

ORGAN SWAPPING: a fair and equitable process?

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DISCLOSURE

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GOALS

- Overview of Kidney Paired Donation (KPD)
- Mathematics of KPD Matching: Role in Fairness/Equity
- Expanding KPD
 - Compatible Pairs
 - Non-directed Donors
 - Organ Shipping
 - Desensitization
- Other Issues of Fairness and Equity

DEFINITION: INCOMPATIBLE PAIR

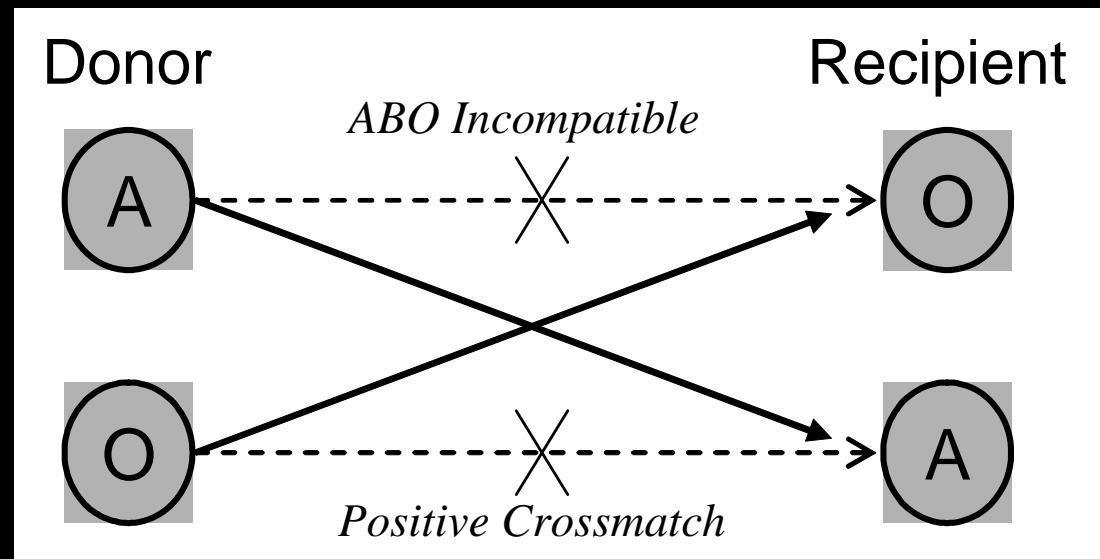
Live kidney donor and intended recipient who are either ABO incompatible (ABOi) or have a positive crossmatch (+XM)

- any two individuals will be ABOi: 35%
- any two individuals have a +XM: 11%
- estimates 1000-3000 patients per year join the deceased donor waiting list because they are incompatible with their willing, healthy live donor

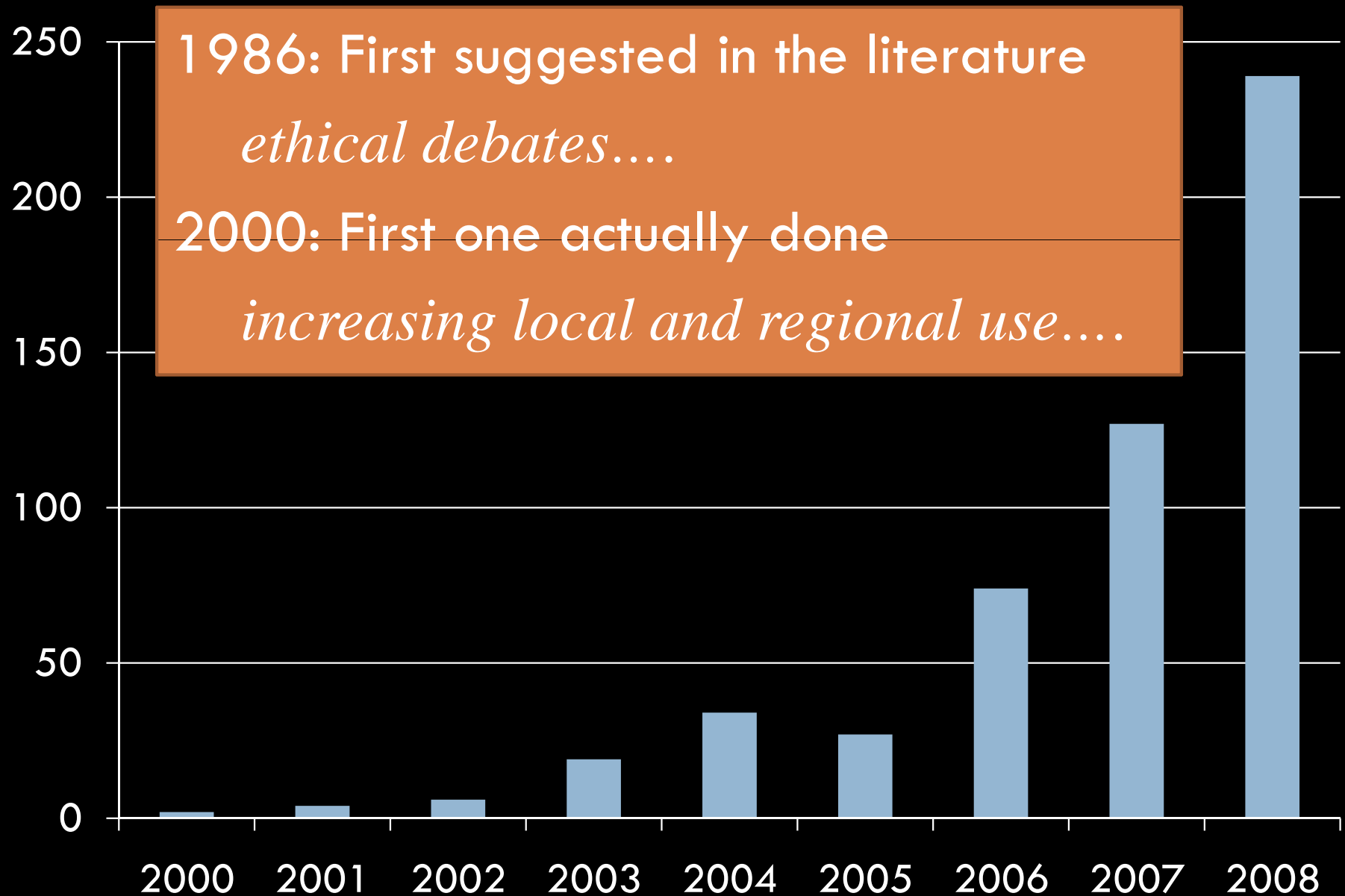
LIVE DONOR KPD

Definition: *(subject to change)*

Procedure by which incompatible pairs (2 or more pairs) exchange donors such that compatible transplants result



HISTORY OF LIVE DONOR KPD



REPRESENTING INCOMPATIBLE PAIRS



**There are over a million
ways to match
100 incompatible pairs**

Hiller J. "The Old Days" Circa 2003.

