Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Scoping Report

Extended Interval Screening by the Diabetic RetinaScreen Programme in Ireland

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Safer Better Care

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Key points

- Diabetic retinopathy is a microvascular complication of diabetes mellitus and is a common cause of vision impairment and sight loss.
- Diabetic retinopathy screening programmes can prevent sight-threatening diabetic retinopathy (STDR) by timely detection and treatment of cases.
- Diabetic RetinaScreen provides free diabetic retinopathy screening, and treatment where appropriate, to all persons with diabetes aged 12 years and older on the Diabetic RetinaScreen register. Annual screening of people with diabetes is current practice. However, it has been proposed that 2 year screening intervals should be introduced for those at low risk of retinopathy progression and who have demonstrated compliance with the programme, in line with international practice.
- The aim of this scoping report is to provide an overview of the evidence pertaining to extending the screening interval for diabetic retinopathy from one to two years for those at low risk of diabetic retinopathy progression.
- There is consistent evidence from multiple systematic reviews of population-based observational studies, that the risk of diabetic retinopathy progression within two years, in people without retinopathy at baseline, is very low. This is supported by evidence from a large randomised controlled trial (RCT) that found that individualised, risk-based screening intervals may be as safe and effective as fixed, annual screening intervals. There is also a greater rate of false positives and unnecessary referrals associated with annual screening.
- There is also consistent evidence from health technology assessments (HTAs), systematic reviews, RCTs and observational studies to suggest that for those at low risk of retinopathy progression, less frequent screening intervals may be more efficient and result in similar patient outcomes (in terms of quality-adjusted life years (QALYs)), compared with annual screening.
- Some evidence suggests that for patients at high risk of retinopathy progression, a shorter screening interval of less than one year may be warranted.
- There is inconsistent evidence for the effect of extending screening intervals on attendance at follow-up visits. No differences were found between intervention and control arms in the included RCT. However, a large number of participants declined to enrol in the trial as they did not want to extend their screening

interval to 24 months and there was greater loss to follow-up in the intervention arm compared with the control arm. Additionally, one systematic review found that loss to follow-up was high in some longitudinal screening studies.

- Evidence from qualitative and mixed-methods studies suggests that although most healthcare professionals and patients were broadly accepting of extended screening intervals, some had significant concerns.
- No evidence was found regarding an effective means of communicating changes to interval screening to patients or healthcare professionals to help allay fears or concerns.
- Worldwide it appears that few national organised screening programmes have been established; organised screening in other countries may be provided at a regional or provider level.
- A one year screening interval is standard practice in some of these national programmes though some (including Ireland) have signalled their intention to move to extended interval screening for those at low risk of retinopathy progression. Other national programmes have safely implemented extended interval screening up to every four years, in those at low risk.
- In conclusion, extending diabetic retinopathy screening intervals from one to two years in those at low risk appears to be safe, and in line with international best practice. However, any planned changes to the national programme would need to be accompanied by a significant communications campaign including all relevant stakeholders, to address potential concerns. Additionally, ongoing audit of coverage and tracking of non-responders is essential to identify changes in adherence in a timely fashion.

List of abbreviations used in this report

COVID-19	Coronavirus disease 2019
DCER	decremental cost-effectiveness ratio
DMO	diabetic macular oedema
DRS	diabetic retinal screening
EQ-5D-5L	EuroQol five dimensions, five level scale
ETDRS	Early Treatment Diabetic Retinopathy Study
EUNetHTA	European Network for Health Technology Assessment
GP	general practitioners
HbA1c	glycated haemoglobin
HES	hospital eye services
HIQA	Health Information and Quality Authority
HSE	Health Service Executive
HTA	health technology assessment
HUI3	Health Utilities Index Mark 3
ICER	incremental cost-effectiveness ratio
IDSR	Individualised Screening for Diabetic Retinopathy
NCCP	National Cancer Control Programme
NDED	non-diabetic eye disease
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPDR	non-proliferative diabetic retinopathy
NPL	no perception of light
NPV	negative predictive value
NRCT	non-randomised controlled trial

NSS	National Screening Service
PDR	proliferative diabetic retinopathy
POP	planned or ongoing projects
PPV	positive predictive value
QALY	quality-adjusted life year
RCT	randomised controlled trial
STDR	sight-threatening diabetic retinopathy

1. Introduction

1.1. Description

Diabetic retinopathy is a microvascular complication of diabetes mellitus and is a common cause of vision impairment and sight loss.[1] It is estimated that approximately one third of all people with diabetes mellitus worldwide have signs of diabetic retinopathy and a further one third of these have sight-threatening diabetic retinopathy (STDR).[2, 3] In Ireland, it is estimated that approximately 190,000 people have diabetes (type one or two), and about 10% of these (or 19,000) are at risk of STDR.[4] Diabetic retinopathy is caused by excess blood glucose, which leads to blockages of the small blood vessels that supply blood to the retina at the back of the eye. These blockages trigger the growth of very small, often poorly developed and leaky, blood vessels.[5] In the early stages of the disease, diabetic retinopathy can go unnoticed as there are usually no symptoms, but if left untreated, it will eventually lead to blindness.[6] Risk factors for diabetic retinopathy include poorly controlled diabetes, longer duration of diabetes, hypertension, high cholesterol, pregnancy, puberty and certain ethnic groups.[3, 7, 8]

There are two main stages of diabetic retinopathy: early diabetic retinopathy (more commonly called non-proliferative diabetic retinopathy (NPDR)) and advanced diabetic retinopathy (more commonly called proliferative diabetic retinopathy (PDR)). In NPDR, there is no growth of new blood vessels, however the walls of existing blood vessel weaken. Small bulges, called microaneurysms protrude from the vessel walls of the smaller vessels, sometimes leaking fluid and blood into the retina. Larger retinal vessels can also begin to dilate and become irregular in diameter. NPDR can progress from mild (also classified as background diabetic retinopathy) to moderate or severe (also classified as pre-proliferative retinopathy), as more blood vessels become blocked. Patients may not experience symptoms during NPDR.[5]

PDR is a more severe stage of diabetic retinopathy where very small, fragile, blood vessels grow from the surface of the retina. Leakage into the vitreous fluid (in front of the retina) can occur resulting in vitreous haemorrhage. This process is the body's attempt to restore blood supply and hence save the retina, however it can lead to scarring of the retina, retinal detachment, glaucoma and eventually blindness if left untreated.[5] PDR may occur in up to 50% of people with type one diabetes and in about 10% of people with type two diabetes who have had the disease for 15 years or more.[6]

Diabetic macular oedema (DMO) is the most common cause of blindness in diabetic retinopathy and can occur during any stage of diabetic retinopathy progression.[9] During DMO, blood can leak into the macula, which can lead to swelling and

thickening of the retina at the back of the eye.[9] The prevalence of DMO among people with diabetes is approximately 7%.[3]

Diabetic retinal screening programmes can prevent STDR by timely detection and treatment of cases. Screening for diabetic retinopathy, followed by treatment of STDR has been shown to be effective.[8, 10] Population-based programmes have been implemented in various jurisdictions globally, including in Ireland.[11] Diabetic retinal screening can be performed in various ways including direct and indirect ophthalmoscopy, dilated slit lamp bio-microscopy, mydriatic (that is, pupil dilation) or non-mydriatic retinal photography, tele-retinal screening and retinal video recording.[8] Additionally, these screening programmes can be delivered by different professionals such as optometrists, general practitioners (GPs), screening technicians, clinical photographers and ophthalmologists.[8] There are also various classification systems used by different screening programmes such as the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system, the International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales, and the English National Screening Committee grading criteria.[8, 12, 13]

The National Screening Service (NSS) is responsible for the development and implementation of Diabetic RetinaScreen – the National DRS Programme in Ireland. The NSS is part of the Health Service Executive (HSE) National Cancer Control Programme (NCCP).[14] Diabetic RetinaScreen is responsible for the provision of free diabetic retinopathy screening, and treatment where appropriate, to all persons with diabetes aged 12 years and older on the Diabetic RetinaScreen register The only exclusion categories are those aged under 12 years (due to the limited occurrence of diabetic retinopathy in this age group)[15] and those who have 'no perception of light' (NPL) in both eyes, in other words those who are clinically blind in both eyes.[14] This national screening programme commenced on a phased basis in 2013, and provides free, annual retinal screening and if necessary, treatment.[4] Although the screening interval in Ireland is currently one year, some national programmes have moved to longer intervals[16, 17] for those considered to be at low risk of diabetic retinopathy progression. Clinical practice guidelines differ on the optimal interval for retinal screening in this population with some guideline groups recommending annual screening while others recommending up to three year intervals in patients with controlled diabetes and no baseline retinopathy.[18] The Diabetic RetinaScreen – the National Diabetic Retinal Screening (DRS) Programme has proposed the accelerated introduction of a planned two year screening pathway (extended interval screening) for people with diabetes at low risk of sight loss and who have demonstrated compliance with the programme.[19]

The aim of this scoping report is to provide an overview of the evidence pertaining to the extension of diabetic retinal screening intervals from one to two years for

those at low risk of diabetic retinopathy progression. As evidence relating to the impact of extending the screening interval will likely include data from other organised national diabetic retinopathy screening programmes, a brief overview of how screening is organised in such programmes is also included for context and to provide evidence of the potential applicability of data from international screening programmes to the Irish healthcare system.

2. Scope

2.1. Research Question

The following three key review questions were identified:

1. In patients who have no reported retinopathy or maculopathy (i.e., those with a worst final grade of R0M0) and no non-diabetic eye disease (NDED) and whose disease is stable, what is the evidence that a change in the interval of diabetic retinopathy screening from one year to two years affects patient outcomes?

