From Many to One - Applying Big Data to Managing Individual Patients

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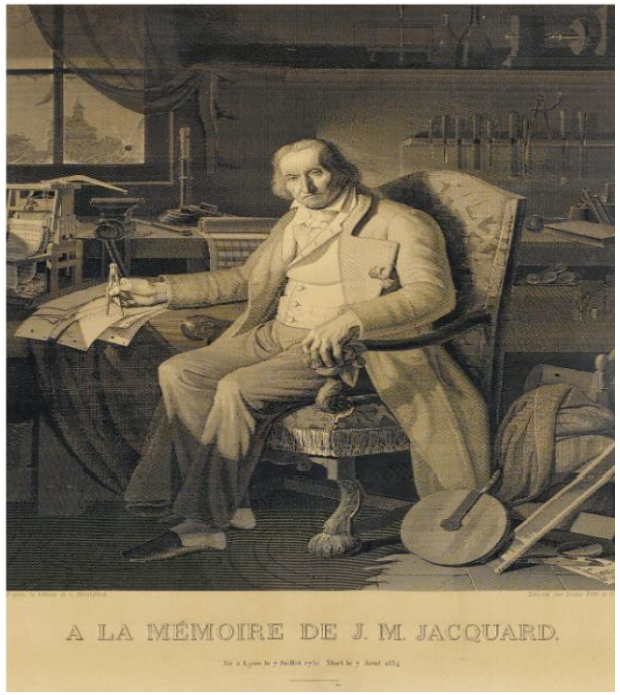
Intermountain Healthcare, Murray, UT

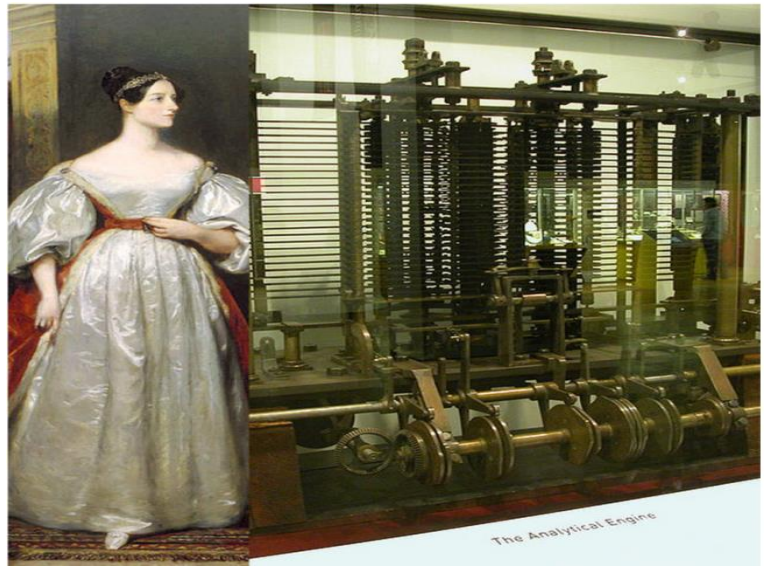
Disclosures

- Research funding from Medeor Therapeutics, CareDx
- Will have material covering Rx Match, a Proprietary pharmacogenomic platform deployed at Intermountain and run and marketed by Intermountain Precision Genomics

Ada Lovelace Byron

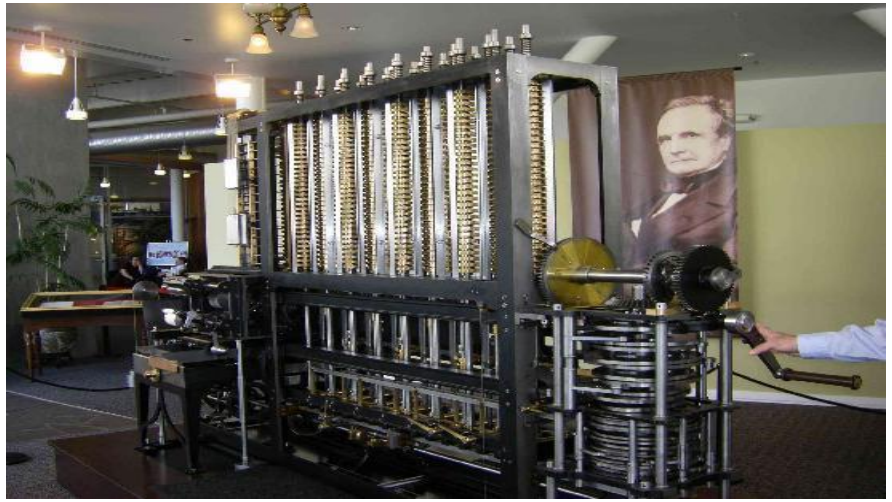


Joseph Marie Jacquard



Ada Lovelace Byron and
Analytical Engine

Punch Cards



Charles Babbage and the Difference Engine

Case

- A 42 year old man transplanted with his second kidney develops acute antibody mediated rejection over the weekend. The surgeon and nephrologist on the case heard a colleague present his preliminary experience with the off label use of bortezomib to treat AMR and decide to use it in this case.
- Bortezomib is used successfully after an emergency consultation with the innovation committee

75 years of collective Experience went into this decision making process !

TIME

10 Questions for Watson's Human

Watson handler — and IBM lead researcher — David Ferrucci talks about the mind of his machine

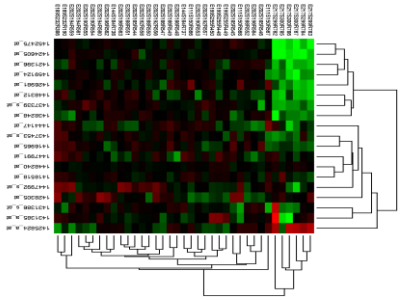
By David Ferrucci | Monday, Mar. 07, 2011

IBM talks about Watson's being used to diagnose diseases. Can a machine make intuitive leaps like the ones Dr. House makes on the TV show?

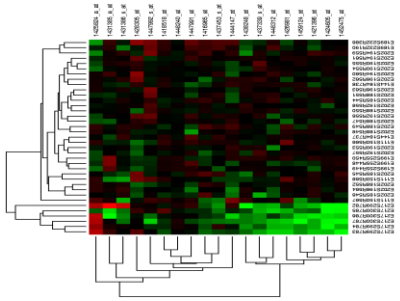
That's a tough question, because I wonder what intuition really is. It's probably a process like connecting the logical dots, but we call it intuition simply because we're not fully conscious of the process.

The Opportunity

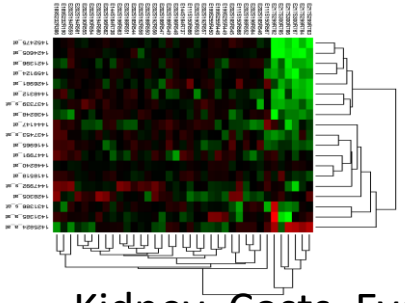
:



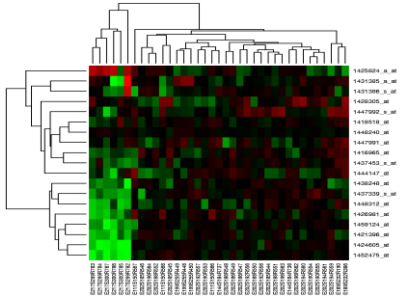
ESRD Patient, Costs/Events



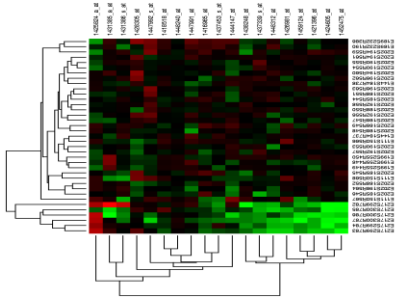
Transplanted Patient Costs/Events



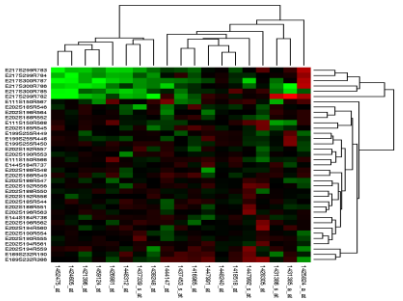
Kidney ,Costs, Events, pathology



Patient at 6 mo, Costs/Events



Transplanted Patient
at 6 mo, Costs/Events



Kidney at 6 mo, Costs/events/pathology

Objectives

- Describe an actionable approach to deployment of a predictive analytics solution in the clinic
- Describe a clinical framework for implementation of precision medicine and genomics in the transplant clinic through a case based approach
- Describe differences between traditional statistics and predictive analytics and how these may apply to building a solution

What Does the expression “Big Data” mean ?

- **Definition**: A term that describes large volumes of high velocity, complex, and variable data that require advanced techniques and technologies to enable the capture, storage, distribution, management, and analysis of the information
- Big data goes beyond size and volume to encompass such characteristics as variety, velocity, and, with respect specifically to health care, veracity.
- Big data can be said to comprise five different categories, or streams, of information

Tech America Foundation 2012

Components of Big Data in Health Care

a) **Web and Social Media Data**
b) **Machine to machine data:** Sensors; Think readings and the electronics that generate readings
c) **Big Transaction Data:** Billing, payments, adjustments, subsidies
d) **Biometric data:** Fingerprints, genetics, handwriting, retinal scans, and similar types of data. This would also include X-rays and other medical images, blood pressure, pulse and pulse-oximetry readings, and other similar types of data
e) **Human-generated data:** Unstructured and semi-structured data such as electronic medical records (EMRs), physicians' notes, email, and paper documents

IBM Whitepaper 2013

Current Data Structure

- OPTN and SRTR data though comprising large data sets, are highly structured
- They do not capture longitudinal evolution of clinical patterns
- Traditional analytic approaches that are model based are appropriate
- Current utilization is mainly regulatory and generates research data that are based on associations

- Cottage industry based on “regulatory workarounds”

Background

- ***Predictive models in kidney transplantation derived from national data (UNOS, SRTR) lack longitudinal patient level data, thereby limiting effectiveness***

- ***Adding patient level data capturing dynamic post-transplant clinical evolution to predictive models, may improve predictive accuracy for graft loss (GL) risk.***

- *Complete capture of patient level clinical data in real time would require an approach that extracts, collates and curates both structured and unstructured data from electronic health records (EHR)*

- *These large amounts of data are notable for volume, velocity, variety and, verified veracity;* ***An operational definition of Big Data***

- *Analytic techniques should be able to handle such data*

Attributes of the Ideal Predictive Model for Graft Loss

- Appropriate to Center's Population and customizable
- Ability to discriminate across levels of risk
- Feasibility of build around clinically actionable variables
- Uses data available within the EMR that are collected in the context of standard patient care
- Biologically relevant to the extent of current understanding including social determinants and care processes
- Ability to inform on individual patient trajectories and capture dynamic longitudinal clinical evolution in the temporal context of routine clinical care

Hyperfiltration in remnant nephrons: a potentially adverse response to renal ablation

T. H. HOSTETTER, J. L. OLSON, H. G. RENNKE, M. A. VENKATACHALAM,
AND B. M. BRENNER
Laboratory of Kidney and Electrolyte Physiology and Departments of Medicine and Pathology,
Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115

AJP Renal 1981

- Hyperfiltration will be associated with a constant serum creatinine level despite ongoing nephron loss

Subtle Acquired Renal Injury as a Mechanism of Salt-Sensitive Hypertension

Richard J. Johnson, M.D., Jaime Herrera-Acosta, M.D., George F. Schreiner, M.D., Ph.D., and Bernardo Rodríguez-Iturbe, M.D.

March 21, 2002

N Engl J Med 2002; 346:913-923

- The transplanted kidney is a substrate for acute and chronic tubulointerstitial injury
- Loss of renal function will be associated with sympatho adrenal activity with variable blood pressure and heart rate
- Loss of interstitial function will manifest as anemia, acid-base and potassium abnormalities

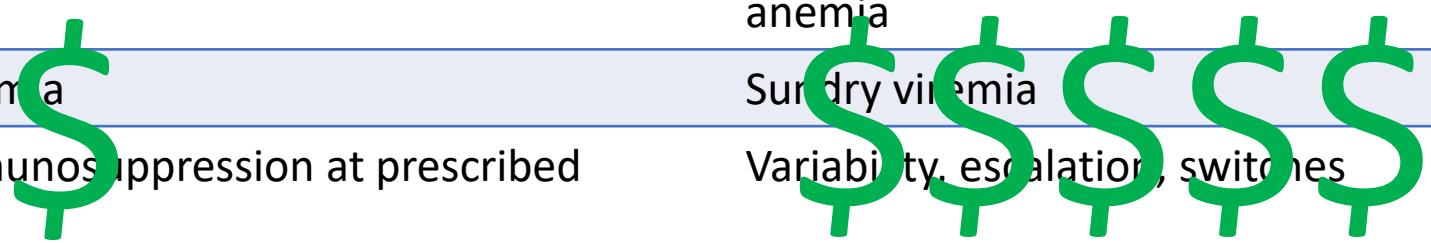
The Auxometric Dimension
A New Method for Using Rate of Growth in Prognostic Staging of Breast Cancer

Mary E. Charlson, MD; Alvan R. Feinstein, MD

JAMA. 1974;228(2):180-185. doi:10.1001/jama.1974.03230270024019

Clinical Evolution

Well Patient	Unwell Patient
Stable creatinine slope	Deteriorating or variable slope
Absence of proteinuria	Presence of proteinuria
Normal acid base status and potassium	Acidosis, hyperkalemia
Improving and stable Hematocrit	Subtle deterioration in hematocrit before manifest anemia
Absence of Viremia	Subdry viremia
Maintenance imunosuppression at prescribed intensity	Variability, escalation, switches
Maintained BP with minimal agents or none	Difficult to control or uncontrolled BP
Metabolic normalcy	Diabetes, obesity, dyslipidemia
Absence of Events: Rejection, Readmission, Death, ESRD, CVD; Time to event ad infinitum	Finite time to event



Objectives

- Articulate an approach to capture longitudinal post-transplant clinical evolution among kidney transplant recipients by capturing structured and unstructured elements from the EHR
- Build predictive models for graft loss and mortality using patient level data
- Compare model performance with those derived of national data
- Deploy predictive models in a clinician facing interface through the electronic medical record to drive post transplant clinical care

Methods

- Structured data were directly extracted from electronic medical records (Epic, Transplant Database and OPTN data elements)
- IBM Watson Content Analytics Studio was applied to unstructured text to extract Banff lesion scores and vital signs from pathology reports and dictated clinician notes
- IBM SPSS Modeler and Essentials for R were used for statistical analyses

