Pre-donation Prescription Narcotic Use: A Novel Risk Factor for Readmission after Living Donor Nephrectomy

American Transplant Congress

June 14, 2016

KL Lentine, MD, PhD,[1] NN Lam, MD, MSc,[2] MA Schnitzler, PhD,[1] GP Hess, MD, MSc,[3] BL Kasiske, MD,[4] **D Axelrod,** MD,[5] **AX Garg,** MD, PhD,[6] **J Schold,** PhD,[7] H Randall, MD,[1] **DC Brennan,** MD,[8] **DL Segev,** MD, PhD[9]

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

1 Saint Louis University, 2 University of Alberta,
3 Symphony Health, 4 Hennepin County Medical Center,
5 Dartmouth University, 6 London Health Sciences Centre,
7 Cleveland Clinic, 8 Washington University,
9 Johns Hopkins University

Disclosures

Krista L. Lentine, MD, PhD
Professor of Medicine
Saint Louis University, St. Louis, MO, USA

I have no financial relationships to disclose within the past 12 months relevant to my presentation. The ACCME defines 'relevant' financial relationships as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.

AND

My presentation does/does not include discussion of off-label or investigational use

(if yes, list company and nature of relationship – e.g. grants, advisory board, etc.).

I do/do not intend to reference unlabeled/unapproved uses of drugs or products in my presentation

(if yes, identify product and unlabeled use).

This work was supported in part by **HRSA contract HHSH-250-2015-00009C**. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of HHS, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

This work was also supported by **NIH/NIDDK R01-DK096008**

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Background

- **Evidence for counseling living kidney donor (LKD) candidates on perioperative risks –** focused on **mortality**
  - Other complications are not well described
- **Readmission –** commonly used measure of **care quality** and **healthcare utilization**
  - Proxy for morbidity and reduced quality of life
- OPTN registry data for U.S. **LKD**, 2005-2012: **2.1% readmitted** within 6 weeks
  - **Center reporting** to the OPTN **underestimates** early surgical complications

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

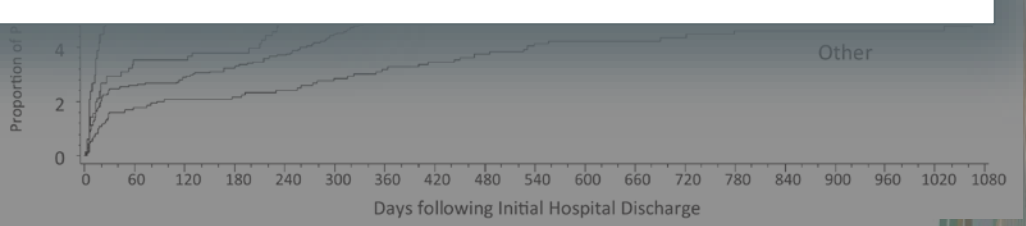
Background

State Inpatient Database (SID) [Schold et al, *CJASN* 2014]

- 4 state inpatient database
-
-

Novel approaches to characterizing perioperative outcomes, including readmission, among confirmed living donor samples are needed

those with predonation **depression** (aHR 1.88) or **hypothyroidism** (aHR 1.63)



- **Limitations: Lack of confirmed LKD status** through patient level-linkages to the national donor registry

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Database Integration

Research Strategy

- Linkage of the **national transplant registry** with other data sources – combine value of:

Confirmed patient status (e.g., LKD, recipient)

+

Baseline patient and **procedure characteristics**

+

Additional **outcome** and **exposure** information

- **Pharmacy fill records**
  - Non-obtrusive measure of **prescribed healthcare**
  - Surrogate **measure of comorbidity** in epidemiologic investigations, including among LKD and transplant recipients

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Database Integration

In context of rising use of prescription narcotics nationally, we asked:

- **Do prescription narcotic fills before living kidney donation predict readmission as a complication after donor nephrectomy?**

Methods: Design & Study Measures

- **Data Sources**
  - Scientific Registry of Transplant Recipients **(SRTR)**
  - Symphony Health Solutions **(SHS)** pharmacy claims warehouse
  - University HealthSystem Consortium **(UHC)**
    - Alliance of 107 academic medical centers & 234 affiliated hospitals – **90% of US non-profit academic centers**
    - **Sept 2008** to **December 2012**
- **Sample Identification**
  - **Patient-Level Linkage, SHS** to **SRTR** – encrypted tokens (transform name, DOB, sex, ZIP code)
  - **Patient-Level Linkage, UHC** to **SRTR** – transplant center, donation date, donor age, sex