2. In relation to a change in the interval of diabetic retinal screening from one years to two years:

    a. How should this change be communicated?

    b. Could this change cause confusion to patients?

    c. Would the reassurance provided by an annual screen be lost?

3. How is diabetic retinopathy screening conducted in other organised, national programmes?

Table 1. Research question outlined in the PICO format

The applicability of each study will be considered in relation to the following PICOS.

Criteria	Definition
Population	Patients with type one or two diabetes mellitus at low risk of diabetic retinopathy progression, i.e. no reported diabetic retinopathy at baseline and whose disease is stable. These are defined as patients meeting either of the following criteria: ▪ patients who have been screened with a worst final grade of R0M0 and no NDED in both eyes for two consecutive years ▪ patients graded R0M0 in one eye and no perception of light in the other for two consecutive years.
Intervention	Diabetic retinopathy screening every two years (extended interval screening).

Comparator	Diabetic retinopathy screening every year (usual care).
Outcomes	**Review Question 1:** ▪ Incidence and progression of diabetic retinopathy (retinal or macular changes), measured according to an internationally recognised grading system (e.g. International Clinical Diabetic Retinopathy And Diabetic Macular Edema Disease Severity Scale). ▪ Attendance at follow-up visits. ▪ Proportion of positive screens. ▪ Cost-effectiveness. **Review Question 2:** Knowledge, experience, attitudes, practices and awareness: communication of changes, confusion caused by changes, reassurance of annual checks. **Review Question 3:** Structure of national programme, screening intervals, technology and grading systems used, service evaluations.
Study design	**Include:** Health technology assessments, systematic reviews, randomised controlled trials, non-randomised controlled trials, cohort studies, case-control studies, cross-sectional studies, qualitative studies, economic evaluations and mathematic modelling studies.‡ **Exclude:** Case reports/series and expert opinions.

±Only the highest levels of evidence will be used and so not all of the study designs listed above will necessarily be included in this scoping report

3. Literature search

Health technology assessment (HTA) databases were checked for relevant published or ongoing HTAs. This included the:

- Centre for Reviews and Dissemination database (https://www.crd.york.ac.uk/CRDWeb/)
- International HTA database (https://www.inahta.org/hta-database/)

- European Network for HTA (EUnetHTA) planned and ongoing projects (POP) database (https://eunethta.eu/pop-database/).

PROSPERO was also searched to identify any relevant published or ongoing systematic reviews (https://www.crd.york.ac.uk/prospero/).

A structured search of the literature was conducted on 23 September 2020 in the *PubMed Clinical Queries Tool* in line with HIQA's standard operating procedure for the conduct of scoping reports.[20] The following search terms were used: ("diabetic retinopathy" AND "screening") OR ("diabetic retinal" AND "screening"). Results were limited to studies conducted in humans. No date or language restrictions were applied. This search was supplemented by a broader search of PubMed, using the following terms ("diabetic" OR "diabetes") AND (("retinal" OR "retinopathy") AND "screening") AND ("attitudes" OR "experience" OR "knowledge" OR "awareness" OR "practices"). Grey literature searching was also conducted using the Lenus repository (www.lenus.ie), National Institute for Health and Care Excellence (NICE) Evidence (https://www.evidence.nhs.uk/), Retina International (http://retina-ded.org/screening-innovation-and-clinical-trials/screening-programs-by-geography/) as well as targeted searches of government websites from countries where national DRS programmes are established.

The findings from the literature search are presented below, prioritising the highest available level of evidence (that is, health technology assessments (HTAs) and systematic reviews). However, lower levels of evidence from randomised and non-randomised controlled trials (RCTs and NRCTs), observational studies (but not case reports or case series) and other study designs (qualitative, mixed-methods studies, economic evaluations and mathematical modelling) are also presented if higher levels of evidence are unavailable and or limited. Hence, primary research studies will only be discussed below if they have not already been synthesised as part of included reviews or HTAs.

4. Potential clinical impact

4.1. HTAs

- Three relevant HTAs published between 1999 and 2019 were identified.[21-23] There is unlikely to be duplication of studies between these HTAs given the different methodologies used to estimate the clinical impact.

- Scanlon et al. published a HTA in 2015 with the overall aim of determining the cost-effective diabetic retinopathy screening interval for the English national programme.[23] A hidden Markov modelling approach was undertaken using a

data set of 65,839 eye grades from a longitudinal cohort of 14,187 people aged 12 years or older with diabetes who underwent diabetic retinopathy screening in England between 2005 and 2012. The objective for this study was to determine the rate of true- and false-positives as well as the rate of true- and false-negatives under various scenarios, including fixed screening intervals of every six months, one year, three years and five years. Two year intervals were not examined. This study used routinely collected screening data to model the natural history of retinopathy and maculopathy and the rates of correct and incorrect assignments using a statistical model. Certain assumptions were made about the model regarding the ability to progress and regress to and from certain stages of diabetic retinopathy. A high risk cohort was also considered for comparison (that is, patients with a 10-year duration of diabetes, poorly controlled glycaemia (baseline HbA1c of 65 mmol/mol) and elevated cholesterol (6 mg/l)).[23]

- In patients with no detectable retinopathy or maculopathy (R0M0) and no clinical risk factors at baseline (low risk group), the number of false negatives were estimated to be 1, 2, 9 and 22 per 10,000 screened at six months, one year, three years and five years screening intervals, respectively. In the same cohort, the number of false positives were estimated to be 54, 66, 111 and 149 per 10,000 screened at six months, one year, three years and five years screening intervals, respectively. We estimated from the data provided that the positive predictive values (PPVs) (that is, the probability that patients with a positive screen result truly had the disease) were 6.90%, 10.81%, 26.97%, and 40.87% for six months, one year, three year and five year screening intervals respectively (Table 2). We estimated that the negative predictive values (NPV) (that is, the probability that patients with a negative screen result truly did not have the disease) were 99.99%, 99.98%, 99.91% and 99.77% for six months, one year, three year and five year screening intervals respectively.[23]

- In patients with no detectable retinopathy or maculopathy (R0M0) considered to be at high risk due to a longer duration of diabetes, poorly controlled glycaemia and elevated cholesterol clinical risk factors at baseline, the number of false negatives were estimated to be 1, 3, 20 and 52 per 10,000 screened at six months, one year, three year and five year screening intervals, respectively. In the same cohort, the number of false positives were estimated to be 61, 80, 159 and 228 per 10,000 screened at six months, one year, three year and five year screening intervals, respectively. We estimated from the data provided that the PPVs were 8.96%, 14.89%, 36.4%, and 52.1% for six months, one year, three year and five year screening intervals, respectively (Table 2). We estimated that the NPVs were 99.99%, 99.97%, 99.79% and 99.45% for six months, one year, three year and five year screening intervals, respectively.[23]

- Misclassification of a retinal photograph to a more advanced stage of any level of retinopathy was found to be more common than misclassification into a lower grade. As the screening interval increases, it was found that the proportion of unnecessary referrals decreases substantially, while the proportion of missed cases only increases slightly. These figures were found to be higher for patients with a higher baseline risk of retinopathy progression. Overall, the number of false positives were found to far outweigh the number of false negatives because the population being screened consisted largely of people with no detectable diabetic retinopathy and, hence, the false positives rates were 'amplified' by the screening which had a lower sensitivity rate (80-85%). Whereas, due to the higher specificity of this screening (97.7-99.5%), the modelling would suggest that not many additional cases with the disease were missed by increasing the screening interval. The authors discussed how such unnecessary referrals to specialist eye clinics are inconvenient for patients and may cause unnecessary anxiety. The probability of misclassifying a photograph at a referable level from all lower grades was found to be very small, but the authors acknowledge that this may have been due to the limitations of the modelling method used. Hence caution is needed when interpreting the findings from this modelling study.[23]

- Martín Sánchez et al. published a HTA in 2019 for the Aragon Institute of Health Sciences in Spain. One of the objectives of this HTA was to determine the most appropriate diabetic retinopathy screening interval based on the findings of a systematic review (which included systematic reviews as well as primary research studies). The authors concluded that two year screening intervals may be safe and effective in patients with diabetes (both type one and two) without retinopathy. The authors also concluded that patients at high risk of retinopathy progression should be screened more frequently than every two years, and patients at low risk could be screened less frequently (potentially every four to five years).[21]

- A HTA published in the UK in 1999 considered a reduction in the diabetic retinal screening interval. The findings of this report supported annual screening and suggested that more patients could become blind with a two year rather than one year screening interval. However, the assessments included in the report all used modelling techniques and the authors noted the limitations of using modelling studies rather than primary research to draw conclusions on appropriate screening intervals. Furthermore, the full text of this HTA, which was published over 20 years ago, was not retrievable and hence the data informing their conclusion could not be reviewed.[22]

Table 2. The modelled number of screening referrals for, and the estimated accuracy of, different screening intervals stratified by patients at low and high risk of retinopathy progression (adapted from Scanlon et al.)[23]

Cohort	Total screened (n)	Number with disease (n)	Correct referrals (n)	False referrals (n)	Not referred when disease present (n)	True positives (n)	False positive (n)	True negatives (n)	False negatives (n)	PPV (%)	NPV (%)	Se (%)	Sp (%)
R0M0 Low risk 6 month interval	10,000	5	4	54	1	4	54	9941	1	6.90	99.99	80.0	99.5
R0M0 Low risk 1 year interval	10,000	10	8	66	2	8	66	9924	2	10.81	99.98	80.0	99.3
R0M0 Low risk 3 year interval	10,000	50	41	111	9	41	111	9839	9	26.97	99.91	82.0	98.9
R0M0 Low risk 5 year interval	10,000	125	103	149	22	103	149	9726	22	40.87	99.77	82.4	98.5
R0M0 High risk 6 month interval	10,000	7	6	61	1	6	61	9932	1	8.96	99.99	85.7	99.4
R0M0 High risk 1 year interval	10,000	17	14	80	3	14	80	9903	3	14.89	99.97	82.4	99.2
R0M0 High risk 3 year interval	10,000	111	91	159	20	91	159	9730	20	36.4	99.79	82.0	98.4

R0M0 High risk 5 year interval	10,000	300	248	228	52	248	228	9472	52	52.10	99.45	82.7	97.7

Key: NPV, negative predictive value; PPV, positive predictive value, R0M0, No retinopathy or maculopathy detected; Se, sensitivity; Sp, specificity.
High risk defined as patients with a 10 year duration of diabetes, poorly controlled glycaemia (baseline HbA1c of 65 mmol/mol) and elevated cholesterol (6 mg/l) at baseline.

