

Validation of center-reported immunosuppressive medication use with an independent pharmacy database

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Introduction

- Data on immunosuppressive (IS) medication use in organ transplant recipients is mandatorily collected by the Organ Procurement and Transplantation Network (OPTN) at time of transplant, 6 months, and 12 months posttransplant.
- After that time, IS data submission is elective at 1-year intervals.
- Data does not capture dosages and is insensitive to medication changes.
- The Scientific Registry of Transplant Recipients (SRTR) sought to describe agreement between OPTN-reported IS information and pharmacy fill data obtained through a linkage with a large national aggregator of pharmacy fills (IMS Health).

Methods

- The study population consisted of primary kidney transplant recipients between January 1, 2006 and December 31, 2011. Patients with a prior history of solid-organ transplants were excluded.
- Three cohorts were constructed by whether at least one immunosuppressive fill was captured by the IMS database during 1) 0-6 months posttransplant; 2) 6-12 months posttransplant; or 3) 30-36 months posttransplant.
- Immunosuppressive medication classes included calcineurin inhibitors, antimetabolites, mTOR inhibitors, and steroids. However, having only steroidal claims was insufficient for inclusion.
- Classes were also split into agents and brands. For example, calcineurin inhibitors were split into CsA and tacrolimus, which were further divided into Neoral and Gengraf (CsA) and Prograf (tacrolimus).
- Cohort 1 was compared to OPTN data at discharge, Cohort 2 was compared to OPTN data at 1-year follow-up, and Cohort 3 was compared to (optional) OPTN data at 3-year follow-up. Only fills occurring between the start of the cohort and the date of the follow-up form were included.
- Kappa statistics and percent agreement were calculated for each cohort.

Results

- Agreement between OPTN and IMS IS data was relatively high, but varied by time and medication type.
- Agreement was best at 12 months in agent-specific comparisons, and at 3 years in class-specific comparisons.
- Kappa is the probability of observed agreement minus the probability of chance agreement, divided by the possible beyond-chance agreement.
- The Kappa statistic can range from -1 to 1, with a value of 0 indicating chance agreement. Values from 0.21 to 0.40 indicate fair agreement; 0.41 – 0.60 moderate; 0.61-0.80 substantial; and 0.81 - 1.00 almost perfect†.
- Kappa was higher in class-specific versus agent-specific comparisons.
- When using an alternate term for the probability of chance agreement††, the Kappas for CsAs, azathioprine, and mTOR inhibitors increased to 0.90 -0.98.
- In cases where more than 50% of the cohort had neither OPTN nor IMS evidence of a drug, IMS was more likely than OPTN to report use of a drug in the remaining portion of the cohort (Figure 1). This suggests that IMS may be better at detecting less common drugs. However, sensitivity and specificity calculations are not possible in absence of an assumed gold standard.
- Figure 1 shows data at baseline; however, the pattern also held for data at 1 and 3 years posttransplant.

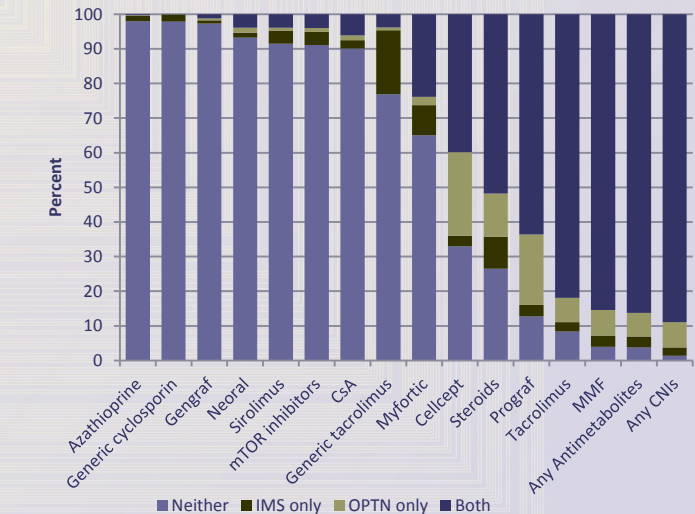
†Landis and Koch, 1977, Biometrics.

†† Brennan and Prediger, 1981, *Educ. Psychol. Meas.*

Table 1. Agreement and Kappa statistics for drug classes and agents

Class or agent	OPTN Report vs. Pharmacy Fills by Months Posttransplant					
	Baseline 0-6 months (n=29,974)		12-month 6-12 months (n=20,642)		3-year 30-36 months (n=8,021)	
	% agree	Kappa statistic	% agree	Kappa statistic	% agree	Kappa statistic
CsA	96.2	0.74	97.3	0.82	96.8	0.81
Neoral	97.2	0.72	97.4	0.73	96.1	0.65
Gengraf	98.6	0.63	98.6	0.68	98.4	0.56
Tacrolimus	90.3	0.58	90.3	0.66	91.6	0.74
Prograf	76.4	0.39	75.9	0.44	68.9	0.36
Mycophenolate Mofetil	89.4	0.38	87.7	0.53	89.7	0.66
Cellcept	72.8	0.48	76.1	0.53	68.9	0.41
Myfortic	88.9	0.73	92.2	0.81	93.1	0.82
Azathioprine	98.2	0.63	99.0	0.73	98.7	0.56
mTOR inhibitor	95.0	0.59	96.8	0.79	97.3	0.85
Steroids	78.2	0.54	80.0	0.60	83.3	0.67

Figure 1. Evidence for immunosuppressives at baseline, by source



Conclusions

- We found a high level of agreement between OPTN center-supplied IS data and IMS data. Kappas ranged from fair to substantial, and were generally highest at 12 months posttransplant, after which IS reporting to OPTN is no longer mandatory.
- Agreement levels and Kappa statistics were highest with CsAs and mTOR inhibitors.