ALEH Clinical Research Workshop: How to Use and Manage Databases

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Outline for today

- Brief introduction to using large databases
- Discuss pros and cons of large databases
- Overview of how to choose the right database and potential databases for research
- How to analyze and interpret large databases
- Pitfalls and helpful tools

Basics of using large databases

- What is a database?
  - Collection of data that is organized so that its contents can easily be accessed, managed, and updated
- Database sizes
  - Small: $<10^5$ records, <10GB data
  - Medium: 10^5-10^7 records, 10-40GB data
  - Large: $>10^7$ records, >40GB data
- Records ≠ patients
  - Patients may have multiple entries
  - Multiple updates (i.e., MELD updates)

Major logistical issues to consider with database research

- Access to statistical software and/or statistical support
  - SPSS is point-and-click
  - Having software ≠ understanding statistics
- Can my computer handle the data (10MB->1GB)
- Do I have/need funding for the data
    - UNOS and SRTR transplant databases: $250-2,500
- Am I able to clean data
  - Why was data collected?
  - Missing data
  - Repeat entries

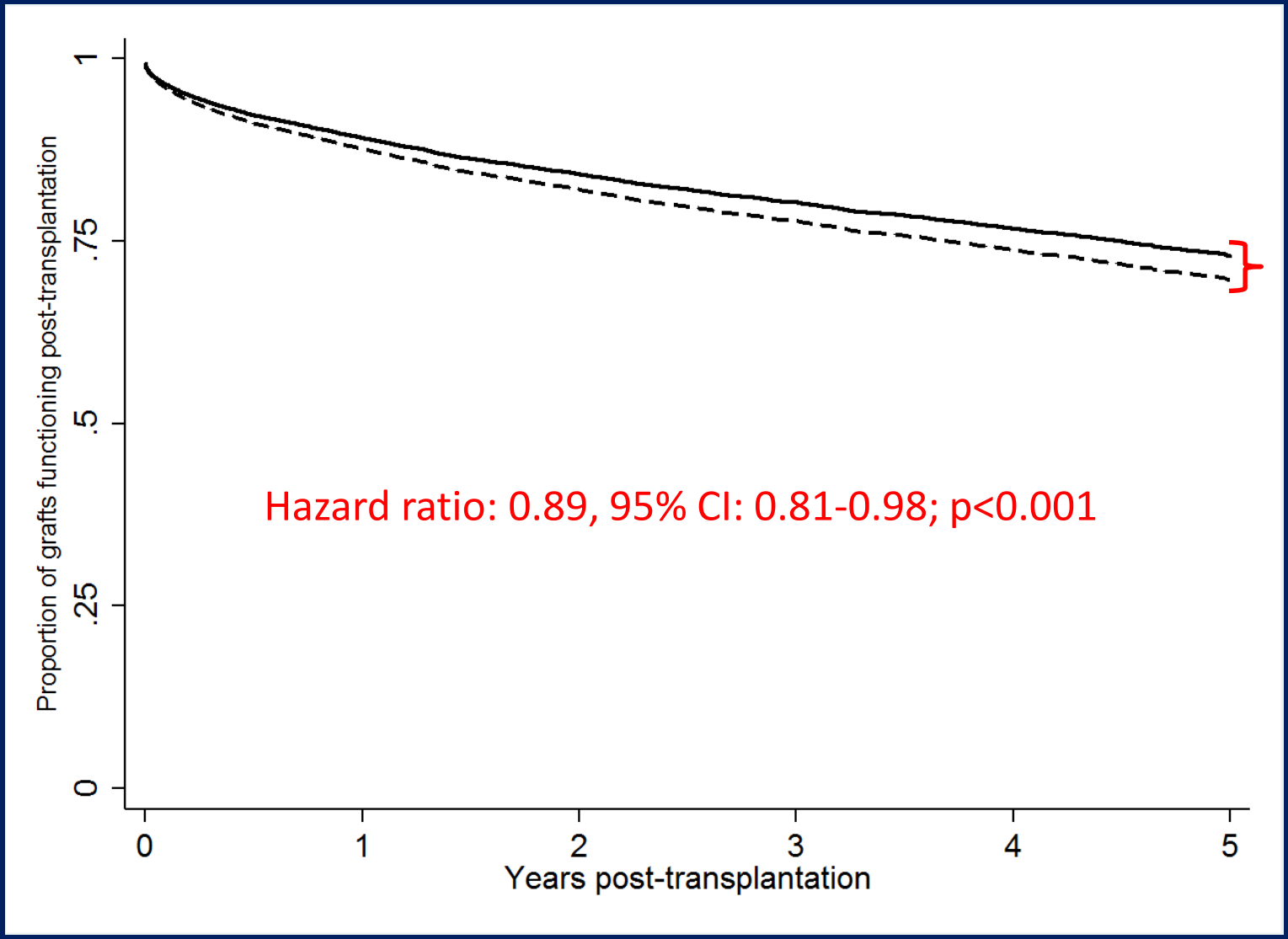
Why use a large database

- When a large sample size needed (rare exposure or outcome)
- Compare outcomes/performance across some measure
  - Variation in transplant center post-OLT outcomes
  - Organ donation rates across donor service areas
- Weigh benefits and tradeoffs of large database vs single-center data
  - Loss of granularity (can't review medical records for 100,000 people)
  - Lack of control for data entry (previously coded or administrative data)
- Potential studies evaluating outcomes of cirrhotics in ICU
  - Single center: Outcomes, reason for admissions, risk factors (MELD, APACHE, SOFA) for adverse outcomes
  - Large database (PHC-4): All cirrhotics in ICUs in PA
    - Evaluate outcomes and reasons for admissions
    - Compare outcomes across hospitals (academic vs community)
    - Don't have lab data data (MELD, ? SOFA)
  - What is the main question/message