4.2. Systematic reviews

- Four relevant systematic reviews published between 2013 and 2019 were identified.[1, 24-26] Although these four systematic reviews had different inclusion criteria, there is potentially some overlap of studies between them.

- A systematic review of the incidence and progression of diabetic retinopathy published by Sabanayagam et al. in 2018 found that progression to proliferative diabetic retinopathy was higher in individuals with mild disease compared with those with no diabetic retinopathy at baseline. This review included 14 population-based studies conducted since 2000. The authors conclude that "data showing the prevalence of progression to proliferative diabetic retinopathy of less than 1% in individuals with no retinopathy supports the notion of extending the screening interval to four years in patients with diabetes and no retinopathy."[1]

- A systematic review of the screening intervals for diabetic retinopathy and incidence of visual loss was published by Echouffo-Tcheugui et al. in 2013. Twenty-five studies were included: 15 evaluations of real-world screening programmes, three modelling studies and seven cost-effectiveness studies. Despite study heterogeneity, the general observation across these programmes was that two year screening intervals among people with no diabetic retinopathy at diagnosis were not associated with higher incidence of STDR. The authors concluded that two year screening intervals for people with no retinopathy at diagnosis may be safely adopted. However, the authors also concluded that for patients with pre-existing diabetic retinopathy, a shorter interval of less than one year is warranted.[24]

- A systematic review of the incidence of STDR in people with type two diabetes was published by Groeneveld et al. in 2019. The systematic review included 17 population-based studies with at least 100 patients in each. The review found that, in people with type two diabetes without any diabetic retinopathy at baseline, the average incidence rate of STDR was approximately 1 per 100 person-years and the average number of people needed to screen to detect one case of STDR was 175. This contrasted with the average incidence rate of STDR of approximately 8 per 100 person-years, and an average of 19 people needed to screen to detect one case of STDR in patients with mild diabetic retinopathy at baseline. Hence, in people with mild retinopathy, progression to sight-threatening diabetic retinopathy was nearly 10-fold higher than in those with no retinopathy. The authors concluded that the screening interval for people with type two diabetes without retinopathy should be extended, but did not suggest an optimal interval.[25]

- A systematic review was published by Taylor-Phillips et al. in 2015 with the aim of determining whether the recommended screening interval for diabetic retinopathy could be safely extended beyond one year, in order to inform screening policy in the UK. RCTs, cohort studies, prognostic or economic modelling studies were included. In total, 11 observational studies, five risk stratification modelling studies and nine economic studies were included. Studies concluded that there was little difference between clinical outcomes from screening at one year or two year intervals in patients at low-risk of progression. However, there was high loss to follow-up (13–31%), heterogeneity in definitions of low risk, and variation in screening and grading protocols for prior retinopathy results. The authors concluded that there was insufficient evidence at that time to recommend a move to extend the screening interval beyond one year. This conclusion was primarily based on the poor quality of the evidence included in the review, as they were all observational or modelling studies, the heterogeneity in definition of 'low risk' among included studies, and hence the inability to reliably predict the outcomes of a change in screening interval. Notably, while the authors did not find sufficiently robust evidence to support the extension of the screening interval, they also did not find persuasive evidence that it should not be extended.[26]

4.3. Non-systematic reviews

- Three relevant non-systematic reviews published between 1998 and 2017 were identified.[27-29] Although these three reviews had different objectives, there is potentially some overlap of studies between them, particularly between the two more recent reviews.[28, 29]

- Scanlon published a literature review in 2017 examining the evidence underpinning extended screening intervals for diabetic retinopathy in people at low risk of progression. Scanlon estimated from the included studies that people with no diabetic retinopathy in either eye are at a low risk of progression to STDR over a two-year period (event rate 4.8 per 1000 person years), irrespective of whether the screening method is one-field non-mydriatic or two-field mydriatic digital photography. Low risk has been defined in the literature as no retinopathy on two consecutive screening episodes or no retinopathy on one screening episode combined with risk factor data. Scanlon concluded that the risk of STDR due to an extension to two year screening intervals is less than 5 per 1000 person years in a population with a national screening programme where the general standard of diabetes care is relatively good, whether low risk is defined as no retinopathy on two consecutive screening episodes or no retinopathy on one screening episode combined with other risk factor data. However, Scanlon states that the generalisability of these findings are dependent on the population

of people with diabetes being screened, and the sensitivity of approaches used to detect eye changes.[28]

- Scanlon noted that some commentators in the field had previously expressed caution regarding extending the screening interval as this "may lead to difficulties in maintaining contact with patients and may give patients the impression that vision loss is unlikely and therefore not a concern." Concerns have also been raised that patients may adversely change their behaviours if they are told that they are at low risk of retinopathy and they may be less likely to attend screening in the future, however, there was no behavioural evidence to support these assertions.[30] Scanlon also discussed the findings of a survey study conducted in Wales in 2009 and 2010, where 85% (N=507 of N=600 respondents), felt that they should have annual diabetic retinopathy screening. However, 65% (N=390) of respondents would accept screening at two or three year intervals if medical evidence showed that it was safe, while 33% reported this extension was not acceptable. For those that disagreed with longer screening intervals, the primary concerns were fear of sight loss and loss of reassurance that changes can be detected early enough to prevent further complications and impairment of vision.[31] Scanlon also discussed the findings of a discrete choice experiment conducted to elicit the preferences for diabetic retinopathy screening in 160 people with diabetes. The authors concluded that respondents were willing to accept a longer screening interval, as long as preferences for other attributes of service provision (the ability of screening to detect other eye changes, explanation of results and shorter travel time) were made available.[28, 32]

- Swanson published a literature review in 2005 regarding retinopathy screening in people with type two diabetes. The author concluded that based on the epidemiological findings of included studies, certain people with well-controlled type two diabetes may not warrant annual examination for diabetic retinopathy, and that longer intervals may be safe. However, the author cautioned against extending the screening interval beyond one year given the low screening uptake among people with diabetes at the review was undertaken.[29]

- A modelling study based on a review of the literature was published by Bachmann and Nelson in 1998. The aim of the study was to quantify case detection and blindness prevention attainable through diabetic retinopathy screening in a British general practice based population. The authors estimated that of those screened, about 4% would be correctly detected as requiring treatment during an initial screening round, but this yield could decrease to about 1% in subsequent annual screening rounds. The authors argued that the efficiency of a diabetic retinopathy screening programme could be improved by

screening those at high risk more frequently, and screening those at low risk less frequently.[27]

4.4. Randomised controlled trials (RCTs)

- Only one relevant RCT, which was published in 2019, was identified.[33] This RCT has not been included in any of the previously discussed reviews or HTAs.

- A large RCT conducted in England between 2014 and 2018 has been published as a non-peer reviewed pre-print in 2019.[33] A peer-reviewed protocol for this study was also published in 2019.[34] The Individualised Screening for Diabetic Retinopathy (IDSR) RCT aimed to investigate the safety, efficacy and cost-effectiveness of an extended screening interval in people with diabetes at low-risk of retinopathy progression, and a more frequent interval in those at high risk. Patients were included if they were 12 years or older, attending for a diabetic retinopathy screening, and provided written informed consent. A risk calculation engine (RCE) developed by the authors was based on a large epidemiological data set. This RCE was used to estimate the risk of retinopathy progression in the study participants based on their risk factors comprising age, diabetes duration, glycated haemoglobin (HbA1c), systolic blood pressure and total cholesterol. The RCE in conjunction with the randomisation process, used the patient's risk factors to calculate and allocate a participant's screen interval. Participants in the intervention arm (individualised screening arm) were allocated by the RCE to a six, 12 or 24 month interval at baseline and at each follow-up visit using the most recent screening and clinical risk factor data. Participants in the control arm (fixed interval) continued with annual screening. A per-protocol analysis was undertaken for the primary analysis, and intention-to-treat was undertaken as a sensitivity analysis, with results found to be similar.

