

Overview on kidney exchange programs

Ana Viana et al

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11 March 2016

- Kidney failure: some figures.
- The past: deceased and living donor transplants.
- The present: Kidney exchange programmes.
 - Current state of practice.
 - Current state of research.
- The future: multi-country kidney exchange programmes.

- 10% of the Portuguese population suffers from chronic kidney disease.
- Over 12 000 people with end stage kidney disease (ESKD); 24 000 people expected in 2025¹.
- It is the 9th leading cause of death each year in the United States (more than breast or prostate cancer).
- Has high economic impact on national health services (NHS)
 - in the UK, the cost of treating ESKD in 2010 was estimated to be 1–2% of the total NHS budget although ESKD patients comprise of only 0.05% of the total population.

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The past

Two treatment options:

- Dialysis
- Transplantation
 - Deceased donors
 - Portugal listed as 2nd country in the world in number of transplants.
 - Living donors (spouse, sibling, ...)
 - In 2010 there were 51 living donor transplants out of a total of 573 in Portugal;
 - Several potential transplants were not performed due to incompatibility between patient and donor.

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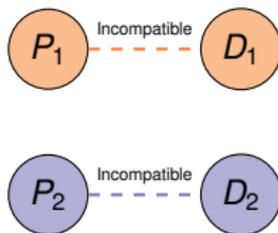
- Blood incompatibility:

Donor	Patient			
	O	A	B	AB
O	V	V	V	V
A	X	V	X	V
B	X	X	V	V
AB	X	X	X	V

- Immunological incompatibility.

Living donor kidney transplants

The past



Transplants could not be done.

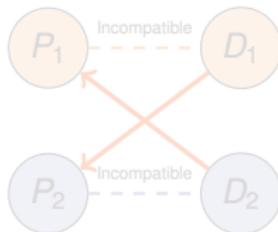
The present

Kidney exchange programmes

Current state of practice

Kidney exchange programmes

Many countries set new policies that allow exchange of organs between incompatible pairs - **Kidney exchange programmes**.

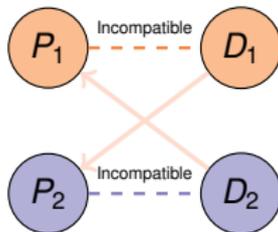


2-way kidney exchange

Two transplants are now possible.

Kidney exchange programmes

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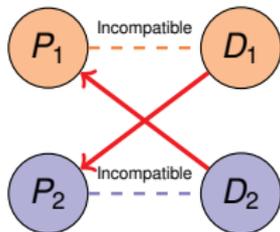


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2-way kidney exchange

Two transplants are now possible.

Kidney exchange programmes

Objective: Maximise number of transplants AND reduce illegal donation.

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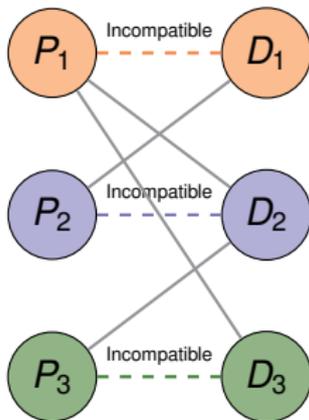
www.CartoonStock.com: GOLD 604.32 CORN 5.72 KIDNEYS 25,375



Kidney exchange programmes

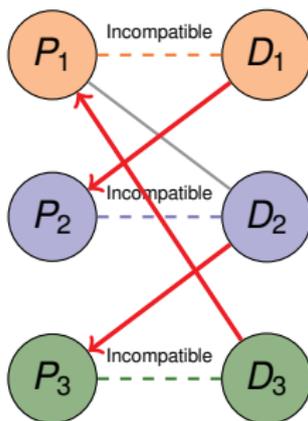
3-way exchange

The idea can be extended to more pairs.



Kidney exchange programmes

3-way exchange

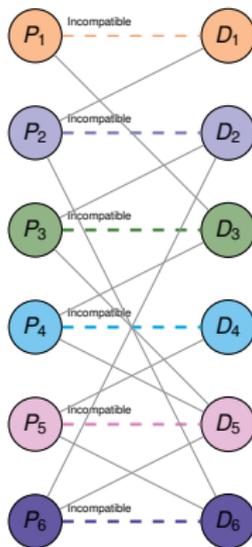


3-way kidney exchange

Three transplants are possible if we allow at most three pairs in an exchange.

