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Diabetische Retinopathie

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Maliebaanzaal, UMC Utrecht

Rijnstate. Voorop in zorg voor jou.

Disclosures

- Geen (financiële) belangen

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Diabetes Mellitus

- Metabole ziekte
- Hoge glucosespiegel in bloed
  - Toegenomen resistentie tegen insuline
  - Verminderde productie van insuline
- Symptomen
  - Veelvuldig urineren
  - Toegenomen dorst
  - Toegenomen honger
- Behandeling
  - Verhogen insuline (endogeen) en celgevoeligheid voor insuline
  - Verminderen glucose uptake en productie door lever
  - Exogene insuline

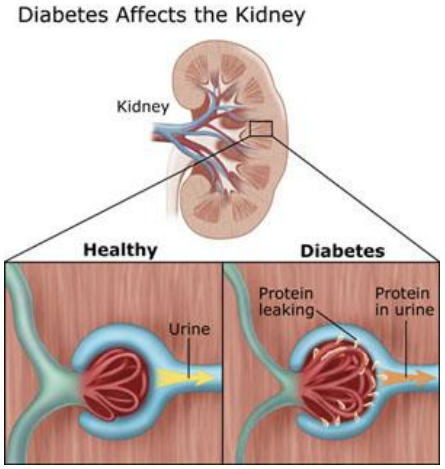


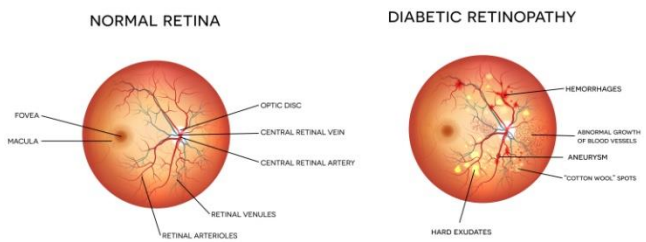
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Diabetische complicaties

- Marcovasculair: CVD, infarct
- Neuropathie
  - Doof gevoel
  - Niet helende wonden
  - Onbalans
- Nefropathie
  - Proteïnurie
  - Niertransplantatie
- Retinopathie
  - Tijdelijk tot blijvend visus verlies
    - Glasvochtbloeding
    - Macula oedeem
    - Netvliesloslating







Vasculaire schade

- Microangiopathie
  - Intracellulaire sorbitol ophoping
  - Oxidatieve stress
  - Stapeling van Advanced Glycation End producten

- Capillaropathie
  - Pericyten
  - Verdikking van basaal membranen
  - Verlies van gladspierweefsel in celwand
  - Proliferatie van endotheel cellen

→ LEKKAGE, OCCLUSIE EN ISCHEMIE



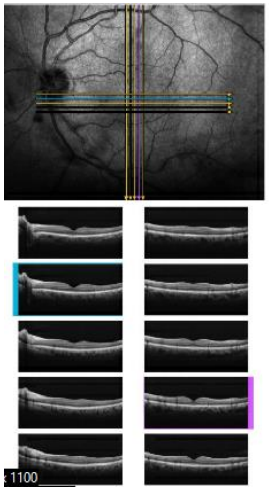
- Neovascularisaties

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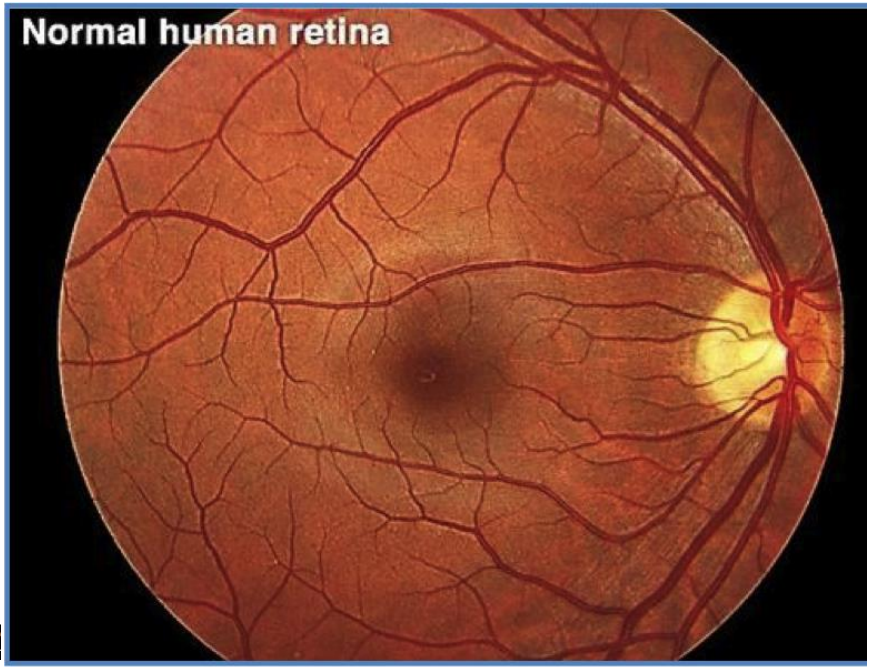
Bron: JJ Kanski Clinical Ophthalmology: A Systematic Approach 7th Edition ISBN-13: 978-0702040931

Funduscopie/fundusfotografie

- Retina: spiegel van het cardiovasculaire systeem in lichaam
- Enige plek waar direct op bloedvaten gekeken kan worden
- OCT scan





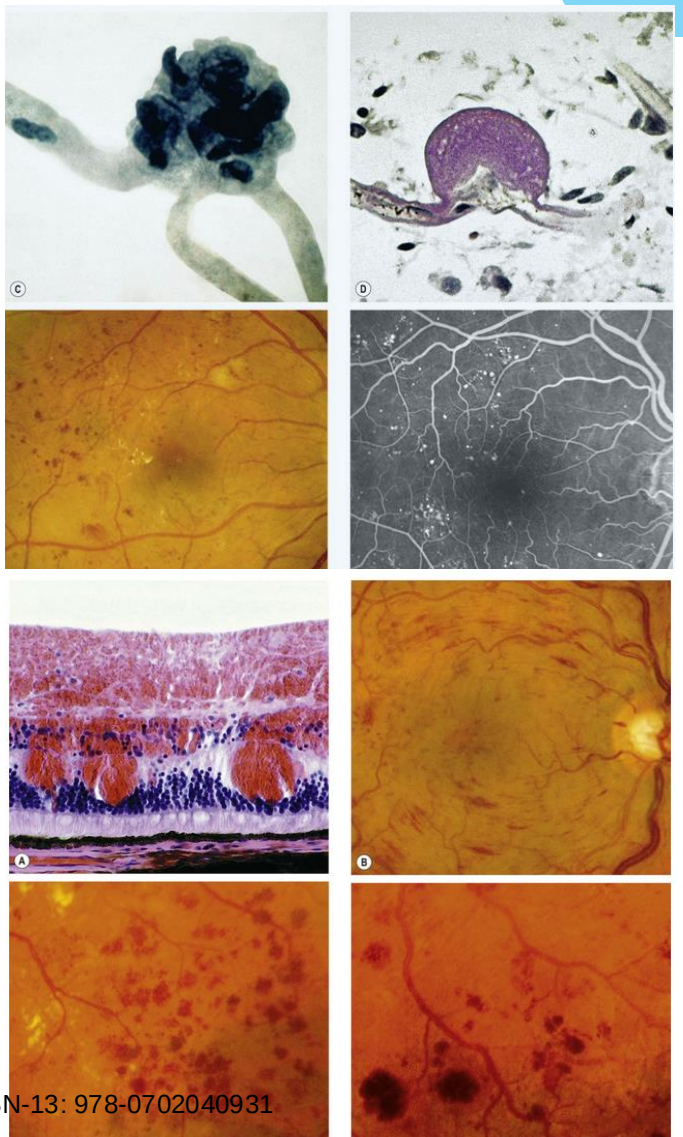


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Diabetische Retinopathie

- Microaneurysmata
  - Dilatatie van capillairen
  - Fusie van een loop

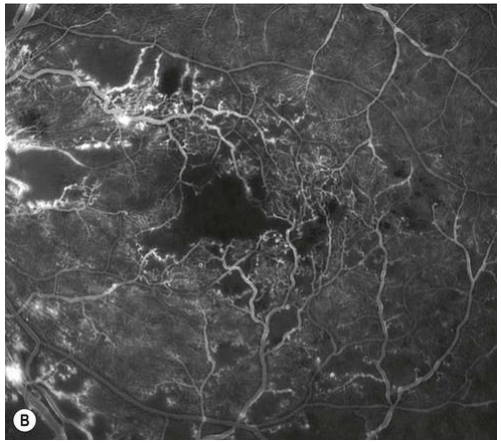
- Bloedingen
  - Zenuwvezellaag
  - Intraretinale bloedingen
  - Diepe retinale infarcten