- In the trial, 4,534 participants were randomised, 2,265 to the individualised and 2,269 to the control arm. Attendance rates at first follow-up were equivalent between individualised (1,754/2,097, 83.6%) and control (1,883/2,224, 84.7%) arms (difference -1.0, 95% CI -3.2 to 1.2). STDR detection rates were non-inferior between groups: individualised 1.4%, control 1.7% (-0.3, -1.1 to 0.5). Loss to follow up was higher in the individualised arm, 101 (4.5%) compared with 41 (1.8%) in the control arm, largely due to the longer follow-up period of 24 months experienced by participants at low risk (who comprised 83.4% of the individualised arm) compared to the 12 months follow-up in the control arm. The 15 participants who prematurely discontinued the intervention were all in the individualised arm and mostly in the 24 month group. There was no evidence of a loss of ability to detect STDR in the individualised arm (28/1,956; 1.4%) compared to the control (35/2,042; 1.7%) with a difference of -0.3 (-1.1, 0.5)

and pre-specified non-inferiority margin of 1.5%. In the individualised arm, 43.2% fewer screening attendances were required (2,008 vs 3,536). Attendance rates in patients at high risk were lower in the individualised arm at 72.3% compared with 77.3% in the control group, but the shorter interval (six month vs one year) allowed more frequent screening and earlier detection of disease. Additionally, the attendance rates observed over a period of 12 months were considerably higher in the individualised arm compared to the annual arm (89.1% versus 77.3%).[33]

- Safety and efficacy outcomes were comparable between groups. The detection rate of STDR was non-inferior, there was no worsening of visual acuity or higher rates of visual impairment, and there was no detectable worsening of glycaemic control in the individualised arm. Generalisation of the findings from this RCT may be limited by the fact that glycaemia and blood pressure control was relatively good in the participants who agreed to take part in the trial, along with the low baseline prevalence of diabetic retinopathy in this population. Of the 3,503 people who did not consent to participating in this trial, the most common reason provided was that they preferred to continue with annual screening (1,167, 14% of those who declined). Hence, this indicates that there may be some reluctance among patients when initially attempting to extend the interval between screenings.[33]

4.5. Observational studies

- Five relevant observational studies published between 2017 and 2020 were identified.[35-39] These observational studies have not been included in any of the previously discussed reviews or HTAs.

- A prospective cohort study was undertaken by Chamard et al. following 21,864 people with diabetes without retinopathy at baseline for 10 years, who were screened as part of a regional diabetic retinopathy screening programme in Paris between 2004 and 2017. The safe screening interval was defined a priori in this study as a 95% probability of remaining without referable retinopathy (moderate NPDR, severe NPDR or proliferative DR or mild NPDR with the presence of macular oedema). The safe screening interval for patients without retinopathy at the first examination for type one and two diabetes was 2.2 (95% CI 2.0 to 2.4) and 3.0 (2.9 to 3.1) years, respectively. In a subgroup of patients at low-risk of progression (type two diabetes, no retinopathy at baseline, no insulin therapy and good glycaemic control), the safe screening interval was 4.2 (3.8 to 4.6) years. Based on these data, the authors concluded that for patients without retinopathy at baseline, screening intervals of two years, three years and four

years may be considered safe for those with type one diabetes, type two diabetes and who are at low risk respectively.[35]

- A modelling study was undertaken by the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group. This study used a longitudinal Markov modelling approach based on data from a prospective cohort of 1,375 patients with type one diabetes (including approximately 24,000 ophthalmologic assessments) followed from 1983 to 2012, in the US. The authors concluded that a practical screening interval would be every four years, three years, six months, and three months for patients with type one diabetes and no retinopathy, mild NPDR, moderate NPDR and severe NPDR at baseline, respectively. The authors considered these to be reasonable, data-driven intervals, based on the estimated cumulative incidence of progression to PDR of 2.9% at four year intervals, 3.7% at three year intervals, 6.6% at six month intervals, and 14.4% at three-monthly intervals for those with no retinopathy, mild NPDR, moderate NPDR and severe NPDR at baseline, respectively.[37]

- A retrospective cohort study was undertaken by Lee et al. of 32,553 patients (with data on 60,254 eyes) who attended initial and follow-up diabetic retinopathy screening at 19 UK hospitals between 2007 and 2014. Progression to PDR in five years differed by baseline retinopathy: no retinopathy (2.2%), mild NPDR (13.0%), moderate NPDR (27.2%), and severe NPDR (45.5%). Compared with no retinopathy at baseline, patients that presented with mild, moderate, and severe NPDR at baseline were 6.71, 14.80, and 28.19 times more likely to develop PDR, respectively. The authors concluded that baseline severity of diabetic retinopathy is predictive of clinical outcomes. The authors also concluded that annual diabetic retinopathy screening may not detect new cases of PDR as often as previously thought, however they acknowledged that screening can detect other, non-diabetic eye problems. The patients in this study had been referred from community screening services and hence were more likely to be at a higher risk of retinopathy progression than the general population of people with diabetes undergoing screening.[38]

- A retrospective cohort study was undertaken by Modjtahedi et al. of 79,445 patients with minimal or no retinopathy on initial diabetic retinopathy screening in a telemedicine programme in Southern California, US. Patients were included if their initial screening occurred in 2012 and they had at least two years of follow-up data. Eleven of 69,364 patients without baseline retinopathy required treatment for diabetic retinopathy in the following two years, and 11 patients of 9,811 with minimal retinopathy required intervention during the same period. The authors concluded that it is rare for patients with minimal or no baseline

retinopathy to require retinal interventions in the two years after retinal evaluation. The authors also concluded that extending the recommended follow-up interval for patients at low risk of progression appears reasonable as long as this does not adversely impact on attendance at follow-up visits.[39]

- A retrospective cohort study undertaken by Estil et al. in a general ophthalmologic practice in Norway examined the impact of the introduction of a risk-based algorithm (RETINARISK) on clinical outcomes and the frequency of screening visits for diabetic retinopathy. A total of 444 patients with diabetes were included in the personal risk profile program and 399 in the fixed interval group during a five year period between 2014 and 2019. The RETINARISK algorithm calculated 563 screening intervals for the variable interval group, which was on average 23 ± 16 months (mean ± standard deviation (SD)), compared with 14 ± 5 months for the group with fixed screening intervals. No delay in detecting diabetic retinal changes and no harms were caused to the patients in the variable interval group. However, selection bias was present as patients could choose for themselves what group they wanted to join, and so significant population differences are apparent between groups. As controlling for confounders was not undertaken by the authors, direct comparisons of effectiveness and safety cannot be made between the two groups.[36]

4.6. Qualitative studies

- Only one relevant qualitative study, which was published in 2020, was identified.[40] This qualitative study has not been included in any of the previously discussed reviews or HTAs.

- A qualitative study was published by Byrne et al. in 2020, with the aim of exploring issues surrounding acceptability and the barriers and enablers for changing from annual diabetic retinopathy screening to shorter or longer screening intervals based on the risk of retinopathy progression.[40] Semi-structured interviews of 30 people with diabetes and 21 healthcare professionals from North West England were performed and the data were analysed using the constant comparative method. Interviews were conducted prior to the commencement of and during the IDSR RCT, which compared fixed annual with variable (6, 12 or 24 month) interval risk-based screening, as described above.[33]

- The data suggested that a move to variable screening intervals was generally acceptable in principle, though highlighted significant concerns and challenges to successful implementation. There were important caveats attached to acceptability and a need for clear safeguards around: the safety and reliability of calculating screening intervals, capturing all people with diabetes, referral or self-referral back into the annual screening programme of all people with diabetic

changes regardless of planned interval. For people with diabetes, the six month interval was perceived positively as medical reassurance, and the 12 month interval seen as usual treatment. Concerns were expressed by many healthcare professionals and people with diabetes that a two year interval was too lengthy, could damage trust in the system and was risky for detecting STDR. Cynicism was also expressed by some patients that the reason for extending the screening interval was largely to save money for the National Health Service (NHS), rather than due to the limited clinical benefit of regular screening for those at low risk. There were also concerns about a negative effect upon diabetes care and increasing non-attendance rates. Among people with diabetes, there was considerable conflation and misunderstanding about different eye-related appointments within the health care system.[40]

- The study authors offered some suggestions to tackle the barriers to extending the screening intervals based on the concerns discussed by participants and drawing on broader behaviour change and implementation science literature. One suggestion was to clearly communicate and make transparent how risk levels are determined, the safeguard mechanisms embedded in the process, along with the guidelines and policies to support the changes. Careful explanation to both patients and clinicians of how risk is calculated, and how the system works was suggested as a way of providing reassurance. In particular, it was suggested that conversations between the healthcare professional and patient could encourage attendance at follow-up screenings if there were concerns about non-attendance, using effective communication skills with supportive materials from public health agencies. The involvement of experts who are respected in their field, to present and discuss the risk classification process to other professionals, where regular updates on the stability and accuracy of variable screening can be fed back to clinicians, was also suggested to be a useful intervention. Additionally, the authors suggested that there should be opportunities for both healthcare professionals and patients to refer or self-refer back into the annual screening programme, if there have been changes in the diabetes severity.[40]

5. Potential economic impact

5.1. HTAs

- Only one relevant HTA published in 2015 was identified.[23] This is the same HTA discussed in section 4.1.

- Scanlon et al. published a HTA in 2015 that aimed to determine the cost-effective diabetic retinopathy screening interval for the English national programme.[23]

The economic evaluation considered screening intervals of six months, one year, two years, three years and five years. In addition, the cost-effectiveness of these screening intervals were assessed in patient subgroups at different risks of developing STDR or maculopathy. A decision analytic model was developed to evaluate the costs, quality-adjusted life years (QALYs) and cost-effectiveness of the different screening strategies under evaluation, using a hidden Markov model, with a lifelong time horizon. Certain assumptions were made about the model regarding the ability to progress and regress to and from certain stages of diabetic retinopathy, and that slit lamp biomicroscopy as the 'gold standard' was 100% specific and sensitive. The model adopted the perspective of the UK NHS and personal social services. All costs and effects were discounted beyond the first year of simulation using an annual discount rate of 3.5%. The price years were 2012 and 2013 and, when necessary, costs were inflated using the UK health sector pay and prices inflation factor. The value of £30,000 was adopted as the maximum willingness to pay for a QALY gained. Data were obtained from an English cohort of 15,877 people with diabetes who were screened for retinopathy between 2005 and 2012. Other model parameters were obtained from the published literature.

