# Index

Note: Page numbers in *italics* refer to figures and tables.

<table>
<thead>
<tr>
<th>Term</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>absorption of drug</td>
<td>42–3</td>
</tr>
<tr>
<td>academic detailing programs</td>
<td>406</td>
</tr>
<tr>
<td>academic institutions</td>
<td></td>
</tr>
<tr>
<td>pharmaceutical industry</td>
<td></td>
</tr>
<tr>
<td>relationship</td>
<td>75</td>
</tr>
<tr>
<td>research funding</td>
<td>451</td>
</tr>
<tr>
<td>academic integrity</td>
<td>68</td>
</tr>
<tr>
<td>academic medical centers (AMCs)</td>
<td>63, 65</td>
</tr>
<tr>
<td>care delivery models</td>
<td>67</td>
</tr>
<tr>
<td>medical therapeutics</td>
<td>65–6</td>
</tr>
<tr>
<td>practice improvement</td>
<td>65</td>
</tr>
<tr>
<td>researcher training/support</td>
<td>67</td>
</tr>
<tr>
<td>role</td>
<td>65–8</td>
</tr>
<tr>
<td>Accident and Emergency</td>
<td></td>
</tr>
<tr>
<td>department data</td>
<td>200</td>
</tr>
<tr>
<td>accountability in regulatory action</td>
<td>85</td>
</tr>
<tr>
<td>acetaminophen</td>
<td>48, 142</td>
</tr>
<tr>
<td>acetazolamide</td>
<td>132</td>
</tr>
<tr>
<td>acetylation polymorphism</td>
<td>46–7</td>
</tr>
<tr>
<td>N-Acetylbenzo-quinoneimine</td>
<td>48</td>
</tr>
<tr>
<td>acne</td>
<td>206–7</td>
</tr>
<tr>
<td>adherence, prescribers to treatment guidelines</td>
<td>404</td>
</tr>
<tr>
<td>adherence to treatment</td>
<td>247, 367–81, 447–8</td>
</tr>
<tr>
<td>antihypertensive drugs</td>
<td>378</td>
</tr>
<tr>
<td>clinical problems</td>
<td>367–9</td>
</tr>
<tr>
<td>electronic medication event monitoring</td>
<td>370</td>
</tr>
<tr>
<td>estimates</td>
<td>369–70</td>
</tr>
<tr>
<td>ethics</td>
<td>374</td>
</tr>
<tr>
<td>medication errors</td>
<td>427</td>
</tr>
<tr>
<td>methodologic problems</td>
<td>369–70</td>
</tr>
<tr>
<td>once-daily dosing</td>
<td>373–4</td>
</tr>
<tr>
<td>terminology</td>
<td>368–9</td>
</tr>
<tr>
<td>time course</td>
<td>367, 369</td>
</tr>
<tr>
<td>twice-daily dosing</td>
<td>376–7</td>
</tr>
<tr>
<td>variations</td>
<td>367–8, 375, 377</td>
</tr>
<tr>
<td>administration route errors</td>
<td>429</td>
</tr>
<tr>
<td>administrative databases</td>
<td>253–4</td>
</tr>
<tr>
<td>adrenergic receptors, cell surface</td>
<td>38</td>
</tr>
<tr>
<td>β₂-adrenergic receptors</td>
<td>289–90</td>
</tr>
<tr>
<td>adverse drug events (ADEs)</td>
<td>477</td>
</tr>
<tr>
<td>aggregate analysis tools</td>
<td>109</td>
</tr>
<tr>
<td>bias</td>
<td>111</td>
</tr>
<tr>
<td>causal relationship</td>
<td>278</td>
</tr>
<tr>
<td>community setting</td>
<td>431–2</td>
</tr>
<tr>
<td>data mining</td>
<td>109</td>
</tr>
<tr>
<td>drug holidays</td>
<td>378</td>
</tr>
<tr>
<td>incidence</td>
<td>10</td>
</tr>
<tr>
<td>density</td>
<td>160</td>
</tr>
<tr>
<td>medication errors</td>
<td>427</td>
</tr>
<tr>
<td>near misses</td>
<td>428</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>311–12</td>
</tr>
<tr>
<td>potential</td>
<td>425, 476</td>
</tr>
<tr>
<td>prescriber behavior</td>
<td>50</td>
</tr>
<tr>
<td>Prescription-Event Monitoring</td>
<td>157</td>
</tr>
<tr>
<td>rare</td>
<td>384</td>
</tr>
<tr>
<td>serious</td>
<td>155</td>
</tr>
<tr>
<td>rates</td>
<td>160</td>
</tr>
<tr>
<td>reappearance</td>
<td>131</td>
</tr>
<tr>
<td>recognition</td>
<td>111</td>
</tr>
<tr>
<td>registry</td>
<td>5</td>
</tr>
<tr>
<td>regulatory action</td>
<td>107</td>
</tr>
<tr>
<td>safety of drugs</td>
<td>78</td>
</tr>
<tr>
<td>studies</td>
<td>4</td>
</tr>
<tr>
<td>time</td>
<td>186</td>
</tr>
<tr>
<td>vaccines</td>
<td>411</td>
</tr>
<tr>
<td>see also reports/reporting</td>
<td></td>
</tr>
<tr>
<td>adverse drug reactions (ADRs)</td>
<td>469</td>
</tr>
<tr>
<td>case reports</td>
<td>57</td>
</tr>
<tr>
<td>causality</td>
<td>278–80</td>
</tr>
<tr>
<td>delayed</td>
<td>60</td>
</tr>
<tr>
<td>denominator for calculations</td>
<td>434</td>
</tr>
<tr>
<td>FDA surveillance program</td>
<td>93</td>
</tr>
<tr>
<td>frequency</td>
<td>83</td>
</tr>
<tr>
<td>hospital-based monitoring</td>
<td>434–5</td>
</tr>
<tr>
<td>immediate</td>
<td>60</td>
</tr>
<tr>
<td>incidence</td>
<td>3, 18</td>
</tr>
<tr>
<td>long latency</td>
<td>161–2</td>
</tr>
<tr>
<td>mechanisms</td>
<td>132–3</td>
</tr>
<tr>
<td>monitoring</td>
<td>447</td>
</tr>
<tr>
<td>population size</td>
<td>18</td>
</tr>
<tr>
<td>post-licensing</td>
<td>80</td>
</tr>
<tr>
<td>profile</td>
<td>83</td>
</tr>
<tr>
<td>rare</td>
<td>33</td>
</tr>
<tr>
<td>serious events</td>
<td>78, 101–2</td>
</tr>
<tr>
<td>signal detection</td>
<td>80–2</td>
</tr>
<tr>
<td>suspected unexpected serious</td>
<td>78</td>
</tr>
<tr>
<td>systematic manual review</td>
<td>81</td>
</tr>
<tr>
<td>time of occurrence</td>
<td>432</td>
</tr>
<tr>
<td>tolerability</td>
<td>59–60</td>
</tr>
<tr>
<td>Types A and B</td>
<td>4, 60, 479</td>
</tr>
<tr>
<td>see also causality; reports/reporting</td>
<td></td>
</tr>
<tr>
<td>adverse effects studies</td>
<td>4</td>
</tr>
<tr>
<td>meta-analyses</td>
<td>357–60</td>
</tr>
<tr>
<td>Adverse Event Reporting System (AERS)</td>
<td>93, 104–5</td>
</tr>
<tr>
<td>applications</td>
<td>113–14</td>
</tr>
<tr>
<td>database</td>
<td>283</td>
</tr>
</tbody>
</table>

*Textbook of Pharmacoepidemiology*  Editors B.L. Strom and S.E. Kimmel © 2006 John Wiley & Sons, Ltd
adverse experiences 94, 473
serious 94, 479
unexpected 94, 479
age
confounding 266
effect modification 267
pharmacodynamic effects 39
see also children; elderly people
Agency for Healthcare Research and Quality (US) 8, 63–4, 447, 451
aggregate analysis tools 109
agranulocytosis 131, 132
airflow limitation, chronic 347
albuterol 269, 289
algorithms of causality 282
requiring scoring of individual judgments 281–3
alkylating agents 72
allergy errors 429
alosetron 7
alternative medicine 449
ambulance data 200
American Dental Association 102
American Hospital Formulary Society therapeutic categories 403
American Medical Association (AMA) 93, 102
analytic studies 22, 76, 473
Anatomic Therapeutic Chemical (ATC) classification 403
angina 284
angiotensin converting enzyme (ACE) inhibitors 45, 83, 290, 335–6
angiotensin receptor antagonists 45
anthrax vaccine 7
antibiotics
acne 206–7
Clostridium difficile association 387–8
antidepressants 177–8
antihypertensive drugs 377
antispsychotic drugs 191–2
Apotek AB 217
appetite suppressants 40–1
aprindine 131
aspirin 360
gastric ulceration 38–9
associations 14, 473
artifactual 14–15
causal 15
criteria 15–17
confounded 15
consistency 16
measures 246–7
strength 16
types 14–15
unsuspected 143–4, 145
astemizole 6
asthma 326, 349, 384, 388, 391
computerized decision support 405–6
Asthma Quality-of-Life Questionnaire (AQLQ) 349
atenolol 378
audit 85
authorization bias 306–7
autobiographical memory, cognitive theory 240–2
autonomy, respect for 305
azapropazone 360
Bayes probability theorem, causality assessment 280, 283–4
Bayesian approach
angina and NSAIDs 284
meta-analysis 356
Bayesian Confidence Propagation Neural Network (BCPNN) 70, 124–5, 128
data mining validation 125–6
BCG vaccination 131–2
Bendectin® 419, 422–3
bendrofluthiazide 373
benefit–risk assessment 82–3, 85
benefits of treatment 50–1
action to increase 85
balance with risk 83
evaluation 82–3
benzodiazepines 40, 46, 145
use reduction 410
benzyl alcohol 36
beta agonists 349, 383–5, 388
beta blockers 38, 60, 289–90, 361
myocardial infarction 324
non-intrinsic sympathomimetic action 379
bias 15, 272, 473
adverse drug events 111
ascertainment 434
authorization 306
case–control surveillance 146–7
cognitive 51
data abstraction 354–5
detection 265, 474
effect measures 244
hypothesized source 357
immortal time 384, 394
incidence 476
information 261, 262–3, 268, 427, 473
misclassification 262–3, 474
National Childhood Encephalopathy Study 261
pharmacoepidemiology 261–71
prevalence 262, 476, 477
protopathic 261, 262, 478
publication 354, 357, 478
recall 146–7, 249, 264, 420, 478
referral 261–2
inpatients 434
reporting 130
sample distortion 262
selection 146, 220, 247, 262, 267–8, 474
self-selection 262
suspicion of clinical event 277
vaccines 411
bioavailability of drugs 48
bioequivalence 330
bioethics 301–9
research 302–5
bioinformatics 448
biological inference 14, 473
biological plausibility 15–16
