

EPIDEMIOLOGY AND
PREVENTION OF
CARDIOVASCULAR
DISEASES: A GLOBAL
CHALLENGE
SECOND EDITION

DARWIN R. LABARTHE, MD, MPH, PHD



JONES AND BARTLETT PUBLISHERS
Sudbury, Massachusetts

World Headquarters

Jones and Bartlett Publishers
40 Tall Pine Drive
Sudbury, MA 01776
978-443-5000
info@jbpub.com
www.jbpub.com

Jones and Bartlett Publishers
Canada
6339 Ormindale Way
Mississauga, Ontario L5V 1J2
Canada

Jones and Bartlett Publishers
International
Barb House, Barb Mews
London W6 7PA
United Kingdom

Jones and Bartlett's books and products are available through most bookstores and online booksellers. To contact Jones and Bartlett Publishers directly, call 800-832-0034, fax 978-443-8000, or visit our website, www.jbpub.com.

Substantial discounts on bulk quantities of Jones and Bartlett's publications are available to corporations, professional associations, and other qualified organizations. For details and specific discount information, contact the special sales department at Jones and Bartlett via the above contact information or send an email to specialsales@jbpub.com.

Copyright © 2011 by Jones and Bartlett Publishers, LLC

All rights reserved. No part of the material protected by this copyright may be reproduced or utilized in any form, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without written permission from the copyright owner.

This publication is designed to provide accurate and authoritative information in regard to the Subject Matter covered. It is sold with the understanding that the publisher is not engaged in rendering legal, accounting, or other professional service. If legal advice or other expert assistance is required, the service of a competent professional person should be sought.

This book was written by Darwin R. Labarthe in his private capacity. No official support or endorsement by the Centers for Disease Control and Prevention, Department of Health and Human Services is intended, nor should be inferred.

Production Credits

Publisher: Michael Brown
Editorial Assistant: Catie Heverling
Editorial Assistant: Teresa Reilly
Production Manager: Tracey Chapman
Senior Marketing Manager: Sophie Fleck
Manufacturing and Inventory Control Supervisor: Amy Bacus
Composition: Auburn Associates, Inc.
Cover Design: Kristin E. Parker
Cover Image: fruit: © Daniel Gilbey/Dreamstime.com; family: © Pavel Losevsky/Dreamstime.com; no smoking: © Rosengaard/Dreamstime.com
Printing and Binding: Malloy, Inc.
Cover Printing: Malloy, Inc.

Library of Congress Cataloging-in-Publication Data

Labarthe, Darwin.

Epidemiology and prevention of cardiovascular diseases : a global challenge / Darwin Labarthe. — 2nd ed.
p. ; cm.

Includes bibliographical references and index.

ISBN-13: 978-0-7637-4689-6 (pbk.)

ISBN-10: 0-7637-4689-4 (pbk.)

1. Cardiovascular system—Diseases—Prevention. 2. Cardiovascular system—Diseases—Epidemiology.
 3. Cardiovascular system—Diseases—Etiology. I. Title.
- [DNLM: 1. Cardiovascular Diseases—epidemiology. 2. Cardiovascular Diseases—prevention & control.
WG 120 L113e 2011]
RA645.C34L33 2011
614.5'91—dc22

2009044199

6048

Printed in the United States of America

14 13 12 11 10 10 9 8 7 6 5 4 3 2 1

Contents

Foreword xi
Preface xiii
Dedication xv
Acknowledgments xvii

PART 1—A PUBLIC HEALTH PERSPECTIVE 1

Chapter 1 Cardiovascular Diseases: A Global Public Health Challenge 3

Summary 3
The Epidemiology and Prevention of Cardiovascular Diseases: Definition and Scope 3
The Basis of Public Health Concern Worldwide 5
Rates of Occurrence in Selected Populations and Changes in Recent Decades 10
Current Burdens of Major Cardiovascular Diseases in the United States and the World 12
Opportunities for Prevention 15
References 17

Chapter 2 Distributions and Disparities 19

Summary 19
Introduction 19
Age and Life Stages 22
Sex or Gender 26
Race or Ethnicity 27
Geography or Place 29
Person, Place, and Time 32
Conclusion 35
References 36

PART 2—THE MAJOR CARDIOVASCULAR DISEASES 39

Chapter 3 Atherosclerosis 41

Summary 41
Introduction 41
Methods of Measurement—Invasive and Noninvasive 42
Manifestations—Above and Below the “Clinical Horizon” 43
Mechanisms of Atherogenesis 46
Person, Place, and Time 47
Atherosclerosis in Childhood, Youth, and Early Adulthood 49
Prevention and Treatment of Atherosclerosis 54
Current Issues 55
References 55

Chapter 4 Coronary Heart Disease 59

Summary 59
Introduction 59
Background 62
Population Studies: Definition and Classification, Diagnostic Algorithms, and Criteria 63
Rates 65
Risks 74
Trends and Explanations 79
Forecasts 83
Current Issues 83
References 83
Appendix 4-A: Key to Population Abbreviations Used by the WHO MONICA Project 87

Chapter 5 Stroke 89

Summary 89
Introduction 89
Background 91
Population Studies: Definition, Classification, and Diagnostic Methods 92
Rates 93
Risks 101
Trends 104
Forecasts 107
Current Issues 107
References 107

Chapter 6 Related Conditions 111

- Summary 111
- Introduction 111
- Peripheral Arterial Disease 113
- Aortic Aneurysm 120
- Chronic Heart Failure 123
- Deep Vein Thrombosis and Pulmonary Embolism 132
- Arrhythmias 135
- References 136

PART 3—THE MAIN DETERMINANTS 139**Chapter 7 Genes and Environment 141**

- Summary 141
- Introduction 142
- Concepts and Strategies of Genetic Epidemiology 144
- Family History 146
- Gene–Environment Interaction 150
- Cardiovascular Applications of Genomic Epidemiology 152
- Current Issues 155
- References 156

Chapter 8 Dietary Imbalance 159

- Summary 159
- Introduction 159
- Concepts and Definitions of Dietary Patterns 161
- Measurement 165
- Determinants 168
- Distribution 170
- Cardiovascular-Related Effects of Diet 172
- Prevention and Control 180
- Current Issues 185
- References 186

Chapter 9 Physical Inactivity 191

- Summary 191
- Introduction 191
- Concepts and Definitions 192
- Measurement 194

Determinants 194
Mechanisms 196
Distribution 197
Cardiovascular-Related Effects 204
Prevention and Control 211
Current Issues 217
References 217

Chapter 10 Obesity 223

Summary 223
Introduction 224
Concepts and Definitions 224
Measurement 229
Determinants 229
Mechanisms 233
Distribution 236
Rates and Risks 244
Prevention and Control 253
Current Issues 262
References 262

Chapter 11 Adverse Blood Lipid Profile 269

Summary 269
Introduction 269
Concepts and Definitions 270
Measurement 273
Determinants 274
Mechanisms 275
Distribution 277
Relation to Rates and Risks 283
Relation to Other Factors 290
Prevention and Control 292
Current Issues 302
References 304

Chapter 12 High Blood Pressure 311

Summary 311
Introduction 312
Concepts and Definitions 312
Measurement 316

Determinants	317
Mechanisms	322
Distribution	323
Relation to Rates and Risks	336
Relation to Other Factors	339
Prevention and Control	341
Current Issues	351
References	352

Chapter 13 Diabetes and the Metabolic Syndrome 361

Summary	361
Introduction	362
Concepts and Definitions	363
Measurement	366
Determinants	367
Mechanisms	368
Relation to Other Factors	369
Distribution	369
Rates and Risks	375
Prevention and Control	382
Current Issues	387
References	389

Chapter 14 Smoking and Other Tobacco Use 395

Summary	395
Introduction	395
Concepts and Definitions	396
Measurement	397
Determinants	398
Mechanisms	398
Distribution	400
Relation to Rates and Risks	404
Relation to Other Factors	414
Prevention and Control	414
Current Issues	424
References	425