- The simulation found that screening every two, three and five years would result in a reduction of 5,375 (95% CI, 5,332 to 5,411), 7,166 (95% CI, 7,111 to 7,213) and 8,617 (95% CI, 8,552 to 8,672) screens, respectively, compared with annual screening. By screening every two years, as opposed to every year, a total of 143 (95% CI, 120 to 162) fewer patients incorrectly diagnosed at screening as having R2–3 or M1 (that is, false positives) would be referred to hospital eye services (HES). These reductions in numbers increase to 190 (95% CI, 159 to 215) and 229 (95% CI, 191 to 259) when screening every three or five years, respectively. By contrast, screening every two years, as opposed to annually, would reduce the number of patients with true R2–3 or M1 grades (that is, true positives) referred to HES, over the lifetime of the cohort, from 277 to 234 people, a reduction of 42 (95% CI, 35 to 50) cases. Increasing the screening intervals to three years and five years would further reduce the number of true positives being referred by 74 (95% CI, 62 to 87) and 119 (95% CI, 100 to 139), respectively. This would result in 8 (95% CI 7 to 10), 15 (95% CI 12 to 17) and 25 (95% CI 21 to 29) fewer true cases of R2–3 or M1 being treated following screening if screening intervals were to be extended to two, three and five years, respectively, compared with annual screening. Over a lifetime, when compared with annual screening, there would be a reduction of 18 (95% CI 15 to 21), 32 (95% CI 27 to 37) and 52 (95% CI 44 to 59) true cases of R2–3 or M1 being treated if screening intervals were extended to two, three and five years, respectively.[23]

- In patients at low risk of progression, the discounted average QALYs gained by patients were 8.3558 when screening every year, 8.3551 when screening every two years, 8.3547 when screening every three years and 8.3541 when screening every five years. Hence, they are comparable. However, the number of screenings over a lifetime was much higher when screening was more frequent. The authors estimated that 21,990, 11,253, 5,878, 4,087 and 2,636 screens would occur over the lifetime of a cohort of 1,000 people with diabetes, if screening occurred every six months, one year, two years, three years and five years, respectively.[23] Hence, there is an over eight-fold increase in the number of screens that would occur, over the lifetime of this simulated cohort, if screening occurred every six months compared with every five years.

- The cost-effective screening intervention for the low-risk group (R0M0 in both eyes in two consecutive episodes) was screening every five years, with a 99% probability of being the cost-effective intervention at the £30,000 per QALY threshold. Other screening intervals for this patient group yielded considerably higher incremental cost-effectiveness ratios (ICERs). For example, when screening every 3 years, 2 years and one year were compared with screening every 5 years, the associated ICERs were £72,217, £113,823 and £225,004 per QALY gained, respectively.[23]

- For the high-risk group (R1M0 in both eyes in two consecutive episodes) the cost-effective screening intervention was screening every two years, where the probability of being the cost-effective was found to be 59%.

- Using the risk-based strategy based on data from the included cohort of patients, the cost-effective option is to screen those at low risk of retinopathy progression every five years and those at high risk every two years. However, there is considerable uncertainty in the evidence informing the model, particularly the natural history of disease progression, association between utility scores and visual acuity and the effectiveness of treatment in diabetic maculopathy. Additionally, English NHS cost data may not be applicable to the Irish healthcare system. Hence caution is warranted when interpreting the findings of this economic evaluation.[23]

5.2. Systematic reviews

- Three relevant systematic reviews published between 2010 and 2015 were identified.[24, 26, 41] Although these three systematic reviews had different inclusion criteria, there is potentially some overlap of studies between them.

- A systematic review of the screening intervals for diabetic retinopathy and incidence of visual loss was published by Echouffo-Tcheugui et al. in 2013.

Twenty-five studies were included: 15 evaluations of real-world screening programmes, three modelling studies and seven cost-effectiveness studies. The authors reported that the aggregated evidence from both the modelling and cost-effectiveness studies favoured a screening interval of between one and two years.[24]

- A systematic review was published by Taylor-Phillips et al. in 2015 with the aim of determining whether the recommended screening interval for diabetic retinopathy could be safely extended beyond one year, in order to inform screening policy in the UK. Nine economic modelling studies were included and the findings were inconsistent with regards to the cost-effective screening interval.[26]

- Jones and Edwards published a systematic review of the economic evidence for diabetic retinopathy screening in 2010. One of the objectives of this review was to determine the cost-effective screening interval for diabetic retinopathy. Three studies evaluated the cost-effectiveness of differing screening intervals, but had inconsistent findings. The authors of this review suggested that these differences may be due to differing assumptions made in the various models, in particular how non-attendance rates may affect the cost-effectiveness when screening intervals are changed.

5.3. Non-systematic reviews

- One relevant non-systematic review was identified.[28]

- Scanlon published a literature review in 2017 examining the evidence underpinning extended screening intervals for diabetic retinopathy in people at low risk of progression. The two included economic evaluations of diabetic retinopathy screening programmes both concluded that annual screening for all people with diabetes may not be cost-effective.[28]

5.4. Randomised controlled trials (RCTs)

- Only one relevant RCT, which was published in 2019, was identified.[33] This RCT, which was described in section 4.4, has not been included in any of the previously discussed reviews or HTAs.

- A large RCT conducted in England between 2014 and 2018 has been published as a non-peer reviewed pre-print in 2019.[33] As described above, the IDSR RCT aimed to investigate the safety, efficacy and cost-effectiveness of an extended screening interval in people with diabetes at low-risk of retinopathy progression, and a more frequent interval in those at high risk. The screening intervals ranged from every six months to every two years dependant on the risk of retinopathy

progression. The costs of routine screening were measured using a mixed micro-costing and observational health economics analysis, from both an NHS and a broader societal perspectives. A detailed work place analysis, measuring resources and staff time to deliver the screening programme, was observed at each of the screening centres. A limited sample (the first 868 to be recruited into the trial of a total of 4,534 participants) completed EuroQol five dimensions, five level scale (EQ-5D-5L) and Health Utilities Index Mark 3 (HUI3) questionnaires at baseline and follow-up visits. A bespoke visit questionnaire asked about out-of-pocket expenses incurred, including travel costs and time lost from paid employment for the patient and companion.[33]

- The incremental QALY scores per patient showed no significant difference between the groups at the two-year time horizon (EQ-5D-5L 0.035 (CI -0.04, 0.13), HUI3 0.009 (CI -0.09, 0.10)). In the individualised arm, 43.2% fewer screening appointments were required. Over the two years, the incremental cost savings per participant were £21.31 (CI 15.24, 26.79) from an NHS perspective rising to £28.87 (CI 21.08, 35.78) with inclusion of societal costs. The economic evaluation found that the annual screening arm (control arm) was dominated by the individualised screening arm (intervention arm).[33]

5.5. Observational studies

- One additional observational study, published in 2020, which has not been included in any of the previously discussed HTAs or reviews, was identified.[42]

- A retrospective cohort study with cost-utility analysis was published in 2020 by Thomas et al. based on data from Diabetic Eye Screening Wales (N=91,393 patients attending screening between 2005 and 2009). The aim of the study was to determine the cost-effectiveness of extending the screening interval from one to two years, in people without reported retinopathy. The authors concluded that the base case and sensitivity analyses, indicated screening every two years to be cost-effective for individuals with type two diabetes irrespective of HbA1c and duration of diabetes. However, the uncertainty around the decremental cost-effectiveness ratio (DCER) indicated that annual screening should be maintained for those with type one diabetes especially when the HbA1c exceeded 80 mmol/mol (9.5%) and duration of diabetes was greater than 12 years.[42]

6. Decision-making and policy considerations

- The National Screening Service (NSS) has proposed the introduction of a 2two year screening interval in the Diabetic RetinaScreen programme for people with diabetes at low risk of progression, in line with international practice. The Diabetic RetinaScreen programme intended to commence extended interval screening as a pathway, through a controlled and pilot phase. However, given the impact that coronavirus disease 2019 (COVID-19) has had on screening services nationally, and the substantial backlog of people awaiting screening, the NSS have proposed accelerating the introduction of this extended interval screening process to assist in the management of this backlog.[19]

- The NSS have proposed that people who have been screened with a worst final grade of R0M0 and who have no non-diabetic eye disease (NDED) in 2018 and 2019 will be considered low risk and eligible for two year screening intervals. People graded R0M0 in one eye and who have no perception of light in the other will also be eligible. People who did not attend or who cancelled their appointment in 2018 or 2019 and who did not attend between 11-13 months of their last appointment will not be eligible, and will be returned to annual routine recall.[19]

- While clinical guidelines consistently recommend screening for diabetic retinopathy, worldwide it appears that few national organised screening programmes have been established; organised screening in other countries may be provided at a regional or provider level. Hence, Ireland as one of the few countries that has implemented a national diabetic retinopathy screening programme is coming from a very strong base.[11] A table comparing the various organised, national diabetic retinopathy screening programmes is presented below (Table 3).

- Annual screening intervals are standard practice in countries such as Ireland, England, Scotland, Wales, Northern Ireland and Singapore. However, some national programmes have moved to two years (for example, Iceland), three years (for example, New Zealand) and even four years (for example, Denmark) screening intervals, for patients at low risk of retinopathy progression. Of note, Public Health England has indicated its intention to accelerate the introduction of two year screening intervals for the national English programme, to manage the backlog of patients arising from the COVID-19 pandemic.[43]

- Different grading classification systems and protocols for screening intervals are used in the various programmes. Uptake and attendance rates in the Irish national programme compares favourably with the other programmes. However,

inherent differences in healthcare systems and populations between countries prevent direct comparisons.

