WORKSHOP
ISPOR Vienna

ISPOR TASK FORCES

W15: BUILDING AND APPLYING CONSTRAINED OPTIMIZATION MODELS IN HEALTH CARE: A CASE STUDY OF OPTIMAL KIDNEY MATCHING

ISPOR
Operations Research Optimization Methods
Emerging Good Practices Task Force

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Session Outline

1) Background on the Optimization Task Force
   - What is Optimization?
   - Potential Applications
2) ESRD
3) Kidney Matching Case Study
4) Reflections from optimization perspective
5) Discussion

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Optimization Methods in Health Care Delivery

Task Force Co-Chairs:

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Task Force Members (1)

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- **Maarten J. IJzerman, PhD**, Professor of Clinical Epidemiology & Health Technology Assessment (HTA); Head, Department of Health Technology & Services Research, University of Twente, Enschede, The Netherlands
- **Deborah A. Marshall, PhD,** Professor, Health Services Research and Health Economics, University of Calgary, Alberta, Canada

Task Force Members (2)

- **Alec Morton, PhD**, Professor of Management Science, University of Strathclyde, Glasgow, Scotland, UK
- **William V. Padula, PhD, MS**, Assistant Professor, Department of Health Policy & Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
- **Mustafa Sir, PhD**, Assistant Professor, Mayo College of Medicine, Rochester, MN, USA

Task Force Members (3)

- **Praveen Thokala, MASc, PhD,** Research Fellow, University of Sheffield, Sheffield, UK
- **Jonathan C. Tosh, PhD,** Senior Health Economist, DRG Abacus, Manchester, UK
- **Peter Wong, PhD, MS, MBA, RPh**, Vice President and Chief Performance Improvement Officer, Illinois Divisions and HSHS Medical Group, Hospital Sisters Health System (HSHS), Belleville, IL, USA

CONOPT Task Force Objectives

(1) Introduce the value of optimization methods in conducting research on health care systems and individual-level outcomes research;

(2) Describe problems for which operations research optimization methods are appropriate; and

(3) Identify good practices for designing, populating, analyzing, testing and reporting high quality research for optimizing healthcare delivery services at both the systems and individual level.

http://www.ispor.org/TaskForces/Optimization-in-Healthcare-background-contd.pdf

CONOPT Task Force & Workshop Objectives

Develop guidance for researchers and decision makers on constrained optimization methods applied in health care delivery system interventions research.

The workshop presentation will:

1) provide an overview of constrained optimization (CONOPT)
2) describe when CONOPT is appropriate to address the problem and treatment for kidney disease
3) provide examples of CONOPT that have been used to address health care delivery problems.

What is Optimization?

- **Optimization** is a key tool in the ***analytics armamentarium.***
  - "**Optimization:** Narrowing your choices to the very best when there are virtually innumerable feasible options and comparing them is difficult" INFORMS, The Science of Better http://www.scienceofbetter.org/what/index.htm
  - "In a mathematical programming or **optimization** problem, one seeks to minimize or maximize a real function of real or integer variables, subject to constraints on the variables." The Mathematical Programming Society http://www.mathprog.org/mps_whatis.htm
- **Take home**: Optimization is an ***applied, practical*** subject, but also a ***highly technical*** one that uses cutting edge math and computation

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Mathematical Formulation of Constrained Optimization Models

Maximize $z=f(x_1, x_2, ... x_n, p_1, p_2, ... p_k)$

subject to

$c_j(x_1, x_2, ... x_n, p_1, p_2, ... p_k) \leq C_j$

for $j=1,2,..m$

where, $x_1, x_2, ... x_n$ are the decision variables,

$f(x_1, x_2, ... x_n, p_1, p_2, ... p_k)$ is the objective function; and

$c_j(x_1, x_2, ... x_n, p_1, p_2, ... p_k) \leq C_j$ represent the constraints.

Constraints can include both inequality and equality constraints and the objective function and the constraints also include non-decision variables $p_1, p_2, ... p_k$, which are not varied in the optimization problem.

