## Index

α-adducin gene 606  
α errors see type I/II errors  
AAAAI see American Academy of Allergy, Asthma and Immunology  
Aarhus University Prescription Database (AUHD) 271, 273–4  
abacavir 153, 609  
ABCB see ATP-binding cassette transporter proteins  
absolute risk 814, 816  
absorption 25  
Abt’s sequential test 855  
abuse of medications 796  
academia  
  funding 899–900  
  future developments 895, 896–901  
  logistical advances 899  
  methodologic advances 896–7  
  new content areas of interest 897–9  
  personnel 900–1  
  scientific developments 896–9  
academic detailing 78–9, 414–15  
ACASI see audio computer-assisted self-administered interview  
ACCA see Advisory Committee on Causality Assessment  
accelerated approval 109, 652  
acceptability  
  meta-analyses 746  
  risk evaluation studies 811–12  
  see also risk tolerance  
acceptance, definition 795  
accuracy of data  
  case–control surveillance 292  
  diagnosis 779–80  
  in-hospital databases 245  
  medical records 230–1  
  recall 769, 771–5  
ACE see angiotensin converting enzyme  
acetaminophen 111–12, 509–10  
activated protein C (APC) 249–50  
active surveillance 477–8  
  see also Sentinel Initiative  
actual knowledge 120  
acute myocardial infarction (AMI) 874  
acute renal failure (ARF) 153–4  
  ad hoc epidemiologic studies 444, 769–75  
ADHD see attention-deficit/hyperactivity disorder  
  adherence see patient compliance/adherence  
ADME studies see pharmacokinetics  
  administrative data  
  medical devices 480  
  medication errors 841–2  
  overview 159–60, 163–4  
  validity 759, 775–87  
ADR see adverse events/adverse drug reactions  
  adulteration 153–4  
  adverse event reporting systems (AERS) 864  
  adverse events following immunizations (AEFI) 423, 427, 430, 432–52  
  adverse events/adverse drug reactions (AE/ADR) 3–5  
  case reports 583–600  
  causation 583–600  
  definitions and concepts 4–5  
  drug utilization 382  
  in-hospital databases 252–4  
  intellectual development 9–11  
  legal factors 65  
  legislation and regulations 6–9  
  legislative instruments 130  
  medication errors 840–1, 843–8  
  meta-analyses 724, 740–1  
  molecular pharmacoepidemiology 606, 618  
  optimization of therapy 4  
  pharmacoepidemiology applications 13–16  
  prescribing practices 417  
  prescription–event monitoring 301–4, 308–17, 320–6  
  risk evaluation studies 819  
  risk management 507–8, 511–12  
  Sentinel Initiative 551  
  sequential statistical methods 861, 864  
  spontaneous reporting 137–57  
  vaccines 423, 427, 430, 432–52  
  see also birth defects  
Advisory Committee on Causality Assessment (ACCA) 438  
AE see adverse events/adverse drug reactions  
AED see antiepileptic drugs  
AEFI see adverse events following immunizations  
AERS see adverse event reporting systems  
age effects  
  Canadian provincial databases 261–4  
  government claims databases 211  
  health maintenance organizations 169–70  
  in-hospital databases 252–4  
  sequential statistical methods 860  
  validity of data 773  
  see also elderly populations  
  age-related macular degeneration (AMD) 90–1  
  Agency for Healthcare Research and Quality (AHRQ) 10, 80–1  
  capacity building and collaboration 115  
  comparative effectiveness research 561–2, 567, 570–1, 573  
  ethics 630  
  future developments 900, 902  
  health maintenance organizations 173, 178, 180  
  medical devices 479  
  registries 334  
  agranulocytosis 348, 357, 874  
  agriculture 827  
  AHRQ see Agency for Healthcare Research and Quality  
  algorithm methods 591–3  
  allergies 843  
  AMA Council on Pharmacy and Chemistry 5–6  
  ambulatory procedures 164  
  AMD see age-related macular degeneration
drug safety evaluations 86–98
future developments 895, 901
legislative instruments 117–34
postapproval safety studies 88–90, 92–4
preapproval safety studies 89–92
research collaborations and initiatives 100–2
risk management 84–6, 88–90
risk mitigation interventions 85–6, 92, 98–100
special populations 94–8
spontaneous reporting 144
study design 86–7
birth defects 487–504
alleged teratogens 490–1
biologic and epidemiologic integration 499–500
biologic plausibility 495
case-control studies 498–9
class action fallacy 491
clinical problems 488–91
cohort studies 496–8
confounding data 495
current solutions 495–9
data quality 492–5
drug safety evaluations 94–6
exposure misclassification 492–3
future developments 499–501
gestational timing of exposures 493
high-risk teratogens 489–90, 491
legal and regulatory factors 500
legislative instruments 122
methodologic problems 491–5
outcome data 494–5
over-the-counter medications 488, 492
predicting teratogenetic effects 488
prescription-event monitoring 314–17
recall bias 493–4, 498–9
relation to drugs 487–8
research collaborations 100–2
risk management 514, 519–20
risk tolerance 68–9
sample size 492
spontaneous reporting 137
unknown risk drugs 490
birth registers 272, 276, 282–3, 340, 547
BLA see Biologics License Applications
black triangle program 143
blinding 645
body composition 28–9, 30–1
bootstrap methods 697
Boston Collaborative Drug Surveillance
Program 6, 9
Boston University Fever Study 651–2
boundary shapes 862–3
