Index

–2log likelihood *see* likelihood ratio statistic
a priori approach to probability 26
addition rule 26
adequacy of fit 97, 98, 167
adjusted odds ratio 88
adjusted R^2 84
administrative censoring 134
aggregate level analysis, clustered data 127, 128
agreement
  limits of 119
agreement, assessing
  categorical variables 118, 120
  measurement variability and error 118
  numerical variables 118–21
  reliability 118
allocation
  bias 42, 104
  clinical trials 40
  random *see* randomization
  systematic 40
  treatment 40
alpha (α) 52, 108
alternative hypothesis, defining the 50
Altman's nomogram 108–9, 149
analysis of covariance 84–5
analysis of variance (ANOVA) 63
  F-ratio 80
  Kruskal-Wallis test 64
  one-way *see* one-way analysis of variance
  repeated measures 125
  table 78–9
ANOVA *see* analysis of variance
antilog 30
area under the curve (AUC) 26, *27*, *125*
arithmetic mean 22, 23
  see also mean
ascertainment bias 102
ASCII files 16
assessment bias 102
  clinical trials 42
association
  in contingency table 72, 73–4
  in correlation 75
assumptions, checking
  linearity 107
  Normal distribution 106
  reasons for 106
  sensitivity analysis 107
  variances, equality of 106
  when assumptions are not satisfied 107
attrition bias 102
automatic selection procedures 99
average 22
  arithmetic mean 22, 23
  geometric mean 22, 23
  median 22, 23
  mode 22, 23
  weighted mean 22, 23

back-transformations 30
backwards selection 99
bar charts 20
  clustered 21
  segmented 20, 21
Bartlett's test 106
  one-way ANOVA 64
Bayes theorem 136–7
Bayesian methods 136
  diagnostic tests 136–7
  disadvantages 137
beta (β) 52, 80
between-subject/group variabilities 25, 63, 118
bias 37, 102
  cohort studies 45
  confounding *see* confounding
  evidence-based medicine 122
  information 102–3
  missing data 18
  on-treatment analyses 43
  selection 102
bimodal distributions 21
binary (dichotomous) variables 14, 122
  explanatory 78, 85, 98–101
  in logistic regression 88–90
  in meta-analysis 130
  in multiple regression 84
binary outcomes and logistic regression 88
Binomial distribution 29
  confidence interval for the proportion 34
  Normal approximation 28
  single proportion test 66
bioequivalence trials 51
Bland and Altman diagram 119
blinding/masking
  clinical trials 42
  evidence-based medicine 122
blocked randomization 40
blocking 38
Bonferroni correction 53
bootstrapping 35
  prognostic scores 139
box (box-and-whisker) plot 21, 24
Brier score 138
British Standards Institution repeatability coefficient 119

calibration, prognostic scores 139
carry-over effects 38
case–control studies 36, 47
  advantages 48
  analysis 48
  cases, selection of 47
  controls, selection of 47
  disadvantages 48
  matched 47–8
  risk factors, identification of 47
  unmatched 48
cases 47
  incident 47
  prevalent 47
categorical data (variables) 14, 66–8
  coding 16, 17
categorical (qualitative) data 14
  agreement, assessing 118, 120
  data entry 16
  diagrammatic display 20
  error checking 18
  logistic regression 90
  more than two categories 72–4
  multiple linear regression 84
causal modelling 105
causal pathway and confounding 105
causality, assessing 37
causality, in observational studies 36
censored data 15, 133
  left- 133
  right- 133
  survival analysis 133, 134
censuses 37
Central Limit Theorem 32
central tendency bias 102
centring, linear regression 81
channelling bias 104
checking assumptions *see* assumptions, checking
Chi-square for covariates *see* model Chi-square test
Chi-squared (χ^2) distribution 28, 143
Chi-squared (χ^2) test
  in 2×2 tables 69
  for covariates (model Chi-square) 88, 97
  independent groups 69
  in $r \times c$ table 72
  for trend in proportions 72–3, 74
  for two proportions
    independent data 69
    paired data 57, 70–1
CI *see* confidence intervals
classification table 89
clinical cohorts 46
clinical heterogeneity 131
clinical trials 36, 40–3
  avoiding bias in 37
  blinding/masking 42
  CONSORT Statement 40, 41–2
  cross-over design 38, 39
  endpoints, primary and secondary 40
  ethical issues 40
  evidence-based medicine 122
  inclusion/exclusion criteria 41
  informed consent 40
  intention-to-treat analysis 42, 122
  patient issues 43
  phase I/II/III 46
  placebo in 40
  protocol 41–2, 43
  sequential 42
  size 42
  subgroup analyses 40
  treatment allocation 40–2
  treatment comparisons 40
cluster randomization
  clinical trials 40–2
  observation, unit of 37
cluster-specific models 127
clustered bar charts 21
clustered data 124
  appropriate analyses 124–5
  displaying 124

