~~New Techniques in Renal Transplantation~~

What's New in Renal Transplantation

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Disclosures

Financial: None

Fiduciary:

- Chairman, Board of Directors, New York Organ Donor Network
- UNOS Region 9 Councilor
- Member, UNOS Board of Directors
- Councilor, American Society of Transplant Surgeons

Disclaimer

- Not comprehensive
- Not limited to technical surgical issues
- Choices:
  - Talk a lot about a little
  - Talk a little about a lot
  - Talk moderate amount selected topics
- Things fellows may not have exposure to
- Are not necessarily ready for prime time
- Things that I think have a future
- Represent conceptual changes

Overview

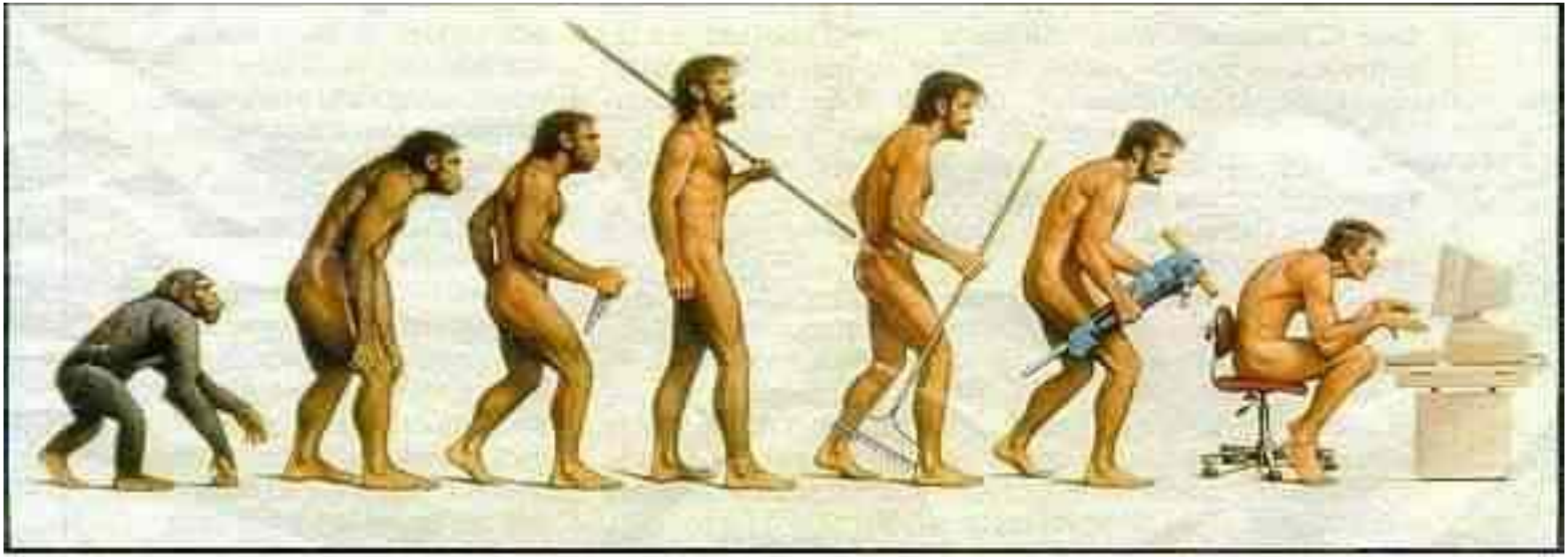
- Technical
  - Difficult Cases: “Show and Tell”
- Pharmacologic
- Organizational
- Financial

Technical

Necessary Steps in the Introduction of New Surgical Techniques

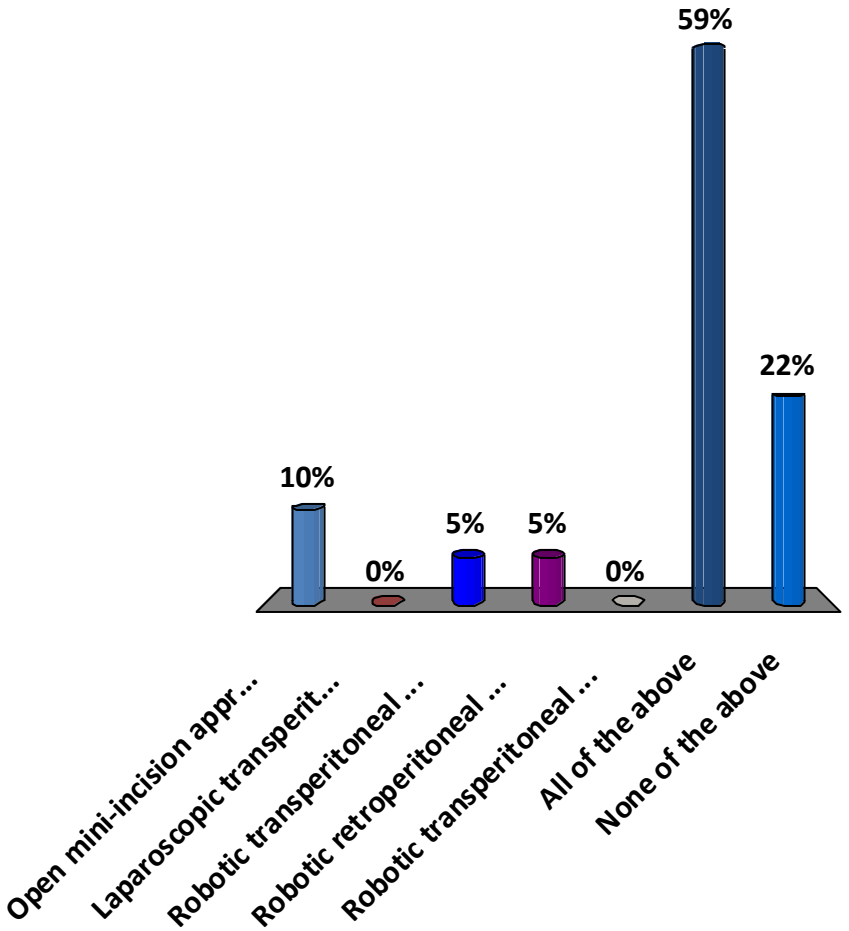
- Conceptualization
- Technical feasibility
- Reproducability
- Optimization
- Safety
- Non-inferiority
- Benefit
- Dissemination/Adoption
- Further evolution

Evolution of Renal Transplantation

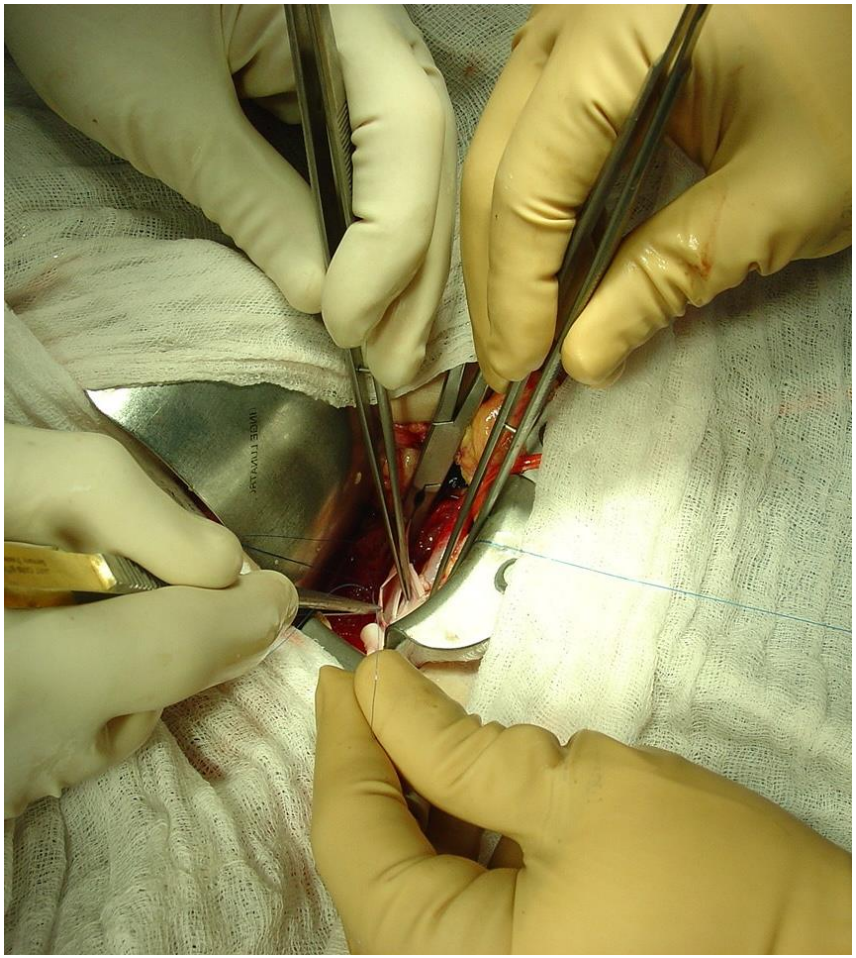


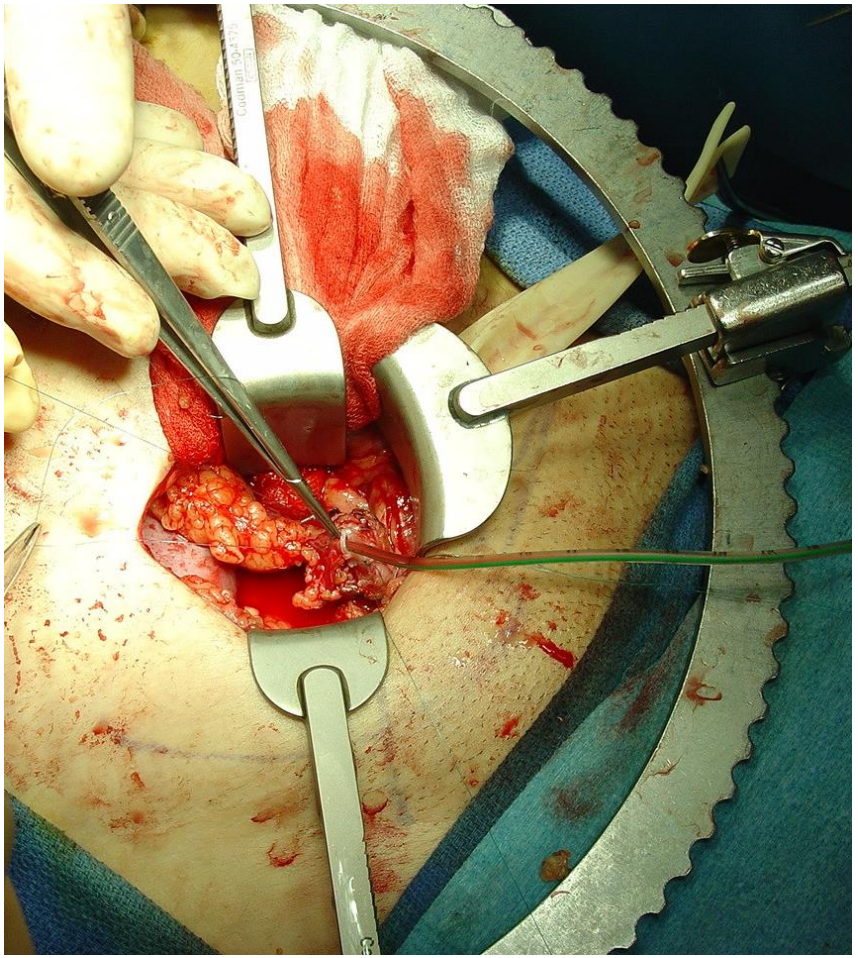
Recent modifications in the renal transplant recipient operations include?:

A. Open mini-incision approach
B. Laparoscopic transperitoneal approach
C. Robotic transperitoneal approach
D. Robotic retroperitoneal approach
E. Robotic transperitoneal with transvaginal insertion of the kidney
F. All of the above
G. None of the above



Mini-Incision Renal Transplantation

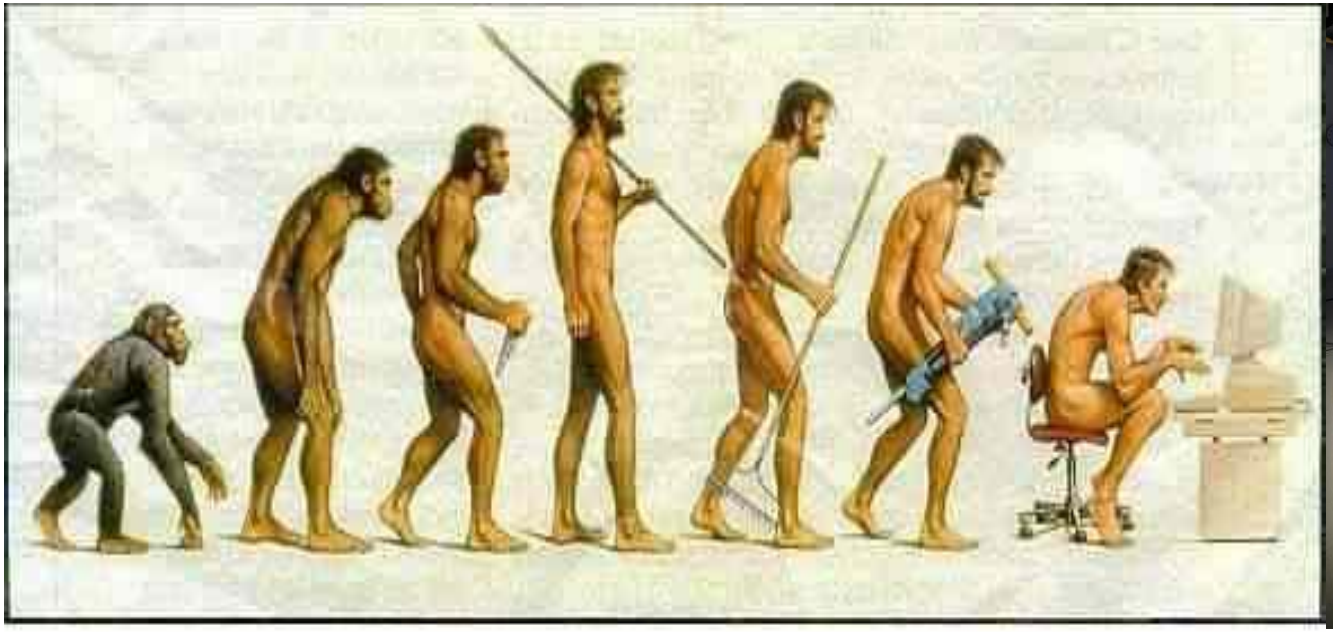




Mini-Incision Renal Transplantation

- 5-7 cm incision in patients with BMI<30
- Extra-peritoneal approach
- Dynamic retraction
- Kidney inserted into the iliac fossa prior to anastomoses
- Back wall of the vascular anastomoses performed from the inside
- No significant advantage compared to open standard open approach

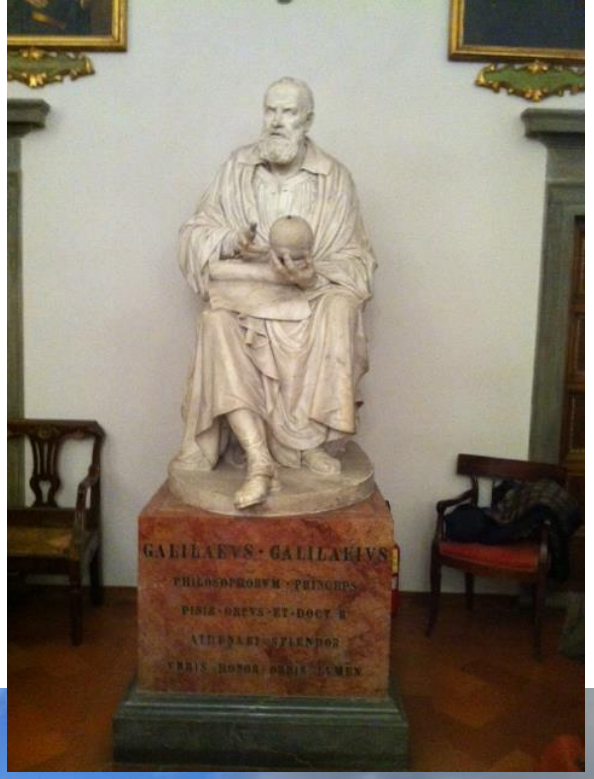
Evolution of Renal Transplantation: Robotics



Minimally Invasive Renal Transplant Recipient Operation

- **Mini-incision**
- **Laparoscopic renal tx – Modi**
- **Robotic transplant routinely performed in a handful of centers**
  - **Usually done transperitoneal**
  - **Robotic SPK – Boggi**
  - **Transvaginal insertion of the kidney – Pietrabissa**
- **Early phases of development**


SOUVENIR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Robotic Renal Transplantation