Kidney exchange programmes

∞ -way exchange

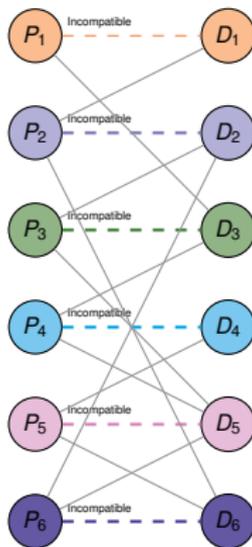


∞ -way kidney exchange

How many transplants?

Kidney exchange programmes

∞ -way exchange



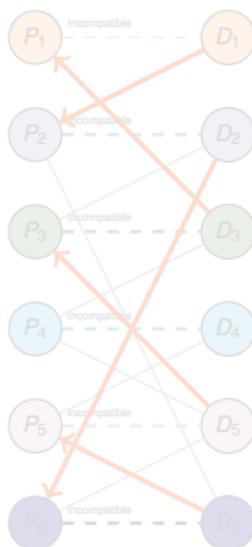
∞ -way kidney exchange

How many transplants?

Kidney exchange programmes

∞ -way exchange

At most **5** transplants: $1 \rightarrow 2 \rightarrow 6 \rightarrow 5 \rightarrow 3 \rightarrow 1$

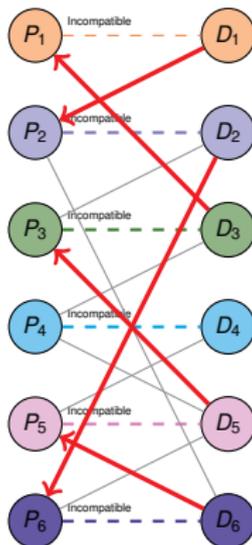


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Kidney exchange programmes

A need for bounded cycle size

But...

– because all transplants in a cycle must be done simultaneously, in practice the maximum number of pairs involved in an exchange must be bounded.

- Logistic/personnel issues constrain the number of such simultaneous operations.

Kidney exchange programmes

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Kidney exchange programmes

A need for bounded cycle size

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- final compatibility tests may detect **new incompatibilities**
- if pairs X and Y in a cycle are found to be incompatible, all transplants in the cycle involving X and Y have to be cancelled: the bigger the cycle the more pairs are affected.

Kidney exchange programmes

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- **Altruistic** donors
- Multiple donors associated to one patient
- Compatible pairs

It is now time for...

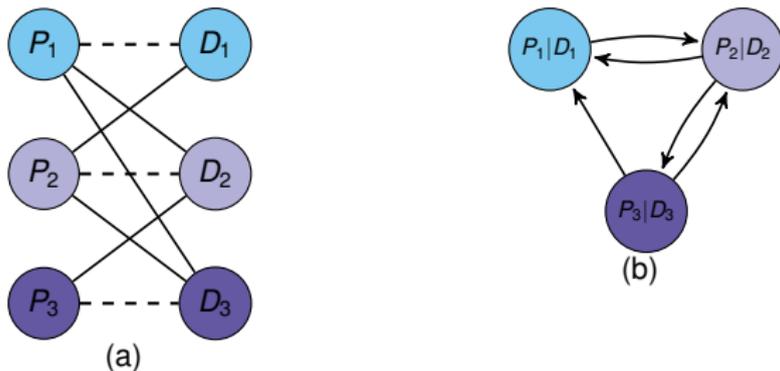
Optimisation

Optimisation problem at hand

Given a pool of N incompatible Patient-Donor pairs, find the maximum number of kidney exchanges (transplants) that involve cycles of size at most K .

Kidney exchange problem

Pre-processing: – transform the bipartite graph of compatibilities into a directed graph in which vertices represent incompatible patient-donor pairs and arcs between vertices represent compatibilities.



Bipartite versus Directed graph

A cycle with k nodes in the directed graph corresponds to a k -exchange.

Let $G(V, A)$ be a directed graph with:

- V – the set of vertices consisting of all incompatible patient-donor pairs;
- A – the set of arcs for designating compatibilities between the vertices.

Two vertices $i, j \in V$ are connected by arc (i, j) if the patient in pair j is compatible with the donor in pair i ².

Definition: The **Kidney Exchange Problem** can be defined as follows:

Find a maximum weight packing of vertex-disjoint cycles having length at most k .

