OPTN/SRTR Registry Analysis: The Devil is in the Details

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*Presenter

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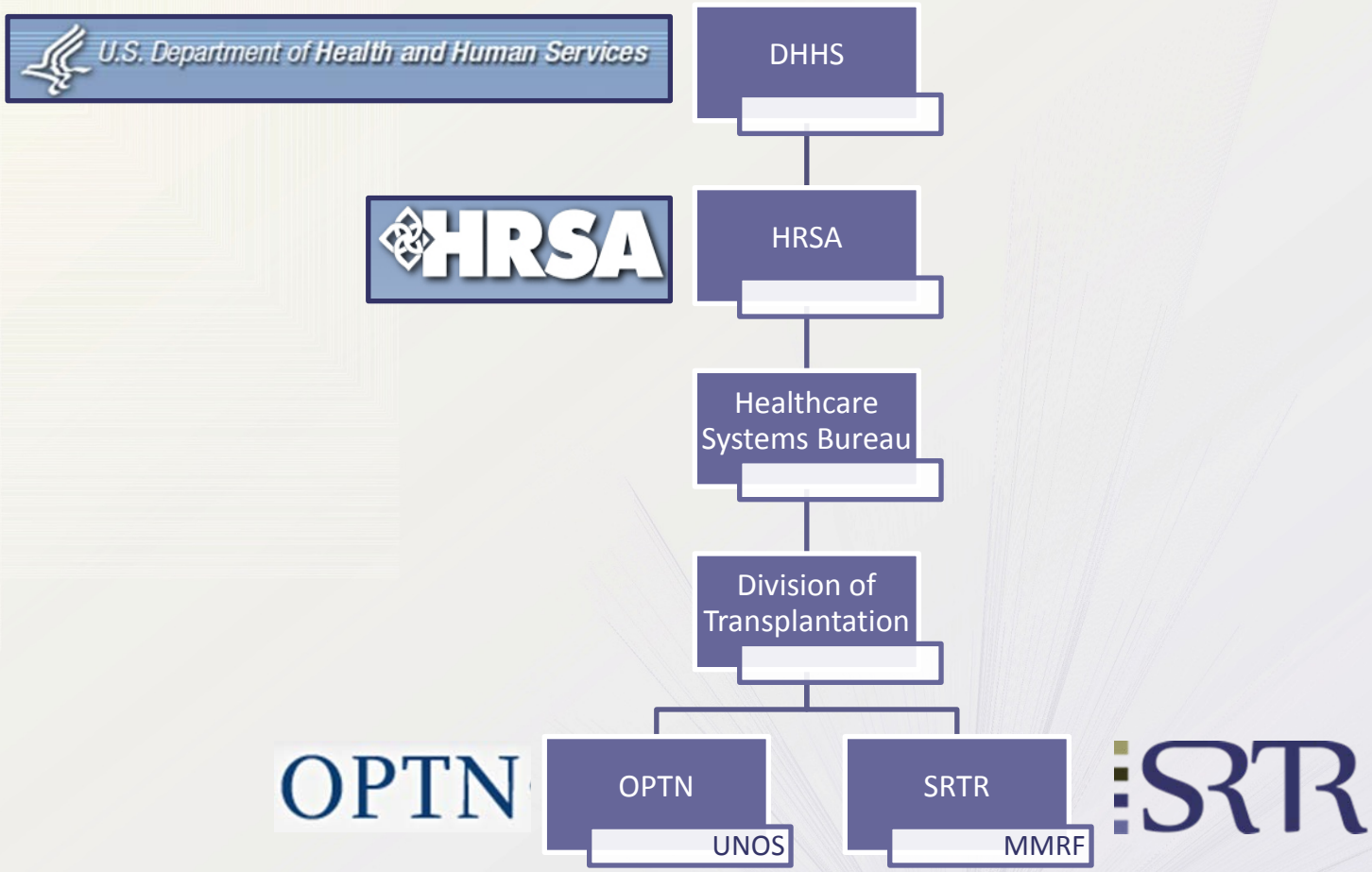
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Outline

- Flow of data to the SRTR
- How to acquire the SRTR data
- Data timeliness and policies
- Data structure, data dictionary, and linkage of datasets within SAF
- Analysis
    a. Converting SAS data files to other formats
    b. How to define a study cohort
    c. How to define key survival endpoints
        i. Death
        ii. Graft Failure
    d. How are multi-organ, multi-visceral transplants handled in the database?
- Data quality
    a. OPTN efforts to bolster the data definitions
    b. Acute rejection
    c. Delayed graft function
    d. Immunosuppressive medications

Relationships: HRSA/OPTN/UNOS/MMRF/SRTR



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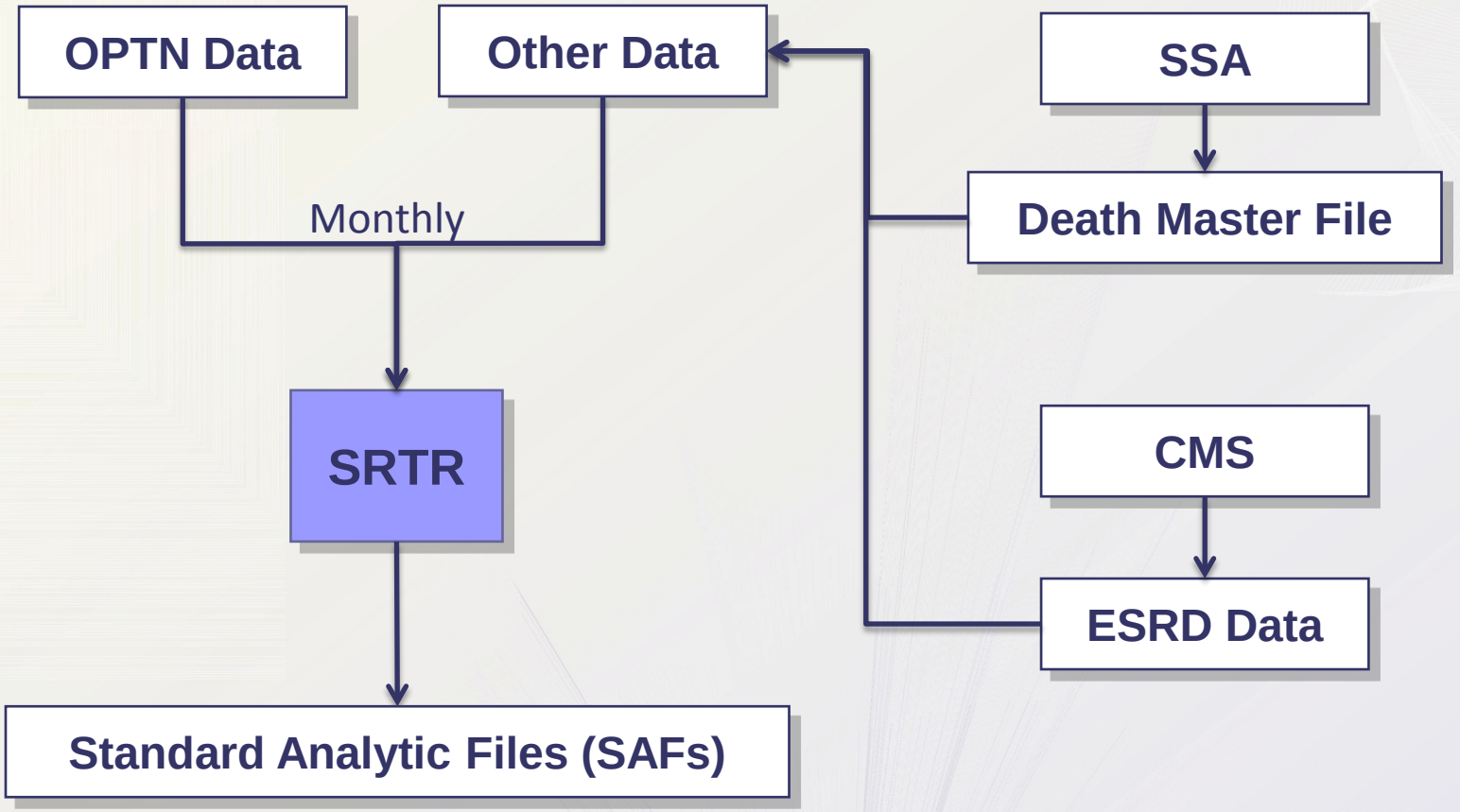
Data Flow Into the SRTR



Standard Analysis Files (SAF)

Standard set of files that include most data fields collected by the OPTN for donors, candidates, and recipients in the US from 1988 to present.

- Includes encrypted patient and program identifiers
- Excludes geographic variables and most text fields
- Requires a Data Use Agreement, Security Plan, and Research plan
- Cost US$1,000

Requestors can request additional variables, such as un-blinded center codes, at an additional fee.

Requests for identifying variables, such as candidate zip code, follow the same process as data linkages.

Linkages and Identifying Data

Any time researchers want to link SRTR data with outside data or want to receive identifiers with SRTR data.

- Requires a Data Use Agreement, Security Plan, and Research plan
- Must demonstrate the research is not feasible without these data/linkage
- Requires review and approval of the SRTR Technical Advisory Committee
- Cost based on the time required for linkage (US$120/hour) and SAF

Examples:

- Linking SRTR SAF to clinical trial data
- Linking SRTR SAF to Medicare/Medicaid data
- Candidate and recipient ZIP code

Acquiring SRTR Data

All inquiries are received by a central phone line (612-347-7787) and/or email address (srtr@srtr.org) and then handled according to the details of the request.