Bradford Hill criteria 122, 586
brand name drugs 666–7
Brighton Collaboration 435–6
British National Formulary 143
bromfenac sodium 510
Burroughs Wellcome Foundation 900–1
calender-time cohorts 871–2
Canadian Institute for Health Information (CIHI) 263, 267
Canadian Institute for Health Research (CIHR) 260
Canadian provincial databases 259–69
access to databases and confidentiality
264–5
applications 266–7
comparative effectiveness research 267
case and overview 259–60
data linkages 264, 265–6
drug utilization 266–7
future developments 267
hospitalization databases 259–60, 263–4
medical records 265–6
medical services databases 259–60, 263
prescription databases 259–63
risk evaluation studies 267
strengths and weaknesses 266
Cancer
beneficial drug effects 668
case-control surveillance 288, 290–1
health maintenance organizations
174, 176–7
registries 272, 276, 281–2, 337
Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) 177
Cancer Communications Research Center (CCRC) 177
Cancer Research Network (CRN) 176–7
CanCORS see Cancer Care Outcomes Research and Surveillance Consortium
candidate gene approaches 614–15
capacity building 107
cardiac structure and function 28–9, 32
cardiovascular disease 174, 179
Cardiovascular Research Network (CVRN) 179
case definition 147
case reports
algorithm/criterial methods 591–3
applications of causality assessment
587–8
causation 583–600
clinical epidemiology 43–4, 48–9
clinical problems 583–90
comparison of methods 594–5
case and overview 583
current solutions 590–5
field studies 351
future developments 595–7
historical development 585–7
methodologic problems 590
pharmaceutical manufacturers 588–9
pharmacoeconomics 689–92
probabilistic methods 593–4, 596
publishers of AE reports 589–90
regulatory factors 589
scoring of individual judgments 592–3
spontaneous reporting 141–3, 147–8
unstructured clinical judgments/global introspection 585–6, 591
verbal judgments 591–2
case series
clinical epidemiology 43, 44, 48–9
prescription-event monitoring 326
sample size 57–60
case-cohort studies 869, 874–5
case-control studies
antibiotics 833–4, 835–6
beneficial drug effects 663–4, 666–8
birth defects 498–9
causation 594
clinical epidemiology 43, 45–9
comparative characteristics of methods
365, 370, 375
confounding data 869, 872–4
drug safety evaluations 95
ethics 631–2
field studies 352–3, 355, 357
molecular pharmacoepidemiology
612–16
prescription-event monitoring 323, 326
sample size 53, 55–7, 59–60
vaccines 430, 448–9
validity of data 759, 761–4
case-control surveillance (CCS) 287–300
applications 293
case and control accrual and classification 287–8
context and overview 287
data analysis 289–91
descriptive characteristics 289
drug information and classification
288–9
future developments 293
prescription and non-prescription medications 291
strengths and weaknesses 291–3
temporal effects 291–2
case-crossover study design 86–7, 89, 875–8
case-time-control studies 878–9
causation
algorithm/criterial methods 591–3
applications of causality assessment
587–8
causation 583–600
clinical epidemiology 43–4, 48–9
clinical problems 583–90
comparison of methods 594–5
case and overview 583
current solutions 590–5
field studies 351
future developments 595–7
historical development 585–7
methodologic problems 590
pharmaceutical manufacturers 588–9
pharmacoeconomics 689–92
probabilistic methods 593–4, 596
publishers of AE reports 589–90
regulatory factors 589
scoring of individual judgments 592–3
spontaneous reporting 141–3, 147–8
unstructured clinical judgments/global introspection 585–6, 591
verbal judgments 591–2
case series
clinical epidemiology 43, 44, 48–9
prescription-event monitoring 326
sample size 57–60
case-cohort studies 869, 874–5
case-control studies
antibiotics 833–4, 835–6
beneficial drug effects 663–4, 666–8
birth defects 498–9
causation 594
clinical epidemiology 43, 45–9
comparative characteristics of methods
365, 370, 375
confounding data 869, 872–4
drug safety evaluations 95
ethics 631–2
field studies 352–3, 355, 357
molecular pharmacoepidemiology
612–16
prescription-event monitoring 323, 326
sample size 53, 55–7, 59–60
vaccines 430, 448–9
validity of data 759, 761–4
case-control surveillance (CCS) 287–300
applications 293
case and control accrual and classification 287–8
context and overview 287
data analysis 289–91
descriptive characteristics 289
drug information and classification
288–9
future developments 293
prescription and non-prescription medications 291
strengths and weaknesses 291–3
temporal effects 291–2
case-crossover study design 86–7, 89, 875–8
case-time-control studies 878–9
causation
algorithm/criterial methods 591–3
applications of causality assessment
587–8
causation 583–600
clinical epidemiology 43–4, 48–9
clinical problems 583–90
comparison of methods 594–5
case and overview 583
current solutions 590–5
field studies 351
future developments 595–7
historical development 585–7
methodologic problems 590
pharmaceutical manufacturers 588–9
pharmacoeconomics 689–92
probabilistic methods 593–4, 596
publishers of AE reports 589–90
regulatory factors 589
scoring of individual judgments 592–3
spontaneous reporting 141–3, 147–8
unstructured clinical judgments/global introspection 585–6, 591
verbal judgments 591–2