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Variety of Optimization Models

- Linear vs. Nonlinear
- Static vs. dynamic
- Continuous vs. Integer
- Deterministic vs. stochastic

Examples of Health Care Decisions for Which Constrained Optimization is Applicable

Type of health care problem	Typical decision makers	Typical decisions	Typical objectives	Typical constraints
Resource allocation within and across disease programs	Health authorities, insurance funds	List of interventions to be funded	Increase population health	Overall health budget
Resource allocation for infectious disease management	Public health agencies, health protection agencies	Optimal vaccination coverage level	Ensure disease outbreaks can be rapidly and cost effectively contained,	Availability of medicines, disease dynamics of the epidemic
Allocation of donated organs	Organ banks, transplant service centers	Matching of organs and recipients	Matching organ donors with potential recipients	Every organ can be received by at most one person
Radiation treatment planning	Radiation therapy providers	Positioning and intensity of radiation beams	Minimizing the radiation on healthy anatomy	Tumor coverage and Restriction on total average dosage
Disease management Models	Leads for a given disease management plan	Best interventions to be funded, best timing for the initiation of a medication, best screening policies	Identify the best plan using a whole disease model, maximizing QALYs	Budget for a given disease or capacity constraints for healthcare providers
Workforce planning/ Staffing / Shift template optimization	Hospital managers, all medical departments (e.g., ED, nursing)	Number of staff at different hours of the day, shift times	Increase efficiency and maximize utilization of healthcare staff	Availability of staff, human factors, state laws (e.g., nurse-to-patient ratios), budget
Inpatient scheduling	Operation room/ ICU planners	Detailed schedules	Minimize waiting time	Availability of beds, staff

Steps in Building an Optimization Model

Stage	Step	Description
Modeling	Problem structuring	Specify the objective and constraints, identify decision variables and non-decision variables, and list and appraise model assumptions
	Mathematical formulation	Present the objective function and constraints in mathematical notation using decision variables and constant parameters
	Model development	Develop the model to estimate the objective function and constraints using decision variables and non-decision variables
	Model validation	Ensure the model is appropriate for evaluating all possible scenarios (i.e. different combinations of decision variables and non-decision variables)
Optimization	Select optimization method	Choose an appropriate optimization method and algorithm based on the characteristics of the model
	Perform optimization/sensitivity analysis	Use the optimization algorithm to search for the optimal solution and examine performance of optimal solution for reasonable values of parameters and decision variables
	Report results	Report the results of optimal solution (i.e. values of decision variables, constraints and objective function)

Speaker

William V. Padula, PhD, MS

Assistant Professor, Department of Health Policy & Management

Johns Hopkins Bloomberg School of Public Health
Baltimore, MD, USA

End Stage Renal Disease

End Stage Renal Disease (ESRD)

- Loss of Kidney Function with a GFR < 15ml/min
- Average life expectancy < 5 years
- Requires dialysis or Kidney Transplant

- Common morbidities:
  - Hypertension
  - Diabetes Mellitus
  - Cardiovascular Disease
  - Elderly patients

ESRD Burden in the E.U. and U.S.

- Effects 1:10 people worldwide
  - 120,000 incidences/year in U.S.
  - 34,000 treated patients in U.K.
  - About 400 per million in all of Europe
- Cost of treatment can exceed $100,000 for ESRD Management
  - Dialysis
  - Drugs (e.g. Erythropoietin Alfa)
  - Kidney Transplant
- Economics of treatment
  - U.S.: CMS pays for dialysis in all incident cases of ESRD
  - U.K.: NHS pays for dialysis in patients <60 y.o.
  - Europe: Varying policies about coverage
- Issue with transplant
  - Limited availability
  - Costly one-time procedure with complex follow-up

IOM Report:
Economics of Kidney Transplant Matching in U.S.

