

Index

- 5-choice serial reaction time task (5CSRTT), 65–67
- 5-fluorouracil, cognitive impairment and, 52, 53
- acidosis, in tumor-induced bone pain, 36
- acid-sensing ion channel-3 (ASIC-3), 36
- actigraphy, 129, 135, 163, 165
- activity/sleep cycles, 135
- acute myeloid leukemia, 181
- adenosine triphosphate hypothesis
cancer-related fatigue, 113
- adenosine, sleep regulation, 175
- adjunctive analgesics, 23
- adriamycin, cognitive impairment and, 52
- advanced sleep-phase syndrome, 161
- advertising claims, 326
- affect, 132
- A-fiber nociceptors, 41
- Agent Pathway, 320
- aggressive behavior, 13
- Agouti-related protein (AgRP), 151
- alendronate, 35
- allergies, 182
- allogenic stem cell transplantation, 181, 224, *See also* hematopoietic stem cell transplantation (HSCT)
- AMD3100, 188
- amifostine, 330
- analgesics, 23
adjunctive, 23
combinations, 27
functional imaging studies, 216
- anemia
cognitive impairment and, 54
fatigue and, 113
- angiogenesis, chemokine role, 182
- animal models, 1–2, 9, 129
cancer symptom mechanisms, 6
cognitive impairment, 67
classical conditioning, 65
Morris Water Maze, 63
operative paradigms, 67
pre-pulse inhibition, 64
treatment-related, 53
depression, 11, 82–84, 89–90
- development of, 1–2, 5, 346–347
- fatigue, 124, 137
emotional and motivational processes, 131–135
fatigue-like behavior, 131
validation, 129
- limitations, 4
- rationale, 5
- tumor-induced bone pain, 1–2
- validation
beyond traditional criteria, 129
traditional criteria, 127
- anorexia/weight-loss syndrome, 142,
See also Food intake
clinical significance, 143
palliative approaches, 145
pathophysiology, 144
proteasome, 149
proteolysis-inducing factor, 146
tumor necrosis factor alpha, 147
- anterior cingulate cortex (ACC), 209, 212
- anti-chemokine therapy, 188
- antidepressant treatment, 83
fatigue, 118
side effects, 83
- antiemetics, posttransplantation
symptom reduction, 231
- anti-IL-6 agents, 187
- anti-IL-8, 187
- anti-TNF agents, 187
- anxiety masquerading as nausea, 252
- apnea, 161
- Apnea-Hypopnea Index, 160
- appetite regulation, 153, *See also* food intake
chemosensory perception of food, 156
functional imaging, 214
signaling molecules, 152
- appetite stimulation, 145, *See also*
anorexia/weight-loss syndrome
- area under the curve (AUC), 278, 298
- aspartate, 44
- association analysis, 197
candidate gene studies, 196
genome-wide association studies, 197
- asthma, 182
- astrocytes, 48
- attachment theory, 77–78
- attention deficit hyperactivity disorders (ADHD), 5
- autologous stem cell transplantation, 225, *See also* hematopoietic stem cell transplantation (HSCT)
- Bayesian adaptive design, 294, 302
head and neck cancer example, 296
area under the curve (AUC), 298
Bayesian adaptive component, 300
factorial component, 298–299
reporting study results, 302
sample size calculation, 302
simulating the operating characteristic of the trial, 301
symptom intervention-related toxicity issues, 300
- illustration of, 295
operating characteristics, 296
sample size calculation, 296
stopping rules, 296
- bexarotene, 330
- biomarkers, 320
- bisphosphonates, 35
- bone pain. *See* tumor-induced bone pain
- bortezomib, 147, 187
- brain
immune message propagation to, 98
network research, 345
- brain-derived neurotrophic factor (BDNF), 87
- breast cancer, sleep disturbance, 164, 166
- Brief Fatigue Inventory (BFI), 115, 272
- Brief Pain Inventory (BPI), 272
- bupropion, 296
- cancer pain syndromes, 20, *See also*
pain
treatment-related, 20
- cancer symptoms. *See* symptoms
- cancer-related fatigue (CRF).