Methods: Study Measures

Covariates	Source
Demographics	• **SRTR:** Age, sex, race, donor-recipient relationship, health insurance (yes/no)
Clinical factors	• **SRTR:** BMI, physical limitations, HTN, smoking • **UHC: "Present on Admission" dx –** obesity, hypertension, & smoking; additional conditions by organ system
Procedure	• **SRTR:** Intended procedure type (laparoscopic or open) and side of nephrectomy (left or right) • **UHC:** robotic nephrectomy
Payer & Center factors	• **UHC:** Payer for donation • **SRTR:** Annual donor nephrectomy volume

Methods: Study Measures

Outcomes	Source
Pre-donation Narcotic Use	• **SHS:** Pharmacy fills for **narcotic medications** in the year prior to donation • Aggregated and normalized **to morphine equivalents (ME)**
Readmission	• **UHC**: Readmissions within 1 year • **Primary diagnosis** for the readmission

- **11.3% filled ≥1 narcotic prescription in the year before donation**
- **Narcotic use in year before donation ranked as tertiles:**
  1) <63 mg, 2) 63 to <157.5 mg, 3) > 157.5 mg

Donor Socio-demographic Information

SRTR Live Donor Registry

- Age, Sex, Race
- Donor/recipient relationship
- Donor insurance
- Physical capacity
- Education, Employment status

Prescription Narcotic Use

SHS Database

- Agent
- Dose (for ME)

Pre-Donation Clinical Information

SRTR Live Donor Registry

- Height, Weight (for BMI)
- HTN, Blood pressure
- Smoking
- Serum creatinine (for eGFR)

UHC 'Present on Admission' Diagnoses

- HTN, Obesity, Genitourinary, Cardiac, Respiratory, Gastrointestinal, Hematologic, Neurologic, Endocrine, Rheumatologic, Psychiatric, Smoking

Procedure and Center Information

SRTR Live Donor Registry

- Procedure: Laparoscopic, Open
- Side of nephrectomy
- Annual volume

UHC Intended Procedure

- Robotic

UHC Payer Information (Donation)

- Private, Medicare, Other

Sample: 14,959 = 55.6% of all U.S. live kidney donations in period

Hospital Readmissions

UHC Hospitalization Records

- Diagnoses and Procedures

Baseline Characteristics

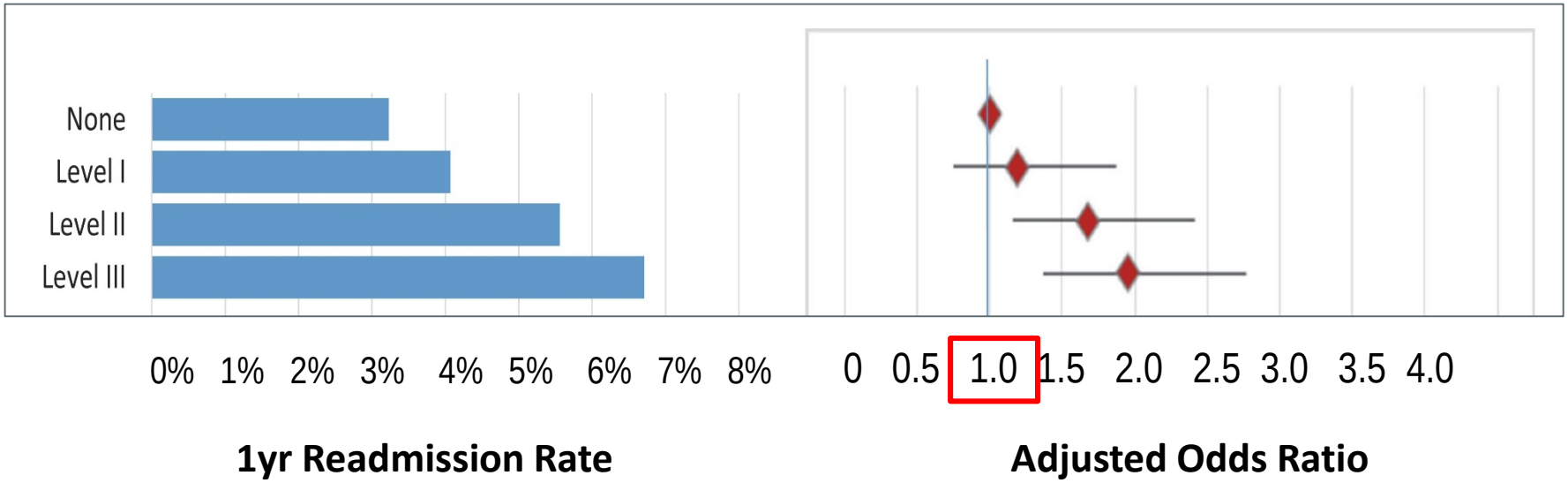
*p<0.05–0.002; †p=0.001–0.0002; ‡p<0.0001	No Narcotics (N=13,266)	Level 1 (N=516)	Level 2 (N=611)	Level 3 (N=566)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age (yrs)	42.1 (11.8)	42.1 (11.8)	41.9 (11.6)	42.9 (11.3)
	(%)	(%)	(%)	(%)
Female	60.9	**70.5‡**	**68.7†**	**65.4***
Race		*	*	‡
White	72.0	**75.4**	**74.6**	**81.5**
African American	11.5	13.8	13.6	11.7
Hispanic	11.3	8.5	8.5	4.8
Other	5.2	2.3	3.3	2.1
Obese (BMI ≥30)	20.7	21.1	24.6	**26.7†**
Comorbidity				
Hypertension	12.1	11.6	12.6	13.3
Genitourinary	1.9	2.5	2.0	2.8
Cardiac	0.9	0.2	1.2	1.6
Respiratory	5.2	7.0	**7.9***	**8.0***