CERT see Centers for Education and Research on Therapeutics
CESR see Comparative Effectiveness and Safety Research
changeability 712
Charlson co-morbidity index 166
CHCA see Child Health Corporation of America
CHF see Commissie Farmaceutische Hulp
CHI see Community Health Index
Child Health Corporation of America (CHCA) 245
children see pediatrics
chloramphenicol 5
CHM see Commission on Human Medicines
CHMP see Committee for Medicinal Products for Human Use
cholestatic jaundice 55–6
clinical conditions
causality 586
patient compliance/adherence 76
pharmacoeconomics 698–9
prescribing practices 75
Clinical Disease Score 166
chronic kidney disease (CKD) 180
chronic obstructive pulmonary disease (COPD) 254–5, 874
Chronic Respiratory Questionnaire (CRQ) 713–14
CIHI see Canadian Institute for Health Information
CIHR see Canadian Institute for Health Research
CIOMS see Council for International Organizations of Medical Sciences
CISA see Clinical Immunization Safety Assessment
cisapride 112
Civil Registration System (CRS) 274
CKD see chronic kidney disease
classification
automated databases 159–60
health maintenance organizations 163–4
medical devices 480
medication errors 841–2
see also commercial insurance databases; government claims databases
case action fallacy 491
clearance 27
clerical errors 196
clinical data 247, 272, 275, 280–1
clinical decision support systems (CDSS) 847–8
clinical economics 680–1
clinical epidemiology 38–51
analyses of secular trends 43, 45, 48–9
case reports 43–4, 48–9
case series 43, 44, 48–9
case–control studies 43, 45–9
cohort studies 43, 46–9
criteria for causation 41–3
errors 39–41
randomized clinical trials 43, 47–9
scientific method 38–9
study design 42–9
Clinical Immunization Safety Assessment (CISA) Network 427, 436–8
clinical pharmacology 23–37
basic principles and concepts 23, 24–5
definition 3
pharmacodynamics 29, 32–5
pharmacoepidemiology relationships 24
pharmacogenomics 35
pharmacokinetics 25–32
risk management 511
clinical practices variation 250–2
Clinical Transaction Codes (CTC) 245
Clinical and Translational Science Awards (CTSA) 571
clinical trials 12, 14–15
antibiotics 832
beneficial drug effects 664–5
birth defects 488
causation 594
comparative effectiveness research 568–9
costs 62
future developments 898
health-care systems 74
hypothesis generating studies 66
legislative instruments 125, 127
marketing 64
medical devices 473–6
meta-analyses 723–5, 729, 740–1, 744–8
patient compliance/adherence 803–4
pharmacoeconomics 679–80, 685–9, 693–4, 699–700
pharmacogenomics 35
pharmacokinetics 29
registries 331–2, 335
regulatory agencies 109–11, 113
reimbursement policies 555–6, 558–9
risk management 511, 517
sequential statistical methods 861–3
spontaneous reporting 137–8
vaccines 426–7, 443
see also randomized clinical trials
clopidogrel 559
closure randomization 834
CMAXSPRT see conditional MaxSPRT
CMS see Centers for Medicare and Medicaid Services
CNV see copy number variants
comorbidities 166
COC see combined oral contraceptives
Cochrane Collaboration
meta-analyses 723, 728–31, 746
prescribing practices 402, 404
coding errors 196–7
coherence 41
comparative characteristics of methods
field studies 355
government claims databases 215–16
randomized clinical trials 650–1
registries 333, 335
follow-up-time cohorts 871–2
Food and Drug Administration (FDA)
academic medical centers 81
antibiotics 829
assessing impacts of regulatory actions
112
beneficial drug effects 657, 659, 662
birth defects 489–90
capacity building and collaboration
114–15
causality 585, 588–9
commercial insurance databases 203, 206
drug safety evaluations 95–6
ethics 630
future developments 899–900
health maintenance organizations
169, 179–80
health-care systems 73, 79
historical development 5–6, 8–10
in-hospital databases 254
legislative instruments 120–1, 124–6
medical devices 477–8, 482–3
meta-analyses 727, 738, 740–1, 746–9
pharmacokinetics 31
registries 338–9, 340, 342
regulatory factors 63–4
responsibilities in drug safety 534–5
risk evaluation studies 810, 820–1
risk management 85–6, 99–100, 505, 508–10, 515, 518–22
spontaneous reporting 141, 152
vaccines 425, 432–4
see also Sentinel Initiative
Food, Drug, and Cosmetic Act (1938) 5
formulation effects 66, 142
FPC see Federal Partners Collaboration
Framingham Heart Study 693–4
French Medicines Agency 144
full-text records 165
funding 572–3, 899–900
funnel plots 736–8
fuzzy-trace theory 821–2
FWA see Federal Wide Assurance
G theory see generalizability
G6PD see glucose-6-phosphate dehydrogenase
gag clauses 127
gastrointestinal (GI) bleeding
comparative characteristics of methods
375
confounding data 884–5
validity of data 757, 768, 775–7, 780–6
gastrointestinal (GI) pharmacokinetics
28–9, 30
Gastrointestinal Toxicity Survey 775
GBS see Guillain–Barré syndrome
gender effects
Canadian provincial databases 261, 264–3
government claims databases 211
health maintenance organizations
169–70
in-hospital databases 253–4
validity of data 770, 773
gene discovery approaches 610–11, 614–15
gene–drug interactions 604–9
general causation 121–2
General Practice Research Database (GPRD)
access to databases 231–2
applications 234–5
context and overview 160, 225–7
data collection and structures 227–30
data quality 230–1, 233–4
future developments 235
pharmacy-based medical record
linkage systems 279
strengths and weaknesses 232–4
validity of data 783, 785
general practitioners (GP)
medical records 225, 231
pharmacy-based medical record
linkage systems 270, 277
prescription–event monitoring 302–3
generalizability
comparative effectiveness research
566
ethics 625–6, 637
health-related quality-of-life 711–12
in-hospital databases 248–9
medical devices 475–6, 480
pharmacoeconomics 686–7, 702
randomized clinical trials 645–6, 650
glucuronosyl transferase (UGT) isoforms
30–1
glutethimide 491
governance 536, 547–8, 573
see also ethics
government claims databases
accuracy of pharmacy claims 216
applications 219–20
data linkages 217
data sources 210–15
data structures 213–15
eligibility and data limitations 218–19
future developments 220–1
limitations in prescription coverage
218
medical records 219
non-representativeness 216–18
out-of-plan care 219
outcome validation 217
population size and follow up length
215–16
program descriptions 209–10, 213–14
recipient characteristics 210–12, 214, 215
strengths and weaknesses 215–19
unavailable information 218
validity of procedure claims 216
GP see general practitioners
GPI see Generic Product Identifier
GPRD see General Practice Research Database
Group Health Cooperative (GHC) 180
H1N1 virus
Group Health Cooperative (GHC) 180
group sequential analysis 857–64
guideline materials 409–10
GWAS see genome-wide association studies
gynecomastia 312
H-2 blockers 557
H1N1 virus
Sentinel Initiative 550–1
sequential statistical methods 861
vaccines 423, 424, 429, 432–4, 440, 447
H5N1 virus 338
HAART OC see Highly Active Antiretroviral Therapy Oversight Committee
Harvard Pilgrim Health Care, Inc. (HPHC) 537
HAS see Haute Autorité de Santé
Haute Autorité de Santé (HAS) 563
HDL see high density lipoprotein
health economics and outcomes research (HEOR) 204–5
Health Information Technology for Economic and Clinical Health (HITECH) 787
health insurance see commercial insurance databases
Health Insurance Portability and Accountability Act (HIPAA) 89

