Propensity Scores Continued

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UNOS Data Example

- UNOS data
- Survival of pediatric kidney rx
- Effect of living v. cadaveric organ on survival
- Build model for propensity to get cadaveric
- Compared cadaveric v. living
  control/match/balanced by propensity

UNOS: Propensity Fit

- Splines for age, age of donor year
- Interactions of these with presence of previous transplant
- logistic txtype prevtx prevtx##c.yearsp* prevtx##c.agesp* prevtx##c.agedonsp* i.hla
- predict prop
- xtile group=prop, nq(5)

Linear in Propensity

```
. logistic death i.txtype prop

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(2)      =      19.30
                                                  Prob > chi2     =     0.0001
Log likelihood = -1400.3094                       Pseudo R2       =     0.0068

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    1.txtype |    1.38542   .2351663     1.92   0.055      .993334    1.932269
        prop |   1.292506   .2855679     1.16   0.246     .8382373    1.992958
       _cons |   .0360183   .0037452   -31.97   0.000     .0293776    .0441602
------------------------------------------------------------------------------
```

Spline

```
. mkspline prop_sp = prop, cubic nknots(7)

. logistic death txtype prop_sp*

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(7)      =      23.23
                                                  Prob > chi2     =     0.0016
Log likelihood = -1398.3454                       Pseudo R2       =     0.0082

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      txtype |   1.399637   .2433085     1.93   0.053     .9955092    1.967821
    prop_sp1 |   144.3345   1024.966     0.70   0.484     .0001302    1.60e+08
    prop_sp2 |   9.0e-203   5.8e-200    -0.73   0.467            0           .
    prop_sp3 |          .          .     0.72   0.470            0           .
    prop_sp4 |   2.6e-213   1.8e-210    -0.71   0.478            0           .
    prop_sp5 |    4.36994    197.448     0.03   0.974     1.52e-38    1.26e+39
    prop_sp6 |   1.03e+67   1.47e+69     1.08   0.281     1.79e-55    5.9e+188
       _cons |   .0241336   .0161688    -5.56   0.000     .0064914    .0897228
------------------------------------------------------------------------------
```


Quintile

```
. logistic death i.txtype i.group

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(5)      =      23.85
                                                  Prob > chi2     =     0.0002
Log likelihood = -1398.0372                       Pseudo R2       =     0.0085

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    1.txtype |   1.460813   .2433996     2.27   0.023     1.053823    2.024982
             |
       group |
          2  |   1.301893   .2544977     1.35   0.177     .8875235    1.909723
          3  |   1.274882   .2676887     1.16   0.247     .8447766    1.923968
          4  |    1.07496   .2522625     0.31   0.758     .6786397    1.702727
          5  |   1.480443   .3480316     1.67   0.095     .9338694    2.346915
             |
       _cons |   .0327919   .0048379   -23.16   0.000     .0245576    .0437872
------------------------------------------------------------------------------
```

Marginal v. Conditional Effects

- Conditional: what you are used to
  unequal populations compared directly by matching, adjustment, stratification
- Marginal:
  populations made equal on average
  compared overall

Marginal Causal Effects

- p_0 = *Probability of death if everyone got living*
- p_1 = *Probability of death " " got cadaveric*
- Can be estimated by "margins"
  based on a particular model
- $p_1 - p_0 = ACE$
- p_1/p_0 = *Causal RR*
- $p_1 (1-p_0)/(1-p_1)\ p_0$ *Causal OR*

Code for Causal RR

- logistic death i.txtype i.group
  could be any model for the data
- *margins txtype, post*
  post saves some key results
- nlcom (RR: _b[1.txtype] / _b[0.txtype])
  SE can be a little off
- nlcom (logRR: log(_b[1.txtype]) - log(_b[0.txtype]))
  then exponentiate -- always better SE/CI

Code for ACE Risk Difference

- logistic death i.txtype i.group
  fits propensity model
- margins txtype
  calculate predicted
- margins dxdy(txtype)
  calculate different

Risk Difference

Margined Over Quintile

```
. margins txtype

------------------------------------------------------------------------------
             |            Delta-method
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      txtype |
          0  |   .0386335   .0041469     9.32   0.000     .0305057    .0467613
          1  |   .0554319   .0046479    11.93   0.000     .0463223    .0645416
------------------------------------------------------------------------------

. margins, dydx(txtype)

------------------------------------------------------------------------------
             |            Delta-method
             |      dy/dx   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    1.txtype |   .0167985   .0072948     2.30   0.021     .0025008    .0310961
------------------------------------------------------------------------------
```


