# Textbook of Diabetes

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# Preface to the Fifth Edition

It is seven years since the last edition of the *Textbook of Diabetes* was published and despite many advances in the understanding of diabetes and its treatment over that time, the management of diabetes still remains a major global burden for people with diabetes, their families, and the wider society in which they live. Whereas the global prevalence of diabetes according to the International Diabetes Federation affected 246 million people in 2010, the current estimate is 415 million and is projected to rise further. One in 10 of the world's population has diabetes and one person dies because of diabetes every 6 seconds. Twelve percent of global health expenditure is spent on diabetes. The challenge to people with diabetes and their healthcare professionals has never been greater.

Despite the ever-increasing numbers, better management is starting to pay dividends. The outlook for those with diabetes appears to be improving, at least in high income countries where an individual's risk of developing complications and losing years to diabetes is falling. If the variation between the best and worst care could be obliterated, much morbidity and mortality would be prevented.

Ironically, as the volume of information and the vast numbers of resources available in this digital age have increased, many are finding it overwhelming to keep abreast of the new advances. It is particularly challenging to determine the validity of many source materials. In this textbook, we aim to bring together a series of *upto-date* chapters from an international group of leading diabetes specialists who provide accurate and clinically relevant information to both academic and practicing diabetes healthcare professionals. Having the key information in one volume still has its merits, and this is further enhanced by *online* access and searchability.

The editors have retained the structure from the previous edition, with a similar length and number of chapters. We begin with a history of diabetes that provides many valuable insights from the past. The book then takes us through the epidemiology of diabetes, the physiology and pathogenesis of diabetes before moving onto management. We have taken a broad view in these sections recognizing that diabetes management encompasses so much more than drug therapy alone. A discussion of the microvascular and macrovascular complications then follows before a new section on the psychosocial aspects of diabetes. Different models of care as well as the management of diabetes in special groups are included before the final section looks into the future. There are new chapters on the biology of glucagon, the microbiome and diabetes, cancer, non-alcoholic fatty liver disease, and end-of-life care. These additions reflect the advances in our understanding of diabetes, its management, and have implications for a variety of related disorders.

As editors, we are only too aware of the hard work that goes into the production of a comprehensive and up-to-date book such as this. Our thanks go to each and every chapter author, who, despite busy academic and professional lives, were prepared to devote the time, energy, and expertise to provide their essential contributions to the text. Thank you for your forbearance of our nagging e-mails!

We are also grateful for the immense help we have received from our publisher, Wiley-Blackwell. Our commissioning editor, Priyanka Gibbons, who took over from Oliver Walter, during the book's development, has provided guidance, encouragement, and support. Our thanks also go to Gill Whitley who kept the momentum going when Rob Blundell left, and to the rest of the production team. The book looks even better than the last edition!

We hope you enjoy reading the book, whether it be dipping in or reading from cover to cover, as much as we did editing it. We have all taken away useful novel information that will aid our daily professional lives and we hope that this book will help you to support those with diabetes in the widest sense of this meaning.

> Richard Holt Clive Cockram Allan Flyvbjerg Barry Goldstein *February 2016*

# List of Abbreviations

AACE	American Association of Clinical	CDC	cardiosphere-derived stem cell
	Endocrinologists	CDC	Centers for Disease Control and Prevention
AAV	adeno-associated vectors	CDE	Certified Diabetes Educator
ABP	ankle blood pressure	CEMACH	Confidential Enquiry into Maternal and Child
ACCORD	Action to Control Cardiovascular Risk in		Health
	Diabetes	CETP	cholesteryl ester transfer protein
ACE	angiotensin-converting enzyme	CGM	continuous glucose monitoring
ACHOIS	Australian Carbohydrate Intolerance Study in	CI	confidence interval
	Pregnant Women	CKD	chronic kidney disease
ACR	albumin : creatinine ratio	CML	carboxymethyllysine
ADA	American Diabetes Association	CNS	central nervous system
ADP	adenosine diphosphate	COC	combination oral contraceptive
AICAR	5-aminoimidazole-4-carboxamide-1β-D-	COX	cyclooxygenase
	ribofuranoside	CPC	cardiac progenitor cell
AMDCC	Animal Models for Diabetes Complications	CRP	C-reactive protein
	Consortium	CSII	continuous subcutaneous insulin infusion
AMP	adenosine monophosphate	CT	computed tomography
Аро	apolipoprotein	CV	coefficient of variation
APWV	aortic pulse wave velocity	CVD	cardiovascular disease
Arx	aristaless-related homeobox	DAWN	Diabetes Attitudes, Wishes, and Needs study
ATP	adenosine triphosphate	DCCT	Diabetes Control and Complications Trial
AUC	area under the curve	DKA	diabetic ketoacidosis
BCAA	branched-chain amino acid	DPP	dipeptidyl peptidase
BMD	bone mineral density	DSN	diabetes specialist nurse
BMI	body mass index	DVLA	Driver and Vehicle Licensing Agency
BM-MNC	mononuclear bone marrow-derived stem cell	EASD	European Association for the Study of Diabetes
BPH	benign prostatic hyperplasia	ECG	electrocardiography/electrocardiogram
bpm	beats per minute	еGFR	estimated glomerular filtration rate
BTX-A	botulinum toxin type A	EMA	European Medicines Agency
CABG	coronary artery bypass grafting	ER	endoplasmic reticulum
CA-MRSA	community-associated methicillin-resistant	ERCP	endoscopic retrograde
	Staphylococcus aureus		cholangiopancreatography
CAPD	continuous ambulatory peritoneal dialysis	ERK	extracellular signal-regulated kinase
CBG	capillary blood glucose	ERM	ezrin-radixin-moesin
CBT	cognitive-behavioral therapy	ESC	embryonic stem cell
CCM	corneal confocal microscopy	ESRD	end-stage renal disease
CDA	Canadian Diabetes Association	ESRF	end-stage renal failure

#### List of Abbreviations

FDA	Food and Drug Administration (USA)	IDRS	Indian Diabetes Risk Score
FDC	fixed-dose combination	IgG	immunoglobulin G
FDKP	fumaryldiketopiperazine	IGR	impaired glucose regulation
FFA	free fatty acid	IGT	impaired glucose tolerance
FGF	fibroblast growth factor	ΙΚΚβ	inhibitor κB kinase-β
FHWA	Federal Highways Administration	IL	interleukin
FMD	flow-mediated endothelium-dependent	IMT	intima-media thickness
	arterial dilation	InsR	insulin receptor
FOXO	forkhead box O	IRMA	intraretinal microvascular abnormality
FXR	farnesoid-X receptor	ISPAD	International Society for Pediatric and
G6P	glucose-6-phosphatase		Adolescent Diabetes
G-6-P	glucose-6-phosphate	IT	information technology
G6PD	glucose-6-phosphate dehydrogenase	IVUS	intravascular ultrasound
GAD	glutamine acid decarboxylase	IWGDF	International Working Group on the Diabetic
GCGR	glucagon recentor	111 021	Foot
GCK	glucokinase	IBDS	Joint British Diabetes Societies
G-CSF	granulocyte colony-stimulating factor	KDIGO	Kidney Disease: Improving Clobal Outcomes
GDF	growth differentiation factor	K	Michaelis constant
GDM	gestational diabetes mellitus		latent autoimmune diabetes in adults
CE	custic fibroois	IDI	low density linoprotein
CI	gestrointecting		low density lipoprotein cholesterol
GIO	gluovalase		low density lipoprotein receptor
	CLD 1 recentor agonist		large for gestational age
GLF-IKA	dur-i receptor agonist	LURVO	liver encodes IncD incodecut
	C protein coupled recentor	LIKKU	linen-specific filsk kilockout
GPK	d-protein-coupled receptor	LP5 Let	line estation
GRPP	glicentin-related pancreatic polypeptide	LST	
GWA	genome-wide association		left ventricular
GWAS	genome-wide association studies	LVEF	left ventricular ejection fraction
НАРО	Hyperglycemia and Adverse Pregnancy	MAOI	monoamine oxidase inhibitor
T T1 A	Outcomes	MDI	multiple daily injection
HbA <sub>1c</sub>	hemoglobin A <sub>1c</sub>	MDRD	Modification of Diet in Renal Disease
HBV	hepatitis B virus	MG53	mitsugumin 53
HCV	hepatitis C virus	mGDP	mitochondrial glycerolphosphate
HDL	high-density lipoprotein		dehydrogenase
HGF	hepatocyte growth factor	MGO	methylglyoxal
нGH	human recombinant growth hormone	MI	myocardial infarction
HHS	hyperosmolar non-ketotic hyperglycemic state	MIBG	<i>m</i> -iodobenzylguanidine
HR	hazard ratio	MIRKO	muscle-specific InsR knockout
HRT	hormone replacement therapy	MODY	maturity-onset diabetes of the young
HRV	heart rate variability	MPGF	major proglucagon fragment
HSC	hematopoietic stem cell	MPO	myeloperoxidase
hsCRP	high-sensitivity C-reactive protein	MRI	magnetic resonance imaging
IADPSG	International Association of Diabetes	MSC	mesenchymal stem cell
	Pregnancy Study Groups	MS	mass spectrometry
IAsp	insulin aspart	mTOR	mammalian or mechanistic target of
IAUC	incremental area under the blood glucose		rapamycin
	curve	mTORC1	mechanistic target of rapamycin complex 1
ICA	islet cell antibody	MTPI	microsomal transfer protein inhibitor
ICU	intensive care unit	NAD	nicotinamide adenine dinucleotide
i.d.	intradermal	NaDIA	National Diabetes Inpatient Audit
IDDM	insulin-dependent diabetes mellitus	NAFLD	non-alcoholic fatty liver disease
IDeg	insulin degludec	NANC	non-adrenergic, non-cholinergic
IDF	International Diabetes Federation	NCV	nerve conduction velocity
IDL	intermediate-density lipoprotein	NEFA	non-esterified fatty acid