²If the objective is other than maximising total number of transplants (e.g., maximise weighted exchange) to each arc can be associated a weight w_{ij} .

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For:

- $k = 2$ – the problem reduces to finding a maximum matching which can be solved efficiently (Edmonds 1965);
- $k = \infty$ – the problem can be formulated as an assignment problem and solved efficiently by the Hungarian algorithm;
- $k \geq 3$ – *NP*-hard.

Integer Programming Formulations

Integer Programming Formulations

- Two Integer Programming models have been presented in (Abraham et al)³
 - Edge formulation;
 - Cycle formulation.
- None of the above mentioned formulations is compact: the number of constraints or variables grows exponentially with k or N .
- **New contribution:** In (Constantino et al)⁴ we propose an Integer Programming formulation whose number of variables and constraints does not depend on k and grows polynomially with N .

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For each cycle c of length less or equal to k in the graph:

$$z_c = \begin{cases} 1 & \text{if cycle } c \text{ is selected for the exchange,} \\ 0 & \text{otherwise.} \end{cases}$$

$$\text{Maximize} \quad \sum_{c \in \mathcal{C}(k)} w_c z_c \quad (1a)$$

$$\text{Subject to:} \quad \sum_{c: i \in c} z_c \leq 1 \quad \forall i \in V \quad (1b)$$

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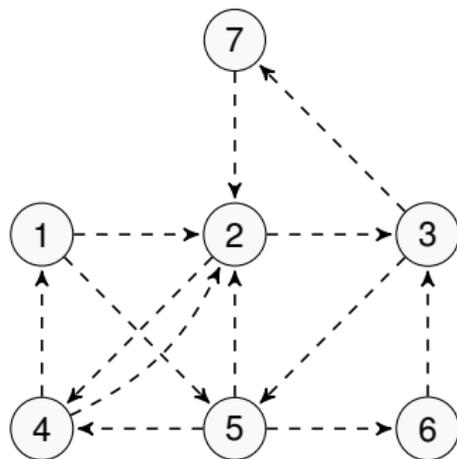
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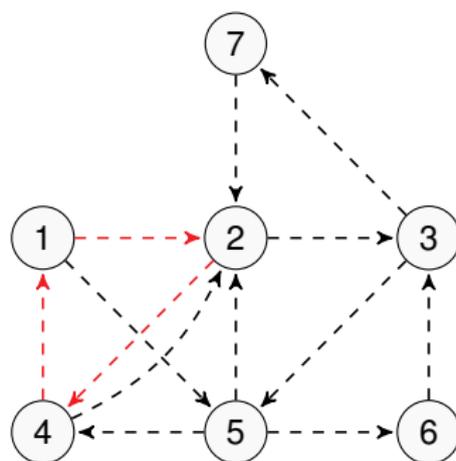
Example



Base graph

Kidney exchange problem

Example

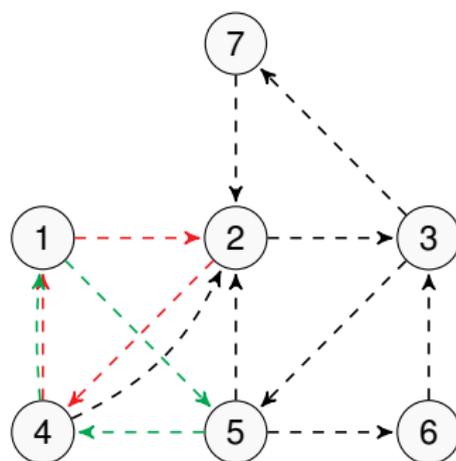


Base graph

C_1

Kidney exchange problem

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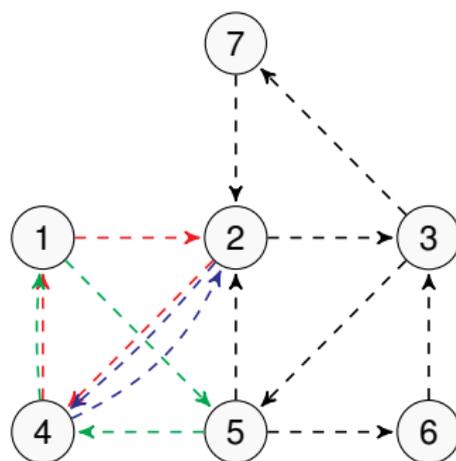


