Complex sampling and R.

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Why are surveys special?

- Probability samples come with a lot of meta-data that has to be linked correctly to the observations, so software was specialized
- Interesting data sets tend to be large, so hardware was specialized
- Design-based inference literature is largely separate from rest of statistics, doesnt seem to have a unifying concept such as likelihood to rationalize arbitrary choices.

In part, too, the specialized terminology has formed barriers around the territory. At one recent conference, I heard a speaker describe methods used in his survey with the sentence, We used BRR on a PPS sample of PSUs, with MI after NRFU

—Sharon Lohr, The American Statistician, 5/2004

Times are changing

- Connections between design-based inference and semiparametric models

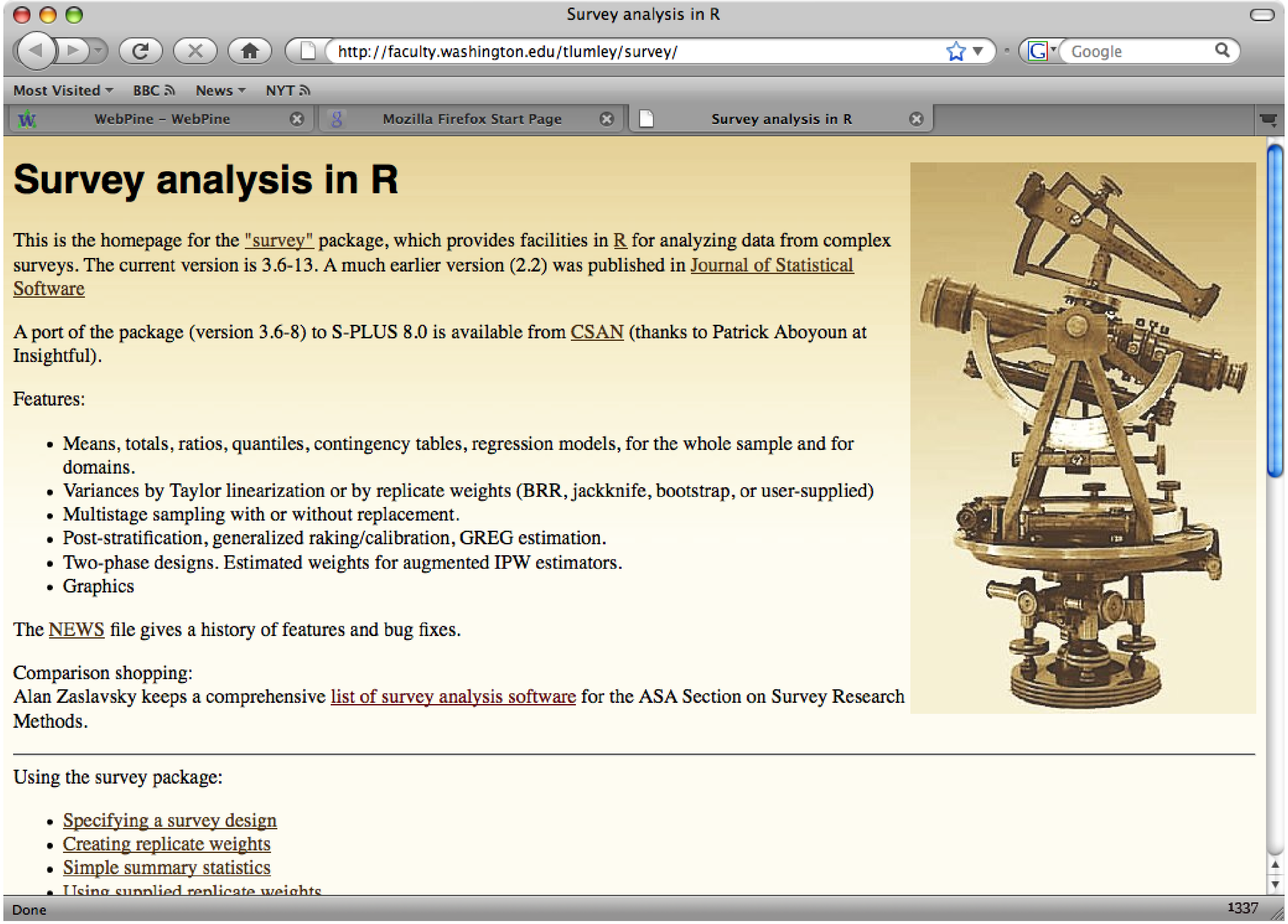
- Increasing use of ‘sandwich’ standard errors in biostatistics

- Connections between sampling weights and causal inference

- Increasing availability of design-based methods in standard software

- Increasing use of complex designs in epidemiology

R Survey package



Survey analysis in R

This is the homepage for the "survey" package, which provides facilities in R for analyzing data from complex surveys. The current version is 3.6-13. A much earlier version (2.2) was published in Journal of Statistical Software

A port of the package (version 3.6-8) to S-PLUS 8.0 is available from CSAN (thanks to Patrick Aboyoun at Insightful).

Features:

- Means, totals, ratios, quantiles, contingency tables, regression models, for the whole sample and for domains.
- Variances by Taylor linearization or by replicate weights (BRR, jackknife, bootstrap, or user-supplied)
- Multistage sampling with or without replacement.
- Post-stratification, generalized raking/calibration, GREG estimation.
- Two-phase designs. Estimated weights for augmented IPW estimators.
- Graphics

The NEWS file gives a history of features and bug fixes.

Comparison shopping:
Alan Zaslavsky keeps a comprehensive list of survey analysis software for the ASA Section on Survey Research Methods.

Using the survey package:

- Specifying a survey design
- Creating replicate weights
- Simple summary statistics
- Using supplied replicate weights

http://faculty.washington.edu/tlumley/survey/

R Survey package

Version 3.6-13 is current, containing approximately 6000 lines of interpreted R code. (cf 250,000 lines of Fortran for VPLX)

Version 2.3 was published in Journal of Statistical Software.

Major changes since then are finite population corrections for multistage sampling, calibration and generalized raking, tests of independence in contingency tables, better tables of results, simple two-phase designs.

Design principles

- Ease of maintenance and debugging by code reuse

- Speed and memory use not initially a priority: dont optimize until there are real use-cases to profile.

- Rapid release, so that bugs and other infelicities can be found and fixed.

- Emphasize features that look like biostatistics (regression, calibration, survival analysis, exploratory graphics)

Intended market

- Methods research (because of programming features of R)
- Teaching (because of cost, use of R in other courses)
- Secondary analysis of national surveys (regression features, R is familiar to non-survey statisticians)
- Two-phase designs in epidemiology

Outline

- Describing survey designs: `svydesign()`

- Summary statistics: mean, total, quantiles, design effect

- Tables of summary statistics, domain estimation.

- Graphics: histograms, hexbin scatterplots, smoothers.

- Regression modelling: `svyglm()`

- Calibration of weights: `postStratify()`, `calibrate()`

Objects and Formulas

Collections of related information should be kept together in an object. For surveys this means the data and the survey meta-data.

The way to specify variables from a data frame or object in R is a formula

```
~a + b + I(c < 5*d)
```

The survey package always uses formulas to specify variables in a survey data set.

Basic estimation ideas

Individuals are sampled with known probabilities π_i from a population of size N to end up with a sample of size n. The population can be a full population or an existing sample such as a cohort.

We write $R_i = 1$ if individual i is sampled, $R_i = 0$ otherwise

The design-based inference problem is to estimate what any statistic of interest would be if data from the whole population were available.

Basic estimation ideas

For a population total this is easy: an unbiased estimator of

$$T_X = \sum_{i=1}^{N} x_i$$

is

$$\hat{T}_X = \sum_{i:R_i=1} \frac{1}{\pi_i} X_i$$

Standard errors follow from formulas for the variance of a sum: main complication is that we do need to know cov$[R_i, R_j]$.

Basic estimation ideas

Other statistics follow from sums: if the statistic on the whole population would solve the estimating equation

$$\sum_{i=1}^{N} U_i(\theta) = 0$$

then a design-based estimate will solve

$$\sum_{i:R_i=1} \frac{1}{\pi_i} U_i(\theta) = 0$$

Standard errors come from the delta method or from resampling (actually reweighting).