See fatigue
- candidate gene studies, 196
- cannabinoid receptors, 154

Index

- cannabinoids, 154
- cardinal symptom, 1
- catecholamines, 185
- catechol-*O*-methyltransferase (COMT), 199
- C-fiber nociceptors, 41
- chemobrain, 51
 - future directions, 55
 - interventions, 55
 - risk factors, 55
 - anemia and fatigue, 54
 - hormonal abnormalities, 54
 - inflammatory response, 54
 - metabolic abnormalities, 54
 - pharmacogenetic factors, 55
 - secondary malignancies, 55
 - treatment-related organ toxicities, 53
 - studies of, 53
 - imaging and electrophysiological studies, 52
 - patient self-report, 52
 - preclinical and animal studies, 53
- chemokines, 180 *See also* inflammatory cytokines
 - angiogenesis role, 182
 - anti-chemokine therapy, 188
 - asthma/allergies and, 182
 - chemosensory perception of food, 156
- chemotherapy
 - chemosensory perception changes, 155–156
 - cognitive impairment and, 51
 - future directions, 55
 - interventions, 55
 - risk factors, 55
 - studies of, 53
 - fatigue and, 112
 - high-dose therapy with hematopoietic stem cell transplantation (HSCT), 224, 228
 - pain management, 22
- Children's Oncology Group (COG), 239
- chronic fatigue. *See* fatigue
- chronic mild stress (CMS) model, 84
- chronotherapy, 165
- circadian rhythm sleep disorders, 161
- circadian rhythms, 165
 - fatigue and, 115
- cisplatin, fatigue and, 130
- classical conditioning, 65
- Clinical Community Oncology Program. *See* Community Clinical Oncology Program (CCOP)
- clinical trials
 - crossover designs, 321
 - endpoint establishment, 321–322
 - hypothesis testing, 321
 - pain management, 27
 - analgesic combinations, 27
 - methodology, 26
 - types of trials, 26
 - randomized discontinuation trial (RDT), 314
 - symptom measurement in oncology trials, 335, 338
 - study design considerations, 337
 - symptom scale selection and use, 338
 - symptom trial design, 348
- cluster analysis, 193
- CNTO 328 antibody, 187
- cognitive behavioral therapy
 - sleep disturbance, 166–167
- cognitive impairment, 12, 51, 60
 - animal models, 67
 - classical conditioning, 65
 - Morris Water Maze, 63
 - operative paradigms, 67
 - pre-pulse inhibition, 64
 - chemotherapy related, 51
 - future directions, 55
 - interventions, 55
 - risk factors, 55
 - studies of, 53
 - inflammatory cytokines and, 54, 61
- Community Clinical Oncology Program (CCOP), 239, 311
 - historical and current symptom management trials, 310–312
- complementary alternative therapy fatigue, 119
- congenital central hypoventilation syndrome (CCHS), 213
- construct validity, 127
- content validity, 276
- convergent validity, 276
- cooperative agreements, 308
- cooperative group system, 238
 - benefits of, 238
 - access to research and cancer populations, 237
 - federal funding, 238
 - intergroup cooperation, 238
 - major contributions, 240
 - advances in symptom management, 240
 - advances in therapy, 239
 - organizational challenges, 244
 - process challenges, 245
 - symptom research challenges, 2
 - symptom research promotion strategies, 244
 - symptom research success factors, 241
 - case example, 248–249
 - cooperative group organizational structure, 241
 - member institution characteristics, 242
 - protocol characteristics, 242
- corticosteroids
 - appetite stimulation, 144–145, 153
 - fatigue interventions, 118
 - side effects, 144
- corticotropin releasing hormone (CRH), 76
- cost-benefit analysis (CBA), 260
- cost-effectiveness analysis (CEA), 260
- cost-minimization analysis (CMA), 260
- costs. *See* economic considerations
- cost-utility analysis, 285–286
- COX-2 inhibitors, 36
- COX2, immune message propagation to brain, 98
- CRISP (Computer Retrieval of Information on Scientific Projects), 308
- Cronbach alpha, 275
- crossover designs, 321
- CTCE-9908, 188
- curcumin, 188
- CXCR4 chemokine receptor, 187
- cyclophosphamide, cognitive impairment and, 52–53
- cytochrome P450 (CYP) enzymes, 200
- cytokines. *See* inflammatory cytokines
- delayed sleep-phase syndrome, 161
- depression, 11, 82
 - animal models, 82–84, 89–90
 - animal tests of, 84