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Diabetische Retinopathie

- Ischemie



- Proliferatie
  - Nieuw vaatvorming



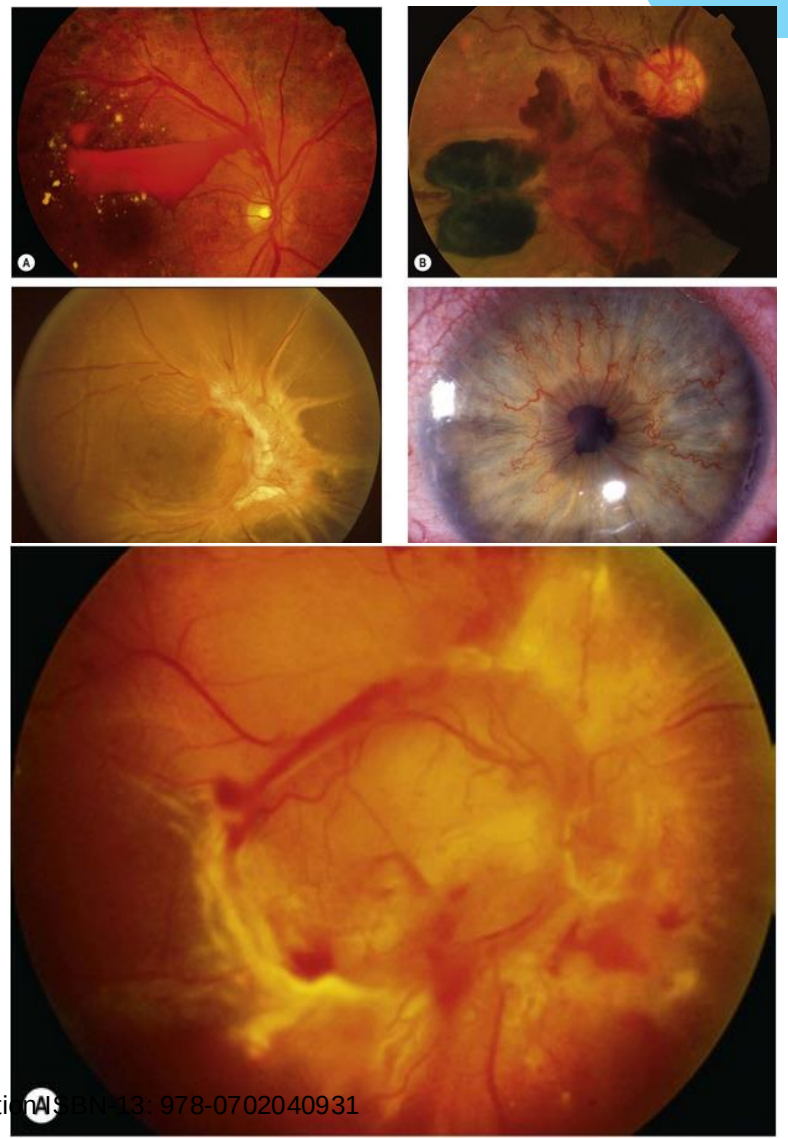
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Diabetische Retinopathie

- Glasvochtbloeding

- Netvliesloslating

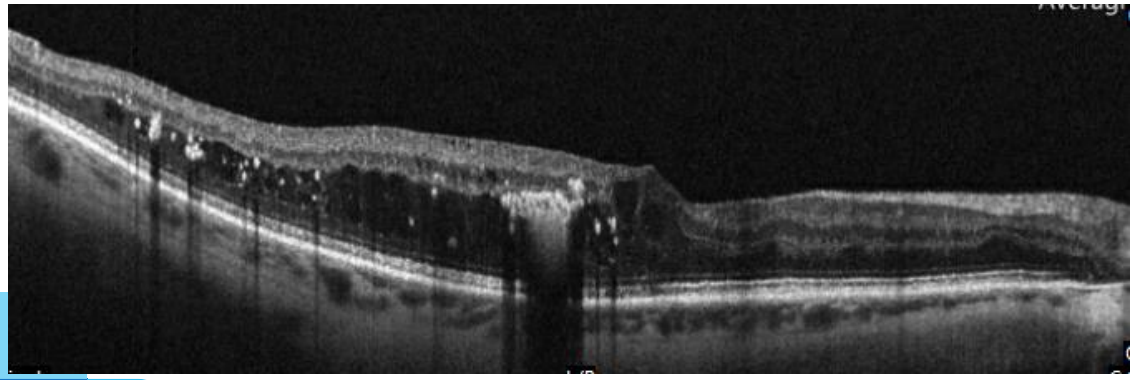


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Diabetisch Maculaoedeem

- Lekkage van vocht in de fovea centralis
  → gebied voor gezichtsscherpte
- Harde exsudaten nabij de fovea

- Bloeddruk reguleren

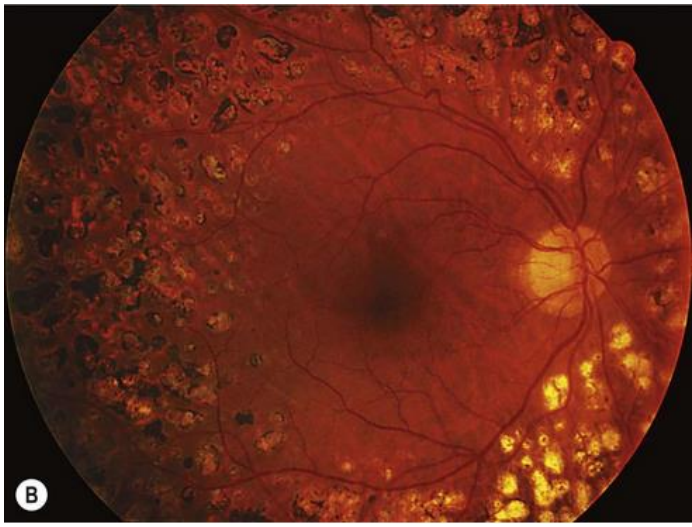




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Behandeling

- Laser photocoagulatie (uitschakelen deel perifere retina)
  - Voorkomen glasvochtbloeding
  - Regressie van neovascularisaties
  - Verlies van perifeer gezichtsveld



- Intravitreale injectie:
  - Anti-VEGF (Avastin, Lucentis,Eylea)
  - Triamcinolon

- Vitrectomie
  - Persisterende glasvochtbloeding
  - Progressieve tractionele netvliesloslating

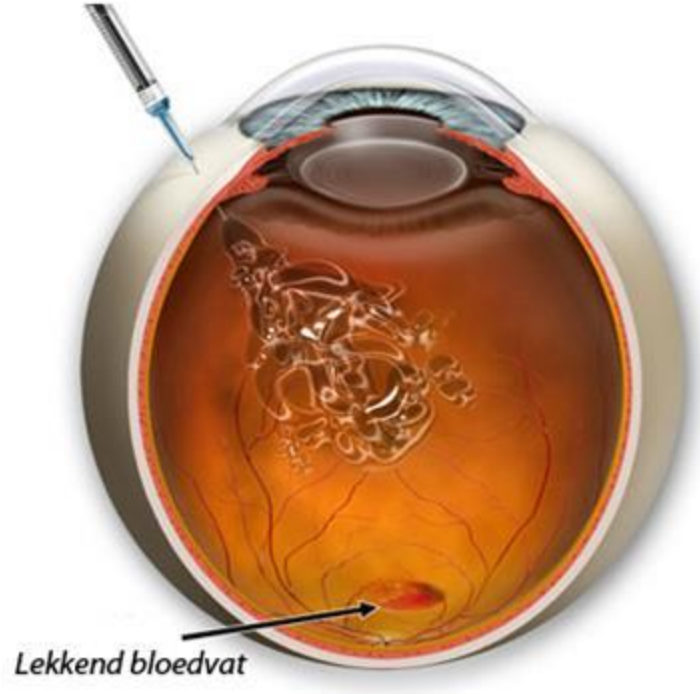
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Behandeling maculaoedeem: anti-VEGF

- Avastin (bevacuzimab): 40 euro per injectie
- Eylea (aflibercept): 800 euro per injectie
- Lucentis (ranibizumab): 900 euro per injectie





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Effect van behandeling



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Wanneer behandelen?