Pros of using large databases

- Large sample size
  - Never underpowered (10:1 ratio outcomes:covariate)
  - Easy to get statistical significance
- Generalizability and external validity
  - Usually capture robust population
  - Single-center study not generalize to broader population
- Can be geographically and demographically diverse
  - Single-center vs national data
- Compare data across areas (geography, centers)

Cons of using large databases



4% absolute difference

Choosing the right database

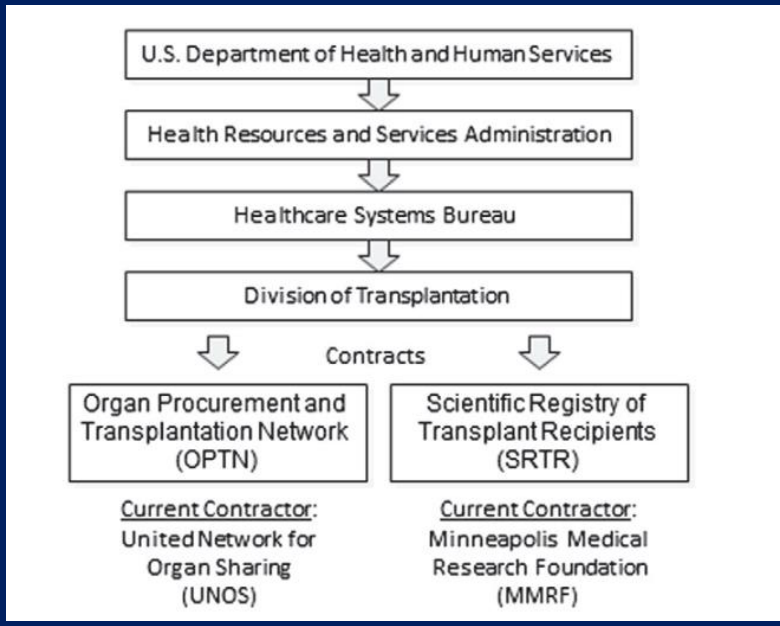
- Depends on:
  - Research question
  - Population of interest
  - Time
  - Budget
- Large database may not be the right answer
- Question and database:
  - Question: What are post-OLT outcomes of patients with PSC
    - Database: UNOS/SRTR
  - Question: What is the success rate of HCC downstaging protocols in the United States
    - Database: UNOS/SRTR (granularity), SEER (no Milan/UCSF), single/multi-center
  - Question: Are there differences in waitlisting for transplant across the United States
    - Database: ???—what is denominator

Using large database vs single-center data

- Depends on research question
- Are all the data available in both datasets
- Examples:
  - Does pre-transplant chronic kidney disease predict post-transplant survival
    - Single-center data better
      - Need to define CKD (i.e., renal ultrasound, proteinuria, trends)
  - Are increasing age and BMI associated with higher risks of early graft failure
    - Large database->more robust numbers

Transplant databases: UNOS and SRTR

- What is the OPTN?
  - Maintains the national registry for organ matching based on NOTA
- What is UNOS?
  - Private non-profit organization that has OPTN contract
  - Responsible for organ matching and collection of data
- What is the SRTR?
  - Organization responsible for analyzing transplant data, creating program-specific reports for center performance and public dissemination
  - Carries out analyses requested by OPTN committees
- SRTR and UNOS
  - Similar data
  - SRTR data “cleaned”
  - Different costs
  - Different request process