MATHEMATICS: OPTIMIZATION

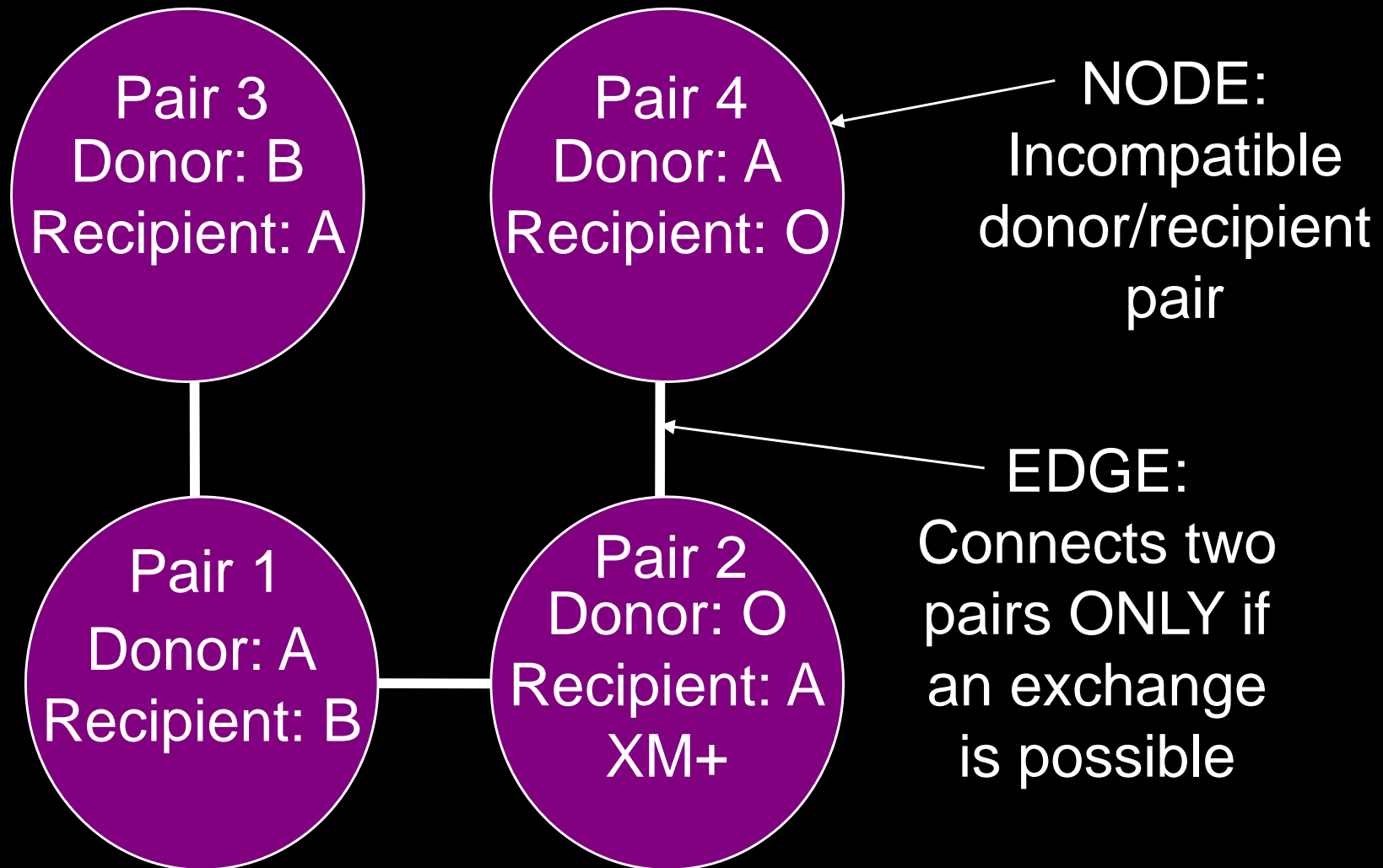
- Field of applied mathematics used in airline scheduling, online driving directions, ...
 - *“the most influential academic discipline you’ve never heard of” (Boston Globe)*
- Optimization technology helps utilize scarce resources by quickly and efficiently considering ALL solutions to a given problem and picking the best
 - Graph Theory
 - Integer Programming

REPRESENTING INCOMPATIBLE PAIRS



Hiller J. "The Old Days" Circa 2003.

REPRESENTING INCOMPATIBLE PAIRS



Segev D, et al. 2005. JAMA.

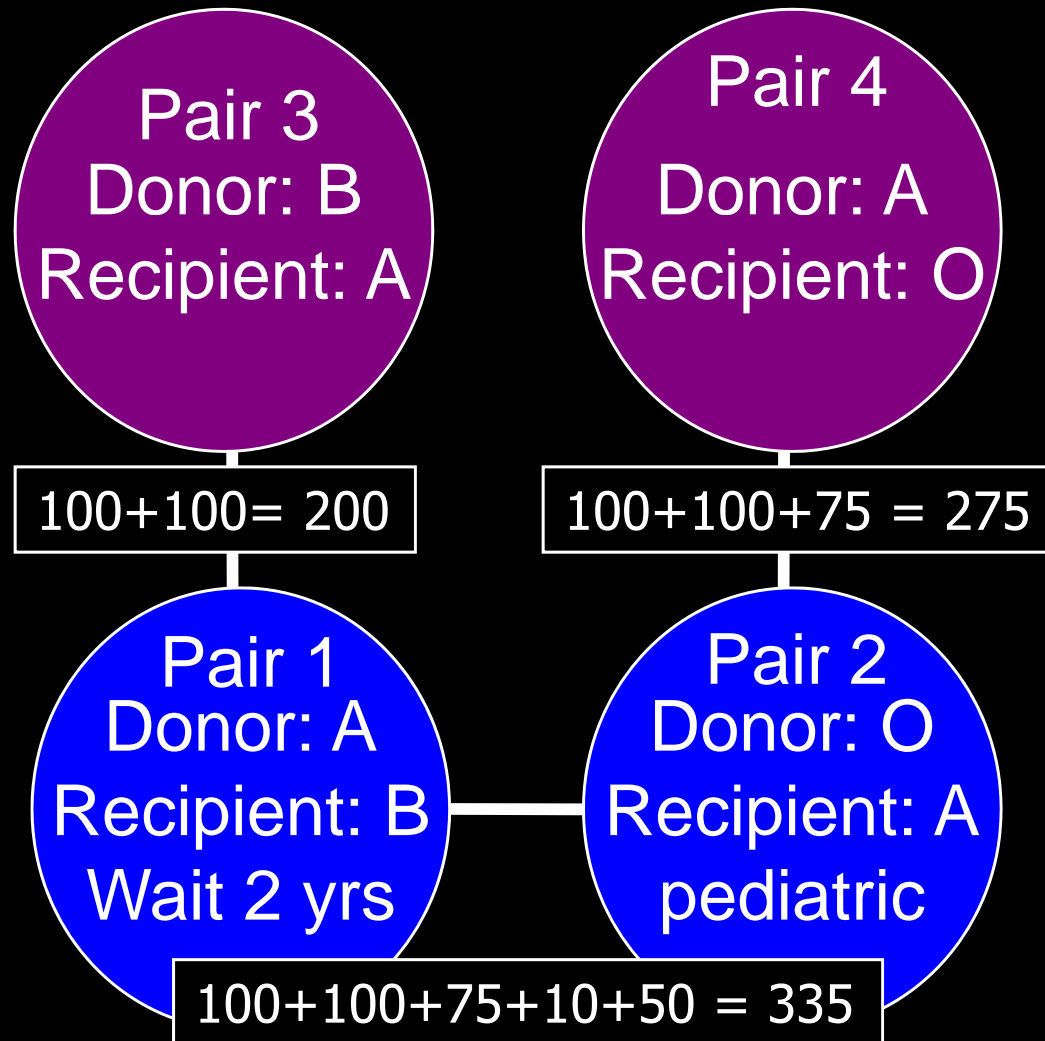
MATHEMATICS: OPTIMIZATION

- **Computational Feasibility:** In a national system, there are too many people to match on the magnetic board
- **Fairness:** For multiple pairs/patients/centers to be willing to participate, there needs to be some assurance that the goals that we've grown to understand in transplantation are met
- **Math will guarantee that the system performs as fairly (or unfairly) as we decide**