- ETDRS
- Voorkomen blindheid tgv diabetes
- Gradering op basis van funduscopische kenmerken
- Ernstige niet-proliferatieve diabetische retinopathie bij DMII
  - In 4 kwadranten (meer dan 20) bloedingen
  - In 2 kwadranten venous beading
  - In 1 kwadrant IRMA's
- Proliferatieve diabetische retinopathie
  - Glasvochtbloeding bij NVD
  - Grote NVD zonder glasvochtbloeding (1/3 papildiameter)
  - Glasvochtbloeding bij NVE (groter dan ½ papildiameter)

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Follow-up

Category/description	*Management*
Non-proliferative diabetic retinopathy (NPDR)	
No DR	Review in 12 months
Very mild	Review most patients in 12 months
Microaneurysms only	
Mild	Review range 6–12 months, depending on severity of signs, stability, systemic factors, and patient's personal circumstances
Any or all of: microaneurysms, retinal haemorrhages, exudates, cotton wool spots, up to the level of moderate NPDR. No IRMA or significant beading	
Moderate	Review in approximately 6 months PDR in up to 26%, high-risk PDR in up to 8% within a year
• Severe retinal haemorrhages (more than ETDRS standard photograph 2A: about 20 medium-large per quadrant) in 1–3 quadrants *or* mild intraretinal microvascular abnormalities (IRMA) • Significant venous beading can be present in no more than 1 quadrant • Cotton wool spots commonly present	
Severe	Review in 4 months PDR in up to 50%, high-risk PDR in up to 15% within a year
The 4-2-1 rule; one or more of: • Severe haemorrhages in all 4 quadrants • Significant venous beading in 2 or more quadrants • Moderate IRMA in 1 or more quadrants	
Very severe	Review in 2–3 months High-risk PDR in up to 45% within a year
Two or more of the criteria for severe	

Proliferative diabetic retinopathy (PDR)	
Mild–moderate	Treatment considered according to severity of signs, stability, systemic factors, and patient's personal circumstances such as reliability of attendance for review. If not treated, review in up to 2 months
New vessels on the disc (NVD) or new vessels elsewhere (NVE), but extent insufficient to meet the high-risk criteria	
High-risk	Treatment advised – see text Should be performed immediately when possible, and certainly same day if symptomatic presentation with good retinal view
• New vessels on the disc (NVD) greater than ETDRS standard photograph 10A (about ⅓ disc area) • Any NVD with vitreous or preretinal haemorrhage • NVE greater than ½ disc area with vitreous or preretinal haemorrhage (or haemorrhage with presumed obscured NVD/E)	
Advanced diabetic eye disease	See text
See text for description	

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Incidentie en Prevalentie

- Proliferatieve diabetische retinopathie bij 5-10%
- Na 30 jaar diabetes: 90% DRP
- 5% van DMII heeft DRP bij presentatie van de ziekte
- In de VS: 20-64 jaar: meest voorkomende oorzaak van blindheid. 12.000-24.000 mensen per jaar
- 90% van blindheid te voorkomen door vroegtijdige opsporing/behandeling

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Screening

- Vroeg ontdekken, voor klachten er zijn
- ETDRS (1979)
- Screening programma
- Jaarlijkse screening, evt frequenter
- Door oogartsen: volledige retina beoordelen
- Duur

- Behandelcriteria uit deze studie nog steeds geldig en in gebruik

Bron: Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study research group. Arch Ophthalmol. 1985 Dec;103(12):1796-806. PMID: 2866759.

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1979 → 2020

- Enorme verbetering diabetes zorg
- Verbeterde insuline
- Pompen/sensors

- Afname diabetische retinopathie
- 90% van de type II diabetes bij huisarts ontwikkelt geen DRP
- Van alle diabetes patiënten in Nederland krijgt nog ongeveer 35% DRP

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‘Nieuwe’ landelijke richtlijn (2017)

- Obv NHIS studie Scanlon (2015)
- Minder frequent screenen → eens per 3 jaar
- Dmv fundusfotografie (45 graden centrale focus en op oogzenuw focus, 2 foto’s per oog)
- Dit is op basis van hoge standaard diabeteszorg

Bron: Federatie Medisch Specialisten – Richtlijn Diabetische Retinopathie (2017)

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Classificatie

R0 (interval 2 of 3 jaar)	Geen zichtbare retinopathie
R1 (interval 1 jaar)	Milde achtergrondretinopathie; Microaneurysmata en/of retinabloeding (puntvormige bloedingen of 'red dots', maximaal 10)
R2 (verwijzing)	Pre-proliferatief: (matige tot ernstige non-proliferatieve retinopathie); Multipele, ronde of vlekkige bloedingen en/of vastomlijnde IRMA en/of 'venous beading' en/of reduplicatie
R3 (snelle verwijzing)	Proliferatieve retinopathie; Alle nieuwe vaten, pre-retinale fibrose, glasvocht- of pre-retinale bloeding met of zonder loslating door tractie
M0	Geen zichtbare maculopathie
M1 (verwijzing)	Gaat gepaard met R1, R2 of R3. Maculopathie: aanwezigheid van tweedimensionale fotografische markers van diabetische maculopathie; Exsudaat binnen 1 disc diameter van het centrum van de fovea, circinate- of groeps-exsudaten binnen de macula, microaneurysma of bloeding binnen 1 disc diameter van het centrum van de fovea.

Noot: ook bij ernstige niet-diabetische fundusafwijkingen is een verwijzing naar de oogarts geïndiceerd.

Bron: Federatie Medisch Specialisten – Richtlijn Diabetische Retinopathie (2017)

JAMA Top Articles of Decade

JAMA. 2016 Dec 13;316(22):2402-2410. doi: 10.1001/jama.2016.17216.

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan [1], Lily Peng [1], Marc Coram [1], Martin C Stumpe [1], Derek Wu [1], Arunachalam Narayanaswamy [1], Subhashini Venugopalan [2], Kasumi Widner [1], Tom Madams [1], Jorge Cuadros [3], Ramasamy Kim [4], Rajiv Raman [5], Philip C Nelson [1], Jessica L Mega [6], Dale R Webster [1]

Affiliations + expand

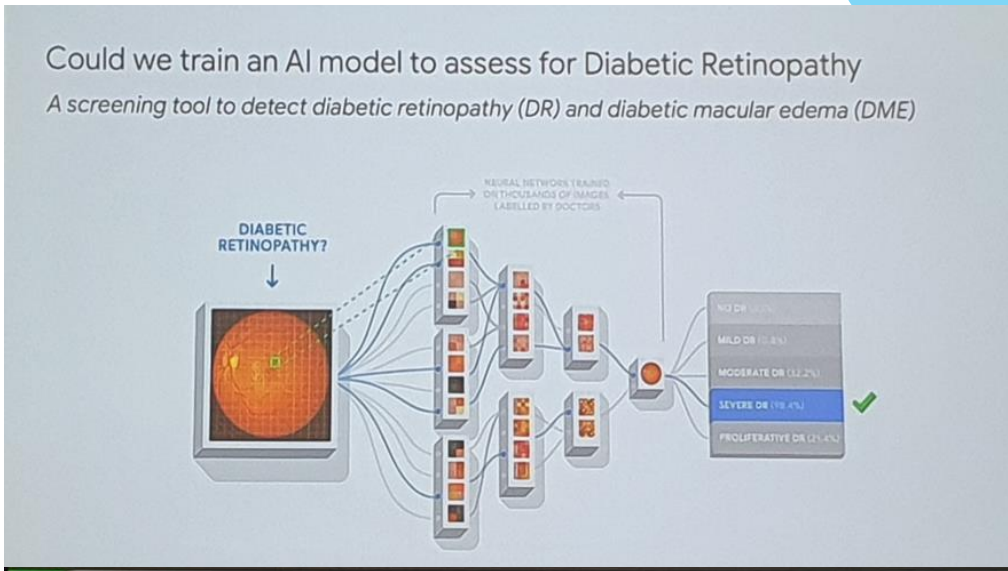
PMID: 27898976 DOI: 10.1001/jama.2016.17216