Tabitha Leighton, MPH & Susan Leppke, MPH

Research and Policy Liaisons
Scientific Registry of Transplant Recipients
Minneapolis Medical Research Foundation
914 S 8th St, Suite S-422, Minneapolis, MN 55404
srtr@srtr.org
612-347-7787

Data Use Agreement

- Data may only be used for specified purposes
- All manuscripts and abstracts must be reviewed prior to submission
- Expires 1 year after date
- Can be renewed free of charge

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Data release agreement

for bona fide research & analysis

Project number:
Date

Pursuant to a contract with the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS), through the Scientific Registry of Transplant Recipients Contractor (SRTR), The Minneapolis Medical Research Foundation (MMRF), with offices at 914 S. 8th Street, Suite S-206 Minneapolis, Minnesota, 55404, will provide the organization identified below (Recipient) with patient-level data (but not patient-identified data unless authorized in writing as described below). The data extracted from the SRTR research database is maintained by MMRF solely for the use identified below. Patient-identified data may only be made available when approved by the SRTR Technical Advisory Committee (S-TAC) and the SRTR Project Officer (PO). The recipient of released data will abide by the terms stated in the Agreement Clauses.

Recipient name _____

Institution _____ Phone _____

Mailing address _____

Contact name _____ Phone _____

email _____

check all that apply ☐ Standard Analysis File (SAF) ☐ LSAM ☐ KPSAM ☐ Additional variables ☐ Other

Description of data to be delivered _____

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Security Plan

- Identifies individuals authorized to have access to the data
- Outlines data protection

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Security plan questions

for data release agreement

Project number:
Date

Researcher name _____

1. On what type of computer system will the data be stored and used? Please answer this for each computer on which the data will be stored or used. Check all that apply.
   - ☐ Laptop with an encrypted hard drive
   - ☐ Personal/home-user computer
   - ☐ Institutional stationary computer
2. Please list the full names and titles of all individuals who will be accessing this data.

_____

_____

_____

Affirmative answers to all of the questions below will certify your compliance with the security agreement. If you cannot check a box to confirm compliance, please contact the SRTR to discuss your situation.

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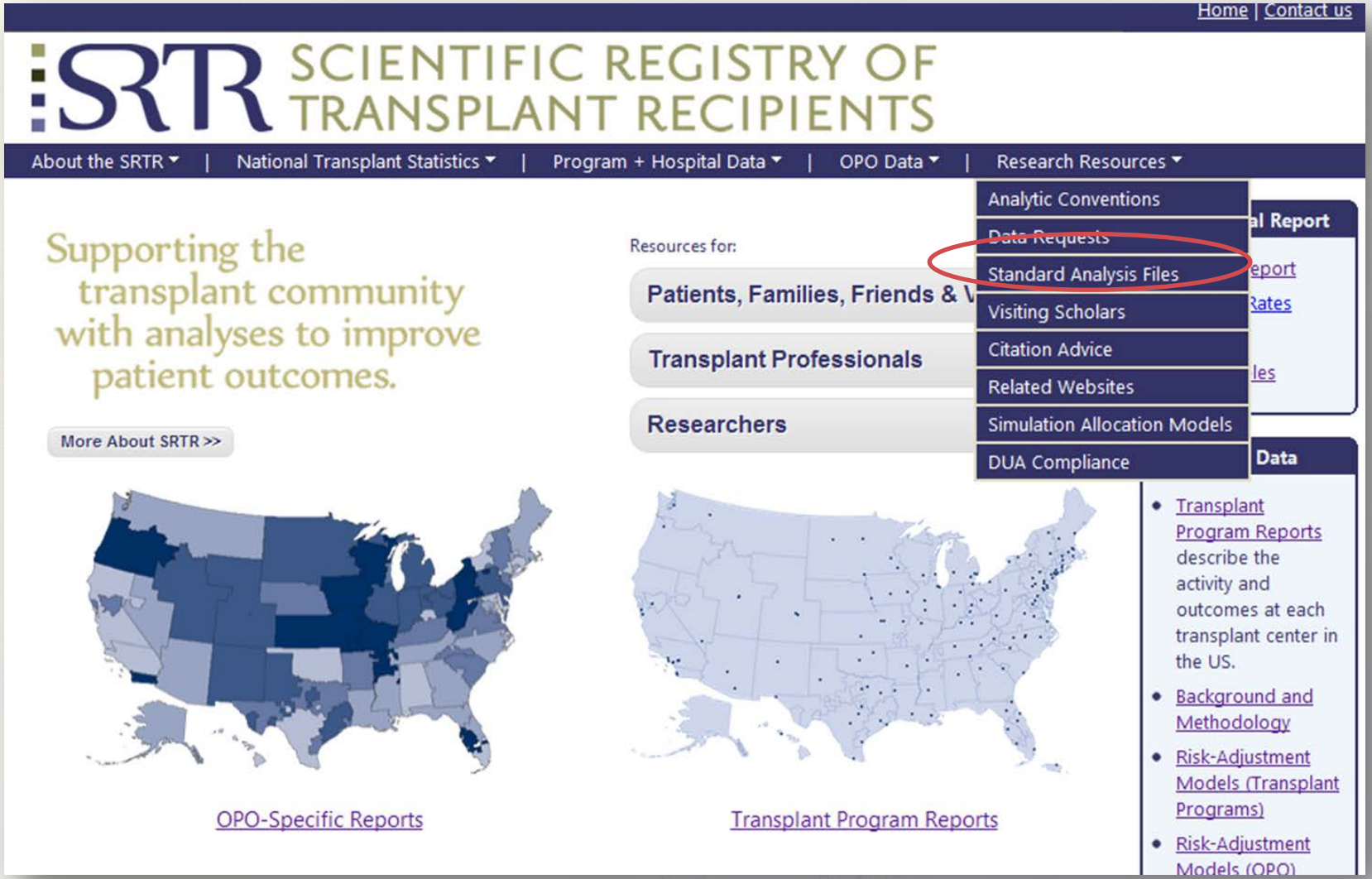
New! Online SAF Data Dictionary (www.srtr.org)



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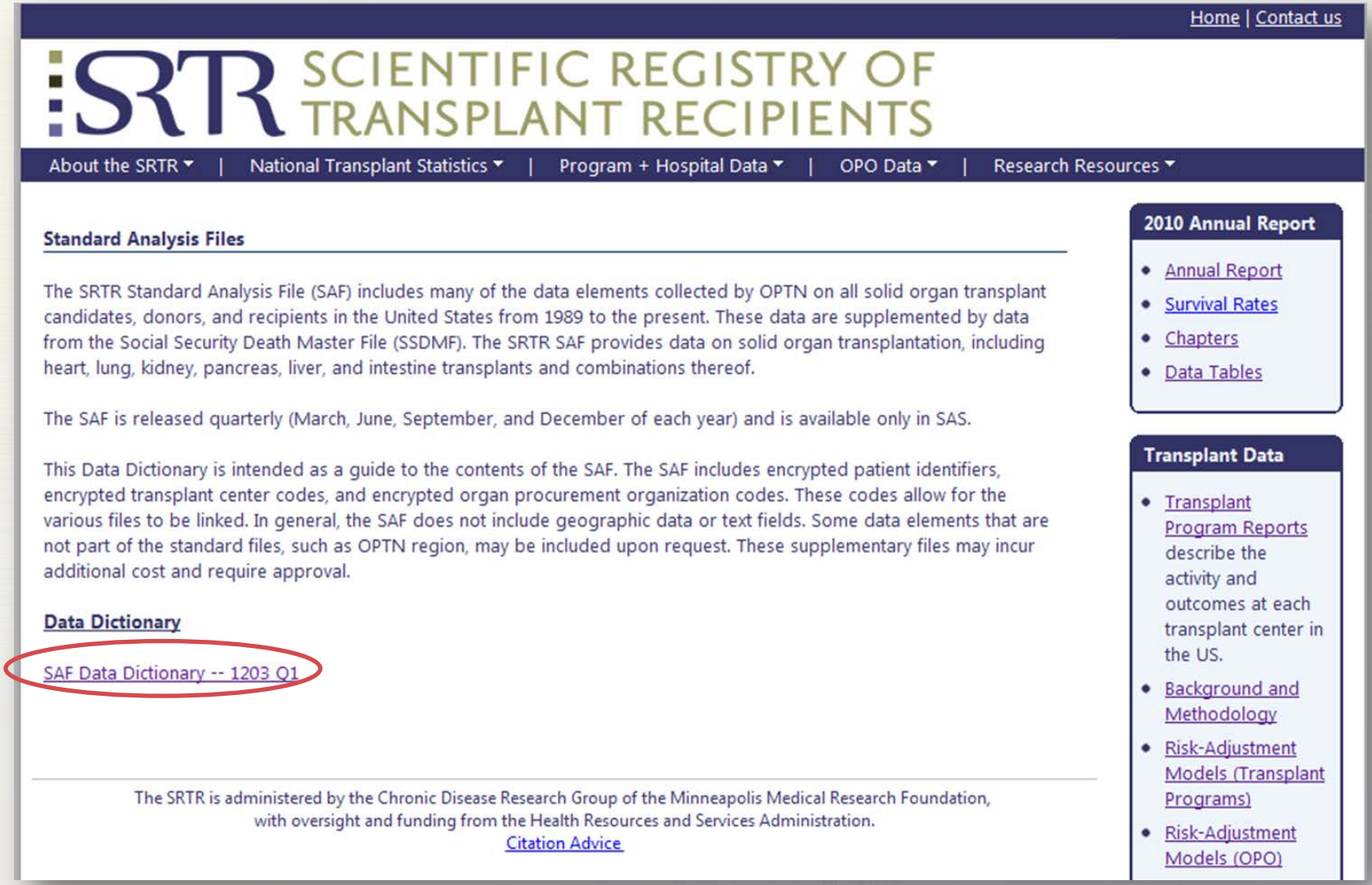

