



# Diabetic retinopathy: management and monitoring

NICE guideline

Published: 13 August 2024

www.nice.org.uk/guidance/ng242

### Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the <u>Yellow Card Scheme</u>.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

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#### Overview

This guideline covers managing and monitoring diabetic retinopathy in people under the care of hospital eye services. This includes non-proliferative and proliferative diabetic retinopathy, and diabetic macular oedema.

The guideline does not include areas covered by the <u>NHS diabetic eye screening</u> 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.

#### Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in <a href="NICE's information on making decisions about your care">NICE's information on making decisions about your care</a>.

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 Managing diabetes to support best eye care

#### Working with the person

1.1.1 All clinicians involved in caring for people with <u>diabetic retinopathy</u> (including macular oedema) should discuss with them how good long-term management of their diabetes can have long-term benefits for their vision. Refer to <u>NICE's</u> <u>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.</u>

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on working with the person</u>.

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

#### Effects of a rapid reduction in HbA1c

1.1.2 When starting a diabetes treatment that is likely to result in a rapid, substantial drop in the person's HbA1c, notify the person's ophthalmologist so they can assess the person's eyes before treatment begins and check for changes afterwards.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on effects of a rapid</u> reduction in HbA1c.

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

# Information that should be available to all people involved in the care of people with diabetic retinopathy

- 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.
- 1.1.4 When making decisions with someone about ophthalmic interventions and frequency of follow-up appointments, take into account their:
  - stage of diabetic retinopathy
  - HbA1c level
  - renal function and
  - blood pressure.

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 about their overall diabetes management.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on information that</u> should be available to all people involved in the care of people with diabetic <u>retinopathy</u>.

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

#### Blood pressure management

- 1.1.6 Refer to <u>NICE's guideline on hypertension</u> for recommendations on blood pressure management for adults with diabetes and hypertension.
- 1.1.7 Be aware that, for people with hypertension, managing blood pressure can reduce progression of non-proliferative diabetic retinopathy.
- 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.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on blood pressure</u> management.

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

#### **Fenofibrate**

1.1.9 Ophthalmologists should consider fenofibrate for people with non-proliferative

retinopathy and type 2 diabetes to reduce the progression of <u>diabetic</u> retinopathy.

In August 2024, this was an off-label use of fenofibrate. See <u>NICE's information</u> on prescribing medicines.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the rationale and impact section on fenofibrate.

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

#### **Statins**

NICE has made a <u>recommendation for research about statins to prevent progression of non-proliferative retinopathy and diabetic macular oedema</u>.

For a short explanation of why the committee made no recommendations, see the rationale and impact section on statins.

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

# 1.2 Cataract surgery for people with diabetic retinopathy or diabetic macular oedema

- 1.2.1 Before cataract surgery for a person with diabetes, the surgeon should obtain information about the person's current diabetic eye disease status. The surgeon can then use this information to tailor the surgery, post-operation medication and follow-up to the person's condition and needs.
- 1.2.2 For guidance on managing cystoid macular oedema as a complication of cataract surgery in people with diabetes, see the <u>section on preventing and managing</u>

complications in NICE's guideline on managing cataracts in adults.

Also see <u>recommendation 1.5.6 on anti-vascular endothelial growth factor (anti-VEGF) treatment as a temporary solution for people with proliferative diabetic retinopathy who need cataract surgery.</u>

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

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

#### 1.3 Treating all active pathologies in each eye

- 1.3.1 After assessing eyes with <u>diabetic retinopathy</u>, treat and monitor each eye separately based on the eye's active pathologies. Depending on the eye's stage of retinopathy, see the recommendations on:
  - non-proliferative diabetic retinopathy or
  - proliferative diabetic retinopathyor
  - diabetic macular oedema.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on treating all active</u> pathologies in each eye.

Full details of the evidence and the committee's discussion are in <u>evidence review G</u>: <u>effectiveness and acceptability of intravitreal steroids, macular laser and anti-VEGFs</u> for treating diabetic macular oedema.

# 1.4 Non-proliferative diabetic retinopathy: monitoring frequencies

- 1.4.1 For guidance on monitoring <u>diabetic retinopathy</u> during pregnancy, see the <u>section on retinal assessment during pregnancy in NICE's guideline on diabetes in pregnancy.</u>
- 1.4.2 Hospital eye services should monitor disease progression in people with moderate, severe or very severe non-proliferative retinopathy who are not currently having treatment and have not previously had treatment. 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.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on when to assess</u> disease status and how often to monitor.

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

#### 1.5 Proliferative diabetic retinopathy

#### Treatment strategies for proliferative diabetic retinopathy

- Discuss with the person with proliferative diabetic retinopathy the benefits and potential side effects of each of the following 3 options: panretinal photocoagulation, anti-vascular endothelial growth factor medicines (anti-VEGFs), and no treatment (observation). As part of this discussion, explain:
  - what proliferative diabetic retinopathy is, and whether they have <u>high-risk</u>

#### characteristics

- that panretinal photocoagulation is usually the first treatment for most people with proliferative diabetic retinopathy
- which treatment is likely to work best for them.

Follow the recommendations on communication and information in <u>NICE's</u> guidelines on patient experience in adult NHS services, <u>babies</u>, <u>children and young people's experience of healthcare</u>, and <u>shared decision making</u>.