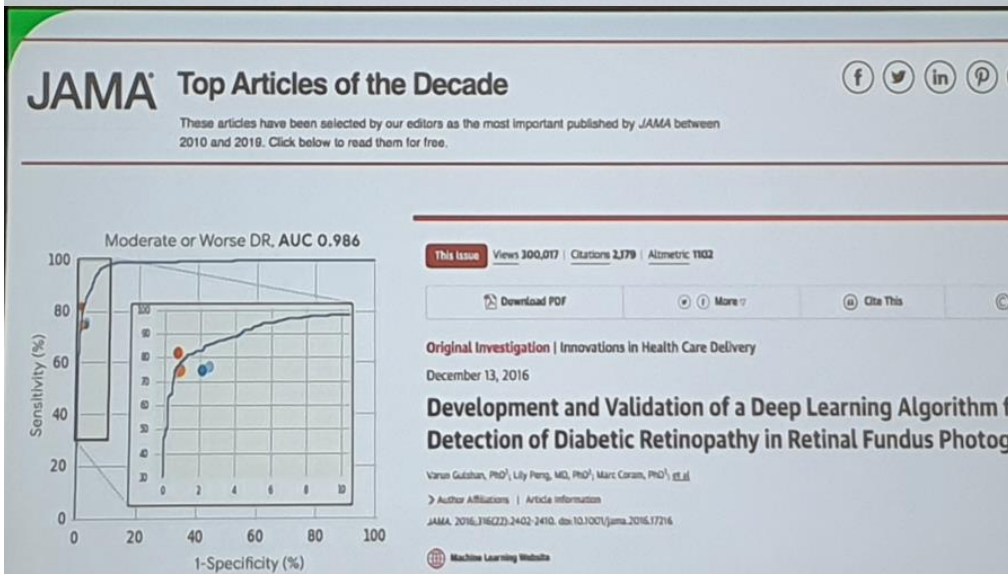
Abstract

Importance: Deep learning is a family of computational methods that allow an algorithm to program itself by learning from a large set of examples that demonstrate the desired behavior, removing the need to specify rules explicitly. Application of these methods to medical imaging requires further assessment and validation.

Objective: To apply deep learning to create an algorithm for automated detection of diabetic retinopathy and diabetic macular edema in retinal fundus photographs.

Design and setting: A specific type of neural network optimized for image classification called a deep convolutional neural network was trained using a retrospective development data set of 128 175 retinal images, which were graded 3 to 7 times for diabetic retinopathy, diabetic macular edema, and image gradability by a panel of 54 US licensed ophthalmologists and ophthalmology senior residents between May and December 2015. The resultant algorithm was validated in January and February 2016 using 2 separate data sets, both graded by at least 7 US board-certified ophthalmologists with high intragrader consistency.



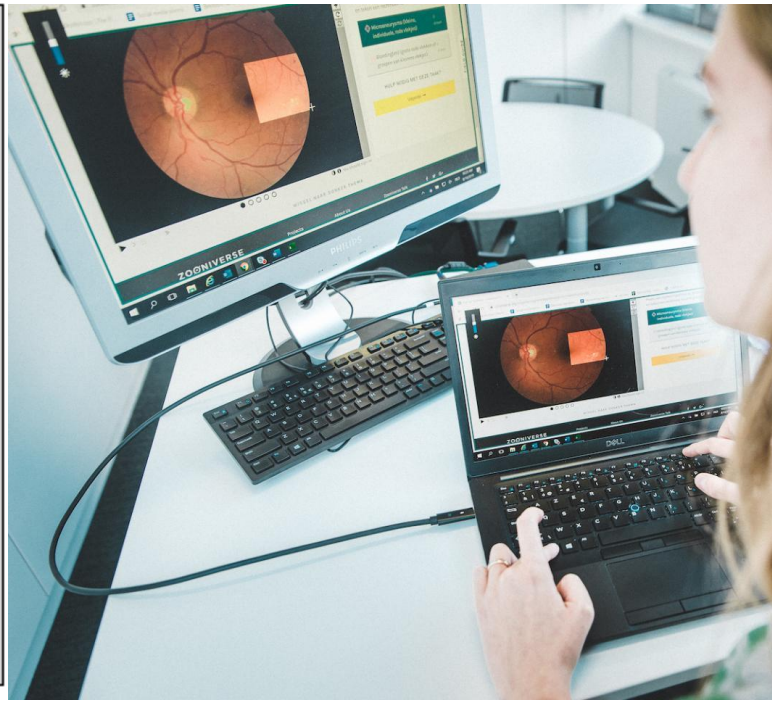


‘Nieuwste’ landelijke richtlijn (2023)

- Geautomatiseerde screening middels AI

Overweeg gebruik van een geautomatiseerd DR-grading-systeem als één van de middelen ter ondersteuning van programmatische screening op diabetische retinopathie bij patiënten met diabetes mellitus:

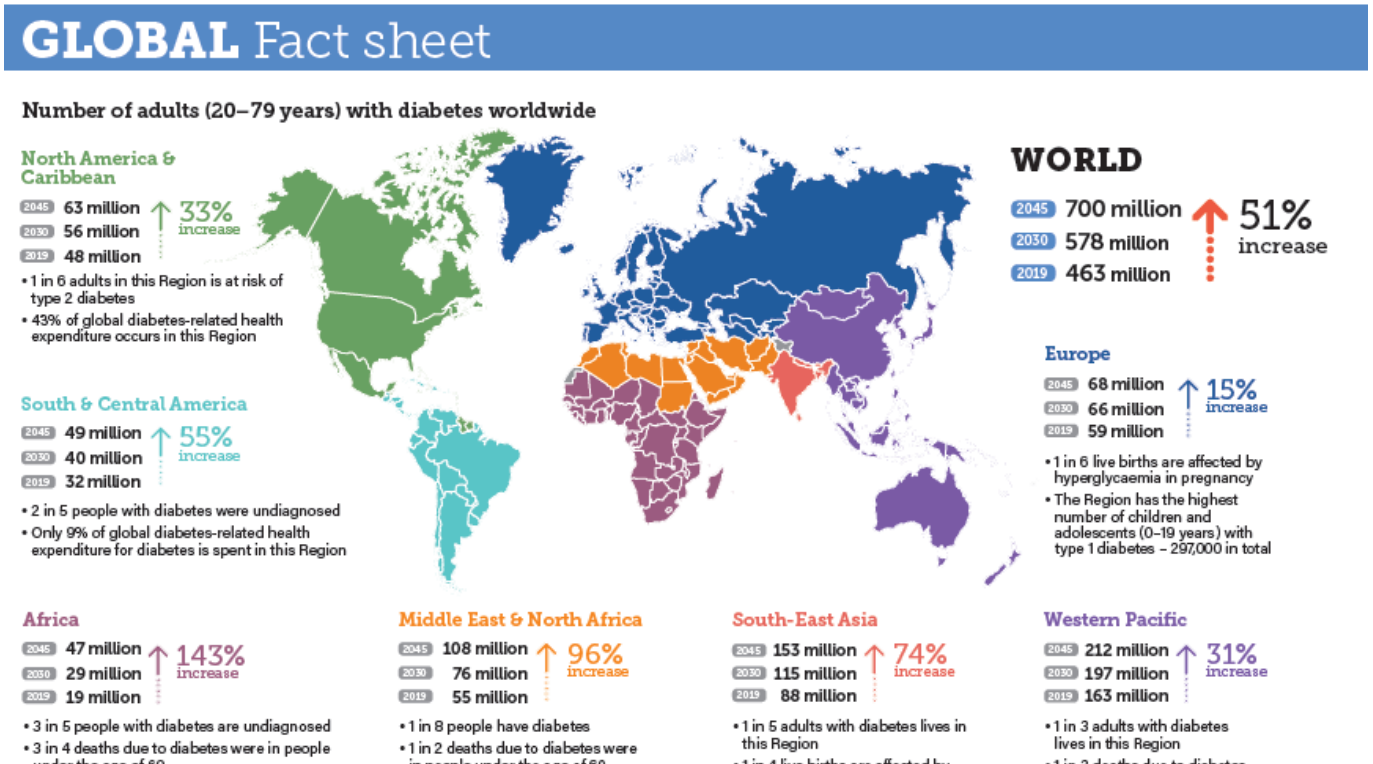
* Zet een automatisch grading-systeem in binnen een ‘triage’ strategie: laat alle positieve uitslagen (referable DR) beoordelen door een humane grader voor doorverwijzing naar een oogarts.
* Gebruik een volgens de Medical Device Directive (MDD) gecertificeerd systeem (klasse IIa CE-geregistreerd) en geef de voorkeur aan een systeem dat additioneel door de FDA goedgekeurd is.
* Wees alert op de uitslag die het systeem geeft, per oog of per twee ogen. Sommige grading-systemen geven alleen een uitslag per twee ogen zodat het niet mogelijk is conform de huidige richtlijn te handelen, dus herhalen van screening bij R1 in een oog, maar doorverwijzen naar oogarts bij R1 in twee ogen.
*Wees bewust dat de performance van automatische grading-systemen met betrekking tot het verschil tussen milde (R1) en geen (R0) diabetische retinopathie niet gerapporteerd is in de literatuur. Daardoor kan mogelijk bij minder patiënten het screening interval van een jaar naar twee of drie jaar verlengd worden.
* Geef voorkeur aan een systeem dat directe terugkoppeling geeft over de kwaliteit van de