Theoretical details can become tricky, especially if $U_i()$ is not a function of just one observation. More information later today.

Describing surveys to R

Stratified independent sample (without replacement) of California schools

```
data(api)
dstrat <- svydesign(id=~1,strata=~stype, weights=~pw,
     data=apistrat, fpc=~fpc)
```

- `stype` is a factor variable for elementary/middle/high school
- `fpc` is a numeric variable giving the number of schools in each stratum. If omitted we assume sampling with replacement
- `id=∼1` specifies independent sampling.
- `apistrat` is the data frame with all the data.
- `pw` contains sampling weights ($1/\pi_i$). These could be omitted since they can be computed from the population size.

Note that all the variables are in `apistrat` and are specified as formulas.

Describing surveys to R

```
> dstrat
Stratified Independent Sampling design
svydesign(id = ~1, strata = ~stype, weights = ~pw, data = apistrat,
fpc = ~fpc)
> summary(dstrat)
Stratified Independent Sampling design
svydesign(id = ~1, strata = ~stype, weights = ~pw, data = apistrat,
fpc = ~fpc)
Probabilities:
Min. 1st Qu. Median Mean 3rd Qu. Max.
0.02262 0.02262 0.03587 0.04014 0.05339 0.06623
Stratum Sizes:
E H M
obs 100 50 50
design.PSU 100 50 50
actual.PSU 100 50 50
Population stratum sizes (PSUs):
E M H
4421 1018 755
Data variables:
[1] "cds" "stype" "name" "sname" "snum" "dname"
[7] "dnum" "cname" "cnum" "flag" "pcttest" "api00"
...
```

Describing surveys to R

Cluster sample of school districts, using all schools within a district.

```
dclus1 <- svydesign(id=~dnum, weights=~pw, data=apiclus1, fpc=~fpc)
```

- `dnum` is a (numeric) identifier for school district
- No stratification, so no `strata=` argument

```
> summary(dclus1)
1 - level Cluster Sampling design
With (15) clusters.
svydesign(id = ~dnum, weights = ~pw, data = apiclus1, fpc = ~fpc)
Probabilities:
Min. 1st Qu. Median Mean 3rd Qu. Max.
0.02954 0.02954 0.02954 0.02954 0.02954 0.02954
Population size (PSUs): 757
Data variables:
[1] "cds" "stype" "name" "sname" "snum" "dname"
[7] "dnum" "cname" "cnum" "flag" "pcttest" "api00"
...
```

Describing surveys to R

Two-stage sample: 40 school districts and up to 5 schools from each

```
dclus2 <- svydesign(id=~dnum+snum, fpc=~fpc1+fpc2, data=apiclus2)
```

- `dnum` identifies school district, `snum` identifies school
- `fpc`1 is the number of school districts in population,`fpc2` is number of schools in the district.
- Weights are computed from `fpc1` and `fpc2`

```
> summary(dclus2)
2 - level Cluster Sampling design
With (40, 126) clusters.
svydesign(id = ~dnum + snum, fpc = ~fpc1 + fpc2, data = apiclus2)
Probabilities:
Min. 1st Qu. Median Mean 3rd Qu. Max.
0.003669 0.037740 0.052840 0.042390 0.052840 0.052840
Population size (PSUs): 757
Data variables:
[1] "cds" "stype" "name" "sname" "snum" "dname"
[7] "dnum" "cname" "cnum" "flag" "pcttest" "api00"
...
```

Summary statistics

`svymean`, `svytotal`, `svyratio`, `svyvar`, `svyquantile`

All take a formula and design object as arguments, return an object with `coef`, `vcov`, `SE`, `cv` methods.

Mean and total on factor variables give tables of cell means/totals.

Mean and total have `deff` argument for design effects and the returned object has a `deff` method.

```
> svymean(~api00, dclus1, deff=TRUE)
mean SE DEff
api00 644.169 23.542 9.3459
> svymean(~factor(stype),dclus1)
mean SE
factor(stype)E 0.786885 0.0463
factor(stype)H 0.076503 0.0268
factor(stype)M 0.136612 0.0296
```

Summary statistics

```
> svymean(~interaction(stype, comp.imp), dclus1)
mean SE
interaction(stype, comp.imp)E.No 0.174863 0.0260
interaction(stype, comp.imp)H.No 0.038251 0.0161
interaction(stype, comp.imp)M.No 0.060109 0.0246
interaction(stype, comp.imp)E.Yes 0.612022 0.0417
interaction(stype, comp.imp)H.Yes 0.038251 0.0161
interaction(stype, comp.imp)M.Yes 0.076503 0.0217
> svyvar(~api00, dclus1)
variance SE
api00 11183 1386.4
> svytotal(~enroll, dclus1, deff=TRUE)
total SE DEff
enroll 3404940 932235 31.311
```

Summary statistics

```
> mns <- svymean(~api00+api99,dclus1)
> mns
       mean     SE
api00 644.17 23.542
api99 606.98 24.225
> coef(mns)
 api00     api99
644.1694 606.9781
> SE(mns)
 api00      api99
23.54224 24.22504
> vcov(mns)
      api00     api99
api00 554.2371 565.7856
api99 565.7856 586.8526
> cv(mns)
api00        api99
0.03654666 0.03991090
```

Domain estimation

The correct standard error estimate for a subpopulation that isnt a stratum is not just obtained by pretending that the subpopulation was a designed survey of its own.

However, the `subset` function and `"["` method for survey design objects handle all these details automagically, so you can ignore this problem.

The package test suite (`tests/domain.R`) verifies that subpopulation means agree with derivations from ratio estimators and regression estimator derivations. Some more documentation is in the domain vignette.

Note: subsets of design objects don't necessarily use less memory than the whole objects.

Prettier tables

Two main types

- totals or proportions cross-classified by multiple factors
- arbitrary statistics in subgroups

Computing over subgroups

svyby computes a statistic for subgroups specified by a set of factor variables:

```
> svyby(~api99, ~stype, dclus1, svymean)
stype statistics.api99 se.api99
E E 607.7917 22.81660
H H 595.7143 41.76400
M M 608.6000 32.56064
```

~api99 is the variable to be analysed, ~stype is the subgroup variable, dclus1 is the design object, svymean is the statistic to compute.

Lots of options for eg what variance summaries to present

Computing over subgroups

```
> svyby(~api99, ~stype, dclus1, svyquantile, quantiles=0.5,ci=TRUE)
  stype statistics.quantiles     statistics.CIs       se      var
E     E                  615 525.6174, 674.1479 37.89113 1435.738
H     H                  593 428.4810, 701.0065 69.52309  4833.46
M     M                  611 527.5797, 675.2395 37.66903 1418.955

> svyby(~api99, list(school.type=apiclus1$stype), dclus1, svymean)
  school.type statistics.api99 se.api99
E           E         607.7917 22.81660
H           H         595.7143 41.76400
M           M         608.6000 32.56064

> svyby(~api99+api00, ~stype, dclus1, svymean, deff=TRUE)
> svyby(~api99+api00, ~stype, dclus1, svymean, deff=TRUE)
  stype statistics.api99 statistics.api00 se.api99 se.api00
E     E         607.7917         648.8681 22.81660 22.36241
H     H         595.7143         618.5714 41.76400 38.02025
M     M         608.6000         631.4400 32.56064 31.60947
  DEff.api99 DEff.api00
E   5.895734   6.583674
H   2.211866   2.228259
M   2.226990   2.163900
```

Computing over subgroups

```
      stype sch.wide statistic.api99 statistic.api00
E.No      E       No        601.6667        596.3333
H.No      H       No        662.0000        659.3333
M.No      M       No        611.3750        606.3750
E.Yes     E      Yes        608.3485        653.6439
H.Yes     H      Yes        577.6364        607.4545
M.Yes     M      Yes        607.2941        643.2353
```