inappropriate analyses 124
rates 92
regression methods 127–9
Cochran's Chi-squared test for homogeneity 132
Cochrane Collaboration 130
coding
data 16, *17*
missing values 16, 17
coefficient
correlation *see* correlation coefficient
intraclass correlation 118, 128
logistic regression 87
partial 84
regression 78
repeatability/reproducibility 118, 120
of variation 25
Cohen's kappa 118
weighted 118
cohort studies 36, 44–6
advantages 45
analysis of 44–5
clinical cohorts 46
confounding 104
disadvantages 45
dynamic 44
fixed 44
follow-up of individuals 44
historical 44
management of study 45–6
outcomes and exposures, information on 44
selection of cohorts 44
collinearity
logistic regression 89
multiple linear regression 85
column charts *see* bar charts
competing risks 134–5
complementary events 26
complete randomized studies 38
composite endpoints 39
computer output 150–62
computer packages, data entry 16–17
conditional logistic regression 90
conditional probability 26, 136
confidence intervals (CI) 34, 35, 122
95% 80
for correlation coefficient 75, 76
for difference in two means 60, 62
for difference in two medians 61
for difference in two proportions
independent groups 69, 70
paired groups 70, 71
interpretation of 34–5, 54, 60, 122
for mean 34, 35
for mean difference 57–58, 59
for median 145
for median difference 57, 58–9
in meta-analysis 130–1, 132
multiplier for calculation of 142, 143
for proportion 34–5
for regression coefficient 80
for relative risk 45, 46
for slope of regression line 80, 81
versus hypothesis testing 51
confidence limits 34
confounding 103
and causal pathway 104–5
clinical trials 40
cohort studies 45
dealing with 103–4
in non-randomized studies 104
time-varying 105
connecting lines in diagrams, use of 21
consent, informed
clinical trials 43
cohort studies 46
CONSORT Statement 40, 41–2, 112
contingency tables
2×2 69
$2 \times k$ 72
$r \times c$ 72
continuity correction
sign test 55
single proportion test 66
continuous data 14
diagrammatic display 20–1
continuous probability distributions 26–7, 28
controls 37, 47
clinical trials 40
see also case–control studies
convenience factor 92
convenience sample 32
Cook's distance 84
correlation 75–7
linear 75–6
correlation coefficient
assumptions 75
confidence interval for 76, 77
hypothesis test of 76, 77
intraclass 118, 128
misuse of 76
non-parametric 76
Pearson 75, 77, 147
Spearman's rank 76, 77, 147
square of (r^2) 75
counts 29
covariance, analysis of 85
covariate, multiple linear regression 84
Cox proportional hazards regression model 90, 134, 135
critical appraisal 122
cross-over studies 38, 39
cross-sectional studies 36, 37
repeated 36, 37
cross-sectional time series models, clustered data 127
cross-validation 139
c statistic 116, 117
cumulative meta-analyses 131
cut-off values 116