Rationale for Variable Inclusion

Variable	Source	Category
KDRI	UNOS	Kidney Quality
Caregiver Status	Transplant Database	Social Determinant
Education Status	Transplant Database	Social Determinant
ICD-10 Comorbidities	EHR;	Comorbidities; Cardiometabolic risk
Banff Lesion Scores	EHR, NLP	Immunologic Risk
CMV, BKV PCRs	EHR	Immunologic Risk
Cardiovascular events	EHR	CV Risk; Access to care
Blood Pressures, Blood sugars	EHR, NLP	Biology, Cardiometabolic risk
Hemoglobin and eGFR Slopes/trajectories	EHR	Biology of Kidney Function
Readmit Counts	EHR	Processes of care, Access to care

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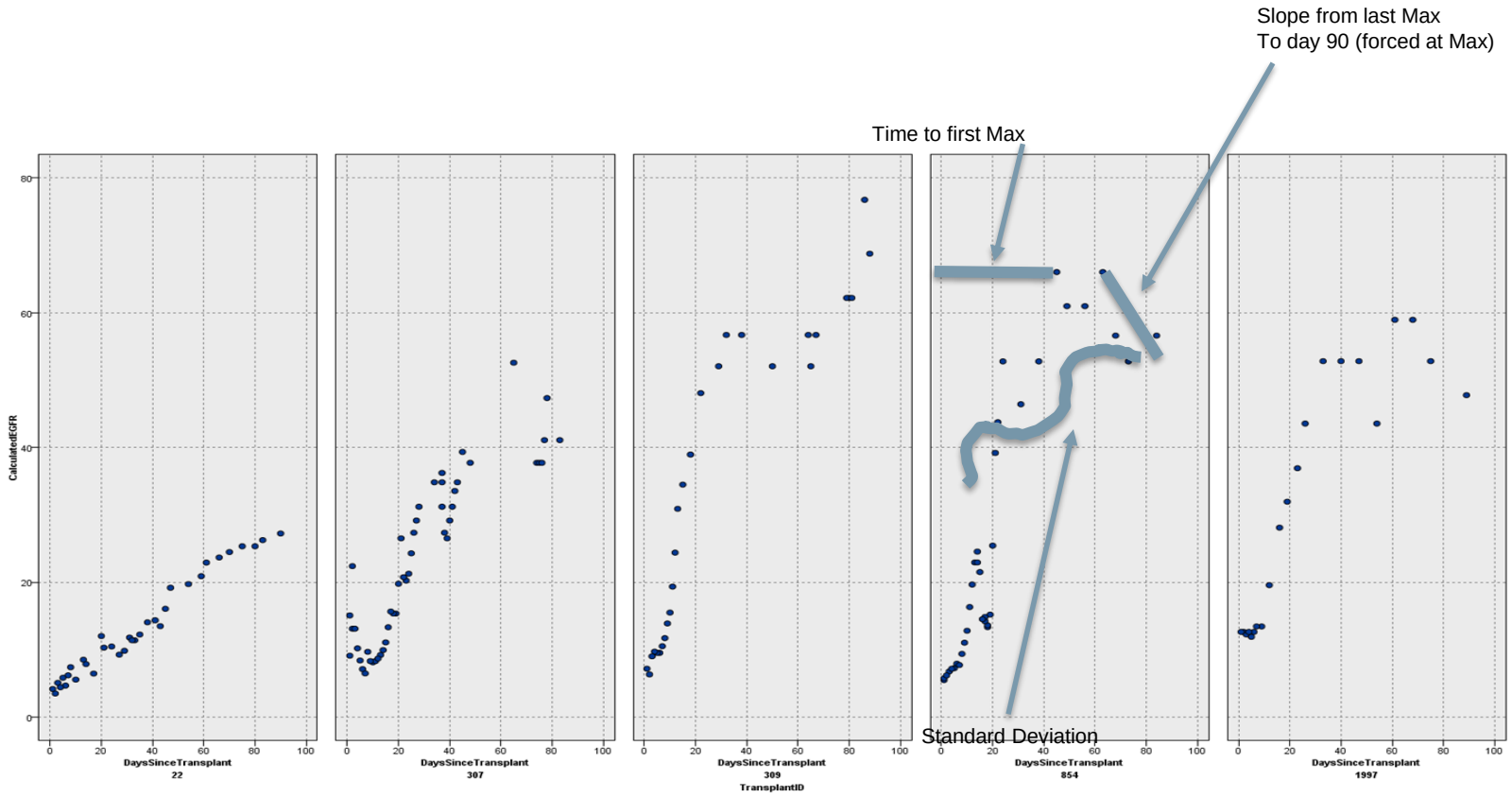
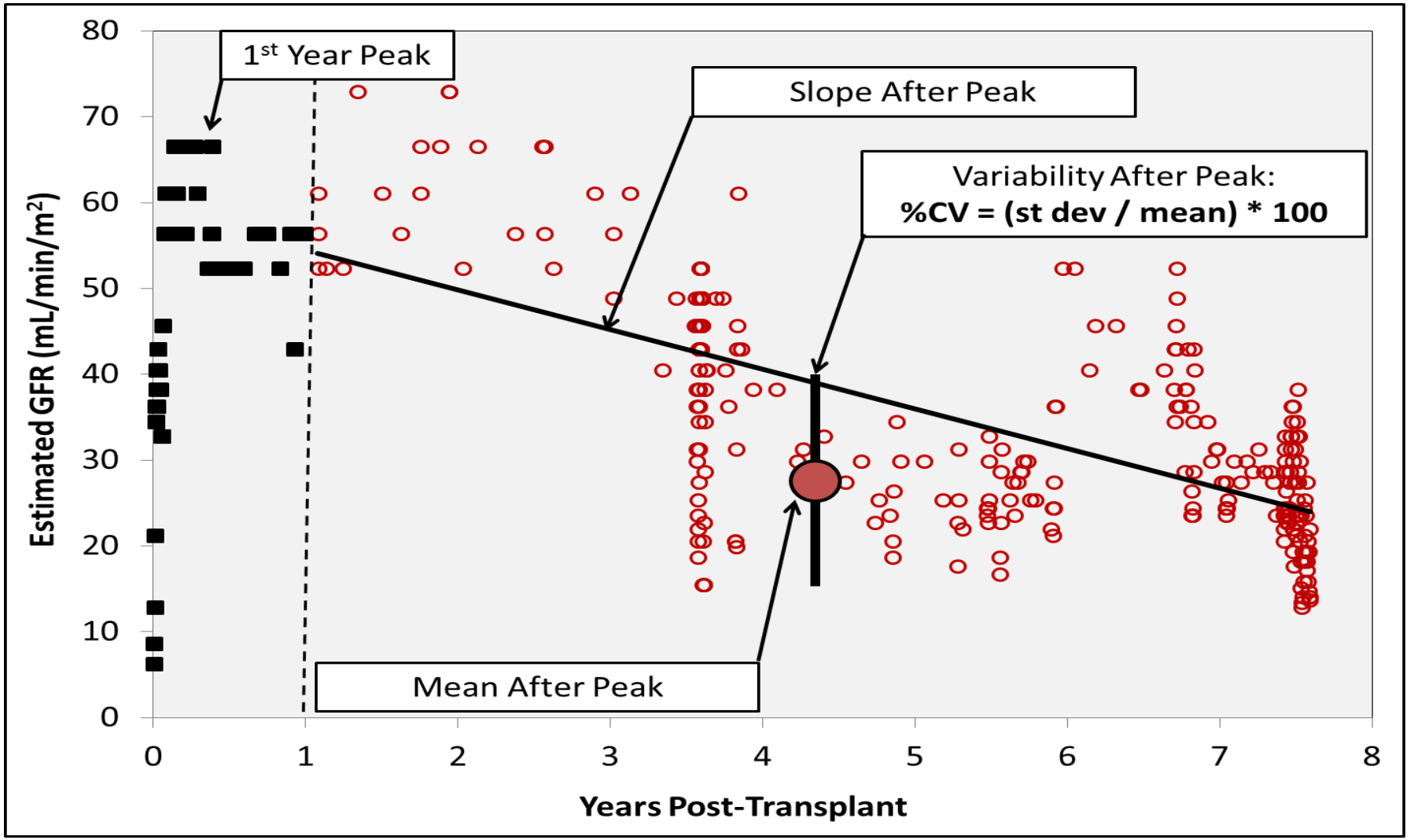
eGFR: TRAJECTORY

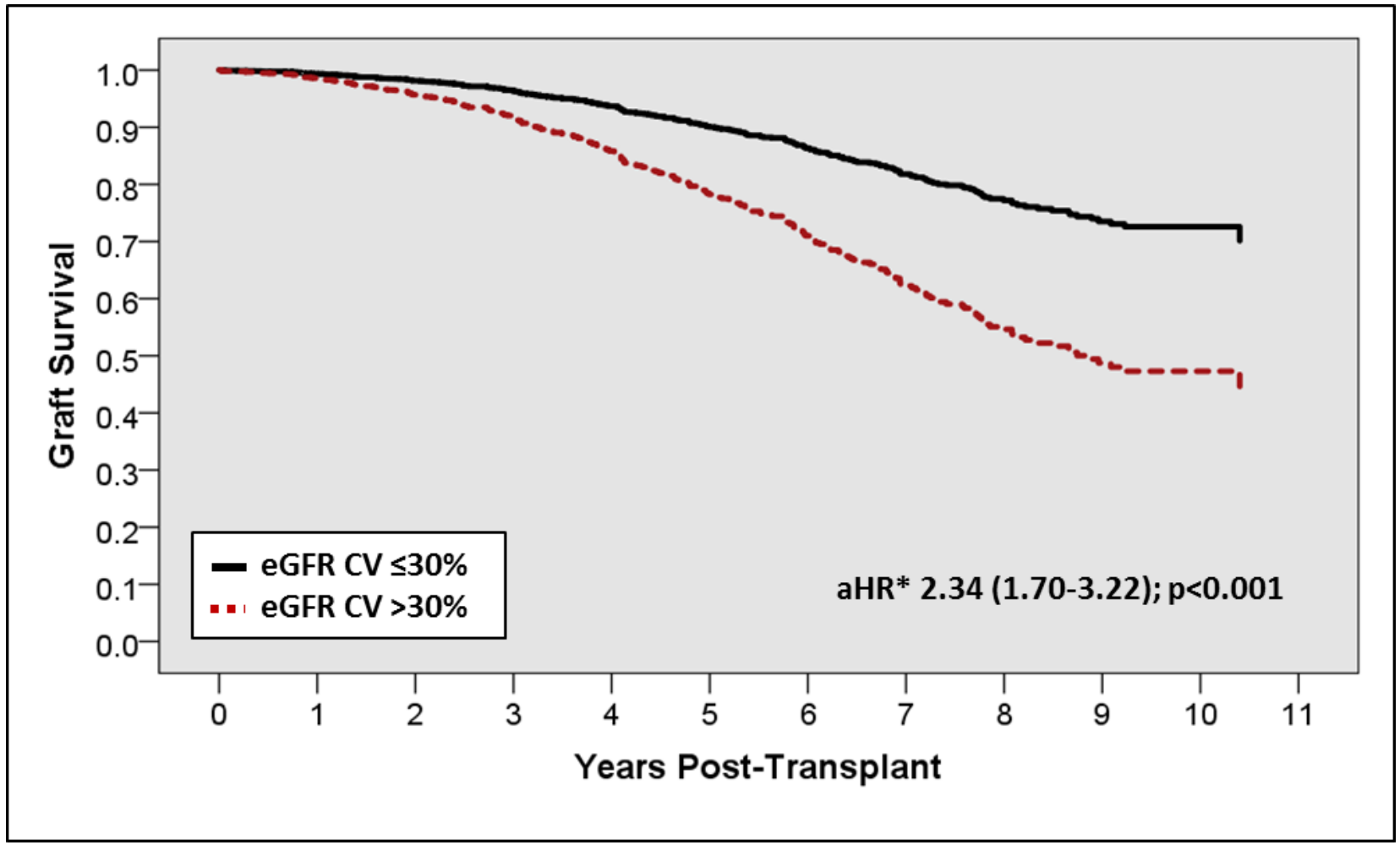


Similar approaches can be used to incorporate hemoglobin, blood pressure and heart rates into longitudinal models

Srinivas TR et al, Am J Transplant 2017



Am Transplant Congress Chicago 2017



- Renal Function Variability is Independently Associated with Graft Loss and Death In Kidney Transplants
- This may reflect dysautoregulation events cumulatively leading to irreversible graft damage

Am Transplant Congress Chicago 2017

eGFR and Tacrolimus Trough Variability and Graft Outcomes

Characteristic	EGFR CV <30% (N=1,229)	eGFR CV ≥30% (n=314)	p-Value
Delayed Graft Function	14.6%	9.9%	0.030
Biopsy Proved Acute Rejection	8.9%	32.5%	<0.001
Tacrolimus Trough %CV (±SD)	44.7±14.1	51.9±13.8	<0.001
eGFR Variables			
1st Year Peak (mL/min±SD)	65.7±20.1	65.9±20.9	0.904
Mean After Peak (mL/min±SD)	56.0±18.1	37.2±14.7	<0.001
%CV (±SD)	14.9±6.5	48.6±17.5	<0.001
Slope After Peak (mL/min/year±SD)	-1.8±8.8	-11.2±13.3	<0.001
Estimated Overall Graft Survival 1-Year 3-Year 5-Year	 95% 91% 86%	 87% 68% 45%	<0.001
Estimated Patient Survival 1-Year 3-Year 5-Year	 97% 95% 91%	 96% 87% 74%	<0.001