MFMU	Maternal–Fetal Medicine Units Network	RDN	renal denervation
NEP	neutral endopeptidase	RECORD	Rosiglitazone Evaluated for Cardiac Outcomes
NFκB	nuclear factor ĸB		and Regulation of Glycemia in Diabetes
Ngn3	neurogenin 3	REMS	Risk Evaluation and Mitigation Strategy
NHANES	National Health and Nutrition Examination	rHuPH20	recombinant human hyaluronidase
	Survey	RMR	resting metabolic rate
NHS	National Health Service	ROS	reactive oxygen species
NICE	National Institute for Health and Care	RR	relative risk
	Excellence	RR	risk ratio
NIDDM	non-insulin-dependent diabetes mellitus	RT-PCR	reverse transcriptase polymerase chain
NIH	National Institutes of Health		reaction
NMU	neuromedin U	SCFA	short-chain fatty acid
Nox	NAD(P)H oxidase	S.C.	subcutaneous
NOD	non-obese diabetic	SDHDL	small, dense high-density lipoprotein
NPH	neutral protamine Hagedorn	sdLDL	small, dense low-density lipoprotein
NRTI	nucleoside reverse-transcriptase inhibitor	SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel
NSAID	non-steroidal anti-inflammatory drug		electrophoresis
NT-3	neurotrophin-3	SGA	second-generation antipsychotics
NT-proBNP	N-terminal pro-brain-type natriuretic peptide	SHP	short heterodimer protein
OCP	oral contraceptive pill	SMBG	self-monitoring of blood glucose
OGIS	oral glucose insulin sensitivity	SML	severe mental illness
OGTT	oral glucose tolerance test(ing)	SNP	sub-basal nerve plexus
OR	odds ratio	SSRI	selective serotonin reuntake inhibitor
ovIDL	oxidation of low-density lipoprotein	T1DM	type 1 diabetes mellitus
PAS	periodic acid-Schiff	T2DM	type 2 diabetes mellitus
PRA	phenylhoronic acid	TAG	triacylglyceride
PC	prohormone convertase	TB	tuberculosis
PCB	polychlorinated binbenyl	TCF7L2	transcription factor 7 like 2
PCI	percutaneous coronary intervention	TF	transient elastography
PCR	polymerase chain reaction	TIND	treatment-induced neuronathy in diabetes
PCSK-9	proprotein convertase subtilisin kexin type 9	TIR	toll-like recentor
PDH	pyruvate dehydrogenase	TNDM	transient neonatal diabetes mellitus
Pdx1	pancreatic duodenal homeobox 1	TNFa	tumor necrosis factor alpha
PGF	placental growth factor	TREG	regulatory T cell
PI	protease inhibitor	TSH	thyroid-stimulating hormone
PI3K	phoenbatidylinositol 3-kinase	TZD	thiazolidinedione
PID	proportional integral derivative	LIKPDS	LIK Prospective Diabetes Study
D/KY	combined pancreas/kidney transplantation		ultrasound
	permanent peopatal diabetes mellitus		University of Texas
PPAR	perovisome proliferator-activated receptor	VEGE	vascular endothelial growth factor
PROactive	Prospective Pioglitazone Clinical Trial in	VLGI	vascular chuothenar growth factor
1 Roactive	Macrovascular Events	VLCD	very low-density lipoprotein
ртом	nost-transplantation diabetes mellitus	VEDL	variable-rate intravenous insulin infusion
DTD1R	protein tyrosine phosphatase 1B	WGS	whole-genome sequencing
DVV	polypentide VV	WHO	World Health Organization
Ool	auality of life	XO	vanthine avidase
R V	recentor agonist	VV1	Vin Vang 1
RAMP	receptor agonisi receptor activity-modifying protein	111	
RCT	randomized controlled trial		
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