distinguish between the effects of hypertension treatments for people who do, or do not, have hypertension at baseline.

Evidence from several randomised controlled trials showed reducing blood pressure had no effect on diabetic retinopathy for people who did not have hypertension so the committee thought it was important to highlight this to ensure that people did not receive unnecessary treatment. However, they emphasised that this is only if the blood pressure medicine was being prescribed with the aim of reducing non-proliferative diabetic retinopathy progression. If the medicines are being offered for other reasons, then it is important that people are still offered them.

Statins

There was no evidence that clearly showed that statins reduce progression of diabetic retinopathy. Some low-quality evidence showed a short-term benefit of statins for people who also had diabetic macular oedema. The committee did not

think the evidence base was sufficient to recommend using statins. Instead, they made a research recommendation to compare the effectiveness of intensive and standard statin treatments for people with diabetic macular oedema.

The committee noted that NICE's guideline on cardiovascular disease recommends that most people with type 1 and type 2 diabetes are offered statins as part of their diabetes management. The committee thought it was important to refer to this guideline in the recommendations.

Fibrates

Evidence from 2 randomised controlled trials showed fibrates are beneficial for people with type 2 diabetes and retinopathy at baseline. However, evidence was only available for retinopathy progression. There was no evidence on other outcomes such as visual acuity or quality of life. Despite this, the committee thought the evidence showed an important effect.

There was no evidence on the effects of fibrates for people with type 1 diabetes, so they were not included in the recommendation. However, the committee was aware of ongoing research on the effects of fibrates for this group, so they decided against making a research recommendation.

The committee highlighted that there is limited evidence on the effectiveness of fibrates for the prevention of diabetic retinopathy progression in people with different ethnicities. They felt this was an important consideration, and therefore made a research recommendation on this.

How the recommendations might affect practice

The recommendations on blood pressure management and statins will not have a significant resource impact because they are consistent with current NICE recommendations.

The recommendation on fibrates is likely to increase the use of fibrates in people with non-proliferative diabetic retinopathy, but this can reduce the risk of progression, thereby reducing the time and costs associated with additional treatment.

Return to recommendations

Cataract surgery

Recommendations 1.2.1 to 1.2.3 and 1.4.6

Why the committee made the recommendations

There was limited evidence on the most effective treatments for people with non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema when they have cataract surgery. This meant the committee could not make specific recommendations about the most effective treatments for these groups.

There was no evidence on the use of different services, such as independent centres, for cataract surgery. But the committee thought it was important to highlight that, in their experience, the use of independent centres can lead to complications for some people. This is because these people's current retinopathy status is not always identified before surgery. Information on current retinopathy status can be identified from a number of sources, such as the NHS diabetic eye screening programme, the Hospital Eye Services medical retina clinic or by examination of the retina. Without this information, surgery may not always be tailored to a person's eye condition, or they may not be given the most effective post-operative medication or follow-up care after surgery. The committee made a recommendation which addresses these concerns.

The committee was aware of recommendations in NICE's guideline on managing cataracts in adults about the use of steroids and non-steroidal anti-inflammatory drugs (NSAIDs) to manage cystoid macular oedema as a complication of cataract surgery, including those with diabetes. They therefore cross-referred to these.

Given the limited evidence base, the committee made 3 research recommendations aimed at developing a greater understanding of how to improve diabetic retinopathy and diabetic macular oedema outcomes following cataract surgery. This will help avoid people with cataracts having to wait until after cataract surgery to have treatment for their diabetic retinopathy or diabetic macular oedema. In turn, this will lower the risk of someone's diabetic retinopathy or diabetic macular oedema progressing further while the person waits for cataract treatment.

Although they recommended temporarily using anti-VEGF treatment for people with proliferative diabetic retinopathy who need cataract surgery, the committee still thought a research recommendation was needed for this group to determine whether there are any more effective management strategies.

How the recommendations might affect practice

The committee made no recommendations on the most effective treatments before, during or after cataract surgery, for people with non-proliferative diabetic retinopathy or diabetic macular oedema, so this will have no impact on practice.

The recommendation for anti-VEGFs for people with proliferative diabetic retinopathy may increase the number of people who are offered this treatment before cataract surgery. However, this may reduce the number of people whose proliferative retinopathy progresses while waiting for cataract surgery, thereby reducing the time and costs associated with additional treatment they might otherwise need.

The recommendation for surgeons to obtain people's current eye disease status before cataract surgery means that more people with diabetic retinopathy should receive the appropriate pre-operative and follow-up care, which will reduce their risk of complications from surgery.