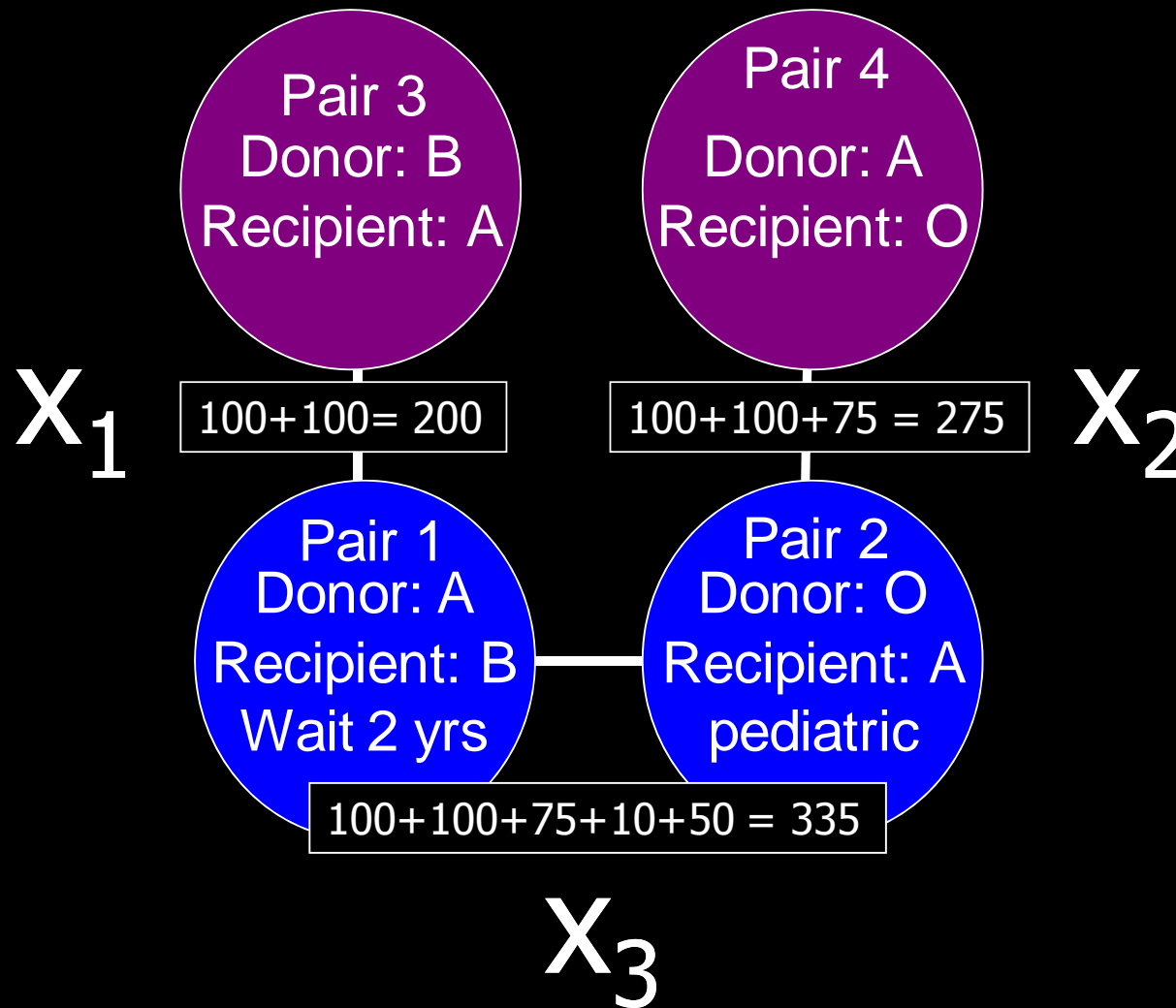
All matches are equal, but some are more equal than others

- Priority for vulnerable populations (highly sensitized recipients, pediatric recipients, those who have been waiting a long time)
- Priority for clinical predictors of good outcome (zero-mismatch)
- Priority for logistically simpler matches, geography (to minimize travel)

Priorities → Points → Edge-Weights



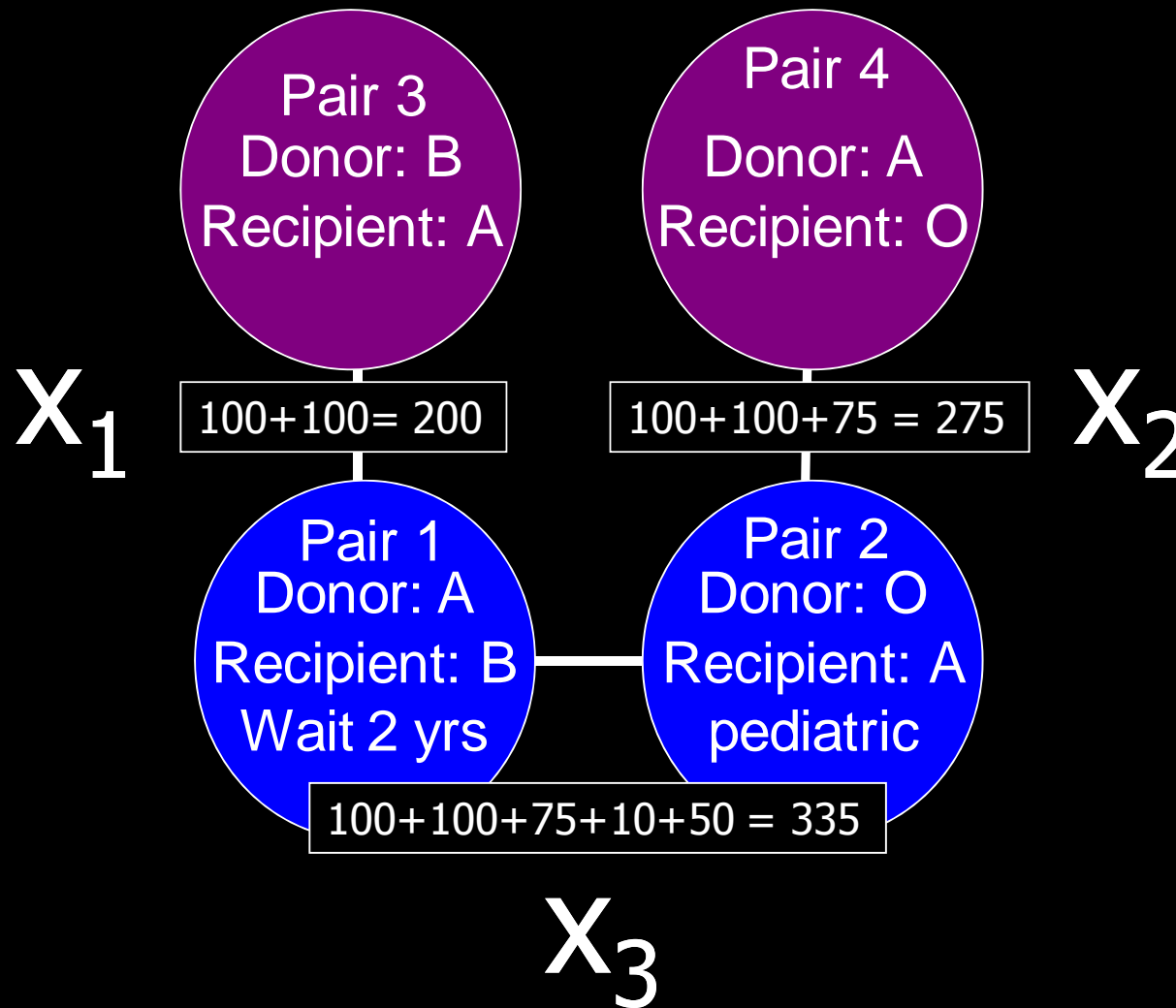
Integer Program Setup: Variables



$x_1 = \text{edge } 1\&3$
 $x_2 = \text{edge } 2\&4$
 $x_3 = \text{edge } 1\&2$
 $x_1, x_2, x_3 \in \{0, 1\}$

