Clinical Obesity in Adults and Children

Fourth Edition

Edited by

Peter G. Kopelman | Ian D. Caterson | William H. Dietz

Associate Editors

Sarah Armstrong | Arianne N. Sweeting | John P.H. Wilding

WILEY Blackwell

Clinical Obesity in Adults and Children

Clinical Obesity in Adults and Children

FOURTH EDITION

EDITED BY

Peter G. Kopelman, MD, DSC, FRCP, FFPH
Professor of Medicine
University of London
London, UK

Ian D. Caterson, AM, MBBS, BSC(MED), PhD, FRACP
Boden Initiative, Charles Perkins Centre and
Boden Professor of Human Nutrition, School of Life and Environmental Sciences, University of Sydney
Sydney, New South Wales, Australia

William H. Dietz, MD, PhD
Chair, Sumner M. Redstone Global Center for Prevention and Wellness
Milken Institute School of Public Health
George Washington University
Washington, DC, USA

WITH ASSOCIATE EDITORS

Sarah Armstrong, MD
Professor of Pediatrics and Population Health Sciences
Duke University
Durham, NC, USA

Arianne N. Sweeting, MBBS, BSC, GRADDIP HL, PhD, FRACP
Staff Specialist Endocrinologist
Department of Endocrinology, Royal Prince Alfred Hospital
Boden Initiative, Charles Perkins Centre, University of Sydney
Sydney, New South Wales, Australia

John P.H. Wilding, DM, FRCP
Professor of Medicine & Honorary Consultant Physician
Department of Cardiovascular and Metabolic Medicine
Institute of Life Course and Medical Sciences
University of Liverpool
Aintree University Hospital
Liverpool, UK

WILEY Blackwell

This edition first published 2022

Edition History
Blackwell Publishing Limited (3e, 2010; 2e, 2005; 1e, 1998)

Registered Offices
John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office
9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print *versions of this book may not be available in other formats.*

Library of Congress Cataloging-in-Publication Data

Names: Kopelman, Peter G., editor. | Caterson, Ian D., editor. | Dietz, William H., editor.
Title: Clinical obesity in adults and children / edited by Peter G. Kopelman, Ian D. Caterson, William H. Dietz ; with associate editors, Sarah Armstrong, Arianne Sweeting, John Wilding.
Description: Fourth edition. | Hoboken, N. J. : Wiley-Blackwell, 2022. | Includes bibliographical references and index.
Identifiers: LCCN 2021043980 (print) | LCCN 2021043981 (ebook) | ISBN 9781119695271 (cloth) | ISBN 9781119695301 (adobe pdf) | ISBN 9781119695325 (epub)
Subjects: MESH: Obesity | Adult | Child
Classification: LCC RA645.O23 (print) | LCC RA645.O23 (ebook) | NLM QU 248.1 | DDC 616.3/98–dc23
LC record available at https://lccn.loc.gov/2021043980
LC ebook record available at https://lccn.loc.gov/2021043981

Cover Design: Wiley
Cover Image: © SEAN GLADWELL/Getty Images

Set in 9.25/12pt Minion by Straive, Pondicherry, India

10 9 8 7 6 5 4 3 2 1

Contents

List of Contributors

Henry W. Ainge-Allen
Sleep and Circadian Research Group (CIRUS)
Woolcock Institute of Medical Research
University of Sydney
Sydney, New South Wales, Australia
and
Centre for Respiratory Failure and Sleep Disorders
Royal Prince Alfred Hospital
Sydney, New South Wales, Australia

Dalal Al-Bazz
Department of Diabetes and Endocrinology
Liverpool University Hospitals NHS Foundation Trust
Aintree University Hospital
Liverpool, UK

Steve Allender
GLOBE (Global Obesity Centre)
Deakin University
Melbourne, Victoria, Australia

Yvonne Anderson
Department of Paediatrics, Child and Youth Health
Faculty of Medical and Health Sciences
University of Auckland
Auckland, New Zealand

Sarah Armstrong
Professor of Pediatrics and Population Health Sciences
Duke University
Durham, NC, USA

Simon Barquera
Centro de Investigación en Nutrición y Salud
Instituto Nacional de Salud Pública
Cuernavaca, Mexico

Louise A. Baur
Sydney Medical School
University of Sydney
Sydney, New South Wales, Australia

John Blundell
Appetite Control and Energy Balance Group
School of Psychology
Faculty of Medicine and Health
University of Leeds
Leeds, UK

Wendy A. Brown
Chair, Monash University Department of Surgery
Alfred Health
Melbourne, Victoria, Australia
and
Program Director of Surgical Services
Alfred Health
Melbourne, Victoria, Australia

Nicola Buckland
Department of Psychology
University of Sheffield
Sheffield, UK

Ian D. Caterson
Boden Initiative
Charles Perkins Centre
University of Sydney
Sydney, New South Wales, Australia
and
Boden Professor of Human Nutrition
School of Life and Environmental Sciences
University of Sydney
Sydney, New South Wales, Australia

Mariachiara Di Cesare
Department of Natural Sciences
Middlesex University
London, UK

Li Kheng Chai
Health and Wellbeing Queensland
Milton, Queensland, Australia
and
Queensland University of Technology
South Brisbane, Queensland, Australia

Ariana M. Chao
Department of Biobehavioral Health Sciences
University of Pennsylvania School of Nursing
Philadelphia, PA, USA
and
Department of Psychiatry
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA, USA

Hélène Charreire
Nutritional Epidemiology Research Unit (EREN)
Inserm/Inrae/Cnam/Sorbonne Paris Nord University
Bobigny, France
and
University Paris Est Créteil
LAB'URBA, Créteil, France

Clare Collins
The University of Newcastle
Callaghan, New South Wales, Australia

Daniel J. Cuthbertson
Department of Metabolic and Cardiovascular Medicine
Institute of Life Course and Medical Sciences
University of Liverpool
Liverpool, UK

Michelle Dalton
Department of Social and Behavioural Sciences
Leeds Trinity University
Leeds, UK

Alessandro Demaio
VicHealth
Carlton, Victoria, Australia

William H. Dietz
Sumner M. Redstone Global Center for Prevention and Wellness
Milken Institute School of Public Health
George Washington University
Washington, DC, USA

Laurence J. Dobbie
Department of Metabolic and Cardiovascular Medicine
Institute of Life Course and Medical Sciences
University of Liverpool
Liverpool, UK

Abdul G. Dulloo
Faculty of Science and Medicine
Department of Endocrinology, Metabolism and Cardiovascular System
University of Fribourg
Fribourg, Switzerland

Chu Shan Elaine Chew
Department of Paediatrics
Adolescent Medicine Service
KK Women's and Children's Hospital
Singapore

I. Sadaf Farooqi
Wellcome-MRC Institute of Metabolic Science
Addenbrooke's Hospital
Cambridge, UK

Nathalie Farpour-Lambert
Head of the Obesity Prevention and Care Program
University Hospitals of Geneva
Geneva, Switzerland

Janet Franklin
Metabolism & Obesity Services
Royal Prince Alfred Hospital
Camperdown, New South Wales, Australia

Luc F. Van Gaal
Department of Endocrinology, Diabetes and Metabolism
Antwerp University Hospital
Edegem, Belgium

Tim Gill
Boden Initiative
Charles Perkins Centre
University of Sydney
Sydney, New South Wales, Australia

Ronald R. Grunstein
Sleep and Circadian Research Group (CIRUS)
Woolcock Institute of Medical Research
University of Sydney
Sydney, New South Wales, Australia
and
Centre for Respiratory Failure and Sleep Disorders
Royal Prince Alfred Hospital
Sydney, New South Wales, Australia

Catherine Hankey
University of Glasgow, Glasgow, UK

Jenna Hollis
The University of Newcastle
Callaghan, New South Wales, Australia
and
Hunter Medical Research Institute
Lambton, New South Wales, Australia
and
Hunter New England Population Health
Wallsend, New South Wales, Australia

Christina M. Hopkins
Department of Psychology and Neuroscience
Duke University
Durham, NC, USA

Peter Hovmand
Center for Community Health Integration
Case Western Reserve University
Cleveland, OH, USA

Lindsay M. Jaacks
Global Academy of Agriculture and Food Security
The University of Edinburgh
Roslin, UK

W. Philip T. James
Department of Population Health London School of Hygiene and Tropical Medicine
London, UK

Fredrik Karpe
Oxford Centre for Diabetes, Endocrinology and Metabolism
University of Oxford
Oxford, UK

Peter G. Kopelman
University of London
London, UK

Bo Kyung Koo
Department of Internal Medicine
Seoul National University College of Medicine
Seoul, Korea
and
Department of Internal Medicine
Seoul Metropolitan Government - Seoul National University (SMG-SNU)
Boramae Medical Center
Seoul, Korea

Soo Lim
Department of Internal Medicine
Seoul National University College of Medicine
Seoul, Korea
and
Department of Internal Medicine
Seoul National University Bundang Hospital
Seoul, Korea

Tim Lobstein
Boden Initiative
Charles Perkins Centre
University of Sydney
Sydney, New South Wales, Australia
and
The World Obesity Federation
London, UK

David Martin
Concord Repatriation General
Royal Prince Alfred and Strathfield Private Hospitals
Sydney, New South Wales, Australia

Emily Oken
Department of Population Medicine
Harvard Medical School and Harvard Pilgrim Health Care Institute
Boston, MA, USA
and
Department of Nutrition
Harvard TH Chan School of Public Health
Boston, MA, USA

Susan E. Ozanne
University of Cambridge Metabolic Research Laboratories and MRC Metabolic Diseases Unit
Wellcome-MRC Institute of Metabolic Science
Cambridge, UK

Jean-Michel Oppert
Department of Nutrition
Sorbonne University
Pitié-Salpêtrière Hospital (AP-HP)
Center for Research on Human Nutrition Ile-de-France
Paris, France
and
Nutritional Epidemiology Research Unit (EREN)
Inserm/Inrae/Cnam/Sorbonne Paris Nord University
Bobigny, France

Rebecca L. Pearl
Department of Clinical and Health Psychology
University of Florida
Gainesville, FL, USA
and
Department of Psychiatry
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA, USA

Kerry M. Quigley
Department of Psychiatry
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA, USA

David Raubenheimer
Charles Perkins Centre and School of Life and Environmental Sciences
The University of Sydney
Sydney, New South Wales, Australia

Yann Ravussin
Faculty of Science and Medicine
Department of Endocrinology, Metabolism and Cardiovascular System
University of Fribourg
Fribourg, Switzerland

Naveed Sattar
Institute of Cardiovascular and Medical Sciences
BHF Glasgow Cardiovascular Research Centre
University of Glasgow
Glasgow, UK

Kyra Sim
Metabolism & Obesity Services
Royal Prince Alfred Hospital
Camperdown, New South Wales, Australia

Stephen J. Simpson
Charles Perkins Centre and School of Life and Environmental Sciences
The University of Sydney
Sydney, New South Wales, Australia

Michael R. Skilton
Boden Initiative
Charles Perkins Centre
University of Sydney
Sydney, New South Wales, Australia
and
Sydney Medical School
Faculty of Medicine and Health
The University of Sydney
Sydney, New South Wales, Australia
and
Sydney Institute for Women, Children and their Families
Sydney Local Health District
Sydney, New South Wales, Australia

Arianne N. Sweeting
Boden Initiative
Charles Perkins Centre
University of Sydney
Sydney, New South Wales, Australia

Boyd Swinburn
School of Population Health
University of Auckland
Auckland, New Zealand
and
GLOBE (Global Obesity Centre)
Deakin University
Melbourne, Victoria, Australia

Mishel Unar-Munguia
Centro de Investigación en Nutrición y Salud
Instituto Nacional de Salud Pública
Cuernavaca, Mexico

Lesly Véjar
Centro de Investigación en Nutrición y Salud
Instituto Nacional de Salud Pública
Cuernavaca, Mexico

Ann Verhaegen
Department of Endocrinology, Diabetes and Metabolism
Antwerp University Hospital
Edegem, Belgium

Thomas A. Wadden
Department of Psychiatry
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA, USA

Wilma Waterlander
Department of Public and Occupational Health
Amsterdam UMC
University of Amsterdam
Amsterdam, the Netherlands

Mariel White
Centro de Investigación en Nutrición y Salud
Instituto Nacional de Salud Pública
Cuernavaca, Mexico

John P.H. Wilding
Department of Diabetes and Endocrinology
Liverpool University Hospitals NHS Foundation Trust
Aintree University Hospital
Liverpool, UK
and
Department of Cardiovascular and Metabolic Medicine
Institute of Life Course and Medical Sciences
University of Liverpool
Aintree University Hospital
Liverpool, UK

Brendon J. Yee
Sleep and Circadian Research Group (CIRUS)
Woolcock Institute of Medical Research
University of Sydney
Sydney, New South Wales, Australia
and
Centre for Respiratory Failure and Sleep Disorders
Royal Prince Alfred Hospital
Sydney, New South Wales, Australia

Preface

Clinical Obesity in Adults and Children originated in 1998 from the Editors' perception of a need for a textbook on obesity which emphasized obesity as a disease entity by reviewing the scientific basis and addressing the clinical and practical aspects of the condition. The introduction concluded that obesity management and research had reached a watershed at the end of the century, given the increasing concerns about the problem for future generations. As we enter the third decade of the new century, such concerns have not only materialized but have been exceeded.

The fourth edition of *Clinical Obesity* has been written during a pandemic caused by the SARs-CoV- 2 coronavirus. Many contributing authors were actively engaged in the frontline of health care treating patients suffering from this virulent virus. The additional morbidity and mortality of COVID-19 infections associated with excess body weight have emphasized the urgent need for the effective prevention and treatment of obesity.

In the context of a pandemic, this new edition of *Clinical Obesity* concludes with a timely chapter on the global syndemic. The notion of a syndemic was first conceived by Merrill Singer, a medical anthropologist, in the 1990s. Writing in *The Lancet* in 2017, Singer argued that a syndemic perspective reveals biological and social interactions that are important for prognosis, treatment, and health policy. A syndemic is not merely a comorbidity; syndemics are characterized by biological and social interactions between conditions and states, interactions that increase a person's susceptibility to harm or worsen their health outcomes. The Lancet Commission on Obesity proposed that obesity, undernutrition, and climate change constitute a syndemic. Malnutrition in all its forms, including obesity, undernutrition, and other dietary risks, is the leading cause of poor health globally. Climate change is a fundamental part of this because of its sweeping effects on the health of humans and the natural systems that we depend on and underpins the way that we live.

In this edition of *Clinical Obesity*, we focus on the textbook's original objectives with chapters on the causes of obesity, obesity as a disease, the management of adult obesity, and childhood obesity. We also include a section on policy approaches that underline the importance of effective and sustainable policies free from political and commercial interference.

We, the editors, have spent long careers concerned about obesity, and we share an exasperation that so little has been accomplished worldwide in reversing its spiraling prevalence and its detrimental effects across all ages. Certainly, the understanding of the science and medical consequences of obesity has grown exponentially, but the drivers of excessive weight gain remain obvious in all societies, yet meaningful policy recommendations fail to be developed or translated into practice, and the economic burden from obesity grows.

We hope that this latest edition of *Clinical Obesity* enables its readers to understand the complexity of obesity better, both within society and the clinical setting, and provides inspiration and knowledge for those tasked with managing and tackling the condition.

We are most grateful to our co-editors for this edition, Sarah Armstrong, Arianne Sweeting, and John Wilding, for their considerable help and support in bringing this new edition to fruition. We hope that the experience will encourage them to take over the "baton" for future editions of Clinical Obesity.

Peter G. Kopelman, Ian D. Caterson, and William H. Dietz
London, Sydney, and Washington, DC

Dedication

Peter G. Kopelman

Peter was an editor for each of the four editions of Clinical Obesity in Adults and Children and lead editor for three. He died just before this edition was completed, but he asked us to ensure it was finished.

Peter was a clinician, a researcher, a teacher, and an academic leader. His research was initially into the genetics of obesity, but this developed into a wider interest in many aspects of obesity, particularly its management. He led the production of clinical guidelines, and his focus was always on the patient with obesity, and with equity. He was a leader in medical education and was executive dean of the Faculty of Health at The University of East Anglia, and then returned as principal at St George's Hospital in London, where he had trained. He became an academic leader within the Royal College of Physicians and the University of London. He was one who cared for others and strove to provide the best care for his patients, and mentoring and leadership for his students and colleagues.

For the two of us, Peter was a wonderful colleague and friend who organised and led us through the production of the last three editions of this textbook. He was a clear thinker, considerate, and helpful to us all.

This textbook, Clinical Obesity in Adults and Children, 4th Edition, is dedicated to him.