Return to recommendations

Monitoring frequencies

Recommendations 1.3.1 to 1.3.2, 1.4.9 to 1.4.12 and 1.5.16 to 1.5.17

Why the committee made the recommendations

The committee made these recommendations based on their clinical experience and one study that compared monitoring frequencies in people with non-proliferative retinopathy.

To reduce the impact on vision, diabetic retinopathy progression needs to be identified early and treated. The committee balanced the importance of detecting progression early with the demands on hospital eye services and costs of monitoring. They also took into account that people with diabetic retinopathy often have comorbidities, including other diabetes-related complications. This means they

attend a large number of hospital appointments to manage their diabetes care. To reduce this burden, it is important to ensure that monitoring is not more frequent than necessary.

People with non-proliferative diabetic retinopathy

Evidence for monitoring frequencies for people with non-proliferative retinopathy showed that risk of progression between monitoring visits is higher for people with severe or very severe retinopathy compared with those with moderate retinopathy.

Based on this evidence and their clinical experience, the committee recommended different monitoring frequencies for people who are not being currently treated and have not been previously treated, depending on the severity of their disease.

People with moderate non-proliferative diabetic retinopathy have a relatively slow rate of progression and so monitoring every 6 to 12 months was considered appropriate.

For people with severe or very severe non-proliferative diabetic retinopathy, whose disease progresses more quickly, monitoring every 3 months was considered beneficial. This will reduce the risk of progression to proliferative diabetic retinopathy or diabetic macular oedema remaining unnoticed for too long. This is important because, once the disease has progressed to proliferative diabetes retinopathy or diabetic macular oedema, it needs to be treated as soon as possible to avoid vision loss.

However, the committee discussed how people with diabetic retinopathy often have to attend multiple appointments for other diabetes-related complications, so attending additional appointments every 3 months might not always be achievable. It was therefore recommended that monitoring should take place between 3 and 6 months for this group. These recommendations reflect current practice. They are similar to the monitoring frequencies recommended in the Royal College of Ophthalmologists guideline, although may result in less frequent monitoring for some of the people who have moderate non-proliferative diabetic retinopathy and are not expected to progress quickly.

People with proliferative diabetic retinopathy or diabetic macular oedema

There was no evidence on monitoring frequencies for people with proliferative diabetic retinopathy or diabetic macular oedema who are receiving treatment or who have previously received treatment. So the committee made recommendations in this area based on their clinical experience, and in line with current practice.

They noted that monitoring during treatment with intravitreal therapies would be determined by the treatment protocol and so did not make recommendations for this area. However, they agreed that some guidance on monitoring frequency after treatment completion is required to improve consistency across the country. Therefore, they made recommendations on follow-up for the first 12 months after the end of treatment, and beyond 12 months. They recommended that, for the first 12 months after the end of treatment, monitoring frequency should be individualised depending on the treatment given and response to treatment.

People with non-proliferative diabetic retinopathy, proliferative diabetic retinopathy or diabetic macular oedema

The committee did not review any evidence that allowed them to clearly differentiate evidence for people under 18 or pregnant people. However, they agreed that the same recommendations should apply to under 18s as to adults. Although the risk of developing diabetic retinopathy is lower in under 18s, if it is identified, it should be monitored in the same way. The committee was aware of existing recommendations on monitoring diabetic retinopathy and the timing of retinal assessments in pregnancy in NICE's guideline on diabetes in pregnancy, so they agreed to refer to this guideline.

Because there was limited evidence on the most effective monitoring frequencies for people with non-proliferative retinopathy who have not started treatment and people with proliferative diabetic retinopathy who have had treatment previously, the committee made 2 recommendations for research on these topics.

How the recommendations might affect practice

The committee highlighted that the monitoring frequency recommended for people with moderate non-proliferative diabetic retinopathy reflects current practice in most

centres and could result in less frequent monitoring for some people who are not expected to progress quickly.

The recommendation for people with severe to very severe non-proliferative diabetic retinopathy may result in more frequent monitoring for some people, but it broadly reflects current practice. Where monitoring frequency is increased, this should result in progression being identified earlier and therefore being less extensive than it would otherwise have been. This will reduce the time and costs associated with the additional treatments needed.

The recommendations for people with proliferative diabetic retinopathy reflect current practice.

Return to recommendations

Treatment strategies for non-proliferative and proliferative diabetic retinopathy

Recommendations 1.4.1 to 1.4.6

Why the committee made the recommendations

People with non-proliferative diabetic retinopathy

There was insufficient evidence to determine which treatment strategies are the most effective to prevent progression to the sight-threatening complications of diabetic retinopathy. The committee was therefore unable to make recommendations for this group. Instead, they made a recommendation for research on treatment strategies for people with severe non-proliferative diabetic retinopathy.