Baseline Characteristics, cont.

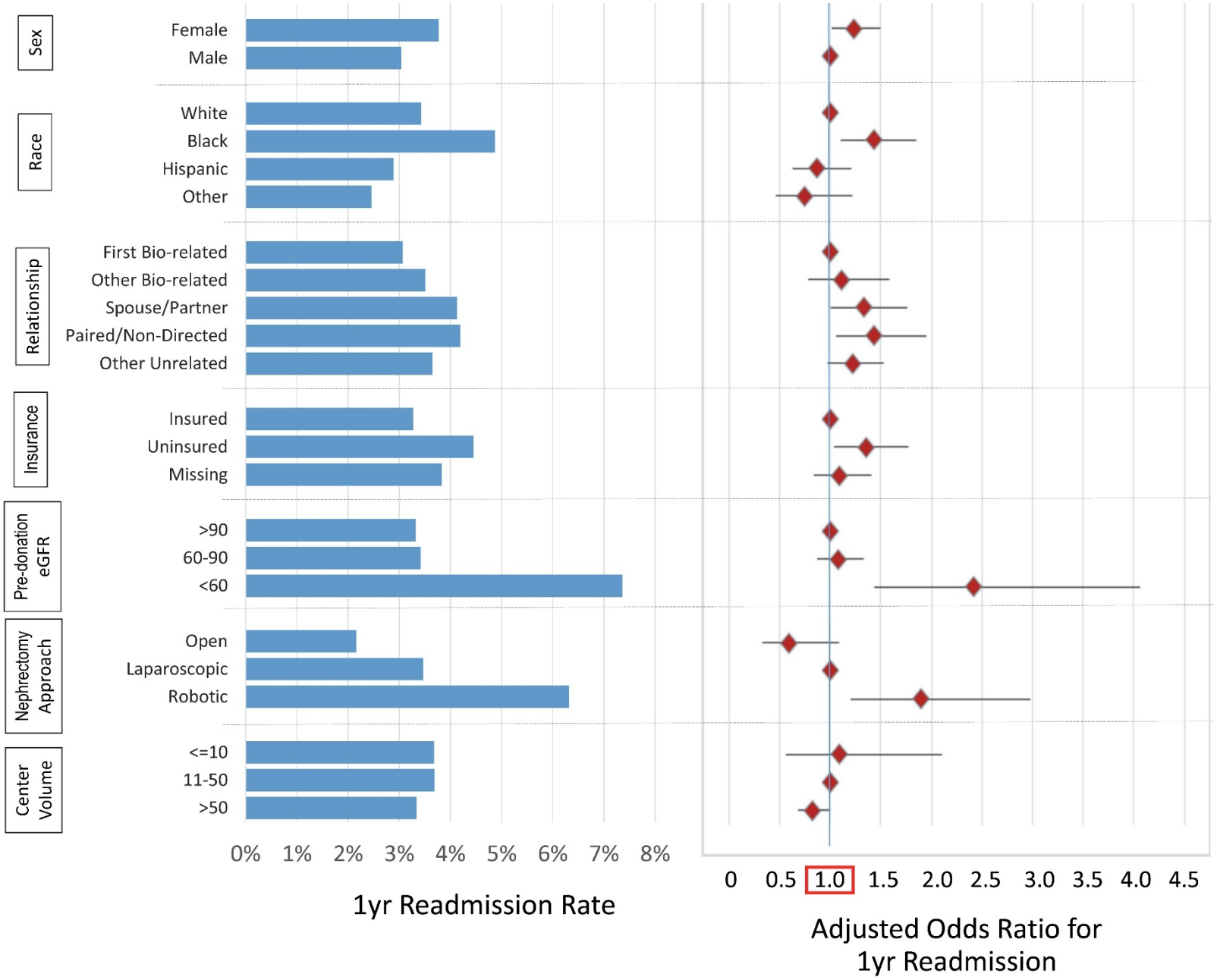
	No Narcotics	Level 1	Level 2	Level 3
	(%)	(%)	(%)	(%)
Gastrointestinal	7.9	8.7	9.7	**10.8***
Hematologic	1.6	1.7	**2.6***	1.6
Neurologic	0.3	0.0	0.5	0.7
Endocrine	11.6	13.0	13.3	**14.8***
Rheumatologic	0.2	0.0	0.3	0.4
Psychiatric	7.0	8.9	**10.2***	**11.0†**
Smoking	8.5	**11.6***	9.3	**14.3‡**
Nephrectomy type				
Laparoscopic	94.0	4.3	3.9	4.6
Robotic	2.4	92.4	93.6	92.4
Left	86.5	3.3	2.5	3.0
Annual center Volume				
≤10	1.9	1.2	1.3	1.8
11-50	41.1	40.3	44.2	44.5
>50	57.0	58.5	54.5	53.7