Ian D. Caterson
William H. Dietz

List of Abbreviations

ACTH	adrenocorticotropic hormone
ADP	air displacement plethysmography
AHI	Apnea/Hypopnea Index
AHO	Albright hereditary osteodystrophy
AHS	*ad hoc* stomach
ART	assisted reproductive technology
ASCVD	atherosclerotic cardiovascular disease
ASP	acylation-stimulating protein
ATP	adenosine triphosphate
AgRP	agouti-related peptide
BAT	brown adipose tissue
BDI	Beck Depression Inventory
BED	binge-eating disorder
BGL	blood glucose levels
BIA	bio-electrical impedance analysis
BIH	benign intracranial hypertension
BMI	Body Mass Index
BMR	basal metabolic rate
BPD	biliopancreatic diversion procedure
CART	cocaine and amphetamine-related transcript
CBT	cognitive behavioral therapy
CKK	cholecystokinin
CETP	cholesteryl ester transfer protein
CHD	coronary heart disease
CHF	congestive heart failure
CI	confidence interval
CNS	central nervous system
COH	controlled ovarian hyperstimulation
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPE	carboxypeptidase E
CPT1	carnitine palmitoyl transferase-1
CRH	corticotrophin-releasing hormone
CRP	C-reactive protein
CT	computed tomography
CVD	cardiovascular disease
DAG	diacyl glycerol
DALY	disability-adjusted life-years
DC	direct calorimetry
DIT	diet-induced thermogenesis
DOHaD	developmental origins of health and disease
DEXA	dual-energy X-ray absorptiometry
EB	energy balance
EBM	evidence-based medicine
ED	erectile dysfunction
EDS	excessive daytime sleepiness
EE	energy expenditure
EI	energy intake
EMCL	extramyocellular lipid
EMG	electromyogram
EMR	electronic medical record
EOG	electro-oculogram
EPOC	postexercise oxygen consumption
FABP	fatty acid binding proteins
FDG-PET	fluorodeoxyglucose positron emission tomography
FFA	free fatty acids
FFM	fat-free mass
FFQ	food frequency questionnaire
fMRI	functional magnetic resonance imaging
GERD	gastroesophageal reflux disease
GDM	gestational diabetes
GH	growth hormone
GHD	growth hormone deficiency

GHS-R1a	growth hormone secretagog receptor 1a
GI	gastrointestinal; Glycemic Index
GIP	gastric inhibitory peptide
GL	glycemic load
GLP-1	glucagon-like peptide-1
GLUT-4	glucose transporter-4 CER ceramide
HCC	hepatocellular carcinoma
HCG	human chorionic gonadotropin
HD	hydrodensitometry
HDL	High-density lipoprotein
HB-EGF	heparin-binding epidermal growth factor like growth factor
HF	heart failure
HSL	hormone-sensitive lipase
IAPP	islet amyloid polypeptide
IBW	ideal body weight
IC	indirect calorimetry
IDF	International Diabetes Federation
IGT	impaired glucose tolerance
IHD	ischemic heart disease
IMCL	intramyocellular lipid
IOTF	International Obesity Task Force
IRS	insulin receptor substrates
IUGR	intrauterine growth restriction
IVF	*in vitro* fertilization
JIB	jejunoileal bypass
KO	knockout
LAGB	laparoscopic adjustable gastric banding
LAUP	laser-assisted uvulopalatoplasty
LDL	low-density lipoprotein
LBM	lean body mass
LED	low-energy diets
LH	lateral hypothalamic; luteinizing hormone
LPL	lipoprotein lipase
LV	left ventricular
MACE	major adverse cardiac event
MAD	mandibular advancement devices
MAFLD	metabolic dysfunction-associated fatty liver disease
MAS	McCune–Albright syndrome
MC4R	melanocortin concentrating hormone receptor 4
MCH	melanin-concentrating hormone
MCP-1	monocyte chemoattractant protein-1
MET	metabolic equivalent
MI	myocardial infarction
MIF	migration inhibitory factor
MMP	matrix metalloproteinase
MR	Mendelian Randomisation
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
MS	metabolic syndrome
MSR	macrophage scavenger receptor
MUFA	monounsaturated fatty acid
NAFLD	nonalcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
NCD	noncommunicable diseases
NCEP	National Cholesterol Education Program
NE	norepinephrine
NEAT	nonexercise activity thermogenesis
NEFA	nonesterified fatty acids
NGF	nerve growth factor
NGT	normal glucose tolerance
NHLBI	National Heart, Lung, and Blood Institute
NMB	neuromedin B
NMR	nuclear magnetic resonance
NPY	neuropeptide Y
NPY/AgRP	neuropeptide-Y/agouti-related protein
NREM	nonrapid eye movement
NST	nucleus of the solitary tract
NTS	nucleus tractus solitarius
OFC	orbitofrontal cortex
OGTT	oral glucose tolerance test
OHS	obesity hypoventilation syndrome
OR	odds ratio
OSA	obstructive sleep apnea
PAI-1	plasminogen activator inhibitor-1
PCOS	polycystic ovary syndrome
PHT	pulmonary hypertension
PMF	protein-modified fast
POMC	pro-opiomelanocortin
PP	pancreatic polypeptide
PSG	polysomnography
PTP1B	protein tyrosine phosphatase 1B
PUFA	polyunsaturated fatty acids
PVN	paraventricular nucleus
PWS	Prader–Willi syndrome

QOL	quality of life
R_a	rate of appearance
RBP-4	retinol binding protein-4
REE	resting energy expenditure
REM	rapid eye movement
RMR	resting metabolic rate
ROS	reactive oxygen species
RPE	rating of perceived exertion
RQ	respiratory quotient
RR	relative risk
RYGB	Roux-en-Y gastric bypass
SCFAs	short chain fatty acids
SD	standard deviations
SES	socio-economic status
SFA	saturated fatty acids
SHGB	sex hormone-binding globulin
SNP	single nucleotide polymorphisms
SNS	sympathetic nervous system
SPA	spontaneous physical activity
T1DM	type 1 diabetes mellitus
T2DM	type 2 diabetes mellitus
TCRFTA	temperature-controlled radiofrequency ablation to the tongue base and palate
TEF	thermic effect of food
TG	triacylglycerol/triglyceride
TIMP	tissue inhibitor of metalloproteinase
TRH	thyrotropin-releasing hormone
TSH	thyroid-stimulating hormone
UCP-1	uncoupling protein 1
UPPP	uvulopalatopharyngoplasty
VAI	visceral adiposity index
VAT	visceral adipose tissue
VBG	vertical banded gastroplasty
VEGF	vascular endothelial growth factor
VLCD	very low-calorie diets
VLDL	very low-density lipoprotein
VLED	very low-energy diets
VMH	ventromedial hypothalamus
WAT	white adipose tissue
WC	waist circumference
WHO	World Health Organization
WHR	waist/hip ratio

1 Obesity

1 Obesity – Introduction: History and the Scale of the Problem Worldwide

W. Philip T. James[1] and Tim Gill[2]

[1] Department of Population Health, London School of Hygiene and Tropical Medicine, London, UK
[2] Boden Initiative, Charles Perkins Centre, University of Sydney, Sydney, New South Wales, Australia

Obesity is a complex condition and, although much remains to be elucidated, our understanding of the many facets of overweight and obesity has advanced greatly over the last few decades. Current research is often focussed on the genetic and molecular pathophysiological drivers which derange energy balance and lead to excess body fat, but it is important that clinicians have an appreciation of the history and context of these findings and an awareness of the significant challenges created by the different features of obesity that continue to be revealed. Different patterns of obesity emerging across the world may also have different impacts on the public health burden and may require a different approach to the development of prevention and treatment strategies.

The condition of obesity has been recognized for millennia, and its historical context was described in detail by George Bray [1], who highlighted the representation of obesity in images and figurines produced in Europe about 23,000–25,000 years ago. These ancient individuals may well have had a severe form of genetic obesity, and Bray suggests that they may have been considered deities – this would not have seemed unreasonable in societies constantly striving to avoid food shortages. This predicament might still have applied to the general population in the early agricultural period 5000–6000 years BC in Mesopotamia and later in Egypt, but by then, with greater food availability, obesity was particularly seen in the ruling classes. However, Bray points out that by then, obesity was considered objectionable rather than reflecting a remarkable and unusual status akin to that of a deity. These individuals most likely suffered from not only the common problems of backache and arthritis but also the impact of comorbidities such as diabetes. Chinese and Indian medicine also dealt with obesity as a problem condition, and the particular propensities for Asians and the people of the Middle East to display ill health on weight gain are discussed later. Further on the Roman Galen distinguished between "moderate" and "immoderate" obesity, so in a European rather than an Asian or Middle Eastern context, there may have been a sizable number of overweight individuals with few complications, whereas others were handicapped by their adiposity without this automatically being a reflection of the degree of obesity.

In this ancient literature, it was clear that obesity was considered a clinically unusual event, and so it is little wonder that the original classification of diseases being steadily developed in France during the 19th century included obesity along with other clearly identified clinical abnormalities, some of which were only really apparent on postmortem examination. This classification of diseases was taken over by the World Health Organization (WHO) on its formation in 1948, so in practice, WHO recognized obesity as a disease entity from its inception. However, at this stage, WHO's primary focus was public health with a heavy emphasis on the poorer countries of the world at a time when obesity was not a problem in lower-income countries.