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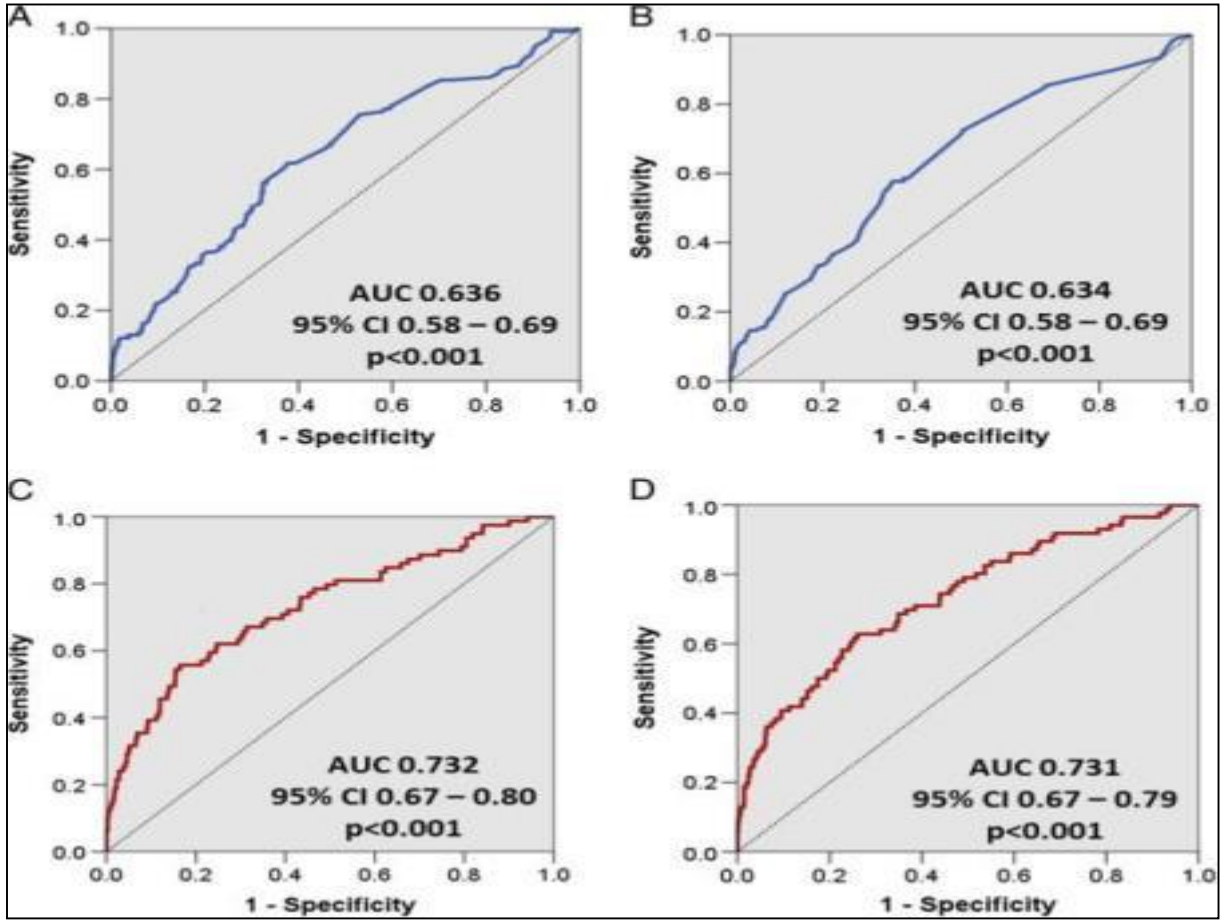


Inclusion of Dynamic Clinical Data Improves the Predictive Performance of a 30-Day Readmission Risk Model in Kidney Transplantation.

Taber, David; Palanisamy, Arun; Srinivas, Titte; Gebregziabher, Mulugeta; Odeghe, John; Chavin, Kenneth; Egede, Leonard; Baliga, Prabhakar

Transplantation. 99(2):324-330, February 2015.
DOI: 10.1097/TP.0000000000000565

FIGURE 1 . Comparison of predictive model accuracy based on the input of fixed and dynamic variables. There are the ROC curves for the 4 predictive models. (A and B) Initial and final ROC curves for the models using fixed variables listed in Table 1, respectively. (C and D) Initial and final ROC curves that use both the fixed and dynamic variables listed in Tables 1 and 2, respectively.

NLP and Banff Lesion Scores

[redacted] 10:25 AM - Lab In HIseven Interface

Component Results

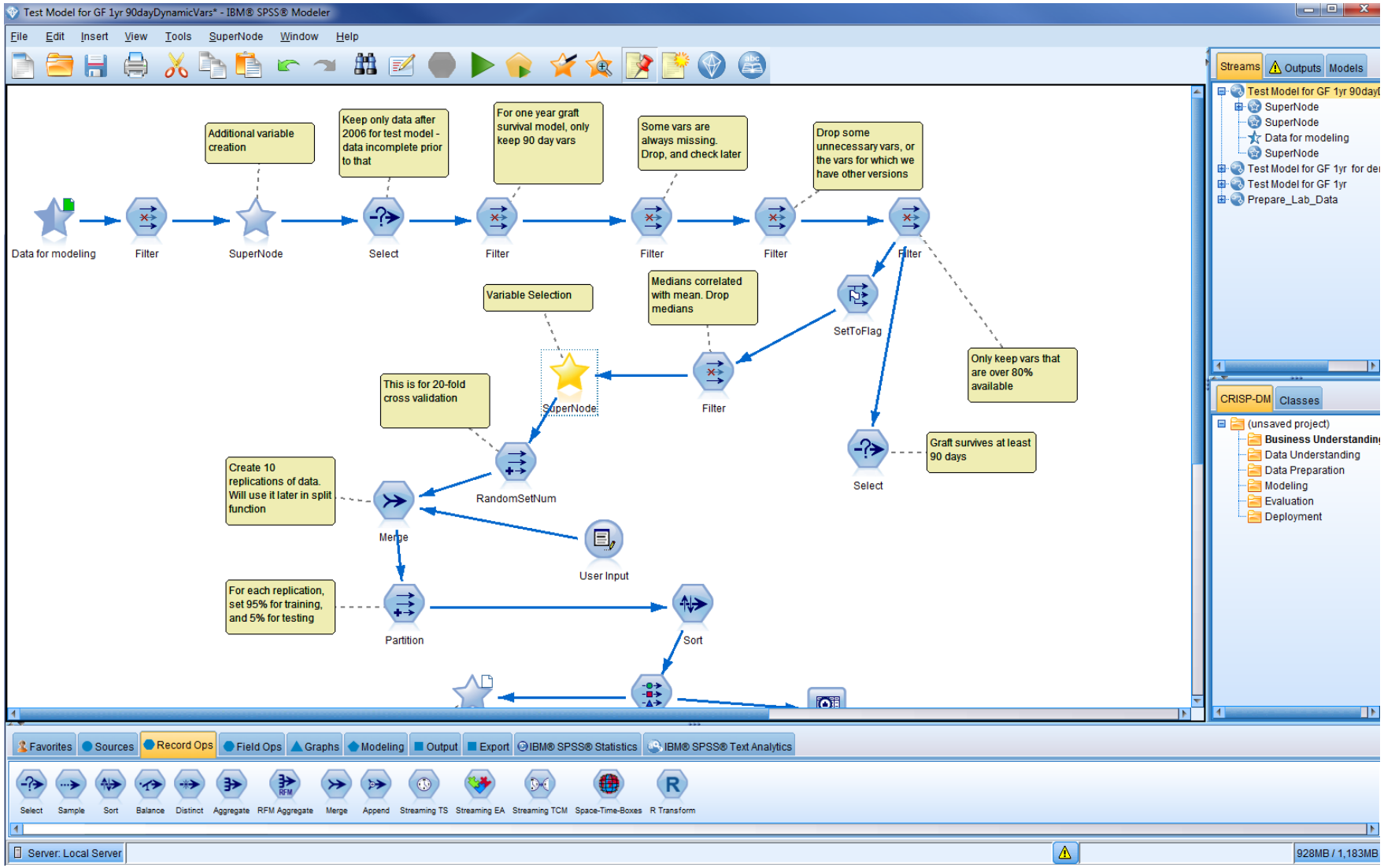
Component

SURG PATH FINAL REPORT

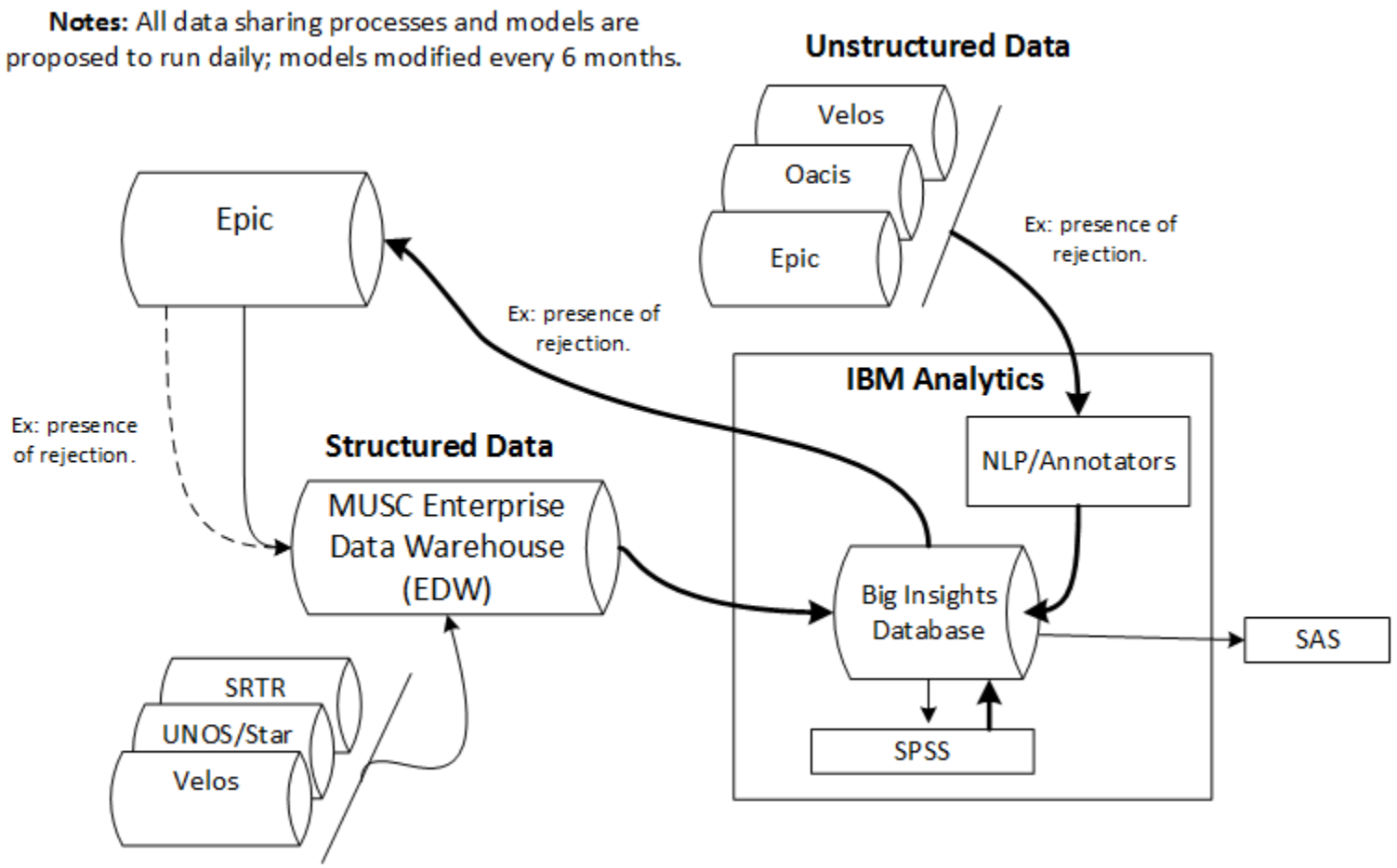
Accession #: [redacted]

Diagnosis
Kidney, clinically transplant, biopsy:
- No evidence of acute rejection
- Banff scores: g0, i0, t0, ah0, v0, cg0, ci0, ct0, ptc0, cv0, mm0, ti0, C4d0

IBM SPSS Modeler



Workflow of Data Extraction, Storage, Analysis and Deployment



Predictive Models

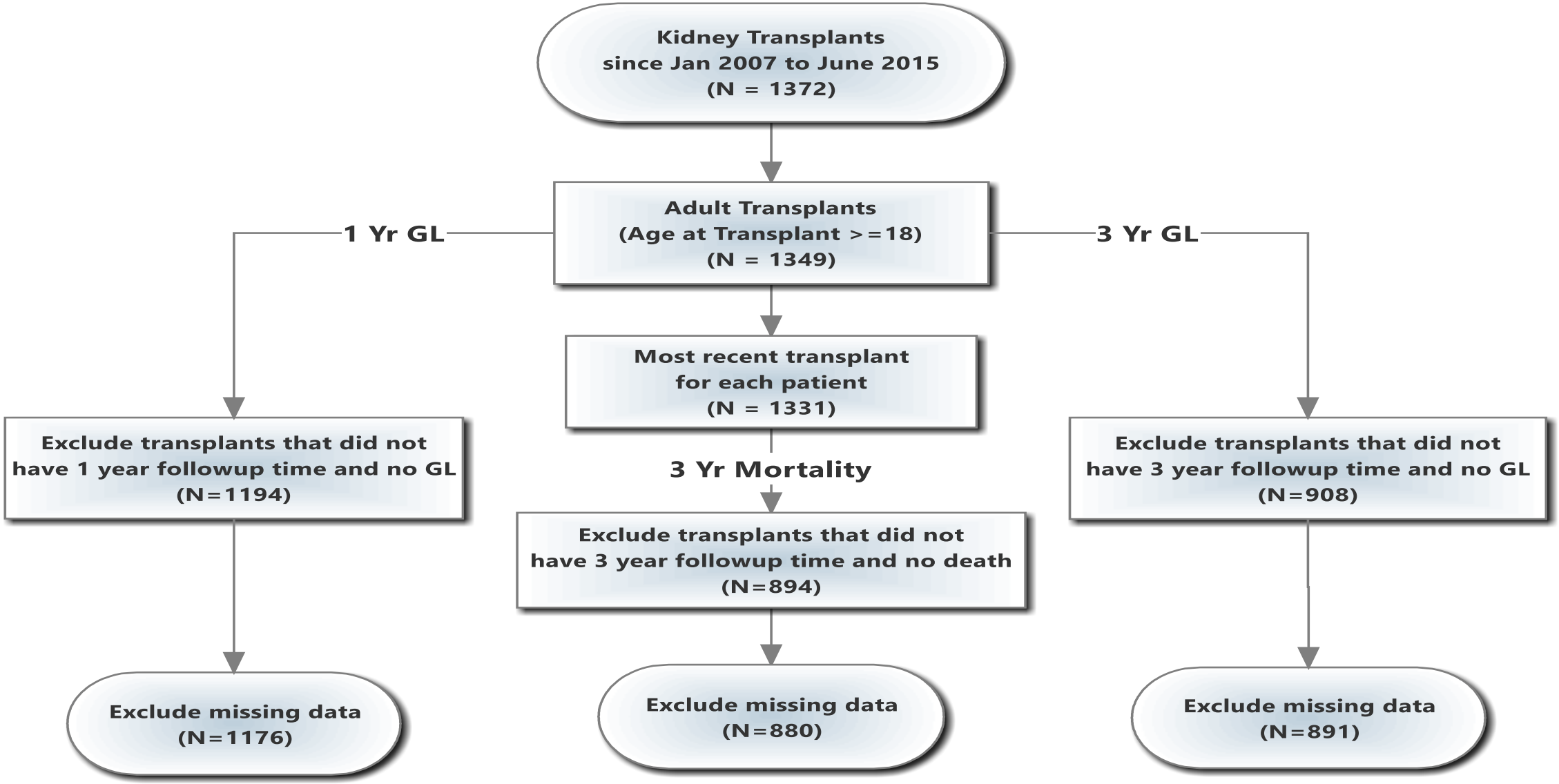
- Data up to 90 days post transplant used for the 1 year graft loss models
- Data up 1 year post transplant used for the 3 year graft loss models