- 1.5.2 Offer panretinal photocoagulation to people when they are first diagnosed with proliferative diabetic retinopathy.
- 1.5.3 Use the following timeframes for panretinal photocoagulation:
  - Start treatment within 4 weeks of offering, if possible.
  - If it cannot be started within 4 weeks, start it within 6 weeks of offering.
  - Complete it within 4 weeks of starting treatment.
- 1.5.4 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.
- 1.5.5 Offer anti-VEGF treatment for people whose proliferative diabetic retinopathy remains active after <u>complete panretinal photocoagulation</u> and discuss the advantages and disadvantages of the available anti-VEGFs with the person.

If the person has vitreoretinal traction or tractional retinal detachment, monitor them closely in collaboration with a vitreoretinal specialist (see also the <u>section</u> on vitrectomy for people with proliferative diabetic retinopathy).

In August 2024, the only anti-VEGF treatment licensed for proliferative diabetic retinopathy was ranibizumab and use of any other anti-VEGF treatment would be off-label. See NICE's information on prescribing medicines.

- 1.5.6 Consider anti-VEGF treatment as a temporary treatment for people with proliferative diabetic retinopathy who:
  - have vitreous haemorrhage secondary to proliferative diabetic retinopathy that is preventing panretinal photocoagulation (see also the <u>section on</u> vitrectomy for proliferative diabetic retinopathy)
  - need cataract surgery and the severity of the cataract is preventing panretinal photocoagulation (see also the <u>section on cataract surgery for</u> people with diabetic retinopathy or diabetic macular oedema).

Discuss the advantages and disadvantages of the available anti-VEGFs with the person.

If the person has vitreoretinal traction or tractional retinal detachment, monitor them closely in collaboration with a vitreoretinal specialist.

In August 2024, the only anti-VEGF treatment licensed for proliferative diabetic retinopathy was ranibizumab, and use of any other anti-VEGF treatment would be off-label. See <a href="NICE's information on prescribing">NICE's information on prescribing</a> medicines.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on treatment</u> strategies for non-proliferative and proliferative diabetic retinopathy.

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

- evidence review B: effectiveness of different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema
- <u>evidence review E: effectiveness and acceptability of anti-VEGFs and laser</u> <u>photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy.</u>

#### Vitrectomy for proliferative diabetic retinopathy

- 1.5.7 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 vitrectomy within 3 months of offering it.
- 1.5.8 Offer vitrectomy to people with proliferative diabetic retinopathy and macula-involving or macula-threatening retinal detachment.
- 1.5.9 Consider vitrectomy for people with non-macula-involving or non-macula-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 or vitreomacular traction.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on vitrectomy</u>.

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

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

#### Assessing disease regression and monitoring

#### Imaging techniques

1.5.10 Consider using ultrawide-field fundus imaging alongside clinical examination when assessing eyes for the presence of proliferative diabetic retinopathy.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on imaging techniques for</u> monitoring diabetic retinopathy and diabetic macular oedema.

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

#### **Frequencies**

- 1.5.11 For guidance on monitoring proliferative diabetic retinopathy during pregnancy, see the <u>section on retinal assessment during pregnancy in NICE's guideline on diabetes in pregnancy.</u>
- 1.5.12 Assess <u>disease regression</u> in people who have received treatment for proliferative diabetic retinopathy. Conduct this assessment 2 to 3 months after the end of treatment (see <u>recommendation 1.5.10 on imaging techniques for proliferative</u> diabetic retinopathy).
- 1.5.13 For people whose disease has regressed after treatment for proliferative diabetic retinopathy, monitor under the care of hospital eye services for 12 months after the end of treatment, using an individualised monitoring frequency.
- 1.5.14 For people whose disease has regressed after treatment for proliferative diabetic retinopathy, after the first 12 months following the end of treatment:
  - Discharge the person to the diabetic eye screening programme if they are eligible for it (see <a href="Public Health England's criteria for referral to the diabetic eye screening programme">Public Health England's criteria for referral to the diabetic eye screening programme</a>).
  - If the person's retina has features that makes it ineligible for the screening programme, monitor the person's eyes under the care of hospital eye services, and consider seeing them every 12 months (see <a href="recommendation">recommendation</a> 1.5.10 on imaging techniques for proliferative diabetic retinopathy).

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on when to assess</u> disease status and how often to monitor.

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

#### When disease does not regress

1.5.15 For people whose disease has not regressed after treatment for proliferative diabetic retinopathy, see <a href="recommendations">recommendations</a> 1.5.1 to 1.5.6 on treatment strategies for proliferative diabetic retinopathy.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on treatment strategies for non-proliferative</u> and proliferative diabetic retinopathy.

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

- evidence review B: effectiveness of different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema
- <u>evidence review E: effectiveness and acceptability of anti-VEGFs and laser</u> <u>photocoagulation (alone or in combination) for the treatment of non-proliferative and proliferative diabetic retinopathy.</u>

#### 1.6 Diabetic macular oedema

# Treatment strategies for clinically significant diabetic macular oedema

1.6.1 Offer treatment to people with <u>clinically significant macular oedema</u> (<u>centre-</u>

involving and non-centre-involving).

- 1.6.2 Discuss with the person with clinically significant 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 whether they have centre-involving or non-centre-involving macular oedema, and which treatment is likely to work best for their particular condition.

Follow the recommendations on communication and information in <u>NICE's</u> guidelines on patient experience in adult NHS services, <u>babies</u>, <u>children and</u> young people's experience of healthcare, and shared decision making.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on discussing and offering treatment for diabetic macular oedema</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review G:</u> <u>effectiveness and acceptability of intravitreal steroids, macular laser and anti-VEGFs</u> for treating diabetic macular oedema.