 - behavioral tests, 85
 - biological assessments, 86
 - antidepressant treatment, 83
 - consequences of, 71
 - diagnosis, 72
 - distinction from sickness, 100
 - inflammation-induced, 75
 - bilateral relationships, 104–105
 - molecular mechanisms, 102
 - neurobiological circuitry of, 104
 - risk factors, 103
 - mechanisms and mediators, 90
 - cytokines, 90, 99
 - hippocampal neurogenesis inhibition, 87
 - HPA axis alteration, 75–76
 - monoamine metabolism alteration, 76–77
 - stress, 74
 - translational implications, 77–78
 - tumor effects, 88
 - predictors in cancer, 71
 - prevalence in cancer, 71
 - sickness behavior as a form of, 99

- dexamethasone
 - appetite stimulation, 144–145
 - fatigue and, 130
- direct costs, 261
- discounting, 262
- doctor-patient relationship
 - establishment, 249
- dopamine, sleep-wake cycle role, 171
- dorsal column nuclei, 43
- drug development. *See* symptom management
- drug metabolism, 201
- cytochrome P450 (CYP) enzymes, 200
- uridine diphosphate
 - glucuronosyltransferase (UGT), 201
- drug treatment. *See* pharmacotherapy
- dyspnea, 212
- functional imaging, 213
- Eastern Cooperative Oncology Group (ECOG), 240
- symptom research program
 - development, 242–245
- economic considerations, 259,
See also quality-adjusted life years (QALYs)
- cost considerations, 262
- discounting, 262
- time horizon, 262
- types of costs, 262
- economic evaluation, 261
- cost-benefit analysis (CBA), 260
- cost-effectiveness analysis (CEA), 260
- cost-minimization analysis (CMA), 260
- cost-utility analysis, 260–261
- sensitivity analysis, 262
- supportive care strategies, 266
- Edmonton Symptom Assessment Scale (ESAS), 271
- eicosapentaenoic acid, 319
- electroencephalography (EEG), 207
- chemotherapy-related cognitive impairment, 52
- emotions, 251
- endocannabinoid system, 154
- endogenous opioid system, 154
- endothelins, tumor-induced bone pain and, 37
- endotoxin. *See* lipopolysaccharide (LPS)
- endotoxin challenge, 1–2
- epidermal growth factor receptor (EGFR) inhibitors, 318
- Epstein-Barr virus (EBV), 13
- estrogen, cognitive function and, 54
- etanercept, 78, 147, 186
- Ethylol®, 330
- etiological validity, 126
- etoposide, 13
- fatigue and, 130
- executive function, 134
- exercise
 - fatigue management, 118
 - posttransplantation symptoms and, 232
- face validity, 125
- fatigue, 110, 120, 124
- animal models, 124, 137
- validation, 129
- as a sickness behavior, 124
- assessment, 117
- application of knowledge gained, 117
- epidemiological research, 114
- fatigue as a syndrome, 113
- instruments, 272
- measurement, 114
- multidimensional measures, 115
- single item and subscale measures, 115
- tool selection, 116
- unidimensional measures, 116
- chemotherapy and, 112
- clinical correlates, 111–112
- cognitive impairment and, 54
- current research, 114
- defining, 335
- diagnostic criteria, 127–129
- functional impairment
 - interpretation, 117
- inflammatory cytokine relationships, 13, 130, 180
- interventions, 119
- antidepressants, 118
- complementary alternative therapy, 119
- corticosteroids, 118
- exercise, 118
- psychological interventions, 118–119
- psychostimulants, 118
- nature of, 111
- neuroimaging, 136, 215
- psychological components, 131
- emotional and motivational processes, 131–135
- fatigue-like behavior, 131
- radiation therapy and, 112
- relationship to other symptoms, 117
- severity interpretation, 117
- response shift effect, 117
- significance of cancer-related fatigue, 110
- translational research approaches, 113
- adenosine triphosphate hypothesis, 113
- anemia hypothesis, 113
- circadian rhythm modulation hypothesis, 113
- growth factor hypothesis, 113
- HPA disruption hypothesis, 113
- proinflammatory cytokine hypothesis, 113
- serotonin dysregulation hypothesis, 113
- vagal-afferent activation hypothesis, 113
- FDA regulations, 326
- approval process, 333
- guidance, 335
- product development, 333
- reviewers, 332
- establishing clinical benefit, 327
- fear conditioning, 134
- fever, 99
- fluoxetine, 83, 89