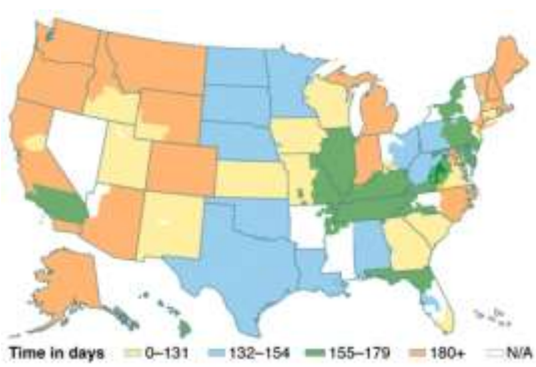
Science

POLICY FORUM PUBLIC HEALTH

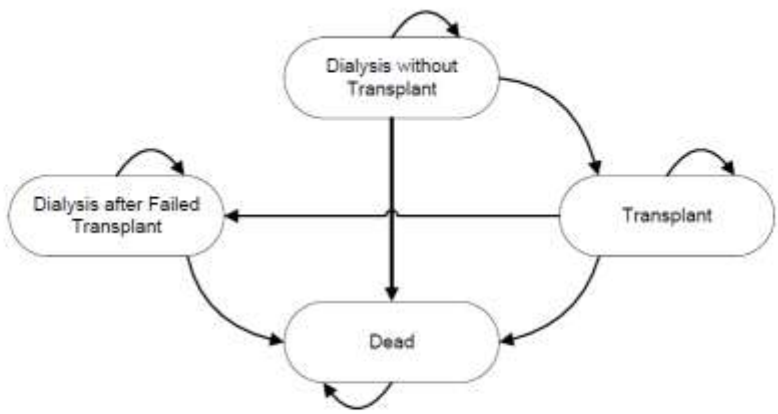
Waiting for Organ Transplantation

Robert D. Gibbons*, David Meltzer, Naihua Duan

Science 14 Jan 2000:
Vol. 287, Issue 5451, pp. 237-238



ESRD Model Conceptual Framework



ESRD Queuing

- Long waiting lists (~100,000 in US) for ESRD patients waiting for a kidney transplant
- Waiting lists continue to increase due to shortage of kidneys available for transplant and potential incompatibility between donors and recipients
- Monetary market is forbidden (i.e. illegal to sell)

Speaker

Praveen Thokala, MASc, PhD,
Research Fellow,
University of Sheffield,
Sheffield, UK

Kidney Matching Example

Overview of Kidney Allocation Problem

- Aim: Highlight the use of optimization techniques in solving important real world clinical problems

- Case study presented here is based on a paper by Anderson et al 2015, titled "Kidney Exchange and the Alliance for Paired Donation: Operations Research Changes the Way Kidneys Are Transplanted"

- More than 1000 lives saved so far

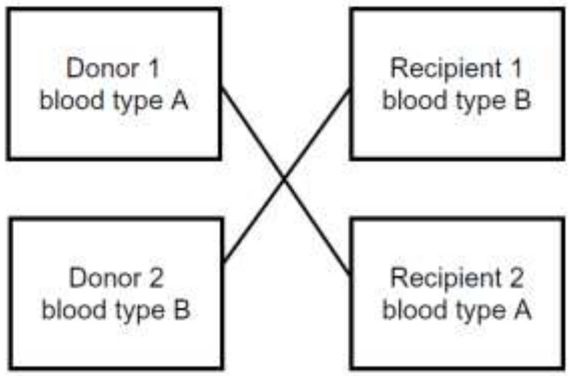
Kidney transplantation for ESRD patients

Two different avenues:

- "Patient-donor" pairs: Donors who are willing to donate their spare kidney to a specific recipient (family members)
  - ➢Potential incompatibility

- "Non-designated" donors: altruistic kidney donors who decide to donate without having an intended recipient
  - ➢Waiting times

Two way cyclic exchange



- Conducted simultaneously, to avoid reneging
- Difficult logistics (four operating rooms for two nephrectomies and two kidney transplants)