data
categorical *see* categorical (qualitative) data
censored 15
clustered 92, 124–6, 127–9
coding 16, 17
derived 14–15
describing 22–5
diagrammatic display *see* diagrammatic display of data
distinguishing between types 14
dredging 53
error checking 18–19
graphical display 20–21, 124
missing 16, 18
numerical *see* numerical (quantitative) data
paired 57
range checking 18
and statistics 14
summarizing 22, 24
transformation 30–1
see also specific types
data entry 16
Data Safety and Monitoring Committee (DSMC) 40
dates
data entry problems 16
error checking 18
deciles 24
decision making in hypothesis testing 52
Declaration of Helsinki 43
degrees of freedom (df) 34–5
Chi-squared distribution 28
F-distribution 28
t-distribution 28
delimiters 16
dependent (outcome, response) variables 78
binary 105
categorical 90
derived data 14–15
design *see* study designs
deviance *see* likelihood ratio statistic
df see degrees of freedom
diagnostic tests 115–16, 136–7
in Bayesian framework 136–7
diagrammatic display of data 20
clustered data 124
connecting lines 21
one variable 20–1
outliers, identifying 21
two variables 21
diagrammatic display of results 112
dichotomous variables 14
discrete data 14
discrete probability distributions 26, 28–9
discriminant analysis 138
disease register 46
dispersion *see* spread
distribution
bimodal 20
continuous probability 28
discrete probability 29
empirical frequency 20
frequency 20, 21
probability 26
sampling 32–3
skewed 20
Standard Normal 27
symmetrical 20
theoretical 26–9
uniform 20
unimodal 20
see also specific types
distribution-free tests *see* non-parametric tests
dot plots 20, 21
double-blind trials 42
dummy (indicator) variables
multiple linear regression 84
sensitivity analysis 107
Duncan's test 63
dynamic cohort studies 44

ecological fallacy 102–3
clustered data 125
meta-regression 103, 131

ecological studies 37, 102–3
effect (of interest) 52
  in evidence-based medicine 122
  in meta-analysis 130–1
  importance of 122
  power of test and 52
  in sample size calculation 108
effect modifiers 45
efficacy 40
empirical frequency distributions 20, 26
  displaying 20–1
endpoints of studies
  choosing 39
  clinical trials 40
  primary 40
  secondary 40
epidemiological studies 36
EQUATOR Network 112
equivalence range 51
equivalence trials 51
error
  residual 78
  Type I 52
  Type II 52
  typing 18
  variation 53
estimated relative risk 45
ethical issues
  clinical trials 43
  cohort studies 46
  power of a test 52
ethics committees
  clinical trials 43
  cohort studies 46
even numbers 22
evidence, levels of 122
evidence-based medicine (EBM) 122
  approach 122–3
  systematic reviews 130
exclusion criteria, clinical trials 43
expected frequency 69
experimental studies 36, 37
experimental units 38
explanatory (independent, predictor) variables 78, 85, 98–101
  in logistic regression 88–89
  in multiple regression 84–5
  nominal 84, 99
  numerical 103
  ordinal 98
Exponential model, survival analysis 134
exposure variable 45, 102–5
external validation 139
extra-Binomial variation 89–90, 94
extra-Poisson variation 93–4

factorial experiments 38–9
Fagan's nomogram 136, 137
false negative rate 89
false positive rate 89
F-distribution 28
  one-way ANOVA 63
  statistical table 142, 144
Fisher's exact test 69, 72
fitted value 70
fixed cohort studies 44
fixed effect model 130
follow-up
  cohort studies 44, 45
  loss to *see* loss to follow-up
  person-years of 92
forest plots 131
forms 16
  multiple 16
forwards selection 98
frailty models 134
F-ratio 80
free format 16
frequency 20, 69, 72
  displaying 20–1
  observed and expected 69
  shape 21
  table of 115
frequency matching, case–control studies 47
frequentist approach to probability 26, 136
F-test *see* variance-ratio test
funding bias 102
funnel plots 131

G see model Chi-square test
Galton, Sir Francis 79
Gaussian distribution *see* Normal distribution
generalized estimating equations (GEE) 128
  example 129
generalized linear models (GLMs) 96
  adequacy of fit, assessing 96–7
  likelihood and maximum likelihood estimation 96
  regression diagnostics 97
  types 96
geometric mean 22, 23
G-estimation 105
gold standard tests 115
Gompertz model 134
goodness of fit
  linear regression 79, 80
  logistic regression 89
  multiple linear regression 85
Gossett, W. S. ('Student') 28
gradient, of regression line 78
graphical display
  of data *see* diagrammatic display of data
  of results 112

Harrell's *c* statistic 138–9
hazard 134
hazard ratios 134
healthy entrant effect 102
  cohort studies 44
Helsinki, Declaration of 43
heterogeneity
  clinical 131
  statistical 130
  of variance 106, 130
hierarchical models, clustered data 127
histograms 20–1
  logistic regression 89
historical cohorts 44
homogeneity, of variance 130
homoscedasticity 106
Hosmer–Lemeshow test 139
  logistic regression 89
  prognostic score 139
hypothesis, null and alternative 50
hypothesis testing 50–1
  categorical data 66
  consequences of 52
  for correlation coefficient 75–6
  errors in 52–3
  likelihood ratio 88
  meta-analysis 130
  more than two categories 72
  more than two means 63
  multiple 53
  non-parametric 51
  presenting results 112
  in regression 80–1
  single mean 54–5
  single proportion 66
  two means
    related groups 57–59
    unrelated groups 60–2
  two proportions
    independent groups 69
    related groups 69–70
  two variances 105, 106
  versus confidence intervals 52
  Wald 88

I^2 130
identity link, generalized linear models 96
inappropriate analyses 124
incidence rate 92
incidence rate ratio *see* relative rates
incident cases 47
inclusion criteria, clinical trials 43
independent variables *see* explanatory variables
indicator (dummy) variables
  multiple linear regression 84
  sensitivity analysis 107
inferences 32
influence plots 131
influential observations
  linear regression 80
  logistic regression 90
  multiple linear regression 85, 107
information bias 102–3
informative censoring 134
informed consent
  clinical trials 43
  cohort studies 46
intention-to-treat (ITT) analyses
  clinical trials 43
  evidence-based medicine 122
interaction 38, 99–100
interdecile range 24
interim analyses
  clinical trials 40
  hypothesis testing 53
intermediate variables and confounding 105
internal–external cross-validation 139
internal pilot studies 108
internal validation 139
interpolation, unpaired *t*-test 61
interquartile range 24
inter-subject/group variation 25, 63, 118
interval estimates 32, 34
intraclass correlation coefficient (ICC) 118, 119
  clustered data 128, 129
intra-subject/group variation 25, 63, 118

jackknifing 35

Kaplan–Meier curves 133
Kappa κ
  Cohen's 118, 120
  weighted 118
k-fold cross-validation 139
Kolmogorov–Smirnov test 106
Kruskal–Wallis test 64
  clustered data 124, 126

lead-time bias 102
least squares *see* method of least squares
leave-one-out cross-validation 139
left-censored data 133
Lehr's formula 109
Levene's test 106
  one-way ANOVA 63
leverage 85
lifetable approach, survival analysis 133
likelihood 96
  –2log 89, 97
  Bayes theorem 136
likelihood ratio (LR) 97
  Bayes theorem 137
  diagnostic tests 116, 117
likelihood ratio statistic (LRS) 97
  logistic regression 88, 89
  Poisson regression 93
likelihood ratio test
  clustered data 128
  logistic regression 88–9
Likert scales, central tendency bias 102
limits of agreement 119
Lin's concordance correlation coefficient 119
linear regression 78
  ANOVA table 78–9
  assumptions 78, 79, 80
  and clustered data 124
  goodness of fit, assessing 80
  improving the interpretation of the model 81
  method of least squares 78
  multiple 84–7
  multivariable 84
  outliers and influential points 80
  regression line 78, 80–1
  regression to the mean 79
  simple 78, 82
  theory 78
linearity
  checking assumptions 107
  transformations 30, 31
link function, generalized linear models 96
location, measures of 22
log log plots 134
logarithmic transformation 30
logistic regression 88
  adequacy of model, assessing 89–90
  conditional 90
  diagnostics 90
  equation 88
  explanatory variables 88–9
  multinomial (polycotomous) 90
  odds ratio and relative risk, comparing 90
  ordinal 90
  prognostic scores 138
logit (logistic) transformation 31
Lognormal distribution 28, 29
  transformations 30
log-rank test 134
longitudinal studies 36, 37
  clustered data 127
loss to follow-up
  bias 102
  cohort studies 44, 45
  sample size adjustment 109

Mann–Whitney *U* test 60
Mantel–Haenszel procedure 69, 103
marginal structural models 105
marginal total 69
masking *see* blinding/masking
matching
  case–control studies 47–8, 90
  conditional logistic regression 90
  confounders 103, 104
mathematical models 96
maximum likelihood estimation (MLE) 96
  clustered data 127
McNemar's test 70
  confounding 103
mean 23
  confidence interval for difference in two 60, 62
  difference 57, 60, 62
  weighted 22, 23
mean Briar score 138
mean square 63
measurement bias 102
measurement error 118
measurement variability 118
measures
  of location 22–23
  of spread 24–25
median 22, 23, 24
  difference between two 57–8, 61
  ranks for confidence intervals for the 142, 145
  survival time 133
  test for a single 54–6
Medline 122
meta-analysis 130
  advantages and disadvantages 131
  sensitivity analysis 107, 131
  statistical approach 130–1
meta-regression 131
  ecological fallacy 103, 131
method agreement 119
method of least squares (ordinary least squares, OLS) 96
  clustered data 127, 129
  linear regression 78
misclassification bias 102
missing data 16, 18
missing values
  coding 16, 19
  handling 18, 19
mixed models, clustered data 127
mode 22, 23
model Chi-square test 97
  logistic regression 89
  Poisson regression 93
models
  Cox proportional hazards regression 90, 134, 135
  Exponential 134
  fixed effect 130
  generalized linear 96–7
  Gompertz 134
  hierarchical 127
  logistic regression 88
  multi-level 78, 84–6
  multivariable 94
  over-fitted 99
  Poisson regression 93–4, 134
  random effects 128
  random intercepts 129
  random slopes 128
  regression 134
  statistical 88–9, 96, 102–4
  univariable 99
  Weibull 134
mortality rates 92
multicentre studies 37
multi-coded variables 16
multi-collinearity 100
multilevel models, clustered data 127
multiple forms per patient 16
multiple hypothesis testing 53
multiple linear regression 84
  analysis 85
  analysis of covariance 84–5
  assumptions 84
  categorical explanatory variables 84
  explanatory variables, choice of 85
  outliers and influential points 85, 107
multiplication rule 26
multivariable regression
  confounding 103, 104
  see also logistic regression; multiple linear regression; Poisson regression
multivariate analysis 84
  hypothesis testing 53
mutually exclusive (categories) 69

negative controls 40
negative predictive value 116
negatively skewed distributions (NPV) 21
  square transformation 31
nested models 97
nominal data 14
  multinomial logistic regression 90
  multiple linear regression 84
nominal significance level 53
non-inferiority trials 51
non-parametric (distribution-free, rank) tests 51, 107
  for more than two independent groups 64
  for single median 54–6
  for Spearman correlation coefficient 76
  for two independent groups 61–2
  for two paired groups 57–8
Normal (Gaussian) distribution 27, 28
  approximation to Binomial distribution 28, 66
  approximation to Poisson distribution 29
  in calculation of confidence interval 34
Normal plot 106
normal range *see* reference intervals
null hypothesis, defining the 50
number of patients needed to treat (NNT) 122
numerical (quantitative) data 14
  agreement, assessing 118–21
  data entry 16
  diagrammatic display 20–1
  error checking 18
  more than two groups 63–5
  single group 54–6
  two related groups 57–9
  two unrelated groups 60–2
numerical results, presenting 112

observation 14
  defining the unit of 36–7
observational databases 46
observational studies 36, 37
observed frequency 69
observer bias 102
odds (of disease)
  adjusted 88
  case–control studies 48
  logistic regression 88, 90
  posterior 137
  prior 137
offsets, Poisson regression 93
one-sample *t*-test 54
one-tailed tests 50
one-way analysis of variance 63–4
  and clustered data 124
on-treatment analyses, clinical trials 43
ordinal data 14
  multiple linear regression 84
  ordinal logistic regression 90
ordinal logistic regression 90
ordinary least squares (OLS) *see* method of least squares
outliers 18
  checking for 18
  handling 18
  identifying using graphical methods 21
  linear regression 80
  logistic regression 90
  multiple linear regression 85
overdispersion
  logistic regression 89
  Poisson regression 93–4
over-fitted models 99
overview *see* meta-analysis