Variable	Giulianotti and Oberholzer *et al.*[14-16]	Boggi *et al.*[18]	Menon *et al.*[19-21]
Patient's position	Left lateral decubitus	Left lateral tilt of patient and table with 15° Trendelenburg	Supine with lithotomy and steep Trendelenburg position
Docking of robot	Right side of patient	Right side of patient	Between two legs
Incision for graft placement	Paraumbilical vertical	Suprapubic horizontal	Paraumbilical vertical
Use of hand assisted device	Yes	Yes	Yes
Placement of camera port	Left lower quadrant, slightly left to midline	Left to the midline below the level of umbilicus	Through gel-point placed at paraumbilical incision
Graft placement	Transperitoneal	Initially transperitoneal shifted to extra-peritoneal for final position	Initially transperitoneal shifted to extra-peritoneal for final position
Selection of patient group	Obese	Non-obese	Non-obese
Use of regional hypothermia	No	No	About 300cc ice-slush
Ureteric reimplantation	Re-docking of robot	Open surgery	No re-docking of robot was required
Creatinine clearance following RAKT versus open surgery	Initial slow clearance; no difference at 3 months	-	Similar clearance from day one onwards in hands of experienced robotic surgeon, slow initial clearance in hands of surgeon less experience for robotic surgery

RAKT = Robot assisted kidney transplantation

Modi P, et al: Indian Journal of Urology 2014, Jul-Sep; 30(3): 287-292

Robotic Renal Transplantation in the Obese Patient

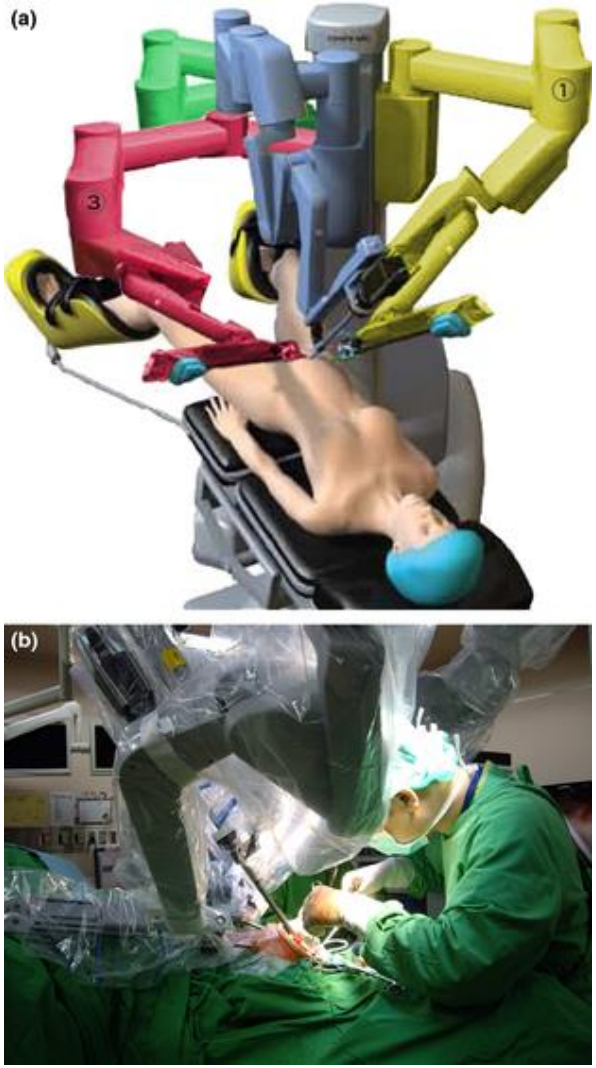
Tzvetanov I, et al: World J Surg. 2013 Dec;37(12):2791-9

Robotic Renal Transplantation in the Obese Patient

	Robotic	Open	P Value
N	28	28	
BMI	38.1±5.4	42.6±7.8	0.002
Wound Infection	0	8 (28.6%)	0.004
Creatinine at Discharge	2.0±1.4	1.4±0.5	0.04
Length of Stay (days)	8.2±4.5	8.1±5.3	0.98
Hospital Costs for Tx	$75,148	$60,552	0.02
6 Month Hospital Days	14.3±10.2	15.8±17.3	0.69
6 Month Total Hospital Costs	$86,272	$66,487	0.04

Oberholzer J: Am J Trans 2013, Mar; 13(3):721-728

Robot-assisted Renal Transplantation In The Retroperitoneum

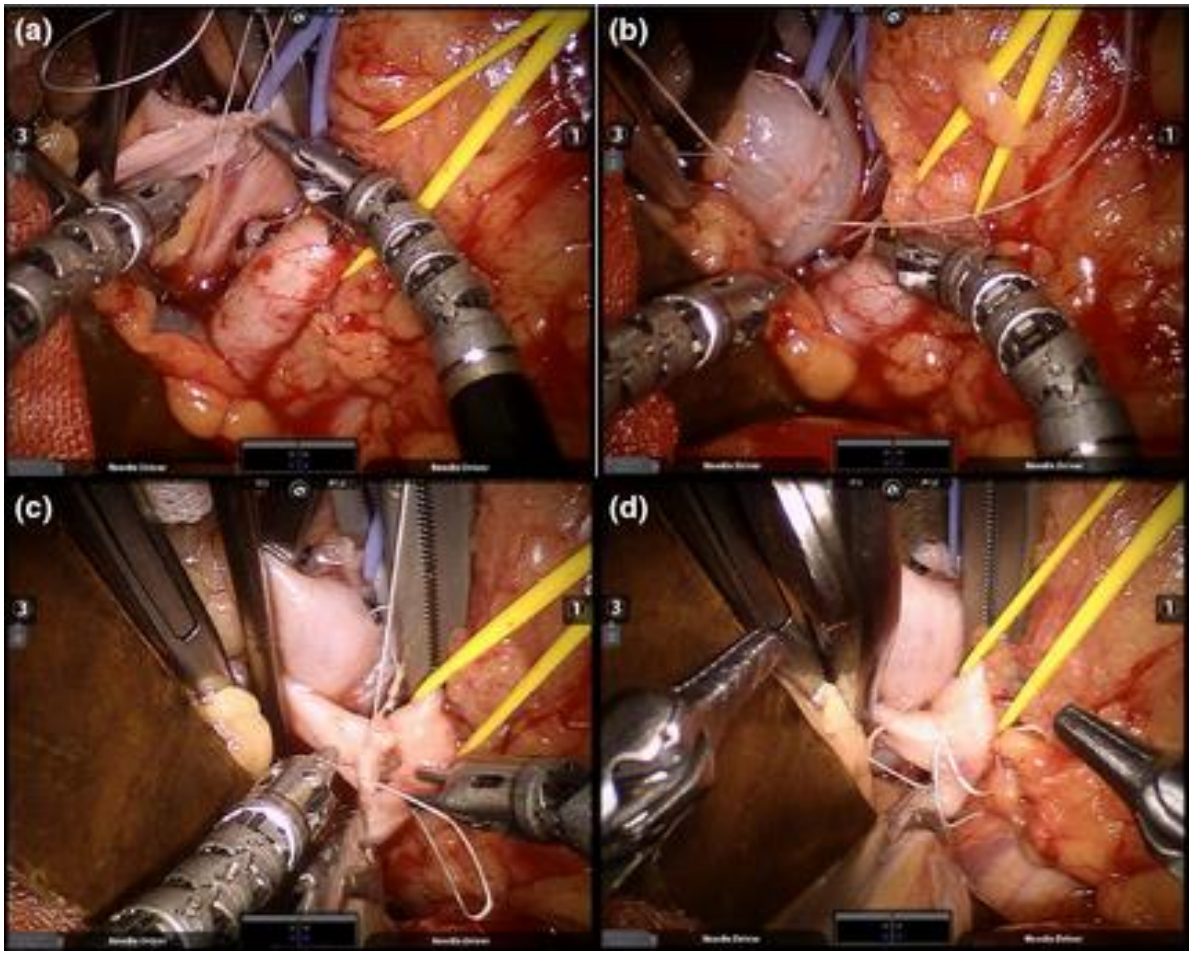


Tsai MK et al: Transplant International Volume 27, Issue 5, pages 452-457, 18 FEB 2014

Robot-assisted Renal Transplantation In The Retroperitoneum

N = 10 patients

Average Anastomosis Time Of 67.4 ± 22.3 Min



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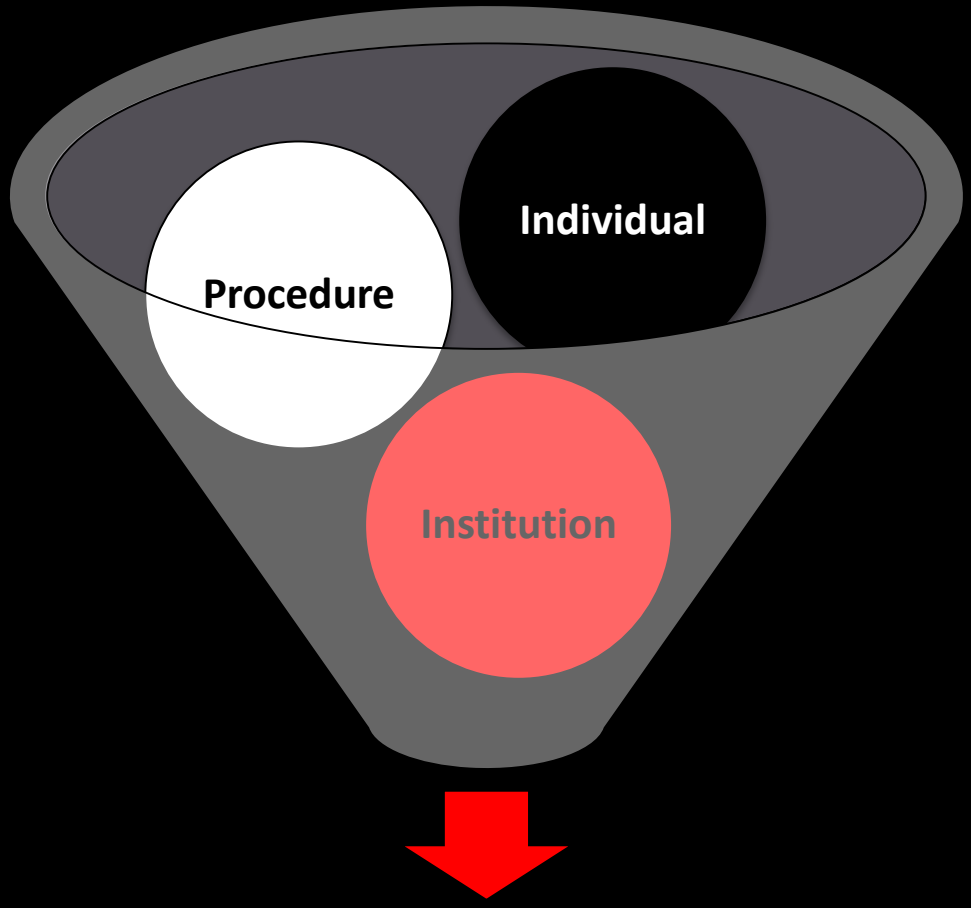
Components of the Learning Curve



Overall Learning Curve

Difficult Cases

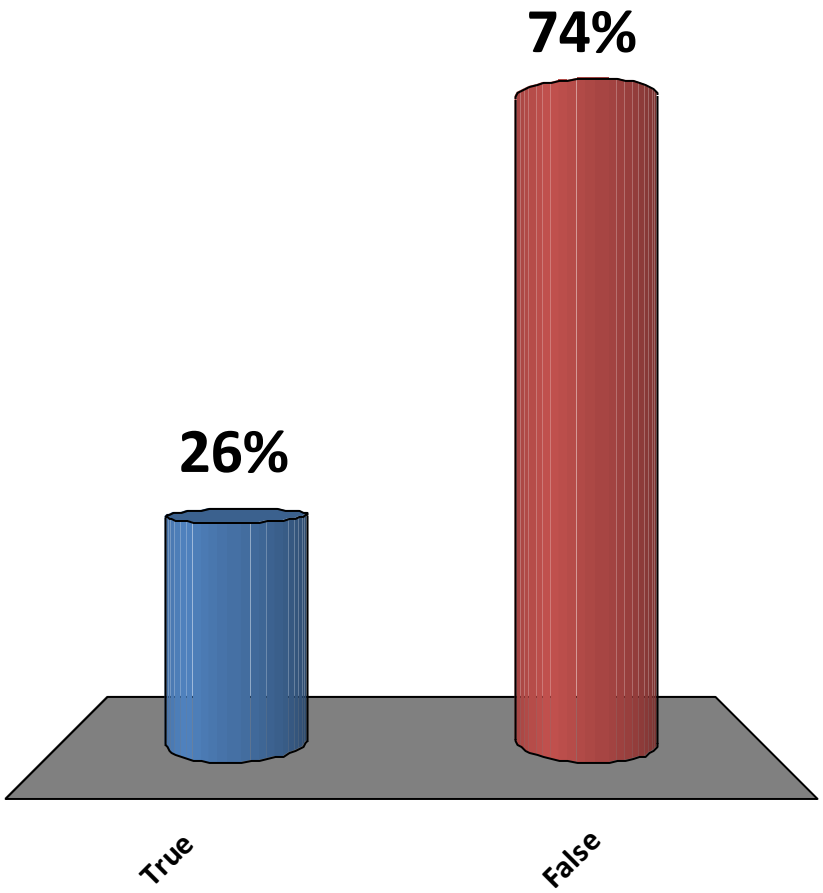
“Show and Tell”

Outside the Box Surgical Approaches

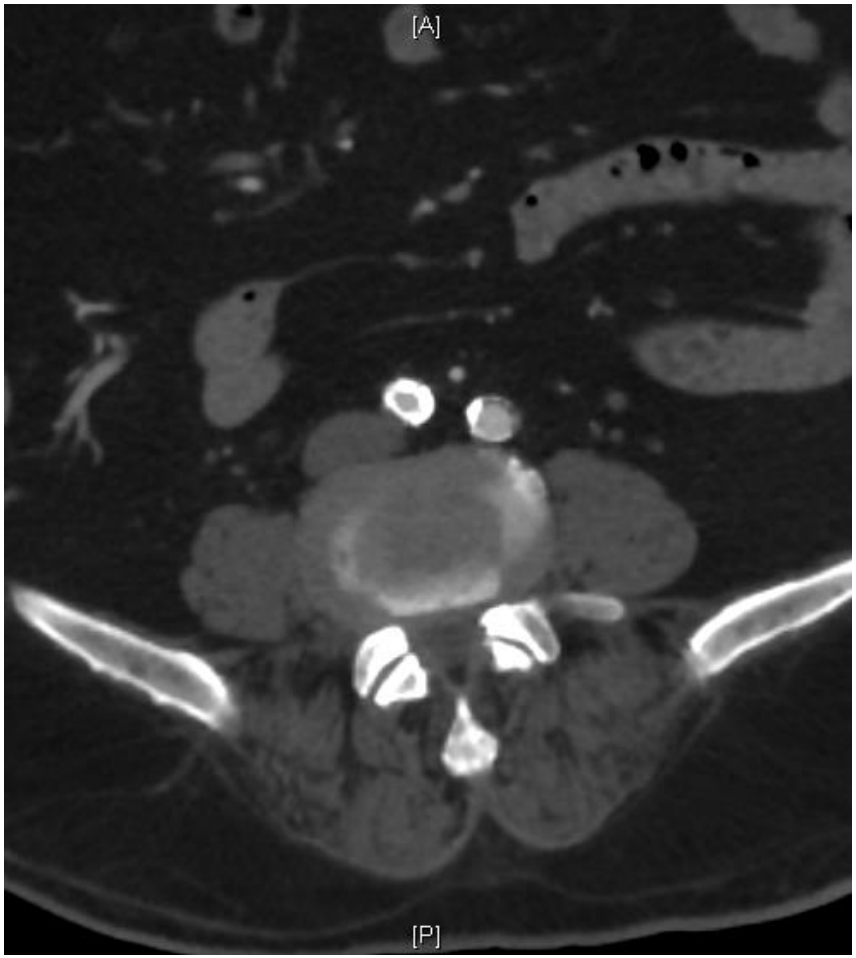
Extensive, diffuse, bilateral aorto-iliac vascular calcification, with bilateral common iliac artery stenoses is a contra-indication to renal transplantation?