biopharmaceutical industry 287

case–control surveillance 287

commercial insurance databases 198

economics 633–4

field studies 356

in-hospital databases 247

Sentinel Initiative 337, 548–9

health maintenance organizations (HMO) 163–88

administrative and claims data 163–4

affiliated organizations and departments 168

applications 167–81

birth defects 496–7

commercial insurance databases 200

data development procedures 165–6

data resources 163–5

future developments 899

government claims databases 213

historical context 169

HMO research network 167–81

medical records 163–5, 167, 172, 176

multi-HMO projects 165–6, 169, 171–81

reimbursement policies 560

research databases and registries 165

Sentinel Initiative 543

standard data layouts 169–73

strengths and weaknesses 166–7

health plans see health maintenance organizations

health profiles 716–17

Healthcare Safety Surveillance System (HSSS) 203, 861

health-care systems 73–83

automated databases 161

Canadian provincial databases 259–60, 263

commercial insurance databases 189, 194, 204–5

drug approval processes 74

economic assessments 79

effectiveness and efficacy 77–8

future developments 81

government claims databases 210

incentive structures 194, 200

interventional pharmacoepidemiology 78–9

medical records 228–9, 235

patient compliance/adherence 75–7

pharmacy-based medical record linkage systems 278–9

policy analysis 78

postmarketing surveillance 73–4

prescribing practices 74–5, 404

registries 332–4

regulatory agencies 108

risk evaluation studies 810, 812–13

risk management 514–15

spontaneous reporting 139–41, 143–4, 149–50

see also health maintenance organizations

health-care-acquired infections 827, 836

health-care-associated meningitis 154

health-related quality-of-life (HRQL) 709–22

clinical problems 710

course and overview 709–10

current solutions 710–19

definitions 710

future developments 719

generic instruments 716–17

health profiles 716–17

methodologic problems 710

multiple QoL measures in clinical studies 718–19

new drug investigations 711–15

specific instruments 717–18

taxonomy of QoL instruments 715–16

utility measurement 717

HealthCore Integrated Research Database (HIRDSM) 199–203, 784

HeartNet 477

Henoch–Schönlein purpura (HSP) 250–2

HEOR see health economics and outcomes research

heparin 641–2, 730–1

hepatic function 30, 31–2, 55–6

hepatitis 55–6

hepatotoxicity

case series 59

case–control studies 57–8

cohort studies 55–6

HER2 oncogene 606

herbal medications 359

heterogeneity 733–5, 738

high density lipoprotein (HDL) cholesterol 880–1

high-dose chemotherapy 701–2

high-risk medication therapies 176

Highly Active Antiretroviral Therapy Oversight Committee (HAART OC) 100–1

HIPAA see Health Insurance Portability and Accountability Act

HIRDSM see HealthCore Integrated Research Database

historical comparison groups 687–8

historical development 5–11

drug crises 6–11

intellectual development 9–11

legislation and regulations 5–9

history taking 765

HITECH see Health Information Technology for Economic and Clinical Health

HIV/AIDS

health maintenance organizations 175

patient compliance/adherence 795, 797–802, 805

research collaborations 100–1

HLA B5701 609

HMO see health maintenance organizations

homogeneity of data 740

hormone replacement therapy (HRT) 642–3, 663–4

hospital procedures 164

hospitalization data

Canadian provincial databases 259–60, 263–4

comparative characteristics of methods 367, 373–4, 375

countounding data 872–3, 878

in-hospital databases 246–7, 249, 252–3

patient compliance/adherence 795

pharmacy-based medical record linkage systems 272, 275, 282

validity 771–5, 779–85

see also in-hospital databases

HPHC see Harvard Pilgrim Health Care, Inc.