biological terrorism 64
Bilologics Control Act (1902) 92
biomarkers
interactions with medication 292–4
intermediate 450
biotechnology revolution 334
birth, drug evaluation of outcomes 73
birth defects, drug-induced 418–23, 440
biologic plausibility 420
case–control studies 420
clinical problems 418
cohort studies 420
confounding 420
data sets for other purposes 421
exposure 417
large population studies 421
methodologic problems 419–20
outcome 418
recall bias 420
sample size 419
secular changes 422
selected exposures 421
statistical power 421
validity 422
see also teratogens
Black Box Warnings 184
blinding 313
economic analysis 341
information bias 268
bootstrap methods, nonparametric 342
Boston Collaborative Drug Surveillance Program 6, 120, 434
Bradford Hill criteria 278
breast cancer, metastatic 334–5
INDEX 483

breast implants, silicone 6
Brigham and Women’s Hospital inpatient database 432–3
Brigham Integrated Computing System (BICS) 435
bromocriptine 6
buccal cell samples, case–control surveillance 142
budgets, prescribing 51
bupropion 162
calcium antagonists 49
calcium channel blockers 197
cancer screening 329
services data 193
in utero drug exposure 73
see also named cancers
candidate gene association studies 292, 295
carbamazepine 418
metabolites 48
cardiac glycosides 38
cardiac output 41
carvedilol 164
case–cohort design 389–90, 474
cases, diagnoses 139
dietary supplements 141, 145
dNA collection 142
drug dictionary 142
drug–disease associations 141
drug/genotype analysis 143
drug information 139, 140, 141
drug use 142–3
duration of use 144
effect modification 143
effects after long intervals 145
gene polymorphisms 146
hospital records information 141–2
hypothosis testing 142–3
interviews 138, 139, 144
methods 138–9, 140, 142
modifying factors 141
non-prescription medications 145
nondifferential misclassification 147
outcome data 146
participation rates 139
statistical power 143, 146
unsuspected associations 143–4, 145
case–crossover designs 391–3, 474
case definitions 219
case identification 186
case–non case method 123
case reports 18, 21–2, 473
adverse reactions 57
causation 277–86, 448
risk management 423
structured approach 280
case series 18–19, 21–2, 474
sample size 31–2
case–time–control design 391, 393
causal inference 377
causal relationships 131
assessment 121–2
observational studies 312
causality 83, 473
accumulated value of evaluations 283
accuracy of judgment 283
adverse drug reactions 278–80
algorithms 281
requiring scoring of individual judgments 281–3
assessment 121–2
applications 285
Bayes probability theorem 279, 281
comparison of methods 283–5
methodologic problems 280–1
uses 279–80
automation of evaluation 285
case reports 277–86, 448
criteria 278–80, 282
Bayesian approach with verbal judgments 281
critical elements 285
gene–drug interactions 290
global introspection 280–2
likelihood assessment 82
determination methods 277–81
number of evaluations 283
probabilistic methods 281–3
proof 110
unstructured clinical judgment 280
vaccine adverse events 411
causation 17
celcoxib 152, 154, 160
cell replication blocking 37
cell surface receptors 37, 38
Center for Drug Evaluation and Research 99–100
Center for Food Safety and Nutrition (CFSCAN), Adverse Event Reporting System 99
Centers for Disease Control and Prevention 453
Centers for Education and Research on Therapeutics (CERT) 8, 63–4, 65, 182, 447
databases 66
public–private partnerships 68
Centers for Medicare and Medicaid Services 188
central nervous system (CNS) depressants 40
cerivastatin 7, 134
challenge–rechallenge 18
change, global ratings 347
changeability 474
HRQL instruments 347
channeling of drugs 392
chart review 428
chelating agents 43
chemotherapy 72
plus autologous stem cell transplantation 334–5
children
drug use 323
medication errors 427
chlamydial infection 372
chloramphenicol 93
cholestyramine 43
Chronic Respiratory Questionnaire 348
cigarette smoking
asthma 389
lung cancer 15, 16, 17, 19
INDEX

cimetidine 18, 49, 56
liver disease 71
postmarketing surveillance 223
claims-based evaluations, medication errors 427, 428
claims databases 168–9, 170, 176, 187
classification validity 246
clearance of drug 42, 474
cleft palate 421
clinical economics 336–8
unstructured 282
clinical outcomes, efficacy of drug 82–3
clinical pharmacology 4, 36, 474
funding 66
clinical significance 33
clinical trials 69–70
economic analysis 338–9
inclusion/exclusion criteria 69–70
patient sample size 69
usual care arm 339
see also named types of trials
clioquinol 6
Clostridium difficile 387–8
clusters of events 131

cognitive bias 51
cognitive processes, temporal questions 241
cognitive theory, autobiographical memory 240–2
cohort effect 386
cohort studies 19–21, 22, 473
ad hoc 222–3, 235
new drugs 235
confounding 265
controls 313
data sources 220
database resources 232
drug exposure changes 384
drug-induced birth defects 418–19
fixed entry 384
losses to follow-up 262
Phase IV 56
postmarketing 137–8
risk sets 386–7
sample size 26–7, 28, 29, 32, 451–9
sampling within 384–8
structures 384–6
study design 383–4
types 386–8
vaccine efficacy 329
variable entry 386
Collaborative Perinatal Project (CPP) 421
colorectal cancer risk and NSAIDs 263–4
common practice, economic analysis 338–9
Common Rule 302–3, 304–5
communications cross-cultural 64
feedback to reporters 122
initiatives 135
regional centers 120
risk 186
safety of drug 85
communitarianism 304
community setting, adverse drug events 428–9
compassionate use 78
complementary medicine 449
compliance large simple trials 317
white-coat 370
see also adherence to treatment
compliance-dependent drugs 375, 378
corticosteroids 326
cost(s) 474
by indication 267–8, 273–4, 313–14, 324–5, 326, 420, 474
indication for prescription 267–8
large simple trials 314
matching 270
mechanism 264–5
modeling 271
multivariate analysis 272
odds ratio 391
partial data 383, 390–1
population admixture 294–5
propensity scores 273
randomization 268–9, 313
stratification 272–3
two-stage sampling 272–3, 391
uncertainty source 384
uncontrolled 312
vaccines 411
confounding variables 15, 474
automated databases 168
case–control surveillance 138, 145
database resources 235
information need 194–5
restriction to one level 271
congenital anomalies 162
consent see informed consent
construct validity 346–7, 474
counter behavior 50–2
consumer reports 118
contact lenses, soft 417
continuous-benefit effect model 341
controls/control groups 22
absence 222–3, 318
choice of treatment 313–14
expected incidence of outcome 26
friend 219–20
identification 186
number of groups 27
number of unexposed subjects 27
placebo 314
recruitment 219
corneal ulcers 417

coronary artery bypass surgery (CABG) 361
Coronary Drug Project 268
correlation coefficients 245
corticosteroids 326
cost(s) 474
analysis methods 341–2
analysis plan 341
development of drugs 74
direct 337–8, 475
drug statistics 400
drug use 10–11
prescriber behavior 52
INDEX

485

department identification 336
indirect 476
intangible 337, 338, 476
medical care 333–4
meta-analysis impact 361–2
productivity 337, 338
studies 55
total 401
types 337–8
unit 401
cost–benefit analysis 336, 474
Cost Containment Program 436–7
cost-effectiveness 51, 474
analysis 336–7
molecular pharmacoepidemiology 297
postmarketing drug surveillance 110
requirements 448
studies 328–9
cost-efficacy analyses 339
cost-identification analysis 474
cost–utility analysis 350
coumarin 46
Council for International Organizations of Medical Sciences (CIOMS) 82
ethics board review 303
international reporting standards 128, 129
monograph IV 133
counterfeit medicines 135
COX-2 inhibitors 39, 152, 160
creatinine clearance 44, 45
plasma concentration 44
Creutzfeldt-Jacob disease (CJD) 72
critical method with verbal judgments 281
criterion validity 346, 474
cyclosporine 45, 49
cYP2C9 polymorphism 291
cytochrome P450 (CYP) 46, 48, 49
data
abstraction bias 354–5
access to existing 307–8
administrative databases 253–4
analysis 314
automated 412
comparative characteristics of resources 228, 229–31, 232–3
comparison with external data 162
completeness 247, 250–5
costs 341
de-identified 307
demographic 183, 192, 200
denominator 131
diagnosis 168–9
disease incidence 217–18, 234