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Grootste zorgen – diabetes pandemie

- Wereldwijd: 1/11 mensen diabetes
- 10% van alle zorgkosten wordt aan diabetes uitgegeven
- 79% met diabetes woont in low-middle income countries



Bron: International Diabetes Federation https://idf.org

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Overgewicht in Ghana

- 48,966 Ghanians
- 43% overweight or obese
- Consistent increase from 1998→2016



RESEARCH ARTICLE Open Access

Overweight and obesity epidemic in Ghana—a systematic review and meta-analysis

Richard Ofori-Asenso[1*†], Akosua Adom Agyeman[1†], Amos Laar[2] and Daniel Boateng[3,4]

Abstract

Background: In many low and middle income countries (LMICs), the distribution of adulthood nutritional imbalance is shifting from a predominance of undernutrition to overnutrition. This complex problem poses a huge challenge to governments, non-state actors, and individuals desirous of addressing the problem of malnutrition in LMICs. The objective of this study was to systematically review the literature towards providing an estimate of the prevalence of overweight and obesity among adult Ghanaians.

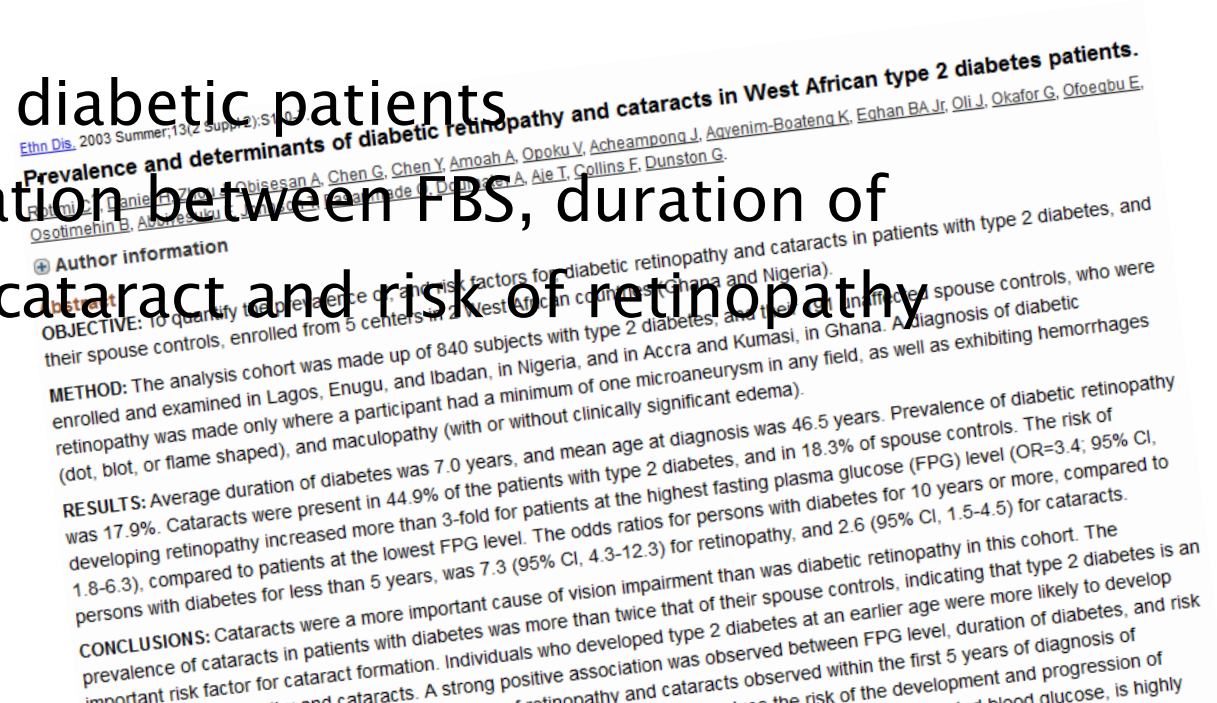
Methods: This study followed the recommendations outlined in the PRISMA statement. Searches were performed in PubMed, Science Direct, google scholar, Africa Journals Online (AJOL) and the WHO African Index Medicus database. This retrieved studies (published up to 31st March 2016) that reported overweight and obesity prevalence among Ghanaians. All online searches were supplemented by reference screening of retrieved papers to identify additional studies.

Results: Forty-three (43) studies involving a total population of 48,966 sampled across all the ten (10) regions of Ghana were selected for the review. Our analysis indicates that nearly 43% of Ghanaian adults are either overweight or obese. The national prevalence of overweight and obesity were estimated as 25.4% (95% CI 22.2–28.7%) and 17.1% (95% CI = 14.7–19.5%), respectively. Higher prevalence of overweight (27.2% vs 16.7%) and obesity (20.6% vs 8.0%) were estimated for urban than rural dwellers. Prevalence of overweight (27.8% vs 21.8%) and obesity (21.9% vs 6.0%) were also significantly higher in women than men. About 45.6% of adult diabetes patients in Ghana are either overweight or obese. At the regional level, about 43.4%, 36.9%, 32.4% and 55.2% of residents in Ashanti, Central, Northern and Greater Accra region, respectively are overweight or obese. These patterns generally mimic the levels of urbanization. Per studies' publication years, consistent increases in overweight and obesity prevalence were observed in Ghana in the period 1998–2016.

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Diabetische Retinopathie in Ghana

- Cohort study in Nigeria and Ghana (Kumasi and Accra)
- 840 patients involved
- 17.9% DRP
- 2x cataract in diabetic patients
- Strong correlation between FBS, duration of diabetes and cataract and risk of retinopathy



Ethn Dis. 2003 Summer;13(2 Suppl 2):S17-24

Prevalence and determinants of diabetic retinopathy and cataracts in West African type 2 diabetes patients.

Rotimi C, Daniel T, Obisesan A, Chen G, Chen Y, Amoah A, Opoku V, Acheampong J, Agyenim-Boateng K, Eghan BA Jr, Oli J, Okafor G, Ofoegbu E, Osotimehin B, Akinkugbe F, Owoaje E, Ogunniyi A, Aje T, Collins F, Dunston G.

Author information

Abstract

OBJECTIVE: To quantify the prevalence of and risk factors for diabetic retinopathy and cataracts in patients with type 2 diabetes, and their spouse controls, enrolled from 5 centers in 2 West African countries (Ghana and Nigeria).