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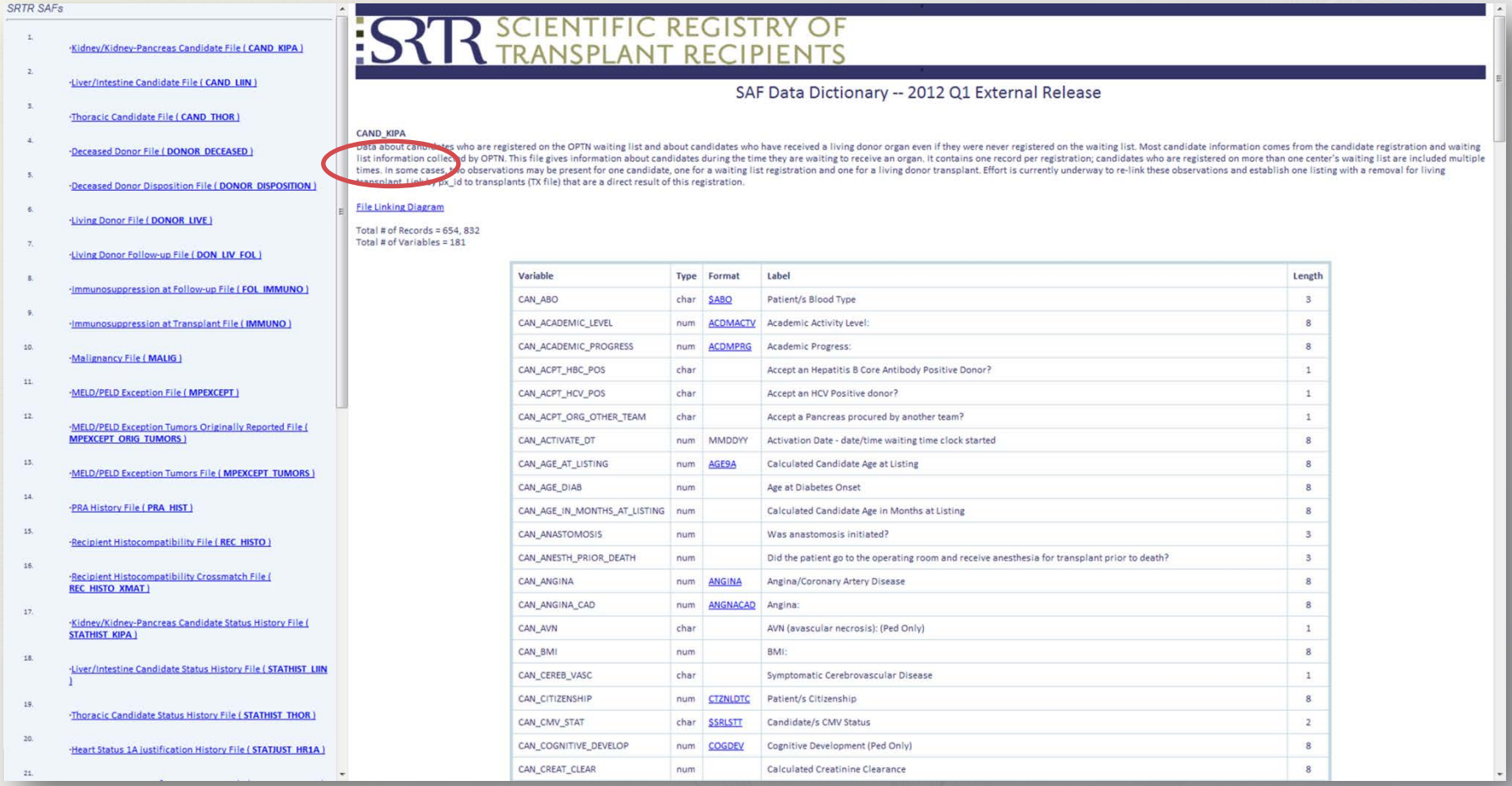

SRTR SAFs

1. Kidney/Kidney-Pancreas Candidate File (**CAND_KIPA**)
2. Liver/Intestine Candidate File (**CAND_LIIN**)
3. Thoracic Candidate File (**CAND_THOR**)
4. Deceased Donor File (**DONOR_DECEASED**)
5. Deceased Donor Disposition File (**DONOR_DISPOSITION**)
6. Living Donor File (**DONOR_LIVE**)
7. Living Donor Follow-up File (**DON_LIV_FOL**)
8. Immunosuppression at Follow-up File (**FOL_IMMUNO**)
9. Immunosuppression at Transplant File (**IMMUNO**)
10. Malignancy File (**MALIG**)
11. MELD/PELD Exception File (**MPEXCEPT**)
12. MELD/PELD Exception Tumors Originally Reported File (**MPEXCEPT_ORIG_TUMORS**)
13. MELD/PELD Exception Tumors File (**MPEXCEPT_TUMORS**)
14. PRA History File (**PRA_HIST**)
15. Recipient Histocompatibility File (**REC_HISTO**)
16. Recipient Histocompatibility Crossmatch File (**REC_HISTO_XMAT**)
17. Kidney/Kidney-Pancreas Candidate Status History File (**STATHIST_KIPA**)
18. Liver/Intestine Candidate Status History File (**STATHIST_LIIN**)
19. Thoracic Candidate Status History File (**STATHIST_THOR**)
20. Heart Status 1A Justification History File (**STATJUST_HR1A**)
21. ...

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SAF Data Dictionary -- 2012 Q1 External Release

CAND_KIPA

Data about candidates who are registered on the OPTN waiting list and about candidates who have received a living donor organ even if they were never registered on the waiting list. Most candidate information comes from the candidate registration and waiting list information collected by OPTN. This file gives information about candidates during the time they are waiting to receive an organ. It contains one record per registration; candidates who are registered on more than one center's waiting list are included multiple times. In some cases, two observations may be present for one candidate, one for a waiting list registration and one for a living donor transplant. Effort is currently underway to re-link these observations and establish one listing with a removal for living transplant. Link by px_id to transplants (TX file) that are a direct result of this registration.

File Linking Diagram

Total # of Records = 654, 832
Total # of Variables = 181

Variable	Type	Format	Label	Length
CAN_ABO	char	SABO	Patient/s Blood Type	3
CAN_ACADEMIC_LEVEL	num	ACDMACTV	Academic Activity Level:	8
CAN_ACADEMIC_PROGRESS	num	ACDMPRG	Academic Progress:	8
CAN_ACPT_HBC_POS	char		Accept an Hepatitis B Core Antibody Positive Donor?	1
CAN_ACPT_HCV_POS	char		Accept an HCV Positive donor?	1
CAN_ACPT_ORG_OTHER_TEAM	char		Accept a Pancreas procured by another team?	1
CAN_ACTIVATE_DT	num	MMDDYY	Activation Date - date/time waiting time clock started	8
CAN_AGE_AT_LISTING	num	AGE9A	Calculated Candidate Age at Listing	8
CAN_AGE_DIAB	num		Age at Diabetes Onset	8
CAN_AGE_IN_MONTHS_AT_LISTING	num		Calculated Candidate Age in Months at Listing	8
CAN_ANASTOMOSIS	num		Was anastomosis initiated?	3
CAN_ANESTH_PRIOR_DEATH	num		Did the patient go to the operating room and receive anesthesia for transplant prior to death?	3
CAN_ANGINA	num	ANGINA	Angina/Coronary Artery Disease	8
CAN_ANGINA_CAD	num	ANGNACAD	Angina:	8
CAN_AVN	char		AVN (avascular necrosis): (Ped Only)	1
CAN_BMI	num		BMI:	8
CAN_CEREB_VASC	char		Symptomatic Cerebrovascular Disease	1
CAN_CITIZENSHIP	num	CTZNLDTC	Patient/s Citizenship	8
CAN_CMV_STAT	char	SSRLSTT	Candidate/s CMV Status	2
CAN_COGNITIVE_DEVELOP	num	COGDEV	Cognitive Development (Ped Only)	8
CAN_CREAT_CLEAR	num		Calculated Creatinine Clearance	8

