

# Index

---

Note: Page numbers followed by an *f* refer to figures. Page numbers followed by a *t* refer to tables. Page numbers in **bold** indicate an in-depth discussion.

## A

- a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS), 55
- abdominal fat mass, 41
- aberrant phosphorylation, 103*t*
  - insulin receptor, 4
- absenteeism costs, 2
- acarbose, 122, 123*t*, 125, 138*t*, **140**, 191
- ACE inhibitors, 62, 62*t*
- acetyl-CoA, 4
- Actos Now for the Prevention of Diabetes (ACT NOW) trial, 122, 123*t*, 138*t*, 140, 187
- acute insulin response to intravenous glucose (AIR), 42*t*
- acute insulin secretory response to glucose (AIRg), 17, 43–44, 116, 138
- acylcarnitines, 83
  - in prediabetes, **90–92**, **91f**
- adalimumab, 59
- adiponectin, 41, 42*t*, **59–62**, **62t**, 117, 118*f*
- ADIPOQ gene, 60
- adipose tissue inflammation, 87
- adiposity, 17, 27, 28*t*, 29, 49, 87, 144, 160
- adrenergic  $\beta$ -3 receptor (ADRB3), 54
- aerobic fitness, 156
- Affordable Care Act, 178
- aging, 3, 25*f*
- air pollutants, traffic-related, 5
- air quality, 5, 6*f*
- alanine, 85*t*
- alanine aminotransferase, 24
- alimentary bacteria, 93
- $\alpha$ -cell
  - dysfunction, 3, 4*t*
  - hyperfunction, 4*t*
- ambient insulin resistance, 126
- American Diabetes Association (ADA), 2, 11–12, 32, 56, 127, 129, 151–152
- American Heart Association, 32
- amino acids, 189
  - aromatic amino acids (AAAs), 83, 93
  - branched-chain amino acids (BCAAs), 83–84, 86, 93
  - catabolism, 86
  - fasting plasma amino acid levels, 85*t*
  - gluconeogenic, 13
  - pattern, 83, 85*t*
  - polar, 87
  - total, 86
- amputation, 1, 151
- amyloid degeneration, 44
- Anaerostipes, 93
- angiotensin II receptor blockers, 62, 62*t*
- anthropometric predictors, 27–29, 28*t*
- antibiotics, 6*f*, 94
- antifungals, 94
- antihypertensives, 6*f*, 56, 139
- antipsychotics, 6*f*, 153*t*, 191
- antiretroviral therapy, 191

anti-virals, 94  
 apoptosis, 44, 44*f*, 77  
 appetite dysregulation, 3  
 arginine, 85*t*  
 aromatic amino acids (AAAs), 83, 93  
 arthritis, 59, 193*t*  
 asparagine, 84, 85*t*, 189  
 aspartic acid, 84, 85*t*, 189  
 asthma, 193*t*  
 atherosclerosis, 101, 189  
 Australian Diabetes Society/Australian  
 Diabetes Educators Association, 128  
 autoimmune disorders, 59, 189  
 autonomic neuropathy, 100  
 awareness, 1

**B**

bariatric surgery, 192–194, 192*t*  
 behavioral e-counseling, 159  
 behavioral predictors, 29  
 $\beta$ -cell. *See* pancreatic islet  $\beta$ -cell  
 $\beta$ -oxidation, 4  
 bile acid sequestrant colesevelam, 49  
 bile acids, 83  
 biliopancreatic diversion, 192  
 bioactive sphingolipids, 61  
 biomarkers, 77  
 blindness, 1, 151  
 blood glucose. *See* glucose  
 blood pressure (BP), 31, 54*f*, 61,  
 113, 118*f*, 138  
   diastolic blood pressure (DBP), 42*t*  
   elevated, 5, 6*f*, 53, 58, 84, 101, 112, 127,  
   153*t*, 191–192, 193*t*  
   hemodynamics, 53–56, 54*f*, 55*f*, 100  
   hypertensive crisis, 191  
   systolic blood pressure (SBP), 42*t*  
 BMI  
   decrease in, 107  
   in diabetes management, 13, 17, 18*f*, 27,  
   29–31, 40, 61, 83, 110, 154, 167, 190  
   threshold, 193*t*  
 body fat distribution, 144  
 branched-chain amino acids (BCAAs),  
 83–84, 86, 93  
 bupropion, 191

**C**

caffeine consumption, 30–32  
 calories, 4, 107, 109, 139  
 Canadian Normoglycemia Outcomes  
 Evaluation (CANOE) trial, 122, 123*t*,  
 141, 187  
 carbohydrates, 3–4, 111, 143  
   *The Diabetes Carbohydrate & Fat Gram  
   Guide*, 163  
 carboxylase, 4  
 cardiac stress testing, 155  
 cardiometabolic risk factors, 41, 42*t*  
 cardioprotection, 190  
 cardiovascular disease, 100, 113, 149, 151,  
 168, 189–190  
 carnitine, 90  
 carnitine acylcarnitine translocase  
 (CACT), 90  
 carnitine palmitoyltransferase (CPT)-1,  
 4, 90  
 carotid plaque, 101  
 catecholamine signaling, 55  
 cell proliferation, 77  
 Centers for Disease Control and  
 Prevention (CDC), 1, 11, 53, 97, 152  
 Centers for Medicare and Medicaid  
 Services, 178–179, 179*f*, 182–183  
 central nervous system  
 (CNS), 3, 4*t*  
 cephalosporins, 94  
 ceramides, 61  
 certolizumab pegol, 59  
 children and adolescents  
   metabolic surgery for, 193  
   with type 2 diabetes (T2D) in, 2,  
   113–115  
 chlorogenic acids, 32  
 cholesterol levels, 127, 189  
   HDL, 42, 42*t*, 49, 61, 84, 112,  
   118*f*, 168  
   LDL, 24, 49–50, 112  
 chronic kidney disease, 1, 53, 99,  
 100*t*, 114, 151  
 cigarette smoking. *See* smoking  
 citrulline, 85*t*  
 collagen, 88

- community, 121  
 diabetes prevention centers, 168–170, 179, 185  
 diabetes prevention practice in, **149–170, 152t, 153t, 156t, 158f, 164f**  
 family-based program, 154  
 school-based program, 154  
 Community Diabetes Prevention Centers (CDCPCs), **168–170, 179, 185**  
 complications, 1–2  
 congestive heart failure, 100  
 coronary artery disease, 100  
 corticotropin-releasing hormone (CRH), 54  
 counseling, 110–111, 159–160, 163, 178  
 Cox proportional hazards regression, 117  
 C-reactive protein (CRP), 41, 58  
 creatinine, 88  
 Cushing syndrome, 53  
 cyclin-dependent kinase 5 regulatory subunit associated protein 1 (CDKAL1), 70  
 cytokines, 58  
 cytosol, 4
- D**
- dairy consumption, 29–30  
 de novo lipogenesis, 4  
 demographic predictors, 24–27, 25f  
 Department of Agriculture, 164  
 Department of Health and Human Services (HHS), 11  
 depression, 6f  
*Diabetes*, 11  
*The Diabetes Carbohydrate & Fat Gram Guide*, 163  
 Diabetes Food Hub, 163  
 diabetes mellitus, 11  
 Diabetes Prevention Program (DPP), 11, 44, 49, 55, 58–60, 70–72, 83  
 data from, 118–120, 120f, 121t  
 lifestyle-mediated, 108t, **138–140, 138t**, 153–158, 163–170, 187  
 mechanisms and mediators, 116–117  
 Medicare, 178–179, 179f  
 medications, 121–122, 123t, 124–129, 141–142, 187  
 metformin, 108–117, 108t, 109f, 119, 138–139, 138t  
 microvascular and macrovascular complications, 111–112  
 for type 2 diabetes (T2D), 98–99, **108–109**, 109t, 144f  
 Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication (DREAM) trial, 122, 123t, 138t, 140  
 diabetic peripheral neuropathy, 100  
 diabetogenic effects, 74  
 diacylglycerol, 4, 103f  
 diagnosis criterion, 11–12, 12f  
 diastolic blood pressure (DBP), 42t  
 dietary approaches, 88, 123t  
 counseling, 163  
 delivery, 162–165, 164f  
 high-fat, high-carbohydrate, 3  
 intervention, 55  
 dietary fat, 4, 139  
 dietary fiber, 144  
 Dietary Guidelines for Americans, 164  
 dietary habits, 29, 144  
 dietary modifications, 107, 110  
 dietitians, 156, 182  
 dipeptidyl peptidase-4 inhibitors, 141, 191  
 disability costs, 2  
 disposition index, 43. *See also* insulin  
 diuretics, 31  
 dopamine agonist bromocriptine-QR, 191  
 dopaminergic tone, 3  
 double prediabetes, 128  
 drug interactions, 191  
 drug-induced, 189–192  
 drugs and toxins, effects, 44, 44f  
 dysglycemia, 5, 24, 29, 40, 49, 115  
 pathobiology, 143  
 dyslipidemia, 90, 112, 127, 168, 191–192  
 as risk factor, 5, 49, 101, 153t
- E**
- early diabetes mellitus, 11  
 eating patterns, 114  
 economic costs, 2  
 education, 150  
 endocannabinoids, 41

endocrine-disrupting chemicals, 5, 6*f*  
endocrinology, 150  
endogenous glucose production, 27  
endothelial dysfunction, 101, 168  
endothelial nitric oxide synthase (eNOS), 103*f*  
endothelium-dependent vasodilation, 101  
environmental risk factors, 5, 144*f*  
epidemiology, 1–2, 2*t*  
epigenetic pathways, 120  
etanercept, 59  
ethnicity/racial disparities, 24–29, 69–70, 83, 100, 153*t*, 169, 191  
exercise, 62*t*, 107, 110, 114, 118*f*, 123*t*, 156  
exploratory prevention approaches  
    preemptive interventions for at risk people, 189–192  
    for type 2 diabetes (T2D), 189–191  
        lifestyle plus cyclical medication, 187–188  
        metabolic surgery, 192–194, 193*t*

## F

familial clustering, 53  
family history, 97, 114, 127, 138, 153, 153*t*  
family medicine/practice, 184  
fasting plasma amino acid levels, 85*t*  
fasting plasma glucose (FPG), 28, 61, 83–84, 129, 151, 155  
    high normal, 39, 153*t*  
fasting plasma insulin levels, 43  
fat intake, 4  
    limitation, 107, 109–110  
fat mass, 41, 42*t*, 43, 71*f*  
fat oxidation, 4, 90  
fat-free mass (FFM), 87*f*  
fatty acids, 50, 61, 90, 92  
fiber intake, 107, 110–111  
fibrates, 49, 62*t*  
fibrinogen, 58  
fibroblast growth factor receptor 1 (FGFR1), 54–55  
fixed-dose combination of metformin and rosiglitazone, 141  
Food and Drug Administration, 122, 126, 178, 182, 188–189  
food habits, 29, 114, 151

food intake, recording/tracking, 166  
frequently sampled intravenous glucose tolerance test (FSIVGTT), 43

## G

gastric bypass surgery, 86  
gastroesophageal reflux disease, 193*t*  
gastrointestinal side effects, 127, 191  
    from medication, 122  
gender, as progressor, 25  
gene  
    environment interactions, 74  
    expression, 77, 117  
    gene interactions, 74  
    variants, 71*f*  
genetic predisposition, 5, 44, 53–54, 118, 144*f*  
genetic risk scoring, 72  
genomic pathways, 120  
genomics, 69–74, 71*f*  
genotyping, 60, 119, 120*t*  
gestational diabetes, 3, 5, 77, 127, 153*t*, 154, 191  
global costs, 2  
global epidemic, 1  
glomerular filtration rate, 99  
glomerular hyperfiltration, 101  
GLP-1 receptor agonists, 191  
glucagon suppression, postprandial, 3  
glucagon-like peptide (GLP)-1 receptor agonist, 124, 141, 188  
glucocorticoids, 62, 62*t*, 153*t*, 189  
gluconeogenic amino acids, 13  
glucoregulation, 12, 28*t*, 40, 56  
glucose  
    abundance, 4  
    disposal  
        insulin-stimulated, 40  
        oxidative, 40  
    disposal rates, 40  
    dysregulation, 5  
    fasting plasma, 1, 19  
        diabetes criterion, 11–12, 12*f*  
        prediabetes criterion, 11–12, 12*f*  
    hepatic, 3, 4*t*  
    homeostasis, 5, 13  
    intracellular, 4

- metabolism, 1
  - oral tolerance test, 1, 11–13, 12*f*, 17, 23, 39, 43, 53, 73, 129, 151, 153, 155
  - production
    - hepatic, exaggerated, 3, 4*t*
  - rebound, 122
  - regulation, 11
  - renal reabsorption, maladaptive, 3, 4*t*
  - slightly elevated, 11
  - tolerance, 19, 86, 191
  - toxicity, 44
  - 2-h plasma, 1
  - glucose area under the glucose curve (AUC), 16*t*
  - glucose disposal rate (GDR), 16*t*
  - glucotoxicity, 39, 44*f*
  - glutamic acid, 84, 85*t*, 87
  - glutamine, 83–84, 87, 87*f*
  - glutaryl carnitine, 91
  - glycemia, 17, 49
  - glycemic and gluoregulatory predictors,
    - in normal glucose regulation (NGR) transition to prediabetes, 39–41, 42*t*, 43–44, 44*f*
  - glycemic control, 168
  - glycemic dysregulation, 28
  - glycemic progression, 25, 142
  - glycemic rebound, 125–126
  - glycine, 83–84, 85*t*, 87–88, 87*f*, 189
  - glycogen, 40, 98
  - glycolysis, 4
  - goal-setting, 114
  - golimumab, 59
  - government and civic responsibilities, 157
  - granulocytes, 58
  - group counseling, 110
  - group therapy, 161
  - gut flora, 30, 93–94
  - gut microbiome, 93–94
- H**
- HAART, 6*f*
  - Hawthorne effect of participation, 115
  - HDL cholesterol, 42, 42*t*, 49, 61, 84, 112, 118*f*, 168
  - Health Improvement Network, 94
  - health insurance, commercial, 178
  - healthy eating habits, 111
  - heart failure, 1
  - heart rate, 100
  - hematocrit, 24
  - hemodynamics.
    - See also blood pressure (BP)
      - microvascular, 100
      - in normal glucose regulation (NGR) transition to prediabetes, 53–56, 54*f*, 55*f*
  - hemoglobin A1c (HbA1c) level, 1
    - increase from medications, 189–190
    - miRNAs and, 78
    - outcomes, 154–155, 161, 192
    - prediabetes criterion, 11–12, 12*f*, 17–18, 23, 26, 39, 101, 137, 143, 149–151
  - hemoglobinopathies, 12
  - hemolytic anemia, 12
  - hepatic enzymatic activity, 41
  - hepatic glucose production, 3, 4*t*, 27
  - hepatic glycolysis, 13
  - hepatic insulin resistance, 73
  - hepatic lipase activity, 168
  - hepatocyte nuclear factor 4 $\alpha$  (HNF-4 $\alpha$ ), 73
  - heritability, of diabetes, 69
  - hexosamine, 101
  - high-sensitivity C-reactive protein (hs-CRP), 42*t*
  - histidine, 84, 85*t*, 87, 189
  - HIV antiretroviral agents, 153*t*
  - HIV-AIDS, 6*f*, 157
  - HLA haplotypes, 3
  - homeostasis model assessment of  $\beta$ -cell function (HOMA-B), 14, 16*t*, 17, 42*t*
  - homeostasis model assessment-insulin resistance (HOMA-IR), 13, 14*f*, 15, 16*t*, 31, 41, 61, 84
  - hormone replacement, 139
  - hs-CRP, 42*t*
  - human genome, 5
  - hydroxybutyrylcarnitine, 90
  - hydroxychloroquine, 59
  - hyperaminoacidemia, 86
  - hyperglycemia, 1, 4*t*, 101, 103*f*
    - development, 3
    - diabetes-grade, 99
    - target tissue damage, 102*f*

hyperinsulinemia, 138  
hyperinsulinemic-euglycemic clamp (ISI-clamp), 14–15, 14*f*, 16*t*, 18, 40–41, 73  
hypersomnia, 5, 6*f*  
hypertension. *See* blood pressure (BP)  
hyposomnia, 5, 6*f*

## I

immunosuppression, 153*t*, 189, 191  
impaired fasting glucose, **11–13**, 16*t*, 108.  
*See also* prediabetes  
impaired glucose tolerance, 109  
incontinence, 193*t*  
incretin deficiency/resistance, 3, 73  
Indian Health Services, 128  
inflammatory cytokines, 194  
inflammatory markers, 118*f*, 144  
inflammatory signals, 44, 44*f*  
    normal glucose regulation (NGR)  
    transition to prediabetes, **58–62**, **62*t***  
infliximab, 59  
insulin  
    action, 13  
    basal  
        fasting, 15  
        overnight, 13  
    biogenesis, 70, 71*f*  
    deficiency, 3, 86  
    demand, 3, 74, 77  
    fasting, 16*t*, 17, 18*f*, 61  
    indices, 16*t*  
    resistance, 4, 4*t*, 6*f*, 17, 53, 86, **98**, 101,  
    144, 168, 189  
        acquired, 3  
        ambient, 126  
        inherited, 3  
        in prediabetes, 13–15, 14*f*  
         $\beta$ -cell dysfunction and, 3  
    secretion, 13, 17, 40, **43–44**, **44*f***, 49, 61,  
    87, 88*f*, 91*f*, 115, 118*f*, 189  
        indices, 16*t*  
        loss, 3  
    secretion (index), 14, 14*f*  
        in prediabetes, 15, 16*t*, 17–19, 18*f*  
    sensitivity, 14*f*, 17–18, **40**, 49, 61, 87*f*,  
    91*f*, 115–116, 118*f*  
    signaling, 4, 103*f*  
insulin receptor substrate 1 (IRS1) gene, 26

insulinemia, 43, 115  
insulinogenic index, 14, 16*t*  
insulinoma cell line (INS-1), 77  
insulinoma  $\beta$ -cell lines, 70  
insulinopenia, 3  
insulin-resistant nonobese (IRN), 42*t*  
insulin-resistant obese (IRO), 42*t*  
insulin-resistant obese and lean  
    phenotypes, 40–41, 42*t*, 43  
insulin-sensitive and insulin-resistant  
    obese and lean phenotypes, 40–41,  
    42*t*, 43  
insulin-sensitive nonobese (ISN), 42*t*  
insulin-sensitive obese (ISO), 41, 42*t*  
insulin-sensitive obese and lean  
    phenotypes, 40–41, 42*t*, 43  
intensive lifestyle intervention  
    group, 110  
interleukin (IL)-6, 58  
intermittent fasting, 165  
internal medicine, 180, 184  
International Diabetes Federation, 1–2  
intracellular diacylglycerol, 4  
intracellular glucose, 4  
intracellular pathways, 102*f*  
intraepidermal nerve fiber density, 142  
intrauterine environment, 5, 6*f*, 114  
iron deficiency, 12  
ischemic stroke, 101  
islet amyloid, 44*f*  
isoleucine, 83–85  
isotope dilution technique, 27

## K

Kaplan-Meier analysis, 53  
ketoacidosis, 191  
ketone bodies, 83  
kidney disease. *See* chronic kidney disease  
Krebs cycle, 4, 86

## L

latent autoimmunity, 44, 44*f*  
LDL cholesterol level, 24, 49–50, 112  
leucine, 83–84  
lifestyle coaches, 159, 179, 183–184  
lifestyle counseling, 178  
lifestyle interventionists, 158

lifestyle modifications/interventions, 60, 99, 108, 111, 113  
 adiponectin levels and, 62*t*  
 Diabetes Prevention Program (DPP), 108*t*, **138–140**, **138*t***, 153–158, 163–170, 187  
 genes, 121*t*  
 group, 107, 110  
 limitations, 121  
 mechanisms and mediators, 115–117, 118*f*  
 metformin, 187  
 randomized controlled trials, 107*t*  
 risk-conferring genes and, 118–121, 120*f*, 121*t*  
 for type 2 diabetes (T2D), 118–120, 120*f*, 121*t*  
 linoleoyl carnitine, 91  
 lipid moieties, 83, 144  
 lipids, 28*t*, 49, 90, 138–139  
 lipogenesis de novo, 4  
 lipogenic transcription factors, 41  
 lipolysis, 3, 4*t*, 13, 55  
 lipotoxicity, 4, 44, 44*t*  
 liquid chromatography, 83  
 liraglutide, 124, 141, 188  
 long-chain fatty acids, diet-derived, 4  
 long-chain fatty acids-coenzyme A (CoA), 4, 90  
 lorcaserin phentermine/topiramate, 191  
 low-dose metformin and low-dose rosiglitazone, 122  
 lymphocytes, 58

## M

macrolides, 94  
 macronutrient derangements, 194  
 macrovascular complications, of prediabetes, 100–103, 102*f*, 103*f*  
 major histocompatibility complex, 5  
 maladaptive renal glucose reabsorption, 3  
 malnutrition, 157  
 malonylcarnitine, 90  
 malonyl-CoA, 4  
 mass spectrometry, 83  
 maternal diabetes, 26  
 Matsuda Index, 41  
 medical community education, 150

Medicare diabetes prevention program, 178  
 fee schedule, 179*f*  
 reimbursement schedule, 179, 179*f*, 182–183  
 medications, 5. *See also* specific medication  
 cyclical, 187–188  
 diabetes Prevention Program (DPP), 121–122, 123*t*, 124–129, 141–142, 187  
 guidelines for use, 126–129  
 hemoglobin A1c (HbA1c) level, 189–190  
 hypertension, 112  
 ideal drug, 125–126, 125*t*  
 interactions, 191  
 limitations, 125–126, 125*t*  
 for prediabetes, **140–144**, **144*f***  
 for prevention, 121–129, 123*t*, 125*t*  
 side effects, 122, 127  
 type 2 diabetes (T2D), 121–122, 123*t*, 124  
 limitations, 125–126, 125*t*  
 use guidelines, 126–129  
 Mediterranean diet, 165  
 metabolic pathways, 80*t*–81*t*  
 metabolic surgery, 192, 193*t*  
 for children and adolescents, 193  
 risks, 194  
 metabolic syndrome, 41, 100, 111, 168, 190  
 metabolically benign obesity, 41  
 metabolically healthy obesity, 41  
 metabolites, 86, 144  
 metabolomics, 28*t*, 117, 188, 194  
 prediabetes and, **83–88**, **85*t***, **87*f***  
 metagenome, 93  
 metformin, 99, 191  
 in Diabetes Prevention Program (DPP), 108–117, 108*t*, 109*f*, 119, 138–139, 138*t*  
 fixed-dose combination with rosiglitazone, 141  
 guidelines, 127–129  
 with lifestyle changes, 187  
 low-dose, 122  
 with low-dose rosiglitazone, 122  
 prediabetes, 60–61, 138*t*, 181–182  
 as preventative, 122, 123*t*, 124–125, 170  
 methionine, 83, 85*t*

methionine sulfoxide, 83  
methylmalonyl carnitine, 91  
methylthioesterase, 70  
microalbuminuria, 99, 100*t*  
microbiome, 5, 6*f*, 117, 144, 194  
microbiota dysbiosis, 93  
micronutrient derangements, 194  
microRNAs (miRNAs), 117, 144  
    differentially expressed, 79*t*  
    in prediabetes, 77–78, 79*t*, 80*t*–81*t*  
    target genes, 80*t*–81*t*  
microvascular and macrovascular complications, with type 2 diabetes (T2D), 111–113, 149  
microvascular complications, of prediabetes, 99–100, 100*t*  
mitochondria, 4  
Modifiable Activity Questionnaire, 29  
molecular target of rapamycin (mTOR), 86  
monocytes, 58  
morbid obesity, 194  
mortality, 149  
myocardial infarction, 1, 100, 190  
myristoyl carnitine, 91

## N

naltrexone/bupropion, 191  
nateglinide, 124  
National Diabetes Fact Sheet, 26  
National Diabetes Prevention Program, 163, 169  
National Health and Nutrition Examination Survey (NHANES), 25, 53, 99  
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 114  
natural killer cells, 41  
“natural” remedies, 188  
neonatal diabetes, 69  
nephropathy, 53, 99  
neuropathy, 99–100, 100*t*, 142  
neuropsychiatric reactions, 191  
neutrophils, 59  
nicotine, 168  
nitric oxide synthase, 102  
nonalcoholic fatty liver, 193*t*

nonalcoholic steatohepatitis, 58  
non-oxidative glucose disposal, 98  
nonprogressors, 79*t*  
normal fasting glucose (NFG), 13, 16*t*  
normal fasting plasma glucose, 11  
normal glucose regulation (NGR), 11, 23  
    restoration, 137–144, 138*t*, 144*f*  
    transition predictors  
        anthropometric, 27–29, 28*t*  
        behavioral, 29  
        dairy consumption, 29–30  
        demographic, 24–27, 25*f*  
        sugar and caffeine, 30–32  
transition to prediabetes  
    biochemical, hemodynamic, and inflammatory predictors, 39–41, 42*t*, 43–44, 44*f*, 49–50, 53–56, 54*f*, 55*f*, 58–62, 62*t*  
    glycemic and gluco regulatory predictors, 39–41, 42*t*, 43–44, 44*f*  
    hemodynamics, 53–56, 54*f*, 55*f*  
    inflammatory signals, 58–62, 62*t*  
    plasma lipid moieties and incident prediabetes, 49–50  
normoglycemia, 23, 29, 97, 140  
nucleotide polymorphism, 60  
nutraceutical approaches, 88, 188–189  
nutritional factors, 53  
nutritionists, 156

## O

obesity, 5, 31–32, 53, 55, 90, 153*t*, 190  
    insulin resistance and, 3  
    morbid, 194  
    risk factors, 6*f*  
    subphenotypes, 40–41  
    visceral, 62*t*  
obesity-hypoventilation, 193*t*  
obstructive sleep apnea, 193*t*  
octanoylcarnitine, 91, 91*f*  
older adults, type 2 diabetes in, 3  
oral disposition index, 14  
oral glucose load, 13  
oral glucose tolerance test. *See* glucose  
orlistat, 122, 123*t*, 125, 191  
ornithine, 85*t*  
oxidative stress, 87, 102*f*



## P

- palmitoylcarnitine (C16), 90–91
- pancreas, 70
- pancreatic islet  $\beta$ -cell, 13, 16–17, 43–44, 44*f*, 58, 77, 88, 144
  - autoimmune destruction, 3
  - dysfunction, **98–99**
  - insulin resistance and, 3, 4*t*
- pancreatic lipase inhibitor, 122
- pancreatitis, 191
- pathophysiology, 2–5, **4*f***, **6*f***
- penicillin, 94
- peripheral vascular disease, 1, 100
- peripubertal age, 114
- pharmacoprophylaxis, 189–191
- phenylalanine, 83, 84, 87
- physical activity, 109, 114, 139, 144
  - energy expenditure, 156*t*
  - increased, 4
  - intervention delivery, 155–163, 156*t*, 158*f*
  - motivation, 156
  - team sports, 157–158, 158*f*
- physical inactivity, 3, 5, 53, 55, 144, 153*t*
- Pickwickian syndrome, 193*t*
- pioglitazone, 101, 122, 123*t*, 124, 138*t*, 140, 187
- plasma glucose
  - fasting, 1, 5, 11
  - 2-h, 1
- plasma levels, 91*f*
- plasma lipid moieties, in normal glucose regulation (NGR) transition to prediabetes, **49–50**
- plasminogen activator inhibitor-1 (PAI-1), 102, 103*f*
- pleckstrin homology domain (PLEKH), 55
- polar amino acids, 87
- polycystic ovarian syndrome, 58
- polygenic type 2 diabetes, 69
- polyol, 101, 102*f*
- population health, weight-focused, 162
- population-based screening, 107
- postprandial glucagon suppression, 3
- preclinical diabetes mellitus, 11
- prediabetes, 40
  - acylcarnitines in, **90–92**, **91*f***
  - complication mechanisms, 101–103, 102*f*, 103*f*
  - criterion, 11–12, 12*f*
  - development of premature microvascular and macrovascular complications from, 97–103, 100*t*, 102*f*, 103*f*
  - double, 128
  - genomics, **69–74**, **71*f***
  - glucose-defined, 18
  - gut microbiome in, **93–94**
  - hemoglobin A1c (HbA1c) level, 11–12, 12*f*, 17–18, 23, 26, 39, 101, 137, 143, 149–151
  - insulin resistance in, 13–15, 14*f*
  - insulin secretion (index) in, 15, 16*t*, 17–19, 18*f*
  - macrovascular complications, 100–103, 102*f*, 103*f*
  - metabolomics and, **83–88**, **85*t***, **87*f***
  - metformin, 60–61, 138*t*, 181–182
  - microRNAs (miRNAs) in, 77–78, **79*t***, **80*t***–**81*t***
  - microvascular complications, 99–100, 100*t*
  - pathogenesis, 144
  - persistent, 99, 137
  - predictors, 28*t*
  - prevalence, 100
  - progression to type 2 diabetes (T2D), 100–103, 100*t*, 102*f*, 103*f*
    - predictors, 97–99
    - prevention approaches, **107–122**, **108*t***, **109*t***, **118*f***, **120*f***, **121*t***, **123*t***, **124–129**, **125*t***
  - reversal
    - Diabetes Prevention Program (DPP), **138–140**
    - drug-induced, **140–144**, **144*f***
    - lifestyle-mediated, **137–140**, **138*t***
    - trials using lifestyle and/or medication interventions, 138*t*
  - risk factors for, 153*t*
  - risk for, 152
  - screening, 152
  - screening and detection, 150
  - sequelae, 97–103, 100*t*, 102*f*, 103*f*

prediabetes (*Cont.*)  
transition from normal glucose regulation (NGR)  
predictors, **23**  
anthropometric, 27–29, 28*t*  
behavioral, 29  
dairy consumption, 29–30  
demographic, 24–27, 25*f*  
sugar and caffeine, 30–32

prediabetes (impaired glucose tolerance), 97

pregnancy, 3, 12. *See also*  
gestational diabetes  
large baby, 153*t*

prehypertension, 53, 54*f*

premature death costs, 2

premature microvascular and macrovascular complications, from  
prediabetes, 97–103, 100*t*, 102*f*, 103*f*

prevalence, 1–2, 5, 178

prevention practice  
in community, **149**  
centers, **168–170, 179, 185**  
knowledge dissemination, 150–152  
strategies, 152–168, 152*t*, 153*t*, 156*t*,  
158*f*, 164*f*

primary care physician (PCP)  
exposure to diabetes patients, 180, 180*f*  
exposure to prediabetes patients,  
181, 181*f*  
prediabetes screening, 181–182, 182*f*  
survey, 180–185, 180*f*, 181*f*, 182*f*, 183*f*,  
184*f*, 184*t*  
survey inferences, 184*t*

Prochaska's transtheoretical model of  
behavior modification, 149

progressors, 79*t*

proinflammatory cytokines, 58–59, 117

proinflammatory markers, 101, 117

proinflammatory signals, **58–59**

proinsulin level, 116

proline, 85*t*

protein degradation, 86

protein kinase C (PKC), 4, 61, 101  
isoforms, 103*f*

protein synthesis, 86

proteolysis, 13, 86

pseudotumor cerebri, 193*t*

public health, 1

purine, 88  
purine degradation products, 83

## Q

quality of life, markedly impaired, 193*t*  
QUICKI, 41  
quinolones, 94

## R

ramipril, 140

randomized clinical trials, 168  
on efficacy of lifestyle intervention, 150

randomized controlled trials, 191

reactive oxygen species, 102

recombinant human IL-1 receptor  
antagonist, 59

reinnervation, 142

renal dysfunction, 191

residency training programs, 150

resting energy expenditure (REE), 42*t*

retinopathy, 99, 100*t*

rheumatoid arthritis, 59

rheumatological disorders, 59, 189

risk allele (TT), 72, 73

risk factors, **5, 6*f***, 114  
cardiometabolic, 41, 42*t*  
dyslipidemia, 5, 49, 101, 153*t*  
environmental, 5, 144*f*  
obesity, 6*f*  
for prediabetes, 153*t*  
for type 2 diabetes (T2D), 153*t*

risk-conferring genes, lifestyle intervention  
and, 118–121, 120*f*, 121*t*

rosiglitazone, 123*t*, 138*t*, 140–141, 187  
low dose, 122

rosuvastatin, 190

Roux-en-Y gastric bypass (RYGB), 192

Ruminococcaceae, 93

## S

salicylates, 59

satiety dysregulation, 3, 4*t*

school-based intervention program, 114–115

screening recommendations, 56

sedentary behavior, 29, 110, 153*t*

self-efficacy, 166

self-monitoring, 165–166

- senescence, 44*f*  
 serine, 59, 83, 85*t*  
 serum triglycerides, 41  
 simple plate method, 164, 164*f*  
 single-nucleotide polymorphisms (SNPs), 69–71  
 sleep apnea, 5, 6*f*, 193*t*  
 sleep disorders, 5, 6*f*  
 sleeve gastrectomy, 192  
 smoking, 55, 62, 113  
   cessation, 61, 62*t*, 168  
 social marketing, 114  
 socioeconomic status, 5, 6*f*, 157  
 sodium glucose-cotransporter-2 inhibitor, 188, 191  
 soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE), 73  
 solute carrier (SLC), 55  
 statins, 6*f*, 49, 62, 62*t*, 189–190  
 steady-state clamp plasma insulin, 16*t*  
 stearoyl carnitine, 91  
 steroid therapy, 191  
 stress, 6*f*  
 stress response, chronic, 168  
 stroke, 100, 190  
   diabetes and, 1  
   ischemic, 101  
 studies, diabetes  
   Atherosclerosis Risk in Communities Study, 98  
   Baltimore Longitudinal Study of Aging (BLSA), 23, 144*f*  
   Da Qing study, 99, 108*t*, 109–110, 137, 141, 144*f*, 149, 153, 158, 167  
   EPIC-Norfolk study, 101  
   Finnish Diabetes Prevention Study (FDPS), 108*t*, 110–111, 115, 118*f*, 121*t*, 141, 144*f*, 149, 158, 163, 166  
     for type 2 diabetes (T2D), 110–111  
   Framingham Heart Study Offspring Cohort, 29–30, 83  
   Framingham Offspring Cohort Study, 5, 25, 41, 72  
   Gutenberg Health Study, 99  
   HEALTHY study, 114  
   Indian Diabetes Prevention Program (IDPP-1), 108*t*, 111, 123*t*, 124, 127, 143, 144*f*, 170, 187  
     for type 2 diabetes (T2D), 111  
   Indian Diabetes Prevention Program-2, 122, 140, 187  
   JUPITER study, 190  
   Malmö Diet and Cancer study, 83  
   Malmö study, 138, 138*t*, 141, 157  
   multiethnic Insulin Resistance Atherosclerosis Study, 83  
   Multi-Ethnic Study of Atherosclerosis (MESA), 100  
   Paris Prospective Study, 100  
   Pathobiology of Prediabetes in a Biracial Cohort (POP-ABC) study, 24–28, 43–44, 49, 78, 144*f*, 151, 189  
   Pima Indian study, 23–29, 40, 44, 98, 144*f*  
   Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM), 122, 123*t*, 138*t*, 140  
   Swedish Obese Subjects study, 192–193  
   UK Prospective Diabetes Study, 1, 113  
   Whitehall II study, 137, 142  
   Xenical in the Prevention of Diabetes in Obese Subjects (XENDOS) study, 122, 123*t*  
 succinyl carnitine, 91  
 sugar consumption, 30–32  
 synaptic-vesicle exocytosis, 73  
 systolic blood pressure (SBP), 42*t*
- T**
- thiazolidinediones, 62*t*, 122, 125, **140–141**, 187, 191  
 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, 189  
 3-OH-hexadecanoylcarnitine (C16-OH), 90  
 threonine, 59  
 tobacco, 168  
 topiramate, 191  
 total amino acids, 86  
 total fat mass, 42*t*  
 transient ischemic attack, 100  
 translational cascade, 149  
 transplantation, 6*f*, 153*t*, 189, 191–192  
 triglycerides, 24, 31, 42*t*, 49, 61, 112, 118*f*, 127  
 trunk fat mass, 42*t*, 43  
 tuberculosis, 6*f*

tumor necrosis factor (TNF)- $\alpha$ , 58–59, 118  
twins, 69, 99  
2-h plasma glucose (2hPG), 1, 11–13, 12f, 14f, 28t, 39, 43, 54, 54f, 72–73  
type 1 diabetes, 2–3  
type 2 diabetes (T2D), 90  
  asymptomatic nature, 1  
  in children and adolescents, 2  
  development, 11  
  Diabetes Prevention Program (DPP)  
    for, 98–99, **108–109**, 109t, 144f  
  early, 1  
  genetic element in, 3  
  hypertension and, 55f  
  insulin secretion and, 43  
  in older adults, 3  
  pathophysiological defects in, 3, 4f, 4t  
  polygenic, 69  
  predictors  
     $\beta$ -cell dysfunction, 98–99  
    insulin resistance, 98  
    weight gain, 98  
  prevention approaches, 110  
    in children and adolescents, 113–115  
    Diabetes Prevention Program,  
      108–109, 109t  
    exploratory, **187–194**, **193t**  
    Indian Diabetes Prevention  
      Program, 111  
    lifestyle intervention mechanisms  
      and mediators, 115–117, 118f  
    lifestyle modification, 107–108, 108t  
    limitations, 121  
    medication limitations, 125–126, 125t  
    medications, 121–122,  
      123t, 124–125  
    microvascular and macrovascular  
      complications, 111–113  
    risk-conferring genes and lifestyle  
      intervention, 118–120, 120f, 121t  
  progress of prediabetes, 97–103, 100t,  
    102f, 103f  
  progression from prediabetes,  
    prevention approaches, **107–122**,  
    **108t**, **109t**, **118f**, **120f**, **121t**, **123t**,  
    **124–129**, **125t**  
  risk factors for, 153t

tyrosine, 83–84, 85t, 87, 87t  
tyrosine kinase, 59  
tyrosine phosphorylations, 59

## U

urbanization, 5, 6f  
urea cycle intermediates, 83  
uremia, 12

## V

valine, 83–84, 85t  
valsartan, 124  
vascular endothelial growth factor  
  (VEGF), 103f  
vascular smooth muscle dysfunction, 101  
venous stasis disease, 193t  
venous thromboembolism, 190  
visceral adiposity, 27, 101  
visceral fat mass, 41  
visceral obesity, 62t

## W

waist circumference, 27–29, 42t, 61, 84,  
  115–116, 151  
weight  
  change, 31  
  gain, 27–28, 62, **98**  
    statin-induced, 189  
  loss, 4, 55, 61, 62t, 86, 109–110, 118f,  
    127, 143  
    apps, 166  
    goal-setting, 166–167  
    massive, 192  
    in obese patients, 107  
  maintenance, 160, 163  
  online management program, 162  
  regain, 107, 117, 125  
white blood cell count, 58  
wolfram, 69  
World Health Organization, 12

## Z

zinc finger nuclear protein, 70  
Zucker diabetic fatty rat model, 50