People with proliferative diabetic retinopathy

Results from a network meta-analysis indicated that some anti-VEGF treatments resulted in slight improvements in visual acuity in comparison to panretinal photocoagulation. However, the committee noted that these differences were not clinically meaningful. Results from some individual studies indicated that anti-VEGFs result in a reduced incidence of diabetic macular oedema, but there was no clear difference between anti-VEGFs and panretinal photocoagulation for any of the other outcomes. It was not possible to distinguish the effectiveness of different treatments

depending on severity of retinopathy at baseline, because this was not clearly reported in the studies. In addition, many of the studies were low-quality and had small sample sizes, making it difficult to be certain of the effectiveness of each treatment option.

Given the similar effectiveness of panretinal photocoagulation and anti-VEGFs, particularly for visual acuity, the committee used their clinical experience to recommend that panretinal photocoagulation should be used as first-line treatment when possible. This is because panretinal photocoagulation does not have some of the risks that are associated with anti-VEGFs, such as endophthalmitis. It also requires fewer hospital visits and reduces the risk of progression that might otherwise be seen if a person is offered anti-VEGF treatment but cannot attend regular appointments.

The committee thought that panretinal photocoagulation was particularly effective for people with high-risk proliferative diabetic retinopathy. They agreed it can also be beneficial for people with early proliferative retinopathy because, for these people, the alternative option is frequent monitoring. They agreed that the risks associated with progression if people do not attend follow-up appointments are greater than the risk of adverse events from panretinal photocoagulation, particularly with modern panretinal photocoagulation. For this reason, they recommended that all people with proliferative diabetic retinopathy are offered panretinal photocoagulation when they are first diagnosed.

Evidence from 2 studies showed that early panretinal photocoagulation reduced the number of people who progressed or developed severe visual loss at 2 years. This supported the committee’s experience that panretinal photocoagulation brings additional benefits if provided early.

The committee discussed how treatment should ideally be offered and started on the day a person is diagnosed with proliferative diabetic retinopathy, especially for those with high-risk characteristics. However, they were aware that this is not always possible, and therefore recommended that treatment should start within 2 weeks of it being offered. It should be completed within 4 weeks of treatment starting to ensure it is delivered effectively. This will reduce the risk of progression between diagnosis

and treatment. The committee also noted that some people find it difficult to attend appointments, such as people who have jobs with zero hours contracts or those who cannot afford the costs of transport associated with repeated hospital appointments. These people should always be offered the option of starting photocoagulation on the day of diagnosis. This will reduce the risk of the potentially serious consequences associated with delayed treatment, such as loss of vision.

The committee highlighted the importance of discussing treatment options with the patient. This is particularly important for treatments such as panretinal photocoagulation and anti-VEGF treatment because, in the committee's experience, the thought of having laser or injections into the eye can cause anxiety. Discussing each treatment option and giving the person the opportunity to ask questions may help to reduce some of their concerns.

The committee was aware that, in some people, proliferative diabetic retinopathy will progress despite full panretinal photocoagulation. Given that network meta-analysis showed anti-VEGF treatments to have a similar level of effectiveness as panretinal photocoagulation for improving visual acuity, the committee thought that anti-VEGFs would be an effective second-line treatment for people with proliferative diabetic retinopathy. There was no clear evidence that any one anti-VEGF was more effective than any other, so the committee recommended that the cheapest option should be used.

The committee was also aware that some people are unable to have panretinal photocoagulation, such as those with cataracts or vitreous haemorrhage. They thought it was important for these people to receive treatment for retinopathy as early as possible, rather than delaying until after surgery. This will reduce the risk of progression that may otherwise occur if clinicians wait until it is possible to use panretinal photocoagulation. For this reason, the committee recommended that anti-VEGFs are considered as a temporary measure for people who cannot have panretinal photocoagulation.

The committee discussed the lack of evidence on combination treatments for people with proliferative diabetic retinopathy, with most of the studies considering either panretinal photocoagulation or single anti-VEGFs. They therefore made a research

recommendation aimed at determining which is the most effective combination of treatments. This is important because it will highlight whether combinations of different anti-VEGFs are more effective than single anti-VEGFs, or which anti-VEGFs are the most effective when combined with panretinal photocoagulation.

The committee was concerned that panretinal photocoagulation is not always delivered using the most effective methods. Questions raised included whether panretinal photocoagulation should be delivered to the whole retina or just to the ischemic areas. The committee therefore made a research recommendation to determine which is the most effective and acceptable method of giving panretinal photocoagulation.

