Improving Kidney Exchange Programs

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Outline

Kidney Failure Treatments

- Kidney failure
  - One kidney $\longrightarrow$ OK
  - Both kidneys $\longrightarrow$ Dialysis or Transplantation
- Dialysis vs Transplantation
  - Transplantation yields longer survivability
  - Transplantation yields a better quality of life
  - Dialysis is more expensive than transplantation; values for Portugal:
    - Hemodialysis $\longrightarrow$ 30K euro per year per person
    - Transplantation: 30K euro once + 10K euro year

Sources of kidneys for transplantation

- Deceased donors
  - very large waiting lists (5 years or more waiting)
- Living donors:
  - relatives, spouse, friends, altruistic donors
  - many ethical and legal issues (varies with country)
    - e.g. no commercial transaction of kidneys is generally accepted

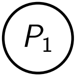
Sources of incompatibility

- Blood type compatibilities

Donor	Recipient			
	O	A	B	AB
O	✓	✓	✓	✓
A	✗	✓	✗	✓
B	✗	✗	✓	✓
AB	✗	✗	✗	✓

- Tissue type incompatibility
  - HLA (Human Leukocyte Antigens)
  - ...

Introduction: background



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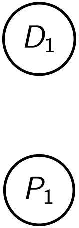

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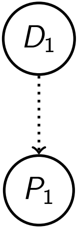

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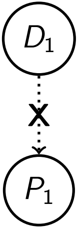

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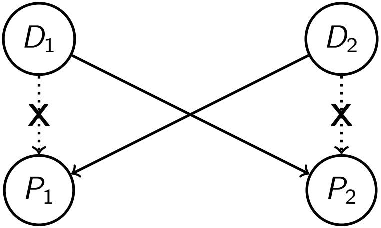

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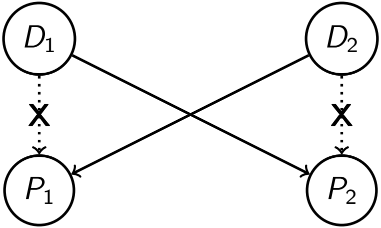

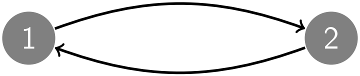

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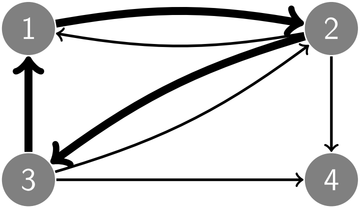

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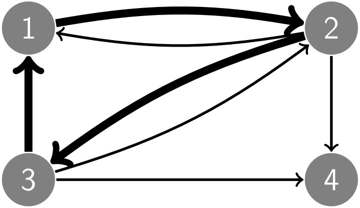
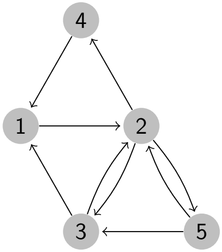


- Exchange between incompatible pairs in a directed graph
    - thin arrows → preliminary assessment compatibility
    - thick arrows → matching

Kidney exchange programs

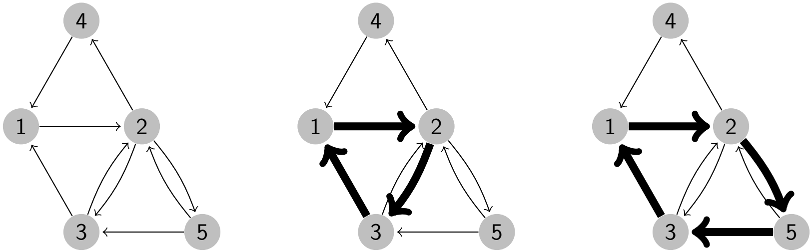
- KEPs were first proposed by (Rapaport, 1986)
- First transplants within a KEP were done in South Korea, 1991
- Many countries have now KEPs (USA, Switzerland, Turkey, Romania, Netherlands, UK, Canada, Australia, New Zealand, Spain)
- A KEP started in Portugal in 2011; presently, transplants are routinely performed

Kidney exchanges: example



- instance with five pairs
- what is the maximum number of transplants?
- what if the allowed number of simultaneous transplants is limited?

