Some mathematical aspects of kidney transplantation

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Here the waiting list in Italy

Tabella 50 - Andamento iscrizioni in lista di attesa al 31 dicembre degli ultimi 10 anni

Organo	31/12/2010	31/12/2011	31/12/2012	31/12/2013	31/12/2014	31/12/2015	31/12/2016	31/12/2017	31/12/2018	31/12/2019	Incremento % ult anno
RENE	8.493	8.361	8.538	8.696	8.735	8.730	8.448	8.255	8.218	7.964	-3,19%
FEGATO	1.149	978	927	955	994	982	968	968	952	1.026	7,21%
CUORE	691	692	643	661	662	675	710	717	703	668	-5,24%
POLMONE	324	349	360	352	364	374	342	347	359	363	1,10%
PANCREAS	248	242	210	225	246	236	235	245	252	257	1,95%
INTESTINO	25	23	26	24	22	20	12	12	12	10	-20,00%
Totale Iscrizioni	*10.930*	*10.645*	*10.704*	*10.913*	*11.023*	*11.017*	*10.715*	*10.544*	*10.496*	*10.288*	*-2,02%*

attesa.png

Attività di Trapianto da Donatore deceduto
Periodo: 01/01/2010 - 31/12/2019

Rete Nazionale Trapianti

Attività di trapianto di Rene

Tabella 19 - Attività di Trapianto di Rene - Trend Annuale

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Totale
RENE	1323	1366	1403	1334	1439	1421	1594	1740	1644	1609	14873
RENE DOPPIO	125	108	107	96	93	105	128	144	125	130	1161
RENE - PANCREAS	27	41	53	43	29	31	56	28	32	33	373
RENE - FEGATO	25	19	21	24	23	18	17	15	27	23	212
RENE - CUORE	3	1	4	2	3		4	4	1	1	23
RENE - SPLIT	5	3	1				1	4		2	16
RENE DOPPIO - FEGATO					2	3			1		6
RENE - POLMONE										1	1
RENE - SPLIT - PANCREAS	1										1
Totale RENE	1509	1528	1589	1499	1589	1578	1800	1935	1830	1799	16666