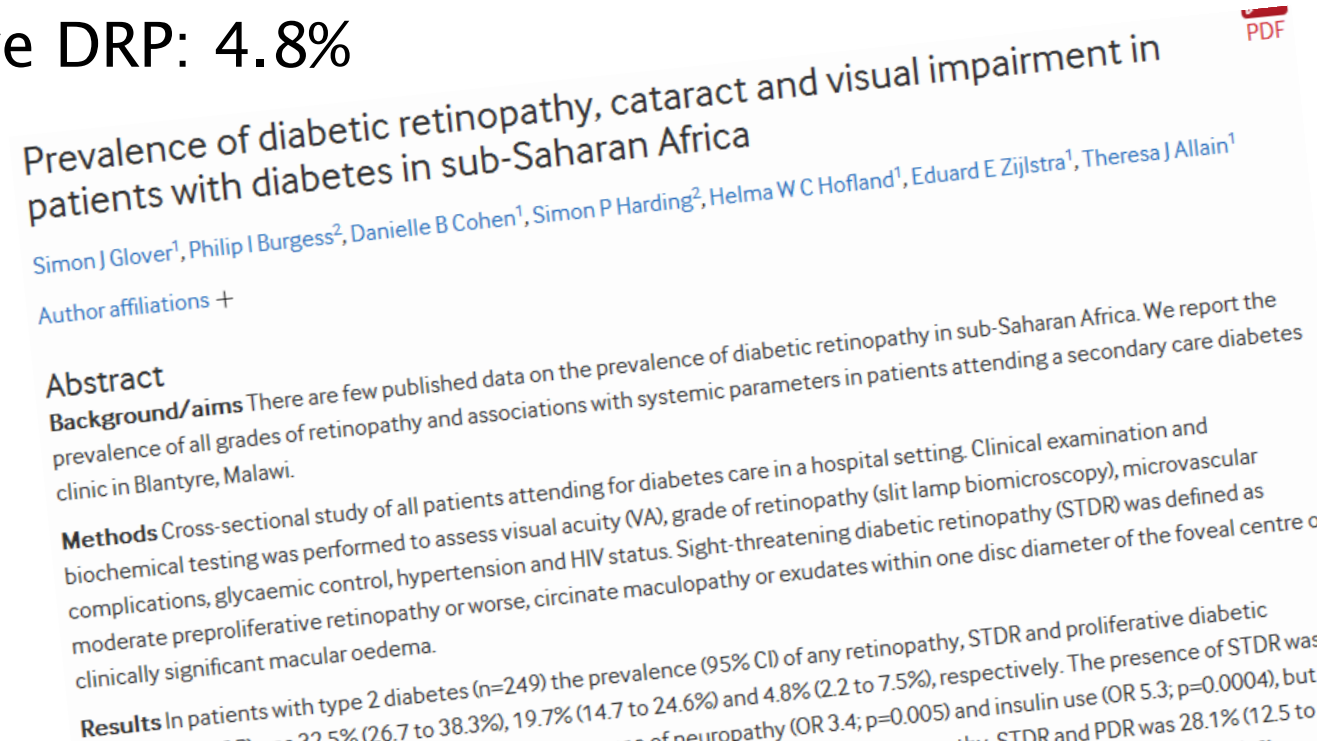
METHOD: The analysis cohort was made up of 840 subjects with type 2 diabetes, and their spouse controls, who were enrolled and examined in Lagos, Enugu, and Ibadan, in Nigeria, and in Accra and Kumasi, in Ghana. A diagnosis of diabetic retinopathy was made only where a participant had a minimum of one microaneurysm in any field, as well as exhibiting hemorrhages (dot, blot, or flame shaped), and maculopathy (with or without clinically significant edema).

RESULTS: Average duration of diabetes was 7.0 years, and mean age at diagnosis was 46.5 years. Prevalence of diabetic retinopathy was 17.9%. Cataracts were present in 44.9% of the patients with type 2 diabetes, and in 18.3% of spouse controls. The risk of developing retinopathy increased more than 3-fold for patients at the highest fasting plasma glucose (FPG) level (OR=3.4; 95% CI, 1.8-6.3), compared to patients at the lowest FPG level. The odds ratios for persons with diabetes for 10 years or more, compared to persons with diabetes for less than 5 years, was 7.3 (95% CI, 4.3-12.3) for retinopathy, and 2.6 (95% CI, 1.5-4.5) for cataracts.

CONCLUSIONS: Cataracts were a more important cause of vision impairment than was diabetic retinopathy in this cohort. The prevalence of cataracts in patients with diabetes was more than twice that of their spouse controls, indicating that type 2 diabetes is an important risk factor for cataract formation. Individuals who developed type 2 diabetes at an earlier age were more likely to develop retinopathy and cataracts. A strong positive association was observed between FPG level, duration of diabetes, and risk of retinopathy and cataracts observed within the first 5 years of diagnosis of the risk of the development and progression of blood glucose, is highly

Diabetische Retinopathie in Afrika

- Blantyre Malawi
- 249 subjects, cross-sectional study
- STDR: 19.7%
- Proliferative DRP: 4.8%



Prevalence of diabetic retinopathy, cataract and visual impairment in patients with diabetes in sub-Saharan Africa

PDF

Simon J Glover[1], Philip I Burgess[2], Danielle B Cohen[1], Simon P Harding[2], Helma W C Hofland[1], Eduard E Zijlstra[1], Theresa J Allain[1]

Author affiliations +

Abstract

Background/aims There are few published data on the prevalence of diabetic retinopathy in sub-Saharan Africa. We report the prevalence of all grades of retinopathy and associations with systemic parameters in patients attending a secondary care diabetes clinic in Blantyre, Malawi.

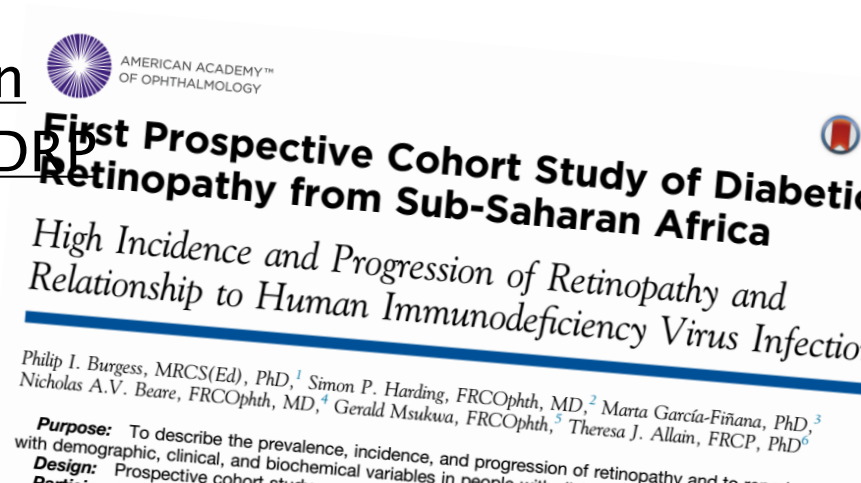
Methods Cross-sectional study of all patients attending for diabetes care in a hospital setting. Clinical examination and biochemical testing was performed to assess visual acuity (VA), grade of retinopathy (slit lamp biomicroscopy), microvascular complications, glycaemic control, hypertension and HIV status. Sight-threatening diabetic retinopathy (STDR) was defined as moderate preproliferative retinopathy or worse, circinate maculopathy or exudates within one disc diameter of the foveal centre o clinically significant macular oedema.