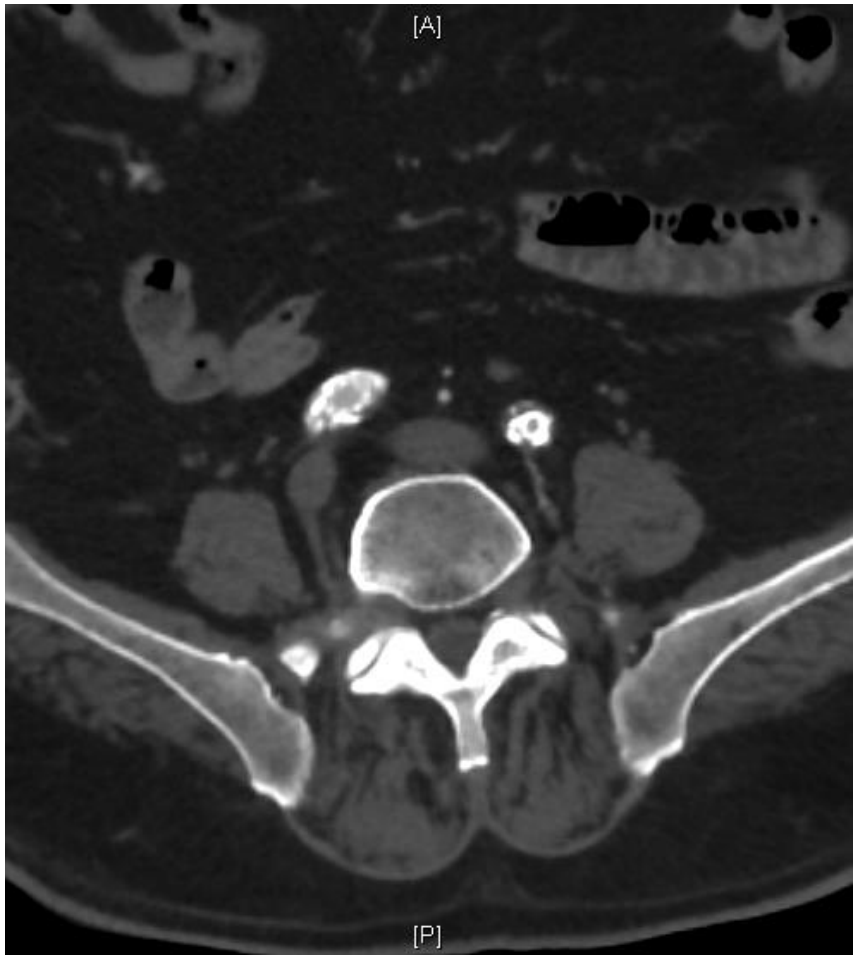
A. True

B. False

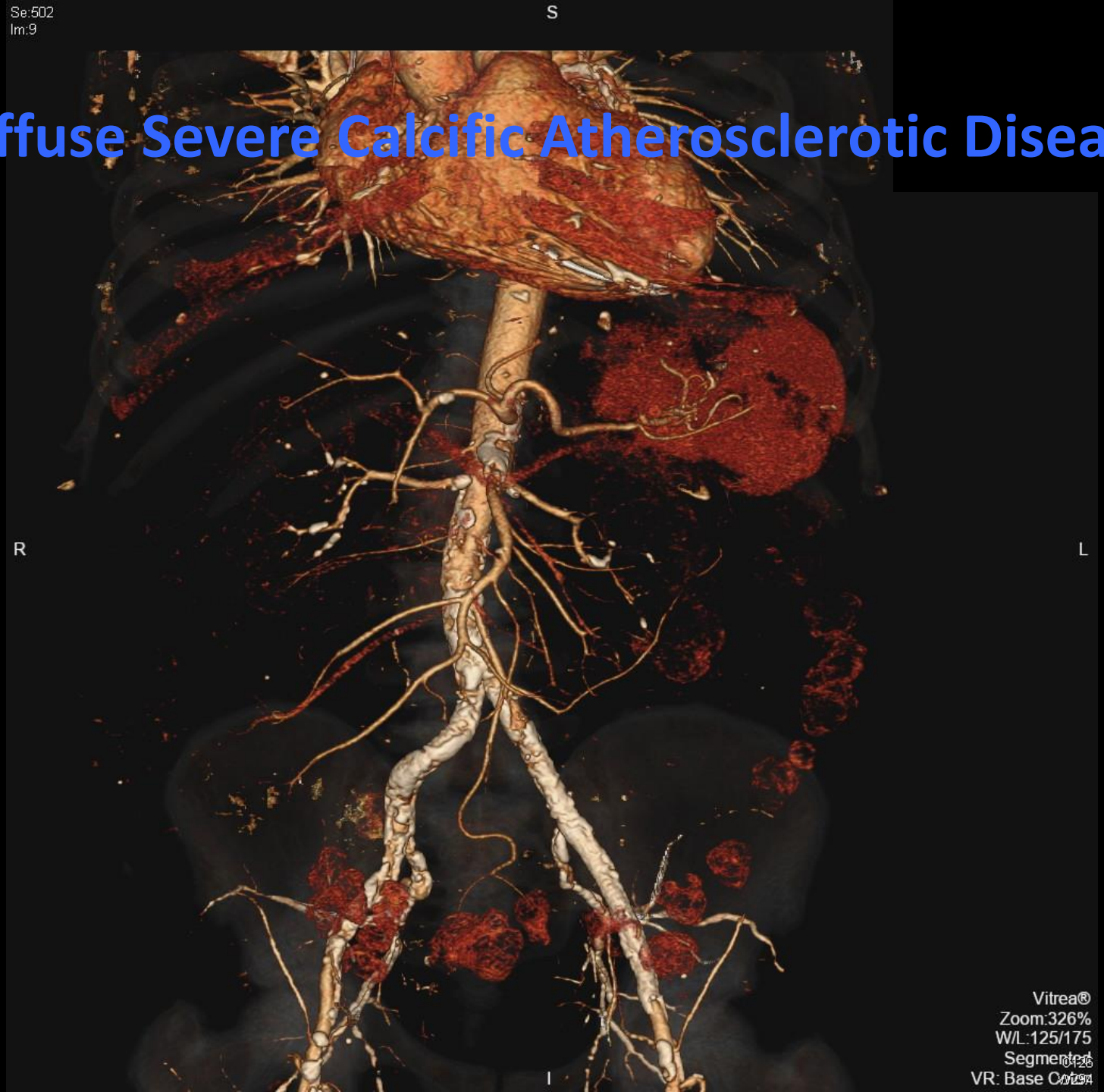


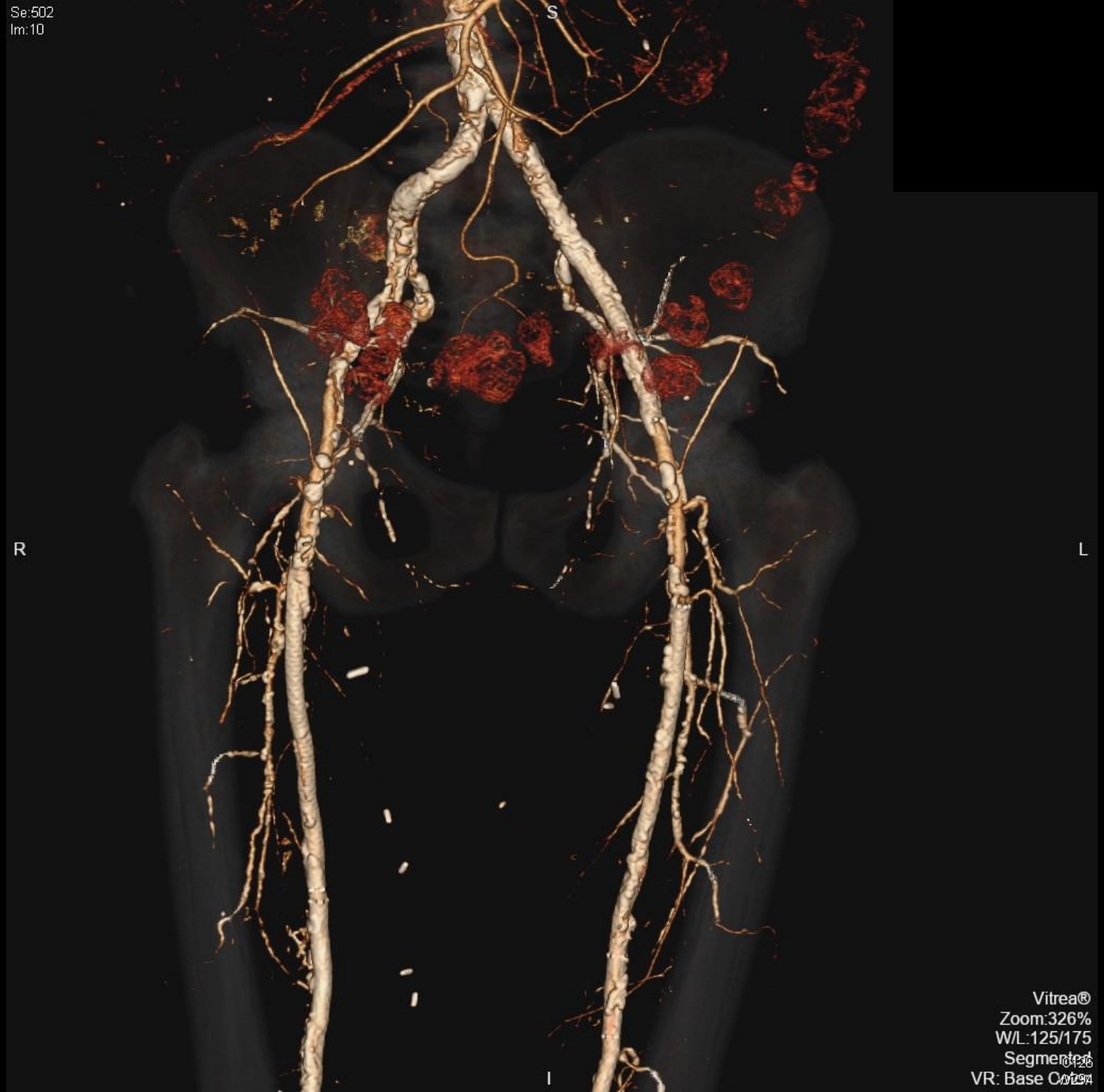
Bilateral Common Iliac Artery Severe Stenosis





Diffuse Severe Calcific Atherosclerotic Disease

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Zoom:326%
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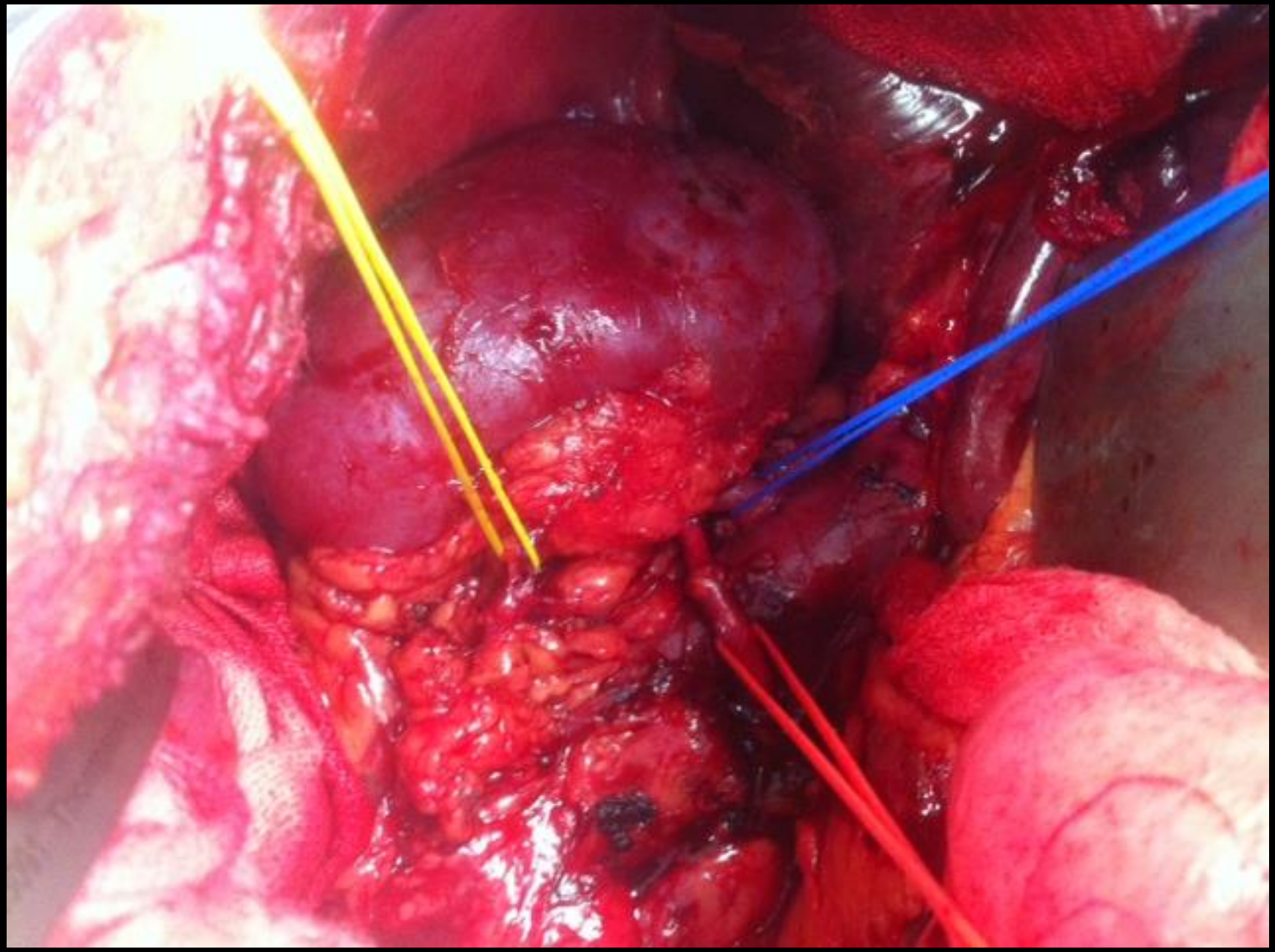
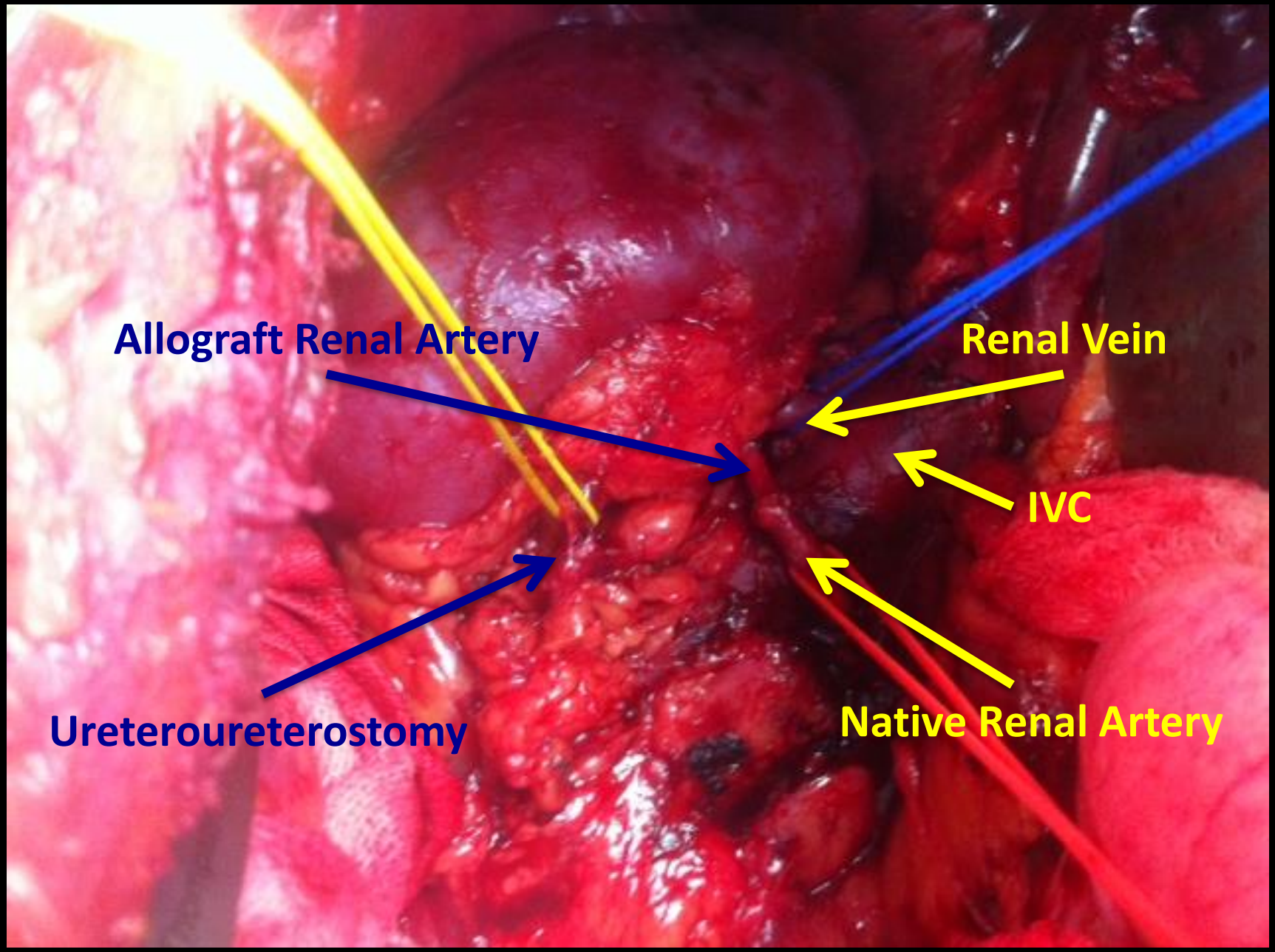
VR: Base