Base graph

C_1, C_2

Kidney exchange problem

Example

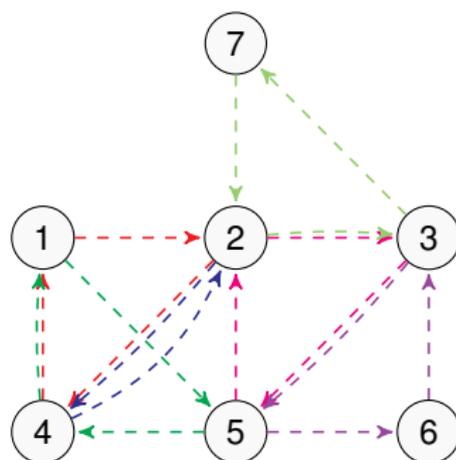


Base graph

C_1, C_2, C_3

Kidney exchange problem

Example

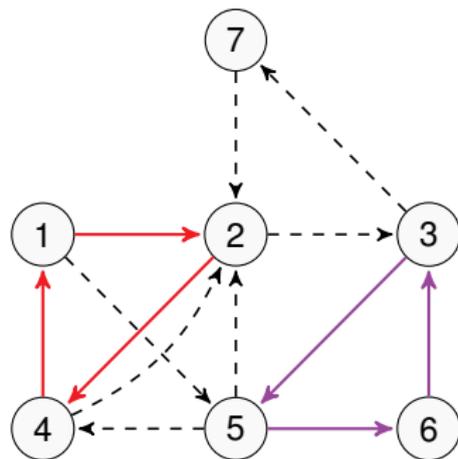


Base graph

$C_1, C_2, C_3, C_4, C_5, C_6$

Kidney exchange problem

Example



(One) optimal solution

- Programmes are now set in several countries, e.g.:
 - Portugal*, South Korea, USA*, Switzerland, Turkey, Romania, Netherlands, UK*, Canada, Australia, New Zealand, Spain.

* – These countries use Integer Programming models to solve the underlying optimisation problem.

Optimisation tools developed under **project KEP⁵** are used by the **National Authority for Transplantation**.

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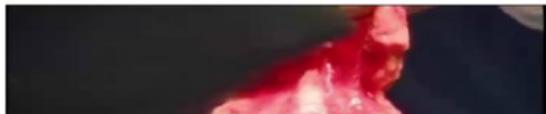
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Primeiro duplo transplante renal cruzado em doadores vivos

Paula Costa/Paulo José Oliveira - RTP

16 Abr. 2013, 23:00 / atualizado em 19 Abr. 2013, 11:15 | País



Seis cirurgias num só dia permitem primeiro transplante renal triplo em Portugal

Paula Rebelo, Rui César, Marcelo Sá Carvalho - RTP

19 Set. 2015, 14:02 / atualizado em 19 Set. 2015, 15:14 | País



A cirurgia, à
Coimbra, em
horas.



Kidney exchange programmes

Web platform used by IPST

KEP Dadores Pacientes Inserir Checklist Compatibilidade Parâmetros Resultados [logout](#)

Ciclo máximo:

Caminho máximo:

Número de soluções:



INESC TEC 2014

The present

Current state of research

The models that are currently used in practice consider that **data is certain** which is **not true**:

- Incompatibilities may be detected between pair matching and actual transplantation (**arc failure**).
- Pairs may dropout of the program (**node failure**).
- Patients and/or donors may be physically unfit when the operation is scheduled (**node failure**).
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- Some sub-optimal solutions obtained under a certain scenario can be much better than the optimal solution, at the time of implementation.
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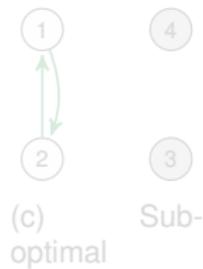
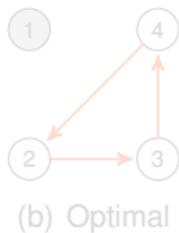
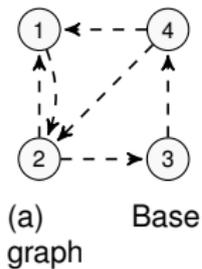
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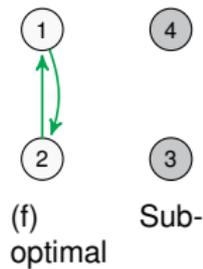
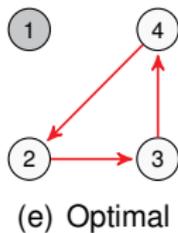
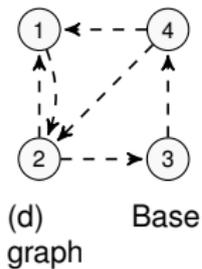
Kidney exchange programmes