paired data 57
  categorical 69, 70
  numerical 57–8
paired *t*-test 57
  Altman's nomogram 109
  confounding 103
  repeated measures ANOVA 125
pairwise matching 47
panel models, clustered data 127
parallel studies 38, 39
parameters
  point estimates 32
  probability distributions 26
parametric tests 51
partial likelihood, survival analysis 134
partial regression coefficients 84
Pearson's correlation coefficient 75–6
  intraclass correlation coefficient 119
  statistical table 142, 147
percentages 14
percentiles 24
  ranges derived from 24–5
pie charts 20
pilot studies 108
placebos 14
point estimates 32
point prevalence 37
Poisson distribution 29, 92
  transformations 30
Poisson regression 92
  coefficients 93
  computer output 93
  equation 92–3
  extra-Poisson variation 93–4
  groups, entering data for 93
  offset, use of an 93
  variables that change over time 93
polychotomous linear regression 90
polynomial regression 99
population 14, 32
positive controls 40
positive predictive value (PPV) 116, 137
positively skewed distributions 21
  logarithmic transformation 30
posterior odds 136, 137
post-hoc comparisons 63
post-test probability 137
power 52–3
  curves 52–3
  sample size 52, 53, 108, 109–10
  statement 109
precision 32–3, 112, 122
  in systematic reviews 130–1
predictive efficiency, indices of 89
predictive values
  negative 116
  positive 116
predictor variables *see* explanatory variables
preferences, analysing 66
pre-test probability 137
prevalence 115, 137
prevalent cases 47
primary endpoint of trial 40
prior odds 137
prior (pretest) probability, Bayes theorem 136, 137
probability 26
  addition rule 26
  a priori 26
  Bayesian approach 136, 137
  complementary 26
  conditional 26, 136
  discrete 26, 29
  frequentist 26, 136
  multiplication rule 26
  posterior (post-test) 136, 137
  prior (pre-test) 136, 137
  subjective 26
  survival 133
probability density function 26
  Normal distribution 26–7
probability distributions 26–9
  continuous 26–7, 28
  discrete 28–9
  theory 26
prognostic index 138
prognostic scores 139
  developing 139
  performance assessment 138–9
  reasons for 138
propensity score approach, confounding 103–4
proportion(s)
  confidence interval for difference in two 69–71
  logit transformation of 31
  sampling distribution 32–3
  sign test for 66–7
  standard error of 33
  test for single 66–8
  test for trend in 72–4
  test for two
    independent groups 69
    related groups 70–1
proportional hazards regression model (Cox) 134, 135
prospective studies
  cohort studies 44
  longitudinal studies 36, 37
protocol 42–3
  deviations 43
protocols, clinical trials 43
publication bias 102
  meta-analysis 131
P-value 50–1
  explanation 50–1
  obtaining the 50
  post-hoc adjustment of 53
  using the 50–1

qualitative data *see* categorical (qualitative) data
quality, of studies in meta-analysis 131
quantitative data *see* numerical (quantitative) data
quartiles 24
questionnaires 16
quick formulae in sample size estimation 108
QUORUM Statement 112
quota sampling 32
quotients 14

r^2 75
R^2 79, 85
  adjusted 85
  linear regression 79, 80
$r \times c$ contingency table 72
random effects
  meta-analysis 130–1
  meta-regression 131
  models, clustered data 127–8, 129
random intercepts linear two-level model 127, 129
random measurement error 118
random numbers table 142, 148
random samples 32
random slopes model 128, 129
random variables 26
random variation 38
randomization 122
  blocked 40
  cluster 40
  stratified 40
randomization, clinical trials 40–2
randomized controlled trials (RCTs) 40
  and confounding 104
  evidence-based medicine 122
randomized studies, complete 38
range 24, 25
  checking 18
  derived from percentiles 24–5
  interdecile 24
  interquartile 24
  normal *see* reference intervals
  presenting results 112
  reference (normal) 24, 26–7, 115
rank correlation coefficient *see* Spearman's rank correlation coefficient
rank (non-parametric) tests 51, 107
ranks for confidence interval for the median 142, 145
rate ratio *see* relative rates