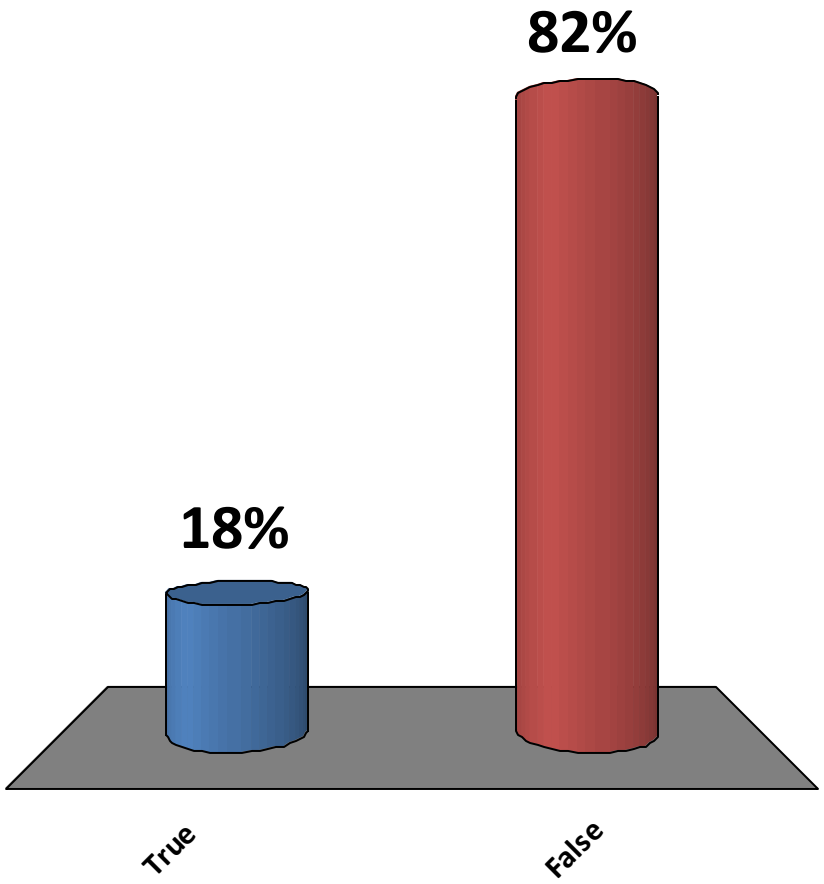


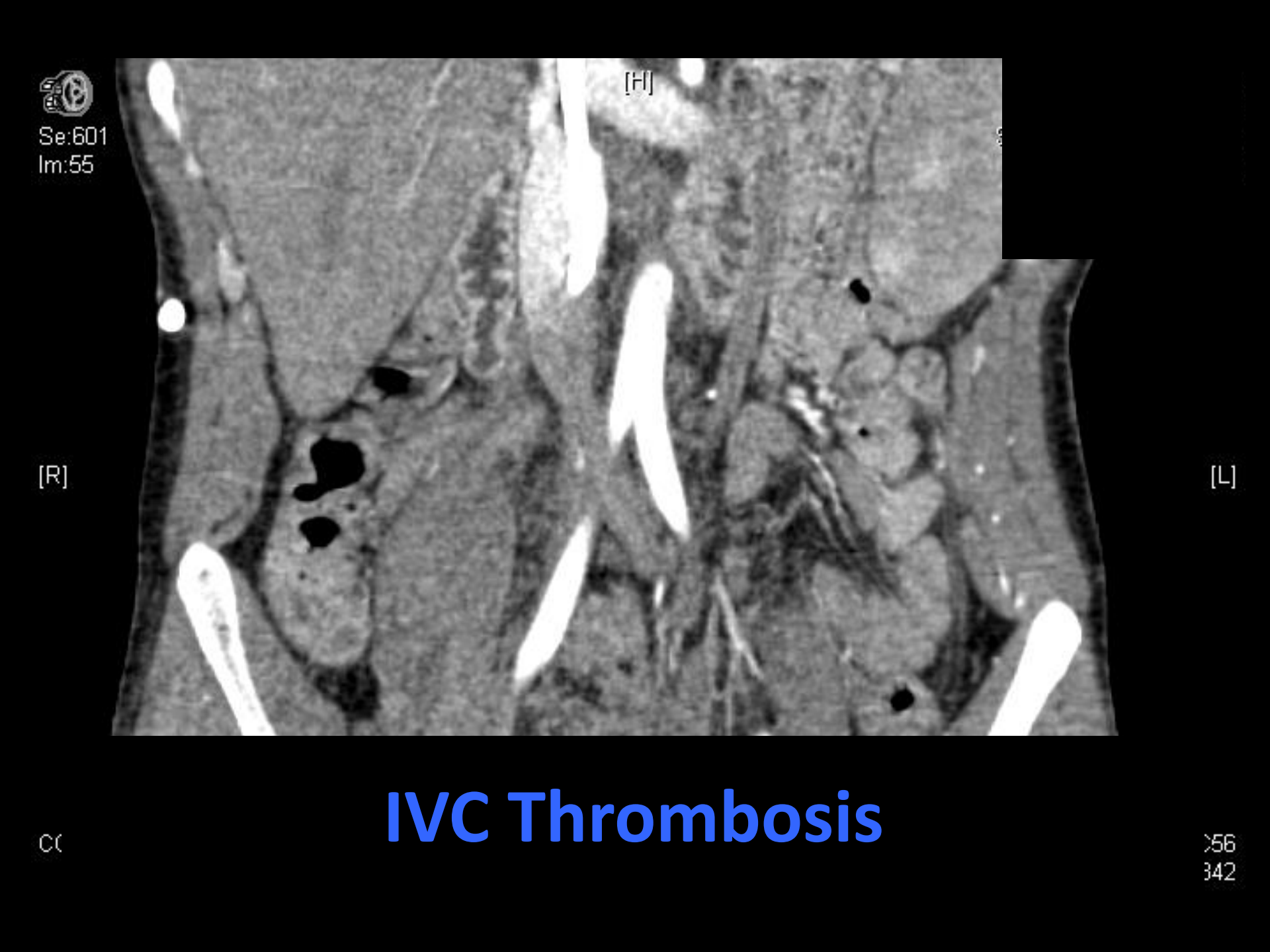

Allograft Renal Artery
Renal Vein
IVC
Ureteroureterostomy
Native Renal Artery

IVC thrombosis is a contra-indication to renal transplantation?

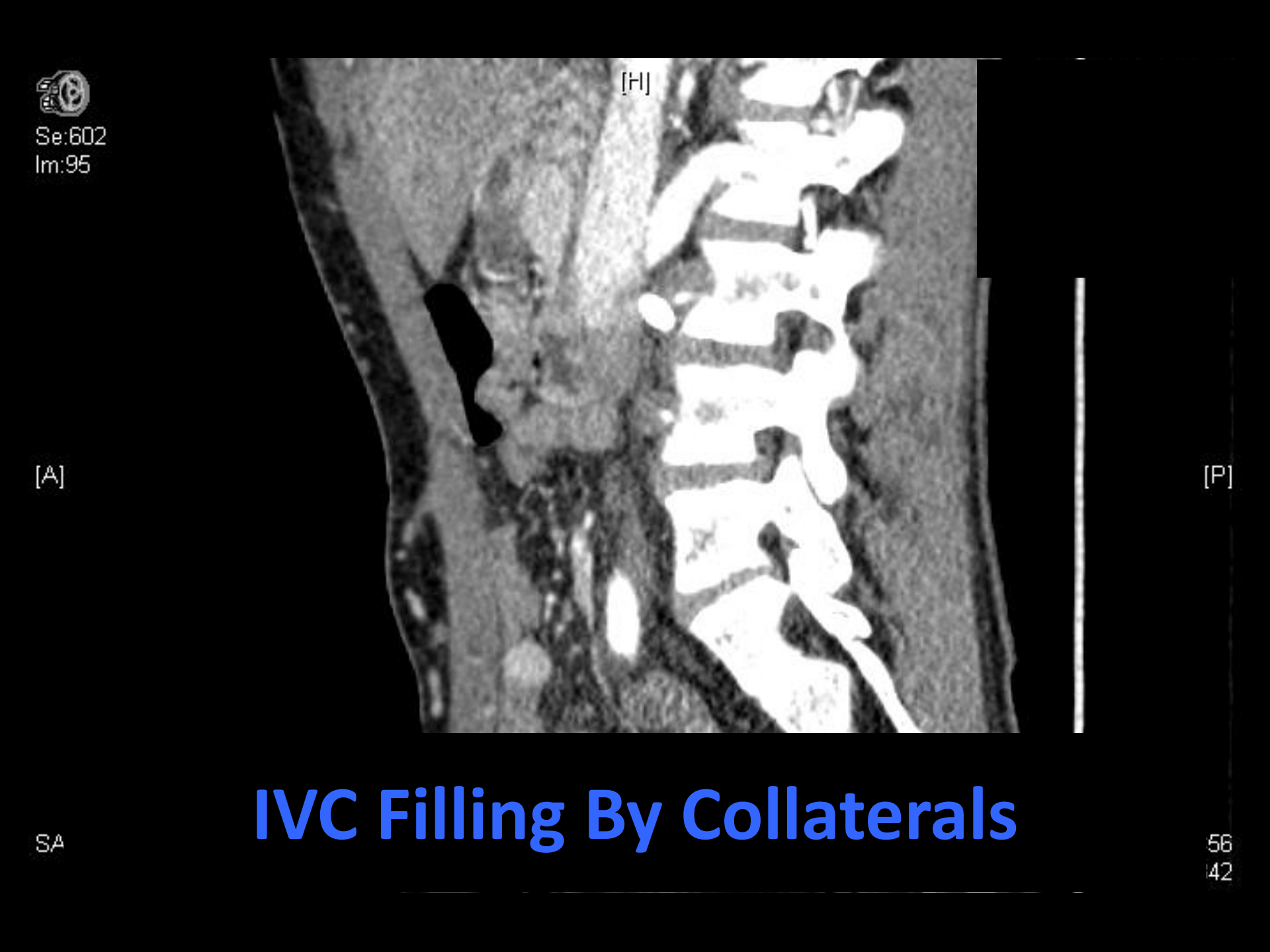
A. True

B. False





IVC Thrombosis



IVC Filling By Collaterals

Pharmaceutical

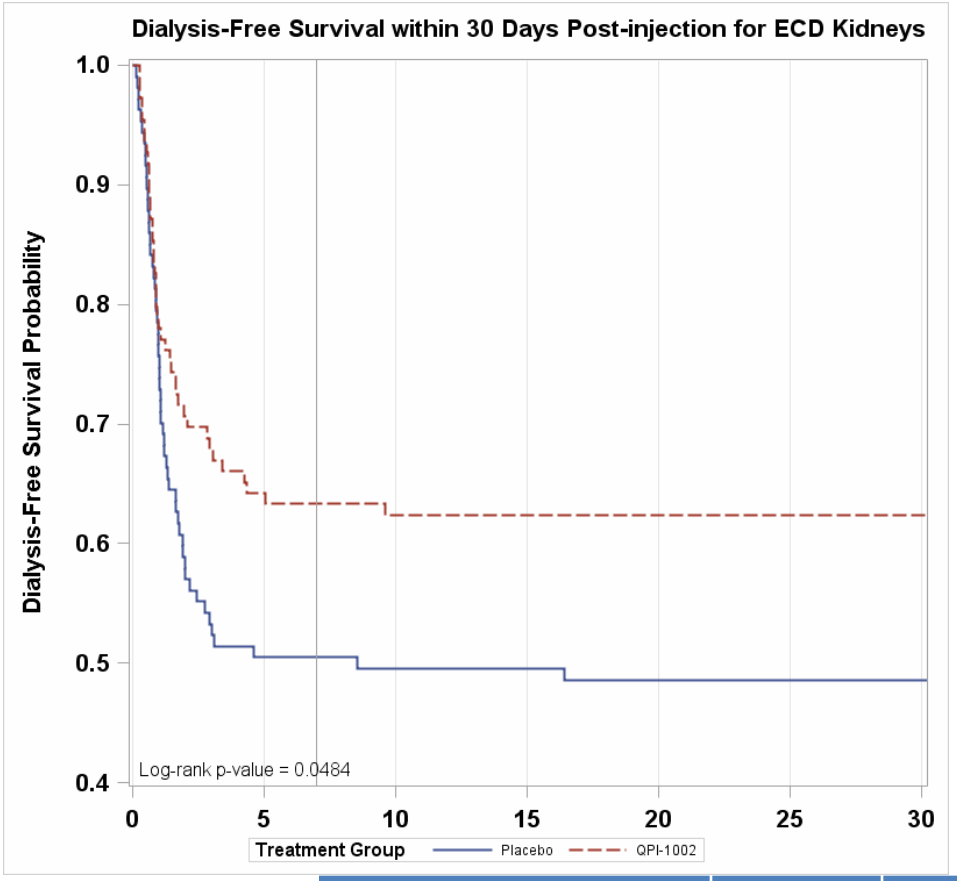
Addressing Delayed Graft Function

- DGF significant problem in DDRT
- Increased LOS = Increased Cost
- More difficult to manage patients with DGF
- Some centers frequently turn down kidneys at high risk for DGF
- Several agents that work by different mechanisms are currently in investigational trials

Anti-Apoptotic Agent

- Quark Pharmaceuticals
- QPI-1002 = 15-NP – small inhibitory RNA against p53
- p53 pro-apoptotic
- p53 plays a central role in the processes of aging and senescence in many tissues
- Increased p53 activation in older kidneys in response to reperfusion injury

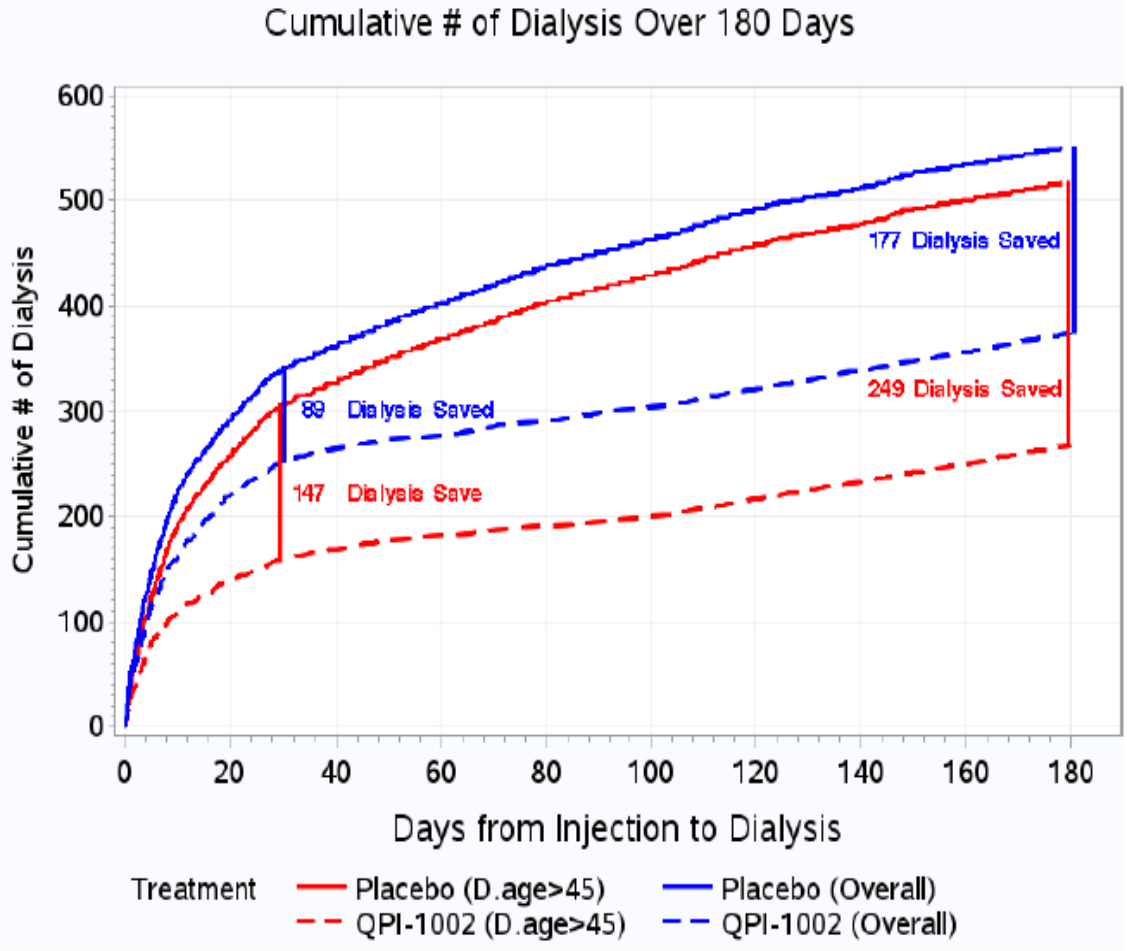
Secondary Endpoint: Dialysis Free Survival



- **QPI-1002 significantly improved the Dialysis Free Survival (time to first dialysis) in the first post transplant month in ECD/CS Strata (Log rank p-value 0.0484)**

Population Unadjusted Analysis)	Hazard Ratio	95% Hazard Confidence Limits		Pr>ChiSq
Overall (N=327)	0.763	0.547	1.064	0.1108
ECD/CS (N=178)	0.626	0.396	0.990	0.0451

Analysis of pharmacoeconomic impact over the 6 month study period

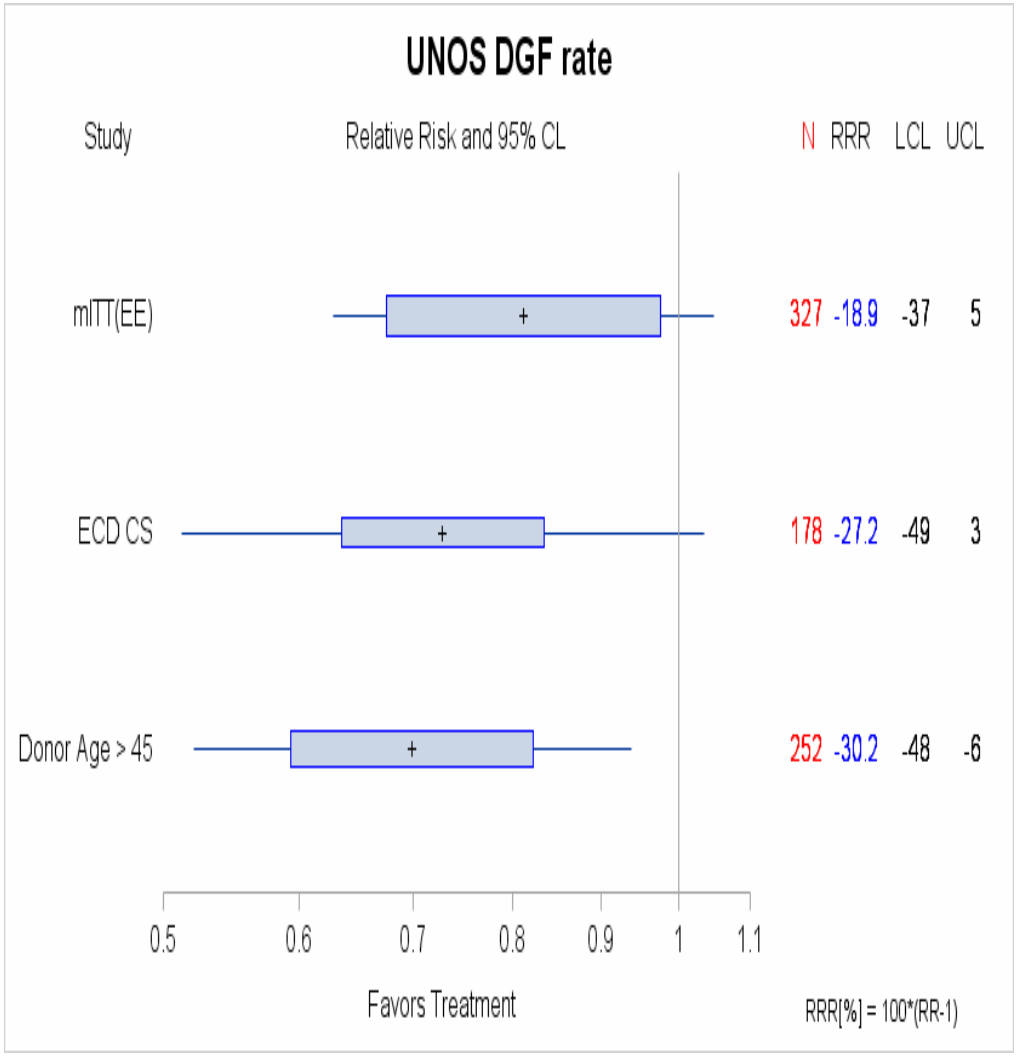


- **There is 39.13% reduction in the number of dialysis events per month for QPI-1002 relative to placebo in the overall population thru 6 mo (p=0.0598)***
- **In the age >45 post hoc population, there was again an increased impact of QPI-1002 (p=0.0256)**

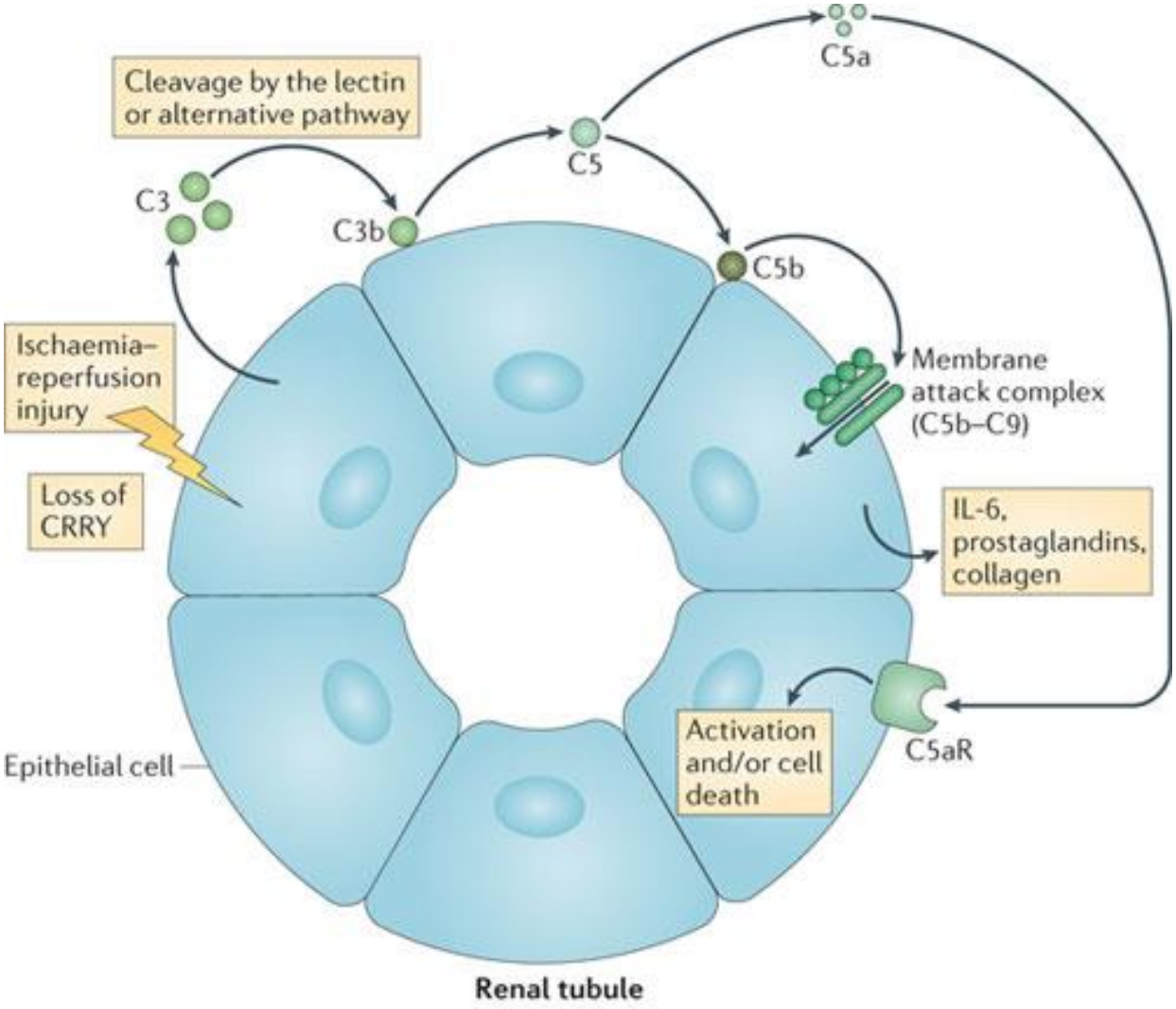
***negative binomial regression model test**

Conclusions

- **Large clinical Phase 2 study with balance in DGF risk factors in overall and key sub populations**
- **Superior efficacy results in favor of QPI-1002**
  - **Statistically significant reduction in incidence of UNOS DGF, freedom from dialysis, and early urine output in older kidney donor sub-population**
  - **Reduction in duration of DGF by more than 30%**
- **Safety Profile: Similar to placebo control**
- **Further study warranted**



Complement In Ischemia/Reperfusion

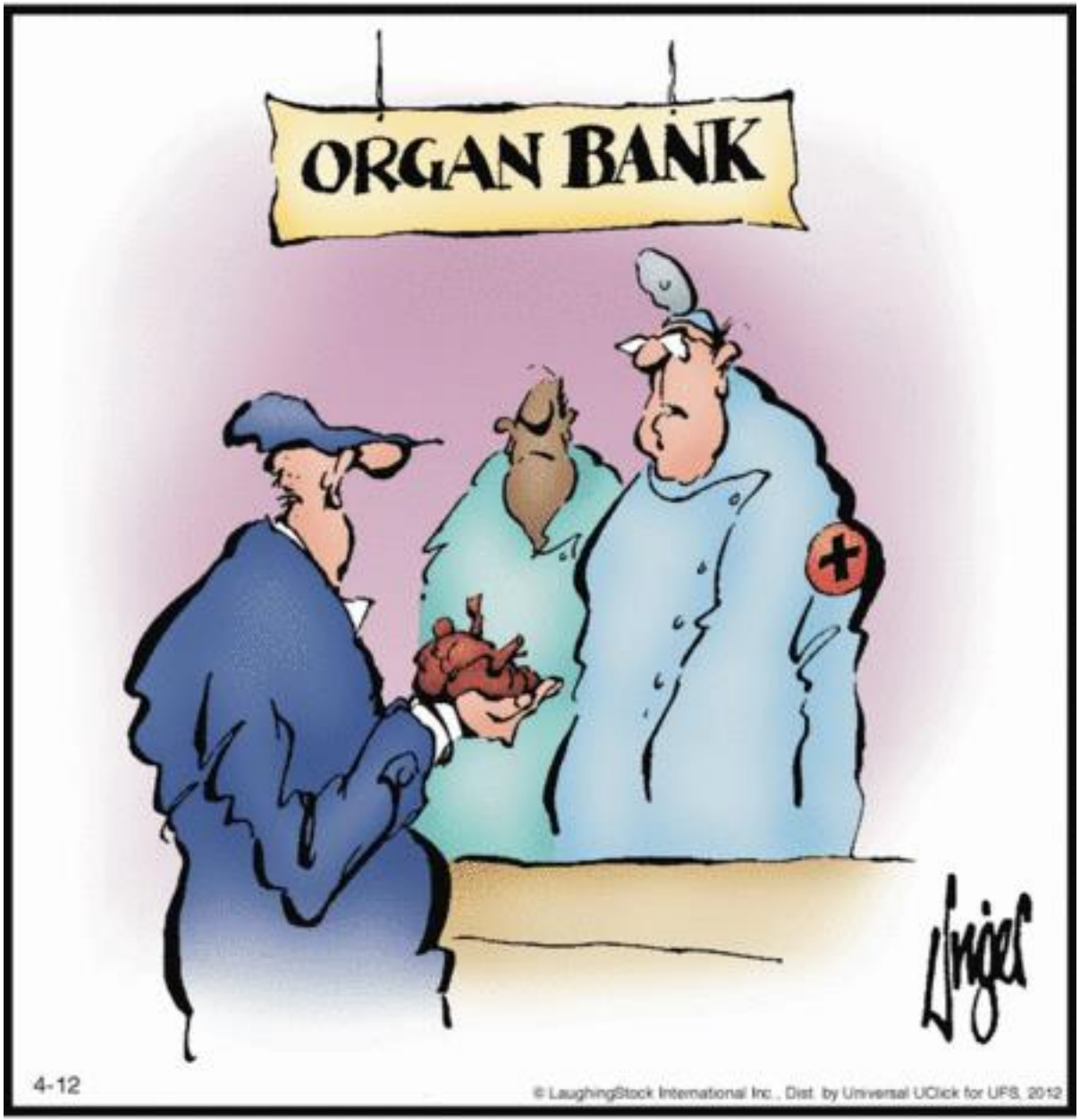


Nature Reviews | Immunology

Complement Inhibition - Eculizumab

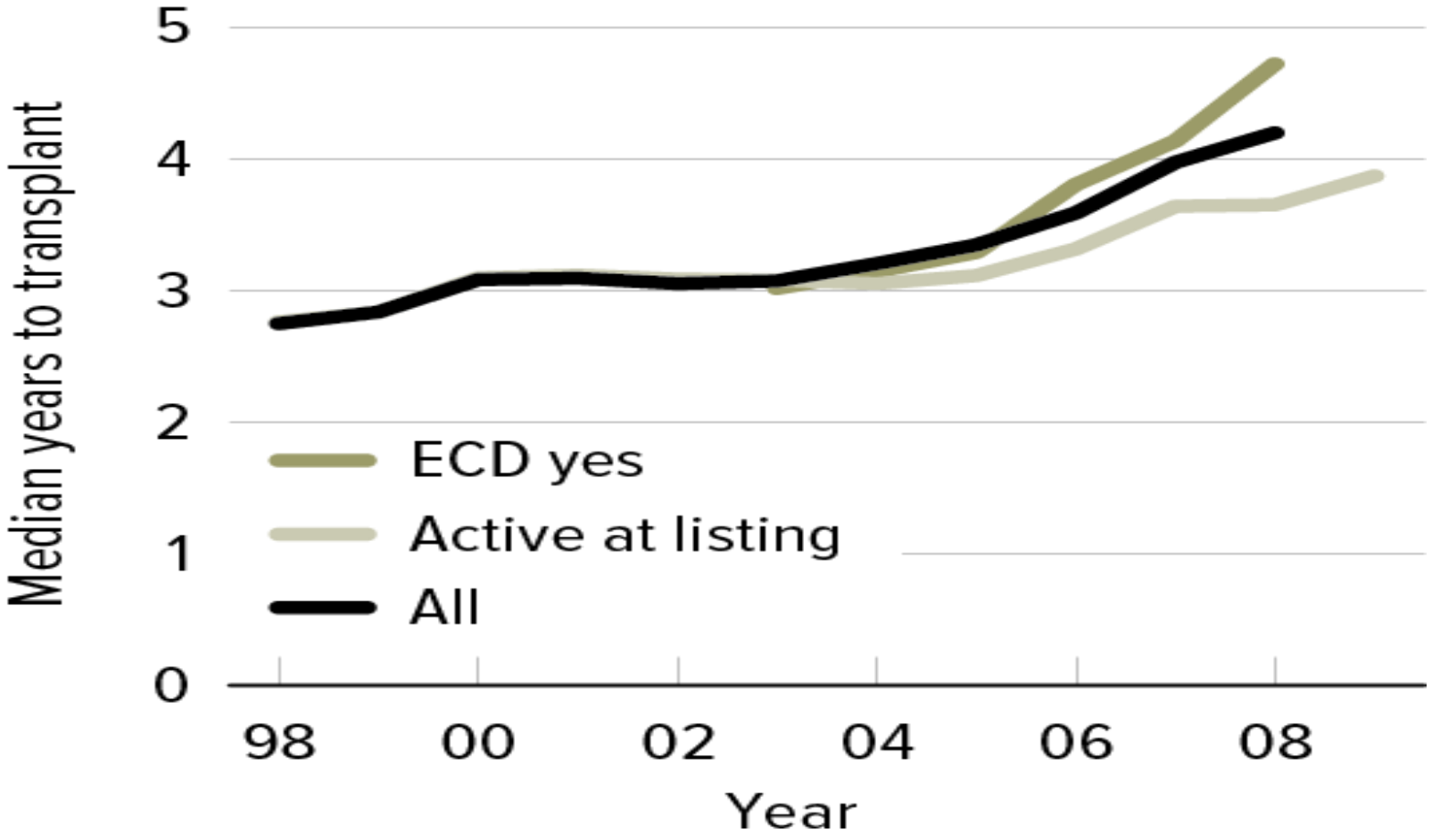
- Made by Alexion
- Monoclonal antibody directed against C5
- Prevents formation of the MAC
- FDA approved for atypical HUS and PNH
- Used for prevention or treatment of AMR
  - Clinical trials underway
- Very expensive - ~$20,000 per dose
- DGF trial recently started

Organizational



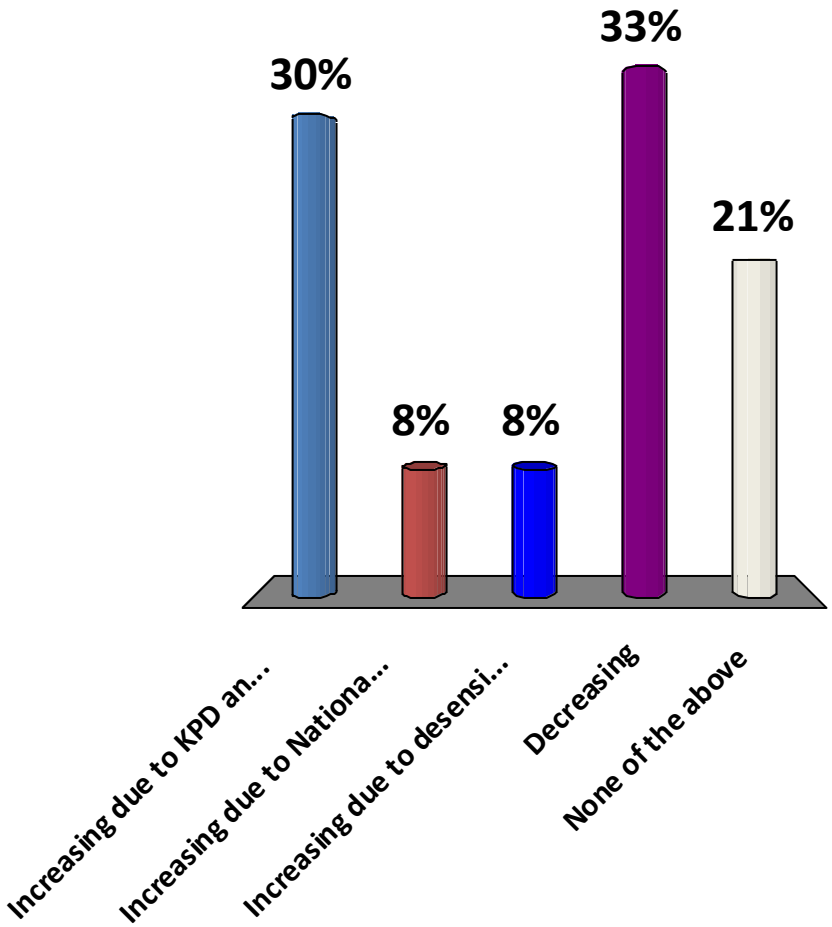
"Yes, we know what it is. We want to know where you got it."