- food intake, 157, *See also* anorexia/weight-loss syndrome; appetite regulation
- chemosensory perception of food, 156
- reduction, 10
- reward systems, 154
- forced swim test, 85
- functional imaging. *See* neuroimaging studies
- funding mechanisms, 308
- cooperative agreements, 308
- grants, 308
- gamma-aminobutyric acid (GABA), 44
- GABAergic neuron role in sleep, 172
- interactions, 176
- gemcitabine, 331
- Gemzar®, 331
- genetics
 - cancer symptoms, 192
 - association analysis, 197
 - drug transport and metabolism, 201
 - genotyping, 195
 - inflammation, 198
 - linkage analysis, 196
 - neurotransmission, 194
 - symptom phenotyping, 195–197
 - variation associated with symptoms, 196
 - genetic marker identification, 345
- genome-wide association studies, 197
- genotyping, 195
- ghrelin, 153
- ginseng, fatigue intervention, 119
- Gleevec®, 331
- glial cells, pain and, 48
- glucocorticoid receptor (GR), 76
- glutamate, 44

Index

- glycine, 44
goals of care, 253
graft-versus-host disease (GVHD), 228
graft-versus-tumor effect, 225
grants, 308
 grant review process, 307
gustatory perception of food, 156
Gynecologic Oncology Group (GOG), 240
- head and neck cancer example, 296
 area under the curve (AUC), 298
 Bayesian adaptive component, 300
 factorial component, 298–299
 reporting study results, 302
 sample size calculation, 302
 simulating the operating characteristic of the trial, 301
 symptom intervention-related toxicity issues, 300
- health-related quality of life (HRQOL), 269
- hematopoietic stem cell transplantation (HSCT). *See also* allogenic stem cell transplantation; autologous stem cell transplantation
 basic concepts, 225
 posttransplantation symptoms, 224, 228
 future directions, 232
 mechanisms, 228
 reducing the burden of, 232
 risk factors, 230
 severity and patterns, 227
 reduced-intensity conditioning (RIC) regimens, 230
 with high-dose therapy, 224
- herpetic neuralgia, 22
- hippocampal neurogenesis inhibition, 87
- histamine, 171
- HPA axis
 depression and, 74–75
 fatigue mechanism, 113
 sleep regulation and, 174
- hunger
 functional imaging. *See* appetite regulation
- Hycamtin®, 331
- hyperalgesia, 44, 48, 98
 physiological changes after nerve injury, 47
 primary, 45
 secondary, 45
- hyperammonemia, 53
- hyperhomocysteinemia, 53
- hypocretin, 171
- hypothesis testing, 321
- ibandronate, 35
- imaging. *See* neuroimaging studies
- imatinib, 331
- imipramine, 83, 89
- immune response. *See also* inflammation
 immune message propagation to brain, 98
 stress and, 74
- indirect costs, 261
- indolamine 2, 3 dioxygenase (IDO), 77, 102
- inflammation, 75, 95, 188
 See also immune response; inflammatory cytokines
 depression and, 75
 bilateral relationships, 104–105
 molecular mechanisms, 102
 neurobiological circuitry, 104
 risk factors, 103
 translational implications, 75
 future research directions, 344
 genetic variation, 198
 sickness behavior induction, 95–96
- inflammatory bowel disease, 182
- inflammatory cytokines, 180, *See also* immune response; inflammation; *specific cytokines*
 allogenic stem cell transplantation and, 181
 angiogenesis role, 182
 asthma/allergies, 182
 brain function and, 180
 cancer symptoms and, 1–2, 6, 131, 317
 cognitive impairment, 54, 61
 depression, 90, 99
 fatigue, 13, 130, 180
 neuropathic pain, 47, 181
 sleep disturbance, 166
 genetic variation, 231, 198
 immune message propagation to brain, 98
 inflammatory bowel disease and, 182
 posttransplantation symptoms and, 228
 rheumatoid arthritis and, 182
 sickness behavior and, 6, 8–13, 88, 99
 animal models, 1–2
 food intake reduction, 10
 molecular mechanisms, 13, 98
 psychiatric abnormalities, 13
 signaling through transcription factors, 184
 sleep regulation, 174
- infliximab, 186
- infraspinal infusion, 23
- Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), 271
- insomnia, 160, *See also* sleep disturbance
 functional imaging, 216
- insula, 209
- Integrated Review Groups (IRGs), 305
- interactive voice response (IVR) technology, 279
- interferon (IFN)
 cognitive impairment and, 61
 depression and, 89
- interleukin-1 (IL-1), 96, *See also* inflammatory cytokines
 cancer symptoms and depression, 90
 food intake reduction, 10
 psychiatric abnormalities, 6, 11–12
 genetic variation, 198
 immune message propagation to brain, 97
 sickness behavior and, 6, 60–61, 88
 sleep regulation, 174
 interactions, 175–176
- interleukin-2 (IL-2), psychiatric abnormalities and, 11–13
- interleukin-6 (IL-6), 187
 anti-IL-6 agents, 187
 cognitive impairment and, 52
 depression and, 89
 genetic variation, 198
 sickness behavior and, 6
 sleep regulation, 173
- interleukin-8 (IL-8), 187
 genetic variation, 198
- internal consistency reliability, 275
- item banks for individual symptoms, 273
- kinase inhibitors, 188
- kinins, tumor-induced bone pain and, 37
- known-group validity, 278
- kynurenine, 103
- labelling. *See* product labeling
- lamina I spinothalamicocortical pathway, 210
- laser therapy, oral mucositis, 232
- learned helplessness model, 84
- learning, 135
- Lee Fatigue Scale, 275
- lenalidomide, 186
- leukemia
 acute myeloid, 181
 depression and, 87
- linkage analysis, 196
- lipopolysaccharide (LPS), 98

- immune message propagation to brain, 98
- LPS challenge, 1–2
- Lung Cancer Symptom Scale, 274
- M. D. Anderson Symptom Inventory (MDASI), 271, 273
- magnetic resonance imaging (MRI)
 - chemotherapy-related cognitive impairment, 52
 - functional (fMRI), 207
- mechanically insensitive afferents, 42
- megestrol acetate
 - appetite stimulation, 144–145
- melanocortin-4 receptor (MC4-R), 153
- melatonin, 146
- Memorial Symptom Assessment Scale (MSAS), 115
- memory, 135
- methotrexate
 - cognitive impairment and, 52–53
 - mechanisms, 53
- methylphenidate, 5, 78, 118
- microglia, 48, 52
- minimum clinically important difference (MCID), 277, 322
 - anchor-based methods, 277
 - cut points to determine treatment responders, 277
 - distribution-based methods, 277
- minocycline, 296
- missing data, 291
- modafinil, 296
- monoamine metabolism, depression and, 76–77
- Morris Water Maze, 63, 134
- Motivation, 132–133
- motor function assessment, 135
- Multidimensional Fatigue Inventory (MFI-20), 116
- nausea and vomiting, functional imaging, 213
- nerve growth factor (NGF)
 - tumor-induced bone pain and, 37
- neuraxial infusion, 23
- neuroimaging studies, 206, 218
 - analgesia, 216
 - appetite, 214
 - chemobrain, 52
 - dyspnea, 213
 - fatigue, 136, 215
 - lamina I spinothalamocortical pathway, 209
 - nausea and vomiting, 213
- pain, 212
 - experimentally induced acute pain, 210
 - neuropathic pain, 212
 - somatic versus visceral pain, 210
- sleep disturbance, 216
- technologies, 207
- neurokinin A, 44
- neurolytic blocks, 23
- neuropathic pain, 19, 48
 - chemotherapy-induced, 47
 - functional imaging, 212
 - glial cells and, 48
 - inflammatory cytokine role, 47, 181
 - neurochemistry of, 47
 - physiological changes after nerve injury, 47
 - tumor-induced bone pain, 38
- neuropeptide Y (NPY), 151, 153
- neuropeptides, 44, 184
- neurotransmitters, 44
- neutotransmission, genetic variation, 199
- nociceptive pain, 19
 - somatic, 19
 - visceral, 19
- nociceptors, 32, 42
 - A-fiber, 41
 - C-fiber, 41
- nonadherence, 256
- noradrenaline, sleep–wake cycle role, 171
- North Central Cancer Treatment Group (NCCTG), 239
- NPY/AgRP-releasing neurons, 152
- nuclear factor KB (NF-KB), 13, 183
 - stress effects, 74
- numerical rating scales (NRS), 274–275
- observational studies, pain management, 26
- Office of Oncology Drug Products (OODP), 332
- olfactory perception of food, 156
- oncology cooperative groups. *See* cooperative group system
- opioid receptors, 154, 199
- opioids, 22, 152–154
- oral cryotherapy, 232
- oral mucositis, 232
- osteoclasts, 35
- osteoprotogerin (OPG), 35
- paclitaxel, cytokine response to, 61
- pain, 31–32, 34, 45, *See also* tumor-induced bone pain
 - assessment, 21
 - cancer pain syndromes, 20
 - evidence base, 20
 - instruments, 272
 - measurement of pain, 18, 21
 - research implications, 2
- functional imaging, 212
- analgesia, 216
- experimentally induced acute pain, 210
- neuropathic pain, 212
- somatic versus visceral pain, 210