Statistical Analysis

- Risk models were developed for 1 year GL and Mortality, and 3 Year GL and Mortality)

Each of these risk models incorporated variables as follow:

- **Model 1:** OPTN/UNOS/SRTR variables
- **Model 2:** UNOS + Tx Database Variables
- **Model 3:** UNOS + Tx Database + EHR Comorbidities
- **Model 4:** UNOS + Tx Database + NLP variables + Trajectory variables


Kidney Transplants
since Jan 2007 to June 2015
(N = 1372)
Adult Transplants
(Age at Transplant >=18)
(N = 1349)
1 Yr GL
3 Yr GL
Most recent transplant
for each patient
(N = 1331)
3 Yr Mortality
Exclude transplants that did not
have 1 year followup time and no GL
(N=1194)
Exclude transplants that did not
have 3 year followup time and no death
(N=894)
Exclude transplants that did not
have 3 year followup time and no GL
(N=908)
Exclude missing data
(N=1176)
Exclude missing data
(N=880)
Exclude missing data
(N=891)

3 year Graft Loss Risk and Data Sources

	Odds Ratios; Logistic (Firth)			
	Odds Ratio	95% Profile-Likelihood Confidence Limits		p-value
Model 1: UNOS				
KDRI	3.953	2.184	7.158	<0.0001
Age at Transplant	0.987	0.970	1.004	0.132
Female	0.588	0.360	0.936	0.025
Blood Type B	1.542	0.883	2.596	0.124
Model 2: UNOS + Transplant Database				
KDRI	4.117	2.265	7.493	<0.0001
Age At Transplant	0.986	0.969	1.003	0.104
Female	0.622	0.380	0.994	0.047
Blood Type B	1.450	0.826	2.451	0.189
Primary caregiver	0.486	0.305	0.784	0.003

Srinivas et al, Am J Transplant 2017

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Srinivas et al, Am J Transplant 2017

3 Year Graft Loss Risk and Data Sources

Model 3: UNOS + Transplant Database + Comorbidity	OR	95 Percent CI		P
KDRI	4.222	2.319	7.705	<0.0001
Age At Transplant	0.985	0.968	1.003	0.095
Female	0.627	0.377	1.017	0.059
Blood Type B	1.462	0.832	2.480	0.181
Primary caregiver	0.507	0.316	0.823	0.006
Cerebrovascular Disease	0.250	0.027	0.984	0.047
Cardiac Arrhythmias	1.705	1.027	2.777	0.039
Alcohol Abuse	2.479	0.807	6.521	0.107
Depression	1.841	0.936	3.433	0.076

Srinivas et al, Am J Transplant 2017

3 Year Graft Loss Risk and Data Sources

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Srinivas et al, Am J Transplant 2017

3 Year Graft Loss Risk and Data Sources

Model 4: UNOS + Tx Database + Comorbidity + Post-Transplant Trajectory	OR	95 % CI		p
KDRI	2.855	1.388	5.848	0.004
Age At Transplant	0.975	0.955	0.995	0.016
Female	0.589	0.328	1.030	0.064
Primary caregiver	0.383	0.222	0.666	0.001
Cerebrovascular Disease	0.264	0.028	1.126	0.076
Cardiac Arrhythmias	1.489	0.829	2.621	0.180
Alcohol Abuse	3.187	0.872	9.822	0.077
Depression	1.908	0.872	3.941	0.103
Pulse Pressure Std Dev 1yr	1.132	1.057	1.211	0.000
Acute MI 1yr	10.550	2.094	48.510	0.006
Cardiac or Vascular Event 1yr	2.514	1.441	4.360	0.001
HGB Mean 7d to 1yr	0.873	0.713	1.063	0.178
HGB Slope 7d to 1yr	0.000	0.000	0.134	0.001
Pulse Mean 1yr	1.022	0.993	1.053	0.134
Calc eGFR S Dev 1yr	0.964	0.926	1.000	0.050
Days SinceTX First Max eGFR 1yr	0.997	0.994	1.000	0.047
Transplant LOS	1.053	0.963	1.128	0.198
Acute Banff Score Max 1yr	1.356	1.212	1.521	<0.0001

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Srinivas et al, Am J Transplant 2017

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Srinivas et al, Am J Transplant 2017

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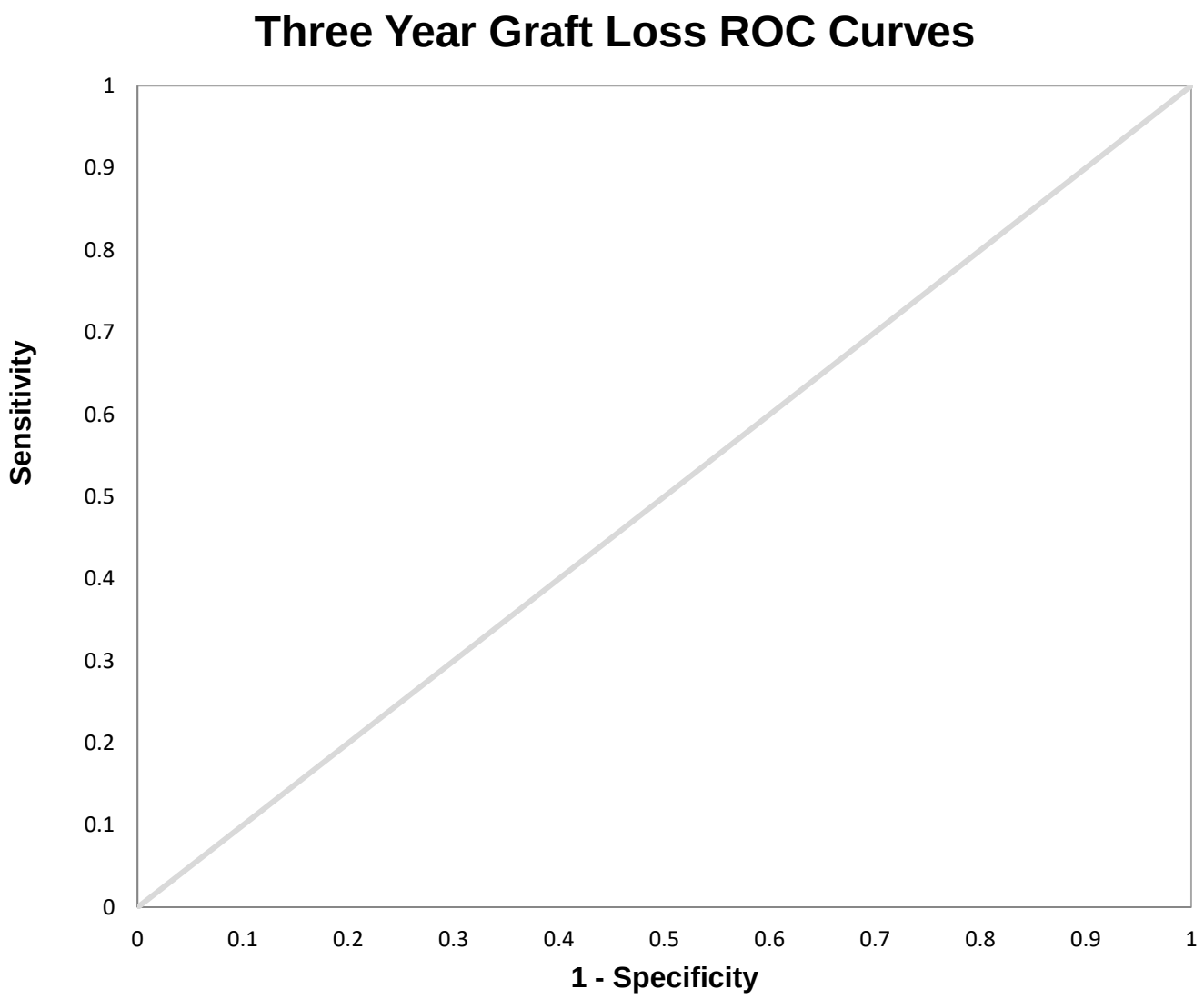
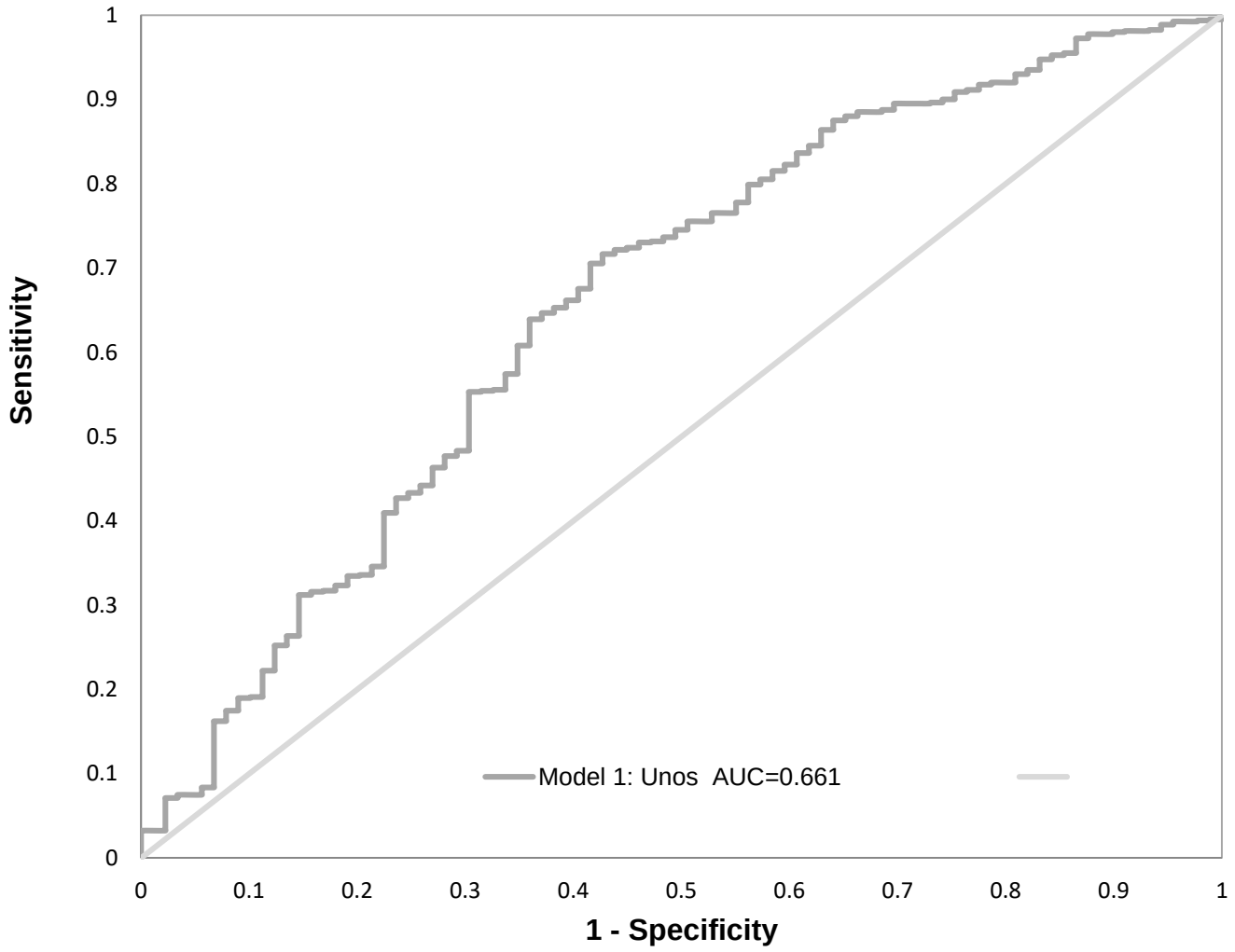
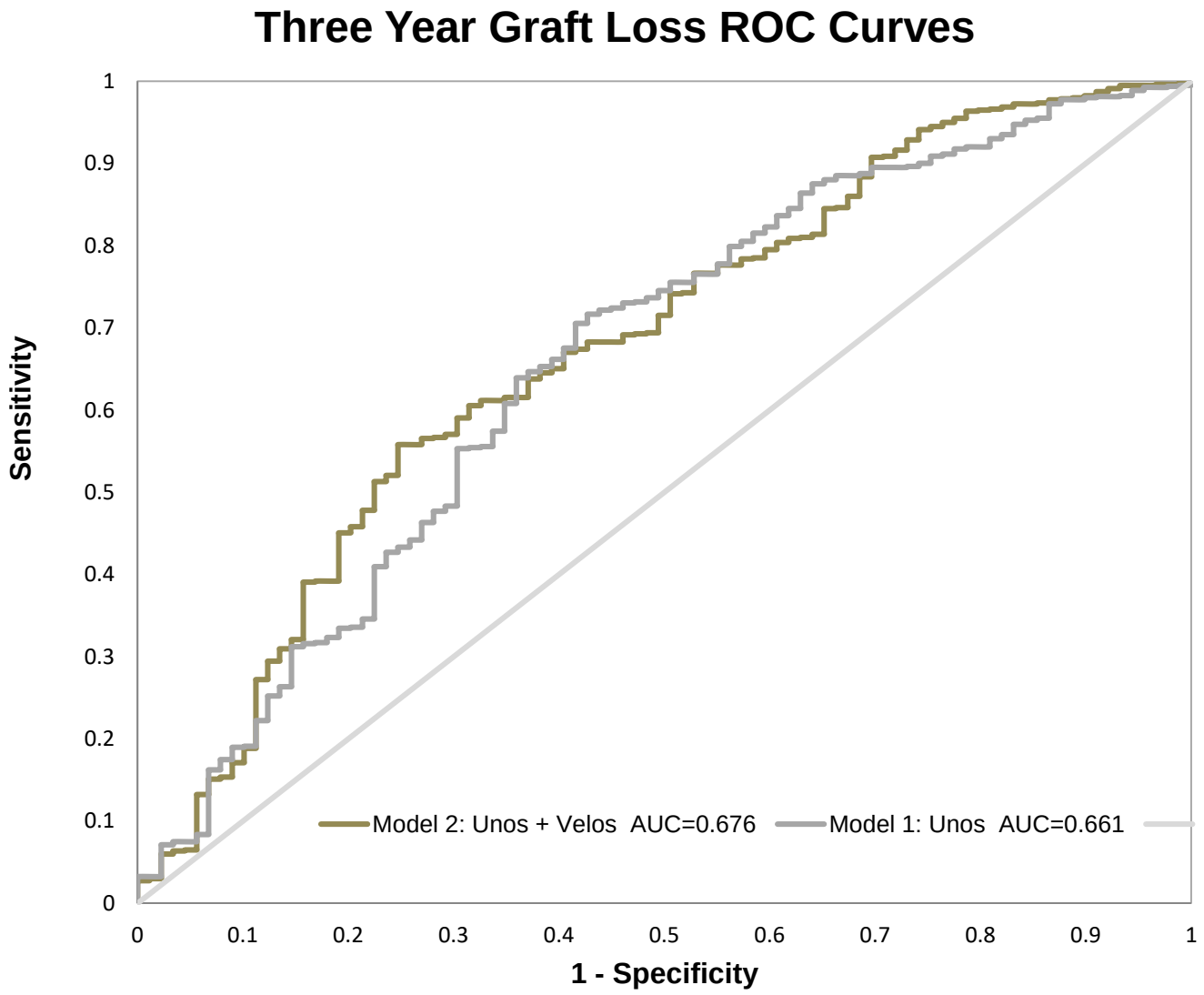
Srinivas et al, Am J Transplant 2017