How the recommendations might affect practice

The recommendations for people with proliferative diabetic retinopathy are in line with current practice and should not increase the number of people who are given panretinal photocoagulation. The recommendation for anti-VEGFs highlights the importance of using the cheapest option. These recommendations therefore should not have a major impact on current practice or cost to the NHS. The recommendation for temporary anti-VEGFs for people who need vitrectomy or cataract surgery will reduce complications for the patient as well as reducing the time and costs associated with additional treatment if their vitrectomy or cataract surgery is delayed.

Return to recommendations

Monitoring diabetic retinopathy and diabetic macular oedema

1.4.7 to 1.4.8 and 1.5.15

Why the committee made the recommendations

Ultrawide-field fundus imaging to detect proliferative diabetic retinopathy in people with non-proliferative diabetic retinopathy

There was no evidence on the diagnostic accuracy of ultrawide-field imaging for detecting proliferative diabetic retinopathy in people with non-proliferative diabetic retinopathy. A range of tests can be used in clinical practice and the committee did

not think they could tell which is the most effective without evidence. Therefore, they made a research recommendation to provide evidence on this in future.

Ultrawide-field fundus imaging to detect proliferative diabetic retinopathy in people with previously-treated diabetic retinopathy

Evidence was available from a single study which assessed the diagnostic accuracy of ultrawide-field fundus imaging for people who had previously had treatment for proliferative diabetic retinopathy. The committee thought that the sensitivity of ultrawide-field imaging was sufficient to consider it as an additional test alongside other tests used to diagnose proliferative diabetic retinopathy.

The committee discussed whether ultrawide-field imaging could be used as the sole diagnostic test for diabetic retinopathy. However, they were concerned about the potential for this form of imaging to miss some important indications such as rubeosis. These other indications can be picked up by current standard techniques, such as slit-lamp biomicroscopy. For this reason, they decided to recommend that ultrawide-field imaging should be used alongside clinical examination to detect proliferative diabetic retinopathy. They also thought it could be a useful tool in diagnostic clinics, which are used for monitoring in between appointments at the eye clinic, and involve images being taken of the patient's eyes, which are then sent to the clinician for evaluation, rather than the evaluation taking place during a face-to-face appointment in the eye clinic. This will help to identify anyone whose disease may be showing signs of progressing. The committee highlighted that this would not be a stand-alone test, as anyone with eyes showing signs of progression would then see an ophthalmologist for further assessment and to make a decision about whether treatment is needed.

The committee noted that using more than one technique was beneficial not only for diagnosing proliferative retinopathy, but also in other ways. While ultrawide-field imaging can be efficient, it is often carried out in diagnostic testing centres. This means that patients miss out on the interaction with healthcare professionals who can answer questions and reduce any anxiety that people may have about their test results. This supported the committee's decision to recommend ultrawide-field imaging alongside other techniques.

Optical coherence tomography for the detection of diabetic macular oedema

Evidence was available from a high-quality systematic review that compared the diagnostic accuracy of optical coherence tomography (OCT) to that of fundus examination or photography. This showed OCT was effective for diagnosing diabetic macular oedema development or progression.

Although the review showed that OCT can result in some false positives, the committee thought this was a result of the ability of OCT to detect subclinical macular oedema. OCT is therefore a useful test to identify people whose disease needs to be monitored until it reaches a threshold where treatment may be needed, as well as identifying people who already have diabetic macular oedema. The committee also discussed how OCT scans play an important role in monitoring treatment response to anti-VEGF treatment. Therefore, the committee decided that OCT should be recommended as the primary diagnostic method for diabetic macular oedema. They highlighted that this reflects current practice.

How the recommendations might affect practice

Recommendations on diagnosing proliferative diabetic retinopathy may result in an increase in the use of ultrawide-field imaging. However, this is considered to be efficient and less costly than clinical examination, and is already used in some centres, so it should not have a major impact on clinical practice.

OCT is already standard practice for diagnosing diabetic macular oedema so recommendations in relation to OCT should not have any major impact on practice.

Return to recommendations

Treatment strategies for diabetic macular oedema

Recommendations 1.5.1 to 1.5.14

Why the committee made the recommendations

People with clinically significant diabetic macular oedema

The committee highlighted that it is important that all people who have clinically significant diabetic macular oedema are offered treatment, whether they have

centre-involving or non-centre-involving oedema. Without treatment, all people with clinically significant diabetic macular oedema are at risk of vision loss.