- future research directions, 27
 - clinical trials, 27
 - observational studies, 26
 - translational approaches, 27
- management, 21–25 *See also specific methods*
 - basic science implications, 25
 - disease-modifying approaches, 22
 - evidence base, 24–25
 - interventional approaches, 23
 - nonpharmacological approaches, 21
 - pain-modifying approaches, 23
 - pharmacotherapy, 23
 - treatment planning, 255–256
 - tumor-induced bone pain, 34
- masquerading as fatigue, 252
- mechanisms
 - assessment of, 19
 - central neural mechanisms, 43
 - peripheral nociceptors, 42
 - primary afferent neurons, 34
- neuropathic, 19, 38, 48
 - inflammatory cytokine role, 181
- nociceptive, 19, 32
 - somatic, 19
 - visceral, 19
- pain crises, 18
- sleep disturbance relationships, 164
- palifermin, 232
- Parkinson’s disease, 4
- paroxetine, 78
- patient-reported outcomes (PROs), 273, 321
 - fatigue, 114
 - in oncology trials, 336
 - measurement of, 321
 - rise of, 330
- Patient-Reported Outcomes Measurement Information System (PROMIS), 268, 320
- peptide hormones, 184
- periodic limb movements in sleep (PLMS), 161
- permeability glycoprotein (P-gp), 200
- personal digital assistants (PDAs), 278
- pharmacological validity, 126
- pharmacotherapy. *See also specific drugs and conditions*
 - FDA-approved treatments, 335
 - pain management, 23
 - analgesic combinations, 27
 - polypharmacy, 256
- Photofrin®, 331
- Piper Fatigue Scale, 275
- pituitary gland, 184

Index

- polypharmacy, 256
- polysomnography, 162
- POMC-producing neurons, 152
- porfimer sodium, 331
- positron emission tomography (PET), 207
 - chemotherapy-related cognitive impairment, 52
- posttransplantation symptoms, 224, 228
 - future directions, 232
 - mechanisms, 228
 - reducing the burden of, 231
 - antiemetics, 231
 - exercise, 232
 - oral mucositis treatments, 232
 - white blood cell recovery, 231
- risk factors, 230
 - patient-related factors, 230
 - regimen-related factors, 230
- severity and patterns, 227
- predictive validity, 126
- pre-pulse inhibition, 64
- primary afferent neurons, 34
 - physiological changes after nerve injury, 46
- sensitization, 45
 - neurochemistry of, 45
- product labelling, 331–336
 - cancer-related symptom claims, 334–337
 - establishing clinical benefit, 327
 - guidance, 335
 - rise of patient report, 330
 - symptom measurement issues, 338
 - symptom palliation versus tumor-reduction treatments, 330
- FDA approval process, 333
 - product development, 332
 - reviewers, 332
- legal and regulatory requirements, 326
- progestational agents
 - appetite stimulation, 144–145
- progressive ratio test, 133
- proinflammatory cytokines, 180
- proinflammatory cytokines, 180, *See also* inflammatory cytokines
- fatigue and, 113
- prostaglandins
 - PGE2, immune message propagation to brain, 98
 - tumor-induced bone pain and, 36
- proteasome, 148
- proteins, 179
- proteolysis-inducing factor, 146
- psychostimulants, fatigue management, 113
- quality-adjusted life years (QALYs), 264
 - application, 265
 - cost per QALY, 264
 - curative versus life-extending versus supportive-care interventions, 263
 - league tables, 264–265
 - utility and, 263
- radiation therapy
 - chemosensory perception changes, 155
 - cognitive impairment, 52
 - fatigue and, 112
 - pain management, 22
- Radiation Therapy Oncology Group (RTOG), 239
- randomized discontinuation trial (RDT), 321
- reliability, 276
- research. *See* symptom research
- Respiratory Disturbance Index, 160
- response shift, fatigue scores, 117
- resting energy expenditure, 143
- restless legs syndrome, 161
- reward systems, food intake and, 154
- rheumatoid arthritis, 182
- rostral areas of the CNS, 43
- S-adenosylmethionine (SAM) deficiency, 53
- Schwann cells, 48
- selective serotonin reuptake inhibitors (SSRIs), 83
- sensitivity analysis, 262
- sensitization
 - neurochemistry of, 45
 - primary afferents, 45
 - spinal neurons, 45
- sensory function assessment, 135
- serotonin
 - cytokine effects on, 77
 - fatigue mechanism, 113
 - inflammation-induced depression mechanisms, 102