Effect of Layering Data Sources on Model Performance


Three Year Graft Loss ROC Curves
Sensitivity
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1 - Specificity

Three Year Graft Loss ROC Curves




Three Year Graft Loss ROC Curves
Sensitivity
1
0.9
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0.7
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0.5
0.4
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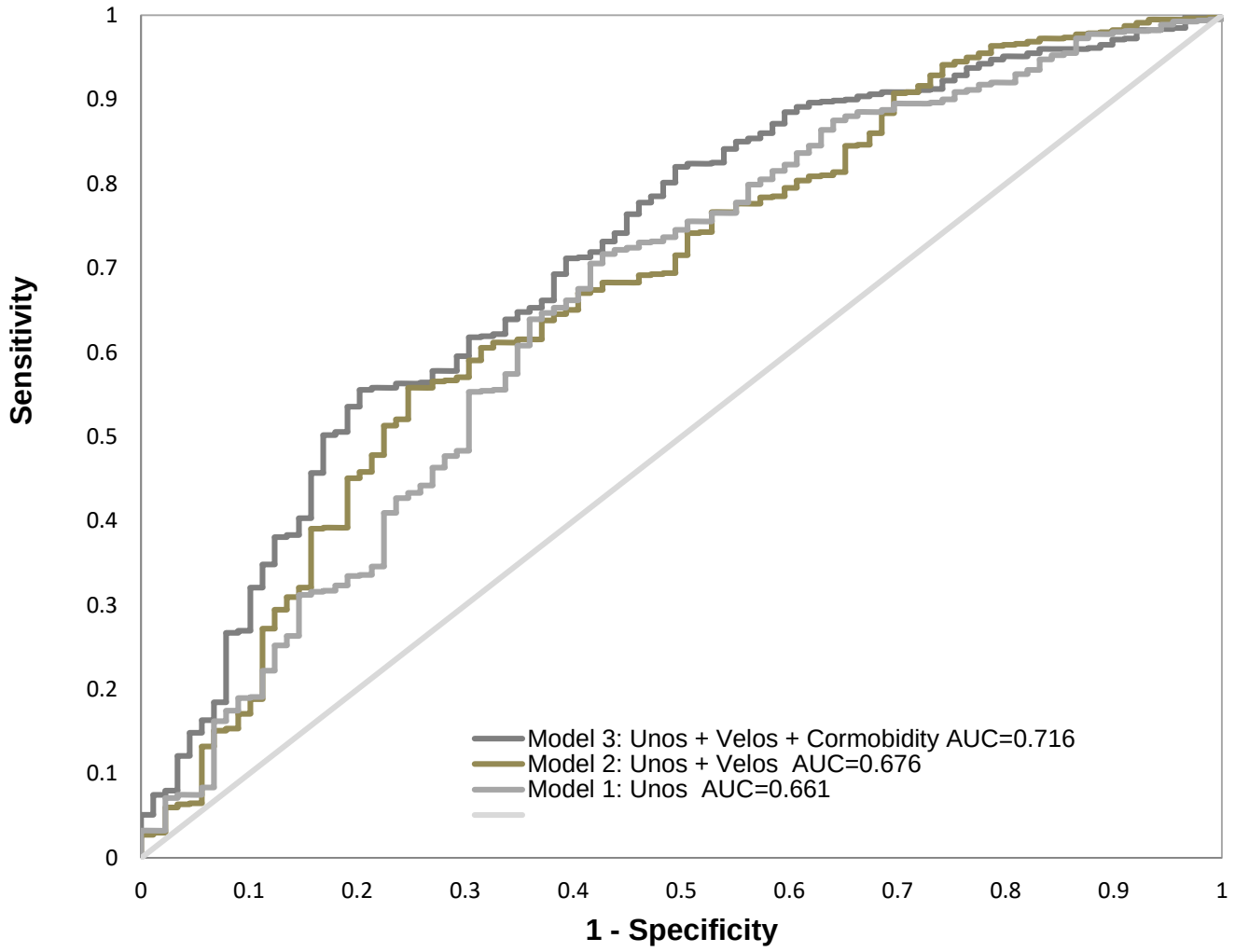
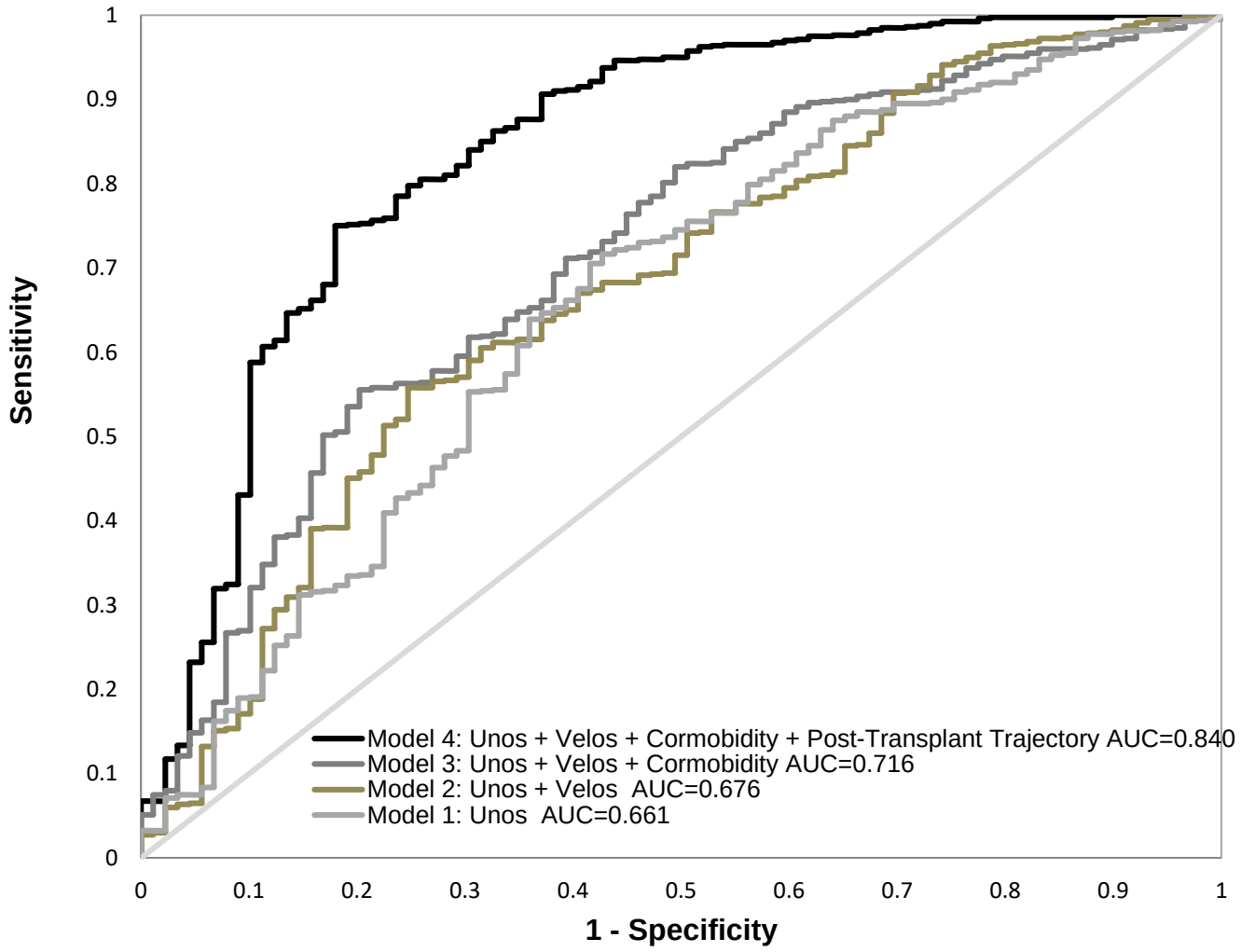
0.2
0.1
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1 - Specificity
Model 2: Unos + Velos AUC=0.676
Model 1: Unos AUC=0.661

Three Year Graft Loss ROC Curves



Three Year Graft Loss ROC Curves

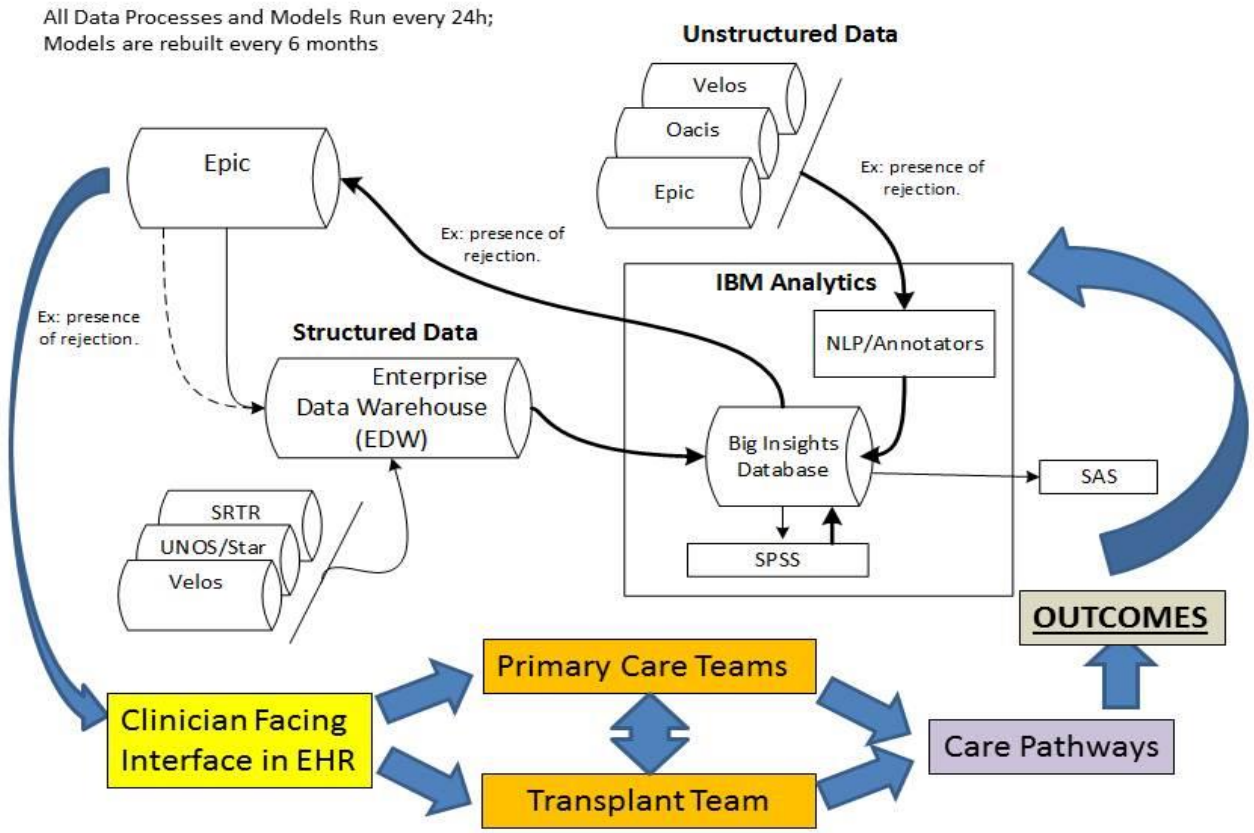


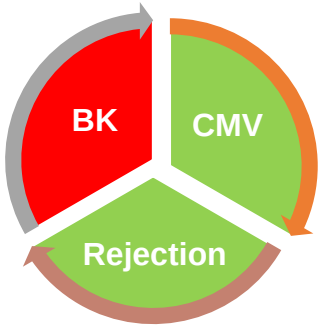
Mutable factors associated with 1 & 3 year graft loss and mortality fall into 2 categories

Transplant associated risk (historically managed by transplant nephrology)

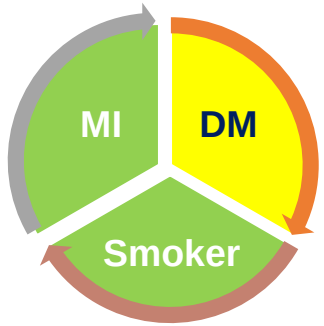
Non-Transplant associated risk (historically managed by primary care)

Model Deployment in The Clinic

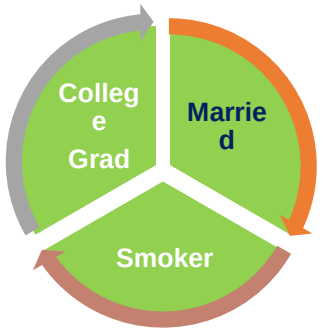




Immunologic



Cardiometabolic



Psychosocial

Date	BK PCR
1/27/16	2.33E4
12/23/15	Neg
11/22/15	Neg

Model Output

Date	Blood Sugar
1/27/16	185
12/23/15	109
11/22/15	93

Model Output

Kidney Tx Summary

PATIENT INFORMATION: "FICTICIOUS FRANK"