Obesity as a public health problem

It is commonly perceived that obesity has only recently been recognized as a public health issue and its potential impact on population health is still yet to be completely acknowledged. However, in his book titled "Fat in the Fifties," Rasmussen [2] describes a period in post-World War II America when obesity was being described as the greatest threat to public health. During the 1940s, heart disease replaced infectious diseases as the major cause of death in the United States. At the same time, data from insurance companies identified that higher body weight (relative to height) was associated with an increased risk of premature death, including those from heart disease, and thus obesity was defined as the major public

Clinical Obesity in Adults and Children, Fourth Edition. Edited by Peter G. Kopelman, Ian D. Caterson and William H. Dietz.

health concern to be addressed. In the 1950s, research by Keys and his colleagues suggested that the three major risk factors for coronary heart disease (CHD) were smoking, high blood pressure, and a high plasma cholesterol level. These findings were seized upon and promoted by vested interests such as the sugar industry that were threatened by the suggestion that excess calories were driving the rise in heart disease and cancer. Although it was recognized that weight gain increased both blood pressure and blood cholesterol levels but obesity per se did not seem to be nearly as important as an independent predictor; in Key's analysis, the olive oil eating, fatter Greek men had one of the lowest CHD rates. As a consequence, obesity lost its prominence as a key public health issue and was buried by the avalanche of concern around what was then described as the "true" risk factors for heart disease.

Obesity was again raised as a serious public health issue in the early 1970s. One author (W.P.T. James) was involved in producing the UK report on obesity for the UK Department of Health and Social Services and the Medical Research Council [3]. At that stage, obesity was being defined as a percentage excess weight above the desirable weight for height listed by the US Metropolitan Life Insurance Company in complex tables with weights in clothes for three personally chosen frame sizes. These figures relating to pre-Second World War mortality statistics that were collected on millions of insurance-eligible Americans. The UK report wanted a standardized measure of body weight that would account for people of different sizes and adopted the approach of the Belgian mathematician Quetelet's from 1835, who recommended that this could be best achieved deriving the index W/H**2** in metric units; a unit now termed the body mass index (BMI). It became apparent that when taking the insurance tables and then considering only the lower limits of the small frame size and the upper limit of the large frame size that the derived Quetelet index was almost the same across a huge range in heights. This ideal body weight from the insurance tables translated into an index of 19.1–24.6 for women and to 19.7–24.9 for men after adjusting for the weight of light clothing and shoe heights. John Garrow, a member of the committee, then rounded these numbers for clinical use to BMI of 20–25. Based on the insurance company's approach of specifying obesity when weights were 20% above ideal, obesity cut-off was set at BMI 30.

Lower limits of BMIs in non-Caucasians?

The BMI limits of 20–25 for minimum mortality rates based on US life insurance data set out in the early 1970s were reaffirmed in the 1983 analysis from the London Royal College of Obesity [4] using data from the US Cancer Society that analyzed data on smokers and nonsmokers separately. Therefore, the big issue was whether these limits applied globally. It was hoped that this could be answered with the establishment of the International Obesity Task Force (IOTF) in 1996, but at that time, there was limited longitudinal data on adult weights and heights and their subsequent mortality in non-Caucasian populations. However, when the IOTF proposed in 1997 cut-off points of 25 and 30 to define new WHO criteria and set out policies for tackling global obesity, the Japanese delegate desired a lower upper normal BMI cut-off point of 23.0, whereas the US delegate favored a higher normal cut point of 28.0 despite the original mortality data being derived from the United States. The Japanese argued that setting the upper normal BMI cut-off point at 25 value did not adequately define overweight in Asian populations, but the United States felt that such a cut point would automatically mean that a large majority of Americans would be defined as overweight which was deemed embarrassing and requiring a rethink of health strategies!

The WHO expert committee decided to continue the long-standing policy of considering the human race as one entity with ethnic differences being unimportant biologically, so they agreed on a universal upper normal BMI cut-off point of 25 [5]. However, it was later proposed [6,7] that the BMI lower limit should be 18.5 rather than 20 as there was little evidence at that stage that mortality increased as BMIs fell below 20 and detailed analyses of ill health in Latin America, Africa, and Asia indicated that there were no health disadvantages at this lower level. However, at that stage, data on large populations examining the relationship of BMI to mortality was limited except in India, where it was clear that mortality rose sharply when BMIs were below 16.

Subsequently, because of the intense concern of many Asian physicians about the burden of ill health, especially diabetes, that arose within the supposedly acceptable BMI range of 20–25, a WHO meeting was convened in Singapore. It concluded that there were differences in the relationship between BMI and the health profile as well as body composition when comparing Western populations to data from several Asian countries. Therefore the option of considering an upper BMI limit of 23 was acceptable in Asian countries [8]. China, however, undertook their own extensive analyses when their Chinese obesity collaboration was formed and then concluded that an upper limit of BMI 24 should be suitable for the Chinese [9], but this judgment, as well as the Singapore conclusion about Asians, was geared more to morbidity relationships than to mortality data.

Morbidity burden starts at much lower BMIs

The setting of these cut points has led many clinicians to assume that a BMI between 20 and 25 is optimum as the mortality risk is minimum. However, it has been known for decades that the risk of diabetes increases progressively from a BMI of about 20, and in the United States is then 5 times higher in women before the BMI of 25 is reached [10]. Furthermore, the incidence of hypertension and increases in blood cholesterol levels, and the risk of both cardiovascular diseases and colon cancer show linear increases as the BMI moves up from a BMI of about 20. So considering a BMI in the range of 20–25 as optimum may result in neglecting all the increasing comorbidities of weight gain within this "acceptable" range. These issues will be considered in greater detail later when we consider the overall hazards of obesity.

Obesity epidemic starts in the early 1980s

Data from the United States suggests that mean population BMI was increasing consistently across the decades from the early 1900s, but the level of overweight and obesity, as defined by a BMI of 25 and 30, only began to increase rapidly in the early 1980s [11]. The Organization for Economic Cooperation and Development (OECD) report on obesity showed that in the 1970s the overall US adult obesity prevalence was already 14% for all adults, but it has risen progressively since then and continued to increase in the 2010s to above 35%. Similar patterns were seen in other developed countries. National surveys of English adults in the 1930s and 1940s reported obesity rates less than 5% in those below the age of 40 years but increasing to 10% in the 50-year-old men. Detailed national representative surveys in England in 1981 showed that overall obesity rates remained relatively low (6% in men aged 16–65 years and 8% in women) [12], but obesity rates had already risen to 11–12% in 40–60-year-olds. Similar prevalences were found in studies in Finland (albeit those data were self-reported), and the Netherlands also reported an average adult prevalence of 5%, but measured prevalence data from Japan on average showed that only 2% adults with obesity.

From the early 1980s, it is clear that obesity prevalences were starting to increase in all Western societies, and by the late 1980s, upper-middle-income countries were beginning to follow the North American and European countries, with increasing obesity rates evident in both men and women from the age of 20 upwards. The pivotal importance of this early part of the 1980s in setting new trends of increasing obesity was vividly illustrated by Norton and others' analysis of children's weights and heights measured in community and other population surveys in Australia over a whole century [13]. By using the IOTF's BMI criteria for childhood obesity [14] (which linked seamlessly with the adult BMI cut-off points), Norton's analysis showed that there was very little increase in childhood obesity until the early 1980s when a remarkable increase started to develop. These IOTF cut-offs have subsequently been refined [15], but the overall picture and analyses are unchanged and reveal something very unusual changed in the environment from the early 1980s onward in affluent societies, with middle-income countries revealing the beginning of a rise in BMIs a little later.

The global epidemic gets underway

The trends in obesity rates from the 1980s to 2008 were beautifully illustrated by Finucaneand others [16] in a comprehensive analysis of huge data sets from around the world, as shown in Figure 1.1. The data reveal marked differences in the prevalences of males and females. In males, it is clear that the more affluent a society in 1980 then the greater the likelihood of some obesity. Thus North America, Latin America, Australia, and Europe had overall prevalences of 10% obesity. In general, the greater the degree of regional affluence, the greater the increase in obesity rates in men over the subsequent 28 years. However, in the early 1980 data, the highest level of obesity among women was not found in North America but rather in emerging counties in Southern Africa, North Africa, the Middle East, and Central Latin America, with Asian women having the lowest levels. In the following three decades, the 1980 regional ranking in women was generally preserved with the fattest regions showing the most significant increases in obesity so that by 2008 several regions of the world were approaching a 40% prevalence of obesity in women.

Since these comprehensive analyses of obesity prevalences, there has been a series of updates both by the Ezzati and Murray groups [17] supported by the Gates Foundation and by the OECD [18] with updates [19] – as well as by a range of national expert groups [20,21]. These data stimulate the question as to why this epidemic had become so striking and seemingly resistant to change and, indeed, how might the problem be tackled? This resistance to change is evident, for example, from surveys conducted by Public Health England who showed that 40% or more of men and over 50% of women aged 25–74 years were trying to lose weight in 2016 [22] and yet the obesity rates remain high suggesting that under current circumstances individuals attempt to slim is very ineffective as a population strategy.