They discussed the importance of making all people with clinically significant diabetic macular oedema aware of their diagnosis and the benefits and side effects of each treatment option. They highlighted that many people with macular oedema are unaware of whether their oedema is centre- or non-centre-involving and are offered treatment without being given a clear explanation of what the treatment is and why it is being offered. This can be very stressful, particularly at a time when people are already concerned about further vision loss. Shared decision making is therefore an important part of managing macular oedema, and will help people understand why a particular treatment may be best for them. It will also ensure that treatment fits their personal needs and circumstances.

People with non-centre-involving diabetic macular oedema

There were very few studies for people with non-centre-involving diabetic macular oedema, making it difficult to determine which is the most effective treatment option for this group. However, the committee discussed how, in their experience, the use of macular laser for people with non-centre-involving macular oedema is current practice and is important, as this can delay the need for anti-VEGF treatment. They thought a recommendation was important for this group because, without treatment, their disease will progress to centre-involving macular oedema and they will be at higher risk of complications, such as vision loss.

The committee's experience was supported by evidence from one study with high- to moderate-quality outcomes in the review on treatment strategies (see evidence review B). This showed that the worsening of visual acuity was slowed when macular laser was provided in the early stages of macular oedema. It was therefore recommended that macular laser should be offered to all people with non-centre-involving diabetic macular oedema, which is an early stage of diabetic macular oedema.

People with centre-involving diabetic macular oedema

The evidence showed that a number of treatments including anti–vascular endothelial growth factor medicines (anti-VEGFs) and some steroids and

combinations of treatments are more effective at improving visual acuity than standard threshold laser alone at 12 months. They are also more effective at reducing central retinal thickness at 12 and 24 months than standard threshold laser. Subgroup analysis showed similar results for people with a central retinal thickness of 400 micrometres or over. Some evidence of the benefits of anti-VEGFs was seen in the subgroup with central retinal thickness less than 400 micrometres. However, the smaller evidence base for this group made it more difficult to be confident in the effects of different treatments.

Improvements in visual acuity and central retinal thickness, even at 12 months, are considered important by people with diabetic macular oedema. Although there was more limited data on effectiveness on visual acuity at 24 months, the committee was confident that the short-term results were enough to make recommendations on the most effective treatments for people with centre-involving macular oedema.

The committee's decisions were mostly based on the results for visual acuity and central retinal thickness because there was limited data for other outcomes at 12 or 24 months. However, the committee noted that anti-VEGFs are not commonly associated with a large number of ocular adverse events and are generally well tolerated, whereas a greater number of adverse events, such as cataracts and increased intraocular pressure, tend to be experienced with steroids. Therefore, they recommended that people with centre-involving diabetic macular oedema, central retinal thickness of 400 micrometres or more and visual impairment should be offered anti-VEGF treatments. The definition of visual impairment was based on the inclusion criteria that are often seen in clinical trials. The committee noted that the dosage and timing guidance differs between anti-VEGFs, and so clinicians should ensure that they follow the information provided in the summary of product characteristics (SPC).

People with central retinal thickness of less than 400 micrometres

The committee was aware that NICE’s technology appraisals already recommend the use of ranibizumab, aflibercept, faricimab and brolucizumab for people with macular oedema. However, these are recommended for people with a central retinal thickness of 400 micrometres and above. They discussed how some groups, especially people of South Asian or Afro-Caribbean descent and some women, tend

to have thinner retinas. Some people in these groups are therefore likely to take longer to reach the 400 micrometre threshold even if they have retinal thickening, which may mean they are not offered treatment until later than other people, and therefore may have worse outcomes. Given that the analysis in this review showed anti-VEGFs to be clinically and cost effective for a wider population, and the meta-analysis indicated that anti-VEGFs may be beneficial for this group, the committee decided to recommend that anti-VEGFs should be considered for people with central-involving macular oedema, visual impairment and central retinal thickness of less than 400 micrometres.

Macular laser was recommended as an alternative treatment option because the evidence and committee's experience indicated that this can also be effective and is current practice for many people in this group. It also has the benefit of delaying the need for anti-VEGF treatment for some people.

Assessing response to treatment

The committee was aware that some eyes do not respond as well as others to anti-VEGF treatments and may need additional treatment. While considering evidence on the criteria for switching or stopping treatment (see evidence review H), they highlighted that response to treatment is usually assessed after the loading phase. At this point, if vision has not stabilised or improved, rescue laser treatment can be used as a short-term option to increase the response. However, they also discussed the importance of assessing response to treatment beyond the loading phase, in case someone's eye has a delayed response. For this reason, the committee recommended that a further review should take place after 12 months, where another class of drug should be considered if necessary.