Transplant Date: 09/12/2016 DGF: Y Age at time of tx: 67 Previous Tx? N

ESRD Diagnosis: _____

HLA Mismatches: 4 CPRA: 10% CIT: 12 hr 23 min WIT: 12 min

Smoking status: 2 packs per day Smoking status date: 9/14/2016

Latest CMV: 520 Date: 9/14/2016 Latest BK: 520 Date: 9/14/2016

Latest creatinine: 1.2 Latest creatinine date: 9/14/2016 Max

eGFR: 75 Date: 09/14/2016 Acute MI Event: Y Date: 9/14/2016

Latest banff grade: IIA Date: 9/14/2016 cg0 ci1 ct1.5 cv3 ah1 mm0 ti1 i0 t1 v1 g0.5 ptc1 c4d0

Post-tx readmission count: 1 Maximum acute banff grade in past year: IIB Date: 10/15/2015

DONOR INFORMATION AT TIME OF TRANSPLANT

Age: 37 Sex: M Race: Hispanic KDPI: 22 Terminal SrCr: xx Weight: 237 BMI: 29

CMV: 027 EBV: xx LD: Deceased Donor ECD: xxx DD: non-beating heart

HLA Mismatches: 4 CPRA: 10% CIT: 12 hr 23 min WIT: 12 min

ADDITIONAL PATIENT INFORMATION

Risk scores

1 year graft loss: 3.7% Date: 9/14/2016 3 year graft loss: Date: 3 year mortality: Date:

Calculated Information (up to 1 year ago if data available)

Maximum eGFR: 75 eGFR slope: 0.7 Systolic BP mean: 155 Pulse mean: 22 Tac mean: nn Tac SD: nn

Intermountain Experience

- Bringing it all together in the clinic
- Tools available: dd CF DNA, Molecular Microscope, Pharmacogenomic Panel
- Standardized cardiovascular evaluation using PET, Echo, Coronary calcium and a dedicated CV physician team
- Routine assessment of frailty and physical performance

RxMatch™ Comprehensive Report

Intermountain® Precision Genomics

Genetic Summary

Gene	Result	Activity †
ADRA2A(C-1291G)	C|C	Normal function
ANKK1	G|A	Altered function
ApoE	Not Tested	See ApoE Genotype Info.
COMT(Val158Met)	G|A	Altered function
CYP2C19	*1|*1	Extensive metabolizer
CYP2C9	*1|*1	Extensive metabolizer
CYP2D6	*1|*1	Extensive metabolizer
CYP3A4	*1A|*1A	Multiple statuses; see per-drug detail
CYP3A5	*1D|*3A; or *1A|*3C; or *1A|*3A or *1D|*3C	Intermediate metabolizer
CYP4F2	*1|*3	Uncertain function

RxMatch™ Comprehensive Report

Intermountain® Precision Genomics

Drug		Finding	Recommendation	Concern	Evidence
Immunosuppressants					
Cyclosporine (Gengraf, Neoral)	✓	CYP3A4: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Sirolimus (Rapamune)	✓	CYP3A4: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Tacrolimus (Prograf, Hecoria)	⚠	CYP3A5: One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have lower dose-adjusted trough concentrations of tacrolimus; the resultant decreased concentrations may increase the probability of pharmacotherapy failure. Consider increasing the recommended starting dose by 1.5 to 2 times (with a total starting dose not exceeding 0.3 mg/kg/day). In liver transplant patients, donor genotype should be considered as well as the recipient's.	Efficacy	

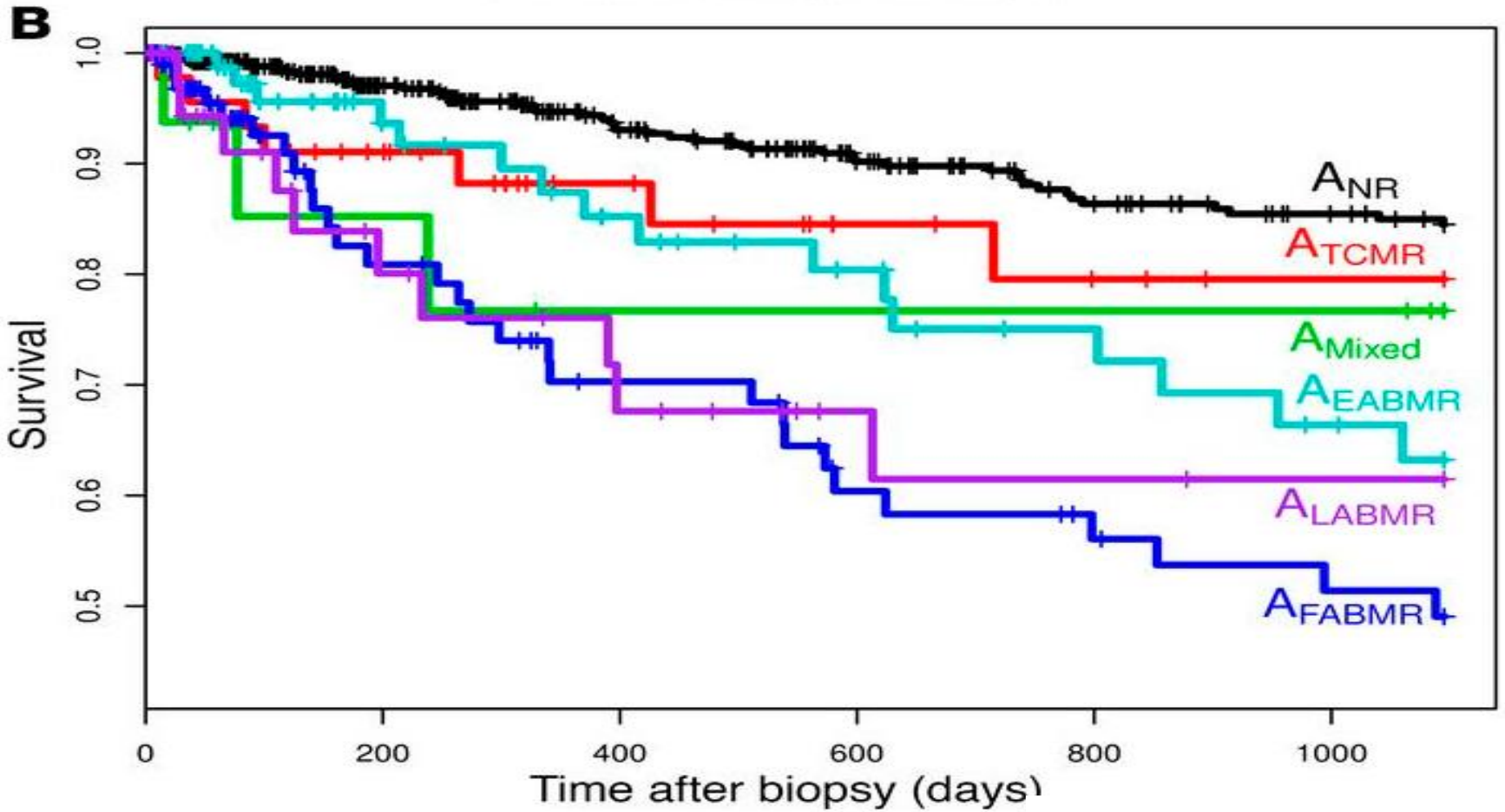
Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Depleting Agents			
Central Nervous System Agents	Dextromethorphan-Quinidine		
Cholinergic Agonists	Cevimeline		
Cholinesterase Inhibitors		Galantamine	
Contraceptives	Estrogen-containing oral contraceptives		
EGFR Inhibitors	Gefitinib		
Endocrine-Metabolic Agents		Eliglustat	
Hypnotics	Eszopiclone		
Immunosuppressants	Cyclosporine Sirolimus	Tacrolimus	
Muscle Relaxants	Carisoprodol		

JCI insight

RESEARCH ARTICLE

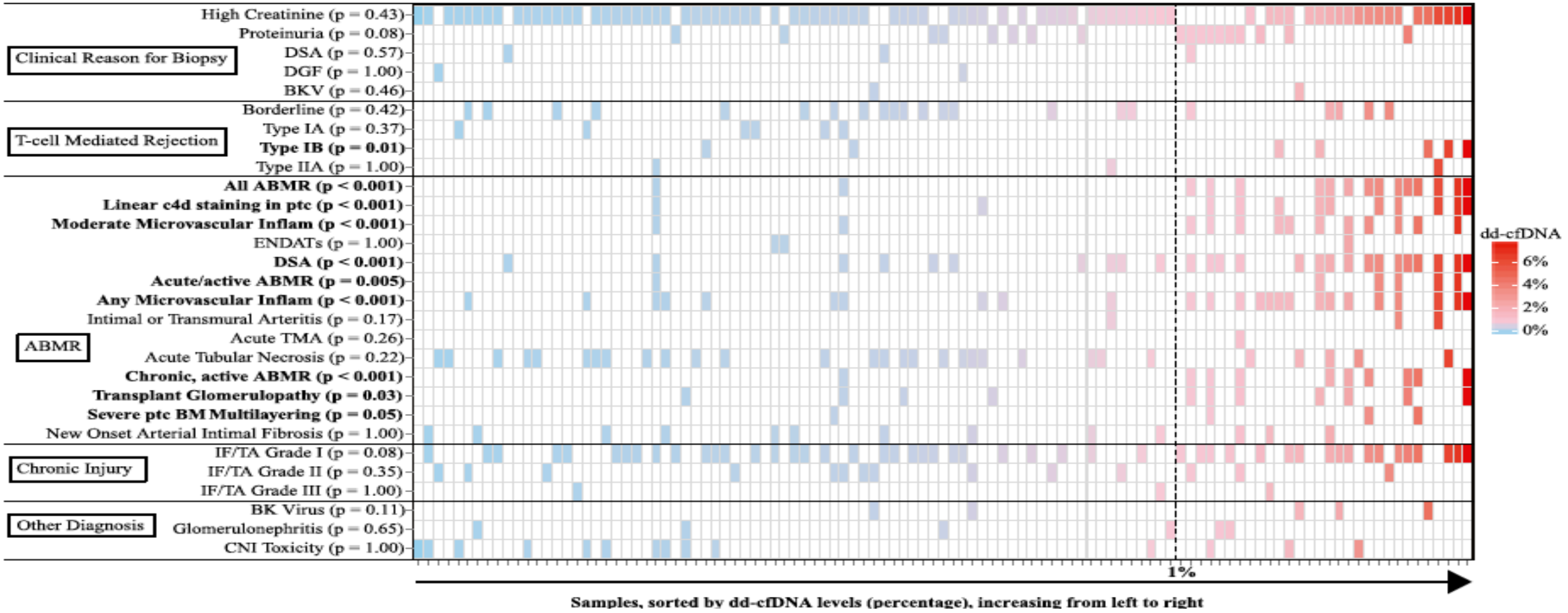
Assessing rejection-related disease in kidney transplant biopsies based on archetypal analysis of molecular phenotypes

Jeff Reeve,[1,2] Georg A. Böhmig,[3] Farsad Eskandary,[3] Gunilla Einecke,[4] Carmen Lefaucheur,[5,6] Alexandre Loupy,[5,7] Philip F. Halloran,[1,8] and the MMDx-Kidney study group[9]