Chapter 15 Other Personal Factors 431

Summary	431
1. Alcohol Consumption	433

2. Adverse Psychosocial Factors 447
3. Hemostatic Factors 464
4. Evolving and Emerging Factors 476
References 491

Chapter 16 Social and Physical Environment 503

Summary 503
Introduction 503
Social Status 505
Changes in Social Conditions 512
Particulate Air Pollution 522
Neighborhood Characteristics 524
Current Issues 527
References 528

PART 4—CAUSATION AND PREVENTION: THEORY, PRACTICE, AND FURTHER RESEARCH 533

Chapter 17 What Causes Cardiovascular Diseases? 535

Summary 535
Introduction 535
Causal Judgment 536
Causal Constructs 540
Caustion of Atherosclerotic and Hypertensive Diseases 543
Conclusion 547
Current Issues 547
References 548

Chapter 18 Strategies of Prevention 551

Summary 551
Introduction 551
Concepts and Language of Prevention 552
Strategies of Prevention 557
Intervention Approaches 560
A Developing Country Perspective 561
Current Issues 563
References 565

Chapter 19 Evidence and Decision Making 567

- Summary 567
- Introduction 567
- Nature of Evidence 569
- Evidence-Based Decision Making 570
- Approaches to Evaluation of Evidence 573
- Current Issues 587
- References 587

Chapter 20 Recommendations, Guidelines, and Policies 591

- Summary 591
- Introduction 592
- Clinical Guidelines 594
- Community Guidelines 607
- Public Policies 609
- Current Issues 613
- References 614

Chapter 21 The Case for Prevention 619

- Summary 619
- Introduction 619
- Experience with Multifactor Primary Prevention 621
- The Burden of Risk 636
- Economic Considerations 640
- Models for Explanation and Prediction 642
- Visions of Success in CVD and Chronic Disease Prevention 647
- Counter-Arguments 649
- Current Issues 649
- References 650

Chapter 22 Taking Action 657

- Summary 657
- Introduction: Calls to Action 657
- Overview: Goals, Strategies, and Action Plans 658
- Case Study: *A Public Health Action Plan to Prevent Heart Disease and Stroke* 665
- Obstacles to Taking Action 669
- Current Issues 673
- References 675

Chapter 23 Epidemiology and a CVD Prevention Research Agenda 679

Summary 679
Introduction 680
Concepts of Epidemiology 681
Goals 682
Strategies of Investigation 683
Proposed Research Agendas 685
Capacity Requirements 690
Populomics: The Population Context of Research on Health 692
Current Issues 693
References 693

INDEX 697

Foreword

Publication of this second edition of Dr. Darwin Labarthe's invaluable book, *Epidemiology and Prevention of Cardiovascular Diseases: A Global Challenge* is most opportune: As Dr. Labarthe emphasizes, the CVD prevention effort at this juncture—50 years down the road—confronts both “. . . considerable challenges and immense opportunities . . .” On the one hand, the CVD epidemic persists; on a global scale it is waxing—indeed a challenge. And the challenge holds also for countries like the United States, where epidemic CVD persists despite substantial declines in coronary/stroke death rates during the latter decades of the 20th century. The current situation in the United States is problematic—as this book documents—making the challenges considerable indeed: tapering or cessation in recent years of down trends in CVD mortality and in major CVD risk factor levels (e.g., for saturated fat and cholesterol intakes, and for diet-dependent serum cholesterol and blood pressure); epidemic obesity with its consequences, including rampant incidence of diabetes and other obesity-driven metabolic CVD risk factors; unabated high salt intake; overall dietary and physical activity patterns still generally adverse population-wide including among children and teenagers; all too many still smoking, all too many teenagers becoming smokers; even more so for lower socioeconomic strata of all ethnicities, hence paltry proportions of all strata at *low CVD risk*—a critical index—and little or no evidence of a sustained upward slope in this index; in the media, especially TV, an on-going flood of promotions of foods/beverages harmful for heart health; in medical practice, overwhelming reliance on a high risk strategy (reactive, not proactive) to cope with these challenges—a focus on detection of people who already have a high level of the established major CVD risk factors and their long-term treatment with medications (in 2008, 320.4 million prescriptions for antihypertensive and 139.6 million prescriptions for antihypercholesterolemic drugs, as reported by the AARP). However useful for patients already at high CVD risk, this limited one-sided strategy relying on pills as the remedy begs the basic issue: Epidemics are due to population-wide exposures to new ways of