Results

- **Overall 1 year readmission rate – 3.6%**
- **Pre-donation narcotic use level bore graded associations with 1-year readmission**
  - LKD with the **highest pre-donation narcotic use** were **twice as likely** to be readmitted as non-users (6.6% *vs* 3.2%, **aOR 1.94**)



Readmission, by Other Factors

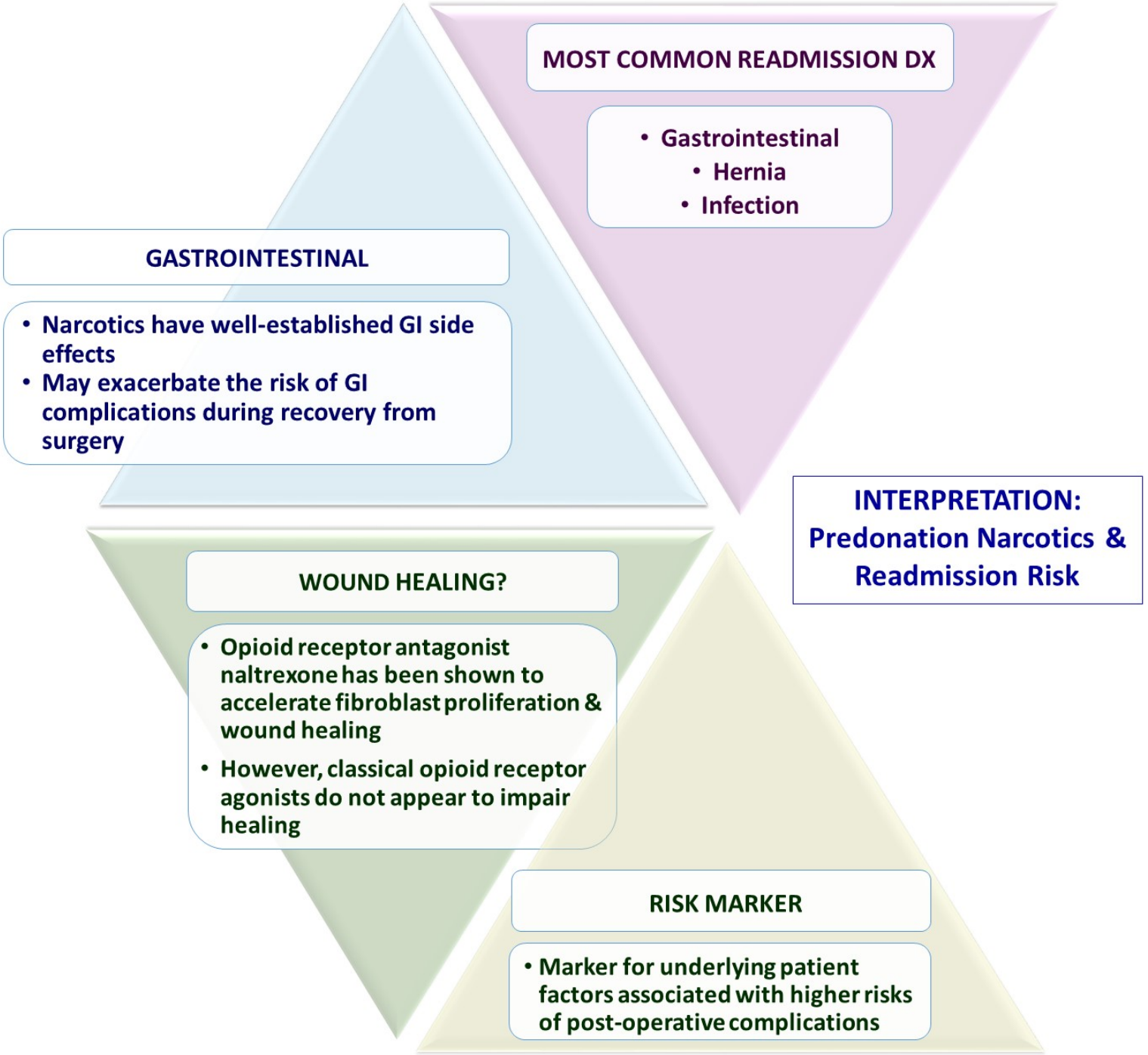


Readmission Diagnoses, by Narcotic Use Level

Most common primary medical diagnoses for readmission after donor nephrectomy, according to pre-donation narcotic use level

No Narcotics		Level 1 Use		Level 2 Use		Level 3 use	
Diagnosis	**%**	**Diagnosis**	**%**	**Diagnosis**	**%**	**Diagnosis**	**%**
Hernia	10.0%	Hernia	19.1 %	Infection	14.7%	Infection	26.2%
Digestive system complications NEC	7.0%	Infection	14.3 %	Digestive system complications NEC	8.8%	Digestive system complications NEC	15.8%
Infection	8.4%	Abdominal pain	9.5%	Abdominal pain	8.8%	Incisional hernia without obstruction	7.9%
Constipation	5.4%	Nausea with vomiting; other digestive complaints	9.5%	Nausea and/ or vomiting	8.8%	Dehydration	5.3%
Dehydration	3.3%	Sprains and strains	9.5%	Paralytic ileus or intestinal obstruction	5.9%	Paralytic ileus	5.3%
Nausea with vomiting	3.0%	Paralytic ileus	4.8%	Unspecified gastritis and gastroduodenitis	2.9%	Other disorders of the peritoneum	5.3%

- Most common readmission diagnoses: **hernias, gastrointestinal complications (GI)**, and **infections**
- **GI complications & infection** appear to predominate in those with the highest predonation **narcotic use**


MOST COMMON READMISSION DX
• Gastrointestinal
• Hernia
• Infection
GASTROINTESTINAL
• Narcotics have well-established GI side effects
• May exacerbate the risk of GI complications during recovery from surgery