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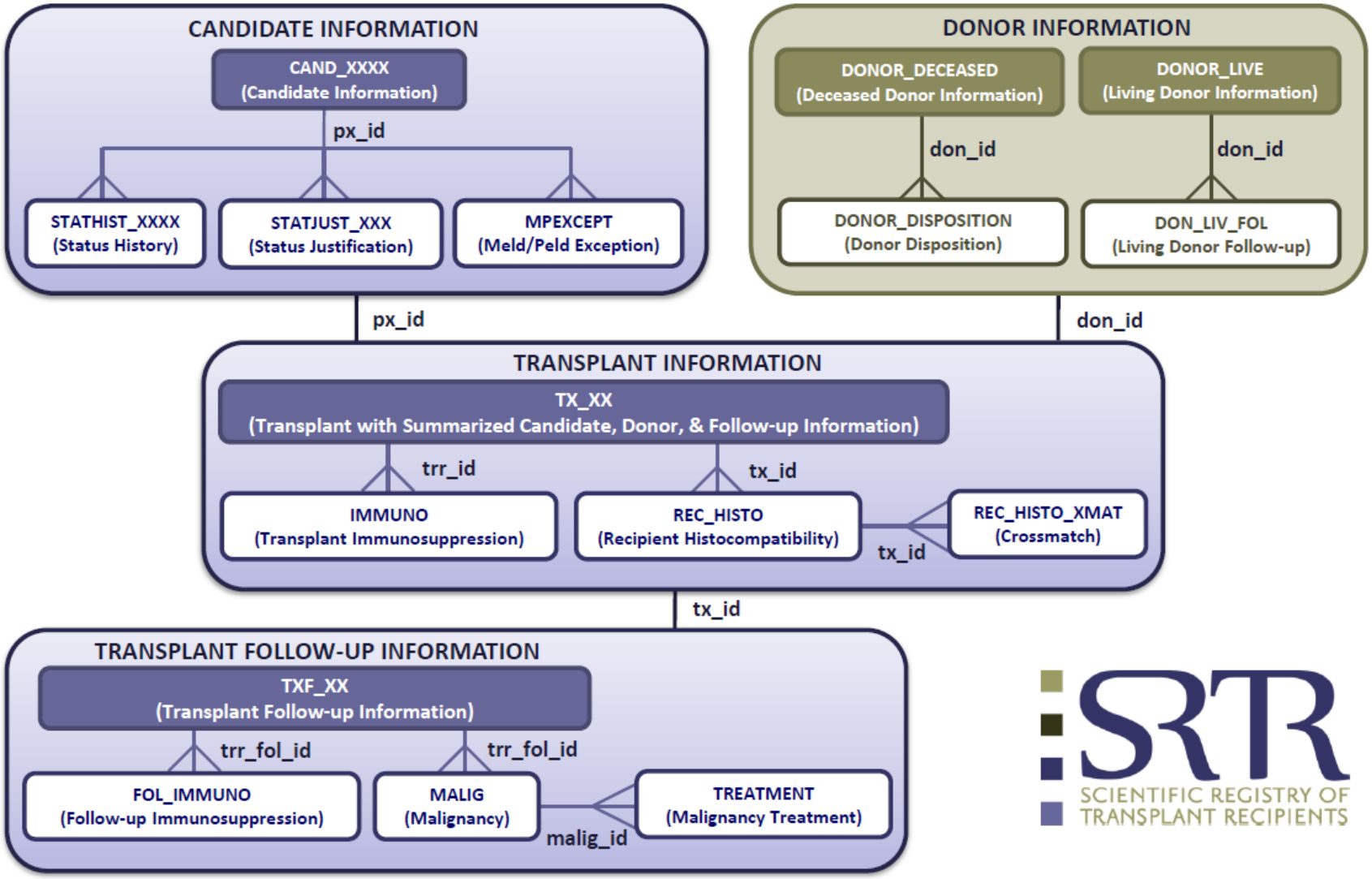
Linking SAF Datasets

The SAS datasets can be linked as diagrammed below. The text along the connector lines indicates the foreign key variable for linkages between the two data sets, used in a "by" statement in a SAS merge. A fork in the link indicates that more than one record may be associated with a single ID.



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How Current are the SRTR Data?

- SAF's are produced quarterly in March, June, September, and December; allows for citable SAF source (current SAF: Mar 2012)
- Current-ness of data is based on OPTN policy for timeliness of form submission
- Transplant follow-up forms collected at 6 months and annually
    - OPTN Policy (7.1.5) allows for submission:
        - Within 30 days for the following forms (Policy 7.2):
            - » Transplant Candidate Registration (TCR)
            - » Deceased Donor Registration (DDR)
            - » Living Donor Follow-Up (LDF)
            - » Recipient and Donor Histocompatibility (RHS & DHS)
            - » Recipient Malignancy (MALIG)
        - Within 60 days for the following forms (Policy 7.3.1)
            - » Transplant Recipient Registration (TRR)
            - » TRR completed when discharged from the hospital or 6-weeks post-transplant, whichever is first
        - Within 30 days of the 6-month follow-up form (Policy 7.1.5)
        - Within 90 days of the annual follow-up forms (Policy 7.1.5)

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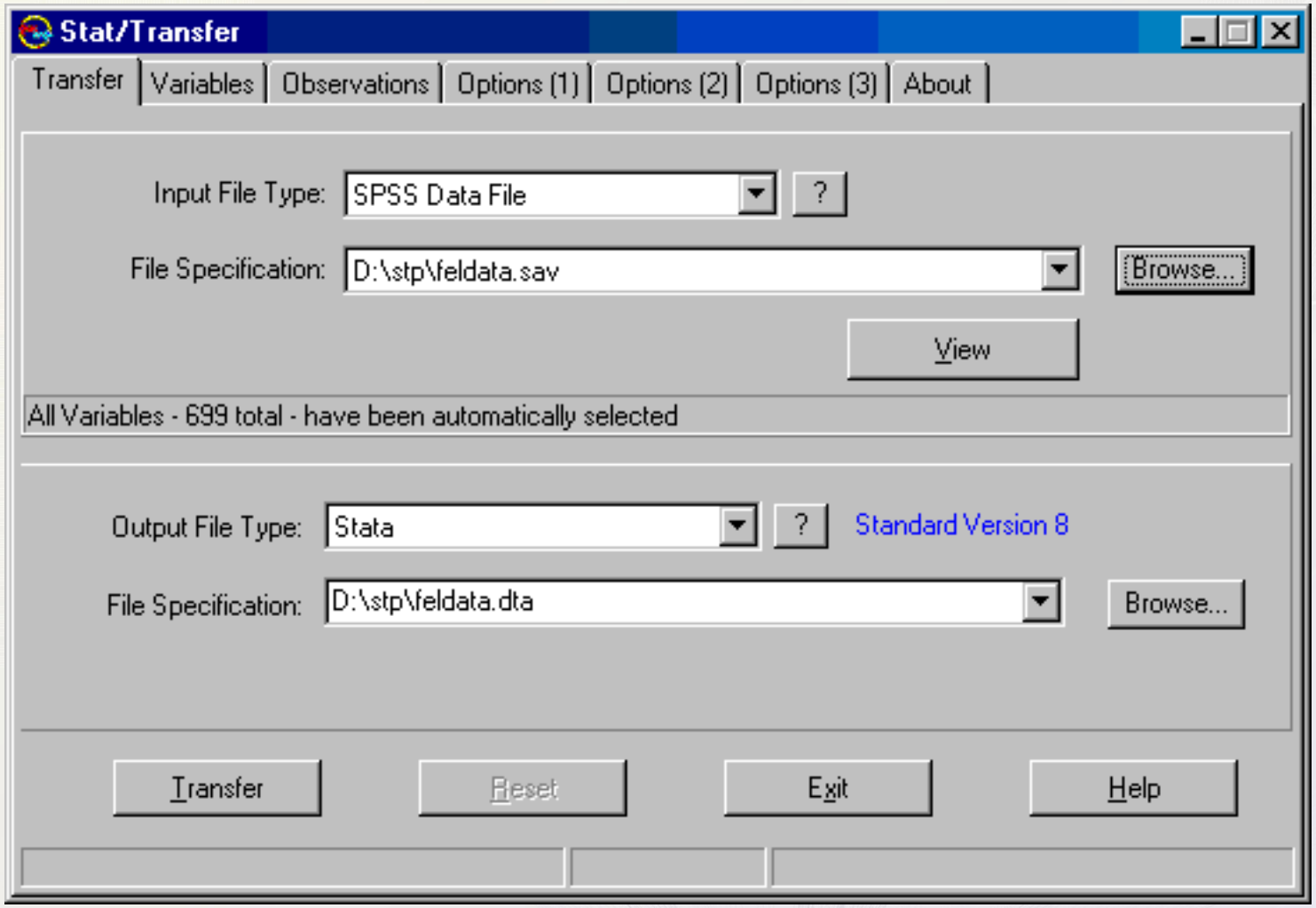
Converting SAS data files to other formats

- SRTR provide data as SAS files ("sas7bdat" extension)
- Most commonly used statistical packages other than SAS include Stata, R, and SPSS
- All packages able to read text files (CSV or fixed format files) but may be cumbersome to manage
- If SAS available, and would like to use different package for data management and analysis, may export datasets directly from SAS into different formats using *proc export*

Converting SAS data files to other formats

- Stata can directly read SAS XPORT transport files using *import sasxport* and can also read value label information from formats.xpf XPORT file, if available
- SPSS has ability to import SAS files directly using pull-down menus
- Can use functions *read.sdd()*, *get.sas()*, or *read.xport()*, the latter for SAS XPORT transport files
- Easiest way to convert datasets to different formats is to use data conversion software such as Stat-Transfer or DBMS/Copy

Stat-Transfer Main Screen



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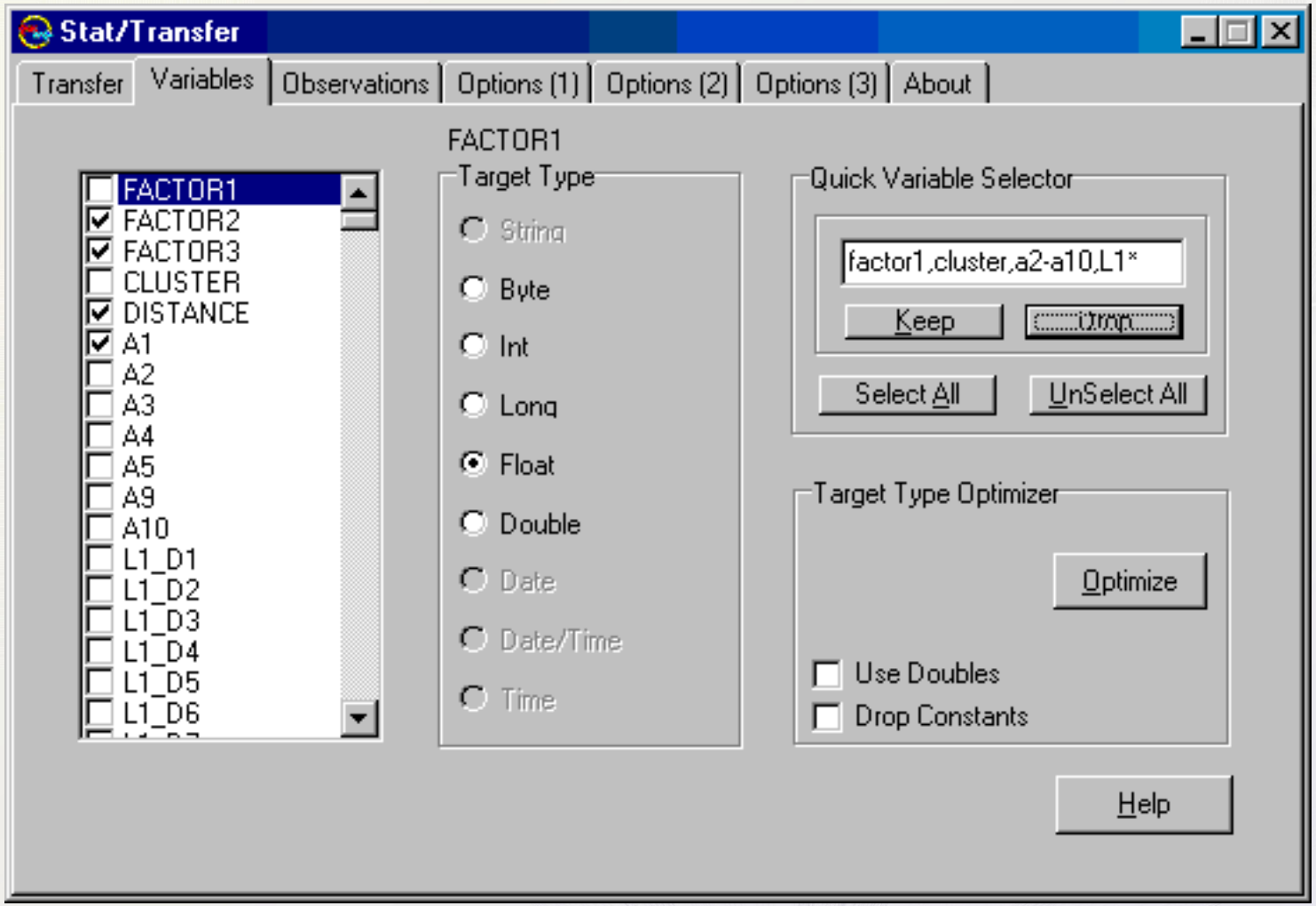
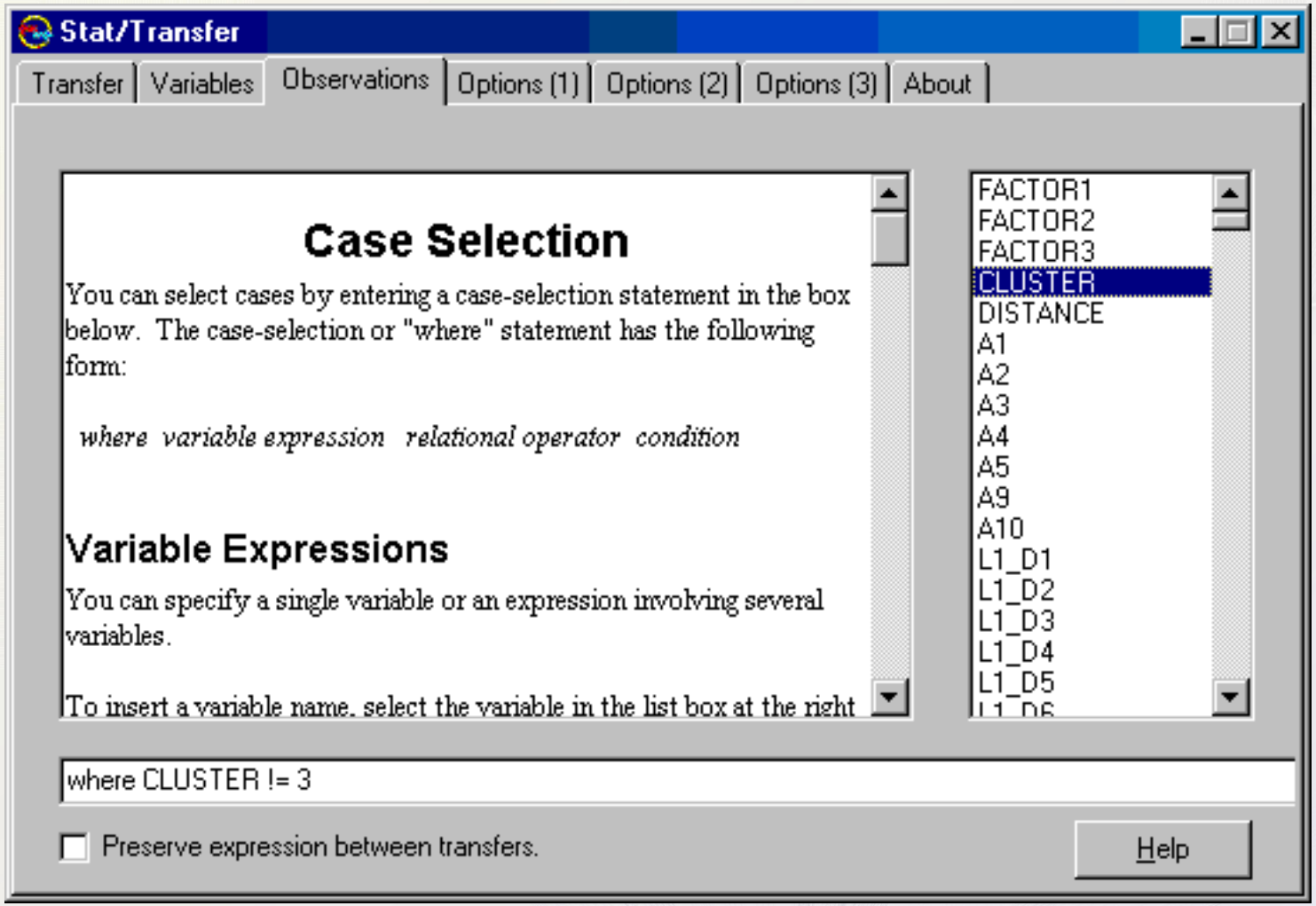
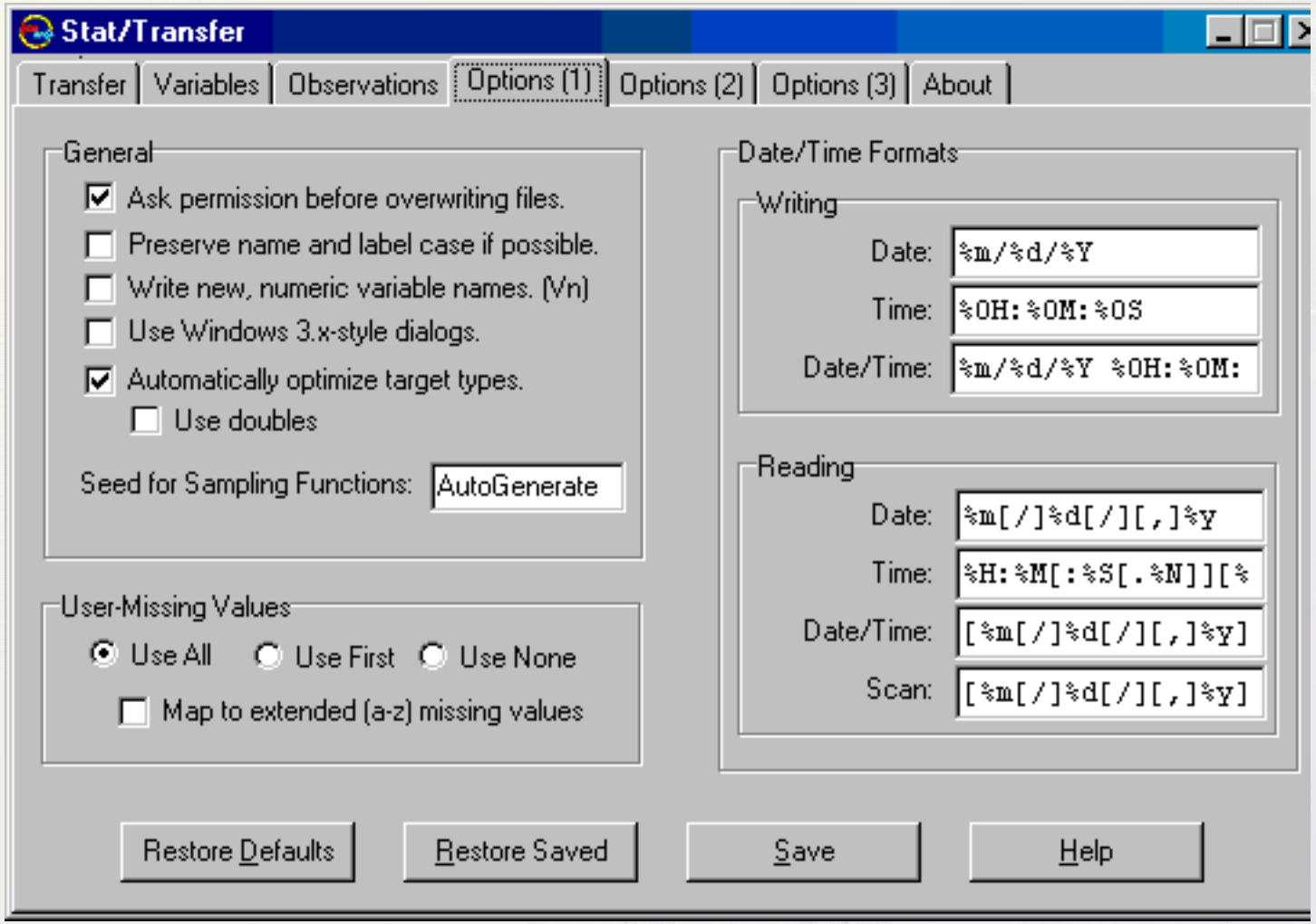
Stat-Transfer Variables Screen



Stat-Transfer Observations Screen



Stat-Transfer Options (1) Screen



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Converting SAS data files to other formats

- http://www.ats.ucla.edu/stat/stata/faq/convert_pkg.htm
- http://www.stata.com/support/faqs/data/convert2.html
- http://rconvert.com/sas-vs-r-code-compare/5-ways-to-convert-sas-data-to-r/
- http://support.sas.com/documentation/cdl/en/movefile/59598/HTML/default/viewer.htm#creattrans.htm
- www.stattransfer.com

Defining Study Cohorts

- Separate data linkage/management section from data analysis section in the statistical code
- Data linkage/management section is where changes to data structure occur while data analysis section is where analytical techniques are applied
- Once datasets are managed and linked, use TX_DATE as time origin for analyses of post-transplant outcomes
- Can condition on survival to some time point post-transplant to perform landmark analyses but need TX_DATE as anchor

Defining Study Cohorts

- Define inclusion and exclusion criteria *a priori* and use relevant variables in dataset to establish conditioning statements
- Apply each criterion or conditioning statement in sequence noting that ordering of sequence may be relevant to ultimate composition of cohort
- These numbers will provide data for study flow diagram that depicts creation of study cohort used for analysis

Defining Study Cohorts: Example using Stata

```
dis _N
drop if txdate<mdy(1,1,2000)|(txdate>mdy(12,31,2009) & !missing(txdate))
drop if dtype==2
drop if ragetx<18
drop if rprvki==1
drop if prevnonki==1
drop if esrddx==7
drop if missing(rbmigp)
drop if missing(dbmigp)
drop if missing(hlamm)
drop if missing(dcd)
drop if missing(kdri)
dis _N
```

Defining Key Survival Endpoints: Recipient's Last Follow-Up Date

- SAF Contains a variable called: TFL_ENDTXFU
- This is the variable to use to identify the last possible follow-up date for transplant recipients
- Built in lag of 3 months to allow for form completion
  - For the Mar 2012 SAF, last form completion would be 31 Dec 2011
  - If < 6 months have elapsed from transplant to 31 Dec 2011, TFL_ENDTXFU = TXDATE, i.e., 0 follow-up available
  - If 6 to 12 months have elapsed, TFL_ENDTXFU = TXDATE+6 Months
  - If > 12 months have elapsed, TFL_ENDTXFU = TXDATE + # of full years from transplant that have elapsed prior to 31 Dec 2011.

Defining Key Survival Endpoints: Death

- SRTR Method: First, use a death reported on the transplant recipient follow-up form for this transplant.
  - Variable: TFL_DEATH_DT (unique to this transplant event)
- If missing, look for death reported by OPTN for this patient
  - Variable: PERS_OPTN_DEATH_DT (waiting list removal reason, recipient registration, follow-up records)
- If still missing, look for death reported by the SSA
  - Variable: PERS_SSA_DEATH_DT
- If still missing, look for a death reported by CMS
  - Variable: PERS_ESRD_DEATH_DT

Defining Key Survival Endpoints: Graft Failure

- Kidney (names differ slightly for KP kidney dates)
  - min(TFL_GRAFT_DT, death_date, PERS_RETX, REC_ESRD_FAIL_DT)
- Heart & Liver
  - min(death_date, PERS_RETX);
- Intestine & Pancreas (names differ slightly for KP pancreas dates)
  - min(TFL_GRAFT_DT, TFL_LAFUDATE, death_date, PERS_RETX)
- Lung & Heart-Lung
  - min(TFL_GRAFT_DT, TFL_LAFUDATE, death_date)

Organ	Graft Failure Date	Last Follow-Up Date	Death Date	Re-Tx Date	CMS Graft Failure Date
Kidney	X		X	X	X
Heart & Liver			X	X	
Intestine & Pancreas	X	X	X	X	
Lung & Heart-Lung	X	X	X		

How are Multi-Organ Transplants Handled in the Database?

- This is dependent on OPTN's program definition:
  - KP and HL programs have their own designation and forms. Therefore, KP and HL transplant recipient information and follow-up information are in their own unique data files, e.g., TX_KP and TX_HL
  - Other multi-organ transplants can be identified as follows:
    - REC_TX_ORG_TY: Indicates multi-organ recipients
    - REC_TX_TY: Provides additional detail regarding number of organs and donors involved.
    - Use TX_ID to link multi-organ recipients across multiple TX_xx files.

REC_TX_ORG_TY and REC_TX_TY

Format Name	Code	Descript
$TXORGTY	HL	HL: Heart-Lung
$TXORGTY	HR	HR: Heart
$TXORGTY	IN	IN: Intestine
$TXORGTY	KI	KI: Kidney
$TXORGTY	KI HL	KI HL: Kidney-Heart-Lung
$TXORGTY	KI HR	KI HR: Kidney-Heart
$TXORGTY	KI IN	KI IN: Kidney-Intestine
$TXORGTY	KI LI	KI LI: Kidney-Liver
$TXORGTY	KI LI 2LD	KI LI 2LD: Two Living Donors, Kidney-Liver TX
$TXORGTY	KI LI HR	KI LI HR: Kidney-Liver-Heart
$TXORGTY	KI LI IN	KI LI IN: Kidney-Liver-Intestine
$TXORGTY	KI LU	KI LU: Kidney-Lung
$TXORGTY	KI PA LD/DD	KI PA LD/DD: Living Donor Kidney, Deceased Donor Pancreas TX
$TXORGTY	KP	KP: Kidney-Pancreas
$TXORGTY	KP HR	KP HR: Kidney-Pancreas-Heart
$TXORGTY	KP IN	KP IN: Kidney-Pancreas-Intestine
$TXORGTY	KP LI	KP LI: Kidney-Pancreas-Liver
…	…	…

Format Name	Code	Descript
TXTYPE	1	1: Single donor, single organ type TX
TXTYPE	2	2: Single donor, multiple organ types TX
TXTYPE	3	3: Multiple donors, single organ type TX
TXTYPE	4	4: Multiple donors, multiple organ types TX

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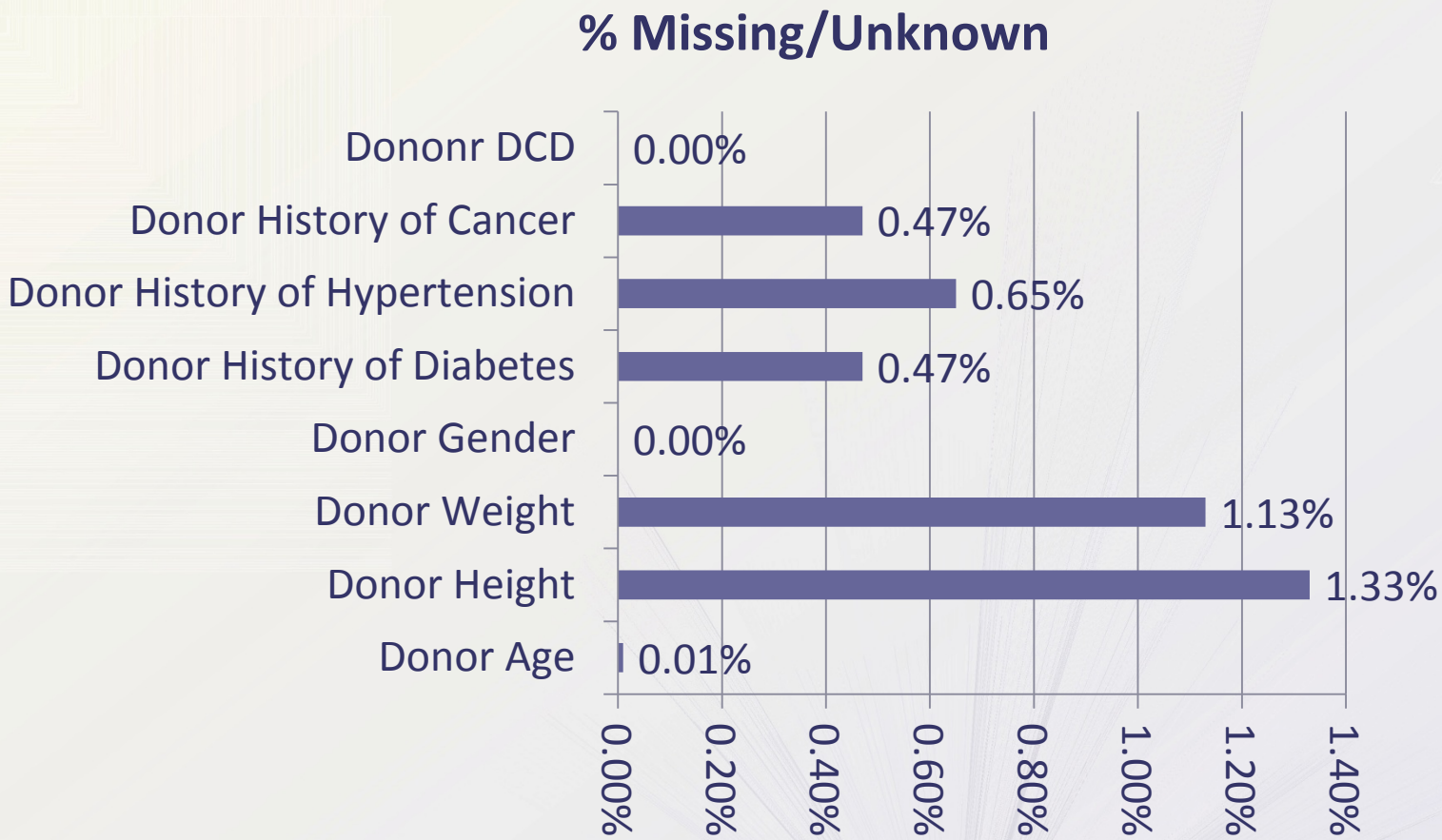
OPTN's Ongoing Data Quality Initiative*:

- Transplant Coordinators Committee (TCC) of OPTN working on initiative to review and bolster data definitions for many of the OPTN forms
- Just completed review of all required Transplant Recipient Registration (TRR) fields
- The Committee then moving to the Transplant Candidate Registration (TCR) form
- Some minor changes (label changes, consistency issues) have already been submitted to IT for modification
- TCC also creating list of issues for the organ-specific committees to address including questions coordinators feel would be better answered by the surgeons
- Recommendations for additional choices or elimination of choices to fields
- Many issues being sent to organ specific committees to request definitions to be developed to add to the documentation (e.g., define portal vein thrombosis, etc.)
- This will be an ongoing effort, with focus turning to follow-up forms after the TRR/TCR forms are completed
- Thanks to Maureen McBride, PhD, Director of Research, UNOS, for the update

Example: Completeness of Common Donor Elements for Kidney Recipients, 2010-2011



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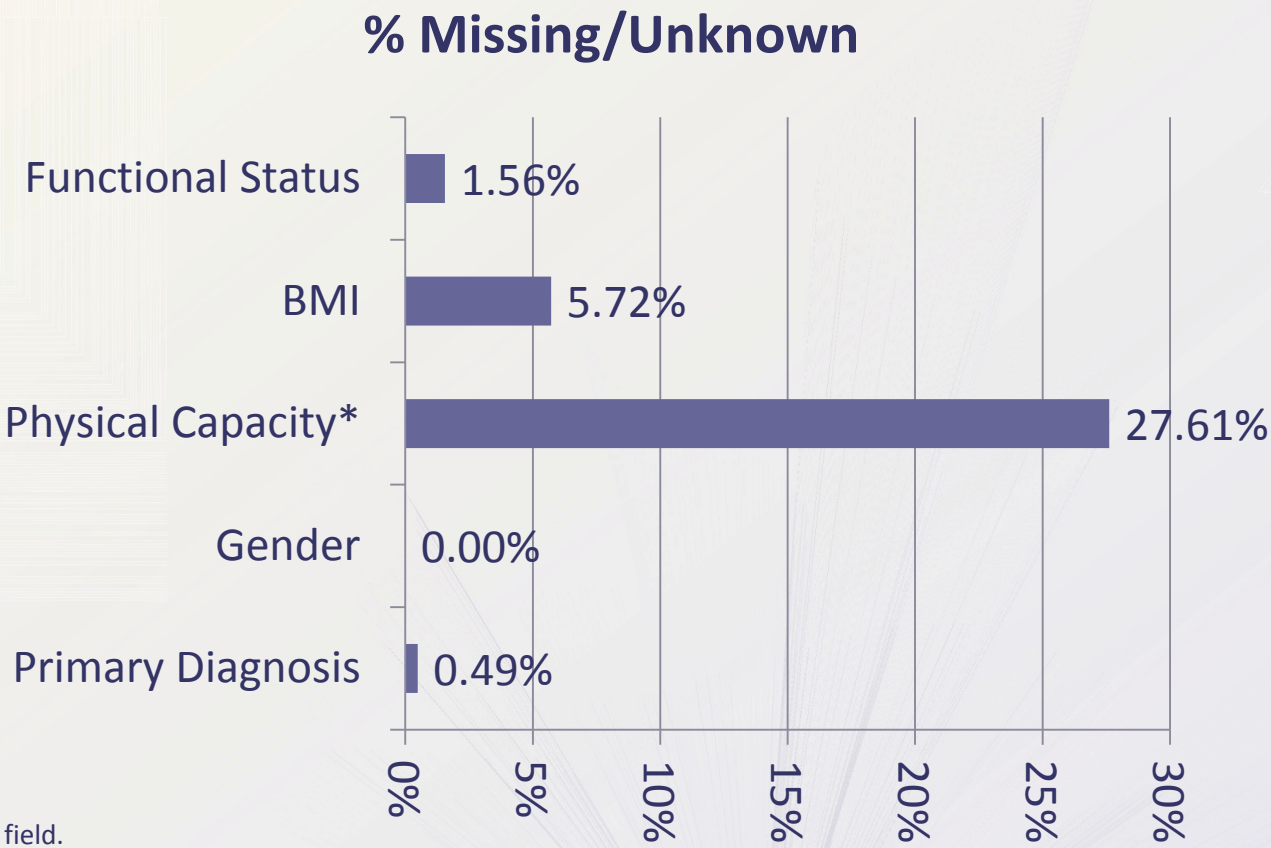
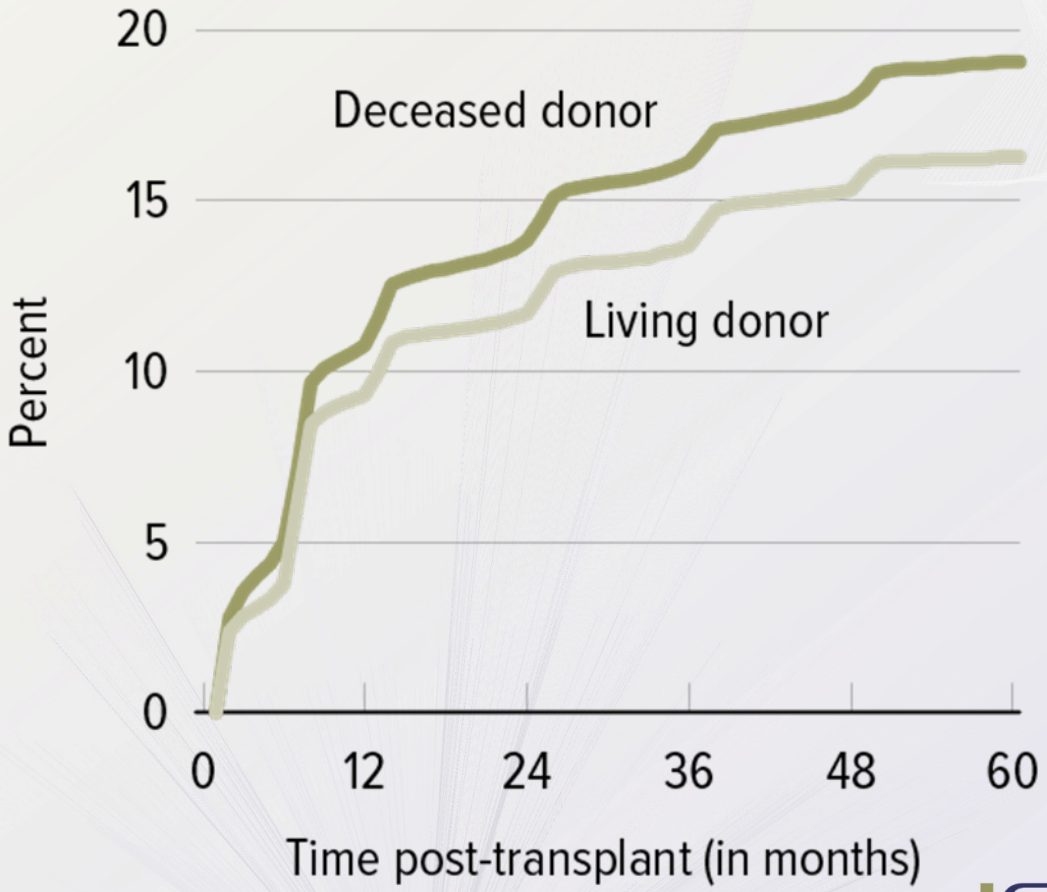
Example: Completeness of Common Recipient Elements for Kidney Recipients, 2010-2011



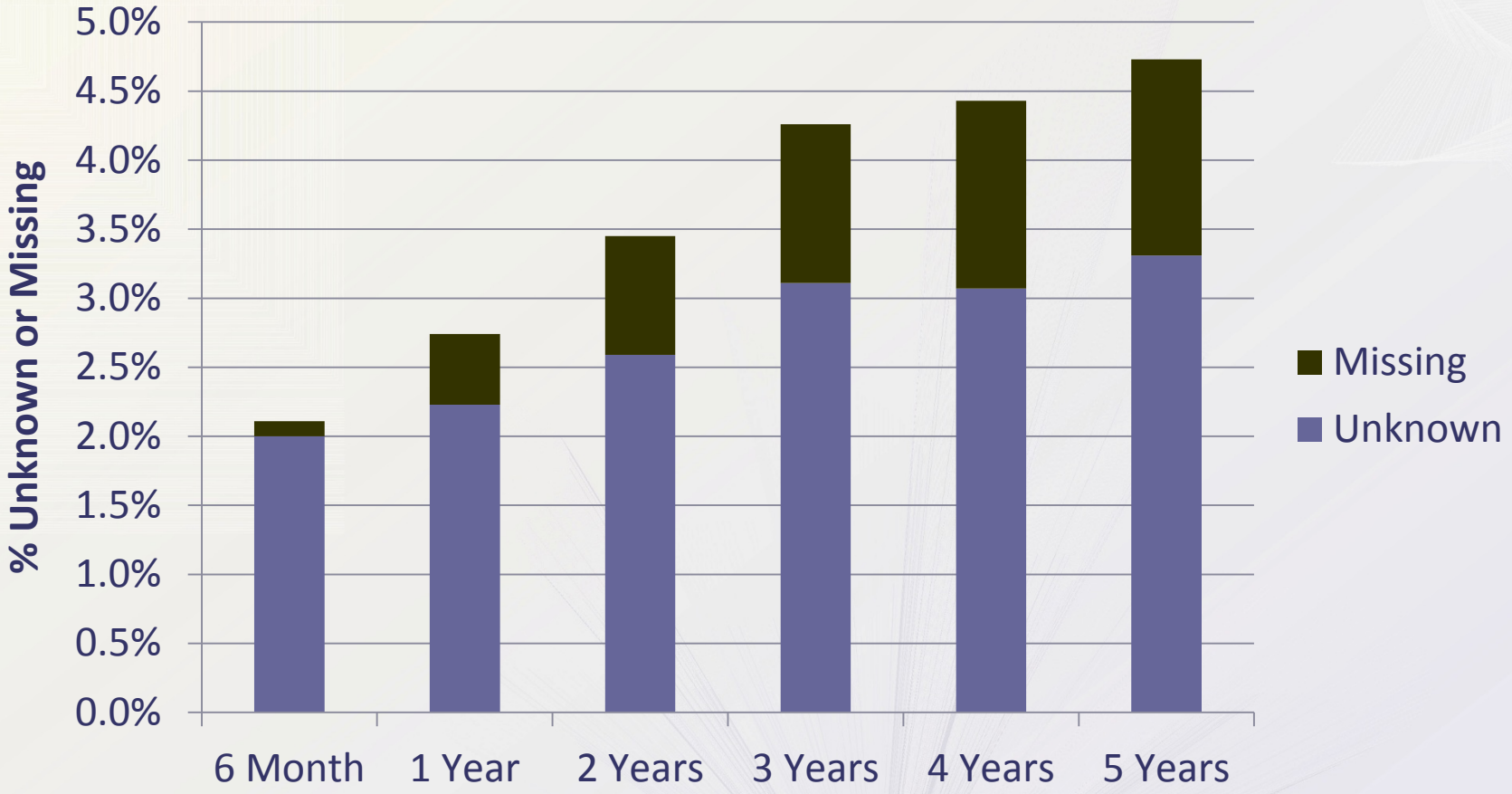
*Not a required field.

Data Completeness: Acute Rejection Data
OPTN/SRTR 2010 Annual Data Report, Figure KI 6.7

- Data on acute rejections are collected on the 6 month and annual follow-up forms.
- Dates are not requested, which yields this "step" function when plotting the incidence of acute rejections.



Ascertainment of Acute Rejection Episodes, 2004-2011 Recipients



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CPRA Implementation Timeline

December 2007

- CPRA added to the OPTN system to be viewed alongside the actual PRA.

October 1, 2009

- CPRA replaced traditional PRA.
- Sensitization points are now based on CPRA.

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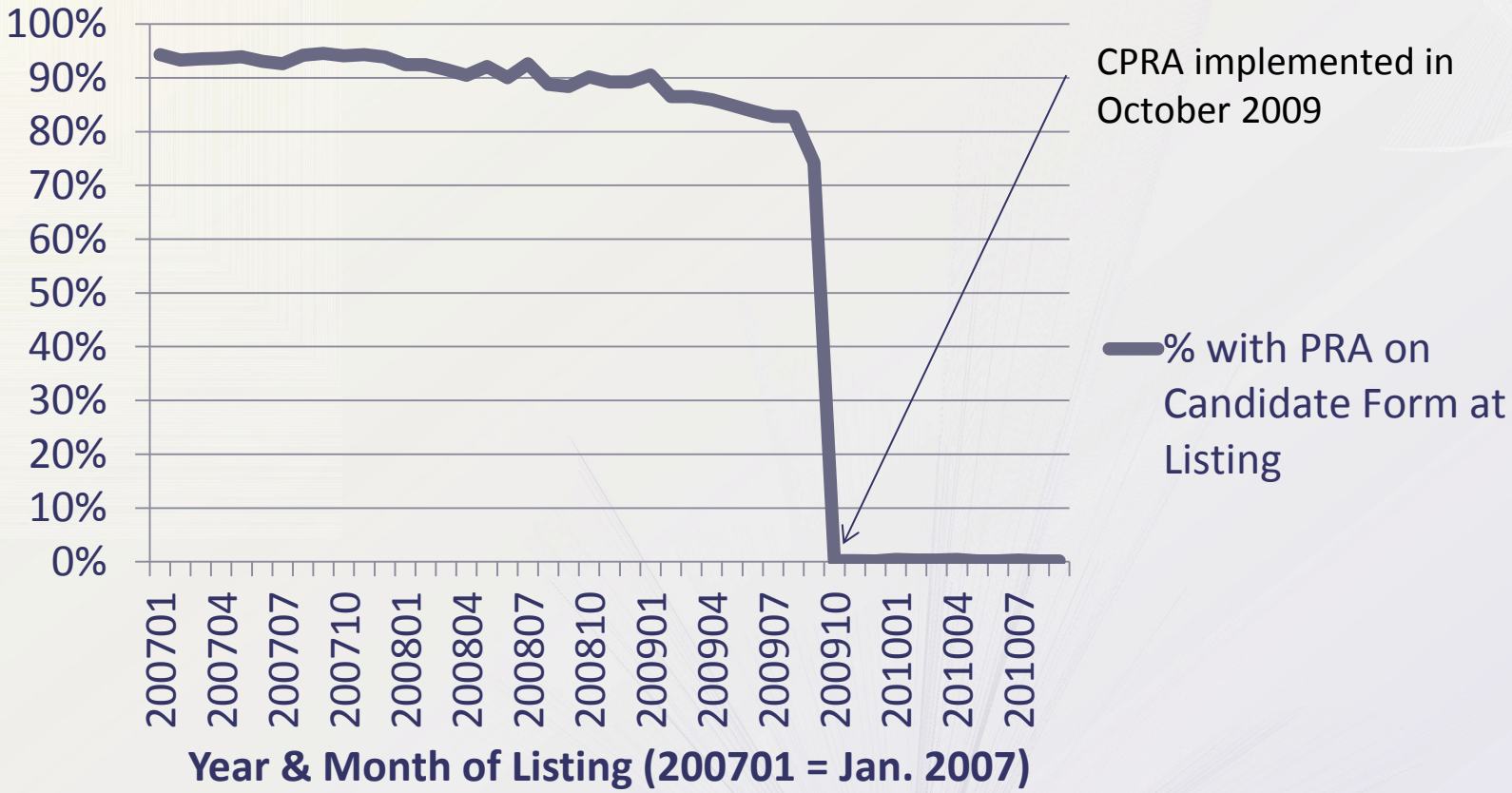
Percent of Patients with Measured PRA Reported to OPTN

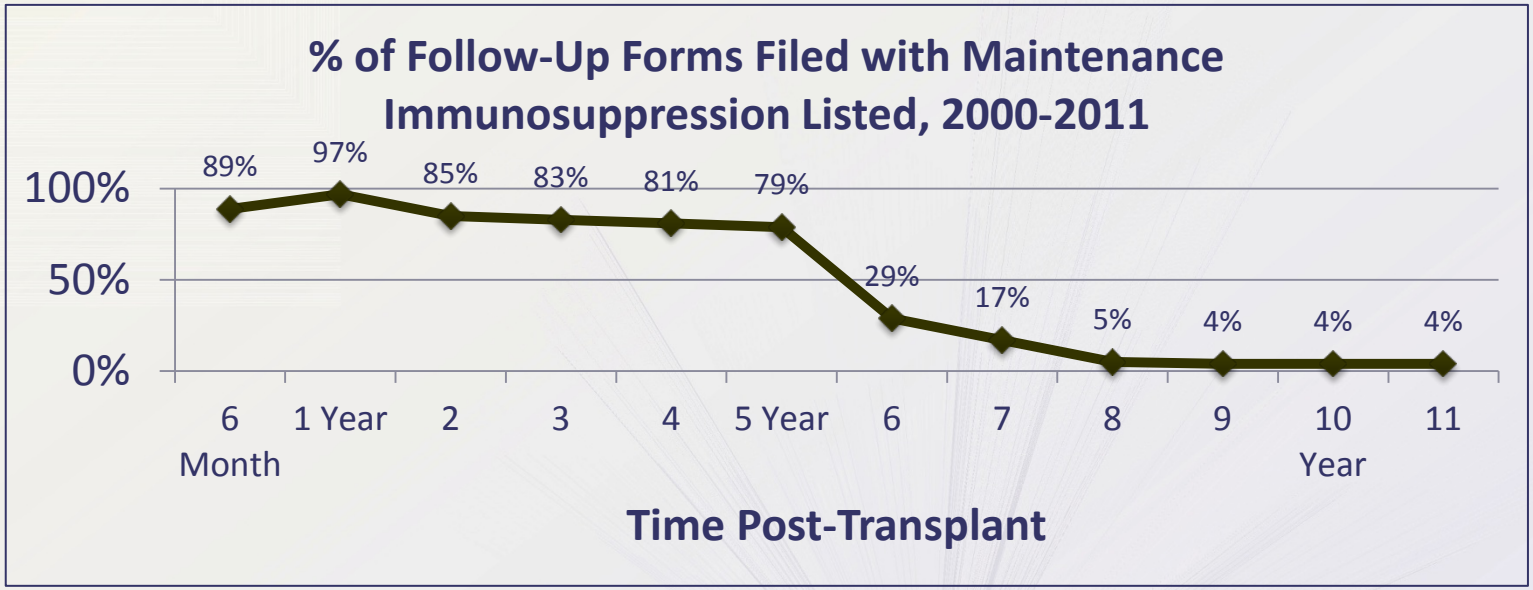


Measured PRA and CPRA in the Current SRTR SAF

- Measured PRA are found in: PRA_HIST.
- CPRA data are currently found in: STATHIST_KIPA.
- SRTR is currently rebuilding PRA & CPRA history files and will supply both measured and CPRA in the PRA_HIST file in upcoming SAF releases.

Immunosuppressive Medications

- OPTN Data Reduction Project, 2/7/2007, IS is only required at baseline and 1 year.
- Immunosuppression is generally provided through 5-years post-transplant.



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