Interpreting results of large databases

- It's not all about the p-value
  - P-value measures likelihood of finding something by chance
  - Largely influence by sample sizes
- Is it clinically meaningful
  - Don't just look at HR/OR
  - Look at actual numbers and predicted outcomes
- Does the result make biological sense or just statistical anomaly (1/20 happen by chance)

Interpreting results: Hypothetical example

- Is the difference in outcomes really that large
- Research question: Is the 1-year post-OLT survival different for LT recipients with PSC vs PBC vs AIH
- Outcome: 1-year post-OLT survival (binary)

```
. xi: logistic died_within_1 i.psc_pbc_aih age dri ldlt final_meld_peld_lab_score
i.psc_pbc_aih     _Ipsc_pbc_a_0-2     (naturally coded; _Ipsc_pbc_a_0 omitted)

Logistic regression                             Number of obs     =      6,063
                                                LR chi2(6)        =      82.56
                                                Prob > chi2       =     0.0000
Log likelihood = -1800.7012                     Pseudo R2         =     0.0224
------------------------------------------------------------------------------
  died_within_1 | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
----------------+-------------------------------------------------------------
          AIH   |   1.383664   .1488621     3.02   0.003     1.120608     1.70847
          PBC   |   .9499216   .1086927    -0.45   0.653     .7590859    1.188734
          age   |   1.023072    .003816     6.12   0.000      1.01562           1
          dri   |   1.206117   .1334843     1.69   0.090     .9709222           1
         ldlt   |   1.398781   .2576449     1.82   0.068     .9749108           2
final_meld_peld_lab_score |   1.026813   .0047798     5.68   0.000     1.017487           1
        _cons   |   .0111116   .0032352   -15.45   0.000     .0062797           .
------------------------------------------------------------------------------
```

```
margins if psc_pbc_aih==0
Predictive margins                              Number of obs     =      2,705
Model VCE    : OIM
Expression   : Pr(died_within_1), predict()
------------------------------------------------------------------------------
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |   .0783734   .0051373    15.26   0.000     .0683045    .0884423
------------------------------------------------------------------------------
```

```
margins if psc_pbc_aih==1
Predictive margins                              Number of obs     =      1,662
Model VCE    : OIM
Expression   : Pr(died_within_1), predict()
------------------------------------------------------------------------------
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |    .11071   .0076355    14.50   0.000     .0957448    .1256752
------------------------------------------------------------------------------
```

```
margins if psc_pbc_aih==2
Predictive margins                              Number of obs     =      1,696
Model VCE    : OIM
Expression   : Pr(died_within_1), predict()
------------------------------------------------------------------------------
             |     Margin   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |   .0902123    .006928    13.02   0.000     .0766336     .103791
------------------------------------------------------------------------------
```

Analyzing UNOS data: You get your STAR file—now what?

-

	wl_id_code	pt_code	rem_cd	age	init_age	region	gender
1	571463	365907	15	28	25	11	F
2	1161229	1035475	4	60	60	11	M