Median Years To Kidney Transplant For Wait-listed Adult Patients

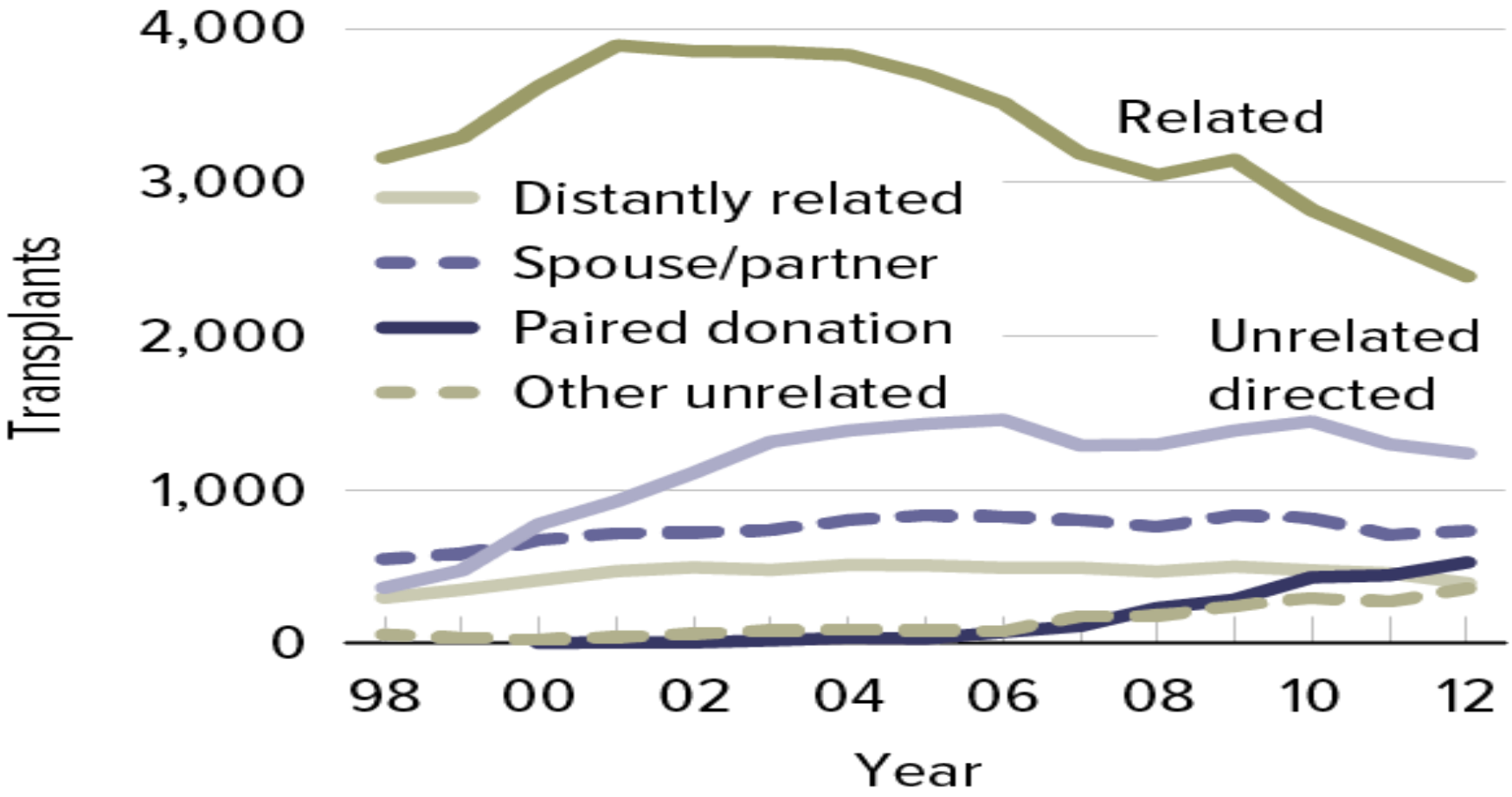


Live donor renal transplantation in the U.S. is?

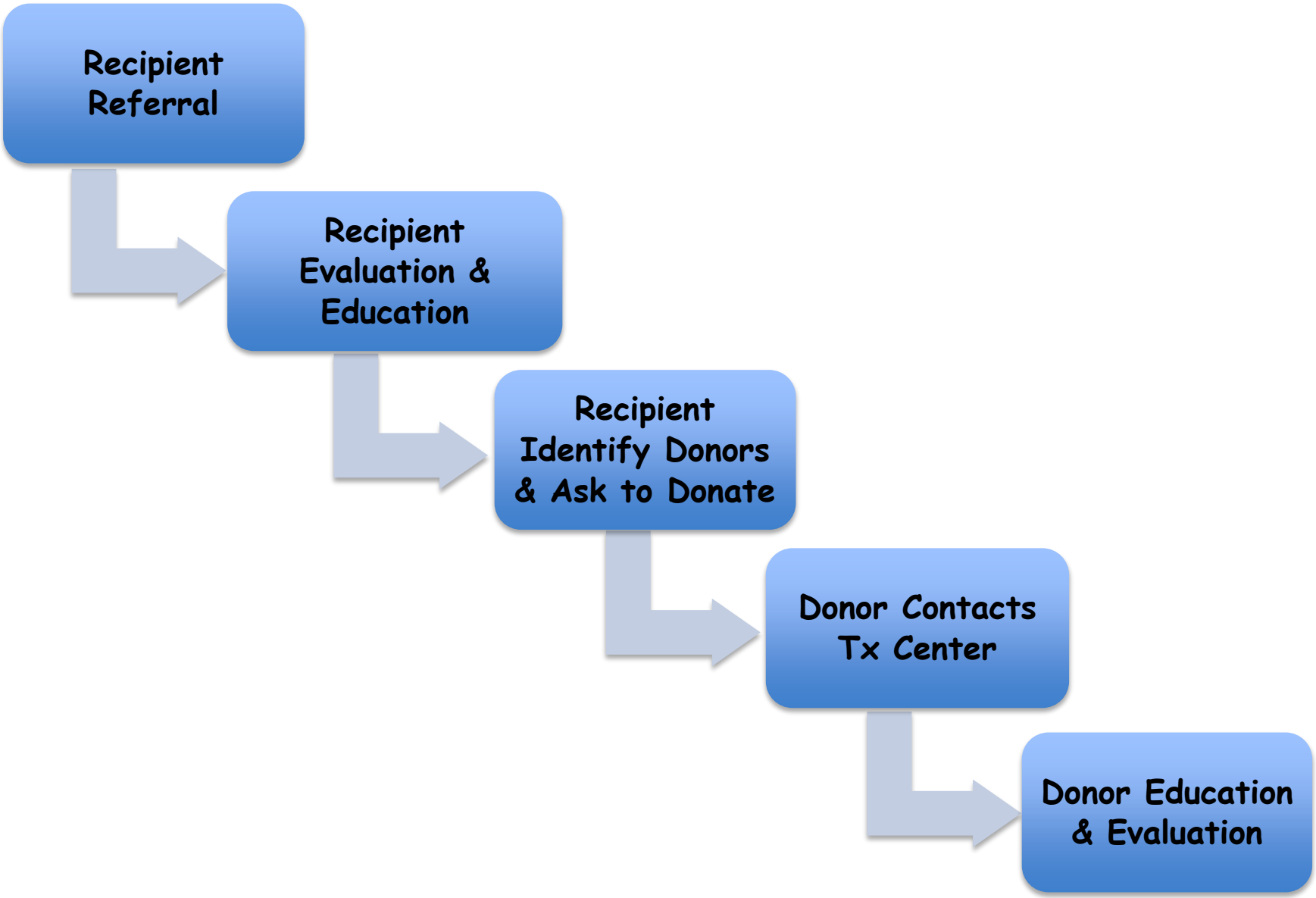
A. Increasing due to KPD and the NKR
B. Increasing due to National Living Donor Assistance Center (NLDAC)
C. Increasing due to desensitization for positive crossmatches and ABO-incompatibility
D. Decreasing
E. None of the above



Kidney Transplants From Living Donors By Donor Relation



Current Standard



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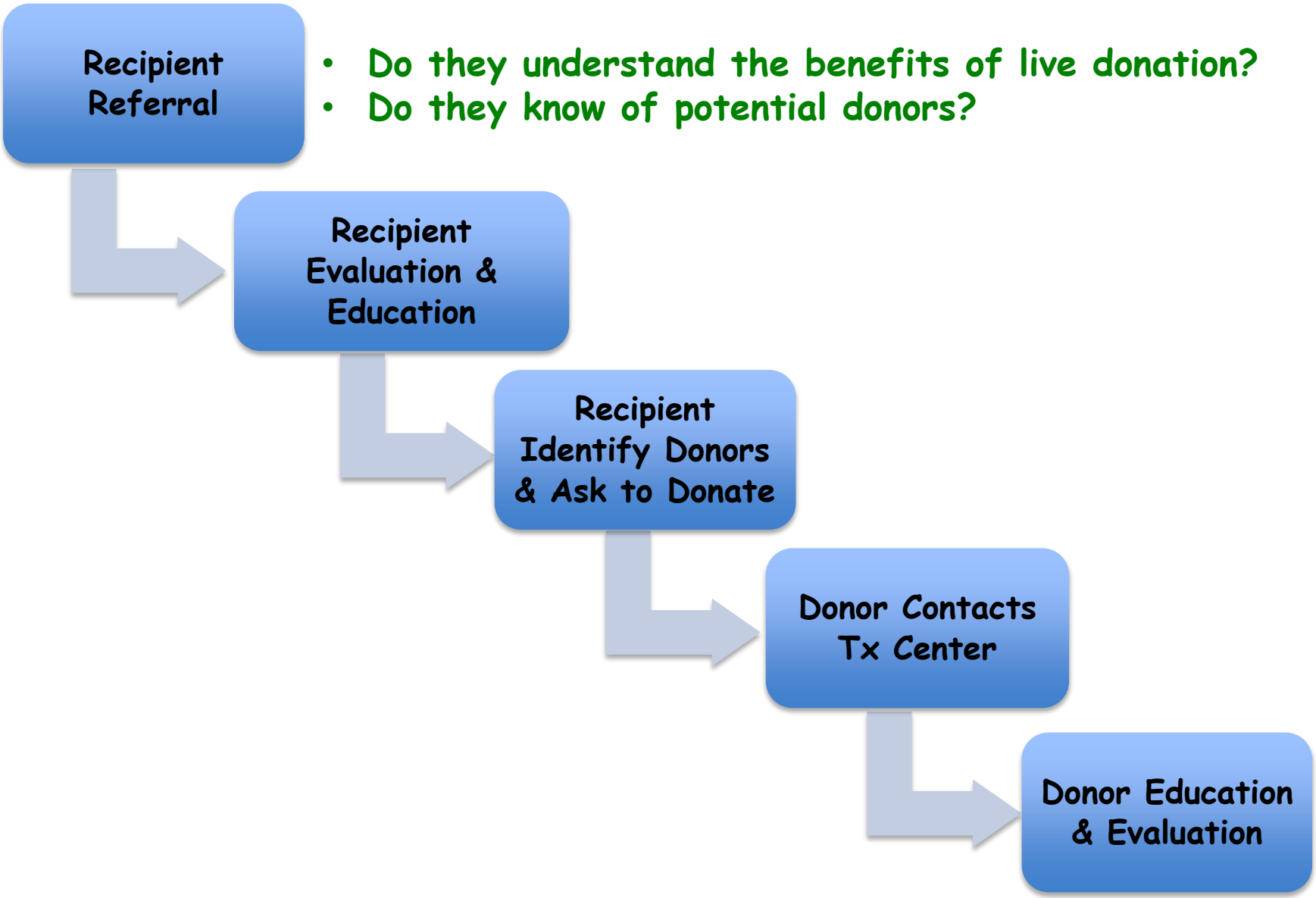

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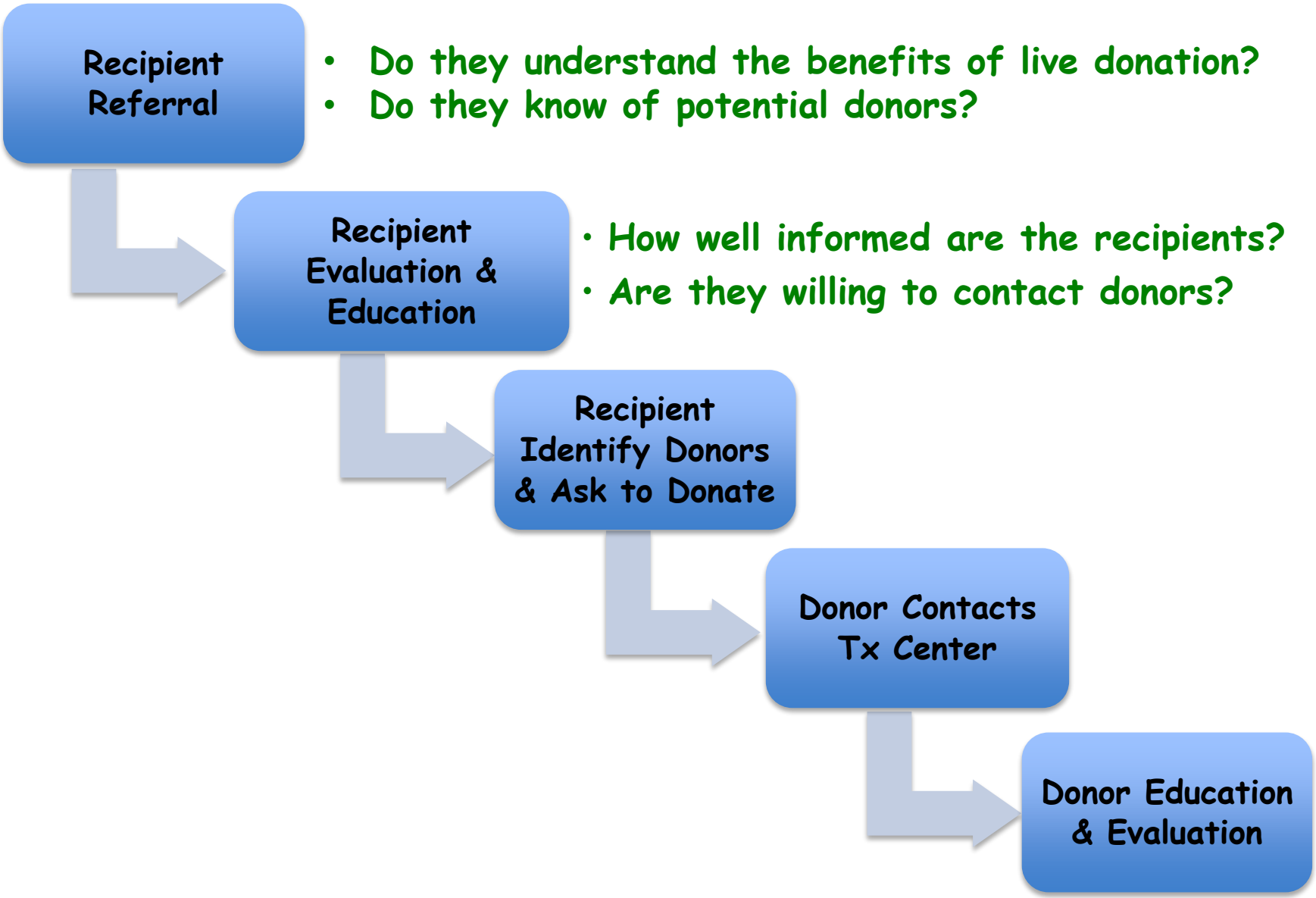