 https://doi.org/10.1172/jci.insight.94197

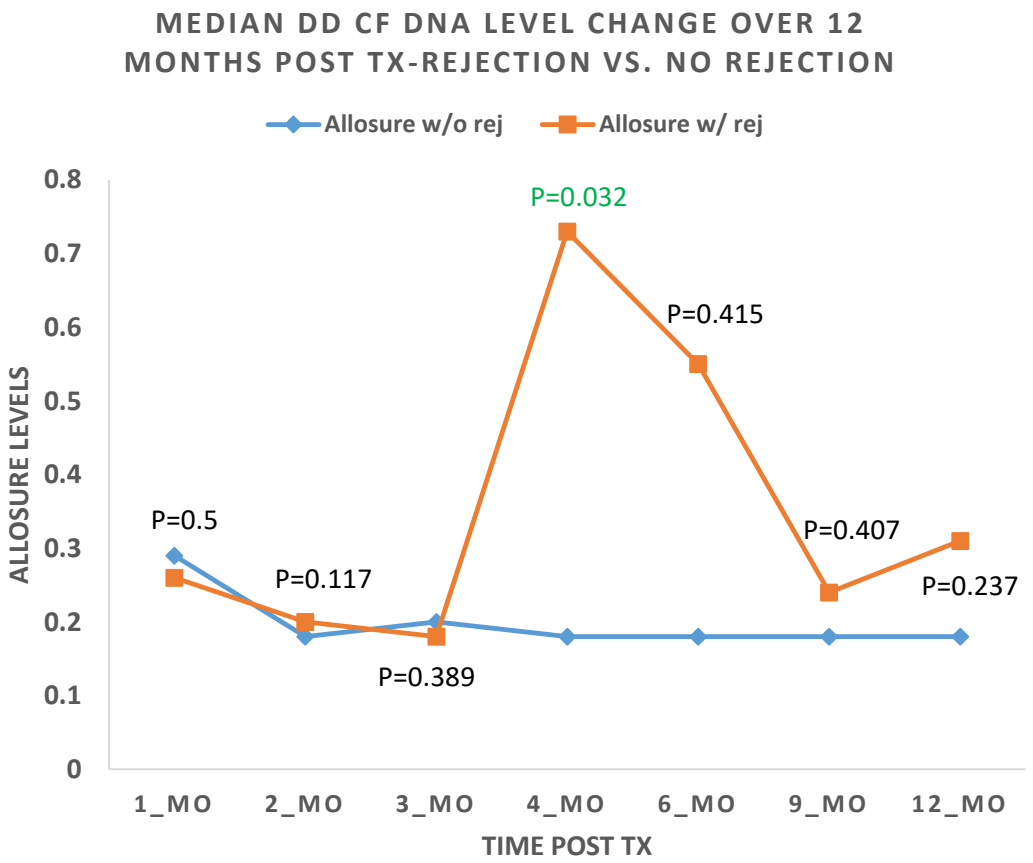
Injury Markers…

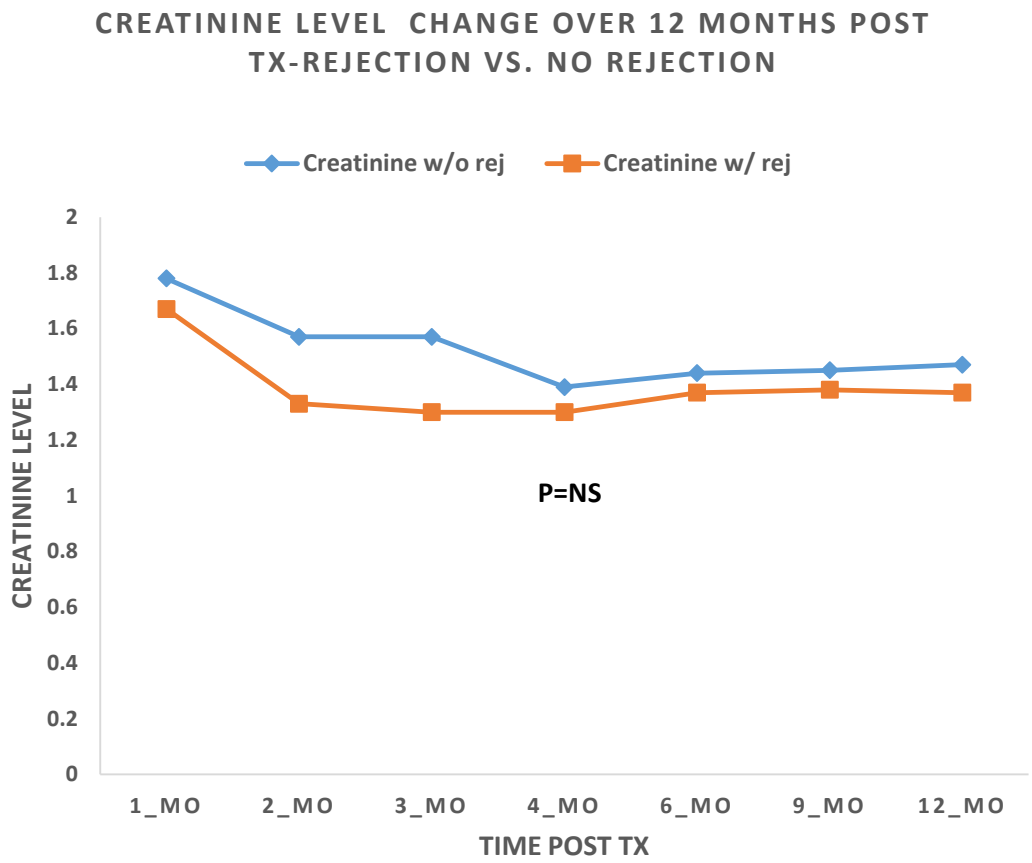


J Am Soc Nephrol 28: ●●●–●●●, 2017

Cell Free DNA

Longitudinal dd-Cf DNA and Creatinine Changes over 12 Months Post Tx-Rejection vs No Rejection





Case Study

Case	Best Creatinine	Biopsy Trigger	Histology	Molecular Microscope	Anti-HLA Ab	Cf-DNA	Treatment	Non HLA Ab
34 yo Asian Indian male; ESRD secondary to SLE ; cPRA-99%; induction r-ATG 6mg/kg; CYP3A5 Intermediate metabolizer	1.43 mg/dL	Pre-existing DSA; surveillance at 4 weeks post Tx	Banff Suspicious ACR	Severe ABMR. No TCMR. Moderate AKI and minimal atrophy-fibrosis	Pre-existing DSA to DRB1 2500 MFI increased to 4900 MFI Denovo Ab to DQ2	0.69	Pulse steroids, IVIG, bortezomib, tocilizumab	Not tested
Repeat Testing	1.2 mg/dL	Surveillance Post Rx at 3 weeks	Banff Suspicious marked improvement	Mild early-stage ABMR. No TCMR. Moderate AKI with mild inflammation and minimal atrophy-fibrosis. Compared to the initial biopsy : overall improvement in ABMR features	DRB1 Ab decreased to 2400 MFI	1.1	Maintenance tac, MMF, Prednisone	Not Tested

Pure Molecular Interpretation (Results Summary)

Abnormal biopsy. Severe ABMR. No TCMR. Moderate AKI and minimal atrophy-fibrosis. Note: This sample is 100% medulla, which may affect the readings, overestimating cg>0 probability, late ABMR (LABMR), and inflammation (Global Disturbance) scores.) Note: the Molecular Microscope® Diagnostic System cannot exclude primary glomerular diseases.	**Percent cortex[1]**
	0%

Result Details

Biopsy Rejection and Injury Scores

	Classifier / Gene Sets	Biopsy Score	Range of Values[2]	Upper Limit of Normal[3]	Interpretation
Injury Scores	Global Disturbance Score	4.68	-3.8 — 5.8	0.02	**Extensive**
	Acute Kidney Injury (AKI) Score	0.87	-0.6 — 1.6	0.61	Moderate
	Atrophy-Fibrosis Score	0.25	0 — 1	0.38	Minimal
Rejection Scores	Rejection Score	0.48	0 — 1	0.30	Mild
	T Cell-Mediated Rejection (TCMR) Score	0.08	0 — 1	0.10	Normal
	Antibody-Mediated Rejection (ABMR) Score	0.52	0 — 1	0.20	**Severe**

Molecular Microscope

Pure Molecular Interpretation (Results Summary)

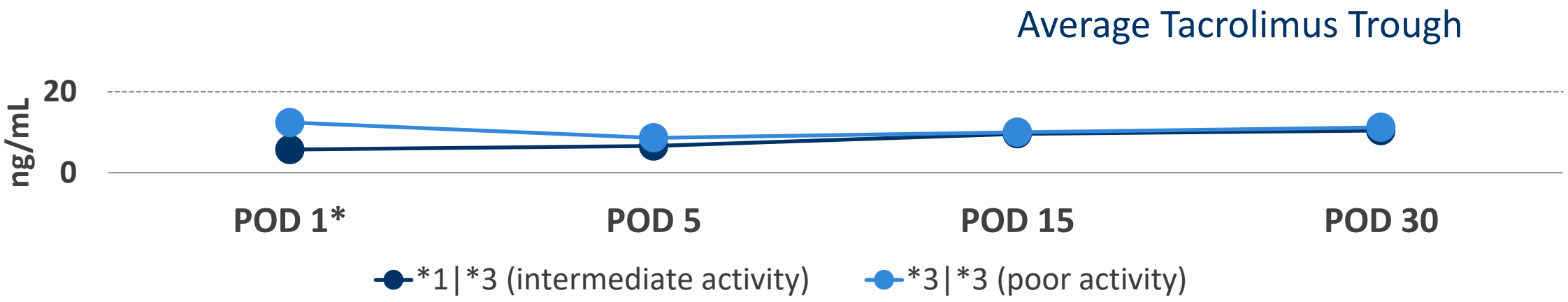
Abnormal biopsy. Mild early-stage ABMR. No TCMR. Moderate AKI with mild inflammation and minimal atrophy-fibrosis. Compared to the biopsy of October 23rd 2018, there has been an improvement in ABMR features. Note: the Molecular Microscope® Diagnostic System cannot exclude primary glomerular diseases.	Percent cortex[1]
	77%

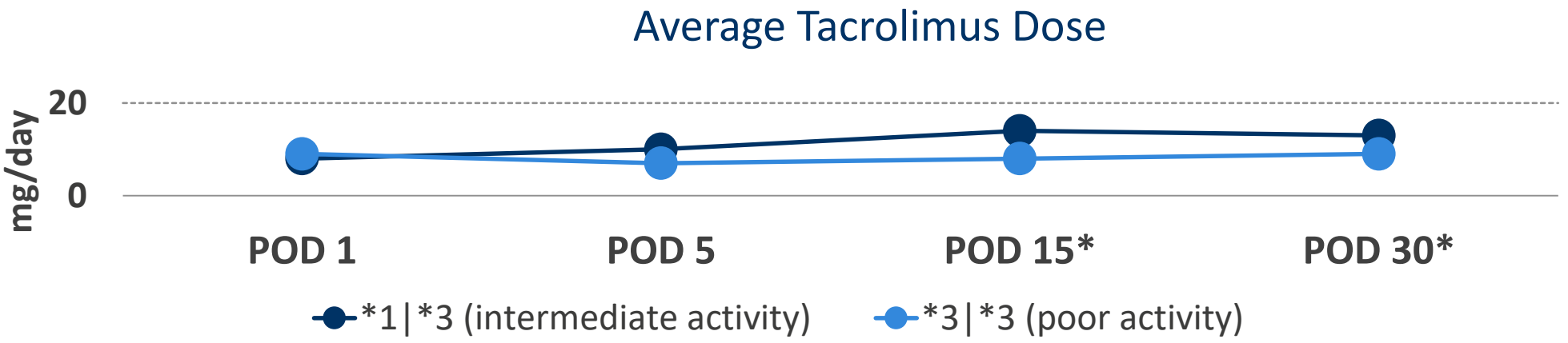
Result Details

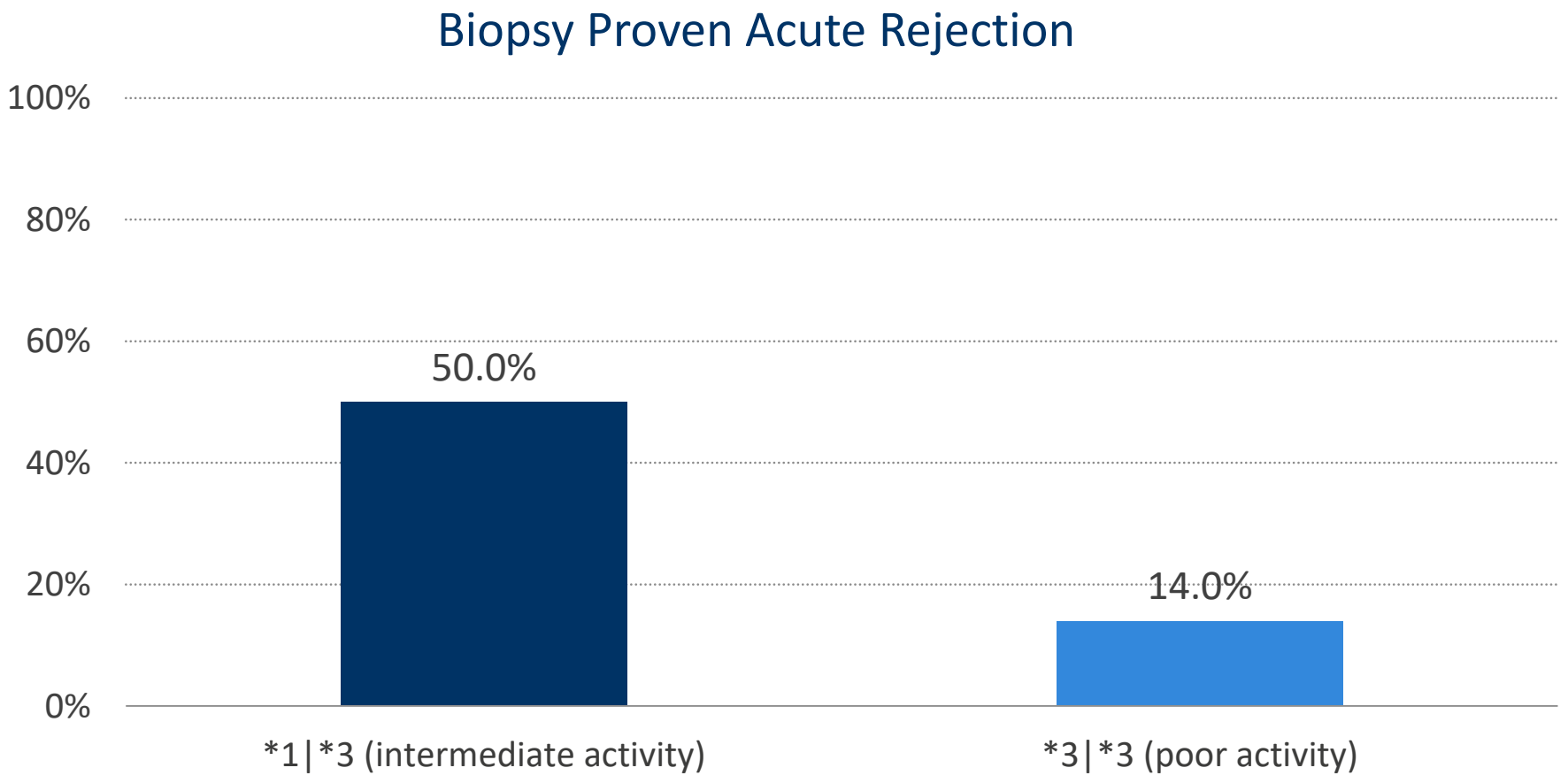
Biopsy Rejection and Injury Scores

	Classifier / Gene Sets	Biopsy Score	Range of Values[2]	Upper Limit of Normal[3]	Interpretation
Injury Scores	Global Disturbance Score	-0.28	-3.8 – 5.8	0.02	Mild
	Acute Kidney Injury (AKI) Score	0.50	-0.6 – 1.6	0.61	Moderate
	Atrophy-Fibrosis Score	0.09	0 – 1	0.38	Minimal
Rejection Scores	Rejection Score	0.39	0 – 1	0.30	Mild
	T Cell-Mediated Rejection (TCMR) Score	0.03	0 – 1	0.10	Normal
	Antibody-Mediated Rejection (ABMR) Score	0.34	0 – 1	0.20	Mild

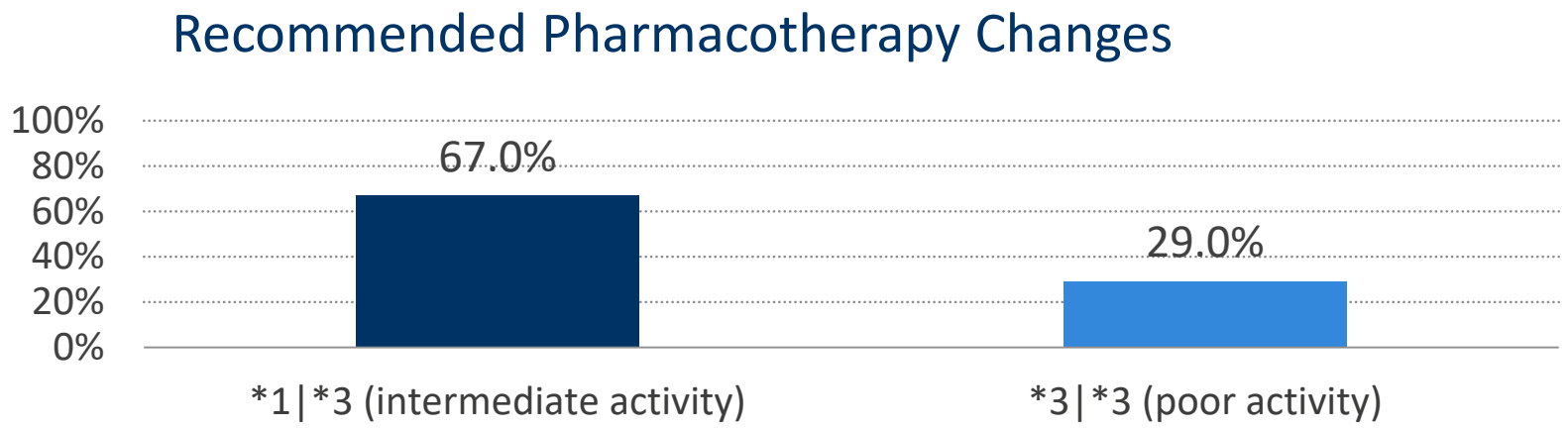
Pharmacogenomics


Average Tacrolimus Trough
ng/mL
20
0
POD 1*
POD 5
POD 15
POD 30
*1|*3 (intermediate activity)
*3|*3 (poor activity)


Average Tacrolimus Dose
mg/day
20
0
POD 1
POD 5
POD 15*
POD 30*
*1|*3 (intermediate activity)
*3|*3 (poor activity)


Biopsy Proven Acute Rejection
100%
80%
60%
40%
20%
0%
50.0%
14.0%
*1|*3 (intermediate activity)
*3|*3 (poor activity)

Change in Drug Dosing or Choice



- Tacrolimus
- Beta Blockers
- Changes in SSRI choice

The Path Ahead

Viewpoint

January 1/8, 2019

More

Humanizing Artificial Intelligence

Sonoo Thadaney Israni, MBA[1]; Abraham Verghese, MD[1]

» Author Affiliations | Article Information

JAMA. 2019;321(1):29-30. doi:10.1001/jama.2018.19398

Osler : “It is more important to know what kind of patient has a disease rather than what disease a patient has”

VIEWPOINT

Monitoring Jet Engines and the Health of People

JAMA December 11, 2018 Volume 320, Number 22

VIEWPOINT

Lionel Tarassenko, MA, DPhil
University of Oxford, Oxford, United Kingdom.