Integer Program Setup: Weights

Edge weights:
 x_1 worth 200
 x_2 worth 275
 x_3 worth 335

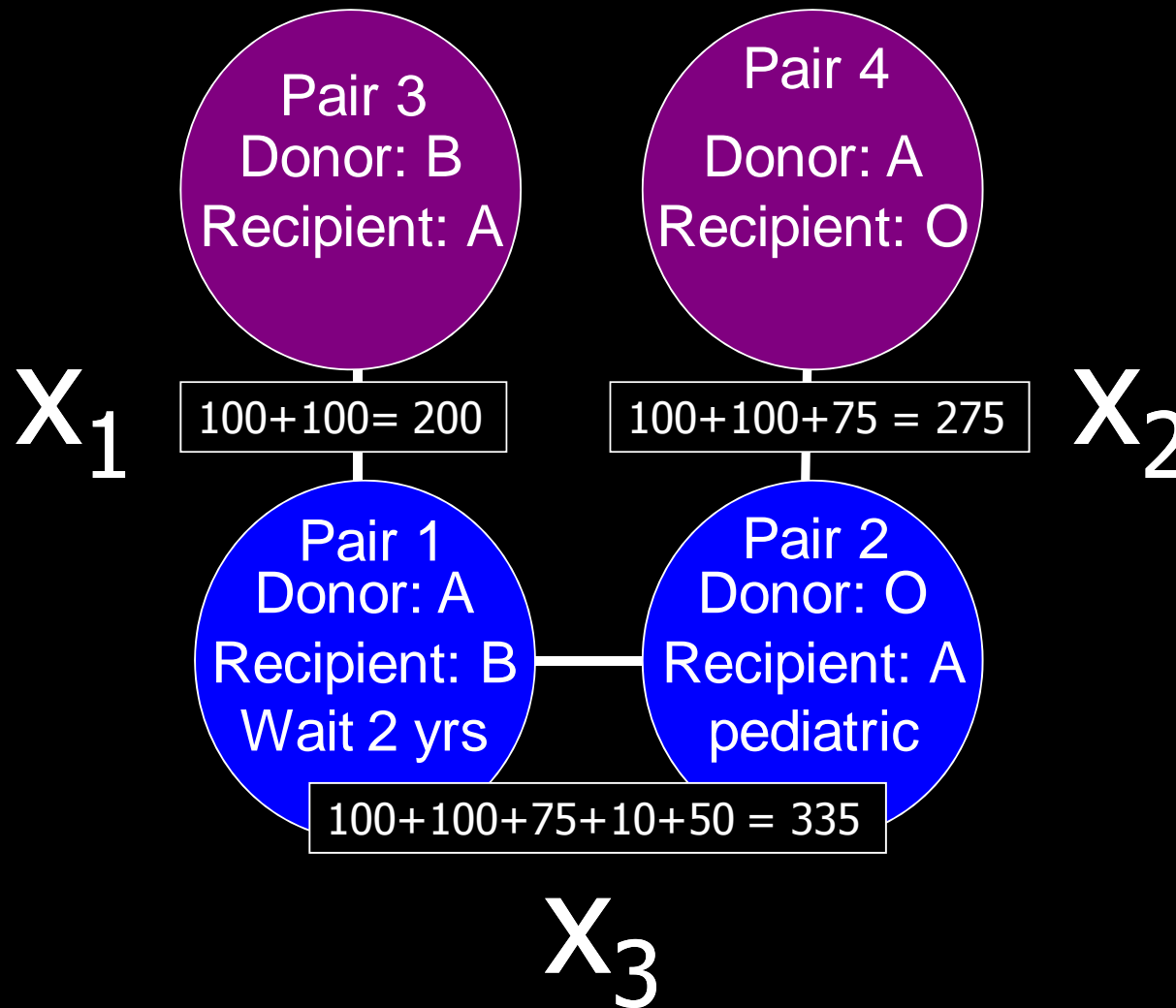


Integer Program Setup: Constraints

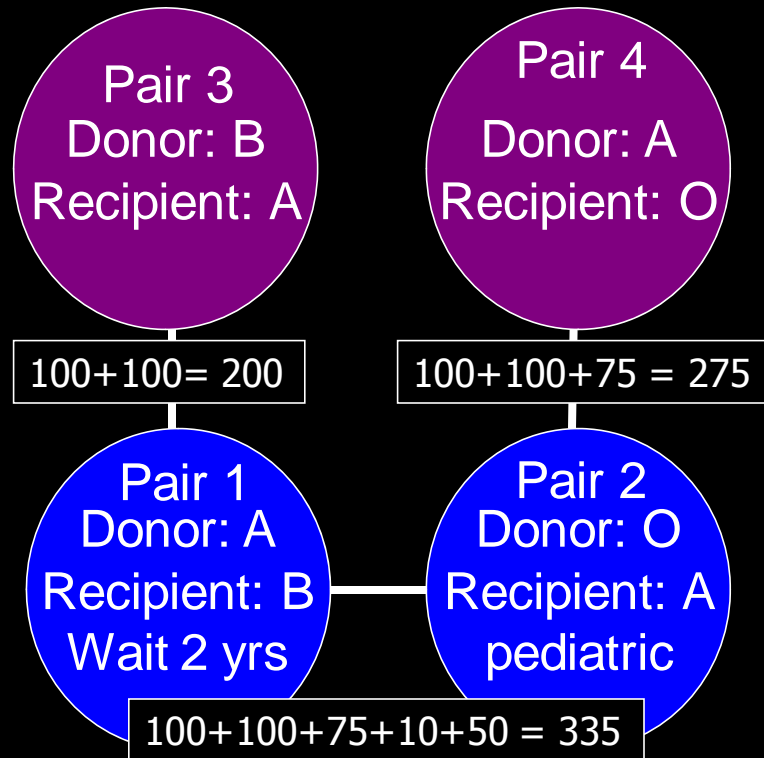
subject to
constraints:

$$x_1 + x_3 \leq 1$$

$$x_2 + x_3 \leq 1$$



Solve IP for Max Edge-Weight



objective:
 $\max(200x_1+275x_2+335x_3)$

subject to constraints:

$$x_1+x_3 \leq 1$$

$$x_2+x_3 \leq 1$$

$$x_1, x_2, x_3 \in \{0, 1\}$$

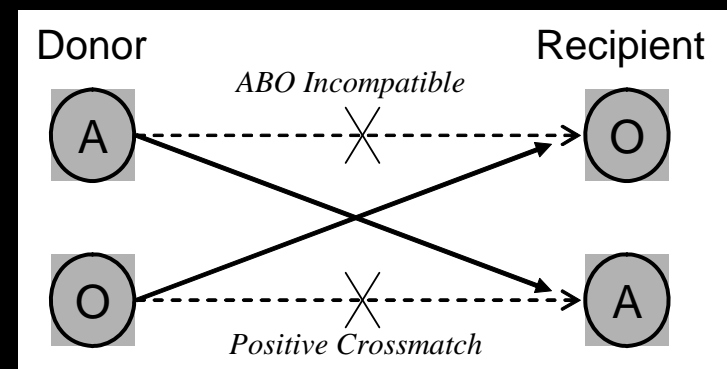
LIMITATIONS OF KPD

- Blood type distribution:
 - O donors are not incompatible unless +XM
 - Most ABOi pairs have O recipients

- Reciprocal match requirements

- Simultaneous requirements

- Need access to lots of pairs



EXPANDING KPD

Definition: *(subject to change)*

Procedure by which incompatible pairs (2 or more pairs) exchange donors such that compatible transplants result

EXPANDING KPD

Definition: *(subject to change)*

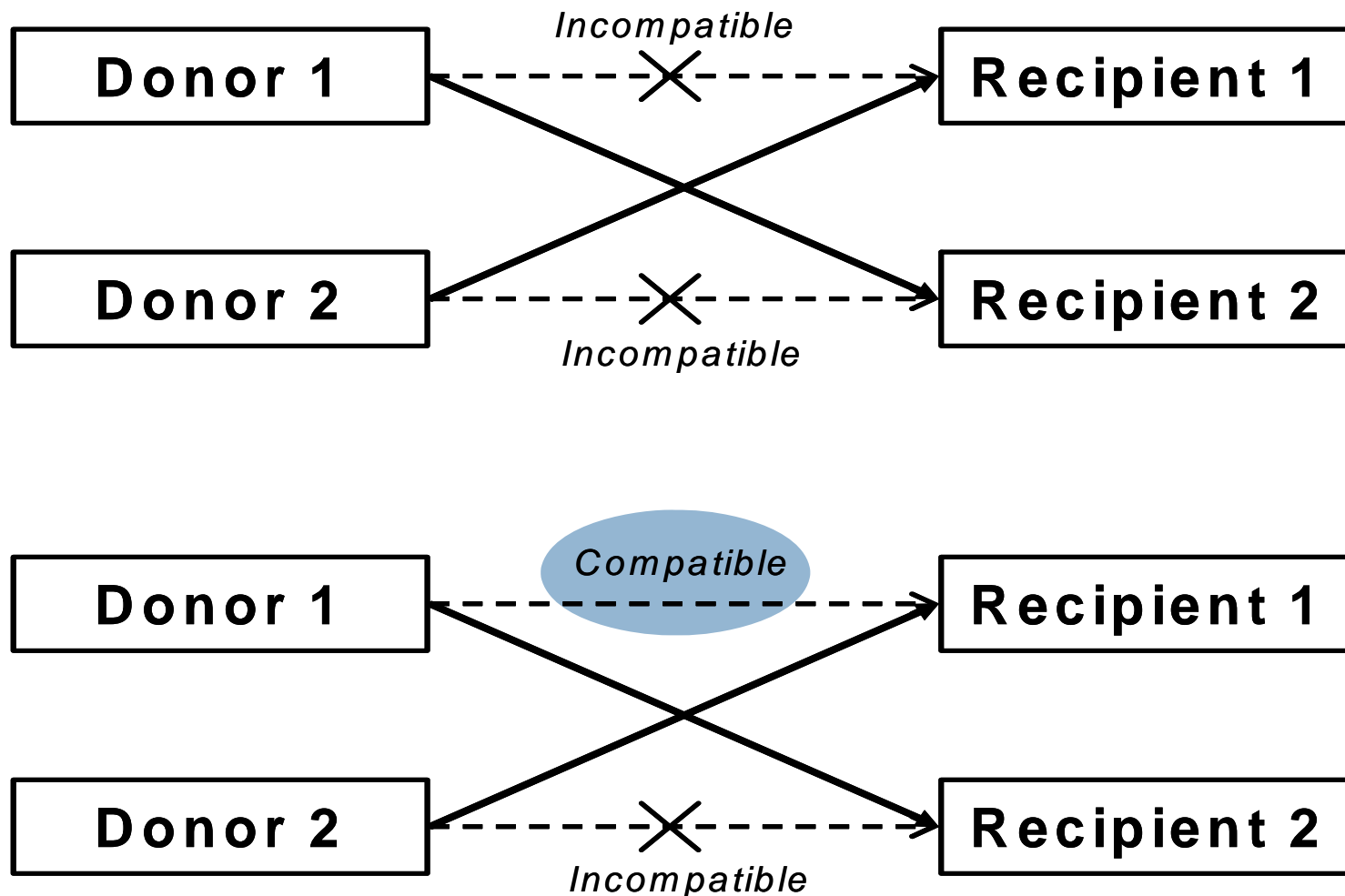
Procedure by which incompatible pairs (2 or more pairs) exchange donors such that compatible transplants result