HRQL see health-related quality-of-life

HRT see hormone replacement therapy

HSP see Henoch–Schönlein purpura

HSSS see Healthcare Safety Surveillance System

human capital development 573

human subjects 624–5, 626

hyperbolic concentration effects 33

hypercholesterolemia 75

hypersensitivity reactions

commercial insurance databases 199

definition 4

spontaneous reporting 142

hypertension 75

hypothesis generating studies 63, 65–6

comparative characteristics of methods 367, 371–2

registries 335–6

hypothesis strengthening 367, 372

hypothesis testing 63, 65

automated databases 158

comparative characteristics of methods 367, 372

prescription–event monitoring 319, 320–2

randomized clinical trials 649

hysteresis 34

i2 statistic 734

IAAAS see International Agranulocytosis and Aplastic Anemia Study

ibuprofen 57–8, 643–4, 652

ICER see incremental cost effectiveness ratio

ICES see Institute for Clinical Evaluative Sciences

ICH see International Conference on Harmonization

ICMJE see International Committee for Medical Journal Editors

ICU see intensive care units

IDIS see Iowa Drug Information Service
data analysis 651–2
feasibility conditions 648–9
future developments 652–3
key conditions 647–8
logistics 649–51
LD see linkage disequilibrium
LDL see low density lipoprotein
learned intermediary defense 123
legal factors
birth defects 500
causation 588–9
future developments 902
historical development 5–9
molecular pharmacoepidemiology 618
pharmacoepidemiological studies 63, 65
prescribing practices 407–8
legislative instruments 117–34
causation 121–3
contract law 117, 126–9
expertise and Daubert 123–4
failure to warn 118–23, 125–6
intellectual property law 117, 129–31
knowledge 119–20
learned intermediary defense 123
product liability 117–26
regulation and product liability 124–6
tort law 117–24
lidocaine 665–6
life-threatening side-effects 509
lifestyle factors 772
linear concentration effects 33
linkage disequilibrium (LD) 605, 615
Lipid Research Clinics Coronary Primary Prevention Trial 804
literature reviews 723, 728–9
liver function 30, 31–2, 55–6
liver toxicity 815–16, 821
LLR see log likelihood ratio
log likelihood ratio (LLR) 854–6, 862
long-acting beta agonists (LABA) 518
long-term care 847
long-term safety 474
long-term surveillance 291–2
longevity of data 248
longitudinal construct validity 711
longitudinal data
automated databases 161
Canadian provincial databases 266
commercial insurance databases 189, 193
confounding data 868, 882
medical records 224
validity 778
low density lipoprotein (LDL) cholesterol 880–1
low molecular weight heparin 730–1
LSD see lysosomal storage disorders
LST see large simple trials
lumiracoxib 304, 306–7
lysosomal storage disorders (LSD) 337–8
M-PEM see modified PEM
MAA see Marketing Authorization Applications
McMaster Health Index Questionnaire 716
MAH see Marketing Authorization Holder
Managed Care Organizations (MCO) 444–5, 448–50
mandated postmarket studies 478–9
Mantel–Haenszel procedure 732, 735, 744, 876
Managed Care Organizations and User Facility Device Experience (MAUDE) 476
marketing 63, 64–5, 404
Marketing Authorization Applications (MAA) 86, 109
Marketing Authorization Holder (MAH) 524–5, 528–31
Markov chain Monte Carlo methods 736, 746
marriage registers 276
Marshfield Clinic Research Foundation 180–1
matched unexposed control design 859
MAUDE see Manufacturer and User Facility Device Experience
maximized sequential probability ratio test (MaxSPRT) 855–63
Mayo Clinic 631–2
MCO see Managed Care Organizations
MCV see meningococcal conjugate vaccine
MDEpiNet see Medical Devices Epidemiology Network
measurement error 758, 760, 761–7
MEB see Medicines Evaluation Board
MedDRA see Medical Dictionary for Regulatory Activities
media reporting 151, 410
Medicaid 9, 112, 209–13
applications 219–20
automated databases 159, 161
beneficial drug effects 667
commercial insurance databases 197, 200
comparative effectiveness research 561–2
data sources 210–13
data structures 213
drug utilization 387–8
future developments 220–1
health-care systems 78
in-hospital databases 253
program description 209–10
recipient characteristics 210–12
strengths and weaknesses 215–19
medical claims 192
medical devices 469–86
active surveillance 477–8
administrative claims data 480
benefit-risk profiles 471, 473–4
characteristics compared with drugs 471–3
classification 471–2
clinical problem 473–4
comparative effectiveness and safety estimation 481
comparative studies 475–6
context and overview 469–73
current solutions 476–82
definitions 469–71
diffusion to clinical practice and utilization 473
enhanced surveillance 477
evidence-based practice and policy 473, 482
future developments 482–3
individual patient exposure 475
international infrastructure 483
long-term safety and effectiveness 474
mandated postmarket studies 478–9
methodologic problems 474–6
national population exposure 475
outcome evaluation methods 480–2
passive surveillance 476–7
registries 339, 479
simultaneous combination of available evidence 481–2
sources of variation 480
treatment assignment mechanisms 481
Medical Devices Epidemiology Network (MDEpiNet) Initiative 482–3
Medical Dictionary for Regulatory Activities (MedDRA) 145, 309
Medical Product Safety Network (MedSun) 477
medical records 224–43
access to databases 231–2
access to original records 233
applications 234–5
automated databases 160
Canadian provincial databases 265–6
commercial insurance databases 196
computer hardware and software requirements 234
context and overview 224–7
data collection and structures 227–30
data quality 230–1, 233–4
ethics 631–2
field studies 352–3, 358
future developments 235
government claims databases 219
health maintenance organizations 163–5, 167, 172, 176
medication errors 841–2
pharmacy-based linkage systems 270–86
population-based data and sample size 232, 235
registries 336
Sentinel Initiative 535, 546–7, 552
strengths and weaknesses 232–4
validity of data 232–3, 767–9, 771, 775–9, 786–7
medical services databases 259–60, 263
Medicare applications 219–20
commercial insurance databases 190, 197
comparative effectiveness research 561–2
confounding data 885–6
data sources 214
data structures 214
field studies 356
future developments 220–1, 899
in-hospital databases 253
pharmacoeconomics 688
program description 213–14
recipient characteristics 214
registries 335
strengths and weaknesses 215–19
validity of data 782
Medicare Prescription Drug, Improvement, and Modernization Act (2003) 10
medication diaries 801
medication errors 840–51
clinical problems 840–2
context and overview 840
current solutions 847–8
definition and classification 840–1
detection 841–3, 844–5
drug class 846
future developments 848
gaps in clinical care 845–7
health-related outcome impacts 845, 848
historical development 10–11
incidence rates 843–5
methodologic problems 842–7
prescribing practices 404–5, 417
prevention strategies 847–8
risk factors 845–6
risk management 507–8, 512
setting 843–4, 846–7
special populations 844
spontaneous reporting 142, 152
Medication Exposure In Pregnancy Risk Evaluation Program (MEPREP) 179
Medicine Monitoring Unit (MEMO) database 273
Medicines Evaluation Board (MEB) 144
Medicines and Healthcare Products Regulatory Agency (MHRA) 13, 225, 308
MEPREP 497
MedSun see Medical Product Safety Network
MedWatch 8–9, 152, 343
membership status 376, 167, 192
MEMO see Medicine Monitoring Unit
menarche 271–2
meningitis 154
meningococcal conjugate vaccine (MCV) 429–30, 434, 527–31
menopause 642, 663–4, 771–2
Menstrual and Reproductive Health Study 771–2
mental health disorders 174, 180
Mental Health Research Network (MHRN) 180
MEPREP see Medication Exposure In Pregnancy Risk Evaluation Program
meta-analyses 723–56
adjusting for covariates 740
adverse events/adverse drug reactions 724, 740, 742
assumptions 740
biases in data abstraction 727, 730–1
biases in original studies 724, 726
case studies of applications 740–8
choice of statistical test 732–3
clinical problems 724–6
combining studies and heterogeneity 726, 733–5
comparative effectiveness research 566–7
conclusions and recommendations 736
cost-effectiveness and time-savings 743–5
cumulative 745–6
current solutions 728–48
data collection 727, 730–1
definitions 723–4
differential effects among patient subgroups 742–3
future developments 748–9
inclusion/exclusion criteria 729–30, 745–6
indirect and simultaneous comparisons of treatments 738–40, 746
literature reviews 723, 728–9
medical devices 476