Code for Causal RR

- logistic death i.txtype i.group
  could be any model for the data
- *margins txtype, post*
  post saves some key results
- nlcom (RR: _b[1.txtype] / _b[0.txtype])
  SE can a little off
- nlcom (logRR: log(_b[1.txtype]) - log(_b[0.txtype]))
  then exponentiate -- always better SE/CI

Causal RR -- Quintile Fit

```
logistic death i.txtype i.group
margins txtype, post

 nlcom (risk_ratio: _b[1.txtype]/_b[0.txtype] )

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  risk_ratio |   1.434816    .228147     6.29   0.000     .9876558    1.881976
------------------------------------------------------------------------------

logistic death i.txtype i.group
margins txtype, post
. nlcom (logRR: log(_b[1.txtype]) - log(_b[0.txtype]))

       logRR:  log(_b[1.txtype]) - log(_b[0.txtype])

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       logRR |   .3610364   .1590079     2.27   0.023     .0493867    .6726861
------------------------------------------------------------------------------
```

marginal RR = 1.43 (1.05, 1.96)

Causal OR -- Quintile Fit

```
logistic death i.txtype i.group
margins txtype, post
. nlcom (OR: (_b[1.txtype]*(1-_b[0.txtype])) / (_b[0.txtype]*(1-_b[1.txtype])) )

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
          OR |   1.460333   .2433062     6.00   0.000     .9834615    1.937204
------------------------------------------------------------------------------


logistic death i.txtype i.group
margins txtype, post
nlcom (OR: log(_b[1.txtype])+log(1-_b[0.txtype])-log(_b[0.txtype])-log(1-_b[1.txtype]) )

  ------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
          OR |   .3786644   .1666101     2.27   0.023     .0521146    .7052142
------------------------------------------------------------------------------
```

marginal OR = 1.46 (1.05, 2.02)

Usual Regression

Basic Model

```
. logistic death txtype prevtx year age age_don i.hla

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(11)     =     109.57
                                                  Prob > chi2     =     0.0000
Log likelihood = -1355.1776                       Pseudo R2       =     0.0389

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      txtype |   1.352607   .2104378     1.94   0.052     .9971076    1.834852
      prevtx |   1.025545    .148438     0.17   0.862     .7722383    1.361941
        year |   .8667789   .0149232    -8.30   0.000     .8380179    .8965269
         age |   .9693932   .0102048    -2.95   0.003     .9495972     .989602
     age_don |   .9976164   .0042928    -0.55   0.579     .9892381    1.006066
             |
      hlamat |
          1  |   1.118378   .2534091     0.49   0.621     .7173287     1.74365
          2  |   .9684949   .2219639    -0.14   0.889     .6180381    1.517677
          3  |   .8122357   .1911163    -0.88   0.377       .51215    1.288151
          4  |   .8067894   .2186669    -0.79   0.428     .4743032    1.372348
          5  |   .9442997   .3425764    -0.16   0.874     .4637757    1.922701
          6  |     .89599   .3324897    -0.30   0.767     .4329461    1.854268
```


Usual Regression

Spine/Interaction Model

```
 logistic death txtype prevtx prevtx##c.yearsp* prevtx##c.agesp* prevtx##c.agedonsp* i.hla

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(32)     =     162.11
                                                  Prob > chi2     =     0.0000
Log likelihood = -1328.9077                       Pseudo R2       =     0.0575

------------------------------------------------------------------------------------
             death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------------+----------------------------------------------------------------
            txtype |   1.472337   .2414501     2.36   0.018     1.067623    2.030471
            prevtx |   6.5e+189   3.3e+192     0.86   0.389     1.8e-242           .
           yearsp1 |    .975281   .1156388    -0.21   0.833     .7730419    1.230429
           yearsp2 |   1.058858   .8618707     0.07   0.944     .2147788    5.220161
           yearsp3 |   .2970671    1.00785    -0.36   0.721     .0003846    229.4555
           yearsp4 |   3.538337   15.02097     0.30   0.766     .0008615    14531.97
                   |
  prevtx#c.yearsp1 |
                1  |   .8033063   .2045974    -0.86   0.390     .4876241    1.323358
                   |
  prevtx#c.yearsp2 |
                1  |   3.321273   6.292198     0.63   0.526     .0810385    136.1187
                   |
```

and more!