Don't need to be incompatible to participate in KPD. Can be:

1. Altruistic donor
2. Compatible pair

COMPATIBLE DONORS IN KPD

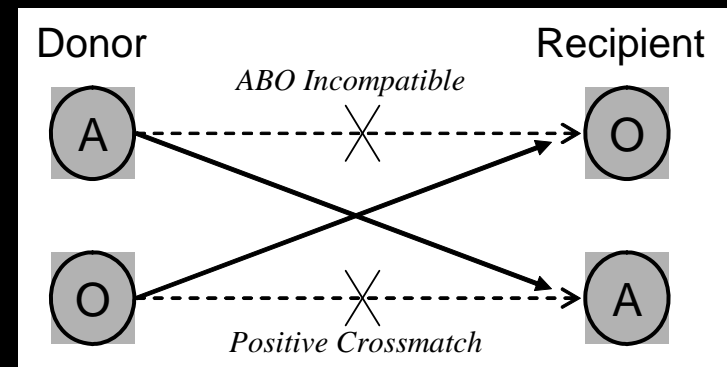


LIMITATIONS OF KPD

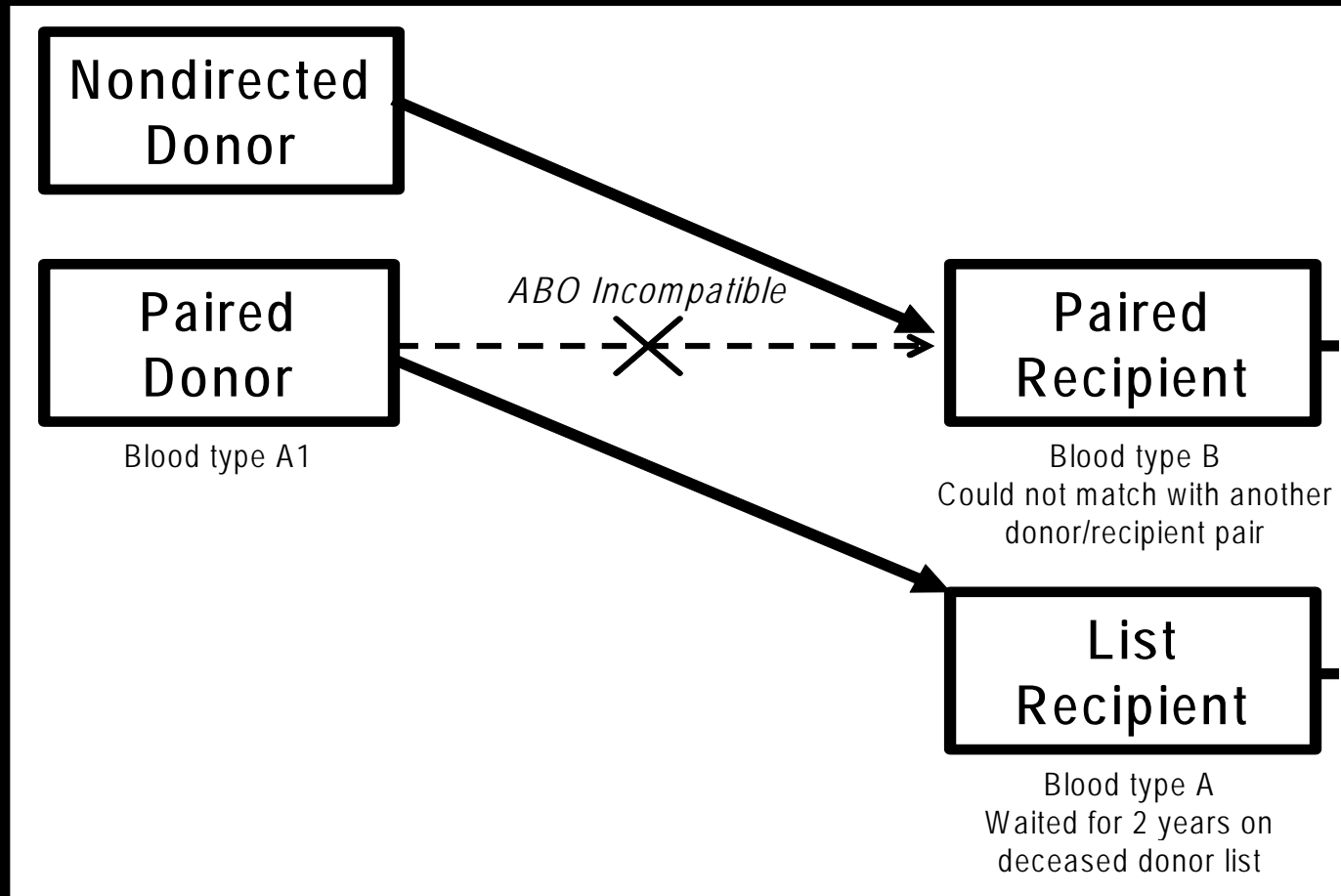
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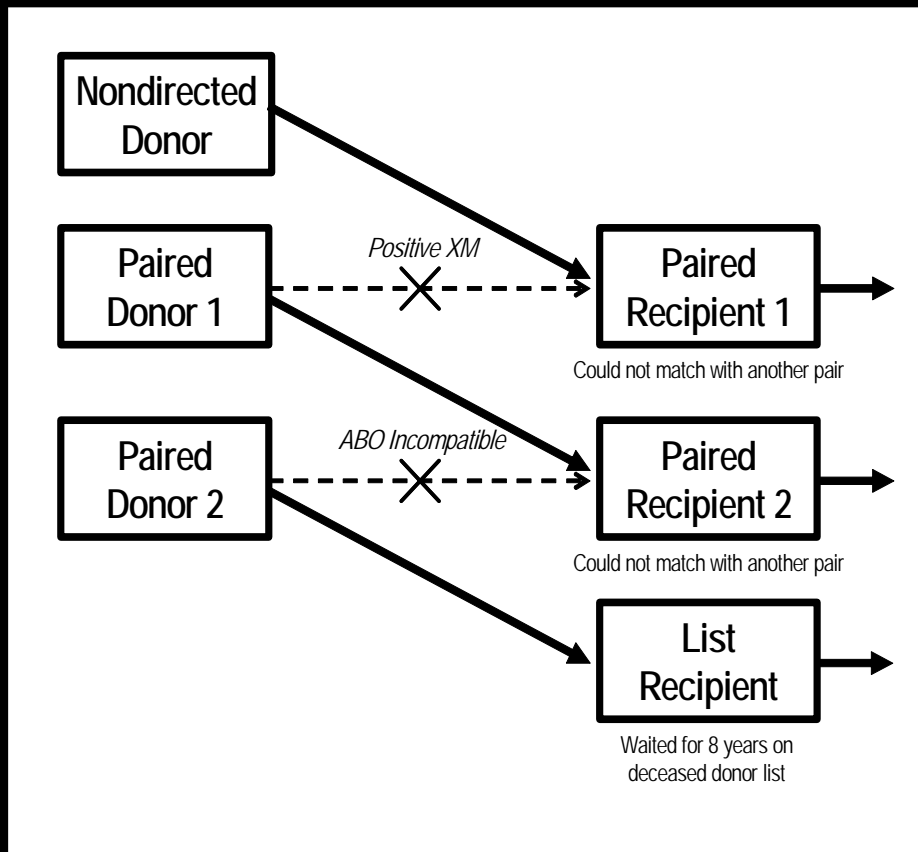


NON-DIRECTED DONORS IN KPD



Lancet. 2006 Jul 29;368:419–21.