life for which the human species has not been adapted over the 2–4 million years of hominid/hominoid evolution; their roots are mass “. . . disturbances of human culture . . .” (Rudolf Virchow)—generalizations fully applicable/valid for the CVD epidemic, as this monograph details. To end the CVD epidemic, the *sine qua non* is rectification of the multiple disturbances in human culture causing it—a proposition repeatedly verified as valid by the history of conquest of earlier epidemics (e.g., tuberculosis, pellagra, rickets).

The opportunities to conquer the CVD epidemic are indeed immense. First and foremost, prerequisite knowledge concerning the *etiology* of the CVD epidemic: the data base (already substantial 50 years ago) is now vast—extensive concordant data, worldwide in scope, accumulated over decades by epidemiology and every other research methodology available to medicine. Critical detailed information on the multiple causes of epidemic CVD is in hand—and for prevention of mass disease, such information on causation, the “question of questions,” is decisive. We know in depth what needs to be done—at every level of prevention—to break links in the chain of causation, including for **primary and primordial prevention**, i.e., the prevention in the first place (from preconception on) of the adverse lifestyles and the lifestyle-related established major risk factors. Crucial to this effort are improved eating patterns, Mediterranean and East-Asian style cuisines updated for this century, especially as to lower salt, plus moderation in intakes of alcohol, fats, and total calories—along with regular frequent exercise and non-smoking. The update for the 21st century—derived from the research achievements of the last 50 years—gives an enhanced nutrient intake pattern: as earlier, low in saturated fats and cholesterol; reduced in total fats; enhanced in polyunsaturated fats; calorie controlled; *plus* free of trans fats; much lower in salt; reduced in sugars especially separated sugars (e.g., from sweetened beverages); enhanced in total protein, especially vegetable protein (lower in animal protein from meats); for those who drink, moderate (not excessive) in alcohol; enhanced in potassium/calcium/magnesium/phosphorus/non-heme iron, the vitamins, and fiber (from whole

grains/beans/vegetables/fruits). As this enumeration indicates, the research findings (including from population-based observational studies and clinical trials) document the *multifaceted dietary imbalances*—concurrent excesses and inadequacies—now implicated in the etiology of the CVD epidemic and its diet-related major metabolic risk factors. Consequent recommendations enable variegated approaches to modern delightful eating styles assuring avoidance/rectification of these imbalances.

These eating styles, along with regular frequent exercise, offer the potential for all population strata (socioeconomic/ethnic) to prevent/check/correct the nowadays still usual development of adverse levels of major metabolic risk factors: serum total/LDL/VLDL/HDL cholesterol; blood pressure; plasma glucose; weight; and they go beyond these merits, since adverse eating patterns produce excess CVD risk over and above their adverse influences on these metabolic risk factors.

So the opportunities are truly immense, as Dr. Labarthe emphasizes. Their scope encompasses potential for realization of the critical goal: *continuous progressive enhancement in the coming years/decades of the percent of the population at low risk*, so that for most people—not just a small minority—CVD risk is miniscule; they are freed of the burden of epidemic CVD, with consequent enhanced longevity with health. High stakes indeed!