- There are some limitations in that this table does not represent an exhaustive list of all national programmes, but rather it represents the national programmes for which data were found. Additionally, there were sometimes conflicting information between different data sources regarding how the screening service is delivered. However, an attempt was made to select the most up-to-date information to populate the table below. The data are correct as of 30 September 2020, but are subject to change.

Table 3. National, organised diabetic retinopathy screening programmes

Country	Methods of screening	Grading classification system	Screening intervals	Database or Quality Assurance programme	Service evaluation outcomes
Denmark[44, 45]	1) Photo screening by ophthalmologist or trained specialist, with mydriatic agent 2) If unclear, indirect ophthalmoscopy by ophthalmologist	ICDRDSS (independent of the possible presence of DMO) Grade: 0 – No DR 1 – Mild NPDR 2 – Moderate NPDR 3 – Severe NPDR 4 – PDR DMO classified as per ETDRS	Flexible and individualised screening intervals: Grade 0 and well-controlled diabetes*: 24-48 months** Grade 0 and uncontrolled diabetes: 12-24 months Grade 1 and well-controlled (no DMO): 24 months Grade 1 and uncontrolled diabetes (no DMO): 12 months Grade 2 and controlled diabetes: 12-24 months (no DMO) Grade 2 and uncontrolled diabetes (no DMO): 6-12 months Grade 3 and controlled diabetes (no DMO): 3-6 months Grade 3 and uncontrolled diabetes (no DMO): 3 months	DiaBase national database	In 2014-2015, 65% of patients attended eye screening within the planned, individualised interval. This compares with 60% in 2013-2014 and 64% in 2012-2013. The standard is at least 90% In 2014-2015, 10% of patients progressed to a more severe level of diabetic eye disease. This compares with 14% in 2013-2014 and 14% in 2012-2013. In 2014-2015, 20% of patients regressed to a milder stage of diabetic eye disease. This compares with 20% in 2013-2014 and 18% in 2012 -2013.
England[43, 46, 47]	1) Digital photograph of both retinas (two-field, 45°), with mydriatic agent. 2) Slit lamp biomicroscopy if digital photo	RxMx grading system (the English National Screening Committee grading criteria): R0 = No retinopathy R1 = Background retinopathy	1 year if R0M0, R1M0 in one or both eyes. 3, 6 or 12 monthly follow-up post-referral if R2, M1 or R3S Changing to 2 years for people with low risk of sight loss (R0M0), in light of backlog due to COVID-19.	Screening quality assurance services. External Quality assurance every 3 years.	A total of 2,144,007 people with diabetes were screened during the 2015-2016 programme (Uptake 82.8%).

	unclear, with mydriatic agent	R2 = Pre-proliferative retinopathy R3A = Active proliferative retinopathy R3S = Stable proliferative retinopathy M0 = No maculopathy M1 = Maculopathy			
Iceland[17]	Determined by an ophthalmologist using slit-lamp examination of the fundus with a 90-diopter lens with dilated pupils	1. No retinopathy 2. Mild NPDR 3. Clinically significant DMO 3. Pre-proliferative DR 4. Proliferative DR	Patients with diabetes without retinopathy are screened every 2 years. Patients with diabetes and retinopathy are screened every year. More frequent eye examinations scheduled for some patients based on the clinical judgement of the ophthalmologist	NR	The 10-year experience from 1995 to 2005 found that 2 year screening is safe and does not risk the visual acuity of patients with diabetes. The patients who developed sight-threatening retinopathy had all first been diagnosed as having mild retinopathy and placed on at least an annual examination schedule. No patient had any undue delay in treatment of sight-threatening retinopathy.
Ireland[14, 48]	1) Digital retinal photography with mydriasis 2) Slit lamp biomicroscopy if digital photo unclear	RxMx grading system (the English National Screening Committee grading criteria): R0 = No retinopathy R1 = Background retinopathy R2 = Pre-proliferative retinopathy R3A = Active proliferative retinopathy	Annual screening (Proposal to increase interval to every 2 years for those with a worst final grade of R0M0 and non-NDED for two consecutive years, or people graded with R0M0 in one eye and NPL in the other)	Quality Assurance Committee. Standards for Quality Assurance in Diabetic Retinopathy Screening, which are	Attendance at follow-up screening visits has been high since commencement of programme in 2013, and has been increasing year on year up until 2018 (from 86.7% to 91.6%). There has also been a declining trend in DED referrals (from 13.2% to 3.7% of all patients screened

		R3S = Stable proliferative retinopathy M0 = No maculopathy M1 = Maculopathy		subject to regular audit. Evidence of EQA should be maintained and available for quality control purposes/audit/inspection. EQA should be done at a minimum every 3 years.	at each round), while there has been an increasing trend in NDED referrals to HES (from 0.4% to 3.2% of all patients screened at each round).
New Zealand[16, 49]	1) Digital retinal photography (minimum field size is two 45-degree fields) 2) Dilated pupil fundus examination, using slit-lamp biomicroscopy, if retinal photography unsuitable. Patients have a choice whether to undergo mydriasis or not	National Diabetes Retinal Grading System: R0 = No DR R1 = Minimal R2 = Mild R3 = Moderate R4 = Severe R5 = Proliferative RT = Stable treated diabetic retinopathy M0 = No macular disease M1 = Minimal M2 = Mild M3 = Mild (with exudates) M4 = Moderate M5 = Severe MT = Stable, treated macular disease	The standard screening interval is 2 years. But can be extended to every 3 years for those without clinical modifiers (below), who have no diabetic retinopathy detected and whose HbA1c has consistently been less than or equal to 64 mmol/mol: ▪ DNA two or more consecutive times ▪ Poorly controlled diabetes: HbA1c > 64 mmol/mol ▪ Duration of diabetes (> 10 years) ▪ Rapid progression of DR ▪ Poorly controlled hypertension (BP ≥ 160/95) ▪ Asymmetrical DR ▪ Renal failure/proteinuria ▪ Type 1 diabetes > 15 years ▪ Foot ulcers	Clinical and service level audits and oversight of reporting information, performed annually. All health practitioners providing retinal screening must participate in professional quality assurance activities, including a peer-review process. Each regional retinal screening service must complete an	None of relevance found since changes in 2016.

			R2 = Rescreen after 12 months R3 = Rescreen after 6 months R4/5 = Referral to ophthalmologist M0 (type 1) = rescreen after 2 years M0 (type 2) = re-screen at 3 years if HbA1c < 64 mmol/mol and clinical modifiers may result in earlier re-screening. M1 = Re-screen at 1–2 years if current HbA1c < 64 mmol/mol. M2 = rescreen after 12 months M3 = Re-screen at 6 months, or review by ophthalmologist within 4 months. M4 = Small exudate around a solitary MA may be re-screened within 6 months. All other cases should be reviewed by an ophthalmologist within 6 weeks. M5 = Referral to ophthalmologist MT = Rescreen after 2 years	annual report with the Ministry of Health	
Northern Ireland[11, 50, 51]	Digital photograph of both retinas (two-field, 45°), with mydriatic agent (if over the age of 50 years), conducted by retinal photographers	RxMx grading system (the English National Screening Committee grading criteria): R0 = No retinopathy R1 = Background retinopathy R2 = Pre-proliferative retinopathy	R0M0 – annual R1M0 – annual R2, M1, R3S – screened every 3, 6 or 12 months depending on progression of disease. R3A, R2, M1 – referral to HES. They are returned to routine screening or surveillance after discharge (Plan to introduce 2 year screening for those at low risk)	Quality assured by the PHA in collaboration with BHSCT who are responsible for the management and delivery of the programme.	69.2% (45,845/66,271) of all those invited for diabetic eye screening across Northern Ireland attended during 2016 to 2017 screening round. The average screening interval for Northern Ireland in 2016/17 was 13 months.

		R3A = Active proliferative retinopathy R3S = Stable proliferative retinopathy M0 = No maculopathy M1 = Maculopathy			
Scotland[52-57]	1) Non-mydriatic retinal photograph (mydriasis required for 1 in 4 patients if image is poor quality) 2) Slit lamp biomicroscopy if digital photo unclear Three levels of grading: <u>Level</u> 1: automated 2: optometrist or nurse practitioner 3: medical retina-trained ophthalmologists	Scottish grading system: R0 = No disease R1 = Mild background DR R2 = Moderate background DR R3 = Severe NPDR or pre-proliferative DR R4 = Proliferative retinopathy M0 = No macular findings M1 = Hard exudates within 1–2 disc diameters of fovea M2 = Blot haemorrhage or hard exudates within 1 disc diameter of fovea	Recall in 12 month if the patient has no visible retinopathy or only mild background retinopathy. Recall in 6 months if the patient has observable background retinopathy or observable background maculopathy (Currently prioritising those at high risk due to backlog as a result of COVID-19)	The Level 3 grader also undertakes internal quality assurance for Level 1 and Level 2 graders, with five hundred random images from each grader included for internal quality assurance each year. All Scottish graders (Level 1 to Level 3) must also participate in external quality assurance once a year.	The yield of referable eye disease was greatest in the first 2 years of the programme where 7% and 6% of individuals successfully screened in the DRS had referable disease in 2006 and 2007, respectively. Since 2008, the annual referral rate has been stable at 4.3% (~5500 referrals per year).
Singapore[8, 58-60]	Non-mydriatic retinal photographs by a nurse	ICDRDSS: No DR Mild NPDR Moderate NPDR	Annual if non-referable (i.e. No DR or mild NPDR)	Regular audits and in-built quality	The national programme, implemented in 2010, was found to be more cost-effective and provided similar

	practitioner, using a tele-medicine model. All retinal images initially analysed by primary professional graders, followed by secondary human assessment by the senior graders to reclassify the eyes.	Severe NPDR PDR No DMO Mild DMO Moderate DMO Severe DMO		assurance processes.	outcomes compared with the previous ad-hoc, family-practice based screening programme
Wales[61, 62]	Digital photograph of both retinas (two-field, 45°), with mydriatic agent, conducted by retinal photographers	Welsh Grading System: R0 = No retinopathy R1 = Mild background DR R2 = Pre-proliferative DR R3s = Stable post-treatment proliferative DR R3A = Active proliferative DR M0 = No maculopathy M1 = Referable maculopathy	R0 or R1 = 12-monthly R2 = Secondary/arbitration grading with annual recall or refer to HES R3S = Secondary/arbitration grading with annual recall if confirmed stable	Quality Assurance monitoring	Uptake of 80% in 2013.