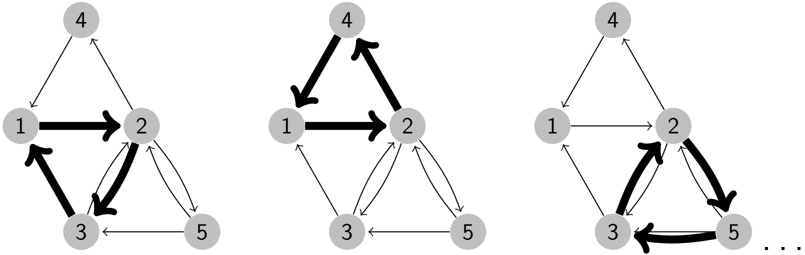
Kidney exchanges: example



- feasible exchange: a set of vertex-disjoint cycles ($e.g.$, $1 - 2 - 3 - 1$)
- size of an exchange: sum of the lengths of its cycles
- maximum exchange in this example: 4 (cycle $1 - 2 - 5 - 3 - 1$)

Kidney exchanges: maximum cycle size

- In many situations the length of each cycle is limited
- If maximum cycle size is $K = 3$, several solutions are possible.



Kidney exchanges: why limiting size

- Two main reasons:
  - usually, all transplants in a cycle should be done at same time
    - someone could withdraw from the program
  - last-minute incompatibility test (crossmatch, just before transplantation)
    - if positive, no transplantation can be done for any pair in this cycle
    - (rearrangements may change the previous limitation)
- However, optimum number of transplants increases with maximum size allowed
- Most programs have $k = 2$ or $k = 3$

Kidney Exchange Model

Problem

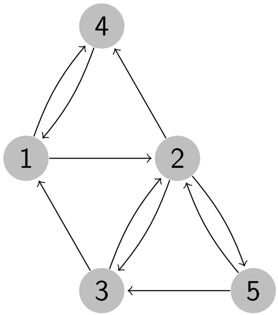
- Given:
  - a pool of n incompatible donor-patient pairs
  - the compatibility between all donors and all patients
- find the maximum number of kidney exchanges with cycles of size at most k

Complexity

- EASY, if $k = 2$ or no limit is imposed on the size of the cycles
- HARD, if $k = 3, 4, 5, \ldots$

Mathematical programming formulations

- There are several possibilities for modeling the problem in mathematical programming
- One of the most successful is the cycle formulation:
  - enumerate all cycles in the graph with length at most K
  - for each cycle c, let variable x_c be 1 if c is chosen, 0 otherwise
  - every feasible solution corresponds to a set of vertex-disjoint cycles



Cycles for $K = 3$:

1. [1,2,3]
2. [1,2,4]
3. [1,4]
4. [2,3]
5. [2,5]
6. [2,5,3]
7. ~~[1,2,5,3]~~

Cycle formulation

$$\text{maximize} \quad \sum_{c} w_c x_c \tag{1}$$

$$\text{subject to} \quad \sum_{c:i \in c} x_c \leq 1 \quad \forall i \in V \tag{2}$$

$$x_c \in \{0, 1\} \quad \forall c$$

- case of $0-1$ weights: $w_c = |c|$, (length of cycle c)
- objective: maximize the weight of the exchange
- constraints: every vertex is at most in one cycle
  - (*i.e.*, donate/receive at most one kidney)
- difficulty: exponential number of variables
  - in our experience: not an issue in practice

Objective

- Ethically, a sensitive subject
- Most common: maximize total number of transplant
  - easy to explain/justify
  - difficult to dispute
- Our claim: this is not adequate
  - KEPs are typically run periodically
  - most of the pairs will eventually be matched, after waiting a few periods
  - hence, we should look for alternatives
    $\rightarrow$ somehow access the quality of the transplants

Objective: our proposal

- For each pair i
  - for each possible matching j for that pair
    - i's patient may receive kidney of j's donor
    - determine expected survival time for patient s_{ji}
- Then, maximize $\sum s_{ji}$, for all arcs in the solution
- This can be done by assigning the weight w_c for each cycle:

$$w_c = \sum_{ji \in c} s_{ji}$$

- Problem:
  - n^2 weights to determine $\rightarrow$ *not practical, if done manually*
  - solution?