NON-DIRECTED DONORS IN KPD



6 Way Domino Transplant

Donor #1: NDD Kenneth Hubbard: 58 y/o wm. Lt. kid: 2A R. Montgomery, MD GOR Room 8			
Donor #2 Joey Small: 34 y/o Lt. Kid: 2A, Rt kid 1A K. Melancon, MD GOR Room 11		Child/ Parent	
Donor #3 Armie Franklin: 29 y/o . Lt. Kid: 1A Li-Ming Su, MD GOR Room 18		Cousins	
Donor #4 Linda Landau: 58 y/o. Lt. Kid 1A T. Jarrett, MD. GOR Room 12		Friends	
Donor #5 Randall Bolten: 55 y/o. Lt. Kid 1A D. Segev, MD. GOR Room 14		Married	
Donor #6: Robin Freedenfeld, 56 y/o Lt. Kid 1A M. Allaf, MD GOR Room 15		Married	

Recipient #1:
S. Finkbeiner: 66 y/o
2nd txp
R. Montgomery, MD
GOR Room 8

Recipient #2:
Robert Reid: 26y/o.
2nd txp.
K. Melancon, MD
GOR Room 11

Recipient #3:
Andrea Roberts: 36 y/o.
2nd txp.
Montgomery/Singer
GOR Room 18

Recipient #4:
Jeanne Heise: 54y/o
1st txp
A. Cameron, MD
GOR Room 12

Recipient #5:
Mark Immerman: 57 y/o
2nd txp.
D. Segev, MD
GOR Room 14

Recipient #6:
Carol Snyder: 61y/o
Melancon/Stewart, MD
GOR Room 15

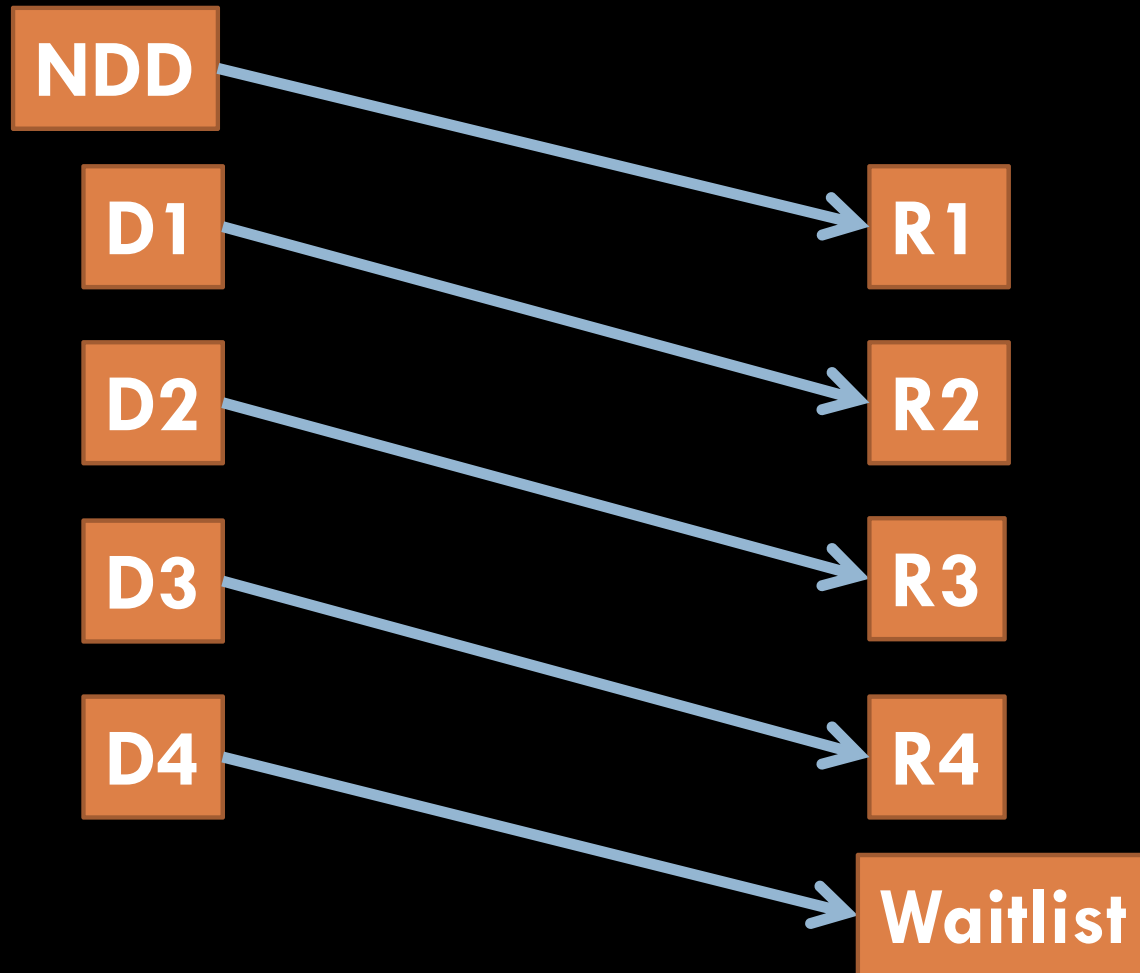
April 5, 2008

LIMITATIONS OF KPD

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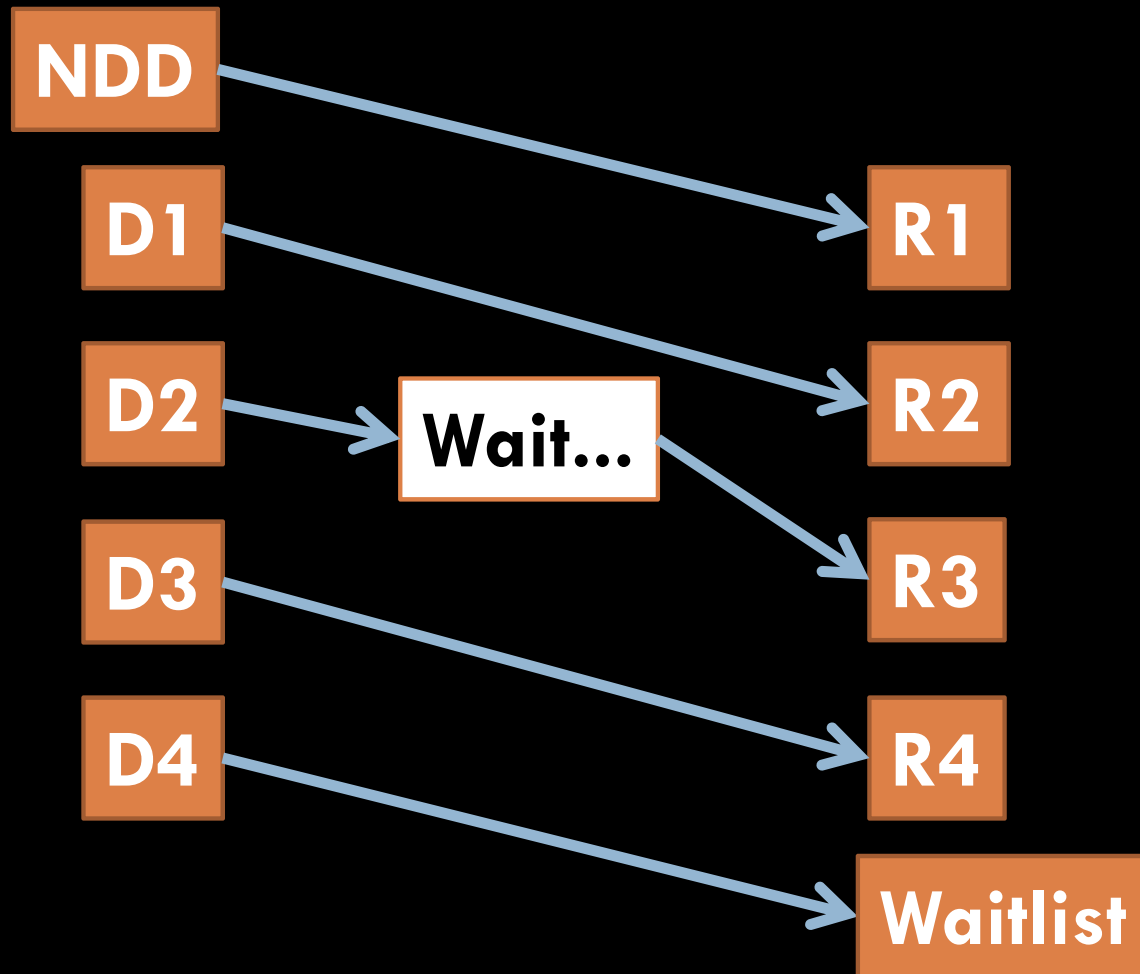