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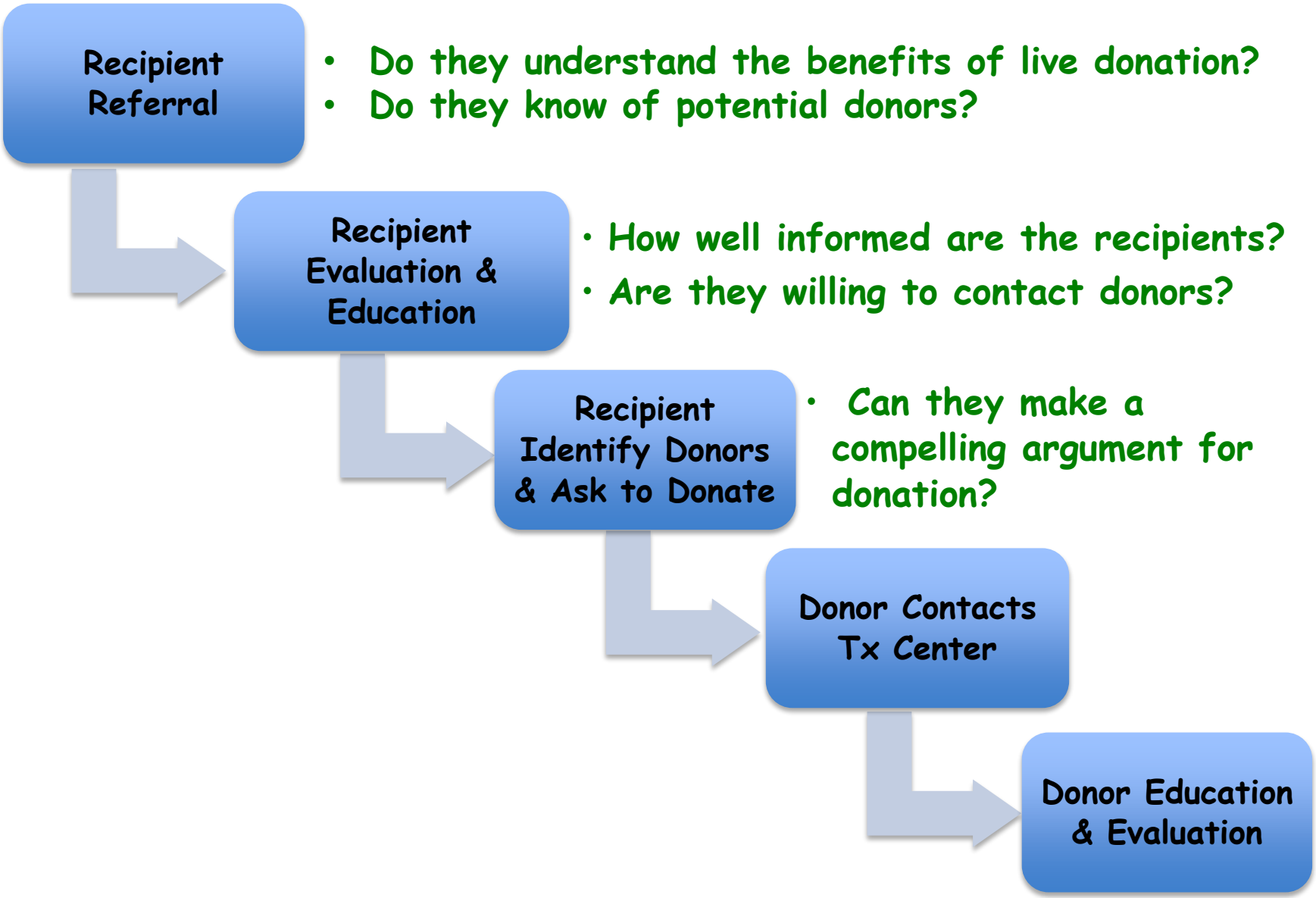

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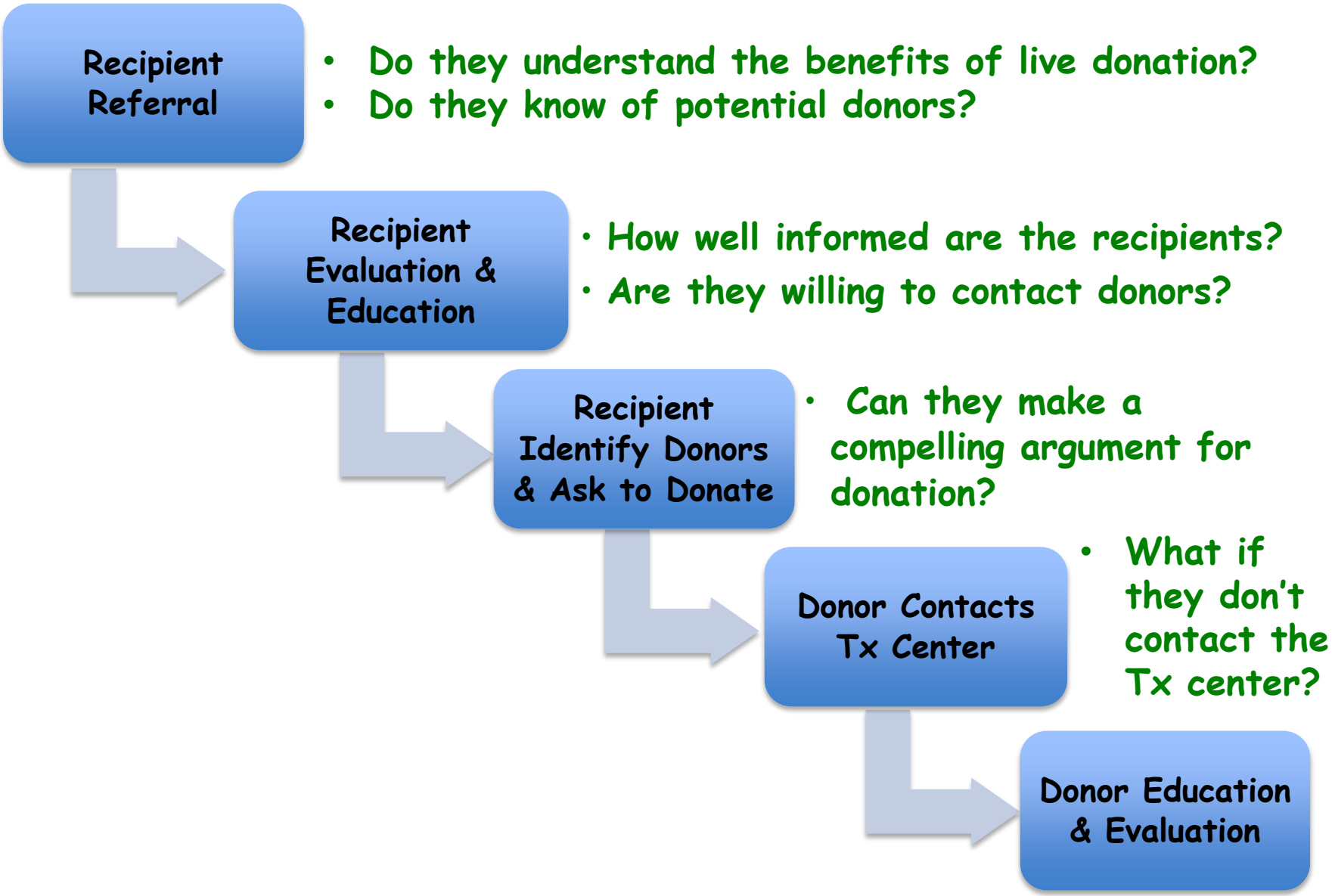

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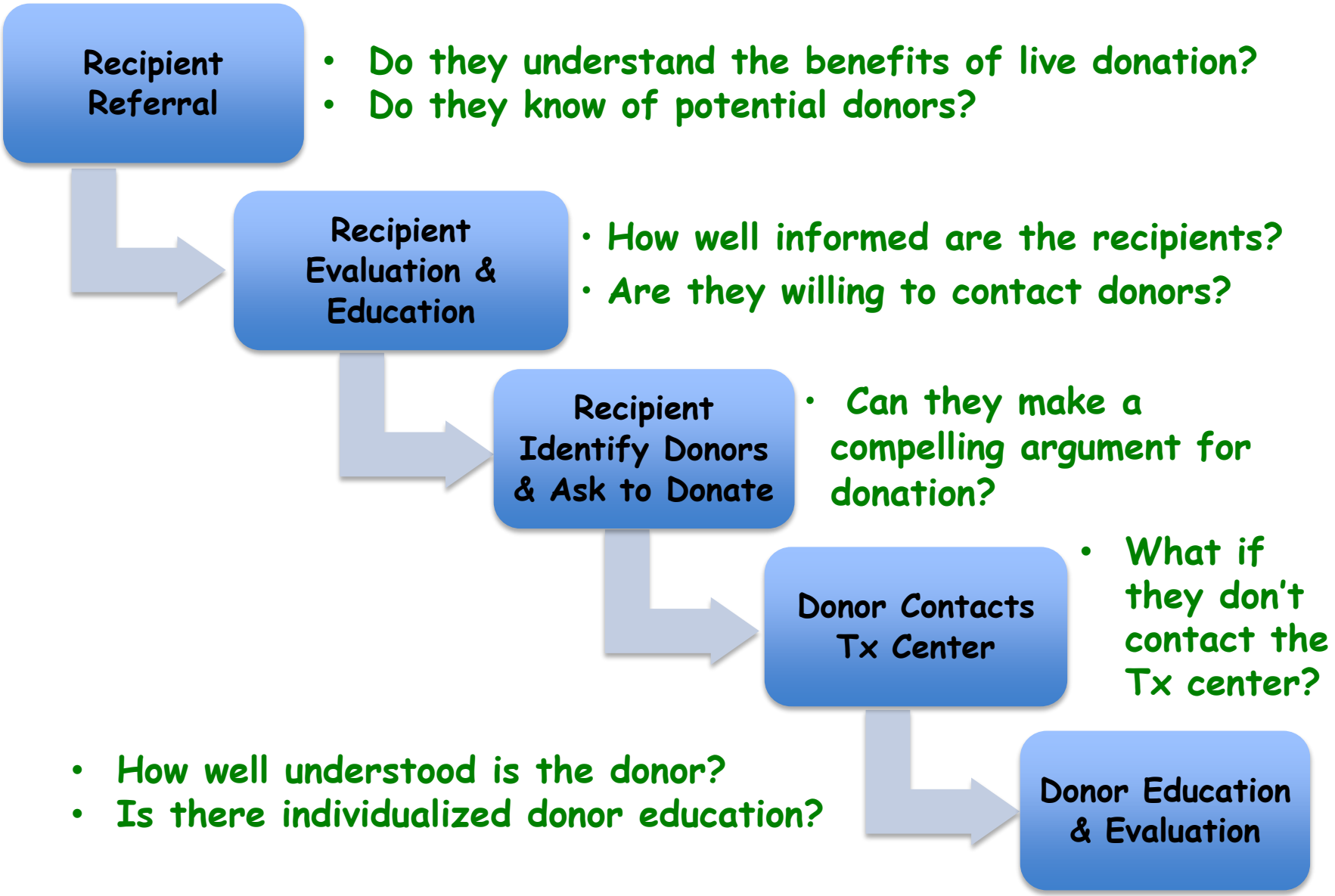
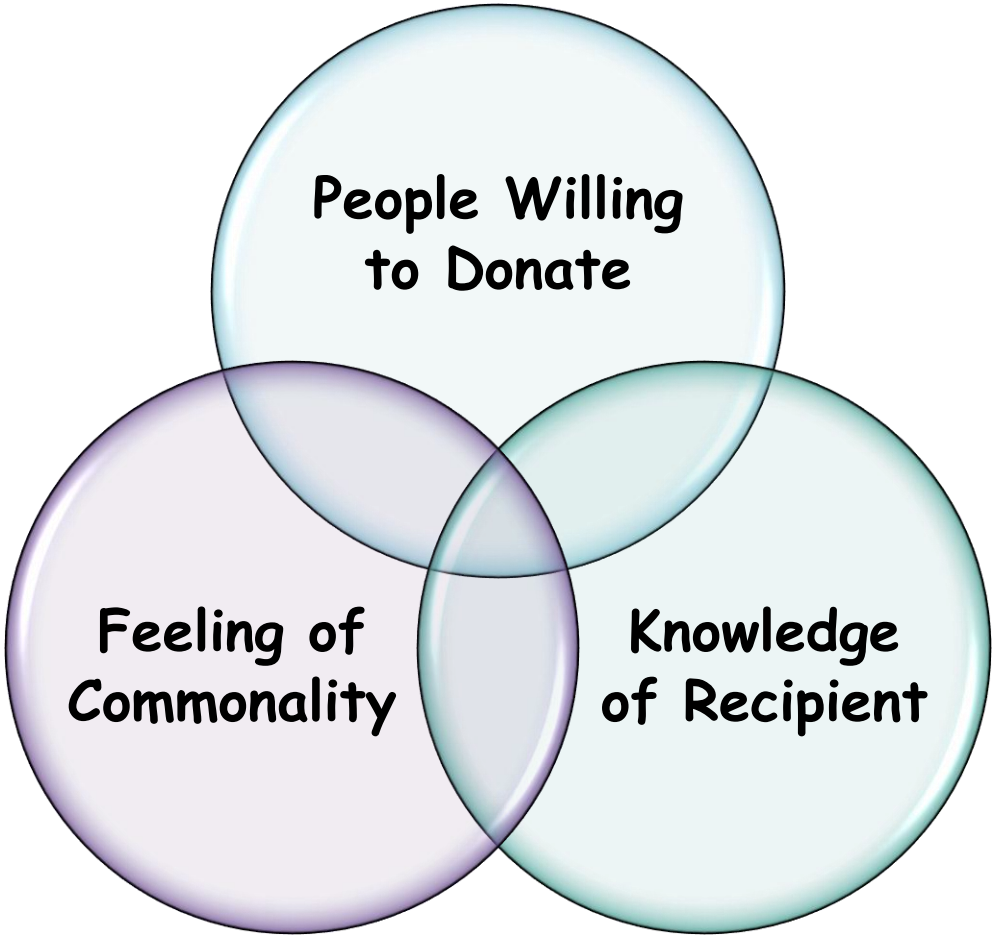


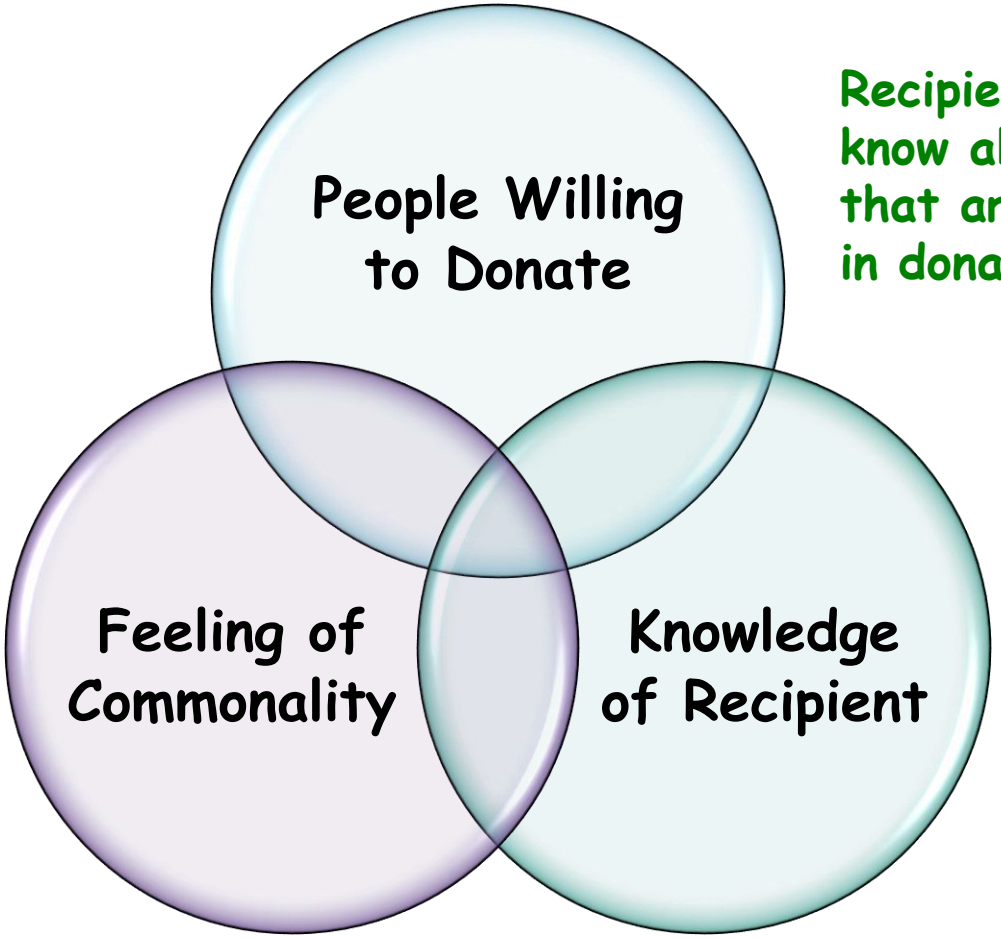
How Can We Best Identify All Potential Donors?