Results In patients with type 2 diabetes (n=249) the prevalence (95% CI) of any retinopathy, STDR and proliferative diabetic 32.5% (26.7 to 38.3%), 19.7% (14.7 to 24.6%) and 4.8% (2.2 to 7.5%), respectively. The presence of STDR was of neuropathy (OR 3.4; p=0.005) and insulin use (OR 5.3; p=0.0004), but STDR and PDR was 28.1% (12.5 to

2012, BMJ

Progressie van DRP in Afrika

- First prospective cohort study of Diabetic Retinopathy
- 357 patients, followed for 24 months
- After 1 year: 10.8% had any form of DRP
- After 2 years: 38% had any form of DRP
- STDR → 3x more common in Africa – Europe
- Background or Preproliferative DRP had 27 – 25% change on STDR
- Negative association between HIV status and progression of DRP OR: 0.2 (95% CI: 0.05-0.85)


AMERICAN ACADEMY™ OF OPHTHALMOLOGY

First Prospective Cohort Study of Diabetic Retinopathy from Sub-Saharan Africa

High Incidence and Progression of Retinopathy and Relationship to Human Immunodeficiency Virus Infectio

Philip I. Burgess, MRCS(Ed), PhD,[1] Simon P. Harding, FRCOphth, MD,[2] Marta García-Fiñana, PhD,[3] Nicholas A.V. Beare, FRCOphth, MD,[4] Gerald Msukwa, FRCOphth,[5] Theresa J. Allain, FRCP, PhD[6]

Purpose: To describe the prevalence, incidence, and progression of retinopathy and to
with demographic, clinical, and biochemical variables in people
Design: Prospective cohort

Behandelopties in tropen

- Laser:
  - Vaak niet beschikbaar
  - Veel hinder van klimatologische omstandigheden
  - Duur in onderhoud
  - Moeilijk om te leren aan eye nurses

- Anti VEGF
  - Bevacuzimab
  - Ziv-aflibercept

- Vitrectomie:
  - Vaak niet verzekerd
  - Alleen in hoofdstad/slechts op 1 of 2 plaatsen

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Laser vs. Intravitreaal anti VEGF

- RCT
- 305 patiënten met proliferatieve DRP
- Prompt panretinale laser behandeling
- Ranibizumab (anti VEGF)

October 2018

Five-Year Outcomes of Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy

A Randomized Clinical Trial

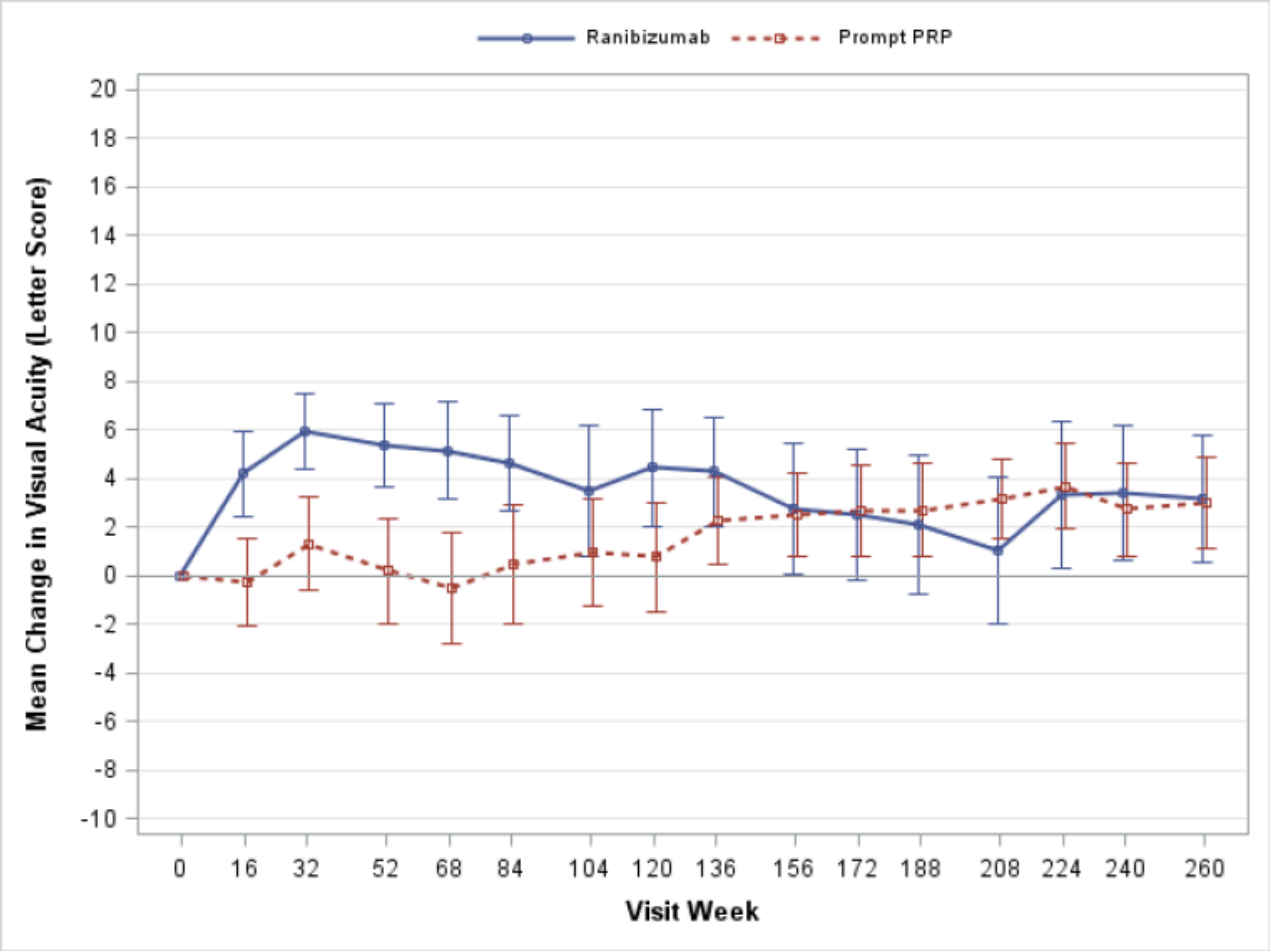
Jeffrey G. Gross, MD[1]; Adam R. Glassman, MS[2]; Danni Liu, MSPH[2]; et al

» Author Affiliations

JAMA Ophthalmol. 2018;136(10):1138-1148. doi:10.1001/jamaophthalmol.2018.3255

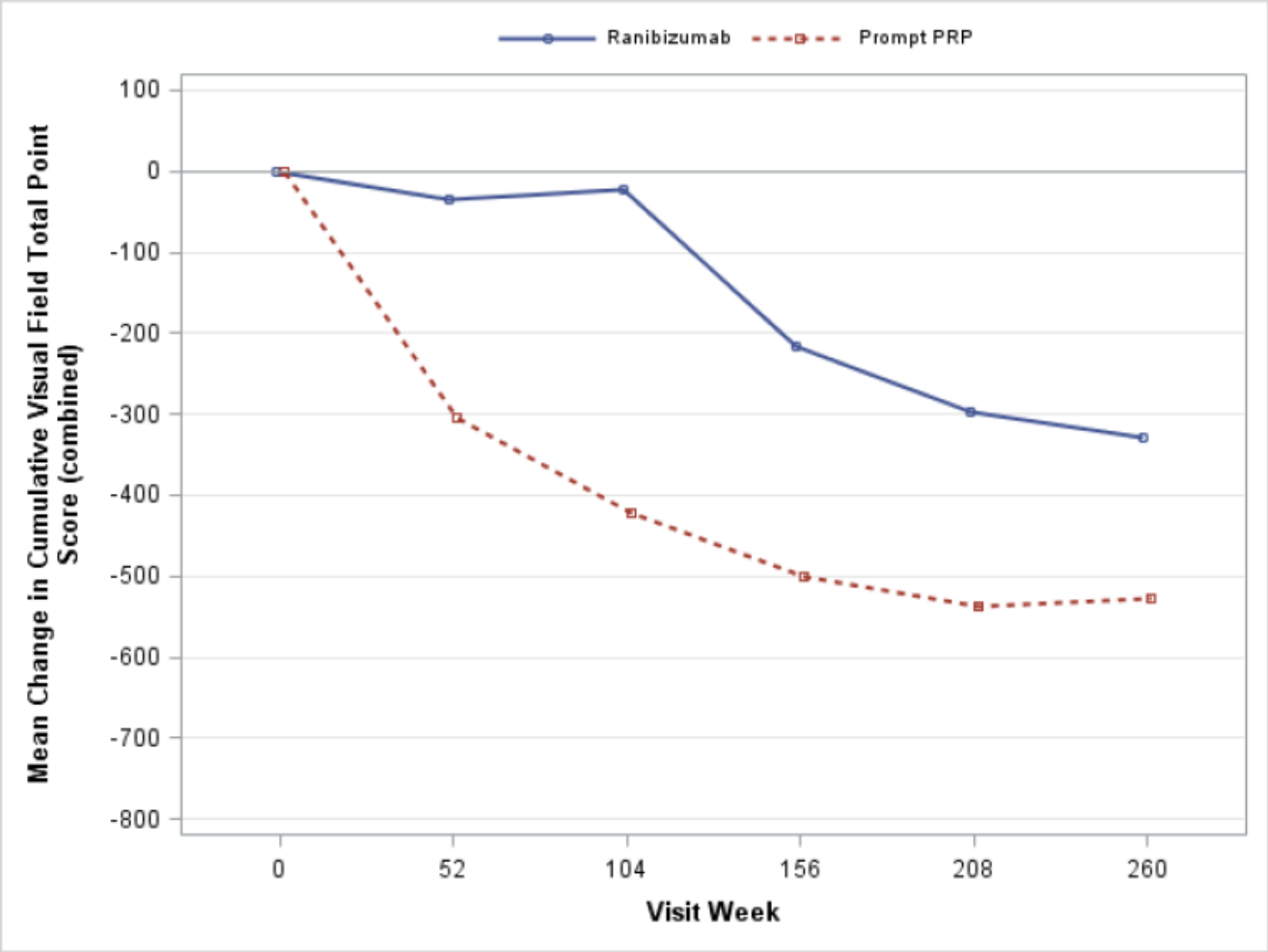
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Visus