SIMULTANEOUS DOMINO



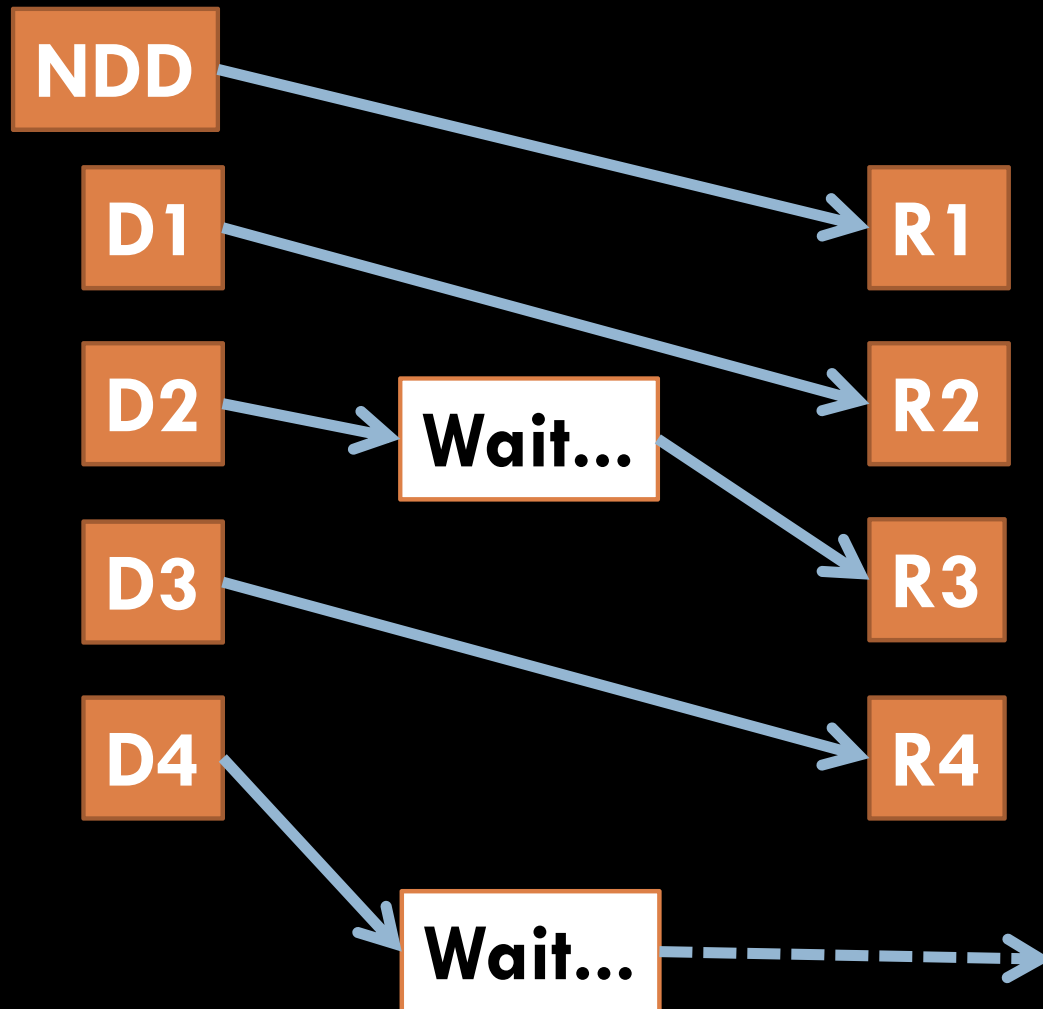
Lancet. 2006 Jul 29;368:419–21.

NON-SIMULTANEOUS DOMINO



AJT. 2009 Jun;9(6):1330-6.

NON-SIMULTANEOUS CHAIN



NEJM. 2009 Mar 12;360(11):1096-101.

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SHIPPING LIVE DONOR KIDNEYS

■ To get more patients transplanted, you have to cross geographic boundaries.

■ In practice, many KPD transplants occur across state and regional lines.

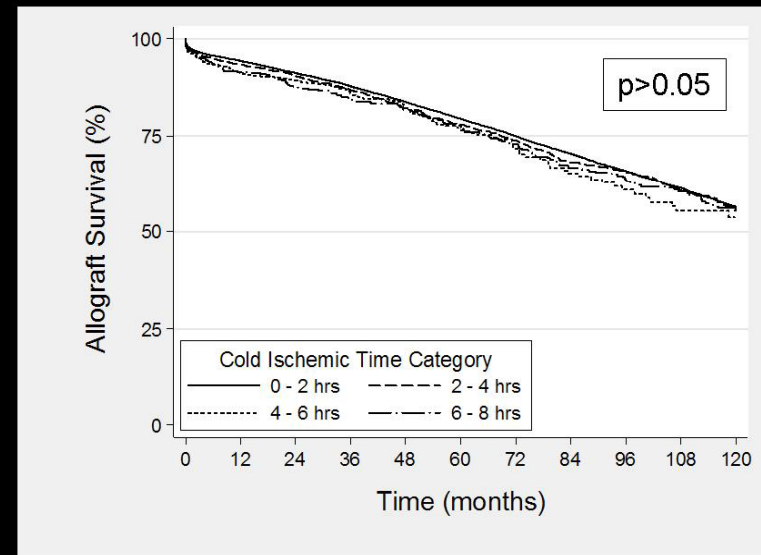
Percent traveling:	
Interstate, recipient	37.6%
Interstate, donor	42.4%
Interstate, both	27.2%
Interstate match	44.0%
Inter-regional, recipient	25.8%
Inter-regional, donor	30.4%
Inter-regional, both	16.3%
Inter-regional match	31.0%

Transplantation. 2008 Aug 27;86(4):502-10.

SHIPPING LIVE DONOR KIDNEYS

- Why not transport the organ instead of the patient?
 - Concerns were mainly related to cold ischemia time.
 - UNOS database analysis of 38,467 adult first-time live donor KT recipients, 1/90-9/05