Computing over subgroups

```
> (a<-svyby(~enroll, ~stype, rclus1, svytotal, deff=TRUE,
+ vartype=c("se","cv","cvpct","var")))
  stype statistics.enroll       se cv.enroll cv%.enroll          var       DEff
E     E         2109717.1 631349.4 0.2992578   29.92578 398602047550 125.039075
H     H          535594.9 226716.6 0.4232987   42.32987  51400414315   4.645816
M     M          759628.1 213635.5 0.2812369   28.12369  45640120138  13.014932

> deff(a)
[1] 125.039075 4.645816 13.014932
> SE(a)
[1] 631349.4 226716.6 213635.5
> cv(a)
[1] 0.2992578 0.4232987 0.2812369
> coef(a)
[1] 2109717.1 535594.9 759628.1

> svyby(~api00,~comp.imp+sch.wide,design=dclus1,svymean,
+ drop.empty.groups=FALSE)
        comp.imp sch.wide statistics.api00 se.api00
No.No         No       No         608.0435 28.98769
Yes.No       Yes       No               NA       NA
No.Yes        No      Yes         654.0741 32.66871
Yes.Yes      Yes      Yes         648.4060 22.47502
```

Functions of estimates

svycontrast computes linear and nonlinear combinations of estimated statistics (in the same object).

```
> a <- svytotal(˜api00 + enroll + api99, dclus1)
> svycontrast(a, list(avg = c(0.5, 0, 0.5), diff = c(1,
0, -1)))
     contrast     SE
avg   3874804 873276
diff   230363  54921
> svycontrast(a, list(avg = c(api00 = 0.5, api99 = 0.5),
diff = c(api00 = 1, api99 = -1)))
     contrast     SE
avg   3874804 873276
diff   230363  54921
```

Functions of estimates

```
> svycontrast(a, quote(api00/api99))
          nlcon     SE
contrast 1.0613 0.0062
> svyratio(~api00, ~api99, dclus1)
Ratio estimator: svyratio.survey.design2(~api00, ~api99, dclus1)
Ratios=
         api99
api00 1.061273
SEs=
            api99
api00 0.006230831
```

Crosstabs

svyby or svymean and svytotal with interaction will produce the numbers, but the formatting is not pretty.

ftable provides formatting:

```
> d<-svyby(~api99 + api00, ~stype + sch.wide, rclus1, svymean,
         keep.var=TRUE, vartype=c("se","cvpct"))
> round(ftable(d),1)
           sch.wide          No                               Yes
             statistics.api99 statistics.api00 statistics.api99 statistics.api00
stype
E     svymean          601.7            596.3            608.3            653.6
      SE                70.0             64.5             23.7             22.4
      cv%               11.6             10.8              3.9              3.4
H     svymean          662.0            659.3            577.6            607.5
      SE                40.9             37.8             57.4             54.0
      cv%                6.2              5.7              9.9              8.9
M     svymean          611.4            606.4            607.3            643.2
      SE                48.2             48.3             49.5             49.3
      cv%                7.9              8.0              8.2              7.7
```

Crosstabs

svyby knows enough to structure the table without help. For other analyses more information is needed

```
> a<-svymean(~interaction(stype,comp.imp), design=dclus1, deff=TRUE)
> b<-ftable(a, rownames=list(stype=c("E","H","M"),comp.imp=c("No","Yes")))
> round(100*b,1)
              stype     E     H     M
comp.imp
No       mean        17.5   3.8   6.0
         SE           2.6   1.6   2.5
         Deff        87.8 131.7 200.4
Yes      mean        61.2   3.8   7.7
         SE           4.2   1.6   2.2
         Deff       137.2 131.4 124.7
```

Testing in tables

`svychisq` does four variations on the Pearson χ^2 test: corrections to the mean or mean and variance of X^2 (Rao–Scott) and two Wald-type tests (Koch et al).

Actual asymptotic distribution of test statistic is linear combination of χ^2_1, which is not hard to compute by numerical inversion of the characteristic function.

I plan to add this for testing in tables, and more importantly because the distribution of the population estimated deviance in generalized linear models is of the same form: allows ‘likelihood ratio tests’.

Graphics

When complex sampling designs are analyzed with regression models it is more important to have good exploratory analysis methods.

Problems with survey data

- large data
- unequal weights.

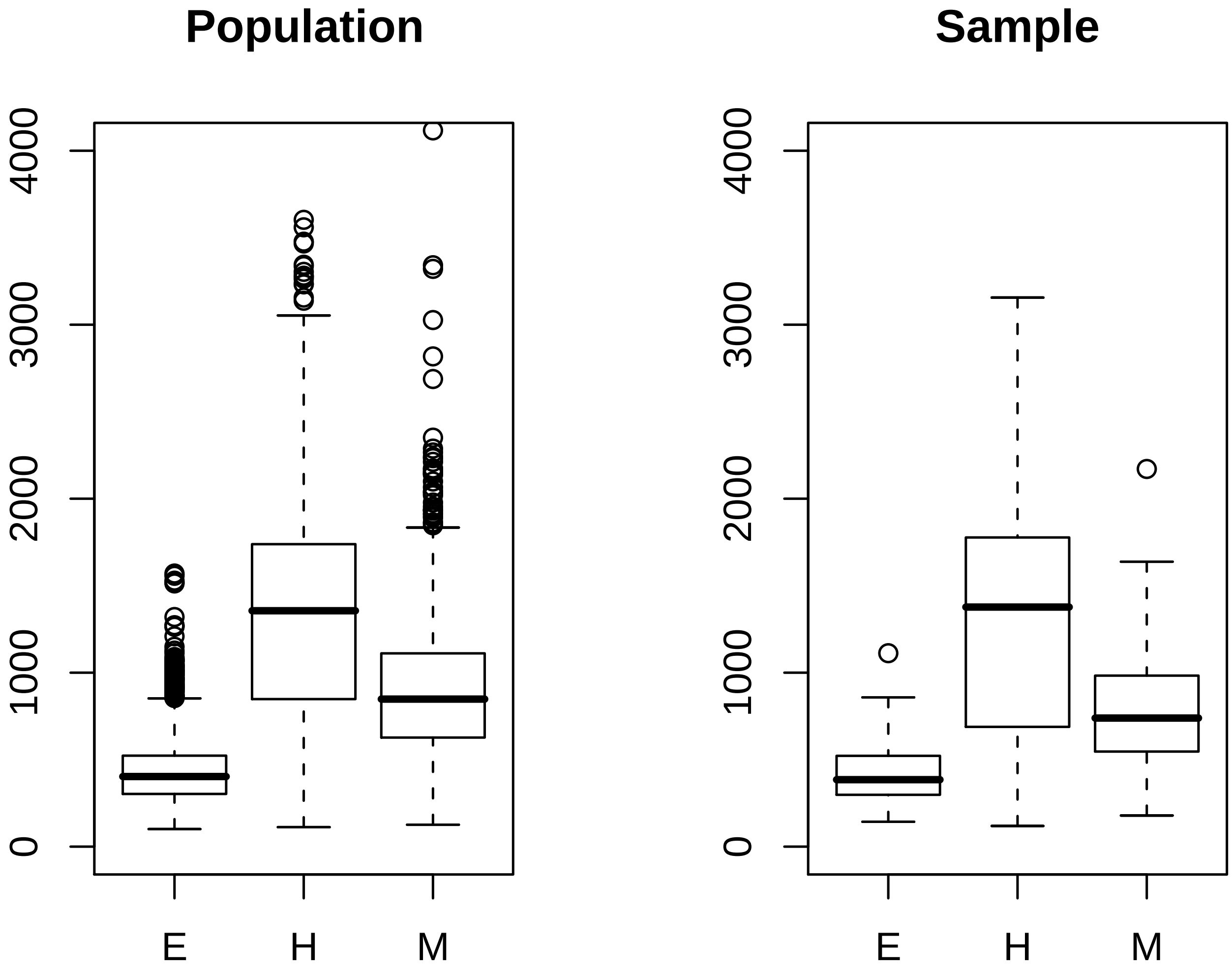
Estimating populations

Boxplots, barplots, and histograms display estimates of the population distribution function for a variable.