Eric J. Topol, MD
Scripps Research Translational Institute, La Jolla, California.

As with jet engines, the full potential of health monitoring for people will only be realized when *individualized* models underpin the monitoring algorithms.

Received: 7 June 2018 | Revised: 5 July 2018 | Accepted: 10 July 2018

DOI: 10.1111/ajt.15027

EDITORIAL

AJT

A call to action—The transplant recipient's expectation of precision in transplant medicine

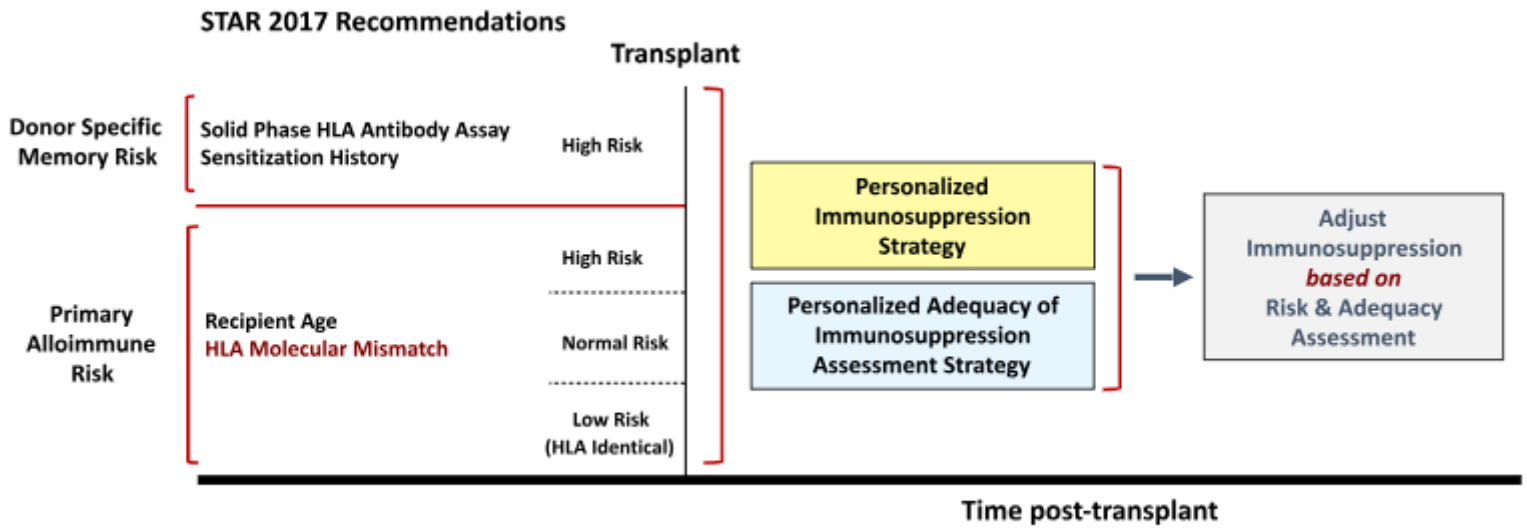


FIGURE 1 Pretransplant alloimmune risk assessment framework linked to posttransplant personalized care (modified from references 3

American Journal of Transplantation

AST | AMERICAN SOCIETY OF TRANSPLANTATION

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PERSONAL VIEWPOINT

Expanding transplant outcomes research opportunities through the use of a common data model

Sylvia Cho, Sumit Mohan, Syed Ali Husain, Karthik Natarajan

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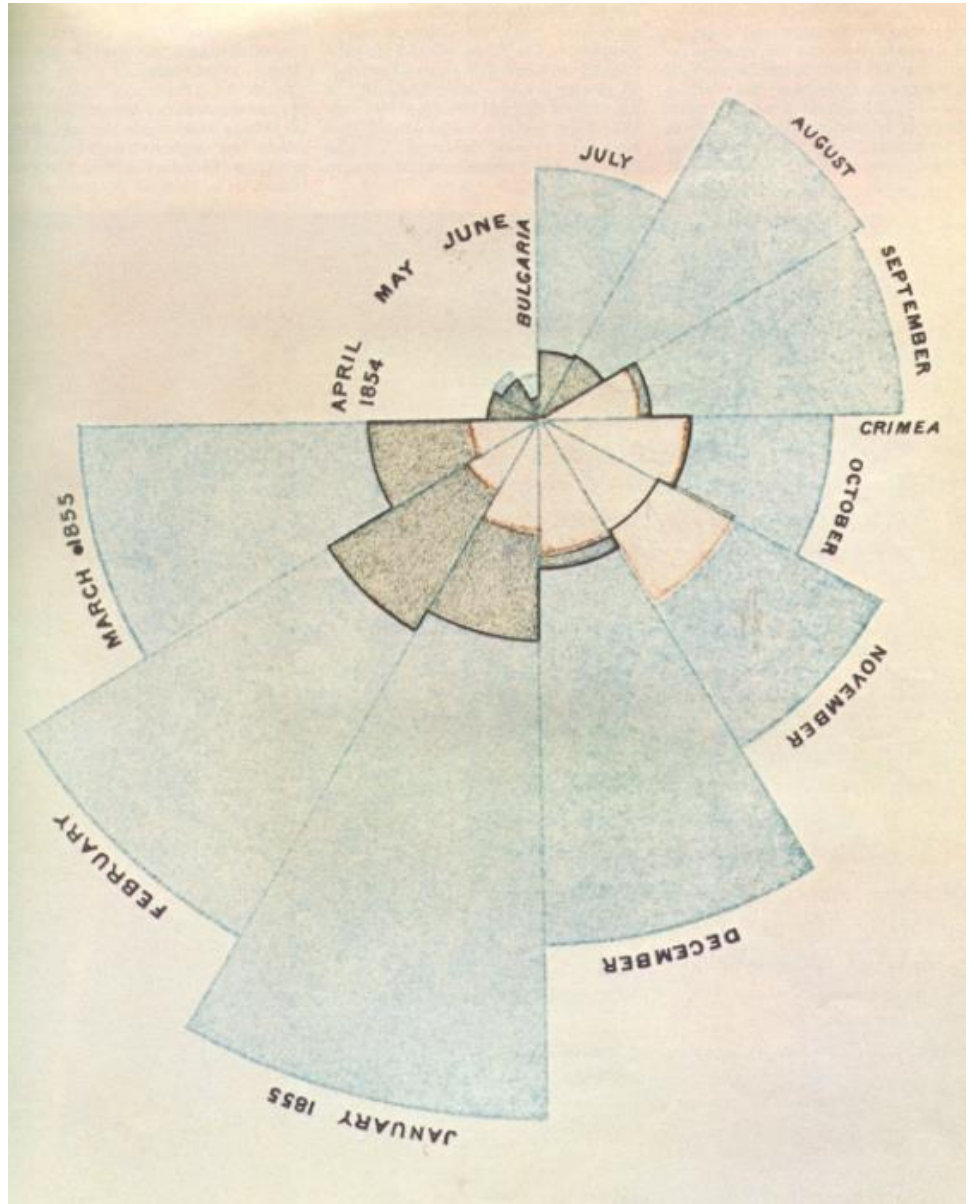
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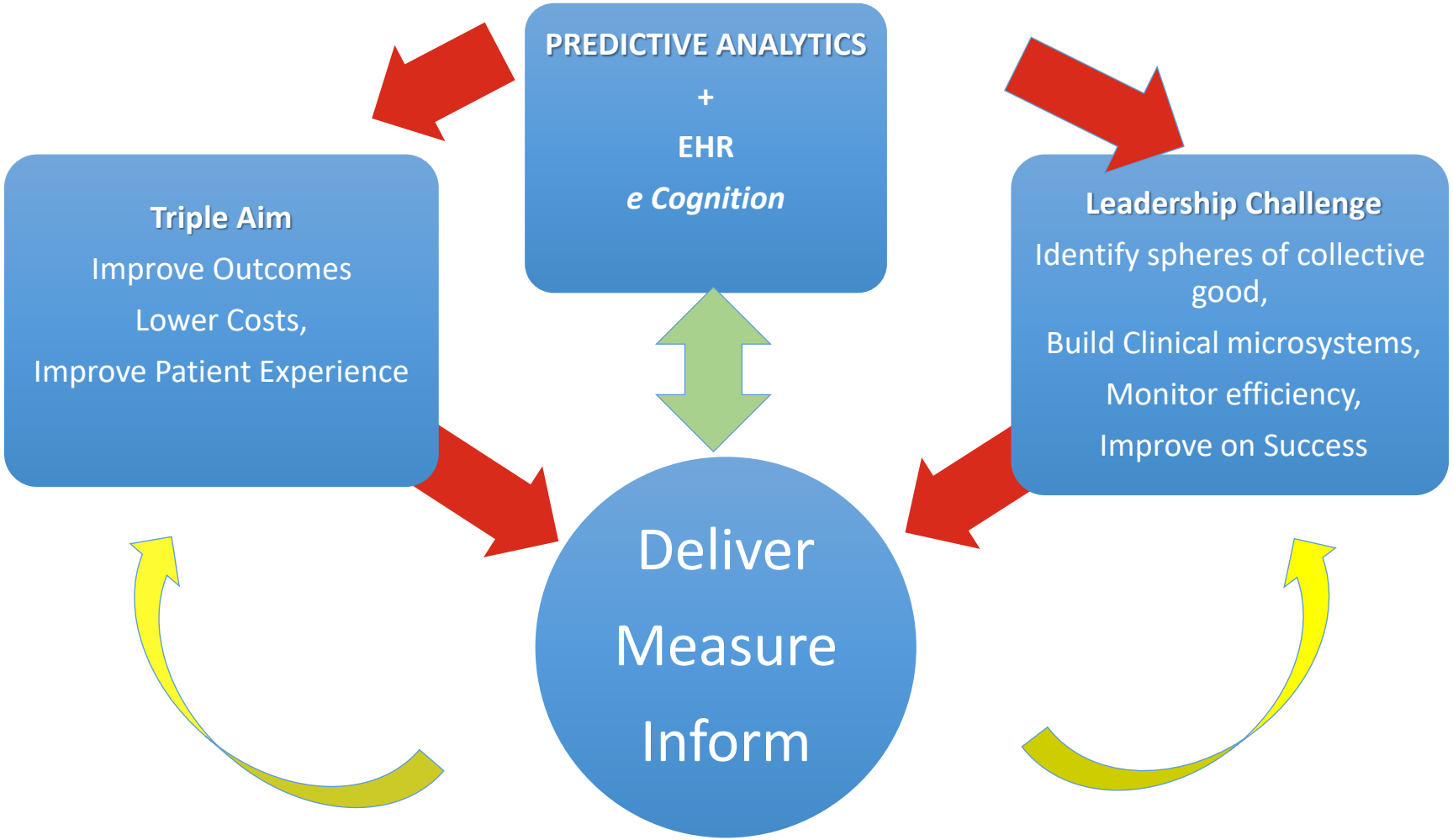
BULGARIA

LEARNING HEALTH SYSTEMS AND CARE DELIVERY PATHWAYS



Berwick DM, et al, Health Affairs 2008
Bohmer RMJ, N Engl J Med, 2013

"A *good* hockey player plays where the puck is.

"...A GREAT hockey player plays where the puck is going to be."

Where we are going at Intermountain

70 percent of the cost of care of CKD and ESRD is locked in unmanaged comorbidity

Total Cost of Care and Per Member Per Month Costs need to be optimized

We are deploying a system of care that goes upstream of CKD and employs cognitive solutions in a learning platform

Teams driven by a predictive model that in full build will incorporate costs in real time

Team

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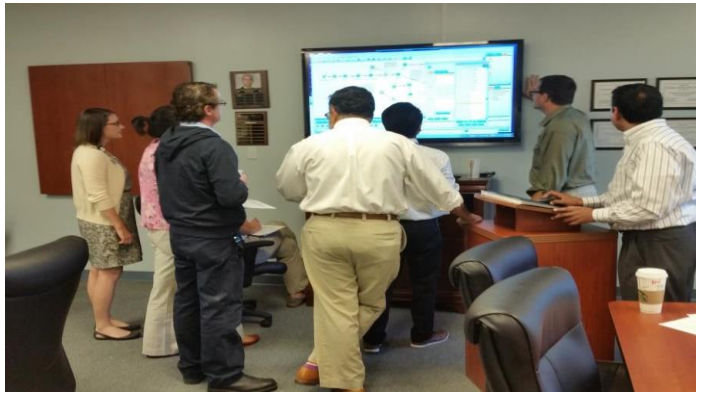

Questions

Thank You !!!