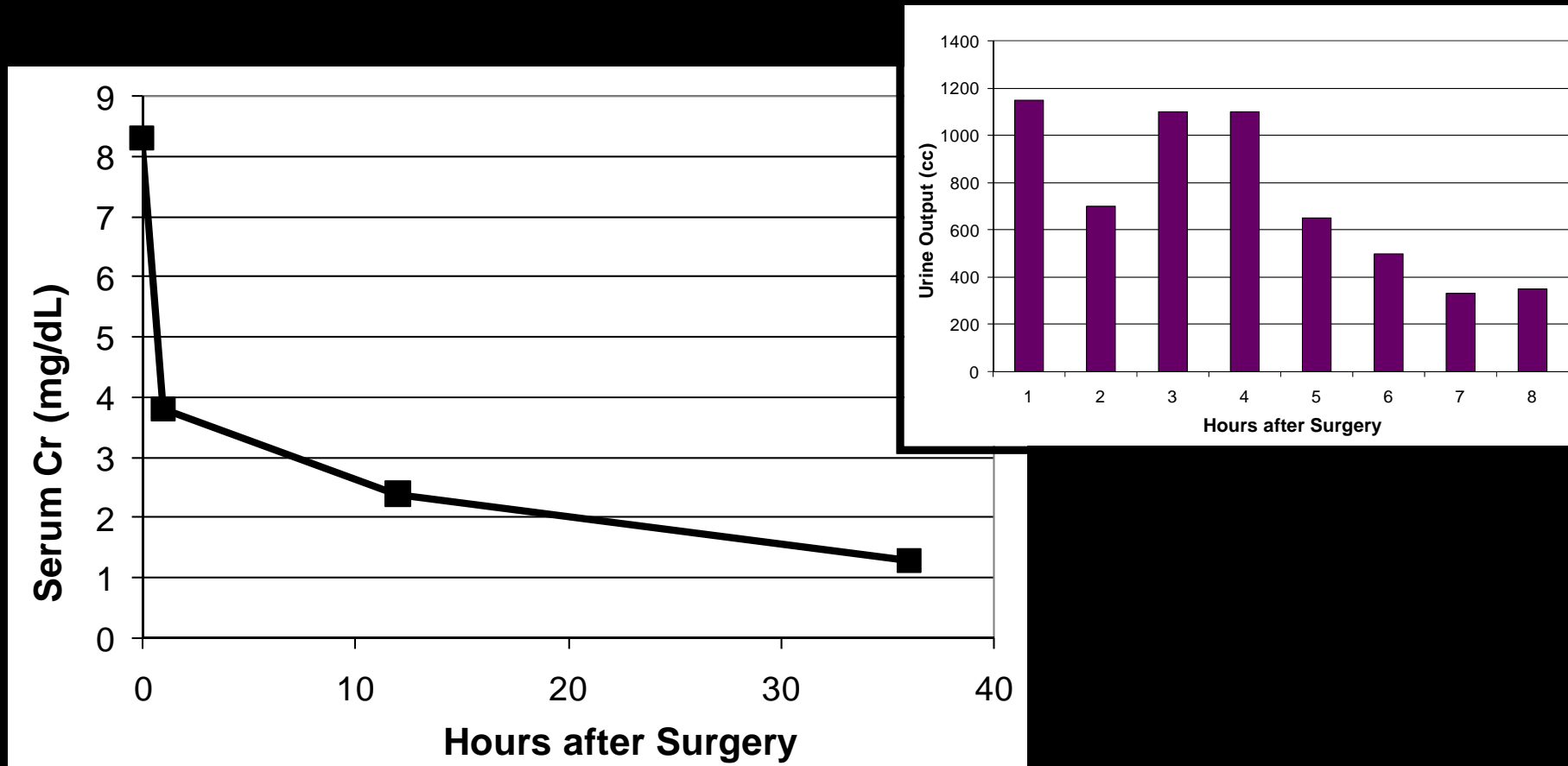
Time	HR	P-value
0-2h	(ref)	(ref)
2-4h	1.09	0.12
4-6h	1.13	0.33
6-8h	1.05	0.69



AJT. 2007 Jan;7(1):99-107.

SHIPPING LIVE DONOR KIDNEYS

- Proof of concept: CPMC → Baltimore (10 hours CIT)



AJT. 2008 Oct;8(10):2163-8.

SHIPPING LIVE DONOR KIDNEYS

- To date, over 35 live donor kidneys have been transported and successfully transplanted: JHU, UCLA, CPMC, Stanford, UCSF, Beth Israel, St. Barnabas, Toledo, Wake Forest, Cornell, Montefiore, Oklahoma City, Henry Ford, Barnes, Yale, McGill.
- CIT 3-14 hours.
- All with immediate graft function (urine output in first 8 hours)

... coming soon ...

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Don't necessarily need to be find
a negative crossmatch in KPD:
Combine KPD and desensitization

MATCHING THE UNMATCHABLE

- From any pool of recipients, many will not match.
- Hard-to-match pairs will accumulate. Most of these are broadly sensitized.
- Results with desensitization low-titer positive XM transplantation are excellent

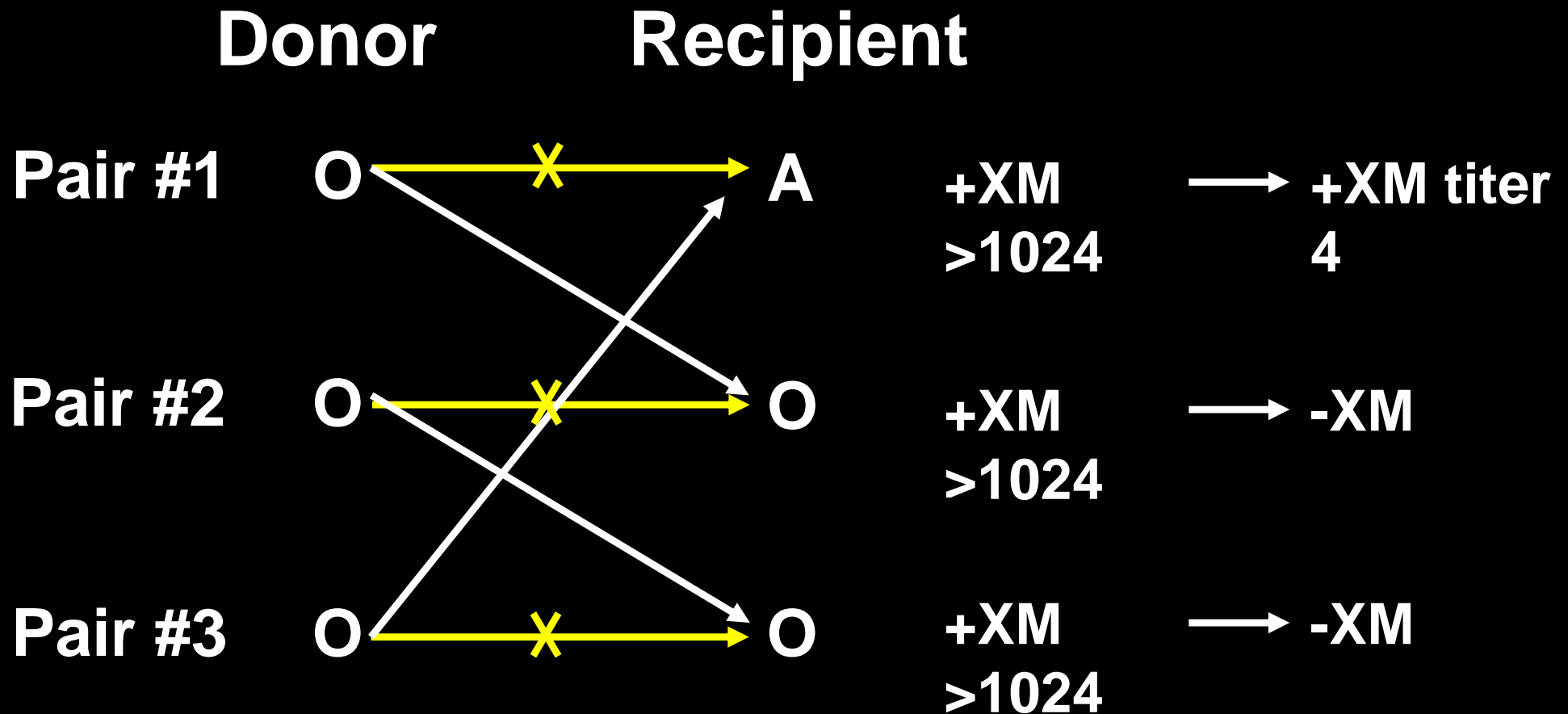
Transplantation. 2006 Jul;82(2):164-5.

MATCHING THE UNMATCHABLE

- For the appropriate patients, change goal from "find a compatible donor" to "find a better donor"
- 1 / 3 patients: titers too high, could not find negative XM donors. KPD + desensitization: no graft losses

Transplantation. 2006 Jul;82(2):164-5.

MATCHING THE UNMATCHABLE



JAMA. 2005 Oct 5;294(13):1655-63.

FAIRNESS AND EQUITY

- Not everybody has access to KPD
 - need a live donor – sort of true
 - people ahead of you get off the list (indirect benefit)
 - dominos (direct benefit)
 - many centers who don't offer KPD don't refer for it
 - patient education
 - mandate KPD info like we mandate multiple listing info?
 - National program!!! (UNOS)
 - geographic disparities in organ availability
 - much of KPD pioneered in poor availability areas

FAIRNESS AND EQUITY

	% live donor recipients	% KPD recipients
Caucasian	68%	68%
African American	14%	13%
Hispanic	13%	9%
Female	40%	43%
PRA>80	4%	13%

FAIRNESS AND EQUITY

- “Allocation” of Non-Directed Donors
 - Normally: NDD gives to someone on waiting list
 - that person didn’t have a live donor
 - Three philosophies:
 - Donor-centric: make the donor’s gift last long
 - Recipient-centric: pick the sickest recipient
 - Socio-centric: Use the waiting list
 - Dominos: the perfect combination?
 - Chains: only people with live donors benefit...

CONCLUSIONS

- KPD facilitates transplantation for patients with incompatible donors
- Mathematical algorithms assure fair and equitable distribution of matching opportunities
- By allowing compatible pairs, non-directed donors, organ shipping, and combined desensitization, KPD opportunities can be significantly expanded
- Although KPD also struggles with allocation equity, in general everybody wins

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