We can substitute the survey estimates: boxplots use quantiles, histograms and barplots need tables. eg boxplot of enrollment by school type (Elementary/Middle/High)

```
svyboxplot(enroll~stype, design=srs)
```

Estimating populations



Scatterplots

This approach doesn't work for scatterplots. We need to incorporate weights in the plotting symbols.

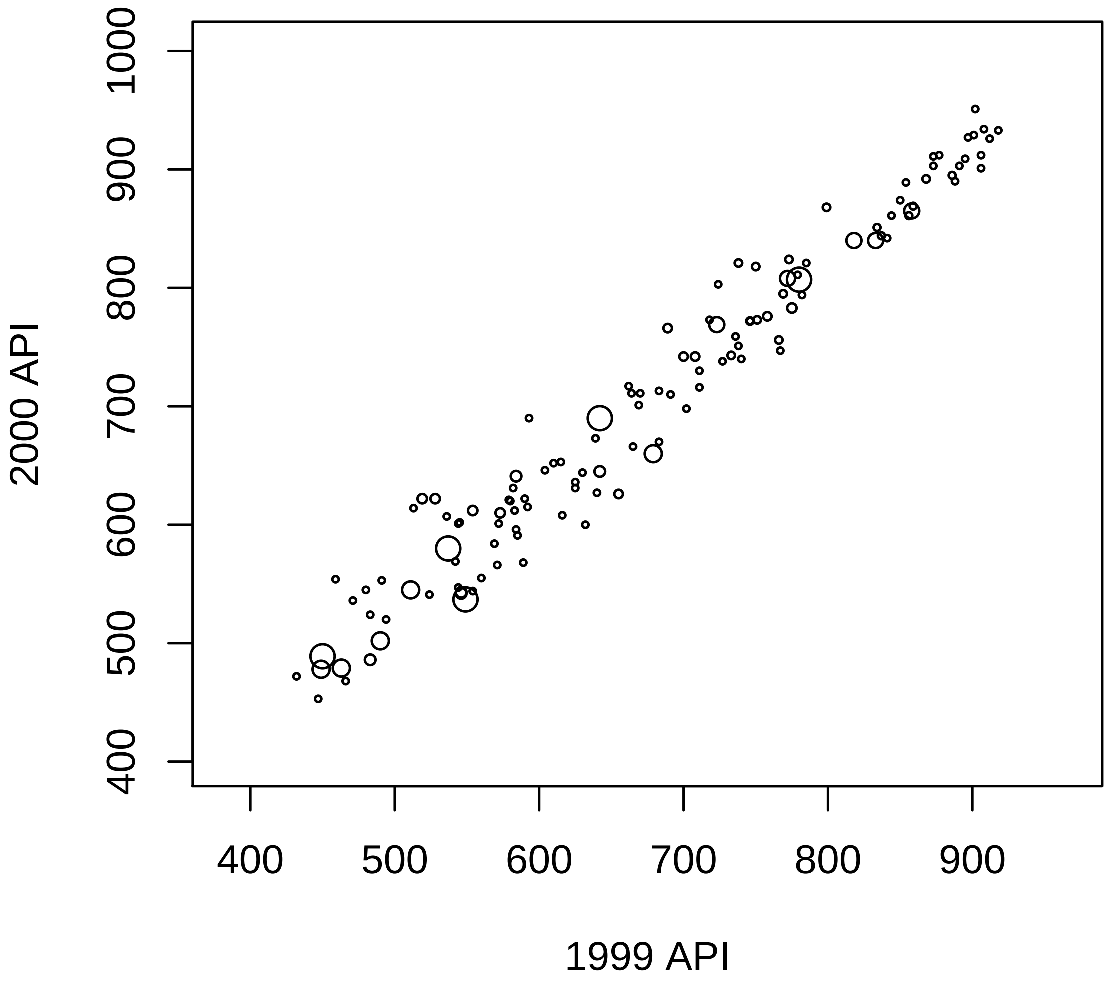
One approach is the bubble plot: radius or area of circle proportional to sampling weight.

Another is transparent color: opacity for each point is proportional to sampling weight, giving a density estimation effect.

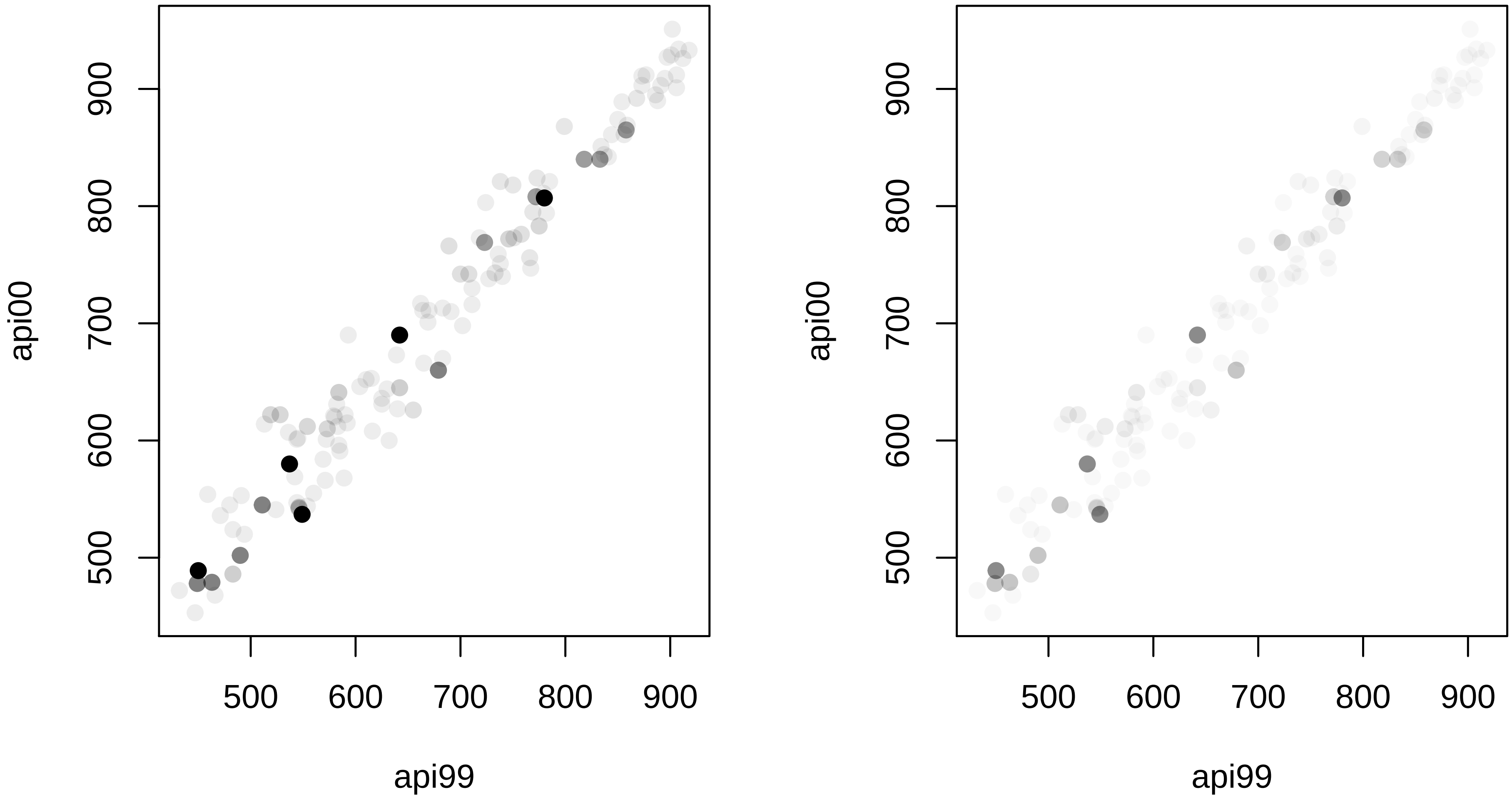
Bubble plots work well with small data sets, badly with large data sets.

Transparency works well with large data sets, badly with small data sets.

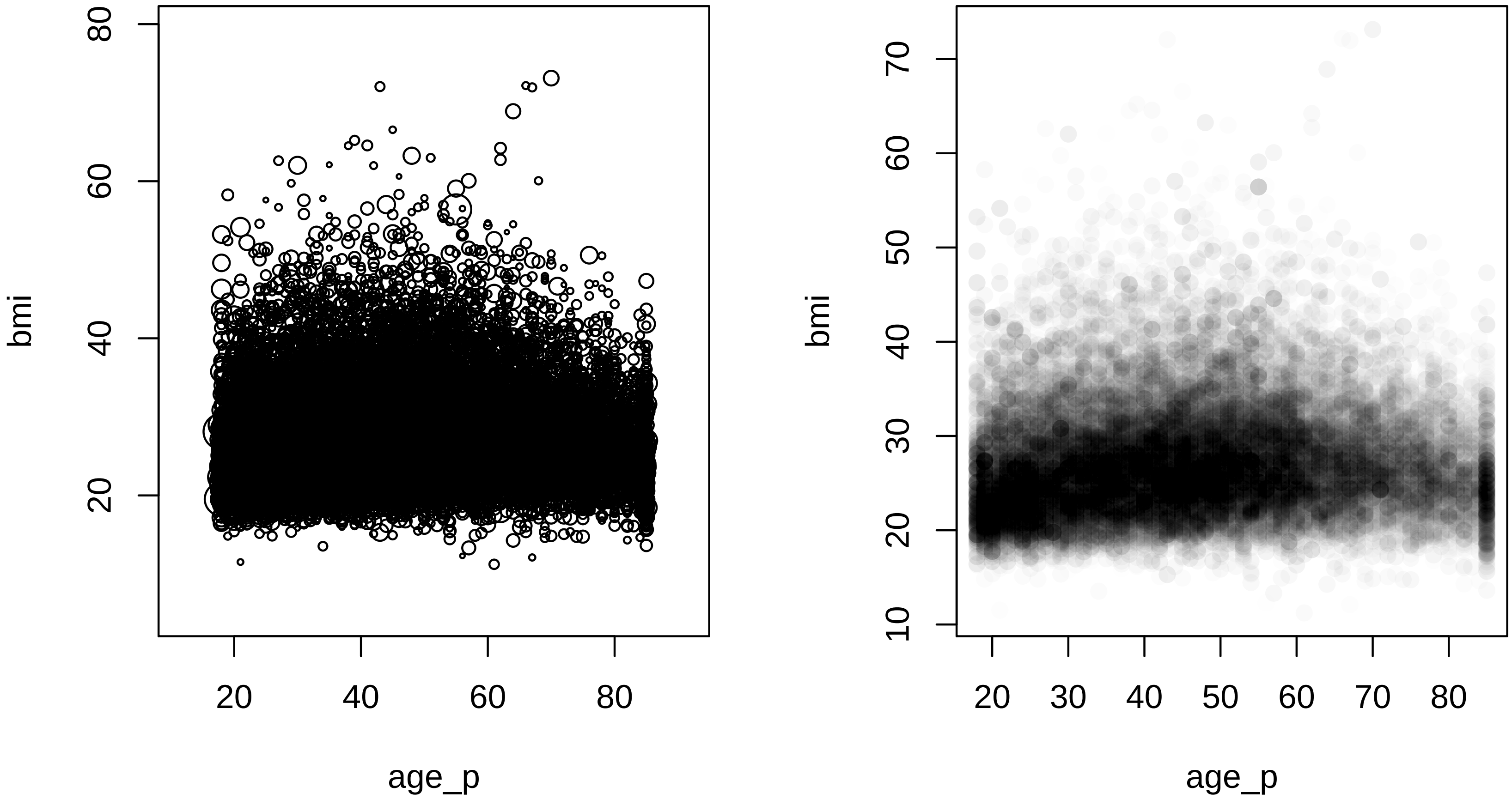
Scatterplots



Scatterplots



Scatterplots



Binning and smoothing

Hexagonal binning divides the plotting area into hexagons, counts the number in each hexagon [Carr, 1987, JASA]. In dense regions this has similar effect to transparency, but allows outliers to be seen, and produces much smaller graphics files.

For survey data we just add up the weight in each bin to get the estimated population numbers in each bin.

In R: `svyplot(bmi˜age_p, design=nhis, style="hex")}`

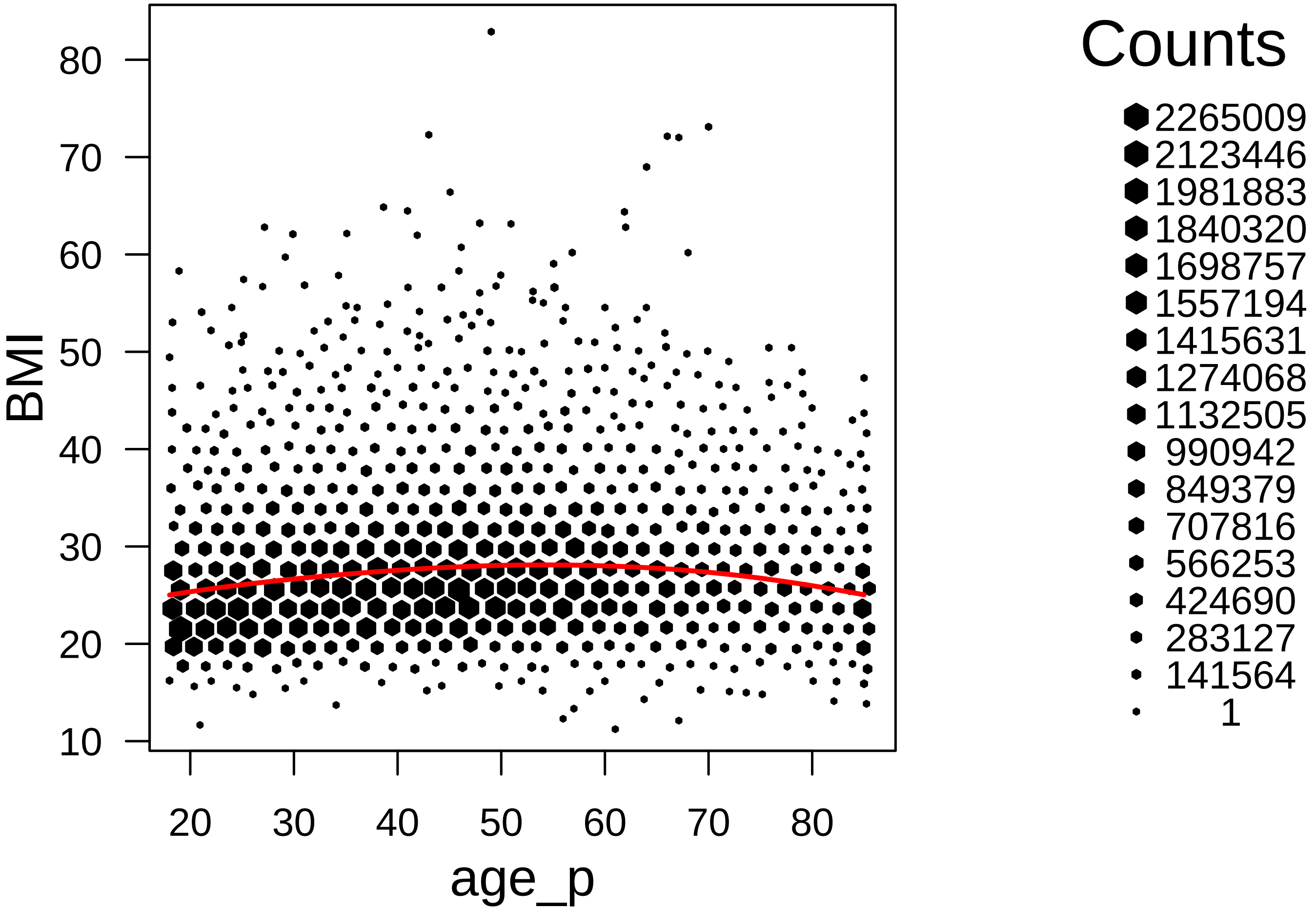
Binning and smoothing

Scatterplot smoothers fit a smooth curve through the middle of the data. There are many variants, but they all work by estimating the mean value of Y using points in a small interval of values of x. `svysmooth()` uses a fast binned kernel smoother (Matt Wand).

In R use `svysmooth` to create a smooth curve and then `plot` to draw it.

```
smth <- svysmooth(api00~api99, stratrs, bandwidth=40)
plot(smth)
```

Binning and smoothing



Regression models

- `svyglm` for linear and generalized linear models

- `svycoxph` for Cox model (no std errors on survival curves yet)

For these models the point estimates are the same for frequency weights, sampling weights, or precision weights, so the point estimation can just reuse the ordinary regression code.

Regression models

More general models eg censored parametric regression models, can be fitted with `svymle`, which takes a loglikelihood and a set of model formulas for one or more of the parameters in the likelihood.

This is harder to get right.

`svymle` is still limited to models where the objective function is a sum of single-observation loglikelihoods: no mixed models.

Simulations

An advantage of using R for survey analysis is easier simulations.

A case–control study could be analyzed as a stratified random sample (stratified on case status), as survey statisticians do, or by maximum likelihood, as biostatisticians do.

We can compare these analyses by simulation [cf Scott & Wild, JRSSB 2000].

```
population<-data.frame(x=rnorm(10000))
expit <- function(eta) exp(eta)/(1+exp(eta))
population$y<- rbinom(10000, 1, expit(population$x-4))
population$wt<-ifelse(population$y==1, 1,(10000-sum(population$y))/600)

one.sample<-function(){
   cases<-which(population$y==1)
   controls<-sample(which(population$y==0),600)
   population[c(cases,controls),]
}
```

Simulations

```
mle<-function(sample) coef(glm(y~x, data=sample, family=binomial()))
svy<-function(sample){
   design<-svydesign(id=~1,strat=~y, weight=~wt, data=sample)
   coef(svyglm(y~x, design=design, family=quasibinomial()))
}
```

Testing shows that it seems to work, and 3 replicates takes about 1 second. 1000 replicates will take about 5 minutes.

```
> replicate(3, {d<-one.sample(); c(mle(d), svy(d))})
                  [,1]       [,2]       [,3]
(Intercept) -1.1575190 -1.1570389 -1.1347550
x            0.9621509  0.9834298  0.9640187
(Intercept) -3.9351437 -3.9335068 -3.8950293
x            0.9514965  0.9725670  0.9194183
```

Simulations

The true parameter values are $(-4, 1)$. Based on 1000 simulations the bias and variability of the estimators are

```
> results<-replicate(1000, {d<-one.sample(); c(mle(d), svy(d))})
> round(apply(results,1,median)-c(-4,1),2)
(Intercept)           x (Intercept)           x
       2.85        0.01        0.08       -0.02
> round(apply(results,1,mad),3)
(Intercept)           x (Intercept)           x
      0.017       0.060       0.035       0.080
```

So the MLE has a relative efficiency of nearly 2 for the slope estimate and is biased for the intercept, as expected.

Misspecified model

Try the analysis when the true model is not linear

$$\text{logit} P[Y = 1|X = x] = e^x - 4$$

but still fit

$$\text{logit} P[Y = 1|X = x] = \alpha + \beta x$$

'True' answer fitting logistic model to population is $(-3.66, 0.75)$

```
> round(apply(results,1,median)-c(-3.6625,0.7518),2)
(Intercept)           x (Intercept)           x
       2.84       -0.16        0.00        0.00
> round(apply(results,1,mad),3)
(Intercept)           x (Intercept)           x
      0.005       0.033       0.013       0.049
```

MLE is biased for population result but has lower variance.

Case-control example

`data(esoph)` in R are data from a case–control study of esophageal cancer in Ile-et-Vilaine, in northern France. The study examined smoking and alcohol consumption as risk factors.

Alcohol consumption is coded into categories 0-39, 40-79, 80-119, 120+ grams/day, smoking into 0-9, 10-19, 20-29, 30+ grams/day.

Age is an extremely strong risk factor, and so is quite likely to be a confounder. It is coded in 10-year categories.

Case-control example

```
> summary(model1)
Call:
glm(formula = cbind(ncases, ncontrols) ~ agegp + tobgp + alcgp,
    family = binomial(), data = esoph)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.6891  -0.5618  -0.2168   0.2314   2.0643

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  -5.9108     1.0302  -5.737 9.61e-09 ***
agegp35-44    1.6095     1.0676   1.508 0.131652
agegp45-54    2.9752     1.0242   2.905 0.003675 **
agegp55-64    3.3584     1.0198   3.293 0.000991 ***
agegp65-74    3.7270     1.0253   3.635 0.000278 ***
agegp75+      3.6818     1.0645   3.459 0.000543 ***
tobgp10-19    0.3407     0.2054   1.659 0.097159 .
tobgp20-29    0.3962     0.2456   1.613 0.106708
tobgp30+      0.8677     0.2765   3.138 0.001701 **
alcgp40-79    1.1216     0.2384   4.704 2.55e-06 ***
alcgp80-119   1.4471     0.2628   5.506 3.68e-08 ***
alcgp120+     2.1154     0.2876   7.356 1.90e-13 ***
```

Case-control example

Alcohol and tobacco both show increasing association with increasing dose. We need tests for the set of coefficients for each of these variables.

Likelihood ratio tests are natural for maximum likelihood

```
>  anova(update(model1,.~.-tobgp), model1, test="Chisq")
Analysis of Deviance Table

Model 1: cbind(ncases, ncontrols) ~ agegp + alcgp
Model 2: cbind(ncases, ncontrols) ~ agegp + tobgp + alcgp
  Resid. Df Resid. Dev Df Deviance P(>|Chi|)
1        79     64.572
2        76     53.973  3   10.599     0.014
```

Case-control example

```
>  anova(update(model1,.~.-alcgp), model1, test="Chisq")
Analysis of Deviance Table

Model 1: cbind(ncases, ncontrols) ~ agegp + tobgp
Model 2: cbind(ncases, ncontrols) ~ agegp + tobgp + alcgp
  Resid. Df Resid. Dev Df Deviance P(>|Chi|)
1        79    120.028
2        76     53.973  3   66.054 2.984e-14
```

Case-control example

Wald tests can be extended more easily to probability-weighted models

```
> library(survey)
> regTermTest(model1,~alcgp)
Wald test for alcgp
 in glm(formula = cbind(ncases, ncontrols) ~ agegp + tobgp + alcgp,
    family = binomial(), data = esoph)
Chisq =  57.89887  on  3  df: p= 1.652e-12
> regTermTest(model1,~tobgp)
Wald test for tobgp
 in glm(formula = cbind(ncases, ncontrols) ~ agegp + tobgp + alcgp,
    family = binomial(), data = esoph)
Chisq =  10.76880  on  3  df: p= 0.013044
```

Case-control example

We do not have the sampling fractions for controls, but the incidence of esophageal cancer is about 5/100,000 per year. We do not know how many years of cases were recruited, but it is reasonable to assume the sampling fraction is between 1/2000 and 1/20000 for controls.

Using the `survey` package we can fit the same model with probability weights. It is necessary first to expand the data to one record per person, then to declare the sampling design, then use `svyglm` to fit the model.

The estimated odds ratios based on a sampling fraction of 1/2000 are very similar to the unweighted analysis, and the intercept is different, as expected.