- Utilize other resources in addition to the recipient
  - Community based resources
- Seek individuals that either don't have a close personal relationship or are unrelated altogether
- Remove the education process from the recipient
  - Recipient advocate
- Remove the "ask" from the recipient
  - Recipient advocate

Advantages of a Community Based Approach

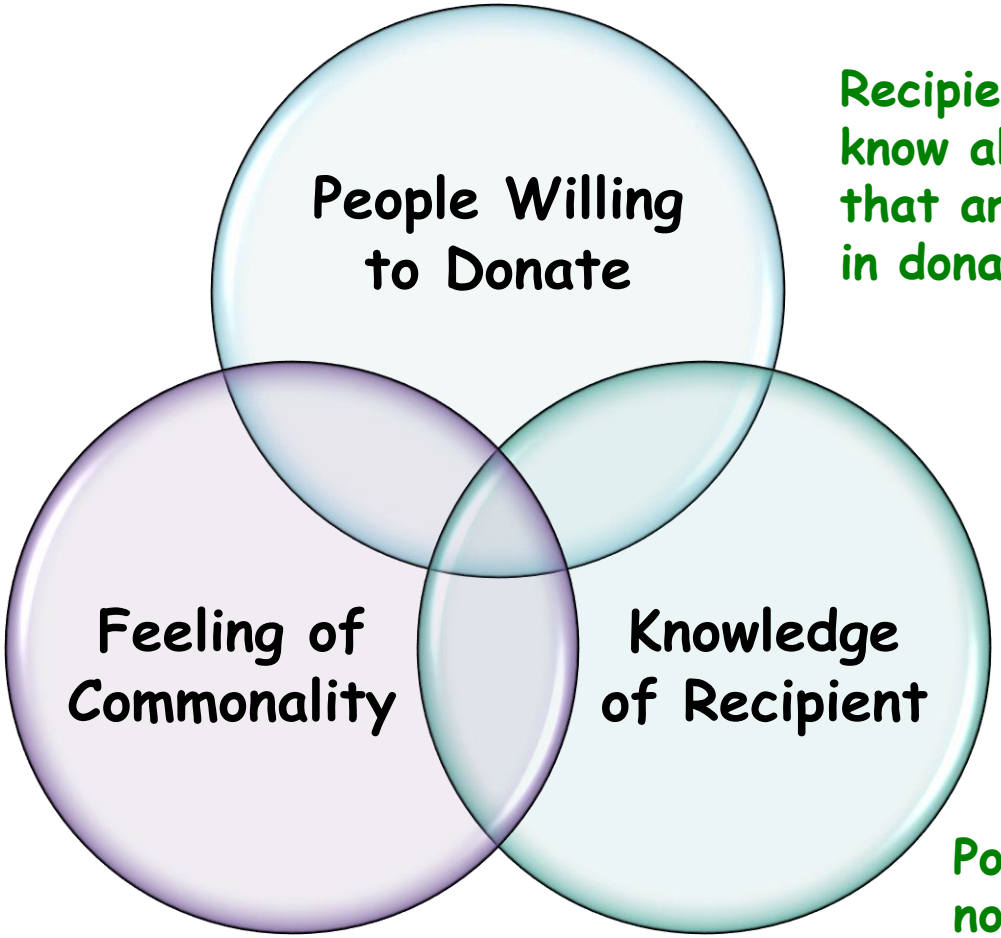


Advantages of a Community Based Approach



Recipient may not know all individuals that are interested in donating

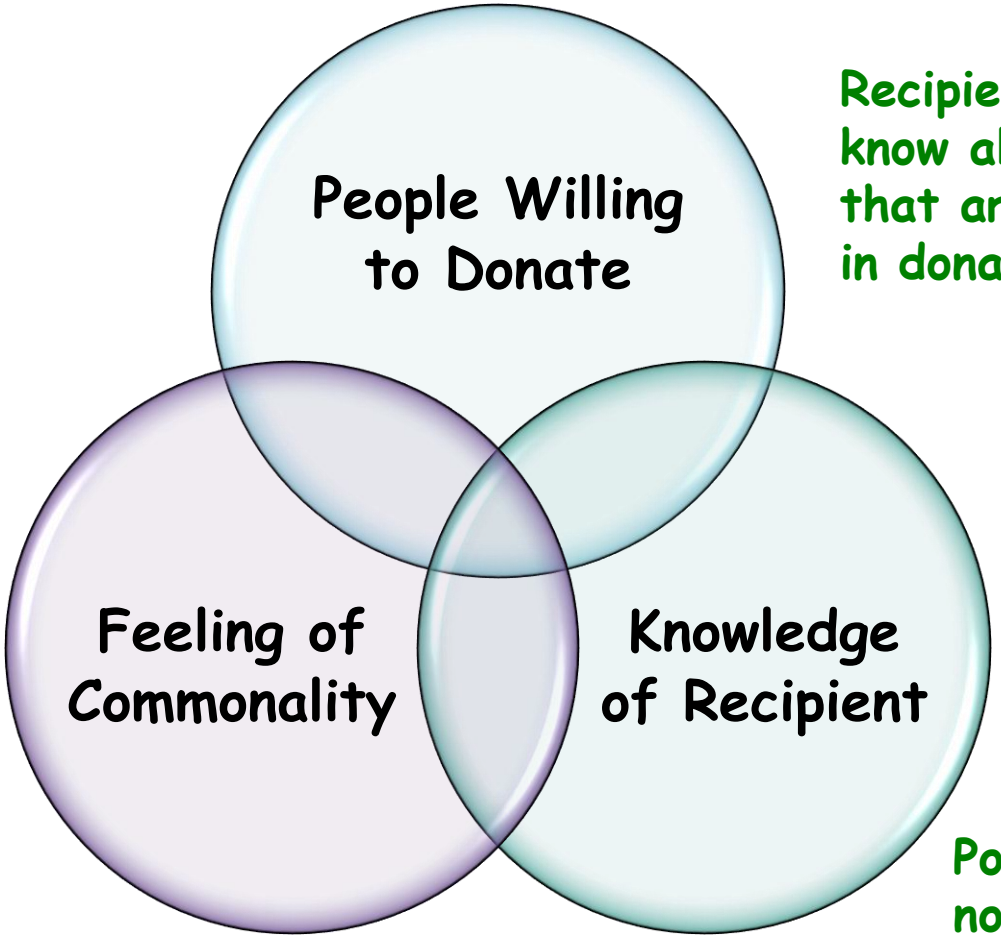
Advantages of a Community Based Approach



Recipient may not know all individuals that are interested in donating

Potential donor may not know all individuals that are in need

Advantages of a Community Based Approach



Recipient may not know all individuals that are interested in donating

Potential donors more likely to donate to someone they share something in common with

Potential donor may not know all individuals that are in need

Advantages of a Community Based Approach

- **Infrastructure**
  - **Publications**
  - **Churches/synogogues**
  - **Websites**
- **Third party recipient advocates**
  - **Clergy**
  - **Organization leaders**
- **“Ask” depersonalized**
  - **Skill, knowledge of recipient minimized**
  - **Interpersonal relations minimized**

Renewal:

Finds Kidney Donors In the Jewish Community

Renewal Outcomes

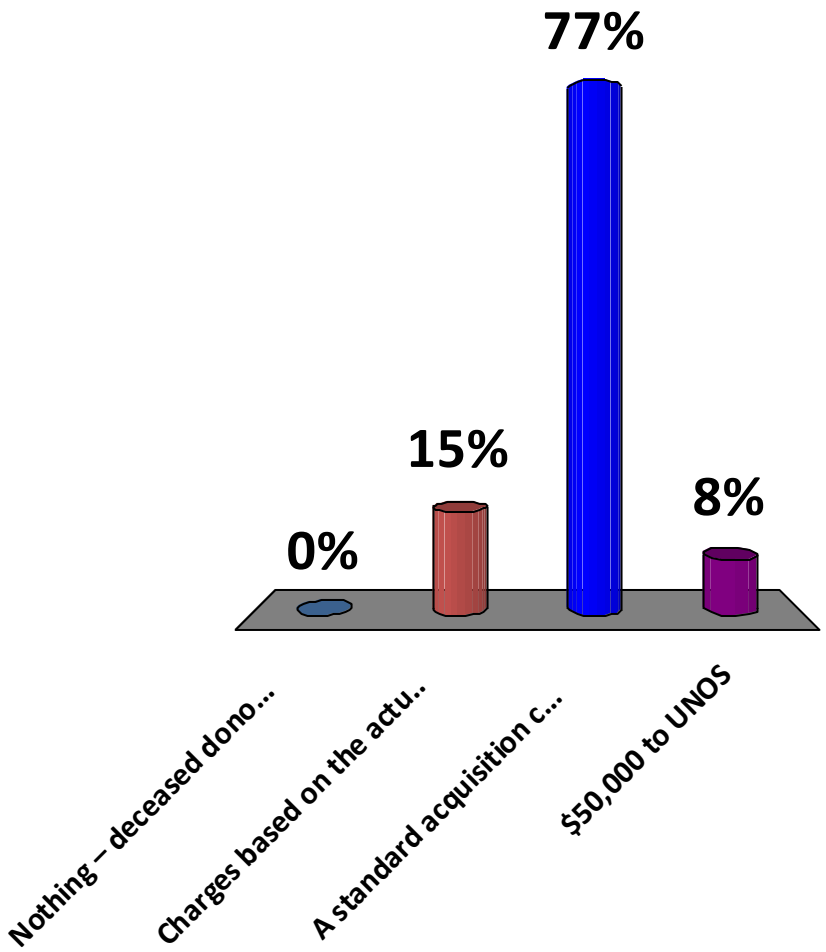
- In first 7 years of existence
- 237 Txs facilitated
- Donor relationship to recipient
  - Family = 95
  - Friends = 13
  - Altruistic = 129
- 8 paired kidney exchanges
- Last year (5774) 57 Txs facilitated
- Estimated that Renewal responsible for 25-33% of non-directed donors in U.S.

Financial

"Frankly, Mr. Ferguson, your case has us baffled. How did you get in here without insurance?"

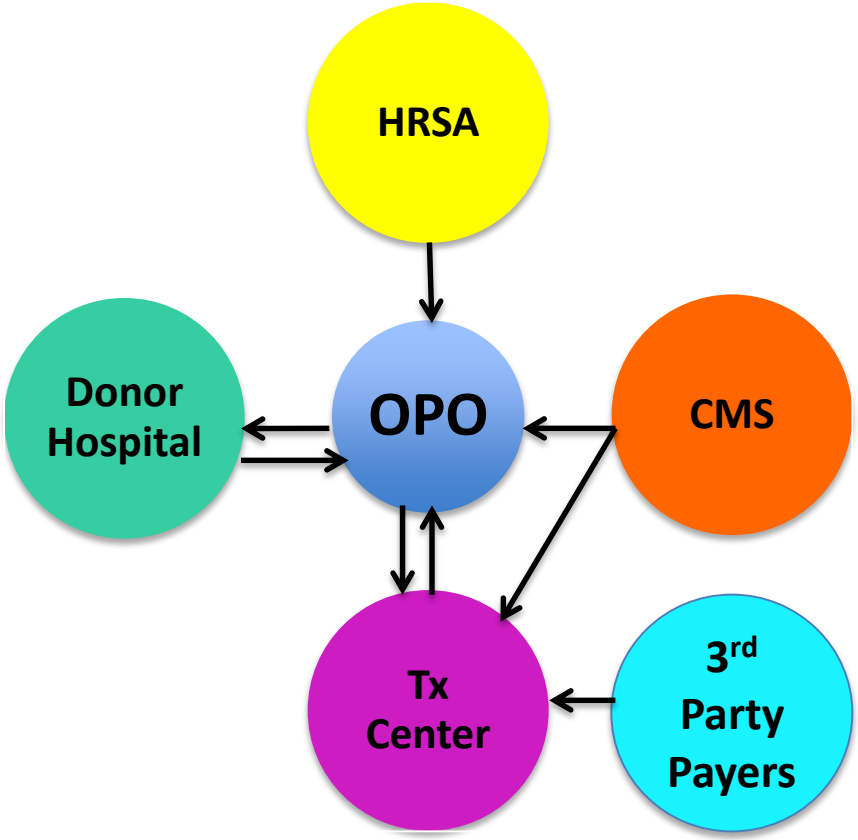
When a Tx center receives a deceased donor kidney, the center pays?

A. Nothing – deceased donor organs are free
B. Charges based on the actual cost to procure that particular organ
C. A standard acquisition charge determined by CMS & the OPO
D. $50,000 to UNOS

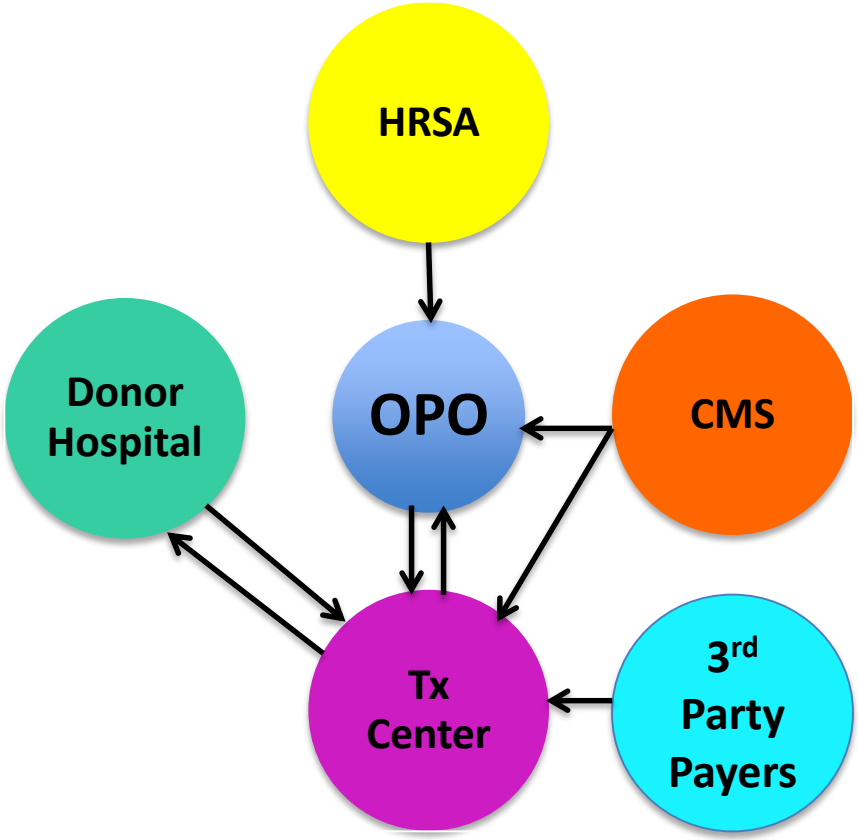


Organ Cost Financial Model

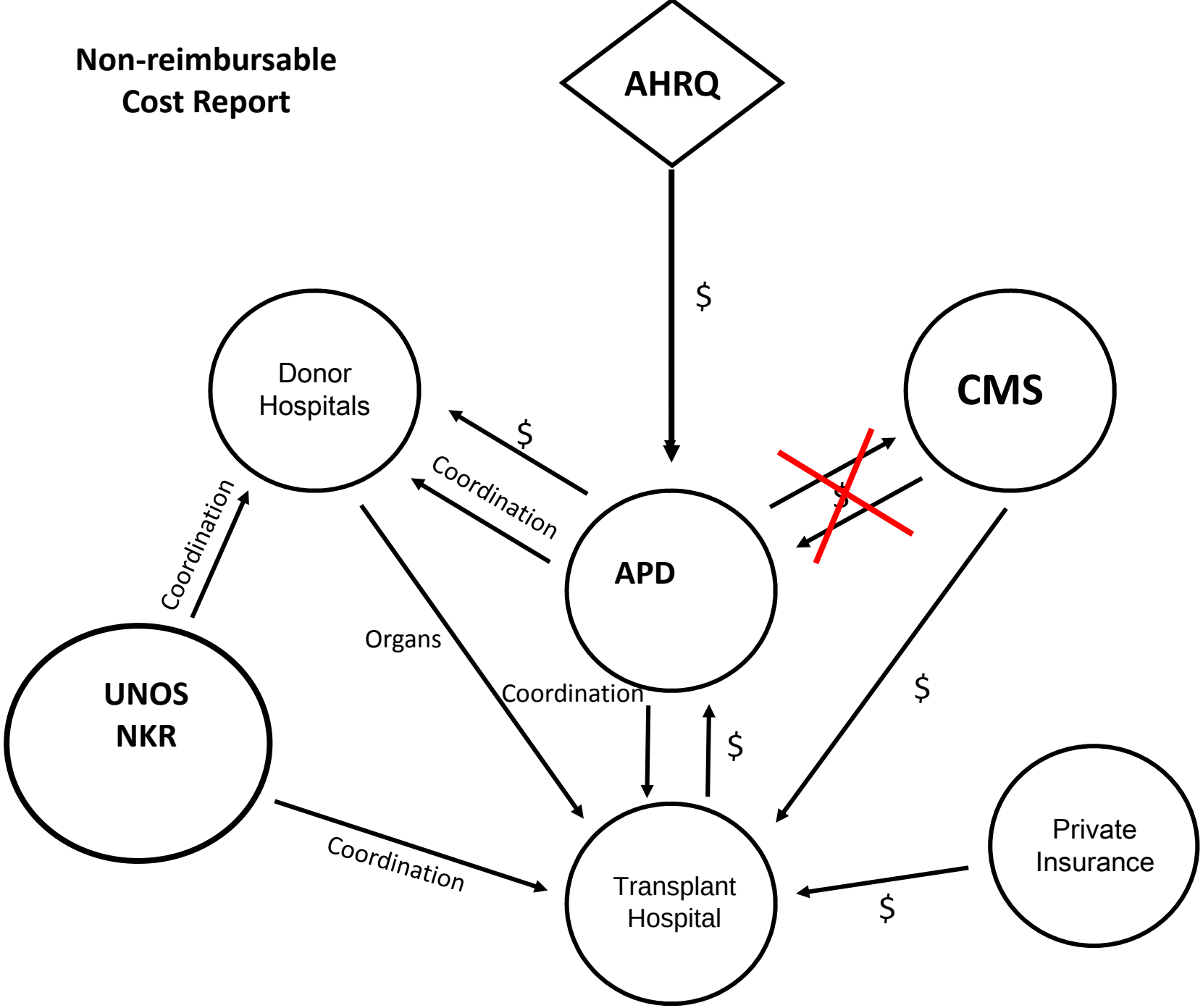
Deceased Donor



Current KPD



Non-reimbursable Cost Report



Summary & Conclusions

- Interesting new developments in all aspects of renal transplantation
- Robotics and new drugs may dramatically change practice in the years to come
- Transplantation is highly dependent upon infrastructure
- Organizational and infrastructure changes are important & necessary to advance care
- Research and service opportunities abound for those interested
- Be dissatisfied with the status quo
- Get involved

“…Dissatisfaction leads to progress.”

Shimon Peres

There's A Lot to Look Out For