methodologic problems 726–7, 736–40
molecular pharmacoepidemiology 616
new indications for existing therapies 741–2
publication bias 726–7, 736–8, 747–8
purpose definition 728
rare events 735–6
regulatory factors 747–8
signal detection 745–6
statistical analyses 731–6
steps involved 728–36
unpublished studies 736–8
metabolism 26–7
metastatic breast cancer 701–2
methicillin-resistant Staphylococcus aureus (MRSA) 828, 835
methodologic studies 219–20
methylphenidate 152
metoclopramide 111
MHRA see Medicines and Healthcare Products Regulatory Agency
MI see myocardial infarction
Michaels–Menken equation 26–7
MID see minimally important difference
Mini-Sentinel Coordinating Center (MSCC) 537
Mini-Sentinel Initiative 179, 206
minimally important difference (MID) 712–15
misclassification errors 761–3
see also exposure misclassification
miscoding 196
missing data 441–2
missing doses 796
misspecification 196
MMR/MMRV see mumps–measles–rubella
modified PEM (M-PEM) studies 304, 306–7, 324–5, 327
molecular pharmacoepidemiology 601–22
applications 607–9
candidate gene approaches 614–15
causal pathway of disease 606–8
clinical problems 604–9
confounding data 609–10, 614, 617
cost and overview 601
current solutions 614–17
definitions and concepts 602–3
effect modifications 611–13, 615–16
future developments 617–18
gene discovery approaches 610–11, 614–15
gene–drug interactions 604–9
genetic variability 601–3, 606–7
historical development 602
methodologic problems 609–14
pharmacodynamics 605–6, 607–8
pharmacogenetics and pharmacogenomics 603–4
pharmacokinetics 604–5, 607–8
population admixture 614, 617
type I/II errors 610, 613–14, 616–17
Monitoring System for Adverse Events Following Immunizations (MSAEFI) 441–2
motor vehicle crashes (MVC) 877–8
MRSA see methicillin-resistant Staphylococcus aureus
MS see multiple sclerosis
MSAEFI see Monitoring System for Adverse Events Following Immunizations
MSCC see Mini-Sentinel Coordinating Center
multicenter evaluations 692
multidrug-resistant Acinetobacter baumannii 828
multidrug-resistant Pseudomonas aeruginosa 828
multi-HMO projects 165–6, 169, 171–81
multimedia campaigns 410
multinational economic evaluations 698–9
multiple sclerosis (MS) 101
multi-source data integration 107, 113
multi-time case–control studies 874
multivariable modeling 321
multivariate analysis 688, 696–7, 879–82, 885
mumps–measles–rubella (MMR) vaccine 423, 425, 433, 440, 445
Sentinel Initiative 550
sequential statistical methods 858, 860
MVC see motor vehicle crashes
myocardial infarction (MI) beneficial drug effects 665–6
meta-analyses 724, 745
prescribing practices 153
validity of data 757, 761–3, 775–7, 780–6
N-acetyl-p-benzoquinone imine (NAPQI) 27
NAEPP see National Asthma Education and Prevention Program
Naranjo scoring method 592
natalizumab 101
National Asthma Education and Prevention Program (NAEPP) 518
National Cancer Institute (NCI) 169, 337, 341
National Cardiovascular Data Registry (NCDR) 479
National Childhood Vaccine Injury Act 432
National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP) 508
National Death Index (NDI) 202, 336, 547
National Disease and Therapeutic Index (NDTI) 387
National Drug Codes (NDC) beneficial drug effects 667
commercial insurance databases 201
health maintenance organizations 164, 166, 172
medical devices 475
National Electronic Injury Surveillance System (NEISS) 478
National Health Service (NHS) 225, 230–1, 302–3
National Healthcare Safety Network (NHSN) 828
National Hospital Ambulatory Medical Care Survey (NHAMCS) 111, 518–19
National Hospital Discharge Survey (NHDS) 111, 519
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) 337
National Institute for Health and Clinical Excellence (NICE) 11, 562–3
National Institutes of Health (NIH) 630, 900–2
national pharmacovigilance systems 143–5
national postmarketing safety databases 145–7
National Registry for Myocardial Infarction 333
natural language processing (NLP) 165
nausea and vomiting 375
NCCMERP see National Coordinating Council on Medication Error Reporting and Prevention
NCDR see National Cardiovascular Data Registry
NCI see National Cancer Institute
NDA see New Drug Applications
NDC see National Drug Codes
NDI see National Death Index
NDTI see National Disease and Therapeutic Index
needs assessment 108
negligence 65, 118
NEISS see National Electronic Injury Surveillance System
nested case–control studies 323, 326, 872–4, 875
net benefit 682–3
New Drug Applications (NDA) 86, 521–2
new drug approval processes 724–5
new drug exposure 367, 374
new indications for existing therapies 741–2
NHAMCS see National Hospital Ambulatory Medical Care Survey
NHDS see National Hospital Discharge Survey
NHI see Normative Health Information
NHS see National Health Service
NHSN see National Healthcare Safety Network
NIAMS see National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICE see National Institute for Health and Clinical Excellence
NIH see National Institutes of Health
NLP see natural language processing
NNT see number needed to treat
nomograms 52
non-diagnosis-linked databases 385–6
non-differential misclassification 761–4
non-malignant diagnoses 288–9
non-parametric bootstrap methods 697
non-pill formulations 803
non-representativeness 216–18
non-response bias 318–19
oral contraceptives 735, 797, 805
oral polio vaccine (OPV) 423, 424, 426, 433
ordinary least squares regression 697
Organization Data Services (ODS) 302–3
Organization for Economic Cooperation and Development (OECD) 624
Organization of Teratogen Information Specialists (OTIS) 501
orphan drugs 84, 108
osteomyelitis 255–6
osteoporosis 663–4
OTC see over-the-counter
OTIS see Organization of Teratogen Information Specialists
out-of-plan care 219
outcome data
antibiotics 831, 834–5
beneficial drug effects 656, 661
birth defects 494–5
comparative characteristics of methods 366, 368, 371, 373–4
medical devices 472–3, 480–2
medication errors 845, 848
patient compliance/adherence 797–8, 805
prescription–event monitoring 317–18
randomized clinical trials 649
vaccines 429–30, 447–8
outcome definition 347–8
outpatient diagnoses
automated databases 160
comparative characteristics of methods 366, 371
health maintenance organizations 164
in-hospital databases 246–7
medication errors 846–7
validity of data 779–80
outpatient resource assessments 689–92
over-the-counter (OTC) medications
automated databases 158–9
birth defects 488, 492
case–control surveillance 291
medication errors 843
randomized clinical trials 641, 643–4
risk management 509–10
validity of data 778
overdose
patient compliance/adherence 796
regulatory agencies 111–12
risk factors 845–6
risk management 509–10
over-reporting 771–3, 801
oxcarbazepine 314–15
P-EHR see payer-based electronic health record
p-values 47
package size 112
packaging 85
pain 175, 796
PALGA see Pathological Anatomy
National Automated Archive
Paling Perspective Scale 815
panel-based methods 713
paracetamol 111–12, 509–10
parallel trials 736
Part D Drug Events (PDE) 214
PAS see postapproval studies
passive surveillance 432, 440, 442, 476–7
see also spontaneous reporting
patent law see intellectual property law
Pathological Anatomy National Automated Archive (PALGA) 276, 281
pathology databases 272, 276, 281
Patient Centered Outcomes Research Institute (PCORI) 81, 562, 571
patient compliance/adherence 795–809
adherence metrics 805
beneficial drug effects 657
birth defects 493
clinical problems 796–7
clinical trials 803–4
confounding data 887
context and overview 795–6
current solutions 798–805
data analysis 797–8, 803–5
definitions 795–6
drug concentration testing 802–3
drug utilization 382, 389
electronic drug monitors 799, 802
evaluation 75–7
future developments 806
health-care systems 75–7
measurement challenges and techniques 797, 798–803
medication diaries 801
methodologic problems 797–8
non-pill formulations 803
pill counts 801
refill data 799–801
self-report data 798–9, 805
temporal effects 804–5
patient information see demographic data
patient information leaflets (PIL) 515–16, 522, 812–13
Patient Package Inserts 85
patient participation 689
Patient Protection and Affordable Care Act (PPACA) 209
patient registries see registries
patient router files 274
patient variation 480
pattern identification 199
payer-based electronic health record (P-EHR) 205
PCORI see Patient Centered Outcomes Research Institute
PDD see prescribed daily dose
PDE see Part D Drug Events
PDP see prescription drug plans
PDUFA see Prescription Drug User Fee Acts
Index 947