Arc/node failure: an example



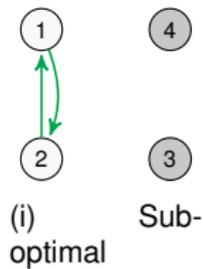
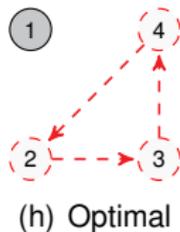
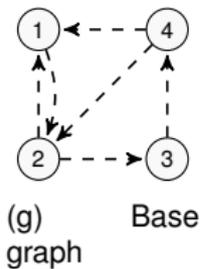
Kidney exchange programmes

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Kidney exchange programmes

Arc/node failure: an example



How have we handled data uncertainty so far?

- Assigning probabilities to node and arc failure
 - Maximise expected number of transplants.
- Robust optimisation
 - Maximise the number of pairs selected in both the initial and the final solution, given a specific scenario.

Plus:

- Recourse policies.
 - Reconstruction policies that can be implemented in a solution if one/some of its nodes and/or arcs fail.

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- **No recourse:**
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 - Robust optimisation: maximise the number of pairs selected in both the initial and the final solution, in the worst case.
- Backarcs recourse
- Subset-recourse (S.O.)
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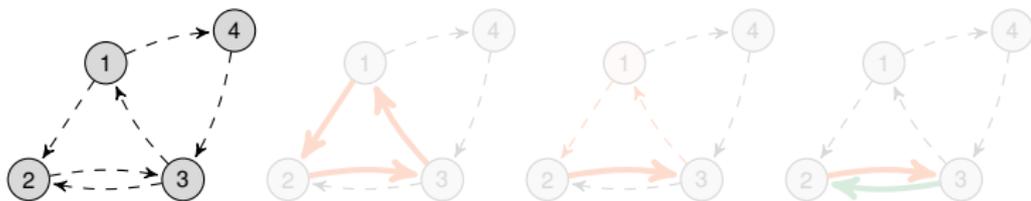
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Kidney exchange programmes

Examples of recourse policies

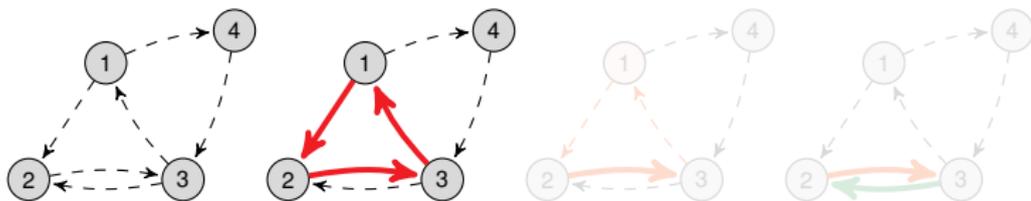
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Kidney exchange programmes

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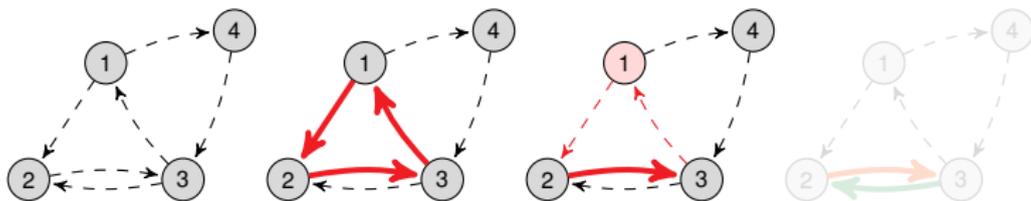
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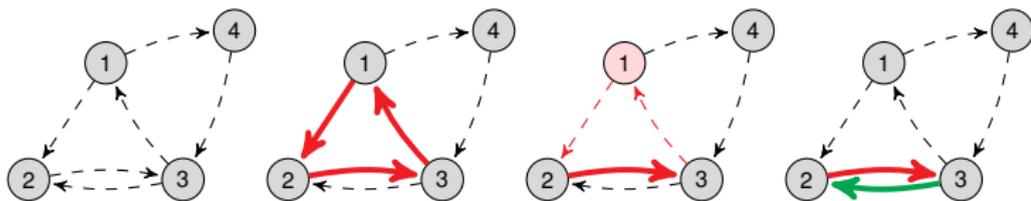
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Kidney exchange programmes