Key: BHSCT - Belfast Health and Social Care Trust; BP – blood pressure; DED – diabetic eye disease; DNA – did not attend; DMO - diabetic macular oedema; DR(S)- diabetic retinopathy (screening); ETDRS - Early Treatment Diabetic Retinopathy Study; EQA - external quality assurance; HbA1c - glycated haemoglobin; HES – hospital eye services; ICDRDSS/IDRMESS - International Clinical Diabetic Retinopathy Disease Severity Scale/ International Diabetic Retinopathy and Macula Edema Severity Scales; PHA - Public Health Agency; NDED – non-diabetic eye disease; NPDR – non-proliferative diabetic retinopathy; NPL – no perception by light; PDR – proliferative diabetic retinopathy.

*Well-controlled diabetes defined as HbA1c ≤ 53 mmol/mol (7.0%) and blood pressure <130/80 mmHg. If the patient's risk factors are not known, the screening interval should follow the recommendations for uncontrolled patients.
** At first screening examination, a maximum interval of 24 months is recommended

7. Discussion and Conclusion

This scoping report has provided an overview of the evidence pertaining to extending the screening interval for diabetic retinopathy from one to two years for those at low risk of diabetic retinopathy progression.

There is consistent evidence from multiple systematic reviews of population-based observational studies that, in people without retinopathy at baseline, the risk of diabetic retinopathy progression within two years is very low. This is supported by evidence from a large randomised control trial (RCT) that found that individualised, risk-based screening intervals may be as safe and effective as fixed, annual screening intervals. There is also consistent evidence from HTAs, systematic reviews, RCTs and observational studies to suggest that for those at low risk, less frequent screening intervals may be more efficient and result in similar patient outcomes compared with annual screening. Notably, the included RCT also decreased the screening interval in the intervention arm to six-monthly for those at high risk of retinopathy progression. Evidence from some systematic reviews and observational studies also supported shorter intervals of less than one year for patients with pre-existing diabetic retinopathy.

However, there is inconsistent evidence for the effect of extending screening intervals on attendance at follow-up visits. No differences were found between intervention and control arms in the included RCT. However, a large number of participants declined to enrol in the trial, as they did not want to extend their screening interval to 24 months, and there was greater loss to follow-up in the intervention arm compared with the control arm. Additionally, one systematic review found that loss to follow-up was high in some longitudinal screening studies. Evidence from qualitative and mixed-methods studies suggests that although most healthcare professionals and patients were broadly accepting of extended intervals, some had significant concerns. There was also some qualitative evidence that these changes might cause confusion and an increased fear of sight loss in some patients. No evidence was found regarding an effective means of communicating extended interval screening changes to patients or healthcare professionals.

No screening programme can prevent all cases. Harms related to taking the screening exam are minimal and short term. Diabetic retinopathy screening tests, like all screening tests, are not 100% accurate. Most adverse effects of a diabetic retinopathy screening programme relate to false negative and false positive test results. False negative test results lead to potentially missed or delayed opportunities to intervene in individuals with treatable retinopathy. False positive test results lead to unnecessary referrals and may lead to increased surveillance, potentially

increasing stress and anxiety. Retinopathy may progress in the time between a negative screening test and the individual's next screening test, however there is strong evidence to suggest that this is highly unlikely in individuals without any retinopathy at baseline.[1, 24-26] This is another potential harm of any screening programme. However, the potential for harm is likely reduced by restricting extended interval screening to those with a low risk of retinopathy progression. The impact of extending the screening interval from one to two years on programme coverage is also not known. An ongoing audit of coverage and tracking of non-responders will allow changes in adherence to be identified in a timely fashion.

National, organised diabetic retinopathy screening programmes have been implemented across several countries, however these are still relatively uncommon. Extending the screening interval for patients at low risk of retinopathy progression is in keeping with developments in other high income countries such as England, New Zealand, Denmark and Iceland.

In conclusion, extending diabetic retinopathy screening intervals from one to two years for those at low risk, appears to be safe, and in line with international best practice. However, any planned changes to the national programme would need to be accompanied by a significant communications campaign, including all relevant stakeholders, to address potential concerns. Additionally, an ongoing audit of coverage and tracking of non-responders is essential to identify changes in adherence in a timely fashion.

References

1. Sabanayagam C, Banu R, Chee ML, Lee R, Wang YX, Tan G, et al. Incidence and progression of diabetic retinopathy: a systematic review. The lancet Diabetes & endocrinology. 2019;7(2):140-9.
2. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond). 2015;2:17-.
3. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care. 2012;35(3):556-64.
4. Diabetic RetinaScreen. Information for Health Professionals 2019 [updated 2019; cited 2020 25 Sep]. Available from: https://www.diabeticretinascreen.ie/health-professionals.24.html.
5. Mayo Clinic. Diabetic retinopathy 2018 [updated 30 May 2018; cited 2020 25 Sep]. Available from: https://www.mayoclinic.org/diseases-conditions/diabetic-retinopathy/symptoms-causes/syc-20371611.
6. Frank RN. Diabetic Retinopathy. New England Journal of Medicine. 2004;350(1):48-58.
7. Morrison JL, Hodgson LA, Lim LL, Al-Qureshi S. Diabetic retinopathy in pregnancy: a review. Clinical & Experimental Ophthalmology. 2016;44(4):321-34.
8. Ting DSW, Cheung GCM, Wong TY. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. Clinical & experimental ophthalmology. 2016;44(4):260-77.
9. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. World J Diabetes. 2011;2(6):98-104.
10. Arun CS, Ngugi N, Lovelock L, Taylor R. Effectiveness of screening in preventing blindness due to diabetic retinopathy. Diabetic medicine : a journal of the British Diabetic Association. 2003;20(3):186-90.
11. Pieczynski J, Grzybowski A. Review of diabetic retinopathy screening methods and programmes adopted in different parts of the world. Journal-Review of Diabetic Retinopathy Screening Methods and Programmes Adopted in Different Parts of the World. 2015.
12. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110(9):1677-82.
13. Shotliff K, Duncan G. Diabetic retinopathy: summary of grading and management criteria. Practical Diabetes International. 2006;23(9):418-20.
14. Diabetic RetinaScreen. Standards for Quality Assurance in Diabetic Retinopathy Screening 2019 [updated 2019; cited 2020 25 Sep]. Available from: https://www.diabeticretinascreen.ie/_fileupload/Documents/Standards-for-Quality-Assurance-in-DRS-Rev-5--04-12-19.pdf.
15. Hamid A, Wharton H, Mills A, Gibson J, Clarke M, Dodson P. Diagnosis of retinopathy in children younger than 12 years of age: implications for the diabetic eye screening guidelines in the UK. Eye. 2016;30(7):949-51.
16. Ministry of Health New Zealand. Diabetic Retinal Screening, Grading, Monitoring and Referral Guidance 2016 [cited 2020 18 Sep]. Available from:

https://www.health.govt.nz/system/files/documents/publications/diabetic-retinal-screening-grading-monitoring-referral-guidance-mar16.pdf.
17. Ólafsdóttir E, Stefánsson E. Biennial eye screening in patients with diabetes without retinopathy: 10-year experience. British journal of ophthalmology. 2007;91(12):1599-601.
18. Sun Y, Cai Y-t, Chen J, Gao Y, Xi J, Ge L, et al. An evidence map of clinical practice guideline recommendations and quality on diabetic retinopathy. Eye. 2020:1-12.
19. National Screening Advisory Committee. Case for the modification of the Diabetic RetinaScreen Programme Dublin: NSAC; 2020 [updated 17 Jul 2020; cited 2020 18 Sep].
20. HIQA. Standard Operating Procedure: Development of Scoping Reports for HTA Prioritisation 2020.
21. Martín Sánchez J, Muñoz Fernández C, Blas Diez M. [Detection of complications of diabetes. Diabetic retinopathy. Economic evaluation of ophthalmoscopy by laser scanning ultra-wide field] Instituto Aragonés de Ciencias de la Salud (IACS)2019 [updated 2019; cited 2020 28 Sep]. Available from: https://www.iacs.es/wp-content/uploads/2019/09/07_IACS_2016_RETINOPATIA_DEF_NIPO.pdf.
22. Mellanby A, Milne R. Reducing the interval for diabetic retinal screening. 1999. Wessex Institute for Health Research and Development DEC Report. 1999;107.
23. Scanlon PH, Aldington SJ, Leal J, Luengo-Fernandez R, Oke J, Sivaprasad S, et al. Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. Health Technology Assessment. 2015;19(74):1-116.
24. Echouffo-Tcheugui JB, Ali MK, Roglic G, Hayward RA, Narayan KM. Screening intervals for diabetic retinopathy and incidence of visual loss: a systematic review. Diabetic medicine : a journal of the British Diabetic Association. 2013;30(11):1272-92.
25. Groeneveld Y, Tavenier D, Blom JW, Polak BCP. Incidence of sight-threatening diabetic retinopathy in people with Type 2 diabetes mellitus and numbers needed to screen: a systematic review. Diabetic medicine : a journal of the British Diabetic Association. 2019;36(10):1199-208.
26. Taylor-Phillips S, Mistry H, Leslie R, Todkill D, Tsertsvadze A, Connock M, et al. Extending the diabetic retinopathy screening interval beyond 1 year: systematic review. British Journal of Ophthalmology. 2016;100(1):105-14.
27. Bachmann MO, Nelson SJ. Impact of diabetic retinopathy screening on a British district population: case detection and blindness prevention in an evidence-based model. Journal of Epidemiology & Community Health. 1998;52(1):45-52.
28. Scanlon PH. Screening intervals for diabetic retinopathy and implications for care. Current Diabetes Reports. 2017;17(10):96.
29. Swanson M. Retinopathy screening in individuals with type 2 diabetes: who, how, how often, and at what cost—an epidemiologic review. Optometry-Journal of the American Optometric Association. 2005;76(11):636-46.

