Choosing ImmunoSuppression regimens in renal Transplant by Efficacy and Morbidity 2 (CISTEM2)

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Background

- The transplant recipient's immune system recognizes new kidney transplant as foreign and attacks it
- Multiple medicines (i.e., immunosuppresants, IS) suppress the immune system but does not always work perfectly
- Therefore, transplant recipients susceptible to life-threatening infections
- Each IS medicine we use has some potentially major side effects; they can add up
- **Q: How do we choose which IS medicines, and how do we adjust over time?**

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First Study: CISTEM1

- **Evaluated association of *initial immunosuppression regimen* with key clinical outcomes**
  - Patient and kidney transplant survival
  - Development of cardiometabolic complications (e.g. diabetes)
  - Infectious complications
- **Data sources**
  - Transplant Registry (SRTR) data on donor and recipient outcomes
  - Medicare FFS claims
  - Pharmacy claims
- **Results and Contribution**
  - Recognize that the choice of IS varies markedly across centers, even those serving nearly identical populations in the same region in the U.S.
  - Developed and piloted a free web-based application for kidney transplant
    - https://neph-calc-i2-wustl.azurewebsites.net/
    - Shared decision making
    - Improve discussion of options with patients
  - Utilize data sources beyond SRTR to assess outcome
    - SRTR/Medicare data to assess long term outcomes

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First Study: CISTEM1

- **Limitations**
  - Medicare claims lack detailed clinical data on kidney function and meaningful outcomes
    - Patients with advanced CKD are equivalent to patients with normal function
    - E.g., serum creatinine levels/eGFR, tacrolimus drug levels, measures of viremia and viruria, malignancy diagnoses, and rehospitalization events
  - Selection bias of patient cohort
    - Only assessed patients with Medicare primary insurance
    - Medicare pays > 60% of transplants but has fewer living donor recipients
  - Paucity of longitudinal data and responsive outcomes
    - How should immunosuppression be adjusted after an episode of rejection

Objective and Aims

Aim 1: establish a novel, robust and curated database (CISTEM2 Database) **integrating transplant registry data with multi-site EHRs, claims and social determinants of health** data for KT recipients, leveraging the PCORnet infrastructure.

Aim 2: develop longitudinal machine learning (ML) algorithms to dynamically suggest immunosuppression (IS) strategies that optimize renal allograft function (at 1-, 3- and -5-years post-KT), reduce cost, and limit IS comorbidities.

Aim 3: validate and fine-tune the temporal-aware ML models to determine reliability in predicting long-term graft function in by additionally incorporating data from other two PCORI networks.

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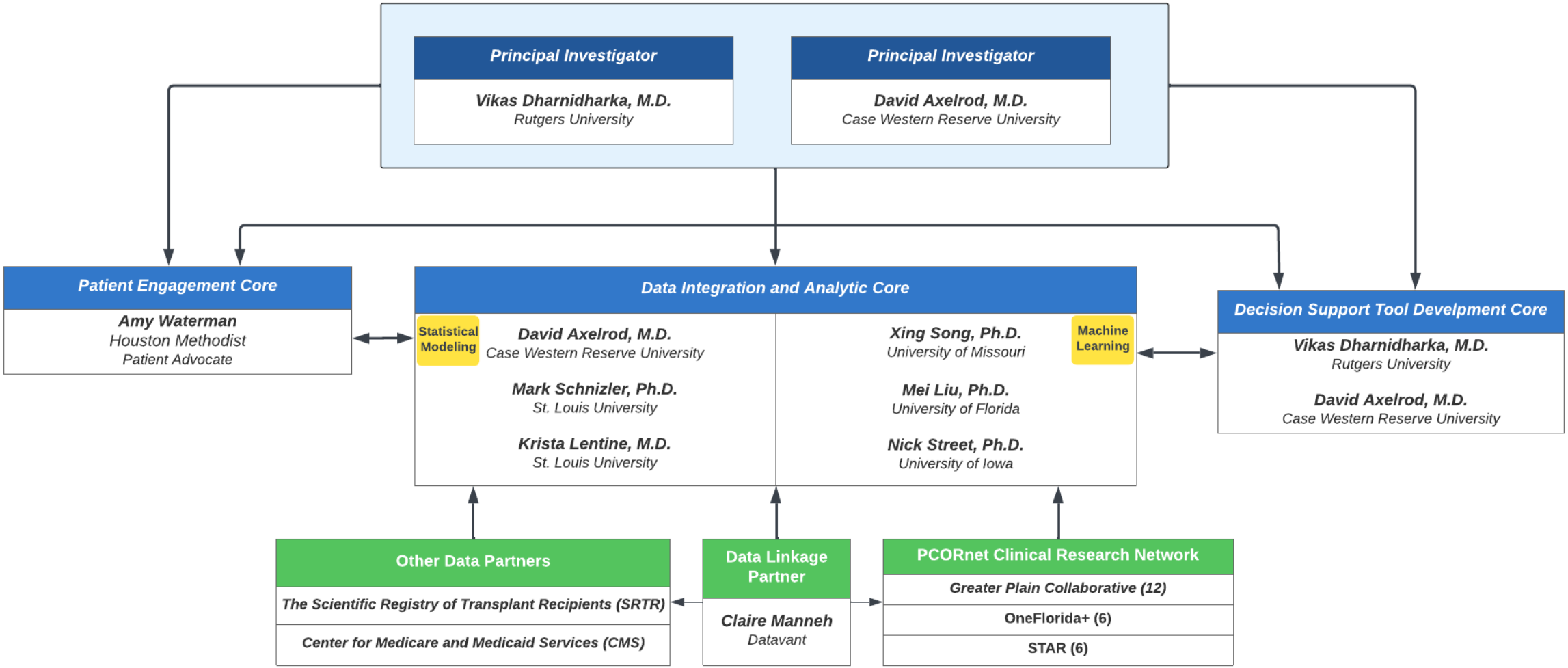
Study Team