#### Non-centre-involving diabetic macular oedema

1.6.3 Offer macular laser treatment to people with <u>non-centre-involving clinically</u> significant macular oedema.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on treatment strategies for</u> non-centre-involving diabetic macular oedema.

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

- evidence review B: different thresholds or criteria for starting treatment for nonproliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema
- evidence review G: effectiveness and acceptability of intravitreal steroids, macular laser and anti-VEGFs for treating diabetic macular oedema.

#### Centre-involving diabetic macular oedema

#### **Good vision**

1.6.4 For people with <u>centre-involving diabetic macular oedema</u> and good vision (79 letters or better) consider either macular laser treatment or observation. Discuss these 2 options with the person with macular oedema.

#### Impaired vision

1.6.5 For people with centre-involving diabetic macular oedema, <u>visual impairment</u> and central retinal thickness of 400 micrometres or more, offer anti-VEGF treatment. Discuss with the person the advantages and disadvantages of the available anti-VEGFs.

In August 2024, NICE technology appraisal guidance recommended ranibizumab, brolucizumab, faricimab and aflibercept as options for treating visual impairment in eyes with central retinal thickness of 400 micrometres or more (see NICE technology appraisal guidance on anti-VEGFs for visual impairment caused by diabetic macular oedema). At that time, these were the only anti-VEGF treatments licensed for visual impairment caused by diabetic macular oedema.

Use of any other anti-VEGF treatment would be off-label (see NICE's information on prescribing medicines).

1.6.6 For people with centre-involving diabetic macular oedema, visual impairment and central retinal thickness of less than 400 micrometres, consider anti-VEGF or macular laser treatment. Discuss with the person the advantages and disadvantages of all available treatments.

In August 2024, anti-VEGF treatments licensed for visual impairment due to diabetic macular oedema were ranibizumab, brolucizumab, faricimab and aflibercept. Use of any other anti-VEGF treatment would be off-label (see <a href="NICE's information on prescribing medicines">NICE's information on prescribing medicines</a>).

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on treatment</u> strategies for centre-involving diabetic macular oedema.

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

- <u>evidence review B: different thresholds or criteria for starting treatment for non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema</u>
- <u>evidence review G: effectiveness and acceptability of intravitreal steroids,</u> macular laser and anti-VEGFs for treating diabetic macular oedema.

### NICE technology appraisal guidance on anti-VEGFs for visual impairment caused by diabetic macular oedema

For anti-VEGFs recommended as options in NICE technology appraisal guidance for treating visual impairment caused by diabetic macular oedema, see the guidance on:

- ranibizumab (TA274, October 2023)
- brolucizumab (TA820, August 2022)
- faricimab (TA799, June 2022)

aflibercept (TA346, July 2015).

#### When to assess response to anti-VEGF treatment, add or switch treatment

- 1.6.7 After the loading phase, assess response to anti-VEGF treatment. Consider using macular laser as adjuvant treatment if the response is suboptimal.
- 1.6.8 Twelve months after starting anti-VEGF treatment, assess response to treatment. Consider switching to an intravitreal steroid implant if the response is suboptimal.
- 1.6.9 At any time after the start of treatment, if a person does not want to continue with regular anti-VEGF injections, consider switching treatment to an intravitreal steroid implant.

See <u>NICE</u> technology appraisal guidance on intravitreal steroid implants for visual impairment caused by diabetic macular oedema.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on when to add,</u> <u>switch or stop treatment</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review H:</u> clinical features for switching or stopping treatment.

#### When non-corticosteroid treatment is not possible

1.6.10 When people with <u>centre-involving diabetic macular oedema</u> have <u>visual</u>
<u>impairment</u> and cannot have non-corticosteroid therapy, consider an intravitreal steroid implant.

See <u>NICE</u> technology appraisal guidance on intravitreal steroid implants for visual impairment caused by diabetic macular oedema.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on when non-</u>corticosteroid treatment is not possible.

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

- evidence review B: different thresholds or criteria for starting treatment for nonproliferative diabetic retinopathy, proliferative diabetic retinopathy, and diabetic macular oedema
- evidence review G: effectiveness and acceptability of intravitreal steroids, macular laser and anti-VEGFs for treating diabetic macular oedema.

### NICE technology appraisal guidance on intravitreal steroid implants for visual impairment caused by diabetic macular oedema

For intravitreal steroid implants recommended as options in NICE technology appraisal guidance for treating visual impairment caused by diabetic macular oedema, see the guidance on:

- <u>fluocinolone acetonide intravitreal steroid implant (TA953, March 2024)</u>
- dexamethasone intravitreal steroid implant (TA824, September 2022).

#### Assessing disease resolution and monitoring

#### **Imaging techniques**

1.6.11 Use optical coherence tomography (OCT) imaging when assessing someone's eyes for the presence of diabetic macular oedema.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on imaging techniques for</u> monitoring diabetic retinopathy and diabetic macular oedema.

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

#### **Frequencies**

- 1.6.12 For people whose <u>disease has resolved</u> after treatment for diabetic macular oedema, monitor under the care of hospital eye services for the first 12 months after the end of treatment, using an individualised monitoring frequency.
- 1.6.13 For people whose disease has resolved after treatment for diabetic macular oedema, after the first 12 months following the end of treatment:
  - Discharge the person to the diabetic eye screening programme if they are eligible for it (see <u>Public Health England's criteria for referral to the diabetic eye screening programme</u>).
  - If the person's retina has features that makes it ineligible for the screening programme, monitor them under the care of hospital eye services, and consider seeing the person every 12 months.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the <u>rationale and impact section on when to assess</u> disease status and how often to monitor.