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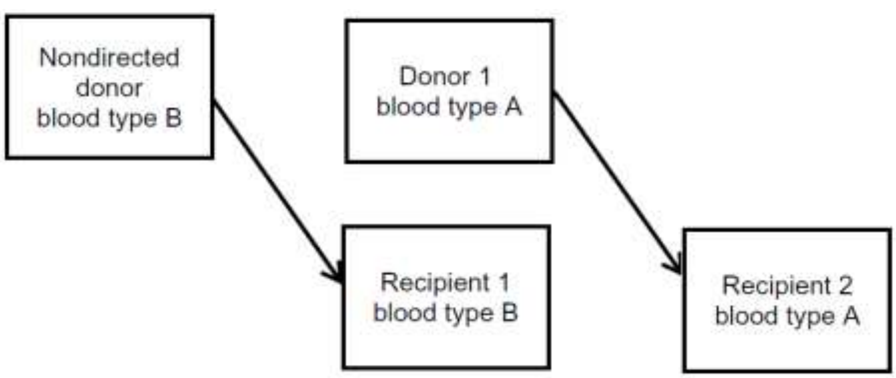
Chains using non directed donors (NDD)



- Chains were short (i.e. 2 or 3) and also conducted simultaneously, the logistics remained a difficult issue

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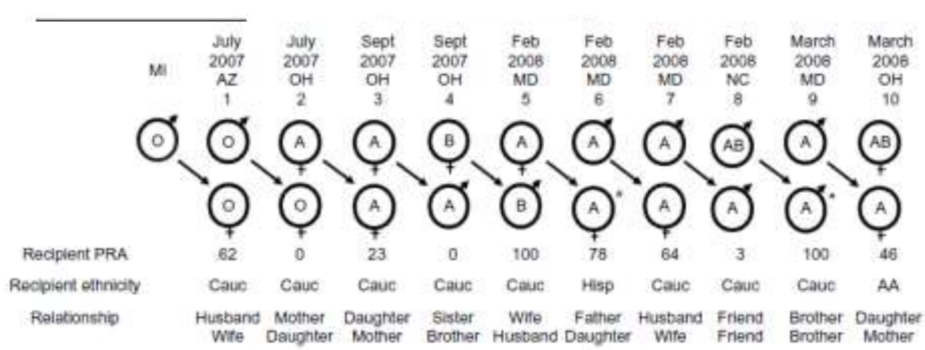
NEAD method

- NEAD stands for non-simultaneous extended altruistic donor chains
- This method was used by Alliance for Paired Donation in the US to save 220 lives (at the time of publication). Others taken up too with over 1000 lives saved
- Key advantages:
  - No need for simultaneous exchange
  - More patients benefit as long chains are used

First use of NEAD



- Good news: the incidence of reneging by bridge donors continues to be very low (about two percent).

Multidisciplinary problem/team

- Conducting kidney exchanges through cycles or chains introduces the challenge of finding a maximal set of compatible matches, a classical OR combinatorial optimization problem, solved using integer programming
- US has more than 200 transplant centers and innumerable dialysis clinics ($50 billion industry), thus market research is essential to deal with participating agents with competing objectives
- A team of physicians and operations researchers worked together to overcome the scepticism and resistance of the medical community to the NEAD innovation

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Speaker

Alec Morton, PhD
Professor of Management Science,
University of Strathclyde
Glasgow, Scotland, UK

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Objective

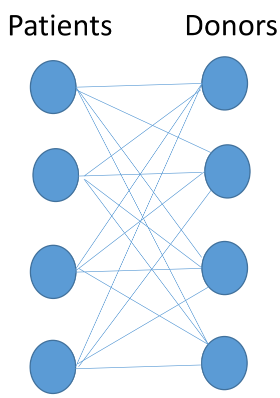
- To give a sense of why optimisation methods are required
- To give a sense of the basic principles of optimisation methods in this example

Simplified problem

- We have N donors and N patients
- Each donor can be paired with one and only one patient
- Each donor-patient matching has a score
- We have to match donors to patients to maximise the total score

Why are optimisation methods required?

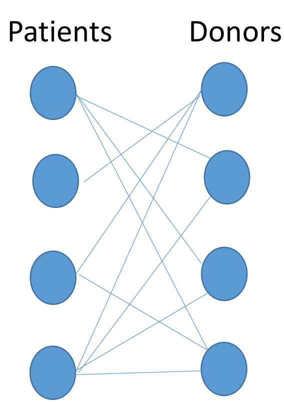
- There are a very large number of possible donor-patient pairs



- Suppose every donor can be matched with every kidney: then n^2 donor kidney pairs, n^2 x $(n-2)^2$ chains of length two…

Principle: Exploit Network Structure

- Not all donor-patient pairs are feasible



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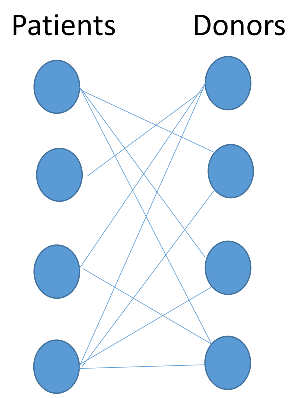

- We can use this observation to reduce the search space

Principle: exploit network structure

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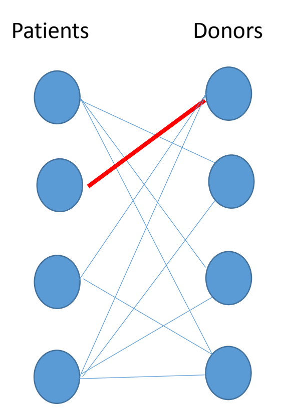

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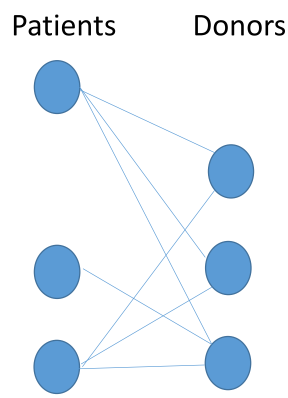

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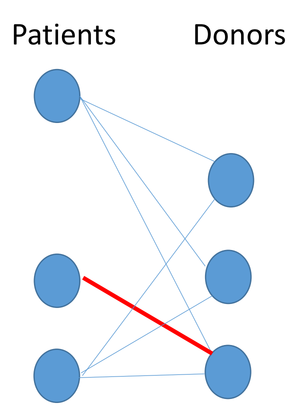

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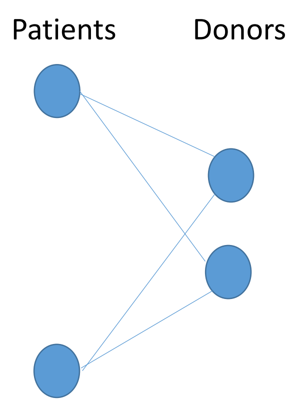
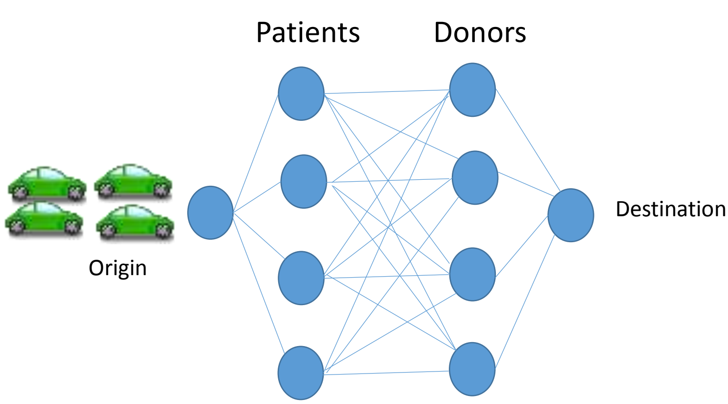


- We can exploit network structure to reduce the size of the problem

There are well-established algorithms for optimising such problems

- Exploits analogy to problems of transportation



Solution Procedure Sketch

- Ignore the helicopters (*relaxed problem)*
- Determines an optimal flow and then check to see if >2 helicopters is used
- If so, we say there is a *violated inequality*
- We resolve, *cutting off* this solution

Take Home Messages About Optimisation Methods?