positive predictive value (PPV) 780, 785
postlicensure Rapid Immunization Safety Monitoring (PRISM) project 547, 550–1, 861
postapproval studies (PAS)
biopharmaceutical industry 88–90, 92–4
medical devices 478–9
regulatory agencies 110–11, 114
risk assessments 511
vaccines 432–44
postmarketing commitments (PMC) 85
postmarketing requirements (PMR) 85
postmarketing surveillance
applications of sequential analysis 860–1
automated databases 158
beneficial drug effects 657–9, 666–7
clinical epidemiology 44
clinical problems 852
commercial insurance databases 205–7
context and overview 852
continuous sequential analysis 854–7
control chart methods 853
costs 62
current solutions 854–64
drug safety evaluations 97–8
future developments 864–5
group sequential analysis 857–64
health-care systems 73–4
historical development 8–9, 11
hypothesis generating studies 66
legislative instruments 125
medical devices 478–9
methodologic problems 853–4
pharmacoeconomics 680
pharmacoepidemiology applications 15
prospective studies 852–67
registries 339
regulatory factors 62–4
sample size 60–1
Sentinel Initiative 534–6
sequential statistical methods 852–67
signal investigation 863–4
study design 858–60, 861–3
see also pharmacovigilance
spontaneous reporting
potentially inappropriate medication (PIM) 253
PPACA see Patient Protection and Affordable Care Act
PPD see Premier Perspective Database
PPI see proton pump inhibitors
PPO see preferred provider organizations
PPV see positive predictive value
PREA see Pediatric Research Equity Act
preapproval review process 138
preapproval safety studies
biopharmaceutical industry 89–92
risk assessments 511
spontaneous reporting 137–8
vaccines 431–2, 443
see also clinical trials
PRECEDE model 408–9
preferred provider organizations (PPO) 200
Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 728, 730
pregnancy
drug safety evaluations 94–6
gestational timing of exposures 493
health maintenance organizations 175, 179
medication errors 843
pharmacokinetics 31
prescription–event monitoring 314–17
registries 339–40
research collaborations 100–2
risk management 514, 519–20
risk tolerance 68–9
see also birth defects
premarketing studies see clinical trials
Premier Perspective Database (PPD) applications 249–56
cost 374
current solutions 244, 246
data structure and elements 246–7
future developments 256–7
strengths and weaknesses 247–9
pre–post with comparison group design 404–5
prescribed daily dose (PDD) 390
prescribing practices 402–22
academic detailing 414–15
audit and feedback systems 411–12
beneficial drug effects 657–9
Canadian provincial databases 259–63
clinical problems 403–4
commercial insurance databases 198
definitions and concepts 408–9
context and overview 402
context and overview 304, 322–3
context and overview 301–2
data analysis 310–17
data collection 303–4
data processing 308–9
data quality 318–19
design and source data 302–3
drug utilization 322–3, 325
epidemiology of diseases and indications 322
ethics and confidentiality 303
events and outcome categories 304, 308
exposure data 317
future developments 326
hypothesis-testing 319, 320–2
incidence/incidence densities 311–16, 322–3
outcome data 317–18
participation in research 318
pediatric drug safety monitoring 323
pharmacogenetics 326
pregnancy outcomes 314–17
qualitative evaluations of events 310
quantitative evaluations of events 310–17, 320, 323–4
questionnaire design 304–7
representativeness 317
retrospective/prospective studies 317
risk predictors 323
sample size and duration 309–10, 317, 319
self-controlled case series analysis 326
setting 319–20
signal strengthening 318, 320–2
single-group cohort design 302–3, 318
logistical issues 407
medication errors 842, 847–8
methodologic problems 404–8
multimedia campaigns 410
opinion leaders 413–14
phenomen-based medical record linkage systems 271, 278
regression toward the mean 406
reminders and computerized decision support 412–13, 416
risk evaluation studies 812
risk management 85, 515
small group learning 410–11
spontaneous reporting 148–9
study design 404–5
unit of analysis 406–7
validity of data 760, 779
prescription drug plans (PDP) 213
Prescription Drug User Fee Acts (PDUFA) 8–9, 10, 85, 98
prescription drugs databases 259–63
prescription–event monitoring (PEM) 9, 301–30
applications 320–6
biopharmaceutical industry 93
comparative characteristics of methods 374
context and overview 301–2
data analysis 310–17
data collection 303–4
data processing 308–9
data quality 318–19
design and source data 302–3
drug utilization 322–3, 325
epidemiology of diseases and indications 322
ethics and confidentiality 303
events and outcome categories 304, 308
exposure data 317
future developments 326
hypothesis-testing 319, 320–2
incidence/incidence densities 311–16, 322–3
outcome data 317–18
participation in research 318
pediatric drug safety monitoring 323
pharmacogenetics 326
pregnancy outcomes 314–17
qualitative evaluations of events 310
quantitative evaluations of events 310–17, 320, 323–4
questionnaire design 304–7
representativeness 317
retrospective/prospective studies 317
risk predictors 323
sample size and duration 309–10, 317, 319
self-controlled case series analysis 326
setting 319–20
signal strengthening 318, 320–2
single-group cohort design 302–3, 318
statistical power 319
stopping medication 314, 316
strengths and weaknesses 317–20
supplemental information 304, 308
therapeutic risk management 324–6
time to onset 314
prescription medications 291, 509, 512, 516
preterm births 175
prevalence studies
  comparative characteristics of methods 367, 373
  medical records 234
  sample size 53–4, 58
primary analysis 651
primary non-adherence 76–7
PRISM
  see Post-licensure Rapid Immunization Safety Monitoring
PRISMA
  see Preferred Reporting Items for Systematic reviews and Meta-Analyses
privacy and confidentiality
  Canadian provincial databases 264–5
  commercial insurance databases 190–1, 198–9, 203–4
  drug utilization 393
  ethics 624, 626–8, 631, 633–4, 637
  medical records 231–3
  pharmacy-based medical record
  linkage systems 279
  prescription–event monitoring 303
  Sentinel Initiative 536, 548–9
  probabilistic linkage 273
  probabilistic methods 593–4, 596
  procedural data 247
  procedure claims 216
  procedure registries 333–4
  product liability 117–26, 588–9
  product lifecycles
    regulatory agencies 107–8
    risk management 508–12
  Sentinel Initiative 536
  spontaneous reporting 137
  product quality 142, 507–8