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

#### Vitrectomy for diabetic macular oedema

1.6.14 For people with diabetic macular oedema that does not respond to anti-VEGF

treatment and also have either vitreomacular traction or epiretinal membrane:

- check for warning signs of <u>permanent damage</u> and
- consider vitrectomy before any permanent damage occurs.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the <u>rationale and impact section on vitrectomy</u>.

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

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

#### When disease does not resolve

1.6.15 For people whose disease has not resolved after treatment for diabetic macular oedema, see <a href="recommendations">recommendations</a> 1.6.1 to 1.6.14 on treatment strategies for diabetic macular oedema.

#### 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 <u>NICE glossary</u> and the <u>Think Local, Act Personal Care and Support Jargon Buster</u>.

#### Centre-involving diabetic macular oedema

Diabetic macular oedema that involves the central subfield of the Early Treatment Diabetic Retinopathy Studies (ETDRS) grid, which has a diameter of 1 mm. Centre-involving diabetic macular oedema is always clinically significant.

#### 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 subfield of the Early Treatment Diabetic Retinopathy Studies (ETDRS) grid, which has a diameter of 1 mm.

#### 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 and
- for people whose proliferative diabetic retinopathy had remained active after this
  original treatment, additional 'fill-in' laser has been applied, if appropriate, adding
  burns in the spaces left by the original treatment.

#### Diabetic retinopathy

Retinopathy includes non-proliferative retinopathy, proliferative retinopathy and maculopathy.

#### 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.

#### Early worsening

Progression of diabetic retinopathy as a result of a rapid, substantial drop in a person's HbA1c from diabetes treatments or other causes, such as pancreas transplant.

#### High-risk characteristics

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

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

#### Macular laser treatment adjuvant to anti-VEGF

The use of macular laser in addition to anti-vascular endothelial growth factor (anti-VEGF) treatment when, following the loading phase, a person's eye has had a <u>suboptimal</u> response to anti-VEGF treatment alone.

#### Permanent damage

Damage such as photoreceptor cell loss, macular atrophy or lamellar macular holes. The time that it takes for permanent damage to occur can vary between people.

#### Resolved macular oedema

Presence of isolated or sparse, small, intraretinal cysts with no other features as seen from optical coherence tomography (OCT) scans.

#### Suboptimal treatment response for diabetic macular oedema

Treatment response for diabetic macular oedema is suboptimal if there is:

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

#### 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 for diabetic macular oedema 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 section on when to add, switch or stop treatment.

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

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

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

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on information that should be available to all</u> people involved in the care of people with diabetic retinopathy.

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

#### 3 Effectiveness of different treatment strategies for nonproliferative diabetic retinopathy

What is the effectiveness and acceptability of observation, anti-vascular endothelial growth factor agents (anti-VEGFs) 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 <u>rationale section on treatment strategies for non-proliferative and proliferative diabetic retinopathy</u>.

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

#### 4 Rapid, substantial reductions in HbA1c

In people experiencing a rapid, substantial reduction in HbA1c, what is the risk of shortterm 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 section on effects of a rapid reduction in HbA1c.

Full details of the evidence and the committee's discussion are in <u>evidence review C:</u> 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 <u>rationale section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.</u>

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

#### Other recommendations for research

# 6 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 <u>rationale section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.</u>

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

# 7 Statins to prevent progression of non-proliferative retinopathy and 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 section on statins.

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

#### 8 Fibrates to prevent progression of diabetic retinopathy

What is the effectiveness of fibrates to prevent progression of diabetic retinopathy in people from a range of ethnic backgrounds?

For a short explanation of why the committee made this recommendation for research, see the rationale section on fenofibrate.

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

#### 9 Most effective and acceptable method of delivering panretinal

#### photocoagulation

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 <u>rationale section on treatment strategies for non-proliferative and proliferative diabetic retinopathy.</u>

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.

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

In people with moderate to severe non-proliferative diabetic retinopathy who are about to have or who have had 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 section on cataract surgery.

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

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

In people with diabetic macular oedema who are about to have, or who have had 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 section on cataract surgery.

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

# 12 Monitoring frequencies for people with non-proliferative diabetic retinopathy

What is the most effective monitoring frequency for non-proliferative diabetic retinopathy in people 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 <u>rationale section on when to assess disease status and how often to monitor.</u>

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

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

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

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on when to assess disease status and how often to monitor</u>.

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

#### 14 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 <u>rationale section on imaging techniques for monitoring diabetic</u> retinopathy and diabetic macular oedema.

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

#### Rationale and impact

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

#### Working with the person

Recommendation 1.1.1

#### Why the committee made the recommendation

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 non-proliferative diabetic 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 people the benefits that keeping their blood glucose levels within the safe range can have for their vision, as this may reduce their risk of vision loss. Sustainably keeping their blood glucose levels within the safe range could also avoid the need for intensive treatments at a later stage, and so avoid potential complications of intensive treatment, including <u>early worsening</u> of diabetic retinopathy.

The committee noted that 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 include recommendations on blood glucose management. They therefore decided that those recommendations should be taken into account in discussions with people about diabetes and vision.

Although no studies evaluated the effects of a rapid, substantial reduction in HbA1c for

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

#### How the recommendation might affect practice

This recommendation will not have a significant resource impact because this should already be part of discussions with people with diabetic retinopathy.

Return to recommendation

#### Effects of a rapid reduction in HbA1c

Recommendation 1.1.2

#### Why the committee made the recommendation

Some of the studies included both short- and long-term follow-up. The committee was interested in the short-term outcomes to see if they showed evidence of <u>early worsening</u>. 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 HbA1c 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 recommendation for research to evaluate the short-term effects from current treatments on early worsening and whether any effects are maintained in the long term.