20 Strata

```
xtile group3=prop, nq(20)
logit death txtype, i.group3

 logistic death txtype i.group3

Logistic regression                               Number of obs   =       7347
                                                  LR chi2(20)     =      50.29
                                                  Prob > chi2     =     0.0002
Log likelihood = -1384.8183                       Pseudo R2       =     0.0178

------------------------------------------------------------------------------
       death | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      txtype |   1.427705   .2478669     2.05   0.040      1.01592      2.0064
             |
      group3 |
          2  |    .326775   .1705254    -2.14   0.032     .1175046    .9087467
          3  |   .7250355    .292959    -0.80   0.426     .3284139    1.600653
          4  |   1.137948   .4122547     0.36   0.721     .5594356    2.314701
          5  |   1.500861   .5153622     1.18   0.237      .765697    2.941874
          6  |   .8503287   .3286302    -0.42   0.675     .3986753    1.813654

ETC
```


Models

Model	Risk Diff	Marginal OR	Cond. OR
Prop: Quint	0.017	1.46	1.46
Prop: Spline	0.015	1.40	1.40
Reg: Simple	0.014	1.35	1.35
Reg: Spline +Int	0.017	1.47	1.46

Regression	Propensity Score
assess confounding	assess confounding
draw DAG	draw DAG
assess predictor size	assess predictor size
select confounders	select confounders
model for outcome	model exposure
check overlap	check overlap
	check for interaction
	compare outcome exposure adjusted for propensity

Major Differences

- Propensity scores (PS) only useful for binary exposure
- Model size can be very different
  PS great for rare outcome/common exposure
- PS involves less modeling of the outcome
- More choices for controlling for propensity
- PS involves many ad-hoc choices

Final Recommendations

- Propensities useful for binary variable or possibly ordinal variable
- Switches modeling to exposure *rather than outcome*
  - Advantage if exposure is common, outcome is rare
- Makes overlap transparent
- Analysis for like "randomized trial" less modeling of the outcome
- Often similar results

Models for Prediction

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Distinct Objectives

for a regression model

1. Developing a Model for Prediction/ Stratification
2. Adjusted Effect of Single Variable
3. Identifying Multiple Predictors of Outcome
4. Adjustment to Improve Efficiency in RCT

Example: Prediction

- Cohort: 11,701 community-dwelling elders
- Predictors: age, co-morbidities, functional status
- 42 candidate predictors
- Follow-up: mortality over 4 years
  1,361 deaths
- Who is at the highest risk of death?

Lee, SJ et al. JAMA. 2006;295:801-808.

Study Context

- Objective: inform patients/risk stratification
- Predictors obtained from patient report
- Wanted index "as simple as possible"
- Combine functional measure + co-morbidities

Statistical Objective

- Develop a regression model
- Discriminates between high and low risk
  how to quantify discriminatory ability?
- Pure prediction is not enough
  want some parsimony/interpretation
  external validity
- Implications for predictor selection
  all 42 significantly associated with death

Getting Best Model

- Need a measure of model predictiveness
- Sift through large # models
  number of models = 2^p
- Handle optimism/overfitting
  "detecting signal v. quirks of the data"
- Consider what will validate externally

Finding Our Model

Look at every possible model and choose the best one in terms of prediction

1. Infeasible in many cases
2. Susceptible to "overfitting"
3. Places no value on simplicity or plausibility

Measures of Prediction

- Log-likelihood
  measure how close model is to the data
  how max. likelihood methods to select model
  analogous to a sum of squares in linear model
- Binary data: C-statistic
  area under ROC curve
  "proportion of person with event has higher risk than someone without event"

A good model optimizes these

Best Subsets

- Consider all possible models
- Each variable may be in or out
  2 possibilities
- Repeated for each predictor
  total number of predictors p
- 2 x .... x 2 (p times) = 2^p
- Increases very fast 2^{42} = 4.4 trillion models
  trillion seconds > 31,000 years
  cut predictors in half: 2.1 million models

Backward Selection

1. Start all variables in the model
2. Fit model
3. Drop term with highest p-value
4. Repeat 2 and 3 until all p-value less than some threshold (e.g., $p < 0.05$)

what is the right threshold? Avoid overfitting

Stepwise Model Selection

- Reduces the model selection immensely
- 42 predictors => 42 possible models
  43 predictors => 43 possible models
- Gives a logical sequence for fitting
  probably don't need to fit all 42
  fit until some criterion is reached
- But will not select the best model

what are limitations of stepwise models?