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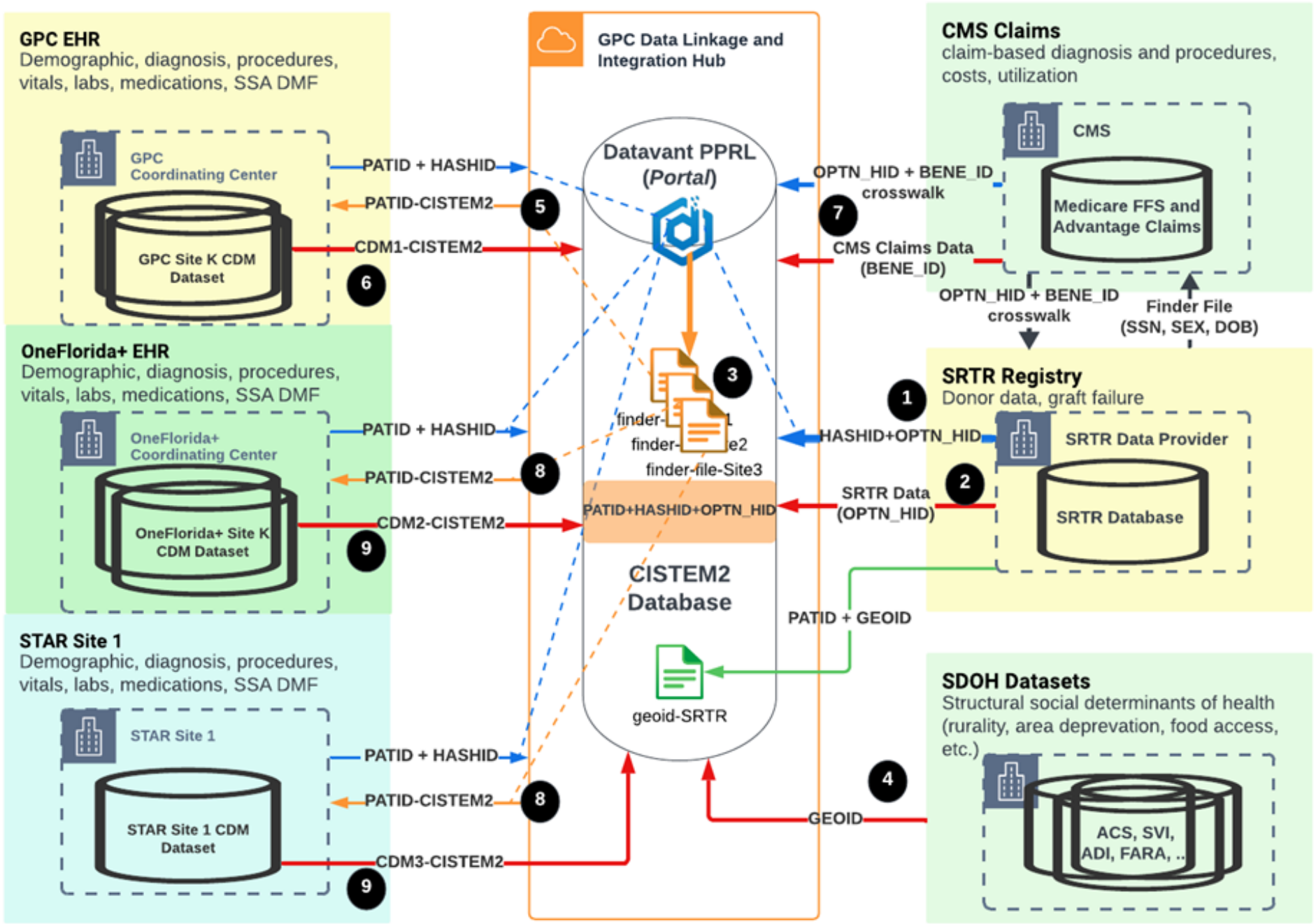
Participating Sites