The opportunities are immense also because on a world scale and in several regions of the world, public policy is in place at the national level (including in the United States), policy committed to the accomplishment of CVD prevention through a two-pronged strategy (population-wide and high risk) emphasizing improved lifestyles. In a few places, public policy specifically includes priority for achieving the decisive goal of progressively increasing the percentage of the population at low risk. In the United States, substantial funds have recently been allocated—specifically to the national Centers for Disease Control and Prevention (CDC)—for the CVD prevention effort.

Opportunities are immense also for this effort because many countries—ranging from Finland to Japan to the United Kingdom and the United States—have already over decades accrued extensive positive experiences with sustained public health efforts to improve lifestyles, thereby control lifestyle-related major CVD risk factors, and contribute to CVD

prevention/control. Repeatedly, the public has been responsive and substantial progress (albeit incomplete) has been achieved, despite opposition from special interests (including sectors of the food and beverage industries, the big tobacco companies)—e.g., in the United States, sizable declines in intakes of saturated and trans fats, total fats, cholesterol; the related decrease in adult population average serum cholesterol from about 240 mg/dl 50 years ago to about 200 mg/dl by the year 2000, achieving a national public health goal; marked falls in the prevalence of cigarette smoking; associated declines—in the order of 50% or more—in mortality from CHD and stroke, with consequent addition of years to life expectancy for young, middle-aged, and older adults. And, in several countries, as well as internationally, there are significant social movements in place, supporting/encouraging the effort, bringing together health professionals and lay leaders in effective alliances. As Dr. Labarthe notes, this too is an important component for a successful prevention effort—important today for CVD, as it was in the 19th century for TB control. All these are indeed solid bases for accomplishment of next key tasks.

As noted repeatedly, this book is replete with many-sided up-to-date information invaluable for every person concerned with the CVD prevention effort. It is a fitting product of Dr. Labarthe's extraordinary capacities and experiences over decades—as a colleague, teacher, researcher, public health leader—in academia, at the CDC, at local/national/international learning venues, including the seminal US and International Ten Day Teaching Seminars on CVD Epidemiology and Prevention he has effectively led for years.

On a personal note, over 40 years ago when I authored an early monograph on this same subject, it was my privilege for it to have a Foreword by Paul Dudley White, MD—distinguished cardiologist, statesman, world leader, humanist/humanitarian. Its opening sentence read, “Dr. Jeremiah Stamler has written the book on Preventive Cardiology that I would liked to have written.” Today these words are mine in regard to this volume by Darwin Labarthe.

Jeremiah Stamler, MD
Professor Emeritus
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Preface

The central messages of this second edition are these:

- (1) Cardiovascular diseases remain the foremost causes of preventable death globally and continue to grow in prominence, because of their attendant burden, disparities, and costs.
- (2) Epidemiology has contributed immeasurably to a vast body of knowledge about the causes and means of prevention of these and related conditions, but this knowledge has yet to be applied on a sufficient scale to confer its potential societal benefit.
- (3) Public health is accountable for putting this knowledge more fully to work by setting goals, devising strategic plans and policies, implementing targeted actions, and documenting their impact in improving the health of populations.

These messages are consistent with the content of the first edition but have gained force from developments in the intervening decade: increased awareness of the global burden of cardiovascular diseases, with their immense social and economic consequences; a growing sense of need to integrate approaches to cardiovascular diseases with prevention of other chronic or noncommunicable diseases, with transformation of health systems to address them coherently; and the ever more urgent goal to reduce the mounting burden, disparities, and costs of these diseases. Epidemiology, through its applications in development, adoption, and implementation of health policy and in public health practice, is fundamental to achieving this goal. It is the author's hope that this new edition will contribute to this effort.

The difference of a decade is due importantly to advances in science and practice that better inform our understanding of the need and opportunity for effective action. From the start of this past decade, the perspective of the author, too, has advanced—from that of the academic epidemiologist to that of the public health practitioner. This was a result of undertaking a US governmental role at the federal level and the greatly enhanced public health experience afforded by this opportunity. The influence of this

change on the context and content of the book is substantial; however, it is necessary to underscore the disclaimer that the views expressed throughout are personal and are not intended to represent the official position of the US Centers for Disease Control and Prevention (CDC) or the US Department of Health and Human Services (DHHS).