Overfitting

Overfitting is a broad term that refers to entering too many terms into the model -- for the amount of available data.

This produces unstable, variable estimates. The extreme ones *tend* to be both spurious and also *tend* to get the most focus.

Hence, results are frequently unreplicable.

Example

- Take 5% sample of Lee data
- Fit all variables to data subset
- 0.05 criterion with backward selection
- Would results be reliable?

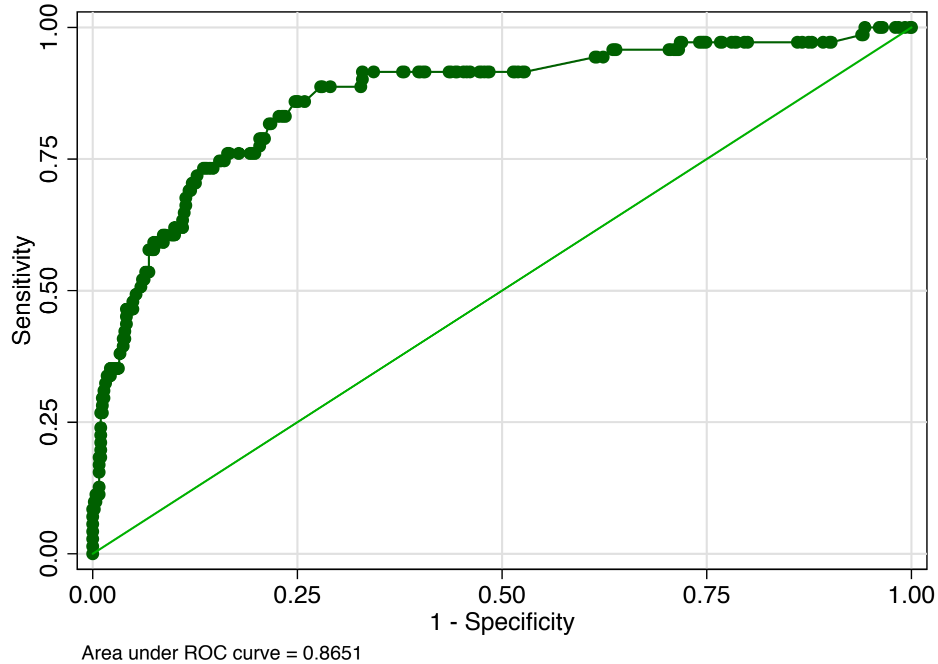
	Odds Ratio	
Variable	test data	full data
walkjog	2.9	3.3
bath	5.0	2.9
couple	0.27	0.58
hrsmemory	15.0	2.9
bmi	2.5	2.3
education (HS)	0.52	0.70
education (college)	0.09	0.49
hrscad	2.2	1.5
hrsincont	0.32	1.0
hrsca	3.4	2.4
gender	0.31	0.45
hrschf	8.7	3.3

Poor Validation

- Odds Ratios consistently overestimated
  consistent overestimation -> bias
- Many estimates outside CI
- More extreme OR -> more overestimated
- Artifact of model selection procedure
  retained only if $p < 0.05$