Transplant Hospital/ Health System	PCORnet CRN	#KTx 2012-23
University of Missouri (DCC)	GPC	179
Allina Health System	GPC	290
Intermountain Healthcare	GPC	1078
Medical College of Wisconsin	GPC	728
University of Iowa	GPC	836
University of Kansas Medical Center	GPC	1383
University of Nebraska Medical Center	GPC	1448
University of Utah	GPC	1276
UT Health Science Center at San Antonio	GPC	1078
UT Southwestern Medical Center	GPC	989
Washington University in St. Louis	GPC	2526
UT Health Science Center at Houston	GPC	637
GPC Total		***12,448***
Vanderbilt University Medical Center	STAR	2286
Duke University Medical Center	STAR	1497
Health Sciences of South Carolina	STAR	2630
Mayo Clinic Arizona	STAR	3407
Mayo Clinic Rochester	STAR	2171
Mayo Clinic Florida	STAR	1673
University of Florida	OneFlorida+	970
University of Miami	OneFlorida+	3726
Advent Health	OneFlorida+	1592
Emory University	OneFlorida+	2766
Tampa General Hospital	OneFlorida+	2749
University of Alabama at Birmingham	OneFlorida+	2620
Total (GPC/STAR/One Florida)		***40,535***

Dataflow


GPC EHR
Demographic, diagnosis, procedures, vitals, labs, medications, SSA DMF
GPC Coordinating Center
GPC Site K CDM Dataset
OneFlorida+ EHR
Demographic, diagnosis, procedures, vitals, labs, medications, SSA DMF
OneFlorida+ Coordinating Center
OneFlorida+ Site K CDM Dataset
STAR Site 1
Demographic, diagnosis, procedures, vitals, labs, medications, SSA DMF
STAR Site 1
STAR Site 1 CDM Dataset
PATID + HASHID
PATID-CISTEM2
CDM1-CISTEM2
CDM2-CISTEM2
CDM3-CISTEM2
GPC Data Linkage and Integration Hub
Datavant PPRL (Portal)
finder-file-Site3
PATID+HASHID+OPTN_HID
CISTEM2 Database
geoid-SRTR
CMS Claims
claim-based diagnosis and procedures, costs, utilization
CMS
Medicare FFS and Advantage Claims
OPTN_HID + BENE_ID crosswalk
CMS Claims Data (BENE_ID)
Finder File (SSN, SEX, DOB)
SRTR Registry
Donor data, graft failure
SRTR Data Provider
SRTR Database
HASHID+OPTN_HID
SRTR Data (OPTN_HID)
PATID + GEOID
SDOH Datasets
Structural social determinants of health (rurality, area deprevation, food access, etc.)
ACS, SVI, ADI, FARA, ..
GEOID
1
2
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Site SOW and Budget

- **Site SOW**
  - Administrative readiness: IRB or NHS, DUA
  - Technical readiness: Datavant license
  - Hash token generation and linkage (Datavant portal access)
  - CDM extraction and submission

- **Site budget**

Budgeted Items	Each Performing Site
1. Infrastructure Cost Recovery (ICR)	$ 10,962
2. Administrative and Startup costs (including small PI oversight effort)	$ 5,000
3. Hash token generation and linkage	$ 7,800
4. Site CDM Data-as-a-Product	$ 5,000
Total	$ 28,762