rates 14, 92
  features 92
  relative 92
  and risk, comparison between 92
ratio 14
  F-ratio 80
  hazard 134
  incidence rate 92
  likelihood 96, 116, 137
  odds 48, 88, 92
  rate 92
recall bias
  case–control studies 48
  cohort studies 45
receiver operating characteristic (ROC) curve 116
  area under the (AUROC) 116, 138
  logistic regression 89
  prognostic scores 138, 140
reciprocal transformation 31
reference categories 84
reference intervals (normal range) 24, 115
  calculation 115
  Normal distribution 27
reference range 24
regression
  clustered data 127–9
  Cox 90, 134, 135
  diagnostics 90, 97
  dilution bias 102
  linear *see* linear regression
  logistic 88–90, 156
  methods 125
  models, survival data 133
  Poisson 92–5
  polynomial 99
  presenting results in 112–13
  simple 78, 80–82
  to mean 79
regression coefficients 78
  linear 78
  logistic 88
  partial 84
  Poisson 93
regression line 78
  goodness of fit 78, 79, 80
  prediction from 80–82
relative frequency distributions 20
  displaying 20–1
relative hazards 134
relative rates 92
  Poisson regression 93
relative risk (RR) 45
  cohort studies 45
  in meta-analysis 45
  logistic regression 88, 90
  odds ratio as estimate of 88
reliability 118
  indices of 119, 121
repeatability 118–19
repeated cross-sectional studies 36, 37
repeated measures
  analysis of variance 125
  data 124
  models, clustered data 127
replication 38
reporting bias 102
reproducibility 118–19
rescaling, linear regression 81
residual error 78
residual variance/residual mean square 63, 79
residual variation 80
residuals 78
  linear regression 78, 80
  multiple linear regression 85
response bias 102
response rates 38
response variables *see* dependent variables
restricted/blocked randomization 40
results, presenting 112–13
retrospective studies
  cohort studies 44
  longitudinal studies 36, 37
right-censored data 133
risk factors
  case–control studies 47
  cohort studies 44–5
risk scores *see* prognostic scores
risks, competing 134–5
robust analysis 107
robust standard errors, clustered data 127, 128
robustness 107
  one-sample *t*-test 54
  one-way ANOVA 64
ROC curves *see* receiver operating characteristic curves

sample 14, 32
  convenience 32
  random 32
  representative 32
  statistic 32
  training 139, 140
  validation 139, 140
  size 38, 52, 106–10
sample size
  Altman's nomogram 108–9, 110, 111, 149
  bias 102
  calculations 108–11
  importance 108
  power of a test 52, 53, 108, 109–10
  quick formulae 109
  requirements 108
  study design 38
sample statistic 32
sampling
  error 32
  distribution 33
  frame 32
  point estimates 32
  quota 32
  reasons for 32
  standard deviation vs standard error of the mean 32
  standard errors 32
  systematic 32
  variation 32
sampling distribution
  of the mean 32
  of the proportion 33
saturated models 97
scale parameter, Poisson regression 93
scaling, linear regression 81
scatter diagrams 20, 21
  correlation analysis 75
  linear regression 78, 80
Scheffe's test 63
scores 14
screening 79
SD *see* standard deviation
SE *see* standard error
secondary endpoints of trials 40
segmented bar charts 20, 21
selection bias 102
  cohort studies 45
sensitivity analysis 107
  logistic regression 89
  meta-analysis 131
  multiple linear regression 84
  outliers 18
sensitivity of a test 115–16
sequential trials 42
Shapiro–Wilk test 106
shrinkage estimates 127
sign test 55
  paired data 57–58
  for a proportion 66–7
significance level 51
  multiple hypothesis testing 53
  and power 52–3
  and sample size 108
significance testing *see* hypothesis testing
significant result 50
Simpson's (reverse) paradox 69
  confounding 103
single-blind trials 42
single-coded variables 16
single proportion test 66
skewed to the left distributions 21
  square transformation 31
skewed to the right distributions 21
  logarithmic transformation 30
software, data entry 16–17
Spearman's rank correlation coefficient 76
  statistical table 142, 147
specificity 115–16, 117
  logistic regression 89
spread 24
  range 24–5
  standard deviation 25
  variation within- and between-subjects 25
square root transformation 30
square transformation 31
standard deviation (SD) 25, 32
  SD vs SEM 32
standard error
  of the mean (SEM) 32, 112
  presenting results 112
  of the proportion 33
  robust 127, 128, 129
Standard Normal distribution 27
  statistical tables 142, 143, 144
standardized difference 108
Standardized Normal Deviate (SND) 27
statistic
  sample 32
  test 50
statistical heterogeneity 130
statistical homogeneity 130
statistical packages, data entry 16–17
statistical tables 142–8
statistics 14
  probability distributions 26
stem-and-leaf plots 21
stepwise selection 99