Poor response to treatment

The committee was aware of NICE technology appraisal guidance for the use of a dexamethasone intravitreal implant or fluocinolone if someone's condition has not responded well enough to anti-VEGFs. Recommendations for the switch to these steroids were supported by the evidence, which showed dexamethasone intravitreal implant is effective at improving visual acuity and reducing central retinal thickness. However, the committee did not recommend this as first-line treatment because additional adverse events can be experienced when using steroids. Fluocinolone

was less effective and cost effective than dexamethasone and so the recommendations for steroids primarily focused on the use of dexamethasone. However, the technology appraisal identified that people who have an intraocular lens may benefit from this treatment, so it was included in the recommendations for this group of people.

People for whom anti-VEGFs are contraindicated or impractical

While anti-VEGFs were recommended for most people with centre-involving macular oedema, the committee recommended that dexamethasone intravitreal implant is considered for 3 subgroups to ensure that they don't miss out on the benefits of treatment. These include people who:

- are not able to regularly attend a clinic to have anti-VEGF injections
- do not want to continue with regular injections
- are not able to have anti-VEGF treatment, such as people who are pregnant.

They highlighted people who are pregnant as an important group to consider, as anti-VEGFs are contraindicated in pregnancy. However, it is important that this group can still receive another type of treatment to avoid further progression of their macular oedema. The recommendations for these 3 groups are in line with NICE's technology appraisal guidance on using a dexamethasone intravitreal implant for treating diabetic macular oedema and NICE's technology appraisal guidance on using fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy.

People with diabetic macular oedema and good vision

Some people with diabetic macular oedema have good vision. These people may have fewer benefits from anti-VEGF, steroids or macular laser treatment than people who have visual impairment, but still experience the adverse effects associated with treatment. However, the committee highlighted that:

- while the benefits may not be as great as for those with visual impairment, the treatments can still reduce the risk of vision loss
- macular laser treatment can be useful in this group to potentially delay the need for anti-VEGF treatment.

Although the analysis for the whole population with diabetic macular oedema suggested that macular laser was not the most clinically effective treatment option, it still showed benefits for improving visual acuity and was the most cost-effective option in comparison to anti-VEGFs or steroids. The committee thought it was important to highlight that macular laser can have benefits for people who still have good vision. They noted that macular laser is not always offered to this group of people even though it can delay progression to the point where a person needs anti-VEGF treatment, thereby benefitting the patient and reducing treatment costs.

However, the committee were aware that macular laser may not be the only option for this group. Evidence from the review on thresholds for starting treatment (see evidence review B) showed that outcomes may be similar for some people whether they are initially offered observation, anti-VEGF or macular laser. Therefore, as the benefits of treatment are likely to be smaller for people with good vision, and there is currently limited evidence comparing macular laser to observation (delayed treatment), the committee recommended clinicians should consider both options. They noted that the most appropriate option needs to be carefully considered for each patient to reduce their risk of progression. Therefore, they recommended that the decision should include a discussion with the patient about the benefits and risks of each option to make a shared decision over which to choose.

How the recommendations might affect practice

The recommendations for people who have non-centre-involving macular oedema reflect current practice and are not expected to have a major impact on practice.

The recommendations for people with diabetic macular oedema and good vision are different to current practice and may increase the number of people who are given macular laser. However, this may reduce the number of people who progress to having visual impairment, thereby reducing the number of anti-VEGF injections that need to be provided to these people, which may have a cost-saving benefit.

For those people who do progress to having visual impairment, the recommendations may increase the number of people who are initially offered anti-VEGFs, as this can include people with a central retinal thickness of less than the 400 micrometre threshold specified in NICE's technology appraisals. However, with

the additional option of macular laser for people who have thinner retinas, and the recommendations to switch treatments if there is a suboptimal response after 12 months, this impact may not be substantial.

Return to recommendations

Effectiveness of different thresholds or criteria for starting treatment

Recommendations 1.4.2 to 1.4.3, 1.4.13 and 1.5.3 to 1.5.4

Why the committee made the recommendations

People with non-proliferative and proliferative diabetic retinopathy

The committee discussed the benefits of panretinal photocoagulation treatment for people with non-proliferative and proliferative diabetic retinopathy. Evidence from 2 studies showed possible benefits of early treatment over deferred treatment for reducing severe visual loss and incidence of progression at 2-year follow-up.

A review of evidence on treatment strategies for people with diabetic retinopathy (see evidence review E) led to recommendations on offering panretinal photocoagulation to all people when they are first diagnosed with proliferative diabetic retinopathy. The committee discussed the timing of this treatment. Based on a combination of the evidence from this review showing that early photocoagulation can reduce vision loss and progression, and on their clinical experience, the committee recommended that this should be started within 2 weeks of proliferative retinopathy being identified.