	VARIABLE NAME	DESCRIPTION	FORM	VAR START DATE	VAR END DATE	FORM SECTION
3	ABO	RECIPIENT BLOOD GROUP @ REGISTRATION	TCR	01-Oct-87		CLINICAL INFORMATION
4	ABO_DON	DONOR BLOOD TYPE	DDR/LDR	01-Oct-87		DONOR INFORMATION
5	ABO_MAT	DONOR-RECIPIENT ABO MATCH LEVEL	CALCULATED			
6	ACADEMIC_LEVEL_TCR	ACADEMIC ACTIVITY LEVEL AT LISTING	TCR	30-Jun-04		CANDIDATE INFORMATION
7	ACADEMIC_LEVEL_TRR	ACADEMIC ACTIVITY LEVEL AT TRANSPLANT	TRR	30-Jun-04		PATIENT STATUS
8	ACADEMIC_PRG_TCR	ACADEMIC PROGRESS AT LISTING	TCR	30-Jun-04		CANDIDATE INFORMATION
9	ACADEMIC_PRG_TRR	ACADEMIC PROGRESS AT TRANSPLANT	TRR	30-Jun-04		PATIENT STATUS
10	ACUTE_REJ_EPI	ACUTE REJECTION EPISODE BETWEEN TRANSPLANT AND DISCHARGE?	TRR	30-Jun-04		POST TRANSPLANT CLINICAL INFORMATION
11	ACYCLOVIR	Biological or Anti-Viral Treatment - Acyclovir	TRR	30-Jun-04	01-Jan-07	Treatment
12	ADMISSION_DATE	RECIPIENT DATE OF ADMISSION TO TX CENTER	TRR	25-Oct-99		PATIENT STATUS
13	ADMIT_DATE_DON	DONOR ADMIT DATE	DDR	26-Apr-06		DONOR INFORMATION
14	AGE	RECIPIENT AGE (YRS)	TRR-CALCULATED	01-Oct-87		RECIPIENT INFORMATION
15	AGE_DON	DONOR AGE (YRS)	DDR/LDR-CALCULATED	01-Oct-87		DONOR INFORMATION
16	AGE_GROUP	RECIPIENT AGE GROUP A=ADULT P=PEDS	CALCULATED			
17	ALBUMIN_DIS	RECIPIENT SERUM ALBUMIN @ DISCHARGE	TRR	01-Oct-87	01-Jan-07	POST TRANSPLANT CLINICAL INFORMATION
18	ALBUMIN_TX	RECIPIENT SERUM ALBUMIN @ TRANSPLANT	WAITING LIST DATA	01-Oct-87		PRETRANSPLANT CLINICAL INFORMATION - SERUM LAB DATA
19	AMIS	A Locus MISMATCH LEVEL	CALCULATED			
20	ANGINA	RECIPIENT ANGINA/CAD @ REGISTRATION	TCR	30-Jun-04	01-Jan-07	CLINICAL INFORMATION
21	ANGINA_OLD	RECIPIENT ANGINA/CAD @ REGISTRATION	TCR	01-Apr-94	30-Jun-04	CLINICAL INFORMATION
22	ANTICONV_DON	DECEASED DONOR-ANTICONVULSANTS W/IN 24 HRS PRE-CROSS CLAMP	DDR	01-Apr-94		CLINICAL INFORMATION
23	ANTIHYPE_DON	DECEASED DONOR-ANTIHYPERTENSIVES W/IN 24 HRS PRE-CROSS CLAMP	DDR	01-Apr-94		CLINICAL INFORMATION
24	ARGININE_DON	DECEASED DONOR-WAS DONOR GIVEN ARGININE VASOPRESSIN WITHIN 24 HRS PRE CROSS CLAMP?	DDR	30-Jun-04		CLINICAL INFORMATION
25	ARTIFICIAL_LI_TCR	RECIPIENT ON ARTIFICIAL LIVER AT LISTING	TCR	01-Oct-87		CLINICAL INFORMATION
26	ARTIFICIAL_LI_TRR	RECIPIENT ON ARTIFICIAL LIVER AT TRANSPLANT	TRR	01-Oct-87		CLINICAL INFORMATION
27	ASCITES_TCR	RECIPIENT ASCITES @ REGISTRATION	TCR	01-Apr-94	30-Jun-04	CLINICAL INFORMATION - LIVER MEDICAL FACTORS
28	ASCITES_TRR_OLD	TRR ASCITES	TRR	01-Apr-94	30-Jun-04	TRANSPLANT CLINICAL INFORMATION - RISK FACTORS
29	ASCITES_TX	RECIPIENT ASCITES @ TRANSPLANT	WAITING LIST DATA	30-Jun-04		WAITING LIST DATA
30	BACT_PERIT_TCR	RECIPIENT SPONTANEOUS BACTERIAL PERITONITIS @ REGISTRATION	TCR	01-Apr-94		CLINICAL INFORMATION - LIVER MEDICAL FACTORS
31	BACT_PERIT_TRR	RECIPIENT SPONTANEOUS BACTERIAL PERITONITIS @ TRANSPLANT	TRR	01-Apr-94	01-Jan-07	TRANSPLANT CLINICAL INFORMATION - RISK FACTORS

19	1176563	1049375	4	53	53	10	M
20	831454	693881	4	60	60	2	M
21	986374	887822	4	55	55	3	M
22	1025735	921721	4	68	68	10	F
23	1177129	1049195	4	61	61	3	M
24	418468	615897	4	53	52	5	F
25	981983	884410	4	69	68	4	F

Knowing the lingo of UNOS

- wl_id_code vs pt_code
  - pt_code
    - One code per patient
    - Tracks through all waitlist entries
  - wl_id_code
    - One code per waitlist entry
    - Can have multiple codes (e.g., dual listing, re-transplant)
- TCR vs TRR
  - TCR=transplant candidate registration
    - Data at time of waitlisting
  - TRR=transplant recipient registration
    - Data at time of transplant

Conclusions and take-home points

- Large databases can be wealth of information
- Large sample sizes allow for important questions to be answered
- Need to be aware of limitations of databases
  - Validity of codes
  - Missing data
  - Lack of labs
  - Know what data initially created for
- Don’t get scooped—anyone can access UNOS data