Despite the limited evidence, the committee was concerned about the potential risk of early worsening from treatments that result in a rapid, substantial drop in HbA1c, which is a

recognised concept among clinicians. Early worsening of diabetic retinopathy does not necessarily mean that the treatment is harmful in the long term. Instead, it highlights the need for close monitoring and early intervention to address any emerging issues with the eyes. An early review allows healthcare professionals to assess the status of the eyes and put appropriate measures in place to manage and monitor potential changes in the eyes during the course of treatment. The committee therefore decided that it is important to be cautious before starting intensive therapies for people whose blood glucose levels are often above the safe range. 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 eyes and identify any changes once they begin treatment.

#### How the recommendation might affect practice

This recommendation may increase the number of people who are seen by an ophthalmologist before starting a treatment that is likely to result in a rapid, substantial drop in HbA1c. However, this is expected to help identify those who are most likely to experience early worsening effects, thereby reducing the number of appointments that are needed after intensive treatment.

Return to recommendation

# Information that should be available to all people involved in the care of people with diabetic retinopathy

Recommendations 1.1.3 to 1.1.5

#### Why the committee made the recommendations

Prognostic factors for 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 bring their blood pressure and HbA1c within recommended ranges.

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, which meant 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 prognostic 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 <u>recommendation for research aimed at identifying other prognostic factors</u>.

## Progression of non-proliferative diabetic retinopathy to diabetic macular ischaemia

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 ischaemia. Therefore, the committee could not make recommendations on this and included progression to macular ischaemia in a recommendation for research on prognostic factors.

## How the recommendations might affect practice

The recommendations are not expected to have a major impact on practice or increase resource use. They 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 put in place to allow clinicians to record and access this information.

Return to recommendations

## Blood pressure management

Recommendations 1.1.6 to 1.1.8

#### Why the committee made the recommendations

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 1 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.

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 do 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.

#### How the recommendation might affect practice

These recommendations will not have a significant resource impact because they are consistent with current NICE recommendations.

Return to recommendations

## **Fenofibrate**

Recommendation 1.1.9

### Why the committee made the recommendation

Evidence from 2 randomised controlled trials showed fenofibrate is 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. They were aware that this is currently (August 2024) an off-label use of fenofibrate. They therefore thought that it should be ophthalmologists who consider prescribing fenofibrate and who initiate their prescription where appropriate. GPs can then renew the prescription.

There was no evidence on the effects of other types of fibrates, or on fenofibrate 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 recommendation for research.

The committee highlighted that there is limited evidence on how effective fibrates are at preventing diabetic retinopathy progression in people from a range of ethnic backgrounds. They felt this was an important consideration, and therefore made a <u>recommendation for research on fibrates to prevent progression of diabetic retinopathy</u>.

#### How the recommendation might affect practice

The recommendation is likely to increase the use of fenofibrate 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 recommendation

#### **Statins**

### Why the committee made no recommendations

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 was sufficient to recommend using statins. Instead, they made a <u>recommendation for research to compare the effectiveness of intensive and standard statin treatments for people with non-proliferative retinopathy and diabetic macular oedema.</u>

Return to recommendation

# Cataract surgery for people with diabetic retinopathy or diabetic macular oedema

Recommendations 1.2.1 and 1.2.2

## 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 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. The committee made a recommendation addressing 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. The recommendations include people with diabetes; the committee therefore cross-referred to these.

Given the limited evidence base, the committee made a <u>recommendation for research on the effectiveness of treatments for non-proliferative diabetic retinopathy before, during or after cataract surgery and another <u>recommendation for research on the effectiveness of treatments for diabetic macular oedema before, during or after cataract surgery.</u> Research will give a greater understanding of how to improve diabetic retinopathy outcomes for people who have cataracts.</u>

## 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 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.

The recommendation for anti-vascular endothelial growth factors (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.

Return to recommendations

## Treating all active pathologies in each eye

Recommendation 1.3.1

#### Why the committee made the recommendation

The committee discussed how people may have different pathologies in each eye. They thought it was important to highlight in the recommendations the importance of treating:

- each eye based on all its active pathologies, rather than only the most severe pathology; this reduces the risk of other pathologies progressing if treatment only focuses on the most severe one
- both eyes, even if 1 eye was considered to have more severe disease; this is essential because it reduces the risk of progression in either eye, thereby reducing the risk of severe consequences of diabetic eye disease, such as vision loss.

#### How the recommendation might affect practice

This recommendation highlights the most effective way to treat diabetic eye disease and reinforces treatment pathways that should already be taking place. As such, it is not expected to result in any changes in practice or have any major resource impact.

Return to recommendation

# Treatment strategies for non-proliferative and proliferative diabetic retinopathy

Recommendations 1.5.1 to 1.5.6 and recommendation 1.5.15

#### Why the committee made the recommendations

#### Non-proliferative diabetic retinopathy

Evidence was insufficient to determine which treatment strategies are the most effective to prevent progression to the sight-threatening complications of diabetic retinopathy (see <a href="evidence review E">evidence review E</a>). Monitoring is generally used in current practice. The committee was therefore unable to make recommendations for this group. Instead, they made a <a href="recommendation for research on treatment strategies for severe non-proliferative diabetic retinopathy">retinopathy</a> and another <a href="recommendation for research aimed at identifying the thresholds or criteria that should be used for starting treatment for non-proliferative diabetic retinopathy</a>.