dredging 123
drug claims to insurers 168
drug utilization 399
economic analysis 340–1
exposure 232
follow-up 318–19
 genetic 201–2
identifiable 307
inpatient systems 436, 438
large simple trials 314
medical record databases 250–1
monitoring 318
outcome 146, 232–3
patterns 123
privacy 307
stratification 125
systematic analyses of automated 412
volume 401
data collection 314, 315, 450
follow-up 318
medical devices 414
MedWatch program 102–3
meta-analyses 354
methods 243
non-spontaneous sources 82
pharmaceutical industry 80
prospective 22
retrospective 22
data mining 109, 123
proportional reporting ratio 126–7
signal detection 109, 123, 128
vaccine safety signal detection 412
validation 125–6
data protection 307
data set
access to 307–8
de-identification 307, 308
limited 308
data sources 256
accuracy evaluation 247–9
case-control studies 218–23
cohort studies 220
current 402
methodologic studies 247–8
secular trend analysis 215–18
data validity 232–3, 239–57
computerized databases 250–5
database resources 250–5
disease 250
hospitalization 250
large simple trials 315
sensitivity/specificity 244
database resources 74–5, 256
case–control studies 232
case–control surveillance 138, 148
cohort studies 232
comparative characteristics 228, 229–31, 233–4
computerized 71
confounding 270–1
data mining 109
data validity 250–5
exposure data validity 232
inpatient 429, 432–3
medication errors 428
new drugs 235–6
population-based 228, 232
relative cost 228
repository 66–7
representativeness 228
research questions 233–6
size 228
speed of studies 228
urgent questions 236
WHO 117–18, 123–6
databases, automated 167–70, 173–209, 449
applications 170
data validity 250–5
design 392
General Practice Research Database 204–7, 209
Group Health Cooperative database 174–8, 207
HMO Research Network 208
Kaiser Permanente Medical Care Program 178–82, 208
Medicaid 188–92, 207
Netherlands Automated Pharmacy Record Linkage 196–8, 207
Saskatchewan health services database 192–5, 207
strengths 169
Tayside Medicines Monitoring Unit (MEMO) 198–203, 209
UnitedHealth Group 184–8, 208
weaknesses 169–70
see also HMO Research Network
Dear Health Care Professional letters 103, 107, 108
debrisoquine 47
decision support, computerized 405–6, 408
deCode project 297
defined daily dose 132, 402
demographic change 64, 218
demographic data
HMO Research Network 183
Saskatchewan health services database 193
Tayside Medicines Monitoring Unit 198
denominator data 131
depression, diagnosis recall 241, 242
descriptive studies 76, 474
developing countries, pharmacoepidemiology programs 134–5
development of drugs
cost 74
economic evaluation 334–6
epidemiology 77–8
process 334–6
regulatory/scientific advice 79
time span 74
dexfenfluramine 40–1
Diabetes Audit and Research in Tayside Scotland (DARTS) database 200
diagnosis
administrative databases 253–6
coding systems 218
information validity 433
self-reported 250
terminology changes 218
diagnostic data validity 168–9, 190
diagnostic databases
General Practice Research Database (UK) 204
Medicaid 189, 190
outpatients 175, 181, 233
Saskatchewan health services database 194
Tayside Medicines Monitoring Unit 198, 207
diaries, prescription 244
adherence to treatment 368
diazepam 46
dietary supplements 137
adverse event reporting 99
case–control surveillance 137, 138
information need 169–70
diethylene glycol toxicity 5, 93
diethylstilbestrol 18, 19
digoxin 38, 40, 49, 361
diltiazem 49
diphtheria–pertussis vaccine 261–2
directly observed therapy 368
disease/disease state
alteration by genetic polymorphisms 290
background incidence 132
benefit–risk impact 82
causal pathways 290
claims databases 168
data validity 250
definition 262
dread 60
incidence 74
data 217–18, 234
low outcome 234
index of suspicion 218
lifestyle impact 250
nondifferential misclassification 246, 472
orphan 79
pharmacodynamic effects 39–40
phenotypic expression 294
postmarketing surveillance 59
prevalence 74
reportable 218
typically drug-induced 130
distribution of drug control 86
systemic 43–4
distribution phase 41–2
DNA 288
collection 142
sequence variation 295
doctors see physicians
dosage of drug
effect modification 267
natural experiments in dose ranging 376
postmarketing reductions 372
dose ranging, natural experiments 371, 376
dose–response relationship 16–17
dosing errors 429
frequency 428
patient 368, 371
pharmacodynamic correlates 371
dosing histories 370, 376–7
electronic monitoring 450
dosing regimen
deviations from 376
forgiveness 373–4
omissions 369, 375–6
optimal 371–2, 373
perfect use 373
selection methods 372–3
typical use 373
variable 376–7
doxycycline 372
dread diseases 60
drug(s) 36–7, 473
active component 36
alternatives 59, 60
channeling 394
co-ingestion with chelating agents 43
comedication 268
comparisons 15
concentration 49
continuity of action 374–5
counterfeit 135
electronic medication event monitoring 370
gene effects on responses 288–9
inactive ingredients 36
mechanisms of action 37
misuse 61
new 235–6
non-prescription 52, 145
outcome of interest 36
patient knowledge 240
plasma concentration 369
plasma half-life 370
post-dose duration of action 374
potency 37
effect modification 267
prescription 52
quality regulation 79
reformulation 36–7
statistics 400, 401
systemic distribution variation 43–4
targeting of therapy 450
undertaken 367–8
user fees 69
drug–ADR combinations 124–5, 128
drug approval process 9
policy 448
drug database design 394
drug dictionary, case–control surveillance 142
drug–disease associations, case–control surveillance 141
drug–drug interactions 40–1, 125, 126, 436
drug metabolizing enzymes 48–9
exposures 429
polypharmacy 432
protein binding 43
renal elimination 45
Drug Efficacy Study Implementation (DESI) process 6
Drug Epidemiology Unit 6
drug-event pairs 71
drug holidays 368, 378–9
drug–laboratory errors 429–30
drug metabolizing enzymes 48–9, 422
drug response
  adaptive 38–9
  genetic determinants 38
pharmacokinetics 41–50
variability 38–41
Drug Safety Research Trust (UK) 6, 155
Drug Safety Research Unit (UK) 152
drug transporters 43–4, 49
Drug Use Evaluation (DUE) Program 436
drug use evaluation (DUE) studies 400
drug utilization 399–400, 473
  see also use of medication
drug utilization review 399, 408–9, 439
  criteria 408
    validity 409–10
    effectiveness evaluation 406
      exceptions 408
    methodologic problems 408
      prospective 408, 478
      research 409
      retrospective 408, 478
drug utilization review programs 400, 408–9, 449
  hospital 408–9
  lack of effect 408
  outpatient
    prospective 408–9
    retrospective 408, 409
drug utilization studies 6, 10, 400–3, 448, 475
classification systems 403
clinical problems 400–1
  data 216–17, 400
  indicator-based approach 402
  measurement units 402–3
  methodologic problems 401
  patient outcome measures 403
  process measures of quality 403
  qualitative 400, 478
  quantitative 400, 478
  research 400–1
duration–response relationship 17
ecological studies 19, 473
economic analysis
  blinding 341
  cost data 341
  data collection 340
intermediate endpoints 341
measurement 341
methodologic problems 336–8
modeling 341
multicenter evaluations 340
patient participation 340
perspective 338
  Phase III study data 334
  sample size 340
  statistical tests 341
  study design 339–41
  types 336–7
  uncertainty 342
  usual care arm 339
economic evaluation 333–43
dimensions 336–8
drug development 334–6
generalizability 342
research 333–4
  economics of drug use 10–11, 52
  see also pharmacoconomics
educational materials, printed 403
efavirenz 106–7
effect measures
  applicability 327
  beneficial 321–31, 473
  bias 244
  confounding 265
cost-effectiveness studies 329–30
  minimum 26
  nonexperimental studies 327–8, 329, 330
  time-window 391
types 321
effect modification 267, 275
  age 266
  confounding 266–7
  dose 267
genetic variants 293
effectiveness studies 321–30, 448, 474
effects of drugs
  antagonistic 40
  beneficial 322–3
  anticipated 322
  unanticipated 322, 478
  delayed 235
  harmful
    anticipated 321
    unanticipated 321, 478
transient 383
  efficacy of drug 324, 475
  clinical outcomes 82–3
data analysis 78
degree of 83
  RCTs 330
  regulation 79