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Gezichtsveld

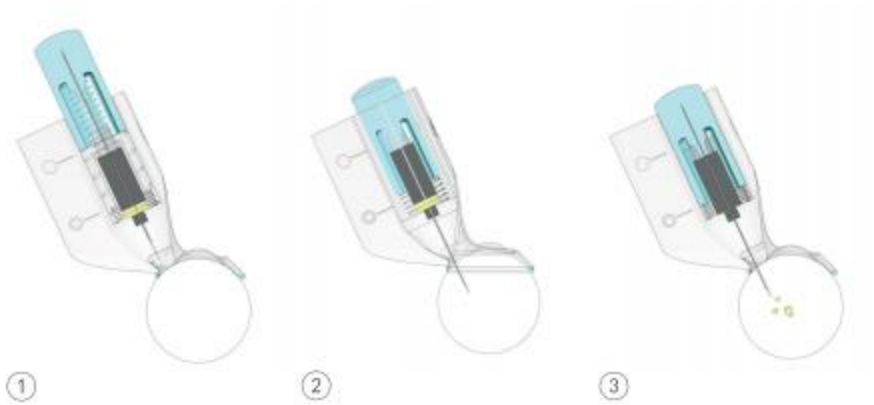


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Mogelijkheden anti VEGF LMIC

- WHO project
- Doelstelling: 1 euro per injectie
- Prefilled
- Biosimilar bevacuzimab
- Geen kans op prikaccidenten
- Geen kans op verkeerd gebruik

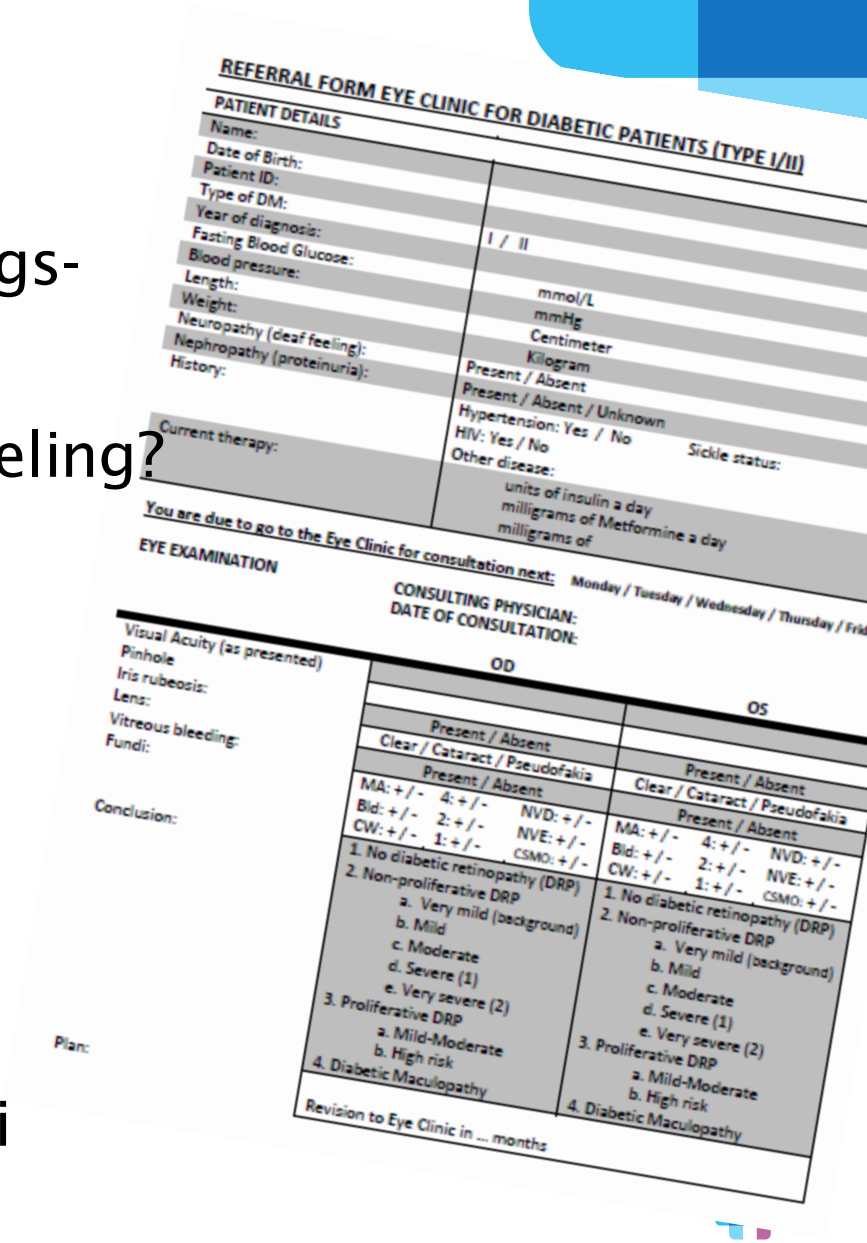




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Screening opzetten

- Informeer naar behandelings-mogelijkheden in land
  - Wie betaalt laser behandeling?
  - Waar staat laser
- Patiënten van reguliere DM poli's doorsturen
- Logistieke uitdaging
  - Overleg met Eye Nurses
  - Fundusfotografie
- Houd behandeling met anti VEGF in achterhoofd



REFERRAL FORM EYE CLINIC FOR DIABETIC PATIENTS (TYPE I/II)

PATIENT DETAILS

Name:
Date of Birth:
Patient ID:
Type of DM: I / II
Year of diagnosis:
Fasting Blood Glucose: mmol/L
Blood pressure: mmHg
Length: Centimeter
Weight: Kilogram
Neuropathy (deaf feeling): Present / Absent
Nephropathy (proteinuria): Present / Absent / Unknown
History: Hypertension: Yes / No Sickle status:
HIV: Yes / No
Other disease:
Current therapy: units of insulin a day
milligrams of Metformine a day
milligrams of

You are due to go to the Eye Clinic for consultation next: Monday / Tuesday / Wednesday / Thursday / Frid

EYE EXAMINATION

CONSULTING PHYSICIAN:
DATE OF CONSULTATION:

	OD	OS
Visual Acuity (as presented)		
Pinhole	Present / Absent	
Iris rubeosis:	Clear / Cataract / Pseudofakia	
Lens:	Present / Absent	
Vitreous bleeding:	MA: + / - 4: + / - NVD: + / - Bid: + / - 2: + / - NVE: + / - CW: + / - 1: + / - CSMO: + / -	
Fundi:	1. No diabetic retinopathy (DRP) 2. Non-proliferative DRP a. Very mild (background) b. Mild c. Moderate d. Severe (1) e. Very severe (2) 3. Proliferative DRP a. Mild-Moderate b. High risk 4. Diabetic Maculopathy	

Conclusion:

Plan:

Revision to Eye Clinic in ... months

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Samenvattend

- Diabetes is een visusbedreigende aandoening waarbij screening EN BEHANDELING een bewezen effect heeft op behoud visus

- Toenemende welvaart in low-middle income countries en pandemie van diabetes

- Screenings en behandelingsstrategieën in de tropen voor diabetische retinopathie kunnen mogelijk anders zijn

- Probeer aansluiting te vinden bij lokale screenings/behandelingsprogramma's

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Vragen?







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