Predicting survival time

- There is a considerable amount of historical data
- Idea: use *historical data* to train a machine learning model
- This has been done in the past, but to our knowledge not to parameterize a KEP optimization model
- See, eg., Living Kidney Donor Risk Index (LKDPI) `http://www.transplantmodels.com/lkdpi/`

LKDPI Score:

9

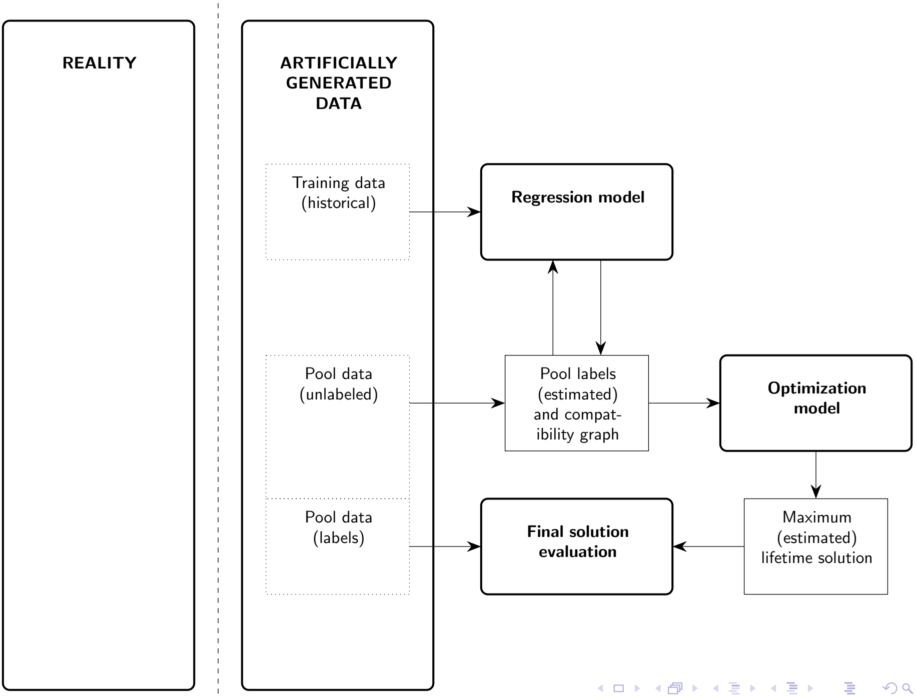
This model calculates a risk score for a recipient of a potential live donor kidney.

Live Donor Characteristics:

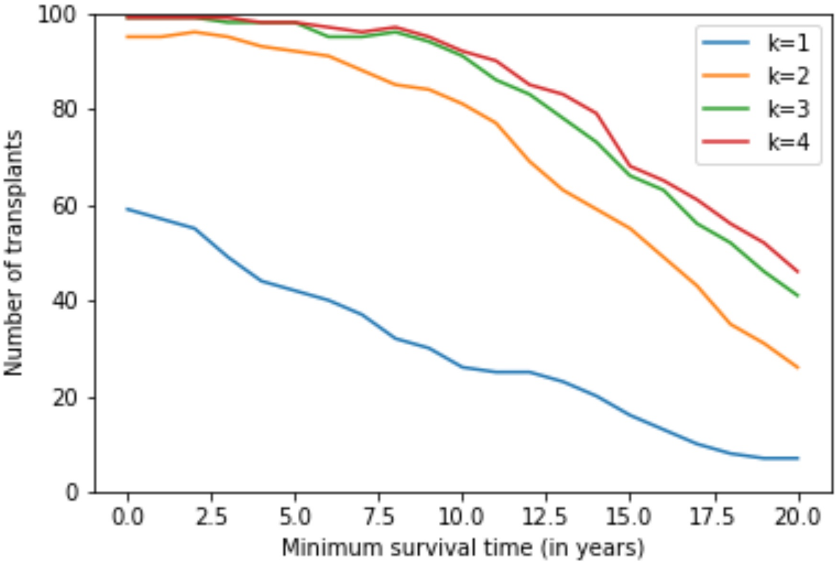
Donor age:	43
Donor sex:	male
Recipient sex:	female
Donor eGFR:	95
Donor SBP:	130
Donor BMI:	24
Donor is African-American:	No
Donor history of cigarette use:	No
Donor and recipient biologically related:	Yes
Donor and recipient are ABO incompatible:	No
Donor Weight:	70 kg/155 lb
Recipient Weight:	80 kg/178 lb
Donor and recipient HLA-B mismatches:	1
Donor and recipient HLA-DR	

Proposed flow:

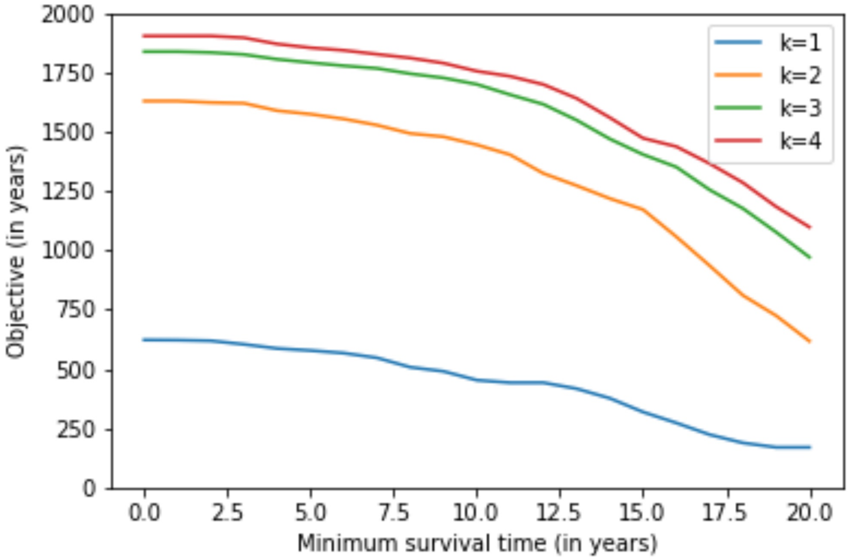
1. Use past data to train regression model
   - features: $\rightarrow$ patients' data
   - output: $\rightarrow$ observed survival times
2. Gather information concerning patients in current pool
3. Parameterize KEP optimization model using
   pool information + predicted survival times


REALITY
ARTIFICIALLY GENERATED DATA
Training data (historical)
Regression model
Pool data (unlabeled)
Pool labels (estimated) and compatibility graph
Optimization model
Pool data (labels)
Final solution evaluation
Maximum (estimated) lifetime solution

Results: number of transplants *vs.* minimum survival time



Results: total survival time *vs.* minimum survival time



Proposed flow: summary

1. Use past data to train regression model → survival times
2. Gather information concerning patients
   → predict survival time for each possible donor-patient assignment
3. Find all cycles of desired length
   → filter cycles with unacceptably low-survival patients
4. Prepare KEP optimization model using this information
5. Execute optimization model, retrieve and analyse solution
6. In the long run: follow transplanted patients, use survival times to improve regression model

Conclusions

- Are current kidney exchange programs wrong?
  - is the objective correct?
- There seems to be room for improvement
  - machine learning + optimization
  - total survival time seems to be a better objective
- Ethics:
  - patient's *minimum acceptable survivable time* should be discussed

Thanks to my former KEP project colleagues and DDDM students!