  product registries 333–4, 339
  product use information 142
  productivity costs 684
  professional data 192
  progressive multifocal leukoencephalopathy (PML) 101
  propensity score calibration (PSC) 886
  propensity score (PS) analysis 661–2, 879–82, 886
  proportional reporting ratios (PRR) 322–3
  propoxyphene 414–15
  prospective studies
    clinical epidemiology 48–9
    pharmacoepidemiology 688–93
    postmarketing surveillance 852–67
    prescription–event monitoring 317
  sequential statistical methods 852–67
protected health information (PHI) 547–9
protocol development 351, 428
protocol–induced testing 685–7
proton pump inhibitors (PPI) 556, 557
proxy adjustment 882–3
P RR see proportional reporting ratios
PS see propensity score
PSC see propensity score calibration
PSUR see Periodic Safety Update Reports
public reporting 149–50
publication bias 726–7, 736–38, 747–8
publicity 151
pulmonary disease 175
Pure Food and Drug Act (1906) 5
QALY see quality-adjusted life-years
QOF see Quality and Outcomes Framework
qualification stickers 520
qualitative drug utilization studies 380–1, 382
quality assurance/control (QA/QC) 358–9
quality improvement registries 341
Quality and Outcomes Framework (QOF) 230
quality-adjusted life-years (QALY) 682–3, 700, 717
quality-of-life see health-related quality-of-life
quantitative drug utilization studies 380–1, 382
quantitative strength of associations 42
quasiexperimental study design 832, 835
questionnaire design
field studies 352
prescription–event monitoring 304–7
validity of data 765–7, 769–70, 773
RA see rheumatoid arthritis
race/ethnicity
  government claims databases 212
  health maintenance organizations 169–70
  in-hospital databases 253–4
  molecular pharmacoepidemiology 614, 617
  patient compliance/adherence 77
  validity of data 767, 770
  radiologic imaging 247
RAIDAR see rare and iatrogenic adverse reactions
RCA see rapid-cycle analyses
RCT see randomized clinical trials
RD see risk difference
READ codes 230
recall bias
  birth defects 493–4, 498–9
  validity of data 762, 766–7, 769–72
  re-challenge 584, 589, 592–4
  Recovery and Reinvestment Act 787
  refill data 799–801
Régie de l’assurance maladie du Québec (RAMQ) 559
registries 331–46
  applications 337–41
  Canadian provincial databases 264
  context and overview 331–2
  data sources 334
  definition 332
  design 332–3
  disease and conditions 333–4, 337–8
  drug safety evaluations 94–5, 98
  effectiveness 338
  future developments 341–3
  health maintenance organizations 165
  medical devices 479
  pharmacy-based medical record
  linkage systems 270, 272, 276
clinical epidemiology 43, 47–9
clinical problems 640–4
comparative effectiveness research 568–9
confounding by indication 644–5, 648
context and overview 640
control treatments 645
current solutions 646–52
data analysis 645–6, 651–2
data collection 645–6, 647, 651
feasibility conditions of LSTs 648–9
future developments 652–3
generalizability 645–6, 650
health-related quality-of-life 715, 718–19
key conditions for LSTs 647–8
large scale trials 646–53
logistics of LSTs 649–51
medical devices 473–6
meta-analyses 723–4, 729, 744–8
methodologic problems 644–6
pharmacoconomics 699–700
prescribing practices 403, 404, 406–8, 413–15
reimbursement policies 556
sample size 645, 647
rapid-cycle analyses (RCA)
  health maintenance organizations 178
  Sentinel Initiative 549–50
  vaccines 440, 445
  rare diseases 337–8, 348
  rare events 735–6
  rare and iatrogenic adverse reactions (RAIDAR) 303–4
  ratings scales 712–13, 746
RCA see rapid-cycle analyses
RCT see randomized clinical trials
RD see risk difference
READ codes 230
recall bias
  birth defects 493–4, 498–9
  validity of data 762, 766–7, 769–72
  re-challenge 584, 589, 592–4
  Recovery and Reinvestment Act 787
  refill data 799–801
Régie de l’assurance maladie du Québec (RAMQ) 559
registries 331–46
  applications 337–41
  Canadian provincial databases 264
  context and overview 331–2
  data sources 334
  definition 332
  design 332–3
  disease and conditions 333–4, 337–8
  drug safety evaluations 94–5, 98
  effectiveness 338
  future developments 341–3
  health maintenance organizations 165
  medical devices 479
  pharmacy-based medical record
  linkage systems 270, 272, 276
clinical epidemiology 43, 47–9
clinical problems 640–4
comparative effectiveness research 568–9
confounding by indication 644–5, 648
context and overview 640
control treatments 645
current solutions 646–52
data analysis 645–6, 651–2
data collection 645–6, 647, 651
feasibility conditions of LSTs 648–9
future developments 652–3
generalizability 645–6, 650
health-related quality-of-life 715, 718–19
key conditions for LSTs 647–8
large scale trials 646–53
logistics of LSTs 649–51
medical devices 473–6
meta-analyses 723–4, 729, 744–8
methodologic problems 644–6
pharmacoconomics 699–700
prescribing practices 403, 404, 406–8, 413–15
reimbursement policies 556
sample size 645, 647
rapid-cycle analyses (RCA)
  health maintenance organizations 178
  Sentinel Initiative 549–50
  vaccines 440, 445
  rare diseases 337–8, 348
  rare events 735–6
  rare and iatrogenic adverse reactions (RAIDAR) 303–4
  ratings scales 712–13, 746
RCA see rapid-cycle analyses
RCT see randomized clinical trials
RD see risk difference
READ codes 230
recall bias
  birth defects 493–4, 498–9
  validity of data 762, 766–7, 769–72
  re-challenge 584, 589, 592–4
  Recovery and Reinvestment Act 787
  refill data 799–801
Régie de l’assurance maladie du Québec (RAMQ) 559
registries 331–46
  applications 337–41
  Canadian provincial databases 264
  context and overview 331–2
  data sources 334
  definition 332
  design 332–3
  disease and conditions 333–4, 337–8
  drug safety evaluations 94–5, 98
  effectiveness 338
  future developments 341–3
  health maintenance organizations 165
  medical devices 479
  pharmacy-based medical record
  linkage systems 270, 272, 276
WHO Drug Dictionary (WHO-DD) 358–9
Wilcoxon rank-sum tests 695–6
within-subject studies 875–9
Women's Health Initiative (WHI) 11, 642, 664
Women's Health Study 649

World Health Organization (WHO)
drug approval processes 12–13
drug utilization 379, 388–91, 394
eyearly legislation 6
spontaneous reporting 137, 143, 145, 148, 152–3
vaccines 425, 432, 435, 438, 447
Wyeth v. Levine 126, 131

Yasmin® 313
Yellow Card system 302, 324
Z-statistics 737
Ziprasidone Observational Study of Cardiac Outcomes (ZODIAC) Study 88–9, 94, 569, 572