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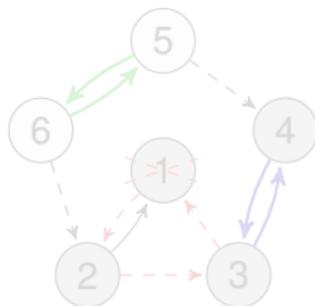
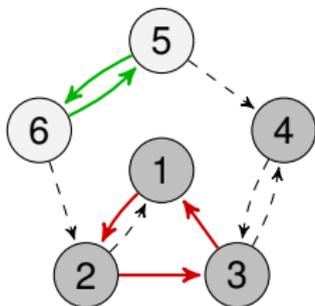
- Backarcs recourse



Kidney exchange programmes

Examples of recourse policies

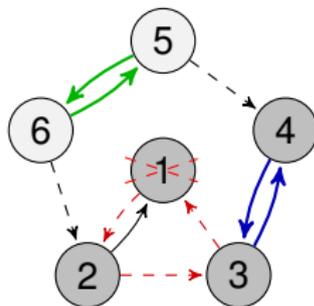
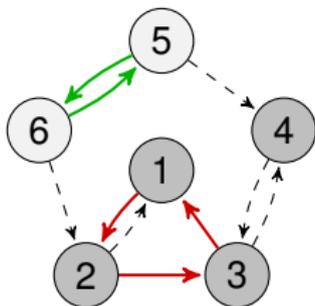
- Subset recourse
 - considers the possibility of involving in the rearrangement vertices not enclosed in the cycle.



Kidney exchange programmes

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Obtaining optimal results for these problems within reasonable computational time requests for adequate formulations and algorithms.

- Klimentova, Pedroso, Viana. “Maximising expectation of the number of transplants in kidney exchange programmes”. Accepted for publication at Computers & OR.
- Glorie et al. “Robust Models for the Kidney Exchange Problem.” Submitted to Operations Research.

The future

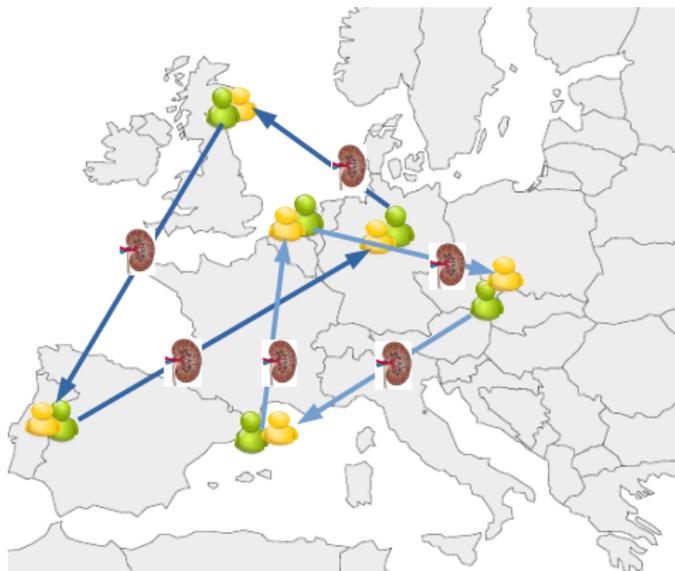
Multi-country kidney exchange programmes

Project mKEP – Models and optimisation algorithms for multicountry kidney exchange programs.