#### Proliferative diabetic retinopathy

A network meta-analysis (see evidence review E) showed 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. Some individual studies showed that anti-VEGFs reduced the 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 tell whether the effectiveness of different treatments changed 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 that panretinal photocoagulation and anti-VEGFs are of similar effectiveness, 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 carry 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. They agreed that panretinal photocoagulation is the standard of care for proliferative diabetic retinopathy.

The committee thought that panretinal photocoagulation was particularly effective for people with high-risk proliferative diabetic retinopathy. They agreed it can also benefit people with early proliferative retinopathy because, for these people, the alternative option

is frequent monitoring. They also 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.

#### Timeframes for panretinal photocoagulation

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 (see <a href="evidence review B">evidence review B</a>). Based on a combination of evidence from the reviews and on their clinical experience, the committee made recommendations on timeframes for panretinal photocoagulation.

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 (see <a href="evidence review E">evidence review E</a>). However, they were aware that this is not always possible. As a result, they recommended that people with high-risk characteristics should be offered to start treatment on the day it is offered, to make sure these people would receive treatment earlier than people without high-risk characteristics. The committee was aware that there may be some instances where it is not possible to start treatment on the same day, but thought that in these cases, panretinal photocoagulation should be completed at the earliest opportunity.

For people who do not have high-risk characteristics, the committee agreed that clinicians should aim to start treatment within 4 weeks but, because they were aware that resources may not always be sufficient for this, they specified that treatment should start no later than within 6 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 to start

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.

#### Discussing diagnosis and treatment options

It is important that people are made aware of what proliferative diabetic retinopathy is, and whether they have high-risk characteristics. This will help them understand why they are being offered treatment, and what this treatment aims to achieve.

The committee was confident that panretinal photocoagulation should be the first-line treatment for people with proliferative diabetic retinopathy (see <a href="evidence review E">evidence review E</a>). However, they also highlighted that, before offering someone treatment, it is important to make them aware of all treatment options, and the associated risks and benefits. Discussing all this with someone and giving them the opportunity to ask questions may help reduce the anxiety related to treatment. This is particularly important for treatments such as panretinal photocoagulation and anti-VEGF injections because, in the committee's experience, the thought of having laser or injections into the eye can cause anxiety.

## When proliferative diabetic retinopathy remains active despite complete panretinal photocoagulation

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 have a similar level of effectiveness to panretinal photocoagulation for improving visual acuity (see <a href="evidence review E">evidence review E</a>), the committee thought that anti-VEGFs would be an effective second-line treatment option for people with proliferative diabetic retinopathy. The action of the anti-VEGFs can result in further progression of vitreoretinal traction or tractional retinal detachment. This is known as anti-VEGF crunch syndrome. The committee therefore recommended additional monitoring for those with these conditions.

#### When people cannot have panretinal photocoagulation at present

The committee was also aware that some people cannot 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 waiting until after cataract surgery (see <a href="evidence review">evidence review I</a>). 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.

#### **Combining treatments**

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 (see <a href="evidence review E">evidence review E</a>). They therefore made a <a href="recommendation for research aimed at identifying the most effective combination of treatments for proliferative diabetes retinopathy</a>. 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.

#### Delivering panretinal photocoagulation effectively

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 ischaemic areas. The committee therefore made a recommendation for research to determine which is the most effective and acceptable method of delivering panretinal photocoagulation (see evidence review E).

#### 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 to use anti-VEGFs if eyes do not respond to panretinal photocoagulation reinforces what should happen in current practice.

The recommendation for temporary anti-VEGF use for people who need vitrectomy or cataract surgery will reduce complications for the person as well as reducing the time and costs associated with additional treatment if their vitrectomy or cataract surgery is delayed.

The recommendations on when panretinal photocoagulation should be offered, and when treatment should start, are not expected to have a major impact on practice.

Return to recommendations 1.5.1 to 1.5.6

Return to recommendation 1.5.15

## Discussing and offering treatment for diabetic macular oedema

Recommendations 1.6.1 and 1.6.2

#### Why the committee made the recommendations

The committee highlighted that it is important to offer treatment to all people who have clinically significant diabetic macular oedema, whether they have centre-involving or non-centre-involving oedema. Without treatment, they are at risk of vision loss.

The committee discussed the importance of making all people in this group aware of their diagnosis and the benefits and side effects of each treatment option. They highlighted that many people with macular oedema do not know 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. Making shared decisions is therefore an important part of managing macular oedema. It 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.

#### Effectiveness of different thresholds or criteria for starting treatment

The committee discussed the effectiveness of early macular laser compared with deferred macular laser for people with diabetic macular oedema. The evidence for this population was from 1 large study that showed that early laser slowed worsening of best-corrected visual acuity at 2- and 3-year follow-ups (see <a href="evidence review B">evidence review B</a>). Eyes receiving early macular laser were also less likely to develop clinically significant macula oedema compared with 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 <a href="evidence review G">evidence review G</a>), to recommend that all people with clinically significant diabetic macular oedema are offered treatment.

#### How the recommendations might affect practice

These recommendations reflect current practice. They are not expected to have a significant impact on practice.

Return to recommendations

# Treatment strategies for non-centre-involving clinically significant diabetic macular oedema

Recommendation 1.6.3

#### Why the committee made the recommendation

There were very few studies on treatment for people with non-centre-involving diabetic macular oedema, making it difficult to determine which is the most effective treatment option for this group (see <a href="evidence review G">evidence review G</a>). 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 it 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 1 study with high- to moderate-quality outcomes in the review on thresholds for starting treatment (see evidence review B). This showed that visual acuity worsened slower when macular laser was provided in the early stages of macular oedema. The committee 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.

### How the recommendation might affect practice

This recommendation for people who have non-centre-involving macular oedema reflects current practice and is not expected to have a major impact on practice.

Return to recommendation

## Treatment strategies for centre-involving diabetic macular oedema

Recommendations 1.6.4 to 1.6.6

## Why the committee made the recommendations

#### **Good vision**

Some people with centre-involving 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:

- although 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 (see <a href="eviewG">evidence</a> review G), it still showed benefits for improving visual acuity and was the most costeffective 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 person and reducing treatment costs.

However, the committee was aware that macular laser may not be the only option for this group. Evidence from the review on thresholds for starting treatment (see <a href="eview">evidence</a>
<a href="eview">review B</a>) showed that outcomes may be similar for some people whether they are initially offered observation, anti-VEGF or macular laser. 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. 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 person to reduce their risk of progression. Therefore, they recommended that the decision should include a discussion with the person about the benefits and risks of each option to make a shared decision over which to choose.

#### Impaired vision

Evidence from the network meta-analysis (see <u>evidence review G</u>) showed that in people with centre-involving diabetic macular oedema, a number of treatments, including anti-VEGFs, some steroids and some combinations of treatments, are more effective at improving visual acuity at 12 months than standard threshold laser alone. 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 more and some evidence of the benefits of anti-VEGFs in people with a central retinal thickness of less than 400 micrometres. However, the smaller evidence base for the latter group meant there was more uncertainty around 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 of treatments 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.

#### Central retinal thickness of 400 micrometres or more

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 (see <a href="evidence review G">evidence review G</a>). 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. The definition of <a href="evisual">visual</a> impairment they used was based on the inclusion criteria that are often seen in clinical trials.

The committee noted that NICE technology appraisal guidance recommends the use of aflibercept, brolucizumab, faricimab and ranibizumab for people with macular oedema and

a central retinal thickness of 400 micrometres and above. The committee also 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).

#### Central retinal thickness of less than 400 micrometres

As noted above, NICE's most recent subgroup analysis, which was carried out for this guideline, showed some evidence of the benefits of anti-VEGFs in people with a central retinal thickness of less than 400 micrometres. However, the smaller evidence base for this group made it difficult to be confident in the effects of the different treatments (anti-VEGFs, some steroids and some combinations of treatments).

The committee 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.

The committee therefore 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.

Although healthcare professionals are actively encouraged to follow the recommendations in NICE guidelines, to help them deliver the highest quality care, these recommendations do not have the same legal status as medicines and treatments recommended through the NICE technology appraisal programme. Therefore, as this recommendation is for a population not included in NICE technology appraisal guidance on anti-VEGFs, the mandatory funding status does not apply to this recommendation.

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.

## How the recommendations might affect practice

The recommendations for people with diabetic macular oedema and good vision differ

from 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 save cost.

For those people who do progress to having visual impairment, the recommendations may increase the number of people who are initially offered anti-VEGF treatment, as this can include people with a central retinal thickness below the 400-micrometre threshold specified in NICE technology appraisal guidance. 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

## When non-corticosteroid treatment is not possible

Recommendation 1.6.10

## Why the committee made the recommendations

Although anti-VEGFs were recommended for most people with centre-involving macular oedema, the committee recommended that an intravitreal steroid implant be considered for 3 subgroups to ensure that they do not 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.

The committee agreed that people may find it difficult to regularly attend appointments for a range of reasons, such as work commitments or caring responsibilities. They also highlighted people who are pregnant at diagnosis, or become pregnant during treatment, 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 committee were aware of the NICE technology appraisal guidance on dexamethasone intravitreal implant for treating diabetic macular oedema and fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema. The mandatory funding status attached to these applies to the population and criteria stated in the technology appraisal.

## How the recommendations might affect practice

The recommendations for the use of intravitreal steroids are not expected to have a major impact on practice.

Return to recommendation

## When to add, switch or stop treatment

Recommendations 1.6.7 to 1.6.9

### 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 did 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 recommendation for research on the effectiveness of clinical features or factors that suggest treatment for diabetic macular oedema should be switched or stopped.

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.

The committee recommended the use of anti-VEGF treatment. However, 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.

#### 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 <a href="evidence review H">evidence review H</a>), they highlighted that response to treatment is usually assessed after the loading phase. At this point, if vision has not stabilised (remaining within 5 letters of what it was before treatment) or improved, <a href="adjuvant laser treatment">adjuvant laser treatment</a> 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. They discussed the timing of this assessment, as they were aware that some people can show this delayed response up to 12 months after the start of treatment. They were also concerned that switching to intravitreal steroids earlier than this could result in people experiencing the additional adverse effects associated with steroids even though they could still respond to anti-VEGF treatment if given more time. For this reason, the committee recommended that a further review should take place after 12 months.

#### Suboptimal response to treatment

The committee was aware of <u>NICE technology appraisal guidance for the use of a</u> dexamethasone intravitreal implant or fluocinolone if someone's condition has not

responded well enough to anti-VEGFs. Recommendations for the switch to an intravitreal steroid implant were supported by the evidence (see <a href="evidence review G">evidence review G</a>), which showed that the 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. There was much more limited evidence for fluocinolone, so the committee referred to the guidance from the NICE technology appraisal.

#### 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.

Return to recommendations

## When to assess disease status and how often to monitor

Recommendations 1.4.1 and 1.4.2, recommendations 1.5.11 to 1.5.14 and recommendations 1.6.12 and 1.6.13

### Why the committee made the recommendations

The committee made these recommendations based on their clinical experience and 1 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.