stratification 38
  stratified randomization 40
STROBE Statement 112
Student's *t*-distribution *see* *t*-distribution
study designs 36, 38
  bias 37
  blocking (stratification) 38
  causality, assessing 37
  controls 37
  cross-over 38, 39
  cross-sectional studies 37
  endpoints, choosing 39
  experimental studies 36
  factorial experiments 38–9
  longitudinal studies 37
  multicentre studies 37
  observational studies 36
  parallel 38, 39
  replication 38
  sample size 38
  unit of observation, defining the 36–7
  variation 38
subgroups
  clinical trials 40
  confounding 103, 104
  hypothesis testing 53
subjective approach to probability 26
summary measures 124–5
  aggregate level analysis 127
  of location 22–3
  of spread 24–5
surrogate marker endpoints 39
surveys 37
survival analysis 94, 133
  censored data 133
  comparing survival data 134
  Cox proportional hazards regression 134
  displaying survival data 133
  Kaplan-Meier log-rank test 134
  problems 134–5
  summarizing survival data 134
survival curves 133
survival probability 133
survivorship bias 102
symmetrical distributions 21
systematic allocation, clinical trials 40
systematic measurement error 118
systematic reviews 130
  meta-analysis 130–2
systematic sampling 32

tables
  2 × 2 table 69
  contingency of frequencies 115
  presenting results as 112
  statistical 142–8
t-distribution 28
  confidence interval for the mean 34
  statistical table 142, 143
test statistic, obtaining the 50
text files 16
text format 16
times, data entry problems 16
time-varying confounding 105
training sample 139
transformations
  method 30
  reasons for 30, 107
  typical 30–1
treatment allocation 40–2
treatment effect 52
trend, Chi-squared test for 72–3
trial size 43
trials *see* clinical trials
true negatives 115
true positives 115
t-test 34
  one-sample 54
  for partial regression coefficients 84
  paired 57
  unpaired (two-sample) 60, 109
two-level structure, clustered data 124, 127
two-sample *t*-test
  see unpaired *t*-tests and Wilcoxon rank sum test
two-tailed tests 50
Type I errors 52
  clustered data 124
  sample size 108
Type II errors 52
  sample size 108
typing errors 18, 19

unbiased estimate 32
underdispersion
  likelihood ratio statistic 97
  logistic regression 90
  Poisson regression 94
uniform distributions 21
unimodal distributions 21
unit, experimental 38
unpaired *t*-test, *see* two-sample *t*-test

validation, prognostic scores 139
validation sample 139
variability
  between-subject 109
  sample size calculation and 109
  within-subject 24
variables 14
  random 26, 38–9
variance 24–5
  Binomial 29
  heterogeneity of 106, 130
  homogeneity of 106, 130
  Poisson 29
  residual 63, 79
  stabilizing 30, 31
  testing for equality of two 64, 106, 107, 153
variance-ratio test (*F*-test) 106
  multiple linear regression 85
variation 38
  between-group 63
  between-subject 24
  coefficient of 24
  explained 80
  extra-Poisson 93–4
  over time 93
  random 38
  unexplained (residual) 80
  within-group 63
  within-subject 25

Wald test 88
  logistic regression 88, 89
  Poisson regression 93
washout period 38
Weibull model 134
weighted kappa 118
weighted mean 22, 23
Wilcoxon rank sum (two-sample) test 60–1
  statistical tables 142, 146
Wilcoxon signed ranks test 55, 57–8
  statistical table 142, 145
within-subject/group variation 25, 63, 118

zero cell count, logistic regression 89
z-test 54
z-value 55, 56, 142