Using historical records, Jaacks and others [23] then examined the evolution of obesity and highlighted four phases in the chronological development of obesity:

Stage 1. Obesity is more prevalent in women than in men and is evident in more affluent groups with low prevalence rates in children. This phase is still evident in many South Asian countries and sub-Saharan Africa.

Stage 2. In stage 2 of the transition, there has been a significant increase in the adult obesity rates with less of a gap between the sexes and in terms of socioeconomic differences. Many Latin American and Middle Eastern countries are at this stage.

Stage 3. In this stage, a swing occurs with those of lower socioeconomic status now having a higher obesity prevalence, but the more affluent women and children do not show any further secular increase. These features are evident in Europe.

Stage 4. This stage is where obesity prevalence actually declines but is a phenomenon we have yet to observe.

In within-country analyses, higher rates of obesity are traditionally associated with urban environments, but Ezzati and colleagues have highlighted that more recently there has also been a marked increase in rural obesity [24]. This implies that the drivers of obesity were originally most evident in urban areas, but as the world has developed, the factors promoting obesity have penetrated the rural communities and/or the rural environment has lost some of the factors which limited the development of obesity.

Abdominal obesity

So far, we have only been considering analyses of obesity epidemiology in terms of BMI, but as previously mentioned, Asian physicians have long been concerned by the onset of obesity's comorbidities

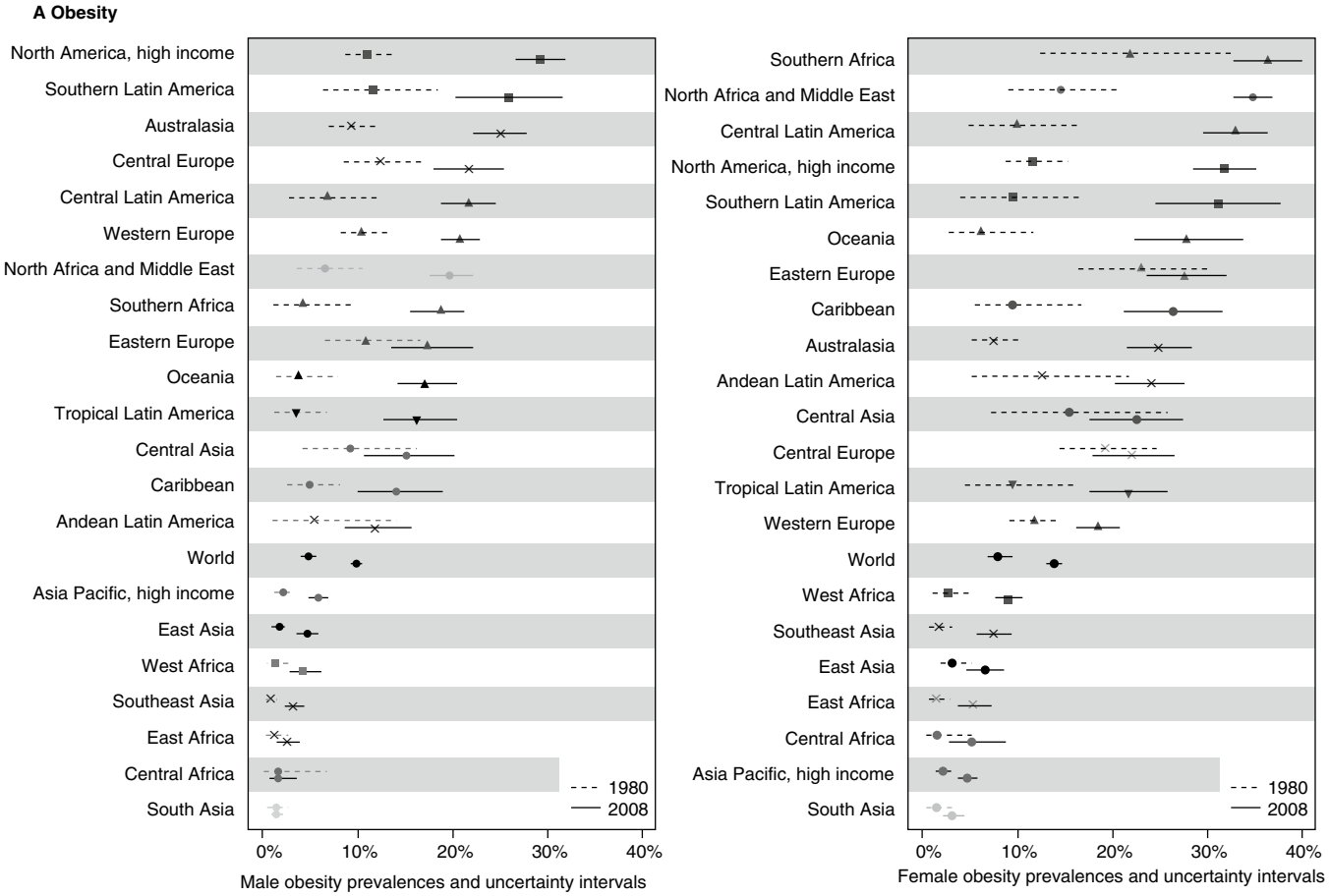

Figure 1.1 Obesity prevalences in different regions of the world. Data for males are in the left block of data and females in the right-hand series. Within each data set, the prevalences for 1980 are on the left and for 2008 on the right. (Source: Reproduced from Finucane et al. [16].)

at much lower BMIs than in Western Europe or North America. The long-standing clinical observation that abdominal obesity was particularly hazardous had led to Vague's identifying decades ago that there was a particular risk if a patient had an android phenotype as distinct from a gynecoid pattern of fat distribution with a small waist/hip (W/H) ratio [25]. The likelihood that abdominal obesity was associated with additional risk was widely accepted, but the definition of what constituted abdominal obesity was uncertain except in terms of a high W/H ratio (>1). The Scottish Royal Colleges of Physicians were preparing a simple guide for general practitioners in 1993 on how to tackle obesity and sought to have the assessment and management summarized on a single page chart which could be placed on a GP's consulting room table. This necessitated a numerical definition of what normal waist measurements were and what the cut-offs should be for specifying abdominal obesity. Based on the data from a population survey of adults in the Netherlands, Mike Lean and Jaap Seidel decided to simply take the waist measurements of 94 and 102 cm in men and 80 and 88 cm in women since these values corresponded epidemiologically to BMIs of 25 and 30 in the Dutch population [26]. They also noted that values exceeding these waist circumferences were associated with higher cardiovascular risks. These values were therefore taken as the cut-off points for abdominal obesity in the Scottish Intercollegiate Guidelines Network (SIGN) guidelines [27] and were then promptly incorporated by the National Institute of Health (NIH) group into their US guidelines for tackling obesity [28] as well as being used in the draft IOTF report for WHO, and then incorporated as the cut-off points in the report of the first WHO Expert Technical Committee to deal with obesity [5].

The INTERHEART international study later showed that waist size and W/H ratios were better indices of the risk of CHD than BMI [29]. W/H values showed marginally better statistical discrimination probably because higher hip values seem to be protective, perhaps relating to the body's ability to safely store fat subcutaneously – on the hips. The importance of abdominal obesity as a predictor of morbidity has been shown many times, but the waist/height ratio expressed in metric units with a simple ratio cut-off of 0.5, rather than hip circumference, seems a better and clinically more practical predictor of disease risk factors, e.g. dyslipidemia, increased blood glucose levels, or higher blood pressures [30] especially in children [31].

Different regional societal burdens of obesity with abdominal obesity

McKeigue et al. described in 1991 the propensity to abdominal obesity and thicker truncal skinfolds as being greater in South Asians than in British adults, and for each increment in waist/hip ratios, there was a greater increase in glucose intolerance, plasma insulin levels, diabetes, hypertension, and plasma triglyceride levels in the South Asians than in the British Caucasians [32]. These findings mirrored the concerns expressed by clinical researchers such as Misra et al. [33] from India, who highlighted the problem of abdominal obesity and its associated dyslipidemia at low BMIs in Indian slum dwellers. This was also noted by the subsequent WHO Singapore meeting [8] and then led the IOTF to assess whether these propensities to diabetes and hypertension were evident on a population basis by comparing Australasian data with large data sets derived from a series of studies across Asia. Iranian data were included in the reference data set from Australia and New Zealand as they were considered for practical purposes Caucasian. This addition may have been a mistake (see below), but their inclusion did not affect the overall conclusion, based on the analysis of 21 population groups with about 263,000 individuals, that those with abdominal obesity had a greater propensity to diabetes but not to hypertension, and that the Asian community was particularly prone to abdominal obesity and its hazardous consequences [30].

Genetic susceptibility could account for this Asian propensity to abdominal obesity and indeed to excess diabetes and lipid disorders at each increment of waist enlargement, or it could be attributed to other factors. A genetic basis is supported by the relatively new analyses of human evolution that have shown the different patterns of genetics as the human race evolved out of East Africa and then left Africa to evolve through the Middle East into Europe, Asia, and then across the Siberian/Alaskan link (now the Behring straits) into North America and down into Central and South America [34]. The most significant changes are those that involve the much more unstable mitochondrial DNA with its faster rate of mutation than nuclear DNA. There are very clear patterns of mitochondrial change, designated by different haplotypes, with a subset leaving Africa and subsequently evolving down multiple haplotype pathways and with some interbreeding with early hominids, the Neanderthals and Denisovans. There are mutations of mitochondrial DNA that are associated with diabetes, but as yet, there are no extensive population studies of genetics that also test for the prevalence of glucose intolerance and diabetes in populations across the world, as well as associated haplotype analyses.

This seemingly special Asian propensity to abdominal obesity and diabetes was then shown to be a more general feature when analyses of the 2006 national survey of Mexican adults found the same features – both a greater propensity to abdominal obesity and a greater prevalence of diabetes and hypertension at each increment of abdominal expansion [35] as shown in Figure 1.2. Furthermore, US studies showed that when ethnic differences were considered, Japanese Americans, as well as Hispanic Americans, were both more likely to have abdominal obesity and greater rates of diabetes at each increment of abdominal expansion than American Whites [36]. African Americans have higher BMIs than Whites or Hispanics, but their diabetes rates are even higher than one would expect for their greater size. However, attempts to identify a genetic basis for this excess diabetes in Africans have so far been unsuccessful [37], with studies of the African diaspora showing marked differences in glucose metabolism in

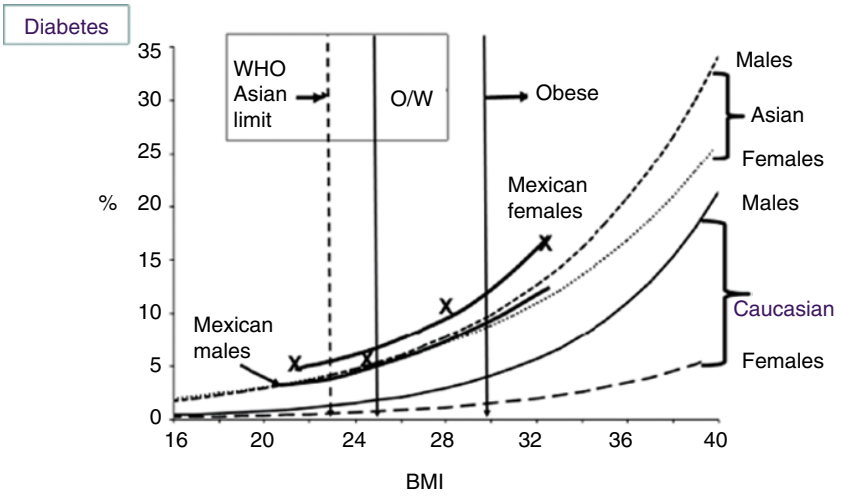

Figure 1.2 The prevalences of obesity in men and women in cohorts with over 263,000 adults either from Asia or from Australasia and Iran (depicted as Caucasians) [30]. Superimposed on this graph are data from the Mexican national survey in 2000 [35]. The Mexican study compared the national survey data with nationally representative data for US non-Hispanic Whites, but these data are not shown in this graph as they were almost identical to those of the Australasian/Iranian data from the Asian study.

different communities with different BMIs and degrees of abdominal obesity enhancing glucose intolerance but they were also eating different diets and with objectively measured differences in physical activity [38]. So there was no suggestion that dilution of the African genome in Jamaica and the United States had distinct weight independent effects as their results did not differ from those observed in Ghana and South Africa.

Furthermore, the seemingly genetically obesity-prone Pima Indians from Mexico and Arizona in the United States show that with similar genetic profiles, there are big national differences in BMI and diabetes prevalences which are largely environmentally determined [39]. Very low obesity and diabetes rates occur in the hard-working, home-farming Pima Mexicans consuming a 25% fat, high fiber diet with a negligible sugar content [40]. So it is difficult to be sure what constitutes a greater genetic propensity to diabetes in different ethnic groups and how this relates to abdominal obesity without taking account of their prevailing diet and physical activity [41]. Indeed, the propensity to develop type 2 diabetes has been related to the duration of being overweight/obese, as well as the magnitude of excess weight [42].

The impression that Caucasians are relatively protected from diabetes associated with weight gain was further amplified by our findings in the Middle East. Carefully conducted randomly selected populations in each of the 21 countries covered by the WHO Eastern Mediterranean Region (EMR), i.e. including not only the Gulf countries, Lebanon, Syria, and the North African countries abutting the Mediterranean but also Djibouti, Somalia, Sudan, Afghanistan, and Pakistan showed (Fig. 1.3) that, despite the wide-ranging levels of average BMI in both men and women, the national average diabetes rates are appreciably higher in the EMR than in the 28 countries of the Europe Union throughout the range of average BMIs.

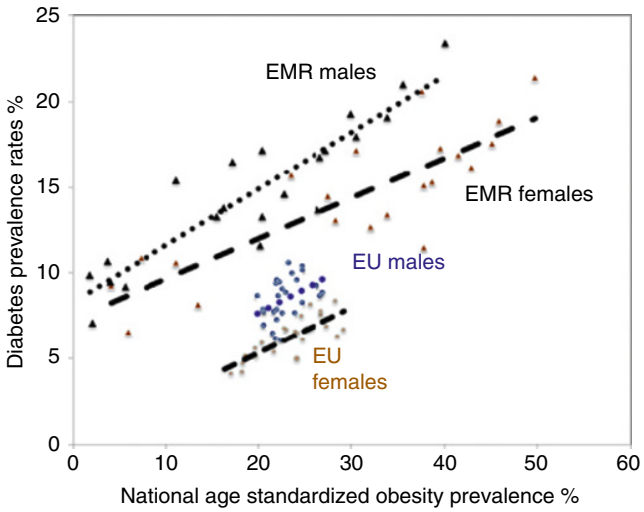

Figure 1.3 The relationship between the prevalences of obesity and diabetes in each of the 21 WHO Eastern Mediterranean countries compared with equivalent data from the 28 countries of the European Union. Diabetes prevalence rates are about twice as high in the Eastern Mediterranean countries as in the European Union at equivalent obesity rates. These data are based on randomly selected adults with measured anthropometry and fasting blood glucose levels in each country undertaken according to a standard protocol (the WHO STEPS program). (Source: Reproduced from Alwan et al. [43].)

If these differences are not genetic, then what might be the basis for the increased susceptibility to abdominal obesity and diabetes? Barker et al. [44], in his original study, claimed that lower birth weight in babies of pre-Second World War women in England seemed to determine an increased propensity of the offspring to develop the metabolic syndrome and diabetes 64 years later. The conditions amongst the working class in England at that time had already been documented as nutritionally

totally inadequate [45], so Barker ascribes the propensity to metabolic syndrome and diabetes as reflecting the impact of maternal malnutrition with induced poor fetal growth. Yajnik in Pune, India, then showed with Barker startling differences between the offspring of mothers in Pune and those of now well-fed mothers in Southampton, England [46]. The Indian children were smaller, with less lean tissue, and relatively fatter with distortions of the organ sizes which already related to increased insulin resistance in the newborn Indian babies. This seemed to be proportional to the degree of vitamin B_{12} deficiency and the discordant folate/B_{12} nutritional status of the mother [47], which has been shown to influence fetal growth. These vegetarian women were often being given inappropriately high doses of folic acid without any B_{12} and most likely would have been eating very modest amounts of food providing nucleic acids. Thus the generation of nucleotides in the crucial phase of early fetal development would have been compromised due to the lack of vitamin B_{12} required to generate methyl groups through folate remethylation.

These early nutritional effects relating to organ metabolism are probably amplified if there is some subsequent childhood malnutrition, because although they can recover their intestinal absorptive capacity on refeeding, their ability to mobilize insulin after a standard glucose test remains markedly reduced despite being extremely well-fed for months and with body weights that had returned to the normal weight for their heights [48]. Further analyses have shown that this effect is long-standing because adults in Jamaica who had been malnourished as children had a persisting impairment of insulin secretion [49], and this defect was also seen in survivors of early fetal deprivation during the Dutch famine [50].

The Millennium report for the United Nations on the global prevalence of persisting childhood malnutrition [51] highlighted the fact that almost all non-Western countries after the Second World War had high prevalences of childhood malnutrition leading to long-standing global, intergenerational malnutrition, which persisted throughout life. So a lifespan approach [52] to considering the problem of adult obesity begins with the nutritional state of the mothers before and during pregnancy with all its pathological and epigenetic implications for the offspring. We already know that the increase in body weight in previously malnourished women as they enter pregnancy leads to a much greater propensity to gestational diabetes [53], and they are then more likely to develop diabetes later themselves as well as having bigger and fatter children.

These global states of malnutrition almost certainly have lasted for millennia, so the early descriptions of obesity associated with ill health described by Bray are in line with the observed debilitating disease such as diabetes resulting from the impact of excess weight gain in people with lifelong malnutrition. In contrast, the Roman description of relatively healthy obese may then have reflected the better overall nutrition of the Romans in their Mediterranean environment.

Historical analyses of contributors to obesity

Weight gain leading to obesity occurs when energy intake from food exceeds energy expenditure from physical activity and metabolic processes over a considerable period. There has been much speculation as to the main driver of the global obesity epidemic, and this has often led to intense debate (see the analysis by Swinburn et al. [54] and the responses this generated). A complex and diverse range of factors can give rise to a positive energy balance, but it is the interaction between a number of these influences, rather than any single factor acting alone, that is thought to be responsible. The genesis of obesity at an individual level often focuses on a lack of cognitive control over personal behaviors that directly influence energy intake and ignores the critical role of physiological processes in driving or attenuating these behaviors. In addition, it is now recognized that powerful societal and environmental forces influence energy intake and expenditure through effects on dietary factors and physical activity patterns and may overwhelm the physiological control of body weight. It is the emergence of these environmental forces and the adjustments brought about by rapid changes in society which are the focus of most attempts to explain the emergence of the global obesity epidemic. The key elements of this transition and the emergence of our understanding around them are now set out below.

Marked declines in society's physical activity

Given how sudden the development of obesity has been on a population basis, one has to ask what happened in the early 1980s to make such a difference to the prevalence of obesity in our environment? One clear societal change is the introduction of computers for a myriad of tasks in the early 1980s but in particular a complete transformation of many people's office hours so now they spend their time sitting while working on their computers for hours on end. Even in such physically active jobs as construction or repairs, the introduction of a myriad of mechanical aids has also drastically reduced the need for sheer physical effort. The major development of the internet has also brought multiple opportunities for home entertainment and thus sedentary leisure time and reduced the need to leave home for entertainment. Life at home has also been transformed by new approaches to food preparation with microwaves, dishwashers, washing machines, etc. becoming a routine addition to kitchen hardware. It is regularly noted that with supermarkets providing ready-to-cook meals, the preparation time for meals has reduced from 2 to 3 hours to as little as 20 minutes.

Given all these changes, it is clear that the demand for energy expenditure has dropped dramatically on a secular basis since the early 1980s. Estimating the extent of this change in energetic terms is difficult in the absence of detailed sequential D_2O^{18} data

on energy expenditure. However, calculations can be made using the latest analyses of energy requirements by WHO [55] based on the original James and Schofield methodology [56]. Thus if a population of young men in their twenties weighing 70 kg was previously moderately active, i.e. with a physical activity level (PAL) of around 1.76 and a similar group are now sedentary (PAL 1.53), then men of this age would have reduced their average energy requirements by 400 kcal/day. Similarly, young women weighing 57 kg and moving from moderate to sedentary activity with PAL changes similar to men would reduce expenditure by 305 kcal/day (see examples in Table 5.1 of the UNU/WHO/FAO 2001 energy requirements report [55]). This would require a substantial and sustained reduction in food intake to match the lower energy expenditure. Originally when assessing UK household intakes in different decades, James estimated that from the 1950s to modern times there might on average have been an average reduction of energy demand for physical activity of about 700 kcal/day on the basis of a marked reduction in the proportion of adults engaged in very active jobs where PALs were 2.0 or more. The overall effects are illustrated in Figure 1.4.

Obtaining independent analyses of secular changes in energy expenditure is not easy, and if one simply relies on questionnaires, then sometimes total physical activity does not seem to have changed over time, e.g. in Finland [58]; but in China, there has been a marked decrease in physical activity [59], and the overall conclusions are that there has been a substantial decline in physical activity demands [60]. Secular studies in Norwegian children studied with accelerometer readings in 2005 and then again up to 2012 showed there was a consistent reduction in more intense physical activity even within this short time interval. In addition, there was an age-related decline in physical expenditure as children became adolescents [61].

Now, as well as the secular decline in physical activity, there is a concomitant reduction in activity as people age. This was shown most vividly in the Baltimore aging studies, where one can recalculate the data on the energy needs of men first when they were 25 years of age and then when the same men were aged 70. If one applies the energetic analyses to the fall in activity and tissue metabolism as the muscle mass slowly declines but adjust the data so that they were the same body weight, then the overall reduction in energy output amounts to a fall of 2100 per day. This means that over the 45 years the falling output is equivalent to an annual average reduction of nearly 50 kcal/day. So in effect the Baltimore men's food intake needed to fall by nearly 50 kcals each day with further equivalent falls in daily intake each year decade after decade to avoid putting on weight as they age [62]. If extra food is eaten, then weight gain occurs, and the classic analyses suggest that about 20–25% of this is lean tissue which then contributes to increasing the maintenance energy requirement.

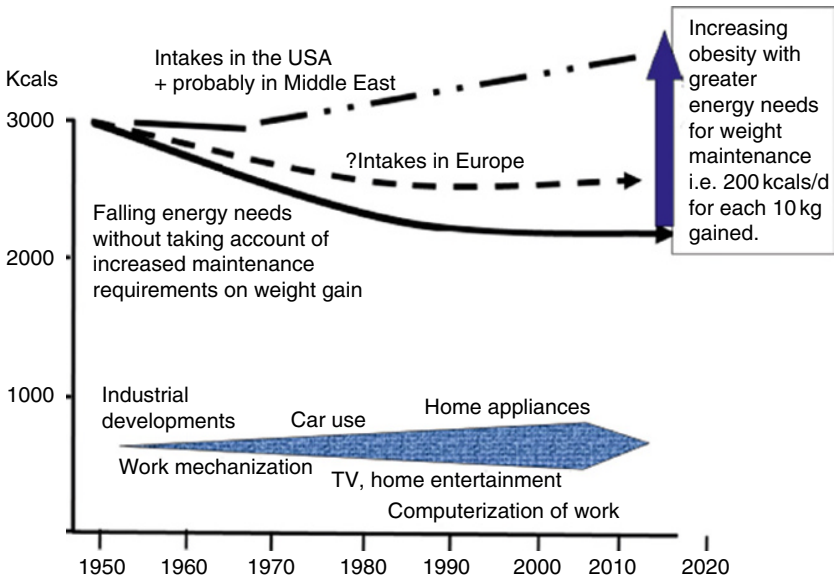

Figure 1.4 An illustration of the principal factors leading to the obesity epidemic. It is assumed that in the 1950s and 1960s, the average intake of the adult male population when weight stable was about 3000 kcal/day when the population was engaged in a lot of physical activity. Then over the next 40–50 years, significant industrial developments occurred, limiting the need for physical activity and in effect reducing the energy needs by perhaps 700 kcal/day on average, as shown by the continuous line falling from 3000 kcal/day. This means that intake should have fallen by the same 700 kcal/day. However, in many European countries, intake did not fall sufficiently, so positive energy balance led to weight gain. This weight gain involved an increase in lean as well as fat tissue, so the total maintenance energy needs of the concomitant lean tissue rose, and there was also an increase in the weight-bearing cost of physical activity. The overall increase in energy maintenance costs amounts to about 239 kcal/day for each10 kg weight gain, as estimated by Hall et al. [57]. However, in the United States, it has been estimated that food intake has risen, which probably applies to many populations in the Middle East, thereby explaining their marked current obesity rates. In European countries and elsewhere, the physiological drive to limit intake at lower expenditure levels was unsuccessful because the food industry developed techniques to enhance food and drink purchases (see below).

Using detailed analyses of lean body mass changes in men and women, James and Reeds showed many years ago that women do not build lean tissue as much as men [63], and so their maintenance energy expenditure does not rise to the same extent as men. Therefore women store more of the excess dietary energy as fat which in part explains why women are likely to gain more weight than men under the same energy imbalance conditions. It is also why women are usually more prone to obesity than men and particularly prone to extreme obesity, i.e. BMIs >40.

This interaction of secular falls in demand for physical activity, together with the natural reduction in physical activity with aging, explains why in the 1970s, obesity was mostly confined to older adults. To prevent obesity, the body's appetite sensing system would need to progressively reduce our food intake as we grow older, and this has become far more difficult with such limited levels of physical activity.

A revolution in food industrial strategies which increase food intakes

In the mid-1980s, one of the authors W.P.T. James was invited by the UK government to join an expert panel examining broad aspects of national industrial policy ranging from financial management to manufacturing and the service sector. The author's remit was to deal with the food, drink, and agricultural industry. Each member led a team with Delphi exercises involving a variety of experts and industrialists and with workshops held in different parts of the country. Given the extraordinary changes in agriculture and food policy that supported self-sufficiency during the Second World War [64], the author was alarmed to discover the proportion of food, including fruit and vegetables, that were now imported from abroad. Discussions with the Treasury Ministry revealed that they were more concerned about the balance of trade than the availability and access to quality food for the British public. At that time, food product development and marketing were unsophisticated, but suggestions around introducing new health criteria for food composition with the recently proposed WHO criteria based traffic light labeling of healthy food [65] were viewed with horror as this was an industrial enhancement, not a health promotion exercise. However, behavioral research began to develop rapidly in the United States and Europe, leading to a very sophisticated understanding of human behavior and how to manipulate it. Exceptionally detailed analyses of human reactions in shops around time spent examining foods, their position in relation to the height of customers, the value of big rather than small displays, the huge bonus of stacking special price inducements at the end of aisles, and the degree of price manipulations needed to stimulate buying all became carefully defined features for selling more product. Then they discovered the value of stimulating people's curiosity and providing unexpected stimuli for purchases at all hours of the day and night through the provision of food and drinks in machines or other facilities wherever people might pass or congregate. A multiplicity of flavors in a variety of products encourages greater consumption as using just one flavor leads to what Rolls termed "sensory-specific satiety." [66]. Then with the discovery of the range of molecular olfactory receptors for different flavors [67] came the special development of food and drinks with specifically added flavors which were known to have a powerful effect on the brain's pleasure and addictive centers. Author W.P.T. James had a detailed account from a major industrialist of the finding that specific flavors were favored by women in both the follicular or luteal phases of their menstrual cycle, so these flavors were then used with vodka to produce alcopops, which then in practice transformed the drinking habits of young women in the United Kingdom. This strategy was so successful that alcohol consumption by young women rose alarmingly in the 5 years following the introduction of these new products leading to medical concerns about the impending problem of alcoholism and indeed cirrhosis of the liver in young women – a feature never seen before in the United Kingdom [68]. Neurological MRI testing is now one of the routine assessments of new food products, many of which have added flavorings aimed at stimulating the pleasure centers with huge factories synthesizing the specific sensory enhancing products. Whether their greater use has anything to do with what Brownell now recognizes as food addiction [69] is still unclear. The subtlety of marketing is also illustrated by the use of a picture of a salad in the options of a famous fast-food chain. This representation of healthy food stimulates young women to not necessarily purchase the salad but to treble their purchases of fried potato chips as the salad image creates a false association with the healthiness of the whole menu and thus provides an excuse to purchase chips. Such sales ensure a good profit margin for the company but have very dubious effects on weight gain and health!

Globalization, modern food supply chains, advanced food processing techniques, and ever more sophisticated and aggressive marketing approaches have created a modern food environment that Swinburn et al. [70] have termed obesogenic (literally designed to induce obesity). The current food supply and consumption patterns are dominated by the wide availability of ultra-processed food products that are highly palatable, cheap, convenient, long-lasting, and heavily promoted. A high level of consumption of these products replaces core foods (such as fresh fruits and vegetables, meat, milk, and wholegrain cereals). Modern lifestyles have also led to changes in eating and lifestyle behaviors. We have fewer formal meals, we eat in front of the TV, we take away more food rather than cook it at home, and at home, we rely more on ready-prepared foods. These behaviors are associated with poorer diet quality. Food is also now cheaper and more widely available than it has been at any point in human history, and the portion size of a single serving has increased dramatically. In addition, we are encouraged by marketing to consume even when we are not hungry. Many of these issues are addressed in later chapters.

So we can conclude that major industrial developments have reduced the need for energy expenditure, but the normal physiological adaptive lowering of food intake to match this new lower requirement is counterbalanced by intense food marketing.

Furthermore, the greater weight and energy requirements of the obese frame mean, for example, that in the United States, the food industry is profiting from the extra food purchases required to maintain the population with obesity. This has been estimated to amount to many hundreds of billions of dollars of extra sales each year if one considers the excess food eaten by children with obesity both in childhood and then in their adult life [71] plus the extra food sales for adults with obesity.

The burden of obesity

For some time, clinicians have recognized that people with obesity have a great deal of backache and are far more prone to osteoarthritis of the weight-bearing joints. It was also well known that weight gain exacerbates hypertension and hypercholesterolemia as well as promoting glucose intolerance and then diabetes. These hazards of obesity were usually presented as a consequence of self-inflicted weight gain, so they were not taken seriously by many clinicians and were even viewed as a means by which one could persuade patients to be slim. However, a more considered understanding of the role of obesity in health was obtained from the WHO Millennium Review of Health conducted by Alan Lopez with Chris Murray and colleagues, which summarized for the first time the amount of death and disability in each of the 14 subregions of the world that was attributable not to particular diseases but to avoidable risk factors. This allowed for much more meaningful public health policy making and led in 2002 to WHO's report on reducing risks globally [72]. The risk factors considered included iron deficiency anemia and vitamin A deficiency as well as childhood and maternal malnutrition, high cholesterol levels, and high blood pressure. The IOTF was asked to undertake the work on global rates of overweight and obesity for this analysis. The relationship of obesity with a host of other diseases, for example arthritis, cardiovascular disease, cancers, and diabetes, was quantified, and all these relationships together with all the other risk factors were linked to data on premature death (i.e. <75 years) and to years of disability. In this analysis, overweight and obesity were ranked the 7th most important risk factor for premature death on a global basis and the 10th most important factor in terms of disability [73]. Since then, overweight and obesity prevalences have escalated, and Murray's team based in Seattle with Gates Foundation support has established an annual analysis of disease burden and risk factors which are published regularly by *The Lancet*. The assessment of the burden of disease in 2017 found a 43% increase in the global male prevalence of overweight (i.e. BMI 25+) from 1990, and in women, the increase was 67% [74]. More detailed analysis of obesity per se came from a special sub-study with the burden being calculated again as a composite of years of life lost because of weight gain and years of life lived with disabilities linked to excess weight, as shown in Figure 1.5 [75]. Note that the figures include both years of life lost

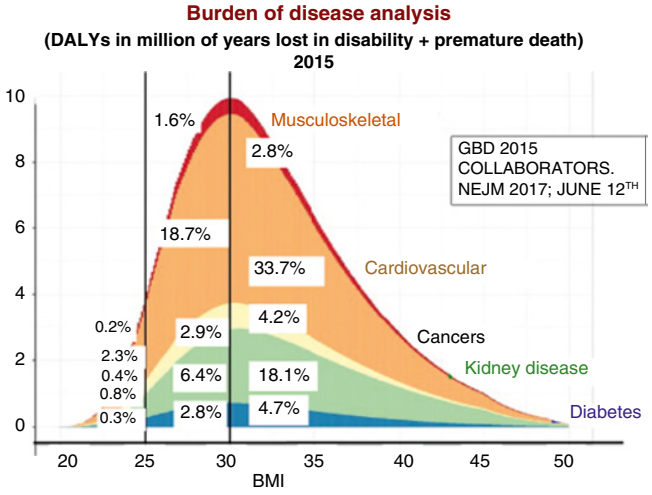

Figure 1.5 The global burden of disease assessed in terms of disability-adjusted life years (DALYs) in millions, which includes the years of life lost due to premature mortality plus the years lived with a disability from the range of different disorders listed. (Source: Redrawn from Figure 1.3b in the global burden analyses [75].)

and the years of earlier disabilities. The greatest burden arises from the excess cardiovascular disease induced by excess weight gain, with kidney disease and diabetes being the next two major burdens. However, the authors recognize that the risk increases from about a BMI of 20, and the major finding is that a substantial burden is induced by just being overweight and not obese. In fact, the overweight burden amounts to about a third of all the burden of obesity and actually accounts for nearly 40% of premature deaths related to excess weight gain. This means that in public health terms, one cannot forget about the large proportion of adults who are overweight. Even with modest increments of risk, their high prevalence means that the overweight group contributes a substantial disease burden.

The economic impact of excess weight gain

Given this burden of obesity-related disease identified in these analyses, policy makers asked obesity specialists to assess the financial damage done by gaining excess weight. These costs are composed of both direct healthcare costs and indirect costs to the community. Although people with obesity have higher rates of illness, the overweight nonobese group still makes a very substantial contribution to the overall hospital and general community cost of general medical care in the community because they make up a much larger proportion of the patient population. Lost productivity associated with failure to attend work because of back pain or other ailments precipitated by the excess body weight together with the loss of efficiency in those who attend work but are unable to work to their maximal capacity also need to be factored into the costings.