#### 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 currently having treatment and have not previously had treatment, 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 diabetic 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. The committee therefore recommended that monitoring should take place every 3 to 6 months for this group. These recommendations reflect current practice.

Because there was limited evidence on the most effective monitoring frequencies for people with non-proliferative retinopathy who have not started treatment, the committee made a <u>recommendation for research on monitoring frequencies for people with non-proliferative diabetic retinopathy</u>.

#### 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. The committee therefore 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 agreed that disease regression in people who have received treatment for proliferative diabetic

retinopathy should be assessed at 2 to 3 months after treatment has ended. This should be an appropriate time so that any progression following the end of treatment can be identified before it leads to more serious consequences. They also 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. After 12 months, people who are eligible for the screening programme should be discharged to this service.

People who are discharged to the screening programme are expected to attend both eye screening appointments and regular appointments with primary care optometrists. This will help identify if further treatment is needed in the future and identify other eye diseases that are not covered by the eye screening programme.

Because there was limited evidence on the most effective monitoring frequencies for people with proliferative diabetic retinopathy or diabetic macular oedema who have had treatment previously, the committee made a <u>recommendation for research on monitoring</u> frequencies for people with proliferative diabetic retinopathy or diabetic macular oedema.

## Under 18 or pregnant people with non-proliferative diabetic retinopathy, proliferative diabetic retinopathy or diabetic macular oedema

None of the evidence reported separate results for people under 18 or pregnant people. However, the committee 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 it agreed to refer to this guideline.

## 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 whose diabetic retinopathy is 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 monitoring frequencies recommended in this guideline are similar to those recommended in the <u>Royal College of Ophthalmologists guideline</u>, although they may result in less frequent monitoring for some people who have moderate non-proliferative diabetic retinopathy and it is not expected to progress quickly.

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

Return to recommendations 1.4.1 and 1.4.2

Return to recommendations 1.5.11 to 1.5.14

Return to recommendations 1.6.12 and 1.6.13

# Imaging techniques for monitoring diabetic retinopathy and diabetic macular oedema

Recommendation 1.5.10 and recommendation 1.6.11

## 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 <u>recommendation for research on diagnostic test accuracy for monitoring disease progression</u> 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. They also highlighted that it is quicker than other imaging tools.

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 other forms of clinical examination to detect proliferative diabetic retinopathy. This could be during face-to-face appointments with a clinician, or at virtual clinics, where imaging takes place and is reviewed later by the clinician. Using ultrawide-field imaging at a virtual clinic would not result in it being 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 1 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 people 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 to diagnose 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 imaging techniques for monitoring proliferative diabetic retinopathy may result in an increase in ultrawide-field imaging use. 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 recommendation 1.5.10

Return to recommendation 1.6.11

## Vitrectomy

Recommendations 1.5.7 to 1.5.9 and recommendation 1.6.14

## 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 (see <u>evidence review F</u>). 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 did not make any recommendations on treatment combinations.

#### **Proliferative diabetic retinopathy**

The evidence did not show that vitrectomy was more beneficial than other interventions. However, the committee thought this was because of 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.

#### Severe proliferative diabetic retinopathy and severe vitreous haemorrhage

Evidence from the Diabetic Retinopathy Vitrectomy Study (DRVS) included in <u>evidence</u> <u>review B</u> (effectiveness of different thresholds or criteria for starting treatment for diabetic retinopathy and diabetic macular oedema) showed early vitrectomy was more beneficial than 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 (see <u>evidence review F</u>). 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.

#### 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 was concerned about the fact that, if this group of people go without treatment, they are at high risk of losing vision. For this reason, the committee agreed that offering vitrectomy to people in this group 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.

#### 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.

#### Diabetic macular oedema

The committee agreed that there was no evidence to support the use of vitrectomy to treat diabetic macular oedema (see <a href="evidence review F">evidence review F</a>).

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 (see <a href="evidence review B">evidence review B</a>). The committee highlighted that, without vitrectomy, these people are at risk of 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 to ensure that the eye does not incur any permanent damage. Although there is limited evidence for people with vitreoretinal traction or epiretinal membrane secondary to diabetic macular oedema, the committee did not make a recommendation for research 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 (see evidence review F).

## How the recommendations might affect practice

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

Return to recommendations 1.5.7 to 1.5.9

Return to recommendation 1.6.14

## 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 is an umbrella term that covers all complications of diabetes that affect the retina. This includes non-proliferative diabetic retinopathy, proliferative diabetic retinopathy and maculopathy. Maculopathy affects the centre part of the retina, called the macula. There are 2 forms of diabetic maculopathy: diabetic macular oedema and diabetic macular ischaemia.

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. 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.

At any stage of retinopathy, people may also develop diabetic macular oedema. It causes fluid to gather in the macula and 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 <u>NHS diabetic eye screening</u> <u>programme (DESP)</u>. Once they show signs of sight-threatening diabetic retinopathy, they are referred to hospital eye services for further tests and treatment. This guideline covers

Diabetic retinopathy: management and monitoring (NG242)	
people who have been referred to hospital eye services, or are already under their ca	are.

# Finding more information and committee details

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

For full details of the evidence and the guideline committee's discussions, see the <u>evidence reviews</u>. You can also find information about <u>how the guideline was developed</u>, including <u>details of the committee</u>.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see <u>resources to help you</u> put NICE guidance into practice.

ISBN: 978-1-4731-6323-2