- High potential value in particular problems
- But does require technical skills and understanding

Next Steps

Finalize & submit Paper 1–Introduction	Early December 2016
Finish Paper 2	November 2017
Review of Paper 2	Early February 2017
Revise as per comments received	March 2017
Final review of manuscript	April 2017
Revise and finalize manuscript	May 2017
Submit Paper 2 to Value in Health	May 2017
Presentation of final papers ISPOR Boston	May 2017

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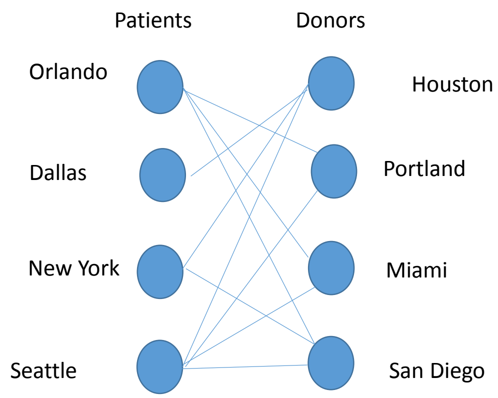
Questions?

For other constraints, use implicit enumeration

- Analogy; suppose that we have helicopters which can be used for long distance transport



There may be constraints which are outside the network structure

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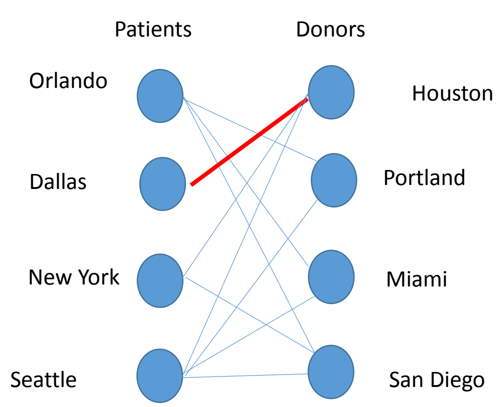

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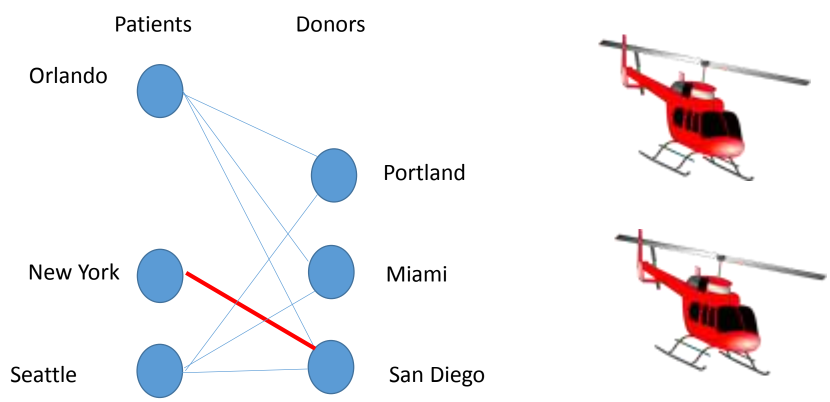

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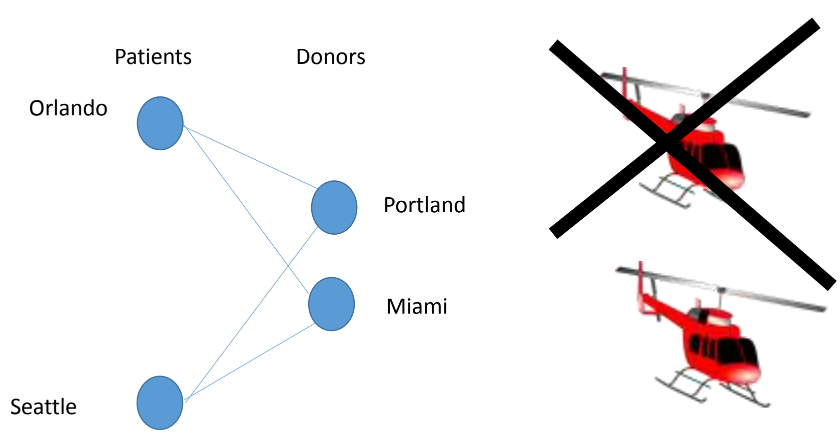

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