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The association between diabetic retinopathy and other complications of diabetes

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Date of preparation: September 2017 | G.MKT.SM.STH.09.2017.1465 | UKMED08170286 | L.PT.MKT.09.2017.1621

The Vision Academy is an educational initiative that is fully funded by Bayer.

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Financial disclosures

- Honoraria / research support from:
  - Bayer
  - BI
  - Lilly
  - MSD
  - Novartis
  - Novo Nordisk
  - Sanofi
  - Takeda

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BI, Boehringer Ingelheim; MSD, Merck Sharp & Dohme.

Diabetes is associated with a variety of complications

- Diabetes and its complications account for more than 2 million deaths every year
- These impose substantial economic costs on:
  - Patients and their families
  - Healthcare systems
  - National economies (e.g. due to loss of work or wages)
- Together with preventing and delaying the onset of diabetes, early detection and management of complications are important for reducing the health and economic burden of diabetes

Could a greater awareness of diabetic eye disease enable the early detection and management of other diabetic complications?

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NCD Risk Factor Collaboration (NCD-RisC). *Lancet* 2016; 387 (10027): 1513–1530.

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The role of the Vision Academy

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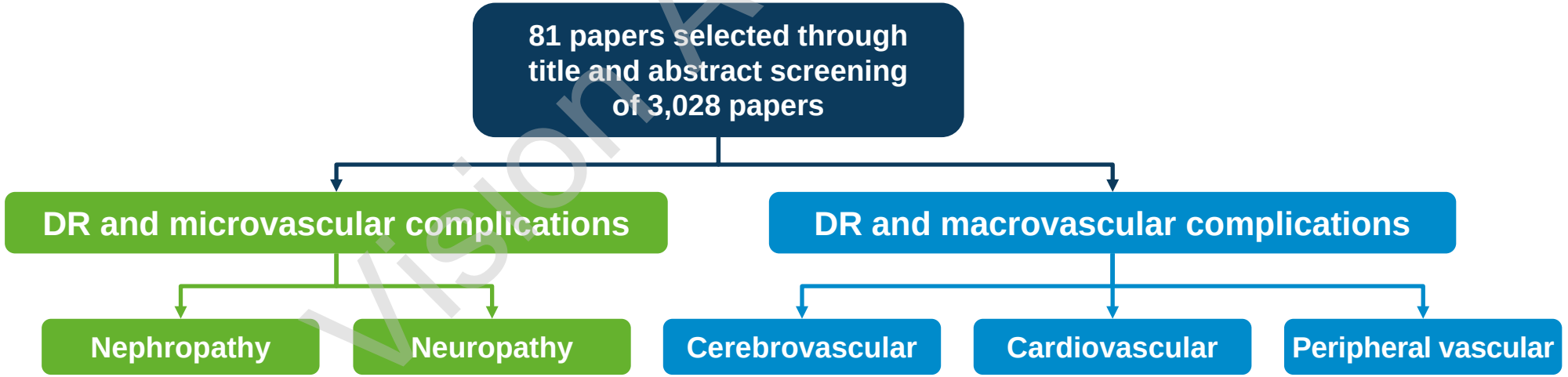
The role of the Vision Academy

- Currently, there is a lack of communication between the various healthcare professionals involved in the treatment of patients with diabetes
- A literature search was performed to examine the relationship between **DR** and other **microvascular** and **macrovascular** complications of diabetes, with the aim of opening up important communication channels between diabetologists and ophthalmologists in order to improve the coordinated care of patients with diabetes



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DR, diabetic retinopathy.

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DR and microvascular complications of diabetes

DR, diabetic retinopathy.

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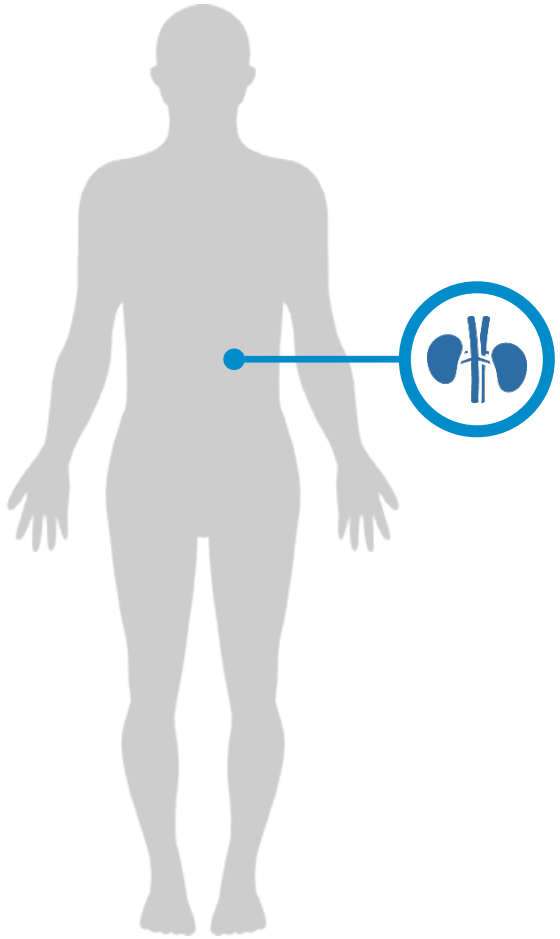
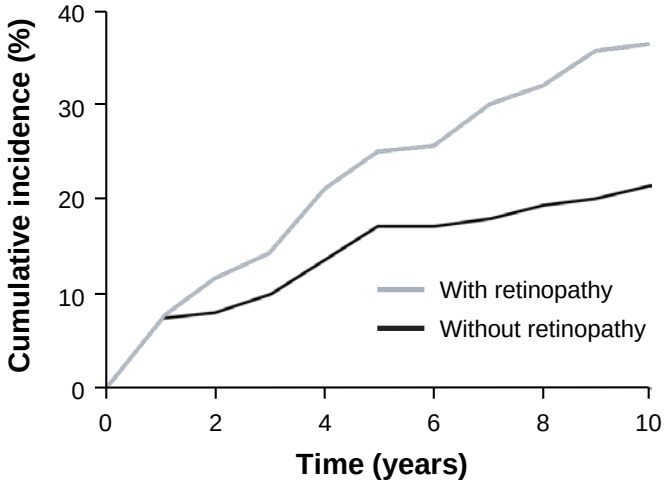
Nephropathy: Literature review findings



DR increases the likelihood of having or developing nephropathy[1–3]

- DR is a significant independent predictor for progression to **micro-** or **macro-albuminuria**[1]
  - However, it is unclear whether albuminuria predicts development of DR[4–6]
- DR is also linked with **declining GFR**[3,7]
  - The severity of DR at baseline can predict the rate of decline in estimated GFR[3]

Cumulative incidence of nephropathy with and without DR*,[1]



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*Follow-up in 537 patients with type 1 diabetes and normal urinary albumin levels at baseline. DR, diabetic retinopathy; GFR, glomerular filtration rate.

1. Rossing P *et al*. *Diabetes Care* 2002; 25 (5): 859–864. 2. Parving H-H *et al. Kidney Int* 2006; 69 (11): 2057–2063. 3. Rossing K *et al. Kidney Int* 2004; 66 (4): 1596–1605.
4. Kotlarsky P *et al*. *Int Ophthalmol* 2015; 35 (1): 59–66. 5. Romero-Aroca P *et al*. *Diabetes Res Clin Pract* 2011; 94 (1): 126–132. 6. Hammes H-P *et al*. *PLoS One* 2015; 10 (7): e0132492.
7. Moriya T *et al*. *Diabetes Care* 2013; 36 (9): 2803–2809.

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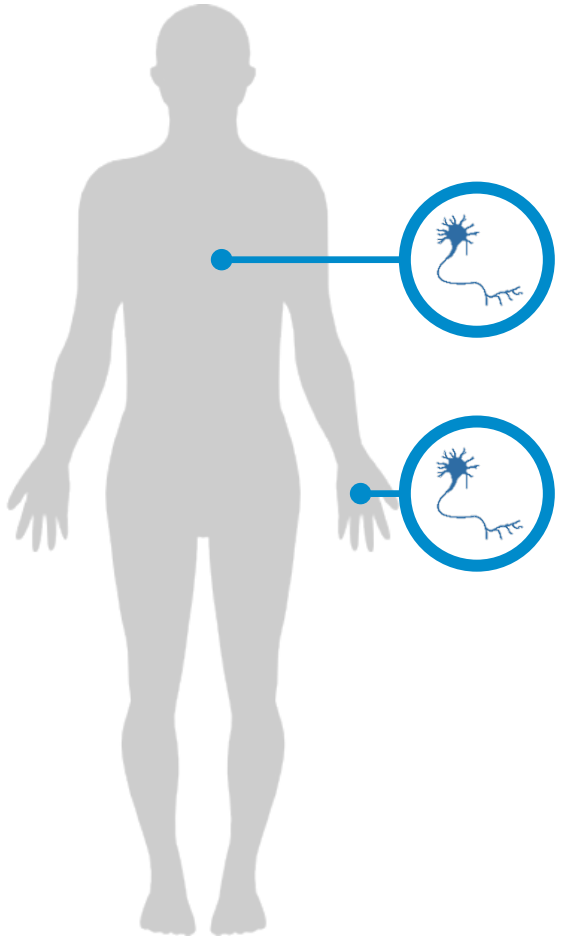
Neuropathy: Literature review findings



DR is associated with cardiac autonomic neuropathy (CAN)[1,2]

- The risk of CAN is increased in the presence of DR[1]
- In patients with T2DM, the stage of DR is independently associated with CAN[2]

DR is associated with diabetic peripheral neuropathy (DPN)[3–6]

- DR is a significant risk factor for DPN, which leads to hospitalization more frequently than other complications of diabetes[3,7]
  - The risk of DPN is greater in patients with proliferative DR than in those with early stage DR[4]

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CAN, cardiac autonomic neuropathy; DPN, diabetic peripheral neuropathy; DR, diabetic retinopathy; T2DM, type 2 diabetes mellitus.

1. Voulgari C *et al. J Diabetes Complications* 2011; 25 (3): 159–167. 2. Huang C-C *et al. J Diabetes Res* 2016; 2016: 6090749. 3. Kostev K *et al. Prim Care Diabetes* 2014; 8 (3): 250–255.
4. Lin I-C *et al. Acta Ophthalmol* 2015; 93 (8): 713–718. 5. Dyck PJ *et al. Diabetes Care* 1999; 22 (9): 1479–1486. 6. Abougalambou SSI *et al. Diabetes Metab Syndr* 2015; 9 (2): 98–103.
7. Bansal V *et al. Postgrad Med J* 2006; 82 (964): 95–100.

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DR and macrovascular complications of diabetes

DR, diabetic retinopathy.

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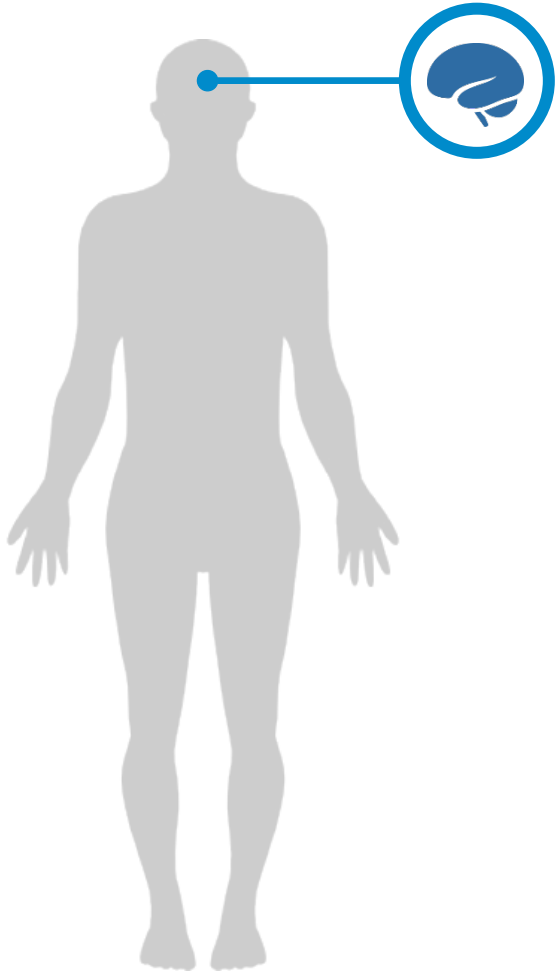
Cerebrovascular complications: Literature review findings



DR is a strong predictor of stroke[1–4]

- Even in mild-to-moderate forms, DR was identified as an independent risk factor for stroke[2,3]
  - Severe DR independently increased the risk of cerebral infarction and cerebral hemorrhage in patients with T1DM[4]
  - A large prospective study in patients with T2DM found DR to be associated only with small artery ischemic stroke[5]

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DR, diabetic retinopathy; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

1. Petitti DB *et al. Stroke* 1995; 26 (4): 593–596. 2. Cheung N *et al. Stroke* 2007; 38 (2): 398–401. 3. Klein BEK *et al*. *Arch Intern Med* 2004; 164 (17): 1917–1924.
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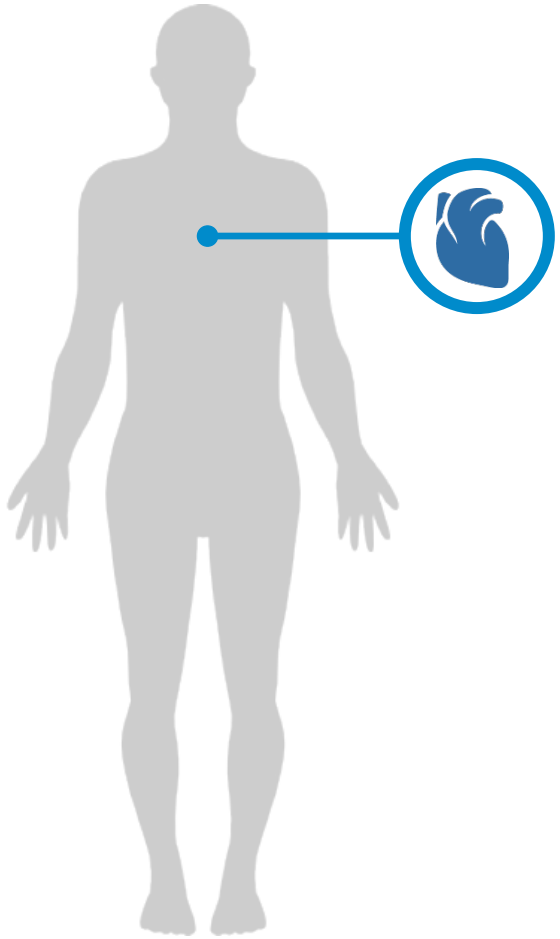
Cardiovascular complications: Literature review findings