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Multi-country KEP



One concern: give countries the incentive to participate fully, in order to achieve the gains that kidney exchange on a large scale makes possible.

$$\begin{aligned} \text{maximize } Z^* &= \sum_{c \in \mathcal{C}} w_c x_c \\ \text{subject to } & \sum_{c: i \in \mathcal{C}} x_c \leq 1, & \forall i \in \mathcal{V} \\ & \sum_{c \in \mathcal{C}} w_{cp} x_c \geq D_p, & \forall p \in \mathcal{P} \\ & x_c \in \{0, 1\}, & \forall c \in \mathcal{C} \end{aligned}$$

Individual rationality (IR) constraints

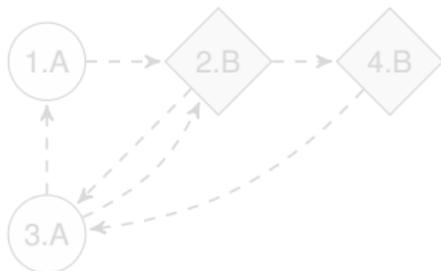
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Individual rationality (IR) constraints

Our vision: IR constraints attack part of the problem but we think there is more...

- New challenges:

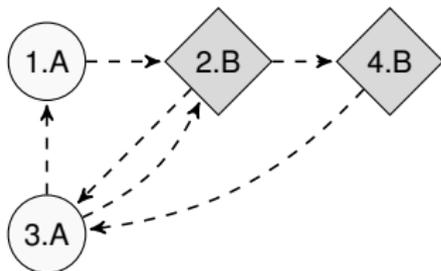


- Country A cannot do any transplants without the help of country B.
- The same is valid for country B.

But...

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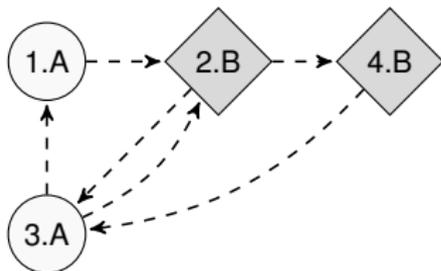


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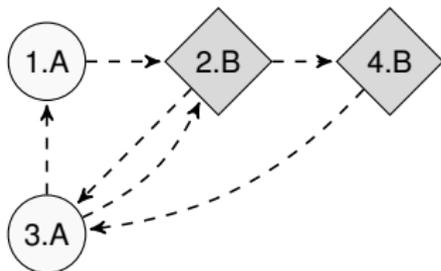


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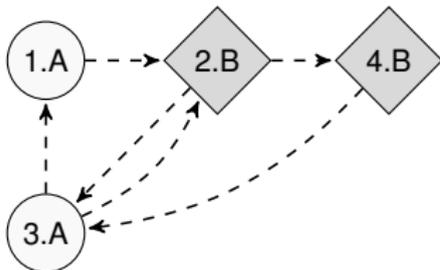


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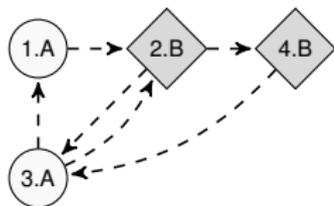
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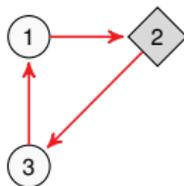


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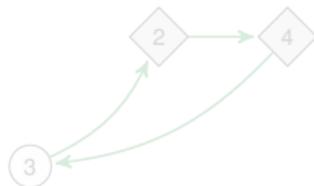
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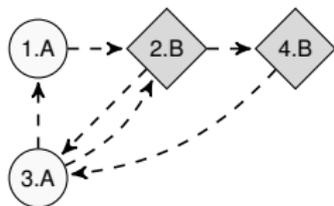
(j)



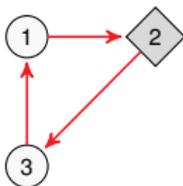
(k) Country A would be happy with this solution...



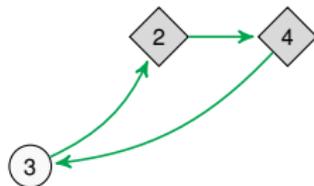
(l) ... while country B would be happy with this one.



(m)



(n) Country A would be happy with this solution...



(o) ... while country B would be happy with this one.

- Current and future research on mKEP will focus on developing models and algorithms for a **fair and equitable share of resources** among the multiple agents (countries, hospitals, etc) participating in the shared pool.
- Approaches followed so far:
 - Game theory: 2-KEG
 - Carvalho et al. "Two-Player Kidney Exchange Game". Submitted to Math. Programming.
 - Integer Programming models: equitable share of resources (kidneys) in the long-term for all countries involved.

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Final remarks

The team



Overview on kidney exchange programs

Ana Viana et al

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11 March 2016