The book has changed principally in presenting greater emphasis on public health in cardiovascular disease prevention while retaining its epidemiologic content. The intent has been to increase the book's value for both epidemiologists and public health professionals by bringing the original content up to date in Parts I–III and expanding discussion of how epidemiology is translated into policy and practice in Part IV.

Currency has been achieved by including more than 1600 citations and nearly 400 tables and figures, many from recent sources; rewriting the chapters on the major cardiovascular diseases and their determinants; introducing a chapter on genomic epidemiology; and expanding discussion of the global dimensions of CVD. For many sources, URLs are included to permit continuing access for interested readers.

New chapters in Part IV address strategies of prevention as part of a recently developed action framework; the nature of evidence for prevention, and methods for its evaluation as practiced by several leading authoritative bodies; current national, regional, and global recommendations, guidelines, and policies for prevention of CVD and other major chronic diseases; the case for CVD prevention at individual and population levels; and action plans adopted for implementation in the United States, Europe, South Asia, and worldwide. Expansion in these areas had one regrettable cost—lack of updates on rheumatic heart disease, Chagas' disease, congenital heart disease, and Kawasaki disease—which are treated only in the first edition.

Features retained in the second edition include the basic structure in which the public health perspective is introduced in Part I; the major atherosclerotic and hypertensive diseases are discussed in Part II;

their main determinants are reviewed sequentially in Part III; and implications of this evidence for theory, practice, and research are discussed in Part IV, which concludes with a chapter on CVD epidemiology of the future—the rich and varied research opportunities presented and the place of epidemiology as the core discipline of “populomics,” the scientific foundation of population health. A historic perspective is also retained, although this is not meant to recount the history of the field, which is being done in a far more effective way elsewhere. The purpose instead is to illustrate wherever appropriate the key studies that, from early in the development of CVD epidemiology, have made fundamental and lasting contributions to our current knowledge.

Throughout the book, the unifying approach of a single author has the advantage of a consistent presentation and coherent interpretation across the many topics addressed. There is room for differing opinion and further exploration of many topics raised. The content reflects one person’s perspective and in no

case represents an exhaustive systematic review, although those of others are cited extensively. Closing each chapter is a more or less speculative suggestion of current issues most important for further discussion. In these ways the text is intended to stimulate thinking and debate. The author welcomes comments, queries, and criticisms from readers.

A Chinese proverb says, “Teachers open the door but you must enter by yourself.”¹ It is hoped that the material that follows will open many doors for students and practitioners of CVD prevention and public health, revealing a world of opportunity for fulfilling our highest obligation: to assure conditions in which people can be healthy.

Reference

-
1. Schiller D. *The Little Zen Companion*. New York: Workman Publishing; 1994.

Dedication

This book is dedicated to all whose work is reflected here and to all who will contribute to advances in the understanding of cardiovascular diseases and reduction of the public health burden they represent throughout the world.

Acknowledgments

Technical assistance in bibliographic work was provided with diligence and skill by T. Christopher Bond; the permissions process was supported by Tiffany Lynn Williams and by Anthony Omokheowa Anani and Elohor Anani.

Contributions of critical points of information were made by Patty Borhani, Ross Brownson, Michele Casper, Elizabeth Barrett-Connor, Rory Collins, Leonard Cook, Jeffrey Cutler, Jack Farquhar, Lawrence Green, Nancy Haase, Millicent and Ian Higgins,

George Howard, William Kannel, Thomas Kottke, Ian MacMahon, Henry McGill, Kenneth Pelletier, Douglas Schocken, Richie Sharrett, Jeremiah Stamler, Elaine Stone, Jack Strong, and Thomas Thom.

Several peer reviewers provided valuable comment and suggestions. Although their anonymity precludes personal recognition, it is hoped that they will see their input reflected in the final product.

Merrily Labarthe deserves boundless gratitude for her support and forbearance throughout this project.