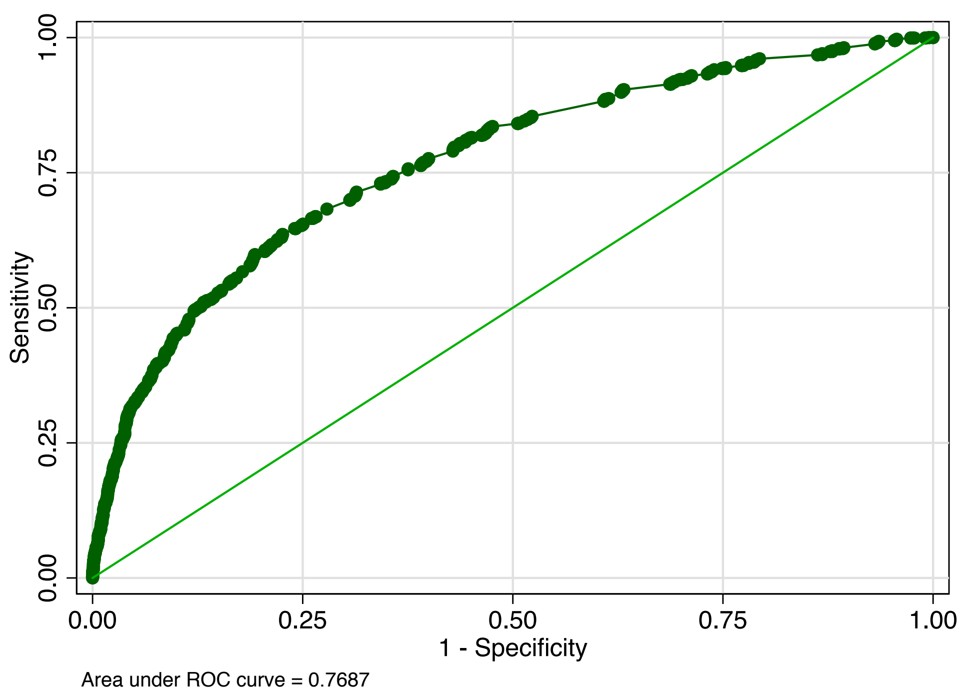
AUROC

Data on which model was built



AUROC

Rest of the data



Cross-Validation

- Correcting for model-based optimism
- Split data into a series of random subsets
  usually 10 of them
- one-at-time, leave subset out
- Build model on 90%
  use other 10% for validation

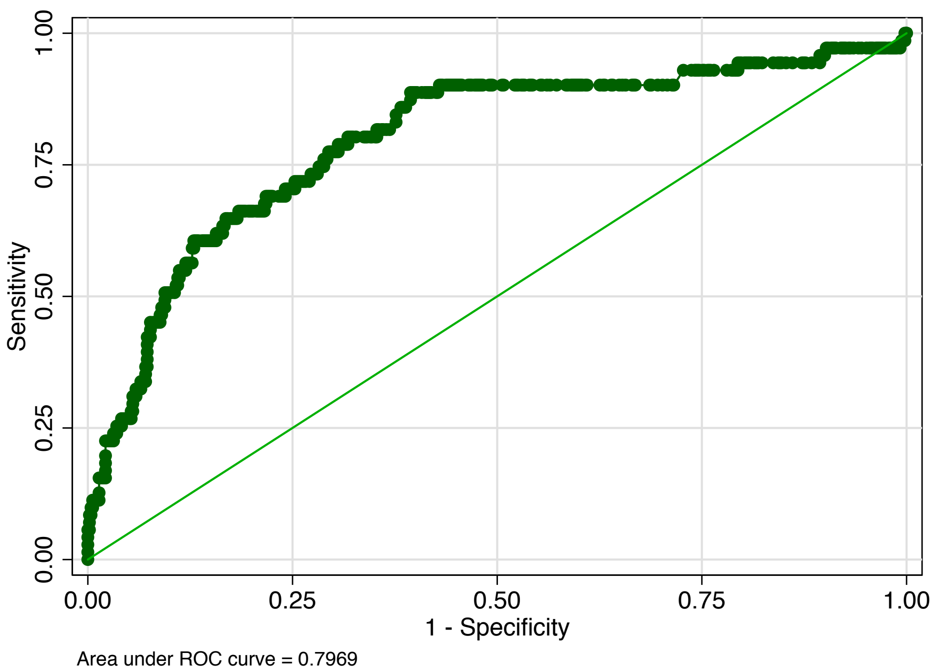
How it works

- Uses data to build and validate model
- 90% builds model, 10% validates it
- Every observation gets used in 1 test set
- Provides an internal validation

Stata Code

- gen u = uniform()
  makes random # and puts in "u"
- xtile cat=u, nq(10)
  creates "cat" 10 groups based on "u"
- stepwise if cat!=`k', pr(.05): logistic died *predictors*
  stepwise leaving out kth group
- predict *prediction* if cat==k
  save prediction for kth group

Cross-Validated



Week After Next

- Fuller discussion of statistical model building
- Approaches to penalize for overfitting
- Non statistical issues in model building