INTERPRETATION: Predonation Narcotics & Readmission Risk
WOUND HEALING?
• Opioid receptor antagonist naltrexone has been shown to accelerate fibroblast proliferation & wound healing
• However, classical opioid receptor agonists do not appear to impair healing
RISK MARKER
• Marker for underlying patient factors associated with higher risks of post-operative complications

Limitations

Design & Data

- Results **may not generalize** to LKD donating at nonacademic centers, or outside the U.S.
- **Retrospective, observational** design identifies associations but cannot prove causation
- **Unable** to account for **illicit drug use, "pharmacy shopping"** behaviors, or narcotic prescription fills outside of insurance benefits
- Unable to capture readmissions **outside the recovery hospital**

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Strengths

Design & Data

- **Verification of donor status** through linkage with the national donor registry
- Capture of **readmission events** independent of center reporting
- **Pharmacy fill records** as a novel **pre-donation exposure**

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Conclusions

- Linkage of the **national transplant registry** with administrative records from a **pharmacy claims database** and an **academic hospital consortium** enabled characterization of **correlates of readmission** after donor nephrectomy
- **Pre-donation narcotic use** is a **novel risk factor** for readmission after donation
  - Associations may in part reflect narcotic use as a measure of comorbidity, but relevant to **risk stratification** and **counseling**
- Future work should investigate **underlying mechanisms** and approaches to **optimizing post-donation outcomes**

SRTR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS