# MODULE 2.5
## Complications - The Human Costs of Diabetes

Diabetes is a metabolic condition defined by a disorder of carbohydrate metabolism, resulting in hyperglycemia. Chronically high levels of blood glucose over time damage blood vessel walls, making them more prone to atherosclerotic plaque formation and restricted blood flow.[1,2] As a consequence, significant complications can develop, including cardiovascular disease (CVD) and stroke, renal disease and failure, eye disease and blindness, lower-limb amputations, neuropathy, and dental disease.[1]

**Cardiovascular Disease**

Not surprisingly, hypertension is a common complication of diabetes. In a US Centers for Disease Control and Prevention (CDC) survey of adults with diabetes conducted between 2009 and 2012, 71% had high blood pressure of 140/90 mm Hg or higher or were taking a prescription antihypertensive agent.[3] According to the American Heart Association, adults with diabetes are 2 to 4 times more likely to have heart disease than adults without diabetes.[4] In fact, the most common causes of disability or death among adults with type 2 diabetes are heart disease and stroke.[4] In up to 65% of individuals with diabetes, death is attributable to heart disease or stroke.[4] In adults with diabetes, comorbid conditions such as hypertension, dyslipidemia, or atrial fibrillation raise the risk of stroke by as much as 4-fold.[5]

**Renal Disease**

Diabetes is a leading cause of renal impairment and failure.[6] Diabetic nephropathy is associated with progressive histologic changes in glomeruli, impairing filtration. Approximately 30% of individuals with type 1 diabetes and 10% to 40% of individuals with type 2 diabetes will eventually develop renal failure.[7] In 2011, 44% of all new cases of renal failure were attributed to diabetes.[3]

**Eye Disease and Blindness**

Diabetes is a major cause of eye disease and the leading cause of new cases of adult blindness.[8] Approximately one-third of all individuals with diabetes develop some form of diabetes-related eye damage.[6] Eye diseases associated with diabetes include[9]:

- Diabetic retinopathy
- Diabetic macular edema
- Cataract
- Glaucoma
- Anterior ischemic optic neuropathy
- Retinal vascular occlusion

Diabetic retinopathy is the most common complication of diabetes and the leading cause of blindness among working-aged adults worldwide.[10,11] A meta-analysis that examined the results of 35 studies conducted between 1980 and 2008 in 22,896 individuals with diabetes living in the US, Australia, Europe, and Asia found the global prevalence of diabetic retinopathy to be 34.6%.[10] A recent CDC-sponsored study found the estimated prevalence of diabetic retinopathy was 28.5% among American adults with diabetes, with 4.4% having vision-threatening diabetic retinopathy.[12] The number of American adults 40 years or older with diabetic retinopathy is projected to reach 16 million by 2050.[13]

The most common cause of vision loss from diabetic retinopathy is diabetic macular edema.[14] The global prevalence of diabetic macular edema among individuals with type 1 or type 2 diabetes varies by geographic region, from as low as 11.4% in European countries to as high as 45.3% in North American countries.[6]

For individuals with type 2 diabetes, the risk of developing a cataract is nearly double the risk for those without diabetes.[15] In a meta-analysis of 8 studies conducted in 20,837 individuals, type 2 diabetes raised the odds ratio of developing a cataract to 1.97 (95% CI, 1.45-2.67; P <.001).[15]

The risk of glaucoma, another eye disease with the potential to cause blindness, is also more prevalent in individuals with diabetes. Based on a meta-analysis of 47 studies conducted in 2,981,342 individuals living in 16 countries, the pooled relative risk for glaucoma in individuals with diabetes relative to those without diabetes was 1.48 (95% CI, 1.29-1.71; P< .001).[16]

Individuals with untreated diabetes are 25 times more likely to become blind than the general population.[17]

**Amputation**

Individuals with diabetes are 25 times more likely to require foot or lower-limb amputation than those without diabetes.[6] In the US in 2010, approximately 60% of nontraumatic lower-limb amputations were performed on adults (20 years or older) with diabetes.[3]

**Neuropathy**

Chronic hyperglycemia and hypertension can also damage nerves throughout the body, leading to neuropathies.[1,6] Bodily functions commonly affected by neuropathies are digestion, urination, and penile erection.[6] In a population-based, longitudinal survey of individuals with type 1 or type 2 diabetes,

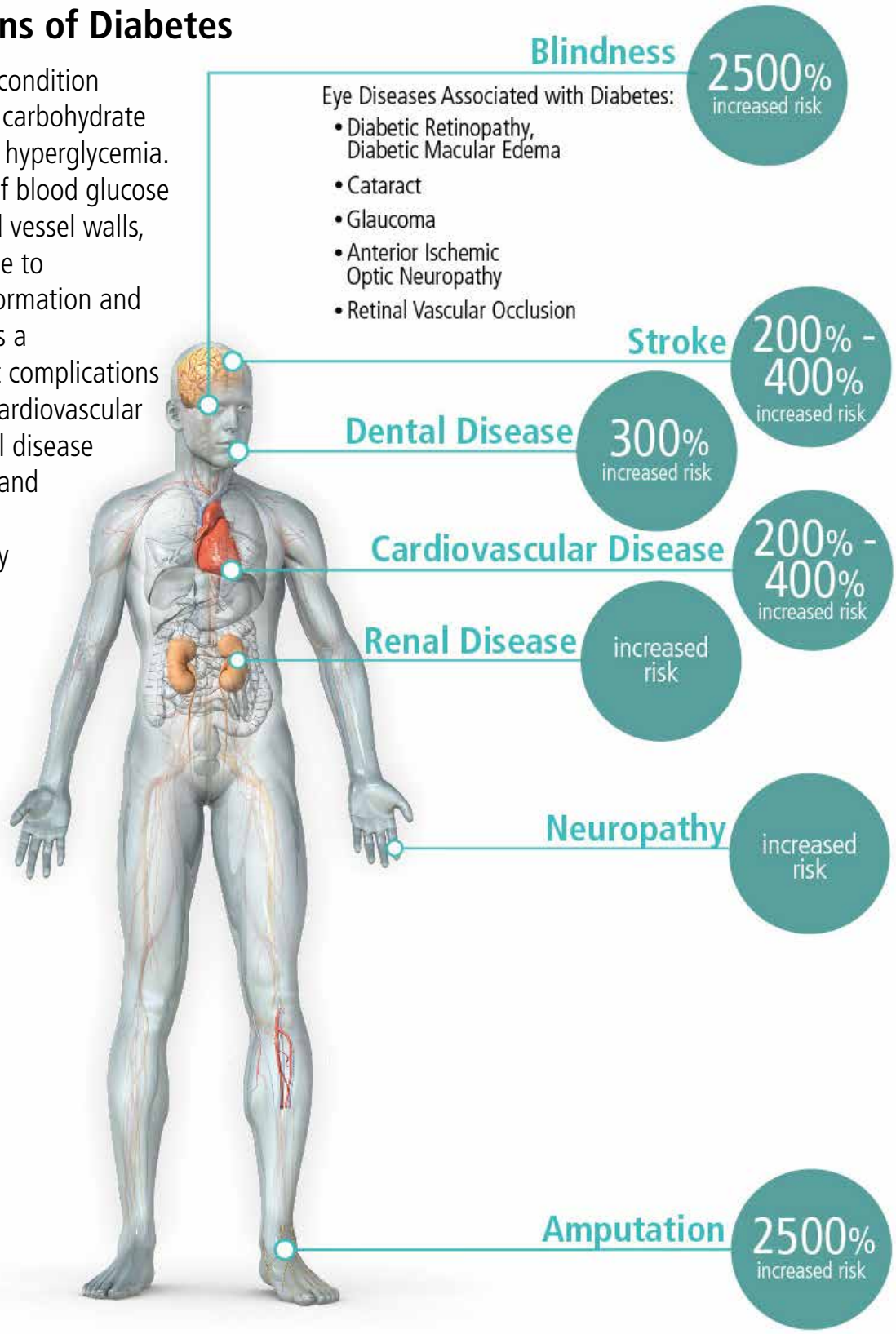
approximately two-thirds of all individuals with diabetes had objective evidence of neuropathy, and 20% had symptomatic neuropathy.[18]

**Dental Disease**

Diabetes increases the risk of gum inflammation (gingivitis) in people with diabetes who have poor glucose control. The clinical significance of gingivitis is that it is a major cause of tooth loss, and may also contribute to the risk of CVD.[6]

## The Complications of Diabetes

Diabetes is a metabolic condition defined by a disorder of carbohydrate metabolism, resulting in hyperglycemia. Chronically high levels of blood glucose over time damage blood vessel walls, making them more prone to atherosclerotic plaque formation and restricted blood flow. As a consequence, significant complications can develop, including cardiovascular disease and stroke, renal disease and failure, eye disease and blindness, lower-limb amputations, neuropathy and dental disease.



## References

1. National Institute of Diabetes and Digestive and Kidney Disease. *Causes of Diabetes*. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; 2014. NIH Publication No. 14-5164. http://diabetes.niddk.nih.gov/dm/pubs/causes/Causes_of_Diabetes_508.pdf. Accessed October 14, 2015.

2. National Institute of Diabetes and Digestive and Kidney Disease. *Causes. Diabetes, Heart Disease, and Stroke.* Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; 2013. http://diabetes.niddk.nih.gov/dm/pubs/stroke/DM_Heart_Stroke_508.pdf. NIH Publicaiton No. 13-5094. Accessed October 14, 2015.

3. Centers for Disease Control and Prevention. *National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014*. Atlanta, GA: US Department of Health and Human Services; 2014. www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf. Accessed October 14, 2015.

4. American Heart Association. Cardiovascular disease & diabetes.. www.heart.org/HEARTORG/Conditions/Diabetes/WhyDiabetesMatters/Cardiovascular-Disease-Diabetes_UCM_313865_Article.jsp. Last updated January 31, 2013. Accessed October 14, 2015.

5. National Stroke Association. Medical risk factors. http://www.stroke.org/understand-stroke/preventing-stroke/-medical-risk-factors?pagename=diabetes. Accessed October 14, 2015.

6. Guariguata L, Nolan T, Beagley J, Linnenkamp U, Jacqmain O. *IDF Diabetes Atlas.* 6th ed. Brussels, Belgium: International Diabetes Foundation; 2013. www.idf.org/diabetesatlas. Accessed October 14, 2015.

7. National Kidney Foundation. Diabetes - a major risk factor for kidney disease. www.kidney.org/atoz/content/diabetes. Accessed October 14, 2015.

8. Centers for Disease Control and Prevention. Diabetic retinopathy. www.cdc.gov/visionhealth/pdf/factsheet.pdf. Accessed October 14, 2015.

9. Chous P. Diabetes and eye disease: what people with diabetes and healthcare professionals need to know. *Diabetes Voice.* 2009;54(3):30-33.

10. Yau JW, Rogers SL, Kawasaki R, et al for the Meta-Analysis for Eye Disease (META)EYE) Study group. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35(3):556-564.

11. Sivaprasad S, Gupta B, Crosby-Nwaobi R, Evans J. Prevalence of diabetic retinopathy in various ethnic groups. *Surv Ophthalmol*. 2012;57(4):347-370.

12. Zhang X, Saaddine JB, Chou C-F, et al. Prevalence of diabetic retinopathy in the United States, 2005-2008. *JAMA.* 2010;304(6):649-656.

13. Centers for Disease Control and Prevention. Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus United States, 2005-2050. www.cdc.gov/visionhealth/publications/diabetic_retinopathy.htm. Last updated August 24, 2009. Accessed October 14, 2015.

14. Mitchell P, Bandello F, Schmidt-Erfurth U, et al. The RESTORE Study. Ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. *Ophthalmology*. 2011;118(4):615-625.

15. Li L, Wan XH, Zhao GH. Meta-analysis of the risk of cataract in type 2 diabetes. *BMC Ophthalmol*. 2014;14:94. doi: 10.1186/1471-2415-14-94.

16. Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis. *Ophthalmology.* 2015;122(1):72-78.

17. Prevent Blindness. Basic diabetes facts. www.preventblindness.org/basic-diabetes-facts. Accessed October 14, 2015.

18. Dyck PJ, Kratz KM, Karnes JL, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort. *Neurology.* 1993;43:817-824.