  vaccine studies 329
efficiency studies 322
elderly people
  chronic use of drugs 134
  HMO representation 177
pharmacodynamic effects of drugs 39
  proportion of population 64
  electronic medication event monitoring (eMEM) 370
  electronic monitoring 450
  elimination of drug, variation 44–5
  elimination phase, terminal 42
  elimination rate constant 42
  endpoints, intermediate 341
  enrolled person-time 191–2
enzymes 37
  drug metabolizing 48–9, 422
  induction 48, 49
  inhibition 49
  EpicCare® 176, 180–1
  EPICURE program 390
epidemiology 4–5, 35–6, 473
  AER report evaluation 105
descriptive studies 71
development of drugs 77–8
  ethics 301–9
guidelines 302
  pharmaceutical industry 69–74
  post-licensing 80
  practice 302
  product planning/development 73–4
  public understanding 75
  quantitative methods 246–7
  randomized 202
  regulations 302
  study designs 17–21
epipodophyllotoxins 72
  EPITOME program 390
  equity in regulatory action 85
errors
  administration route 428
  allergy 428
  reduction 427
  system-based interventions 429
type I 14–15, 26, 294, 296–7, 479
type II 14–15, 26, 294, 297, 479
  see also dosing errors; measurement error; medication errors
erythromycin 49
estrogens 327
ethics
  adherence to treatment 377
  epidemiology 301–9
geneic testing 298
  prescribing behavior RCTs 403
  research 77, 301–9
  Tayside Medicines Monitoring Unit (MEMO) 201
  ethics review boards 303
  process 308
ethinylestradiol 48
ethnicity, confounding by 294–5, 297
European Medicines Evaluation Agency (EMEA) 68, 119
international reporting standards 128–9
European Union
Directive on data protection 307
pharmacovigilance system 119
Euroqol (EQ5) 350
evidence hierarchy 76
expert medical reviewers 70
exposure 36
causal relationship 278
changes 384
defining criteria 270
dichotomous 293–4
differential misclassification 263
drugs in hospital 432–3
genetic polymorphism interactions 294
hospital stays 432
improper definitions 394
measures 244, 274, 449
misclassification 244
nondifferential 243, 245–6, 264
status 412
multiple variables 32
prediction 325–6
report accuracy 248
variations 376
exposure–genotype interaction 143
extension phase 78
face validity 346, 475
factor V Leiden mutation 290
fail-safe N 357
Federal-Wide Assurance (FWA) 303
feeling thermometer 350
fenfluramine 40–1
fenoprofen 360
fenoterol 6, 269
Finland, medical record linkage system 224
first line therapy 83
first pass metabolism 48
fluoxetine 6
Food, Drug and Cosmetic Act (1938) 5, 93
Food and Drug Administration (FDA) 4, 5
NDA fees 7
regulatory action 107
spontaneous reporting of adverse reactions 91–115
foods, drug metabolism effects 49
forgiveness, dosing regimen 371, 373–4
formulation of drugs 58–9
Friuli Venezia Giulia (FVG) database (Italy) 225
funding
clinical pharmacology 66
training 447–8
funnel plot 357
gemfibrozil 133
gene(s)
discovery 292, 295
drug response effects 289–91
mutations 38
gene–drug interactions 290–1
case–control studies 295
causality 290
multiplicative 293
pharmacodynamic 289–90
pharmacokinetic 289
General Practice Research Database (GPRD) 67, 204–7, 209, 252
comparative characteristics 228, 232, 233
completeness 205–6
counter complexity 206
data collection 204–5
diagnoses 204
medical attention 235
medical records 206
access 206
population-based data 205
prescriptions 204
quality assessment 255
size 205
validity 204–5
general practitioners (GP) 152
Netherlands 196–8
Scotland 198, 199–200
generalizability
economic evaluation 342
medication errors 428
generalized linear model 342
genetic data, phenotypic linkage 201
genetic factors
clinical measurement 448–9
metabolism of drugs 47–8
genetic polymorphisms 38, 163
β2-adrenergic receptors 289–90
case–control surveillance 146
disease state alteration 290
exposure interactions 294
metabolism of drugs 46–7, 422
prevalence 294
genetic testing 298
general variability 288–9
phenotypic expression of disease 294
variant 293–4
genome-wide scans 292, 295
genomic controls 297
genotype 163, 448
drug exposure 143
drug metabolism alteration 290–1
orphan 298
glibenclamide 133
global introspection 278, 281
Global Medical Device Nomenclature (GMDN) 415
glomerular filtration 44
glomerular filtration rate (GFR) 45
glucocorticoids 203
glutathione 48
good clinical practice (GCP) 77
good epidemiological practice (GEP) 201, 447
G-protein-coupled receptors 37
green form questionnaires 152, 157, 158
meloxicam 158, 159
prompting effect 156
Group Health Cooperative clinical trials 223
Group Health Cooperative databases 173–8, 207, 251
accessibility 176
cancer surveillance 175
cause of death data 175
claims databases 176
clinical information systems 176
community health services 175
comparative characteristics 228, 233
completeness 176–7
enrollment 174
hospitalization 175
immunizations 175–6
inpatient 254
laboratory data 175
outpatient visits 175
pharmacy files 175
quality of data 176
radiology data 175
rare events 176
strengths 176
INDEX 489

Utilization Management/Cost Management Information System 175
weaknesses 176–8
Guillain–Barré syndrome 131
haloperidol 191–2
haplotypes 295
harms of treatment 50–1
Harvard Pilgrim Health Care 252
database 254
hazards
increase 82
risk levels 61
health care
access with pharmacogenetic testing 298
delivery models 67
practice 64–5
quality measurement in delivery 67
transactions 65
Health Evaluation through Logical Processing (HELP) System 225
Health Insurance Portability and Accountability Act (HIPAA) 190
case–control surveillance 138
combining 300
confidentiality 256
medical data privacy 307
Privacy Rule 255, 256, 307
health maintenance organizations (HMOs)
174–5, 334
ey elderly people 177
network models 179
out-of-plan care 177
poor people 177
uninsured people 174, 184
health profiles 350, 475
health-related quality-of-life (HRQL) 345–6, 350, 475
anchor-based approach 348
clinical problems 346
distribution-based approach 348–9
instruments 346–51
methodologic problems 346
research 346
health surveys 217–18
Health Utilities Index 350
Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS) 417
heart disease 407–8
heart failure 335–6
Helsinki Declaration (1964) 303
herbal supplements 137, 449
information need 256
HIV infection 82–3
HMO Research Network 66, 178, 182–4, 208
Black Box Warnings 184
Center for Education and Research on Therapeutics 182
comparative characteristics 228, 233
external registry linkages 180–1
medical records 183
member health plans 182–3
membership status 183
new drugs 235
homeostatic regulation 39
hormone replacement therapy (HRT) case–control surveillance 138, 148
combination 8, 21
selection bias 220
hospital(s)
admissions 425
adverse drug reaction monitoring 436–8
care outcomes 432
diagnosis information validity 433
drug exposure 432
drug information validity 433
drug use 432–3
evaluation programs
intensive surveillance 434–5
staff participation in studies 434
see also inpatients; outpatients
Hospital Discharge Survey 218
hospital pharmacoepidemiology 432–9, 440
case–control surveillance 138
clinical problems 428–30
methodological problems 430–1
hospitalization 203
administrative databases 253–6
data validity 250
self-reported 250
human growth hormone (hGH) 72
human subjects, research 301–3
hydralazine 133
hydroxylation polymorphism 47
hypertension, unresponsive 378
hypotension, postural 39
hypothesis generation 58–9, 76, 162, 233, 476
hypothesis testing 58, 167
case–control surveillance 138, 142–3
large simple trials 316
randomized controlled trials 312, 314
studies 234, 476
ibuprofen 311–12, 360
Icelandic people, genetic data 297
immortal time bias 383, 394
impact analysis concept 81
implants, long-term 414
IMS Disease Analyzer 224–5
IMS HEALTH 216, 224–5
incidence
bias 476
density 160
prevalence 324–5, 326, 474
birth defects 418
measure 326
indomethacin 6
induction therapy in renal transplantation 360–1
information
coherence with 15–16
framing 50–1
sources 135, 243
see also bias, information
information technology 429
informed consent
case–control surveillance 138
ethical requirement 309
genetic data of Icelandic people 297
large simple trials 317
pharmacogenetic testing 298
research 304–5, 306–7
waiving 304–5
inpatients
data systems 433, 436
databases 429, 432–3
drug use 233, 235, 430
health status 430
information link to outpatient information 433, 438
intensive drug monitoring 434–5
records 431
referred bias 434
see also hospital(s)
Institute of Medicine (IOM), vaccine safety review 411
institutional review boards (IRBs) 301, 303
patient authorization waiver 308
### INDEX

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>insulin, human</td>
<td>6</td>
</tr>
<tr>
<td>intention-to-treat analysis</td>
<td>318</td>
</tr>
<tr>
<td>interaction</td>
<td>265</td>
</tr>
<tr>
<td>effect modification</td>
<td>268–9</td>
</tr>
<tr>
<td>International Classification of Diseases (ICD) coding</td>
<td>253</td>
</tr>
<tr>
<td>International Classification of Diseases–Ninth Revision–Clinical Modification (ICD-9-CM)</td>
<td>168, 183, 190</td>
</tr>
<tr>
<td>international collaboration</td>
<td>64</td>
</tr>
<tr>
<td>International Conference on Harmonisation (ICH) guidelines</td>
<td>79</td>
</tr>
<tr>
<td>postmarketing surveillance</td>
<td>100–1</td>
</tr>
<tr>
<td>International Society for Pharmacopoeidiology</td>
<td>64, 447</td>
</tr>
<tr>
<td>interpretability, HRQL instruments</td>
<td>347</td>
</tr>
<tr>
<td>interrupted time-series</td>
<td>405, 476</td>
</tr>
<tr>
<td>intervention, purpose</td>
<td>82</td>
</tr>
<tr>
<td>intussusception</td>
<td>412</td>
</tr>
<tr>
<td>Investigational New Drug Application (IND)</td>
<td>5–6</td>
</tr>
<tr>
<td>causality assessment</td>
<td>280–1</td>
</tr>
<tr>
<td>Iowa Drug Information System (IDIS)</td>
<td>403</td>
</tr>
<tr>
<td>isoniazid</td>
<td>46–7</td>
</tr>
<tr>
<td>isotretinoin</td>
<td>6, 61, 418</td>
</tr>
<tr>
<td>Joint Commission on Accreditation of Healthcare Organizations</td>
<td>436</td>
</tr>
<tr>
<td>Joint Commission on Prescription Drug Use</td>
<td>6</td>
</tr>
<tr>
<td>Kaiser Permanente Medical Care Program</td>
<td>178–82, 208, 254</td>
</tr>
<tr>
<td>administrative database</td>
<td>179–80, 254</td>
</tr>
<tr>
<td>cancer incidence data</td>
<td>180</td>
</tr>
<tr>
<td>clinical database</td>
<td>179–80, 254</td>
</tr>
<tr>
<td>comparative characteristics</td>
<td>228, 232, 233</td>
</tr>
<tr>
<td>death certificates</td>
<td>180</td>
</tr>
<tr>
<td>electronic medical records</td>
<td>180–1</td>
</tr>
<tr>
<td>hospital discharge records</td>
<td>180</td>
</tr>
<tr>
<td>laboratory test records</td>
<td>180</td>
</tr>
<tr>
<td>member dropout rates</td>
<td>181</td>
</tr>
<tr>
<td>membership</td>
<td>179, 181</td>
</tr>
<tr>
<td>multiphasic health check-up</td>
<td>180</td>
</tr>
<tr>
<td>outpatient diagnostic databases</td>
<td>181</td>
</tr>
<tr>
<td>outpatient visits</td>
<td>180</td>
</tr>
<tr>
<td>pharmacy databases</td>
<td>179–80</td>
</tr>
<tr>
<td>research centers</td>
<td>178–9</td>
</tr>
<tr>
<td>socioeconomic status data</td>
<td>180</td>
</tr>
<tr>
<td>Kefauver–Harris Amendments (1962)</td>
<td>5–6, 93, 323</td>
</tr>
<tr>
<td>ketorolac</td>
<td>58, 438–9</td>
</tr>
<tr>
<td>pharmacy-based study</td>
<td>221, 222</td>
</tr>
<tr>
<td>knowledge base</td>
<td>64</td>
</tr>
<tr>
<td>deficits</td>
<td>65</td>
</tr>
<tr>
<td>improvement</td>
<td>66</td>
</tr>
<tr>
<td>labeling</td>
<td>107, 113–14</td>
</tr>
<tr>
<td>laboratory results data</td>
<td>431</td>
</tr>
<tr>
<td>large simple trial (LST) design</td>
<td>71–2, 314–18</td>
</tr>
<tr>
<td>analysis</td>
<td>318</td>
</tr>
<tr>
<td>compliance</td>
<td>317</td>
</tr>
<tr>
<td>confounding</td>
<td>316</td>
</tr>
<tr>
<td>cooperative population</td>
<td>317</td>
</tr>
<tr>
<td>data</td>
<td>315</td>
</tr>
<tr>
<td>monitoring</td>
<td>318</td>
</tr>
<tr>
<td>feasibility</td>
<td>316–17</td>
</tr>
<tr>
<td>follow-up</td>
<td>317–18</td>
</tr>
<tr>
<td>informed consent</td>
<td>317</td>
</tr>
<tr>
<td>logistics of conducting</td>
<td>317–18</td>
</tr>
<tr>
<td>objectivity</td>
<td>316–17</td>
</tr>
<tr>
<td>outcome measurement</td>
<td>316–17</td>
</tr>
<tr>
<td>power of study</td>
<td>315, 316</td>
</tr>
<tr>
<td>registration documents</td>
<td>317</td>
</tr>
<tr>
<td>research question</td>
<td>315</td>
</tr>
<tr>
<td>sample size</td>
<td>315</td>
</tr>
<tr>
<td>simple treatments</td>
<td>316</td>
</tr>
<tr>
<td>subgroup analysis</td>
<td>318</td>
</tr>
<tr>
<td>uncertainty principle</td>
<td>315–16</td>
</tr>
<tr>
<td>validity</td>
<td>317</td>
</tr>
<tr>
<td>latent interval analyses</td>
<td>143</td>
</tr>
<tr>
<td>legal issues</td>
<td></td>
</tr>
<tr>
<td>genetic testing</td>
<td>298</td>
</tr>
<tr>
<td>postmarketing surveillance</td>
<td>58</td>
</tr>
<tr>
<td>prescribing behavior RCTs</td>
<td>403</td>
</tr>
<tr>
<td>teratogens</td>
<td>419–20</td>
</tr>
<tr>
<td>liberalism</td>
<td>304</td>
</tr>
<tr>
<td>licensing</td>
<td>79–80</td>
</tr>
<tr>
<td>safety of drug</td>
<td>78–9</td>
</tr>
<tr>
<td>life cycle of drugs</td>
<td>77–86</td>
</tr>
<tr>
<td>life expectancy, disability-free</td>
<td>64</td>
</tr>
<tr>
<td>LifeLink™</td>
<td>216</td>
</tr>
<tr>
<td>lifestyle impact on disease</td>
<td>250</td>
</tr>
<tr>
<td>linezolid</td>
<td>113–14</td>
</tr>
<tr>
<td>linkage disequilibrium</td>
<td>295</td>
</tr>
<tr>
<td>literature search for meta-analyses</td>
<td>355</td>
</tr>
<tr>
<td>lithium</td>
<td>49</td>
</tr>
<tr>
<td>liver disease</td>
<td></td>
</tr>
<tr>
<td>drug sensitivity</td>
<td>40</td>
</tr>
<tr>
<td>metabolism of drugs</td>
<td>47–8</td>
</tr>
<tr>
<td>liver failure, acute</td>
<td>187–8, 426</td>
</tr>
<tr>
<td>logistic regression, conditional</td>
<td>389</td>
</tr>
<tr>
<td>long latency outcomes</td>
<td>72</td>
</tr>
<tr>
<td>longitudinal histories</td>
<td>186</td>
</tr>
<tr>
<td>lower limit factor</td>
<td>31</td>
</tr>
<tr>
<td>lung cancer, cigarette smoking</td>
<td>15, 16, 17, 19</td>
</tr>
<tr>
<td>lung disease, drug sensitivity</td>
<td>40</td>
</tr>
<tr>
<td>Lyme vaccine</td>
<td>7</td>
</tr>
<tr>
<td>managed care organizations (MCOs)</td>
<td>373</td>
</tr>
<tr>
<td>Manitoba data files</td>
<td>219</td>
</tr>
<tr>
<td>Manitoba Health Services Insurance Plan</td>
<td>219</td>
</tr>
<tr>
<td>Mantel–Haenszel odds ratio</td>
<td>272, 356, 359, 392</td>
</tr>
<tr>
<td>markers</td>
<td></td>
</tr>
<tr>
<td>interactions with medication</td>
<td>293–5</td>
</tr>
<tr>
<td>intermediate</td>
<td>450</td>
</tr>
<tr>
<td>market repositioning of drug</td>
<td>56</td>
</tr>
<tr>
<td>marketing</td>
<td>57–9</td>
</tr>
<tr>
<td>postmarketing drug surveillance studies</td>
<td>223</td>
</tr>
<tr>
<td>timing</td>
<td>57</td>
</tr>
<tr>
<td>matching, study design</td>
<td>270</td>
</tr>
<tr>
<td>Mayo Clinic system</td>
<td>219</td>
</tr>
<tr>
<td>measurement error</td>
<td></td>
</tr>
<tr>
<td>correcting measures of association</td>
<td>246–7</td>
</tr>
<tr>
<td>differential</td>
<td>242</td>
</tr>
<tr>
<td>nondifferential</td>
<td>242</td>
</tr>
<tr>
<td>quantitative indices</td>
<td>243–5</td>
</tr>
<tr>
<td>research</td>
<td>242–3</td>
</tr>
<tr>
<td>measurement process standardization</td>
<td>270</td>
</tr>
<tr>
<td>MedDRA</td>
<td>129</td>
</tr>
<tr>
<td>media</td>
<td></td>
</tr>
<tr>
<td>informing</td>
<td>67</td>
</tr>
<tr>
<td>misinterpretation of studies</td>
<td>75</td>
</tr>
<tr>
<td>safety issues</td>
<td>85</td>
</tr>
<tr>
<td>Medicaid</td>
<td></td>
</tr>
<tr>
<td>claim validity</td>
<td>253–4</td>
</tr>
<tr>
<td>comparative characteristics</td>
<td>228, 233</td>
</tr>
<tr>
<td>data</td>
<td></td>
</tr>
<tr>
<td>sources</td>
<td>188</td>
</tr>
<tr>
<td>validity</td>
<td>190</td>
</tr>
<tr>
<td>databases</td>
<td>188–92, 208, 252, 254–5</td>
</tr>
<tr>
<td>delayed drug effects</td>
<td>235</td>
</tr>
<tr>
<td>diagnosis accuracy</td>
<td>255</td>
</tr>
<tr>
<td>diagnostic terminology</td>
<td>190</td>
</tr>
<tr>
<td>diagnostic validity</td>
<td>190</td>
</tr>
<tr>
<td>enrolled person-time</td>
<td>191–2</td>
</tr>
<tr>
<td>enrollment</td>
<td>177, 191</td>
</tr>
<tr>
<td>generalizability of population</td>
<td>190</td>
</tr>
<tr>
<td>lack of benefits</td>
<td>65</td>
</tr>
<tr>
<td>medical attention</td>
<td>235</td>
</tr>
<tr>
<td>new drugs</td>
<td>235</td>
</tr>
<tr>
<td>overrepresented populations</td>
<td>189</td>
</tr>
</tbody>
</table>
program 188
recipients 188
UnitedHealth Group
members 185
medical care
costs 333–4
reimbursement 342
medical devices
care claims 415
clinical problems 414
data collection 415
definition 414
exposure assessment 415
medical records 415, 417
methodologic problems 414
national population exposure
assessment 415
public health impact 415
registries 415
safety surveillance 416
studies 414–24, 438
hypothoses 412
techniques 417–8
surveys 415, 416
Medical Outcomes Study instruments 350
medical record databases 169, 180–1
data 251–2
use 256
medical records
abstractions 186
completeness 247
confidentiality 256
electronic 180–1, 183, 429
General Practice Research Database
205, 206
inpatients 431
linkage
in Netherlands 196–7
system 224
medical devices 414, 415
organization 434
permission for use 304
research 306–7
retrieval 247
Saskatchewan health services database
194
Tayside Medicines Monitoring Unit
198
validation 186, 247
Medicare
data structure 189
diagnoses 189
drug benefits 232, 448, 450
UnitedHealth Group members 185
medication errors 92, 427–31, 476
chart review 428
claims-based evaluations 428
clinical problems 428–9
data sources 430
database resources 428
generalizability 430
handoffs 428
information bias 430
methodological problems 430–1
patient safety 425–6
safety theory 427
sample size 430
types 426
medication event monitoring, electronic
(eMEM) 370
Medicines and Healthcare Products
Regulatory Agency (MHRA) 76, 129
Medicines Monitoring Unit (MEMO) see
Tayside Medicines Monitoring Unit (MEMO)
medroxyprogesterone, depot 6
MedWatch Adverse Event Reporting
Form 94, 95–8
MedWatch program 102–3, 108
MedWatch to Manufacturer Program
(MMP) 103
meloxicam 158, 159, 160
membership databases
HMO Research Network 183
Kaiser Permanente Medical Care
Program 178, 182
memory
autobiographical 240–2
organization 241
retrieval 241
MEMS® Monitors 371
meta-analyses 76, 353–63, 476
adverse effects studies 357–60
applications 357–62
Bayesian approach 356
clinical problems 354
combinability of studies 354, 356–7
conclusions 356
cost implications 361–2
cumulative 361–2, 363
data
abstraction bias 354–5
collection 355
definition 353–4
diversity of studies 356–7
group-level 362
heterogeneity 356–7, 362–3
inclusion/exclusion criteria 355
individual-level data availability 362
induction therapy in renal
transplantation 360–1
literature search 355
methodologic problems 354–5
new indications for existing therapies
360–1
nonexperimental studies 356–7
prospective 363
publication bias 354
purpose 355
quality of original studies 354
recommendations 356
research 354–5
selection of therapies 361
statistical analyses 356
steps 355–6
time saving 361–2
meta-regression techniques 362
metabolic reactions 45–6
metabolism of drugs
alteration by genotype 290–1
disease effects 47–8
geneic factors 46–7
slow 448
variation 45–9
metabolites, active 48
methadone 18
methodologic advances 448
metiamide 18
mitoxantrone 110–11
modeling 271, 325
continuous-benefit effect
model 341
economic analysis 341
generalized linear model 342
one-time effect model 341
pharmacokinetic 370–1
molecular pharmacoepidemiology 287–98, 476
cost-effectiveness 298
methodological problems 292–5
research 291–2
type I errors 294, 296–7
type II errors 294, 297
monitoring centers, national 119–20
mortality data 217
Multi-item Gamma Poisson Shrinker (MGPS) method 70
Multicenter studies, economic evaluation 340
multiple regression 325
multiple sclerosis 392–3
multivariate analysis 272
predictive power 342
myelo-optic-neuropathy, subacute 6
myelosuppression 113–14
myocardial infarction 324
naloxone 18, 325
named patient use 78
naproxen 360
National Ambulatory Medical Care Survey 74
National Birth Defects Prevention Study 421
National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program 175
National Center for Health Statistics (NCHS) 216, 217
National Childhood Encephalopathy Study (NCES) 261–2
National Death Index (US) 217
National Disease and Therapeutic Index™ 216, 217
National Institute of General Medical Sciences (NIGMS) 452
National Institutes of Health (NIH) 451, 453
biomedical research 75
Roadmap 67
training funding 448
National Prescription Audit Plus™ 216
National Sales Perspective™ 216
Netherlands automated pharmacy record linkage 196–8, 209, 228, 252
validation studies 255
community pharmacy system 196
general practice 196
medical record linkage 196–7
neural networks, Bayesian approach 123–5
neural tube defects 418
New Drug Applications (NDA) 92
fee 7
nifedipine 43
non-prescription medications 52, 145
non-steroidal anti-inflammatory drugs (NSAIDs)
adverse events 311–12, 358–60
angina 284
case–control surveillance 143–4
colorectal cancer risk 263–4
database resources 236
gastric ulceration 38–9
recall accuracy 248–9
renal function 40, 45
study types 236–7
nondifferential misclassification 246, 476
nonexperimental studies 327–8, 329, 330, 448, 476
meta-analyses 356–7
uncertainty in risk assessment 384
nonparametric bootstrap methods 342
number needed to harm 83
number needed to treat 83, 349
numerator data 132–3
obesity, young people 64
objectivity in regulatory action 85
observational studies 71–2, 74, 476
causal relationships 312
confounding by indication 313
oculomucocutaneous syndrome 6
odds ratio 20, 143, 147, 476
case–time–control 391
combination 356
confounding 389
reporting 127
stratification 272
Office of Drug Safety (ODS) 92, 93
Olmsted County medical records 219
omeprazole 49
one-step method for meta-analysis statistics 356
one-time effect model 341
opiates 40
opinion leaders 406
oral contraceptives 18, 19, 21
case–control study 242–3
case–control surveillance 144, 145
combined 156
confounding 270
dosing regimen 371
ethinylestradiol 48
meta-analysis of nonexperimental studies 356–7
perfect use 373
post-dose duration of action 374
thromboembolic disease 133
typical use 373
unsuspected associations 144
orphan medicines 79, 298
osteoporotic fractures 327–8
outcome data 146
validity 232–3
defining criteria 270
differential misclassification 264
expected incidence 26
hospital care 432
of interest 36
measurement 85
large simple trials 316–17
measures 243
multiple variables 32
nondifferential misclassification 264
patient of physician prescribing 404
patient-reported 201
pregnancy 162
outcomes research 322
outpatients diagnostic databases 175, 181, 233
information 430, 435
prescription encounters 189
therapeutic transaction 65
see also hospital(s)
over-the-counter (OTC) drugs adverse events 94
information need 169–70, 177, 202, 256
teratogenic 418
package inserts 129
pancreatitis 114
passive diffusion 42
patient(s) authorization for data use 308
behavior 52
comparision groups 339
demand 50
dosing errors 368, 369
expectations 50
handoffs 428
hospitalized 429–30
information sources 135
knowledge of drugs 240
preferences 61
responsibility for medication 368
INDEX

postmarketing, risk management 423
potassium chloride formulation trials 223
practice
epidemiology 302
health care delivery 64–5
practolol 6
pravastatin 195
prazosin 10, 18, 31, 56
postmarketing surveillance 223
pre-approval period, risk management 69
pre-licensing stage 77–9
PRECEDE model 406
pregnancy
antidepressant safety 177–8
drug evaluation 73
drug use 323
exposure registry 73
medication errors 428
outcomes 162
see also birth defects, drug-induced; teratogens
premarketing studies 9, 10, 71, 312
efficacy 322
prescribed daily dose 132, 403
prescriber behavior 50–2
adherence to treatment guidelines 404
cost containment 51
modification 401, 403
patterns 51
pecuniary interests 51
pharmaceutical industry influence 52
physician prescribing 10
postmarketing drug surveillance 57
prescribing
behavior modification 403
budgets 51
conceptual framework 406
coverage limitations in Medicaid 190
databases 189, 192, 198–9
errors 404, 477
General Practice Research Database 204
internal validity 405
intervention effectiveness 405
physician 10, 436–7
clinical feedback 406
clinical problems 404
evaluation 404
improving 404–7
methodologic problems 405–6
research 402–4
prescriber data 199
reasons for 267
records 175
trend monitoring 74
unit of analysis 405
prescription(s) 152
indication for 267–8, 273–4
information for medication errors 428
number 400
sequence analysis 394
unclaimed 251
unique identifier number 199
prescription diaries 244, 369
Prescription Drug User Fee Act (US, 1992) 7, 69
Prescription-Event Monitoring (PEM) 6, 151–64
applications 157–8, 159, 160–3
background effects 163
data analysis 153
data comparison with external data 162
database resources 234, 235
event analysis 158, 160
event data collection 153
event rates 160
GP response rate 153, 155
incidence density 160
long latency adverse reactions 160–2
modified studies 163
pregnancy outcomes 162
process 152–3, 154, 163
prompting effect 156
reasons for stopping drug use 157, 160
risk management 163–4
signal detection 157, 158, 159, 160–2
signal generation 160
strengths 155–7
weaknesses 157
Prescription Pricing Bureau 223
press, informing 67
presystemic clearance 48
prevalence 476
bias 264, 476
low exposure 234–5
PREVEND (Prevention of Renal and Vascular End-stage Disease) study 196–7
privacy 303, 477
authorization waiver 308
data 307
inpatient data systems 436
Privacy Board 308
probeneicid 45
products
name recognition 57–8
planning 73–4
quality problems 92
withdrawals 107
Programme for International Drug Monitoring (WHO) 117–36
propensity scores 271, 273, 325–6, 448, 477
proportional reporting ratio (PPR) 70, 126–7, 412
propranolol 38, 379
prospective studies 22, 478
protease inhibitors 370–1
protein binding 43
protocol-induced testing 338–9
protopathic bias 262, 264, 478
public
informing 67
understanding of epidemiology 75
public health 76
protection 79
publication bias 474
meta-analyses 354, 357
public–private partnerships 68
Pure Food and Drug Act (1906) 5, 93
p-values 20, 21, 477
quality-of-life measurements 345–51, 475
anchor-based approach 348
distribution-based approach 348–9
instruments 346–51, 474
discriminative 347
disease-specific 350–1
evaluative 347
generic 349–50
potential use 349–51
score interpretation 347
specific 349, 350–1, 479
taxonomy 349–51
Quality of Well-Being Scale 350
quasi-experimental designs 405
questionnaires 241
random-effects models 356
randomization
by cluster 409
confounding control 268, 313
large simple trials 314–15
randomized controlled trials (RCT) 9, 19, 21, 22, 71, 76, 311–19
blinding 313–14
classic 313–14
confounding control 268–9
control groups 314
data analysis/collection 314
INDEX 495

medical care 342
reinforcements, positive 407
reliability 478
HRQL instruments 346, 348
quantitative measurement 245
renal dosing errors 429
renal elimination
drug–drug interactions 45–6
variation 44
renal function, NSAIDs 40
renal transplantation, induction therapy 360–2
renal tubular reabsorption, passive 44
renal tubular secretion, active 44
replication studies 296–7
reporting odds ratio (ROR) 128
reports/reporting
accuracy 248
bias 130
causality assessment 279–80
characteristics 163
computerized storage 93
15-day 129
electronic 99–100, 101
evaluation 105–9, 121–2
feedback to reporters 122
handling 121–2
international standards 128–9
mandatory 91, 94, 97–8, 99, 120–1
modifications 101–2
publishers 281
quality 112
quantitative 128
requirements 120–1
for generation 129–30
schemes 119
selective 130
sources 121
underreporting 111, 132
voluntary 91, 95–6
see also spontaneous
reporting
reproducibility 478
HRQL instruments 346–8
research 474
adherence to treatment 365–8
beneficial effects 322–3
bioethics 302–5
clinical problems 239–40, 261–2
economic evaluation 334–6
ethics 77, 301–9
ethics board review
funding 451
Health Insurance Portability and Accountability Act impact 256
health-related quality-of-life 345
human subjects 301–3
informed consent 304–5, 307
investment 64
measurement error 242–3
meta-analyses 353–5
methodologic problems 313–14, 323–5
minimal risk 304
molecular pharmacoepidemiology 291–2
outcomes 322
participant confidentiality 75, 77, 303–4, 305–6, 307–8, 447
randomized controlled trials 312
regulation 77
social services 309
study designs 383
validity 306
research questions
beneficial effects of drugs 234
data base resources 233–6
see also hypothesis generation
resources, pharmacoepidemiology 74–5
responsiveness 478
HRQL instruments 346, 348
retrospective studies 22, 478
rhabdomyolysis 134
rights of patients 305
risk 55, 474
acceptability 59–61
action to reduce 85
adverse reaction types 93
balance with benefits 82–3
characterization 424
communication 186
comparative 71
evaluator perceptions 61
excess 21, 132
hazards 61
identification 424
impact 83
minimal 304–5
quantification 81–2
relative 20–1, 132, 474
versus safety 59
summarizing 79
tolerance 59–61
voluntary assumption 61
risk group identification 424
INDEX

risk management 8–9, 423–5, 440, 448
case reports 424
case reports 424–5
design 425
effectiveness 424, 426
evaluation 425
goal setting 425
methodological problems 424
Phase IV studies 424
postmarketing 424, 425
pre-approval period 69
Prescription-Event Monitoring 163–4
product usage 424
programs 425–6
risk sets 386–8
RNA 288
rofecoxib 7
root cause analysis 285
rosiglitazone 164
rotavirus vaccine 7, 412
rule of threes 32, 69
safety alerts 103
safety data
clinical trials 78
collection by pharmaceutical industry 80
comparator-controlled 78–9
management 80
Safety Information and Adverse Event Reporting Program (FDA) 102
safety of drugs 58, 59
adverse event data collection 78
assessment 78–9
communication 85
degrees 59
evaluation 69
history of regulation 92–4
licensing 77–8
post-approval studies 74
postmarketing profile 70
regulation 79
specification 79–80
safety theory 427
salbutamol 349
sample size 25–33
birth defects 418
calculation 26, 29, 32
case series 31–2
case–control studies 29, 30, 31, 32, 33, 464–70
clinical trials 69
cohort studies 26–7, 28, 29, 32, 455–62
economic analysis 340
large simple trials 314
medication errors 427
randomized controlled trials 313
vaccine studies 413
sampling strategies 383
two-stage 272, 391
Saskatchewan health services database 192–5, 209, 253–4
cancer services data 193
comparative characteristics 228, 233
data linking 194
demographic data 192
diagnostic information 195
eligible population 192
exposure data limitation 194
health services data 192–4
health services number 192, 194
hospital services data 193
medical records 194
physician services data 193
prescription drug data 192
reliability 194
validity 194, 255
scientific advice, development of drug 79
scientific inference 14, 478
scientific method 13–14
screening tests, cancer 329
second line therapy 83
secular changes, drug-induced birth defects 422
secular trends analyses 19, 21–2, 473
data sources 215–18
selection see bias, selection
selective serotonin reuptake inhibitors (SSRIs) 83–5, 177–8
sensibility 346, 478
sensitivity 478
calculation 244
low 247
sensitivity analysis 246, 256, 273, 479
cost-effectiveness 337
Serious Adverse Drug Reaction (SADR) Reporting Proposed Rule 101–2
serotonin 40–1
SF-36 350
Sickness Impact Profile (SIP) 350
side effects, known 92
signal(s) automated 160
evaluation 122–8
false 130
generation 160
follow-up 237
signal detection 70–1, 80–1, 122–8
adverse event reports 105, 107
data mining 109, 123, 127–8
evaluation 81–2
HRQL instruments 347
postmarketing drug surveillance 110
Prescription-Event Monitoring 157–8, 159, 160–2
prioritization 81
proportional reporting ratio 126–7
stains 134
Uppsala Monitoring Center 124–5
vaccine adverse events 412–13
vaccines 411
signal-to-noise ratio 347
sildenafil 40, 152, 162
silicone breast implants 6
single nucleotide polymorphisms (SNPs) 288, 295
Slone Epidemiology Center 6
case–control surveillance 228
Slone Survey 216–17
slow acetylators 46–7, 448
small study effects 357
smallpox vaccine 7
social implications of genetic testing 298–9
Social Security death tapes (US) 217
social services research 308–9
societies for pharmacoepidemiology 447
sparteine 47
specificity 479
of associations 16
calculation 244
low 247
spirometry 347
spontaneous reporting 70, 80, 81, 82, 91–115, 118, 478
case–control studies 219
limitations 129–30
mechanisms for adverse reactions 132–3
new drugs 235–6
risk estimation 132
risk group identification 132–3
strengths 129
Spontaneous Reporting System (SRS) 93
standard error of measurement (SEM) 349
standard gamble 350
standardized incidence rate (SIR) 389
standardized mortality rate (SMR) 389
statins 133–4, 195
statistical analyses for meta-analysis 356
statistical inference 14, 479
statistical power, birth defects 421
statistical significance 33, 476
economic analysis 341
statistics 14
drug 398, 399
steady state concentration 42, 479
stem cell transplantation, autologous 334–5
Stevens–Johnson syndrome misclassification 248
stratification, study design 272–3
studies
approaches 227–37
interpretation 75
programs 441
reasons to perform 55–9
subjects 13–14
timing 55–62
study designs 13–23, 383–95
clinical problems 384
confounding control 268–71
descriptive 21–2
epidemiologic 17–21
matching 269
methodologic problems 384–5
observational 21
pharmacoeconomics 339–42
post-licensing studies 77
regulatory agencies 76
research 382–3
restriction 269
sampling within a cohort 384–8
standardization 269, 270
stratification 272–3
two-stage sampling 272–3
within-subject 383, 391–4
see also named types
sulfanilamide elixir 5, 93
Summary of Product Characteristics package insert 129
supraventricular arrhythmias 361
suprofen 6, 133, 219
suspected unexpected serious adverse drug reaction (SUSAR) 78
Sweden, data sources 217
syndrome detection 125
synergy index 296
system-based interventions, errors 429
system changes, error reduction 427
tampons 60
Tayside Medicines Monitoring Unit (MEMO) 198–203, 209, 252
admissions 203
birth cohort 200
clinical laboratory data 200
comparative characteristics 228, 233
confidentiality 201, 202
demographic data 200
diagnostic accuracy 202, 255
drug exposure data 202
episode of care 203
ethics 201
gene tic data 201
good epidemiological practice 201
hospital data 199–200
inpatient admissions 255
medical records accessibility 202
patient access 202
patient identification 199, 201
patient-reported outcomes 201
population-based data 201
population size 202
prescribing data 198–9
primary care data 200
randomized trials 202
temafloxacin 6, 113
temazepam 46
teratogenesis
class action 419
unknown risk 416
see also birth defects, drug-induced
teratogens 5, 6, 61, 418–23
alleged 419
high risk 418
legal issues 419–20
moderate risk 418
over-the-counter drugs 419
pregnancy outcomes 162
regulation 422
study of effects 73
terfenadine 6
tests
one-tailed 26, 29, 31
two-tailed 26, 27, 31
thalidomide 5–6, 117, 418
theophylline 49, 391
therapeutic alternatives 82
therapeutic ratio 49, 479
therapeutic risk management see risk management
thiazolidinediones 181–2
third-party payers 342
thromboembolic disease 133, 156
ticrynafen 6
time sequence of associations 16
time-stamping microcircuitry 449–50
time trade-off 350
tissue partition coefficient 41
tolmetin 57, 58
toxic shock syndrome 60
toxicity information 57–8
tracheoesophageal fistula 421
traditional medicines, co-medication 135
training 447–8
transdermal drug absorption 43
transparency in regulatory action 85
treatment
acceptance 368
benefits 50–1
discontinuing 367
harm s 50–1
identification 186
outcomes 50
tracking 186
triazolam 6
trolgitazone 107, 181–2, 187–8, 426
L-tryptophan 6
Tylenol 142
uncertainty
about products 92
economic analysis 343
principle 315–16
risk assessment 384
UnitedHealth Group 184–7, 208, 252
claims data 187
comparative
characteristics 228, 229
health plans 183
affiliated 252
health professional data 185
medical claims 185
membership data 185
new drugs 235
pharmacy claims 185, 186
research databases 184–5
upper limit factor 32
Uppsala Monitoring Center 117
Bayesian Confidence Propagation Neural Network 124
signal detection system 124
<table>
<thead>
<tr>
<th>Term</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>use of medication</td>
<td>63</td>
</tr>
<tr>
<td>adverse event reporting rate</td>
<td>131</td>
</tr>
<tr>
<td>case–control surveillance</td>
<td>141–2</td>
</tr>
<tr>
<td>chronic</td>
<td>134</td>
</tr>
<tr>
<td>common uses</td>
<td>81</td>
</tr>
<tr>
<td>duration</td>
<td>142, 144, 161, 245</td>
</tr>
<tr>
<td>effectiveness measures</td>
<td>327</td>
</tr>
<tr>
<td>effects after long intervals</td>
<td>145</td>
</tr>
<tr>
<td>frequency</td>
<td>141</td>
</tr>
<tr>
<td>hospital-based evaluation</td>
<td>434–5</td>
</tr>
<tr>
<td>hospitals</td>
<td>428</td>
</tr>
<tr>
<td>indications</td>
<td>192</td>
</tr>
<tr>
<td>inpatient</td>
<td>233, 235</td>
</tr>
<tr>
<td>multiple</td>
<td>135</td>
</tr>
<tr>
<td>nondifferential misclassification</td>
<td>147</td>
</tr>
<tr>
<td>patterns</td>
<td>74</td>
</tr>
<tr>
<td>regulatory control</td>
<td>85–6</td>
</tr>
<tr>
<td>stopping in Prescription-Event Monitoring</td>
<td>157, 160</td>
</tr>
<tr>
<td>timing</td>
<td>142–3</td>
</tr>
<tr>
<td>see also</td>
<td></td>
</tr>
<tr>
<td>drug utilization entries</td>
<td></td>
</tr>
<tr>
<td>user fees, drugs</td>
<td>69</td>
</tr>
<tr>
<td>usual care arm of clinical trials</td>
<td>339</td>
</tr>
<tr>
<td>utility measurement</td>
<td>350</td>
</tr>
<tr>
<td>vaccine(s)</td>
<td>7, 131</td>
</tr>
<tr>
<td>adverse events</td>
<td>411</td>
</tr>
<tr>
<td>bias</td>
<td>412</td>
</tr>
<tr>
<td>clinical problems</td>
<td>411</td>
</tr>
<tr>
<td>confounding factors</td>
<td>393</td>
</tr>
<tr>
<td>diphtheria–pertussis</td>
<td>261</td>
</tr>
<tr>
<td>efficacy studies</td>
<td>329</td>
</tr>
<tr>
<td>epidemiologic studies</td>
<td>411</td>
</tr>
<tr>
<td>exposure status</td>
<td></td>
</tr>
<tr>
<td>misclassification</td>
<td>412</td>
</tr>
<tr>
<td>methodologic issues</td>
<td>411</td>
</tr>
<tr>
<td>multiple sclerosis relapse</td>
<td>392</td>
</tr>
<tr>
<td>outcome event rarity</td>
<td>412</td>
</tr>
<tr>
<td>safety studies</td>
<td>411</td>
</tr>
<tr>
<td>sample size for studies</td>
<td>412</td>
</tr>
<tr>
<td>signal detection</td>
<td>412</td>
</tr>
<tr>
<td>universal exposures</td>
<td>411</td>
</tr>
<tr>
<td>vaccine adverse event reporting system</td>
<td>(VAERS) 103, 412, 413</td>
</tr>
<tr>
<td>Vaccine Safety Datalink (VSD)</td>
<td>176, 412</td>
</tr>
<tr>
<td>valdecoxib</td>
<td>107</td>
</tr>
<tr>
<td>validation studies</td>
<td>244, 249</td>
</tr>
<tr>
<td>validity</td>
<td>433</td>
</tr>
<tr>
<td>criterion</td>
<td>346, 474</td>
</tr>
<tr>
<td>diagnosis information</td>
<td>433</td>
</tr>
<tr>
<td>drug-induced birth defects</td>
<td>418</td>
</tr>
<tr>
<td>drug information in hospital</td>
<td>433</td>
</tr>
<tr>
<td>face</td>
<td>346, 474</td>
</tr>
<tr>
<td>internal</td>
<td>405</td>
</tr>
<tr>
<td>medication events</td>
<td>370</td>
</tr>
<tr>
<td>quality-of-life measurement</td>
<td></td>
</tr>
<tr>
<td>instruments</td>
<td>346–7</td>
</tr>
<tr>
<td>research</td>
<td>306</td>
</tr>
<tr>
<td>see also</td>
<td></td>
</tr>
<tr>
<td>data validity</td>
<td></td>
</tr>
<tr>
<td>valproic acid</td>
<td>114, 419</td>
</tr>
<tr>
<td>valsartan</td>
<td>335–6</td>
</tr>
<tr>
<td>variables</td>
<td></td>
</tr>
<tr>
<td>continuous</td>
<td>32–3, 245</td>
</tr>
<tr>
<td>misclassification</td>
<td>243</td>
</tr>
<tr>
<td>predisposing</td>
<td>406</td>
</tr>
<tr>
<td>ventricular tachycardia</td>
<td>384</td>
</tr>
<tr>
<td>verapamil</td>
<td>39, 49, 361</td>
</tr>
<tr>
<td>visual analogue scales</td>
<td>350</td>
</tr>
<tr>
<td>vital statistics</td>
<td>19</td>
</tr>
<tr>
<td>Saskatchewan health services database</td>
<td>193</td>
</tr>
<tr>
<td>volume data</td>
<td>401, 402</td>
</tr>
<tr>
<td>volume of distribution</td>
<td>475</td>
</tr>
<tr>
<td>apparent</td>
<td>42</td>
</tr>
<tr>
<td>voluntariness</td>
<td>304, 479</td>
</tr>
<tr>
<td>Walker Data Set</td>
<td>200</td>
</tr>
<tr>
<td>warfarin</td>
<td>48, 49, 291–2</td>
</tr>
<tr>
<td>Weber effect</td>
<td>112</td>
</tr>
<tr>
<td>welfare of patients</td>
<td>305</td>
</tr>
<tr>
<td>white-coat compliance</td>
<td>371</td>
</tr>
<tr>
<td>winner’s curse phenomenon</td>
<td>297</td>
</tr>
<tr>
<td>World Health Organization (WHO) database</td>
<td>117–18, 123–6</td>
</tr>
<tr>
<td>drug utilization definition</td>
<td>400, 475</td>
</tr>
<tr>
<td>Programme for International Drug Monitoring</td>
<td>117–36</td>
</tr>
<tr>
<td>World Medical Association Declaration of Helsinki (1964)</td>
<td>303</td>
</tr>
<tr>
<td>Yasmin</td>
<td>156</td>
</tr>
<tr>
<td>young people, obesity</td>
<td>64</td>
</tr>
<tr>
<td>zidovudine</td>
<td>57, 60</td>
</tr>
<tr>
<td>ziprasidone</td>
<td>7</td>
</tr>
<tr>
<td>zomepirac</td>
<td>6, 58</td>
</tr>
<tr>
<td>Z-statistics</td>
<td>357</td>
</tr>
</tbody>
</table>