There was some evidence for people who have severe proliferative diabetic retinopathy and severe vitreous haemorrhage, which indicated that an early vitrectomy results in better visual acuity and fewer retinal detachments at 2 years than deferred vitrectomy. This supported the committee's experience about the benefits of early vitrectomy. This evidence was therefore taken into account when deciding on recommendations for vitrectomy (see evidence review F).

There was very limited evidence for people with non-proliferative diabetic retinopathy. There is currently limited knowledge about the most effective treatment

options for this group, as monitoring is generally used in current practice. The committee therefore decided that they could not make specific recommendations and instead made a research recommendation aimed at identifying the best treatment strategies for people with non-proliferative diabetic retinopathy.

People with diabetic macular oedema

The committee discussed the effectiveness of early macular laser compared to deferred macular laser for people with diabetic macular oedema. The evidence for this population was from one large study that showed that early laser slowed worsening of best-corrected visual acuity at 2- and 3-year follow-ups. Eyes receiving early macular laser were also less likely to develop clinically significant macula oedema compared to eyes that received deferred treatment. The committee thought these improved outcomes were important and matched their clinical experience. They therefore used this information, combined with evidence of cost-effectiveness from the treatment strategies review (see evidence review G), to recommend that all people with clinically significant diabetic macular oedema are offered treatment.

One study compared 3 different management strategies for people with centre-involving diabetic macular oedema with good vision. No significant differences were reported for visual outcomes whether people were initially managed with either aflibercept, laser or observation. The committee interpreted this to mean that it is safe to consider initially observing some people with centre-involving diabetic macular oedema and good vision. This evidence was considered when discussing treatment strategies for people with diabetic macular oedema (see evidence review G), and led to a recommendation that observation should be one of the options considered for people in this group.

How the recommendations might affect practice

No recommendations were made for people with non-proliferative diabetic retinopathy.

The recommendations for people with proliferative diabetic retinopathy are not expected to have a major impact on practice.

The recommendations for people with diabetic macular oedema and good vision are different to current practice and may increase the number of people who are given macular laser. However, this may reduce the number of people who progress to having visual impairment, thereby reducing the number of anti-VEGF injections that need to be provided to these people, which may have a cost-saving benefit.

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Clinical features for switching or stopping treatment

Recommendation 1.5.10 to 1.5.12

Why the committee made the recommendations

For people with non-proliferative and proliferative diabetic retinopathy

There was no evidence for people with non-proliferative or proliferative diabetic retinopathy and so the committee did not think they could make recommendations for this group.

For people with diabetic macular oedema

Evidence was available from 2 studies. Each study used different clinical indicators to determine if treatment should be switched, as well as using different types of treatment. Neither study showed a clear effect of switching treatments based on their switching criteria, so there was insufficient evidence to determine which clinical features best indicate the need to switch treatments for people with diabetic macular oedema.

There was no evidence of which clinical features might indicate the need to stop treatment, so the committee could not make recommendations on this.

The committee discussed how, ideally, there would be a list of biomarkers that can be used to define responsiveness to anti-VEGF therapy to help determine whether to continue, switch or stop treatment. Therefore, they made a research recommendation so that this can be better defined in the future.

Although the committee did not think they could recommend a specific switching criteria, they thought it important to highlight when a decision about switching or

changing treatments should be made. If the decision to switch is made too soon, there may not be sufficient time for the treatment to show an effect. This may have been reflected in the evidence, where one of the studies used a 3-month loading phase.

When discussing treatment strategies for diabetic macular oedema (see evidence review G), the committee recommended the use of anti-VEGF treatment. They could not recommend a specific amount of time for the loading phase before assessing a response because different anti-VEGFs have different recommended loading phases. Instead, they advised that this should first be done after the loading phase of anti-VEGF treatment, and then 12 months after the start of treatment to assess for a delayed response.

How the recommendations might affect practice

The recommendations for people with diabetic macular oedema are not expected to have an impact on practice or resource use as they direct to the summary of product characteristics (SPC) which is used in current practice.

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Vitrectomy

Recommendations 1.4.13 to 1.4.15 and 1.5.18

Why the committee made the recommendations

Vitrectomy in combination with other treatment strategies

The committee reviewed evidence on the effectiveness of vitrectomy alone or in combination with other treatments for proliferative diabetic retinopathy and macular oedema.