 - sleep regulation, 171
 - interactions, 176
- serotonin norepinephrine reuptake inhibitors (SNRIs), 34
- serotonin transporter, 199
- sickness behaviour, 1–2, 5, 8–9, 88
 - animal models, 1–2, 89
 - as a form of depression, 99
 - distinction from depression, 100
 - fatigue as, 13, 124
 - induction by inflammation, 96
 - inflammatory cytokines and, 6, 8–13, 89, 99
 - food intake reduction, 9
- molecular mechanisms, 12, 98
- psychiatric abnormalities, 11–13
- motivational component, 133
- symptoms of, 9
- signal transducers and activators of transcription (STATs), 184
- signaling pathways, 188
- signs, 1
- single nucleotide polymorphisms (SNPs), 196
 - candidate gene studies, 196
- sleep, 170
 - sleep-wake regulatory mechanisms, 170
 - immunomodulators, 174
 - interactions between, 175–176
 - NREM sleep, 172
 - REM sleep, 172
 - wakefulness, 171
- sleep disturbance, 160, 170, *See also* sleep
 - combination therapies, 167
 - common sleep disorders, 161
 - functional imaging, 216
 - in cancer, 163, 167
 - inflammatory markers and, 166
 - objective measures, 163
 - precipitating factors, 164
 - prevalence, 162
 - nonpharmacological therapy, 167
 - pain relationships, 164
 - pharmacotherapy, 160
- sleep-related breathing disorders, 161
- sleep-related movement disorders, 161
- Social support, 77–78
- Soliris®, 335
- somatic nociceptive pain, 19
- somatosensory neurotransmission, 44
- Southwest Oncology Group (SWOG), 239
- spinal dorsal horn, 43
 - neuron sensitization, 45
 - neurochemistry of, 45
 - physiological changes after nerve injury, 47
- standard gamble (SG), 263
- starvation, 143
- stem cell transplantation. *See* hematopoietic stem cell transplantation
- stress
 - depression and, 74
 - translational implications, 74
 - immune response and, 74
 - psychological, 73
- subgenual anterior cingulate cortex (sACC), 136
- substance P, 44
- suffering, 247
- surgery, pain management, 22

- sympathetic nervous system, 185
- symptom management, 247, 257, 293, *See also specific symptoms*
- decision making, 257
- doctor–patient relationship establishment, 249
- drug development, 314, 319, *See also clinical trials*
 - Agent Pathway, 320
 - defining the problem, 315
 - future directions, 322
 - target validation, 320
- goals of care, 253
- novel therapy development, 320
- paucity of evidence, 248
- symptom assessment, 250
 - reassessment, 251
- translational pathway to therapy development, 348
- treatment planning, 257
 - anticancer therapies, 255
 - guidelines and resources, 257
 - invasive pain management procedures, 260
 - nonadherence, 256
 - polypharmacy, 256
 - unmet needs, 253
 - versus cancer treatment, 294
- Symptom Management and Health-related Quality of Life (SxHRQOL) Steering Committee, 322
- Symptom Management and Quality of Life (SxQOL) Intergroup committee, 240
- symptom measurement, 257, *See also specific symptoms*
 - approach to, 270
 - area under the curve (AUC), 278
 - data gathering, 279
 - desirable properties of measures, 264
 - in context, 280
 - clinic, 279
 - clinical trials, 280
 - in oncology trials, 340
 - defining symptoms, 335
 - study design considerations, 337
 - symptom scale selection and use, 338
 - instruments, 272
 - multisymptom measures, 273
 - single-item measures, 271
 - single-symptom, multi-item measures, 273
 - length of instrument, 274
 - longitudinal analysis, 278
 - patient report, 320, 336
 - rise of, 330
 - psychometric validity, 276
 - reliability, 276
 - sensitivity to change, 276
 - validity, 276
 - response options, 275
 - choice of response scale, 275
 - number of response options, 275
 - types of response scale, 274
 - symptom report, 268, 278
 - minimum clinically important difference (MCID), 277
 - relationship to other patient-reported outcomes, 269
 - symptom research, 2, *See also cooperative group system*
 - barriers to, 316
 - Community Clinical Oncology Program (CCOP) trials, 310–312
 - current challenges, 342
 - lack of interdisciplinary research, 342
 - need for mechanism-focused research, 342
 - subjective nature of symptoms, 341
 - federally supported projects, 309–310
 - funding mechanisms, 308
 - cooperative agreements, 308
 - grants, 308
 - future directions, 346
 - animal model development, 1–2
 - brain networks involved in symptom expression, 345
 - genetic marker identification, 345
 - inflammation effects, 344
 - symptom development studies, 343
 - intervention research, 346
 - NIH grant review process, 307
 - support for, 306, 312
 - primary NIH institutes and centers, 305
 - symptoms, 1–2, 318, *See also specific symptoms*; symptom management; symptom measurement; symptom research
 - burden of, 1–2, 270
 - interference with function, 270
 - symptom clusters, 270
 - cancer-related, 8
 - biological pathways to, 317
 - clinical trial designs, 348
 - defining, 335
 - functional imaging, 206, 218
 - appetite, 214
 - dyspnea, 213
 - fatigue, 215
 - lamina I spinothalamocortical pathway, 209
 - nausea and vomiting, 213
 - pain, 212
 - sleep disturbance, 216
 - genetics, 192
 - association analysis, 197
 - genotyping, 195
 - linkage analysis, 196
 - symptom phenotyping, 194
 - variations associated with symptoms, 198
 - immunoneurological pathway model, 1–2
 - inflammatory cytokines and, 1–2, 6, 179, 180
 - longitudinal models, 285
 - average trajectory, 287
 - between-subject and within-subject variation, 288–291
 - impact on quality of life measures, 288–289
 - missing data, 291
 - masquerading symptoms, 252
 - mechanisms, 9–13
 - animal models, 6
 - molecular mechanisms, 13
 - research needs, 342
 - posttransplantation symptoms, 228
 - mechanisms, 228
 - reducing the burden of, 232
 - risk factors, 230
 - severity and patterns, 227
 - sickness behavior, 9
 - subjective nature of, 341
 - treatment-related, 315
 - biological pathways to, 317–318
 - syndrome of inappropriate antidiuretic hormone secretion, 54
 - tachykinins, 184
 - tail-suspension test, 85
 - Targretin®, 330
 - taste perception, 156
 - test-retest reliability, 275
 - thalidomide, 146, 186
 - time horizon, 262
 - time trade-off (TTO), 263
 - tocilizumab, 187
 - topotecan hydrochloride, 331
 - transcription factors, cytokine signaling through, 184
 - transient receptor potential vanilloid-1 (TRPV1), 36
 - translational approaches, pain relief, 27
 - Translational Research Working Group (TRWG), 318

Index

- treatment planning, 257
 - anticancer therapies, 255
 - guidelines and resources, 257
 - invasive pain management procedures, 255–256
 - nonadherence, 256
 - polypharmacy, 256
- treatment-related symptoms, 1
 - cognitive impairment. *See* chemobrain, 54
 - pain, 20
- tryptophan 2, 3 dioxygenase (TDO), 101
- tryptophan depletion, 86
 - inflammation-induced depression mechanisms, 102
- tumor necrosis factor (TNF)-alpha
 - anorexia/weight loss and, 147
 - anti-TNF agents, 187
 - cognitive impairment and, 61
 - genetic variation, 198
 - sickness behavior and, 6
 - sleep regulation, 173
- tumor-induced bone pain, 34
 - acidosis in, 36
- animal models, 1–2
 - management, 34
 - bisphosphonates, 35
 - osteoprotogerin (OPG), 35
 - neuropathic component, 38
 - tumor-derived products and, 37
 - endothelins, 36–37
 - kinins, 37
 - nerve growth factor (NGF), 37
 - prostaglandins, 36
- ubiquitin-proteasome pathway, 148
- unmet needs, 253
 - uridine diphosphate glucuronosyltransferase (UGT), 201
- utilities, 263
- vagal-afferent activation hypothesis
 - cancer-related fatigue, 113
 - Val158Met* polymorphism, 199
- validity, 276
 - construct validity, 131–132
 - content validity, 276
 - convergent validity, 276
 - etiological validity, 126
 - face validity, 125
 - known-group validity, 276
 - pharmacological validity, 126
 - predictive validity, 126
- vascular endothelial growth factor (VEGF), 113
- verbal rating scales (VRS), 274
- visceral nociceptive pain, 19
- visual analog scales (VAS), 263, 274–275
- vomiting. *See* nausea and vomiting VP-16. *See* etoposide
- W/REM neurons, 171
- wakefulness, 171
- weight loss, 151 *See also* anorexia/weight-loss syndrome
 - prognostic significance, 142
- white blood cell recovery, 231
- Zung Self-Rating Depression Scale, 115