Case-control example

```
> desoph<-svydesign(id=~1, weight=~prob, data=expanded)
> pmodel1<-svyglm(cancer~agegp+tobgp+alcgp, design=desoph, family=binomial)

> round(rbind(unweighted=coef(model1), weighted=coef(pmodel1)),3)

           (Intercept) agegp35-44 agegp45-54 agegp55-64 agegp65-74 agegp75+
unweighted      -5.911      1.610      2.975      3.358      3.727    3.682
weighted       -13.422      1.607      2.995      3.321      3.644    3.657

           tobgp10-19 tobgp20-29 tobgp30+ alcgp40-79 alcgp80-119 alcgp120+
unweighted      0.341      0.396    0.868      1.122       1.447     2.115
weighted        0.275      0.340    0.782      1.104       1.437     2.004
```

Case-control example

In this example the standard errors are also similar

```
> round(rbind(unweighted=SE(model1), weighted=SE(pmodel1)),2)

            (Intercept) agegp35-44 agegp45-54 agegp55-64 agegp65-74 agegp75+
unweighted        1.03       1.07       1.02       1.02       1.03     1.06
weighted          1.01       1.06       1.02       1.01       1.02     1.06

           tobgp10-19 tobgp20-29 tobgp30+ alcgp40-79 alcgp80-119 alcgp120+
unweighted       0.21       0.25     0.28       0.24        0.26      0.29
weighted         0.21       0.25     0.29       0.24        0.27      0.30
```

Sometimes the probability-weighted analysis is very inefficient, sometimes it is reasonably efficient.

Two-phase sampling

- Phase 1: sample people according to some probability design $\pi_{1,i}$, measure variables

- Phase 2: subsample people from the phase 1 sample using the variables measured at phase 1, $\pi_{2|1,i}$ and measure more variables

Sampling probability $\pi_i = \pi_{1,i} \times \pi_{2|1,i}$ and use $1/\pi_i$ as sampling weights.

These are **not** (in general) the marginal probability that i is in the sample, because $\pi_{2|1,i}$ may depend on which other observations are in the phase-one sample.

Two-phase sampling

For all the designs today $\pi_{1,i}$ is constant, so its value doesn't affect anything except estimated population totals.

We don't care about population totals in this setting, so we don't need to know the value of $\pi_{1,i}$ (eg can set to 1).

An alternative view is that we are using model-based inference at phase one, rather than sampling-based inference.

Two-phase sampling

Two sources of uncertainty:

- Phase-1 sample is only part of population
- Phase 2 observes full set of variables on only a subset of people.

Uncertainties at the two phases add.

Designs (survey)

The classic survey example is ‘two-phase sampling for stratification’. This is useful when a good stratifying variable is not available for the population but is easy to measure.

- Take a large simple random sample or cluster sample and measure stratum variables

- Take a stratified random sample from phase 1 for the survey

If the gain from stratification is larger than the cost of phase 1 we have won.

Designs (epi)

Many large cohorts exist in epidemiology. These can be modelled as simple random samples. They have a lot of variables measured.

It is common to want to measure a new variable

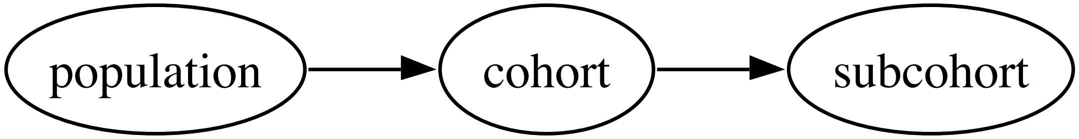
- New assay on stored blood
- Coding of open-text questionnaire
- Re-interview

The classic designs are a simple random sample and a case–control sample.

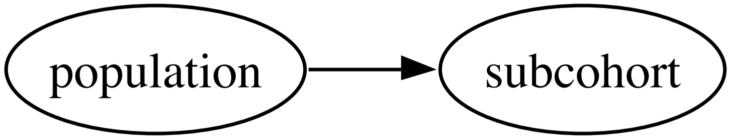
It is often more useful to sample based on multiple phase-1 variables: outcome, confounders, surrogates for phase-2 variable.

Analysis

The true sampling is two-phase



We can ignore the first phase and pretend that we had an unstratified population sample



This is conservative, but sometimes not very. It was used before software for eg Cox models in two-phase samples were developed.

Two-phase case–control

The case–control design stratifies on Y. We can stratify on X as well

	X=0	X=1	
Y=0	a	b	m_0
Y=1	c	d	m_1
	n_0	n_1	

The estimated variance of β is

$$\mathrm{var}[\widehat{\beta}] = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$$

Ideally want all cells about the same size in this trivial case.

Example: Wilm's Tumor

- Wilm's Tumor is a rare childhood cancer of the kidney. Prognosis is good in early stage or favourable histology disease.
- Histology is difficult to determine. NWTSG central pathologist is much better than anyone else.
- To reduce cost of followup, consider central histology only for a subset of cases.
- Sample all relapses, all patients with unfavorable histology by local pathologist, 10% of remainder

[Breslow & Chatterjee (1999) Applied Statistics 457–68]

Analyses: sampling weights

Phase 1

```
          relapse
instit       0     1
good      3207   415
bad        250   156
```

Phase 2

```
          relapse
instit     0     1
good     314   415
bad      250   156
```

Weight is 1/sampling fraction in relapse × local histology strata: 1.0 for cases, controls with unfavorable local histology, $3207/314 = 10.2$ for controls with favorable local histology.

Analyses: sampling weights

Effect of unfavorable histology

	log OR	SE
Full data	1.81	0.11
Subcohort		
(ignoring sampling)	-0.02	0.12
two-phase	1.78	0.155
single-phase	1.78	0.159

Can use any analysis, eg RR rather than OR

	log RR	SE
Full data	1.39	0.07
Subcohort		
(ignoring sampling)	-0.01	0.06
two-phase	1.36	0.101
single-phase	1.36	0.107

Computation in R

Declaring a two-phase design

```
dccs2 <- twophase(id = list(~id, ~id), subset = ~in.ccs,
              strata = list(NULL, ~interaction(instit, rel)),
              data = nwt.exp)
```

- Data set has records for all phase-one people, `subset` variable indicates membership in second phase

- Two `id`, two `strata`.

- Second-phase `weights` and `fpc` are worked out by R

Computation in R

We can compare to the conservative approximation: single-phase sampling with replacement

```
dcons<-svydesign(id=~seqno, weights=weights(dccs2),
       data=subset(nwtco, incc2))
```

Almost no advantage of two-phase analysis in this example; but wait until this afternoon and calibration of weights.

Computation in R

```
>  summary(svyglm(rel~factor(stage)*factor(histol),design=dccs2,
                         family=quasibinomial()))
                             Estimate Std. Error t value Pr(>|t|)
(Intercept)                     -2.6946     0.1246 -21.623  < 2e-16 ***
factor(stage)2                   0.7733     0.1982   3.901 0.000102 ***
factor(stage)3                   0.7400     0.2048   3.614 0.000315 ***
factor(stage)4                   1.1322     0.2572   4.401 1.18e-05 ***
factor(histol)2                  1.1651     0.3196   3.646 0.000279 ***
factor(stage)2:factor(histol)2   0.3642     0.4462   0.816 0.414511
factor(stage)3:factor(histol)2   1.0230     0.3968   2.578 0.010056 *
factor(stage)4:factor(histol)2   1.7444     0.4973   3.508 0.000470 ***
```

```
>  summary(svyglm(rel~factor(stage)*factor(histol),design=dcons,
                         family=quasibinomial()))
                               Estimate Std. Error t value Pr(>|t|)
(Intercept)                     -2.6946     0.1355 -19.886  < 2e-16 ***
factor(stage)2                   0.7733     0.1982   3.902 0.000101 ***
factor(stage)3                   0.7400     0.2047   3.615 0.000314 ***
factor(stage)4                   1.1322     0.2571   4.403 1.17e-05 ***
factor(histol)2                  1.1651     0.3208   3.632 0.000294 ***
factor(stage)2:factor(histol)2   0.3642     0.4461   0.816 0.414408
factor(stage)3:factor(histol)2   1.0230     0.3974   2.574 0.010169 *
factor(stage)4:factor(histol)2   1.7444     0.4977   3.505 0.000474 ***
```

Computation in R

We are not restricted to logistic regression: eg, log link gives log relative risks rather than log odds ratios. SInce relapse is not rare for unfavorable histology these are noticeably different.

```
>  summary(svyglm(rel~factor(stage)*factor(histol),design=dccs2,
                     family=quasibinomial(log)))
                               Estimate Std. Error t value Pr(>|t|)
(Intercept)                     -2.7600     0.1167 -23.644  < 2e-16 ***
factor(stage)2                   0.7020     0.1790   3.922 9.30e-05 ***
factor(stage)3                   0.6730     0.1849   3.640 0.000285 ***
factor(stage)4                   1.0072     0.2207   4.564 5.58e-06 ***
factor(histol)2                  1.0344     0.2690   3.845 0.000127 ***
factor(stage)2:factor(histol)2   0.1153     0.3405   0.339 0.734920
factor(stage)3:factor(histol)2   0.4695     0.3118   1.505 0.132495
factor(stage)4:factor(histol)2   0.4872     0.3316   1.469 0.142020
```

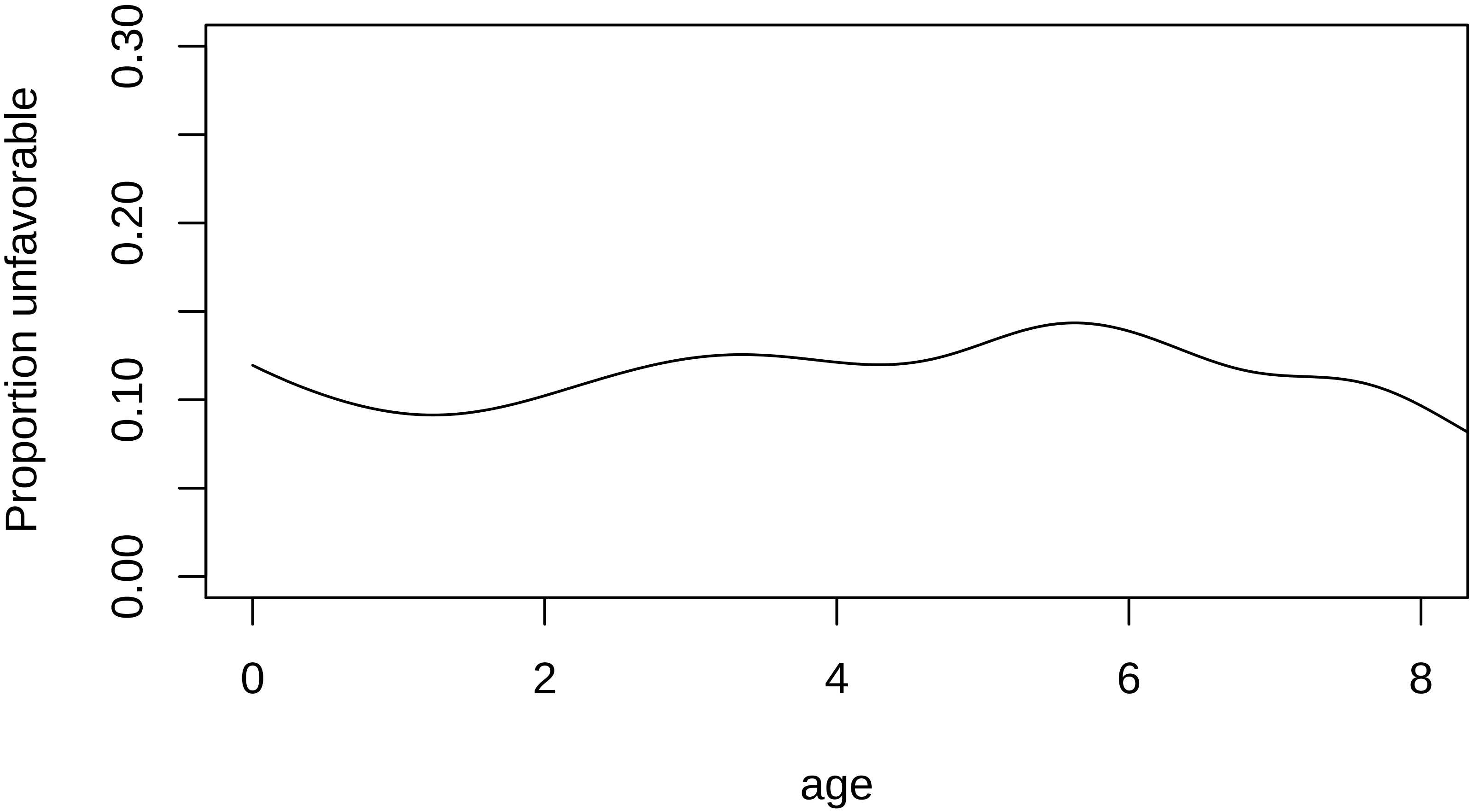
Computation in R

Other exploratory and descriptive analyses are also possible: how does histology vary with age at diagnosis?

[Really needs more detailed classification to be useful analysis]

```
s<-svysmooth(I(histol==2)~I(age/12),design=dccs2,bandwidth=1)
plot(s,ylim=c(0,0.3),xlim=c(0,8),
       xlab="age",ylab="Proportion unfavorable")
```

Computation in R



Case–cohort design

Cox model estimation involves solving

$$\sum_{\text{events}} Z_{\text{event}} - E(\beta, t) = 0$$

where Z_{event} is the covariate for the person having an event and $E(\beta, t)$ is the expected covariate based on a weighted average over everyone at risk at that time.

Case–cohort design

- Prentice (1986) suggested estimating $E(\beta, t)$ from the current case plus a subcohort selected at random at baseline, saving money and computation time.
- Self & Prentice suggested dropping current case from $E(\beta, t)$ for mathematical simplicity.
- Barlow used the subcohort and all cases, with the conservative single-phase sampling standard errors
- Lin & Ying used the same estimates as Barlow, but the correct standard errors.
- Borgan et al (2000) allowed stratified sampling and time-dependent sampling weights.

Advantages

Case–cohort and nested case–control studies have similar power, but in a case–cohort design

- The same subcohort can be used for more than one outcome and for different lengths of followup
- Subcohort defined at baseline allows exposure measurement spread over whole study (for some measurements)
- Information from whole cohort can easily be incorporated when selecting subcohort (eg surrogate exposure) or with post-stratification at time of analysis

Design has been used in ARIC, CHS for measuring genotypes or biomarkers.

Historical artifact

Mathematical techniques in 1980s,1990s, required viewing the Cox model estimating equations

$$\sum_{\text{events}} Z_{\text{event}} - E(\beta) = 0$$

as a process evolving over time.

A member of the subcohort who was in the future going to be a case still had to be treated the same as someone who was not going to become a case, because that information was not predictable. Weight might be 10 until the event and then 1 at the event.

Survey techniques allow a simpler view *sub specie aeternitatis*; no hang-ups about predictable weight processes: weight of 1 for any future case.

Computation

- Prentice, Self & Prentice methods are not just weighted Cox regression, so need some trickery. Mayo Clinic Biostatistics Technical Report #62 describes the trickery and gives S-PLUS and SAS code fragments. `cch()` in R `survival` package is based on these methods.

- Barlow's method, using the conservative single-phase approximateion, is just weighted Cox regression and works in any software with survey or robust standard errors.

- Lin & Ying's method is two-phase weighted Cox regression, needs software for two-phase analysis.

Computation in R

Estimators based on survey-weighted Cox models (Lin & Ying)

```
dcchs<-twophase(id=list(~seqno,~seqno), strata=list(NULL,~rel),
              subset=~I(in.subcohort | rel), data=nwtco)
svycoxph(Surv(edrel,rel)~factor(stage)+factor(histol)+I(age/12),
              design=dcchs)
```

Traditional estimators based on the Therneau & Li trick.

```
fit.ccSP <- cch(Surv(edrel, rel) ~ stage + histol + age,
               data =ccoh.data, subcoh = ~subcohort, id=~seqno,
               cohort.size=4028,  method="SelfPren")

stratsizes<-table(nwtco$instit)
fit.BI<- cch(Surv(edrel, rel) ~ stage + histol + age,
            data =ccoh.data, subcoh = ~subcohort,
            id=~seqno, stratum=~instit, cohort.size=stratsizes,
            method="I.Borgan")
```