Evidence for people with proliferative retinopathy or macular oedema did not clearly show that any of the adjuvant treatment regimens to a vitrectomy can improve outcomes following treatment. However, the trials that were reviewed were small and the inclusion criteria varied, which was not helpful in decision making. With no clear evidence, the committee could not make any recommendations on treatment combinations.

People with proliferative diabetic retinopathy

The evidence did not show a clear benefit of vitrectomy compared to other interventions. However, the committee thought this was due to limitations in the evidence base, such as mixed populations. This made it difficult to draw conclusions about the benefits of vitrectomy for groups of people with different complications.

People with severe proliferative diabetic retinopathy and severe vitreous haemorrhage

Evidence from the Diabetic Retinopathy Vitrectomy Study (DRVS) included in evidence review B (effectiveness of different thresholds or criteria for starting treatment for diabetic retinopathy and diabetic macular oedema) showed benefits of early vitrectomy over delayed vitrectomy for people who have severe proliferative diabetic retinopathy and severe vitreous haemorrhage. This supported the committee's experience that early vitrectomy can be beneficial. The committee also highlighted that vitrectomy can avoid other complications for this group, such as when vitreous haemorrhage obscures the view of the retina so that retinal tears and retinal detachment may be missed if they develop. The committee therefore recommended that vitrectomy should be considered for people with vitreous haemorrhage that has not cleared within 3 months. They used their clinical experience to recommend that the vitrectomy should be performed within 3 months of being offered.

People with proliferative diabetic retinopathy and tractional retinal detachment

There was no evidence for people with proliferative diabetic retinopathy and tractional retinal detachment that involves or threatens the macula. However, the committee were concerned that if this group of people go untreated, they are at high risk of losing vision. For this reason, the committee agreed that offering vitrectomy for these people is justified.

The committee highlighted that vitrectomy can also benefit people with proliferative diabetic retinopathy and tractional retinal detachment that does not involve or threaten the macula. Therefore, they recommended that when proliferative diabetic retinopathy progresses despite complete panretinal photocoagulation, a vitrectomy should be considered as the next line of treatment.

People with proliferative retinopathy with no retinal detachment

For people with proliferative retinopathy with no retinal detachment, there is no evidence that an early vitrectomy is beneficial. The committee agreed that panretinal photocoagulation is effective and appropriate for this group.

People with diabetic macular oedema

The committee agreed that there was no evidence to support the use of vitrectomy to treat diabetic macular oedema.

However, for people with diabetic macular oedema that does not respond to anti-VEGF treatment and evidence of vitreoretinal traction or epiretinal membrane, vitrectomy should be considered. The committee highlighted that without vitrectomy, these people are at risk of developing permanent damage to the eye. With no evidence on timing of vitrectomy for this group, the committee did not think they could specify when this should be done. However, they said this should be done early enough after a person's condition shows no response to anti-VEGF treatment so that the eye does not incur any permanent damage. Although there is limited evidence for this group, the committee did not make a research recommendation on this topic because the small number of people in the group has made it hard to meet targets for trial recruitment in the past.

How the recommendations might affect practice

The recommendations are in line with current practice and so should not have any resource impact on the NHS.

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Context

This is a new guideline on diagnosing and managing diabetic retinopathy. It includes information on monitoring and treatment for people in hospital eye services with:

- non-proliferative diabetic retinopathy
- proliferative diabetic retinopathy and
- diabetic macular oedema.

Diabetic retinopathy is one of the leading causes of visual impairment and blindness in the UK. Retinopathy is a direct consequence of raised glucose levels so, within 20 years of being diagnosed with diabetes, most people with type 1 or type 2 diabetes will have some degree of retinopathy.

Diabetic retinopathy can be non-proliferative or proliferative. Non-proliferative diabetic retinopathy is an early stage of the disease with fewer symptoms. Some people with non-proliferative diabetic retinopathy progress to having proliferative diabetic retinopathy or diabetic macular oedema. Proliferative diabetic retinopathy refers to abnormal blood vessels that grow in the optic nerve, in the retina, or both, which can lead to vitreous haemorrhage. It can also cause scarring that can, in turn, lead to tractional retinal detachment and central and peripheral vision loss. Diabetic macular oedema causes fluid to gather in the macula and this can lead to loss of central vision. Without the correct monitoring and treatment, proliferative diabetic retinopathy and macular oedema can both lead to permanent vision loss.

The eyes of people with diabetes are monitored as part of the NHS diabetic eye screening programme (DESP). Once they show signs of sight-threatening diabetic retinopathy, they are referred to hospital eye services for further tests and treatment. This guideline relates to people who have been referred to hospital eye services, or are already under their care.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on diabetes.

For details of the guideline committee see the committee member list.