30. Klein R. Screening interval for retinopathy in type 2 diabetes. Lancet (London, England). 2003;361(9353):190-1.
31. Yeo ST, Edwards RT, Luzio SD, Charles JM, Thomas RL, Peters JM, et al. Diabetic retinopathy screening: perspectives of people with diabetes, screening intervals and costs of attending screening. Diabetic medicine : a journal of the British Diabetic Association. 2012;29(7):878-85.
32. Yeo ST, Edwards RT, Fargher EA, Luzio SD, Thomas RL, Owens DR. Preferences of people with diabetes for diabetic retinopathy screening: a discrete choice experiment. Diabetic medicine : a journal of the British Diabetic Association. 2012;29(7):869-77.
33. Broadbent D, Wang A, Cheyne CP, James M, Lathe JG, Stratton IM, et al. Safety, Efficacy and Cost Effectiveness of Individualised Screening for Diabetic Retinopathy: The ISDR Randomised Controlled Trial. Available at SSRN 3387513. 2019.
34. Broadbent DM, Sampson CJ, Wang A, Howard L, Williams AE, Howlin SU, et al. Individualised screening for diabetic retinopathy: the ISDR study-rationale, design and methodology for a randomised controlled trial comparing annual and individualised risk-based variable-interval screening. BMJ open. 2019;9(6):e025788.
35. Chamard C, Daien V, Erginay A, Gautier J-F, Villain M, Tadayoni R, et al. Ten-year incidence and assessment of safe screening intervals for diabetic retinopathy: the OPHDIAT study. British Journal of Ophthalmology. 2020.
36. Estil S, Steinarsson ÆÞ, Einarsson S, Aspelund T, Stefánsson E. Diabetic eye screening with variable screening intervals based on individual risk factors is safe and effective in ophthalmic practice. Acta Ophthalmologica. 2020;98(4):343-6.
37. Group DER. Frequency of evidence-based screening for retinopathy in type 1 diabetes. New England Journal of Medicine. 2017;376(16):1507-16.
38. Lee CS, Lee AY, Baughman D, Sim D, Akelere T, Brand C, et al. The United Kingdom Diabetic Retinopathy Electronic Medical Record Users Group: Report 3: Baseline Retinopathy and Clinical Features Predict Progression of Diabetic Retinopathy. American journal of ophthalmology. 2017;180:64-71.
39. Modjtahedi BS, Theophanous C, Chiu S, Luong TQ, Nguyen N, Fong DS. Two-Year Incidence of Retinal Intervention in Patients With Minimal or No Diabetic Retinopathy on Telemedicine Screening. JAMA ophthalmology. 2019;137(4):445-8.
40. Byrne P, Thetford C, Gabbay M, Clarke P, Doncaster E, Harding S. Personalising screening of sight-threatening diabetic retinopathy-qualitative evidence to inform effective implementation. BMC Public Health. 2020;20:1-12.
41. Jones S, Edwards R. Diabetic retinopathy screening: a systematic review of the economic evidence. Diabetic medicine. 2010;27(3):249-56.
42. Thomas RL, Winfield TG, Prettyjohns M, Dunstan FD, Cheung W-Y, Anderson PM, et al. Cost-effectiveness of biennial screening for diabetes related retinopathy in people with type 1 and type 2 diabetes compared to annual screening. Eur J Health Econ. 2020;21(7):993-1002.

43. Public Health England. Diabetic eye screening intervals extended for people at lowest risk 2020 [updated 23 Sep 2020; cited 2020 29 Sep]. Available from: https://www.gov.uk/government/publications/diabetic-eye-screening-longer-intervals-for-people-at-lowest-risk/diabetic-eye-screening-intervals-extended-for-people-at-lowest-risk.
44. Dansk Ophthalmological Society. [Danish national guideline for screening for diabetic retinopathy] 2018 [updated 21 Sep 2018; cited 2020 29 Sep]. Available from: http://www.dansk-oftalmologisk-selskab.dk/arkiver/2902.
45. Andersen N, Hjortdal JØ, Schielke KC, Bek T, Grauslund J, Laugesen CS, et al. The Danish registry of diabetic retinopathy. Clinical epidemiology. 2016;8:613.
46. UK National Screening Committee. NHS Diabetic Eye Screening Programme 2018 [cited 2020 29 Sep]. Available from: https://www.hct.nhs.uk/media/1227/diabetic-eye-screening-information-sheet-for-healthcare-professionals.pdf.
47. Scanlon PH. The English national screening programme for diabetic retinopathy 2003–2016. Acta diabetologica. 2017;54(6):515-25.
48. Diabetic RetinaScreen. Overview of Programme Impact of Covid 19 Move to Extended Interval Screening 2020 [updated 2020; cited 2020 30 Sep].
49. Hutchins E, Coppell KJ, Morris A, Sanderson G. Diabetic retinopathy screening in New Zealand requires improvement: results from a multi-centre audit. Australian and New Zealand Journal of Public Health. 2012;36(3):257-62.
50. Public Health Agency NI. Diabetic Eye Screening Programme Annual Report 2016-2017 2018 [updated 10 Dec 2018; cited 2020 30 Sep]. Available from: https://www.publichealth.hscni.net/publications/diabetic-eye-screening-programme-annual-report-2016-2017.
51. Public Health Agency Northern Ireland. Diabetic Eye Screening: Information for Health Professionals 2020 [cited 2020 30 Sep]. Available from: https://www.publichealth.hscni.net/directorate-public-health/service-development-and-screening/information-health-professionals.
52. NHS Inform Scotland. Coronavirus (COVID-19): Immunisation and screening 2020 [updated 21 Sep 2020; cited 2020 29 Sep]. Available from: https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/coronavirus-covid-19/healthy-living/coronavirus-covid-19-immunisation-and-screening#diabetic-retinopathy-screening-resumes.
53. Public Health Scotland. Your guide to diabetic retinopathy screening 2020 [updated 6 Jan 2020; cited 2020 29 Sep]. Available from: http://www.healthscotland.com/documents/22216.aspx.
54. Zachariah S, Wykes W, Yorston D. The Scottish Diabetic Retinopathy Screening programme. Community Eye Health. 2015;28(92):s22-s3.
55. Healthcare Improvement Scotland. Diabetic Retinopathy Screening: Standards 2016 [updated June 2016; cited 2020 29 Sep]. Available from: http://www.healthcareimprovementscotland.org/our_work/standards_and_guidelines/stnds/diabetic_retinopathy_screening.aspx.
56. Zachariah S, Wykes W, Yorston D. Grading diabetic retinopathy (DR) using the Scottish grading protocol. Community Eye Health. 2015;28(92):72-3.

57. Looker H, Nyangoma S, Cromie D, Olson J, Leese G, Black M, et al. Rates of referable eye disease in the Scottish national diabetic retinopathy screening programme. British Journal of Ophthalmology. 2014;98(6):790-5.
58. Xie Y, Nguyen QD, Hamzah H, Lim G, Bellemo V, Gunasekeran DV, et al. Artificial intelligence for teleophthalmology-based diabetic retinopathy screening in a national programme: an economic analysis modelling study. The Lancet Digital Health. 2020;2(5):e240-e9.
59. SingHealth. Singapore Integrated Diabetic Retinopathy Programme (SiDRP) 2018 [updated 2 Apr 2018; cited 2020 30 Sep]. Available from: https://www.singhealth.com.sg/news/medical-news/singapore-integrated-diabetic-retinopathy-programme-sidrp#:~:text=In%20July%202010%2C%20the%20Singapore,by%20family%20physicians%20with%20a.
60. Nguyen HV, Tan GSW, Tapp RJ, Mital S, Ting DSW, Wong HT, et al. Cost-effectiveness of a National Telemedicine Diabetic Retinopathy Screening Program in Singapore. Ophthalmology. 2016;123(12):2571-80.
61. Wales Eye Care Services. Diabetes Eye Screening Wales 2020 [cited 2020 30 Sep]. Available from: http://www.eyecare.wales.nhs.uk/drssw.
62. Thomas RL, Dunstan FD, Luzio SD, Chowdhury SR, North RV, Hale SL, et al. Prevalence of diabetic retinopathy within a national diabetic retinopathy screening service. British Journal of Ophthalmology. 2015;99(1):64-8.

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