DR is associated with subclinical atherosclerosis[1–3]

- The presence of DR was independently associated with **carotid intima media thickness** and **carotid plaques** in patients with T2DM[3–5]

DR is an independent risk factor for cardiovascular disease[6–9]

- In patients with T2DM, DR was associated with an increased risk of **CHD-related events/deaths**[10,11]

DR (number at risk)	Incident CHD events		Fatal CHD events	
	Number (%) of events	Multivariate HR (95% CI)	Number (%) of events	Multivariate HR (95% CI)
Absent (n=1,242)	153 (12.3)	1.0	19 (1.5)	1.0
Present (n=214)	44 (20.6)	**1.99** (1.33–3.00)	13 (6.1)	**3.00** (1.27–7.09)

Table adapted from Cheung *et al.* 2007[11]

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CI, confidence interval; CHD, coronary heart disease; DR, diabetic retinopathy; HR, hazard ratio; T2DM, type 2 diabetes mellitus.

1. Liu Y *et al. Diab Vasc Dis Res* 2015; 12 (5): 366–372. 2. Saif A *et al. Endocr Pract* 2015; 21 (3): 226–230. 3. Rema M *et al. Diabetes Care* 2004; 27 (8): 1962–1967.
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10. Kawasaki R *et al. Ophthalmology* 2013; 120 (3): 574–582. 11. Cheung N *et al. Diabetes Care* 2007; 30 (7): 1742–1746.

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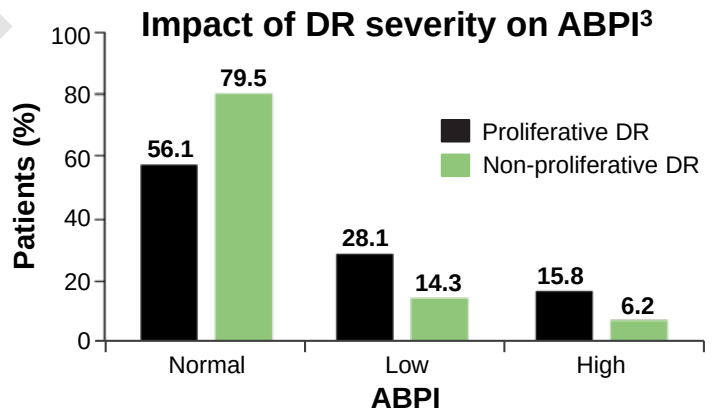
Peripheral vascular complications: Literature review findings

DR is associated with peripheral arterial disease (PAD)[1–3]

- Patients with proliferative DR are more likely to have an **abnormal ABPI** than patients with non-proliferative DR[3]



DR is associated with soft tissue complications[4–7]

- DR is an independent risk factor for **foot ulceration,** and a key risk factor for **lower extremity amputation**[4–7]
  - Similarly, patients who have non-healing foot ulcers or who have had lower extremity amputations are high risk of developing and progressing DR[8,9]

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ABPI, ankle–brachial pressure index; DR, diabetic retinopathy; PAD, peripheral arterial disease.

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4. Baba M *et al. Diabetes Res Clin Pract* 2014; 106 (1): 42–49. 5. Leymarie F *et al. Diabetes Metab* 2005; 31 (6): 603–605. 6. Bruun C *et al. Diabet Med* 2013; 30 (8): 964–972.
7. Parisi MCR *et al. Diabetol Metab Syndr* 2016; 8: 25. 8. Nwanyanwu KH *et al. Diabetes Care* 2013; 36 (6): 1562–1568. 9. Mohammedi K *et al. Cardiovasc Diabetol* 2016; 15 (1): 129.

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Session summary

- A literature review of **81 studies** in **>400,000 patients** found that DR can be a predictor of numerous microvascular and macrovascular complications of diabetes

- Conversely, some systemic complications of diabetes are linked to a higher risk of developing or progressing DR

- These findings demonstrate the need for **prompt referral** and **screening** for DR and other complications of diabetes, and highlight the need for a **coordinated approach** to diabetes management

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DR, diabetic retinopathy.