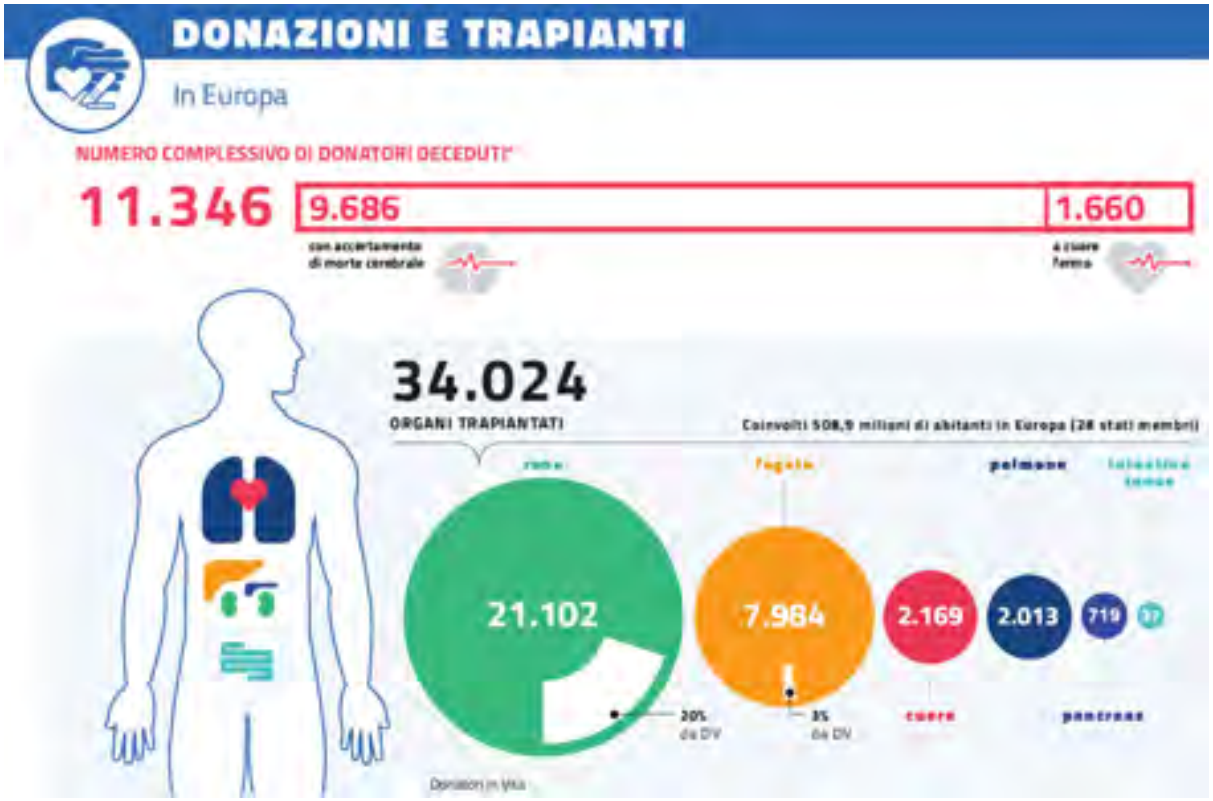
deceased.png

Fig. 13 - Trend annuale attività complessiva trapianto di RENE

Transplants with living donors

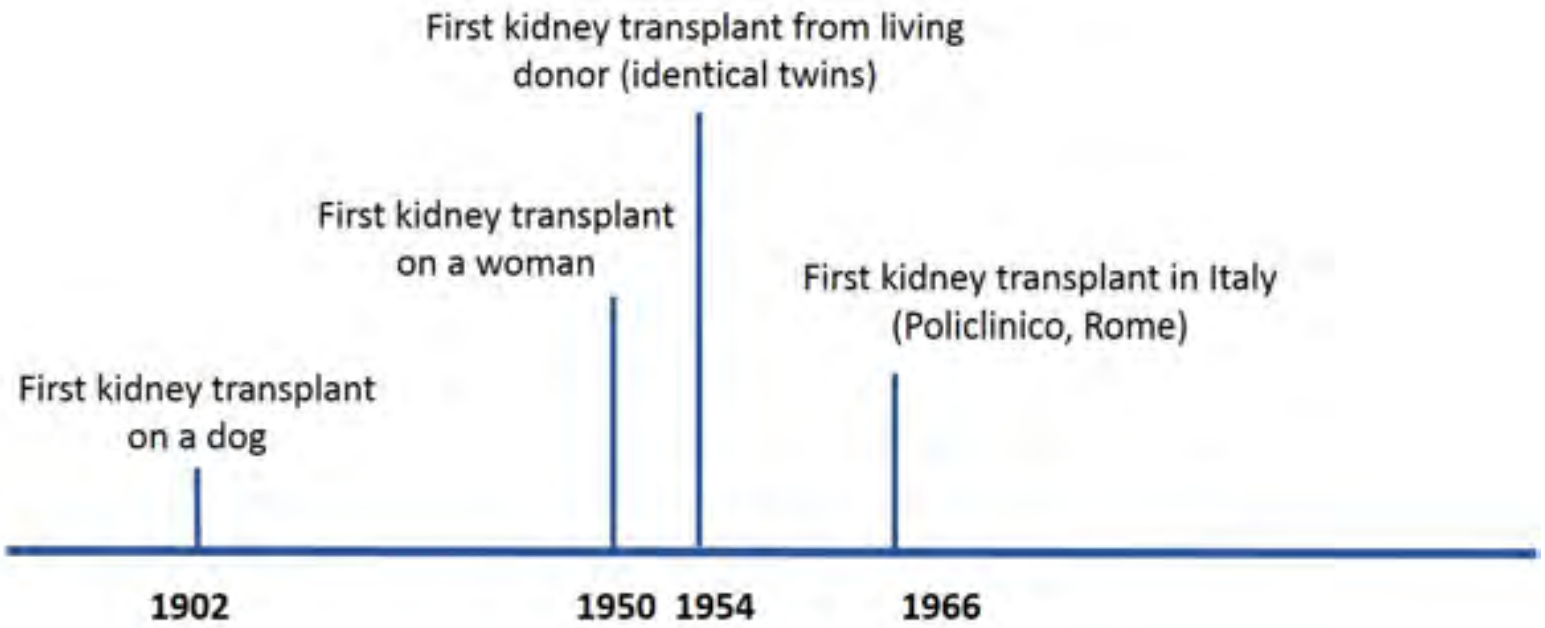
living.png

The situation in Europe (2017)

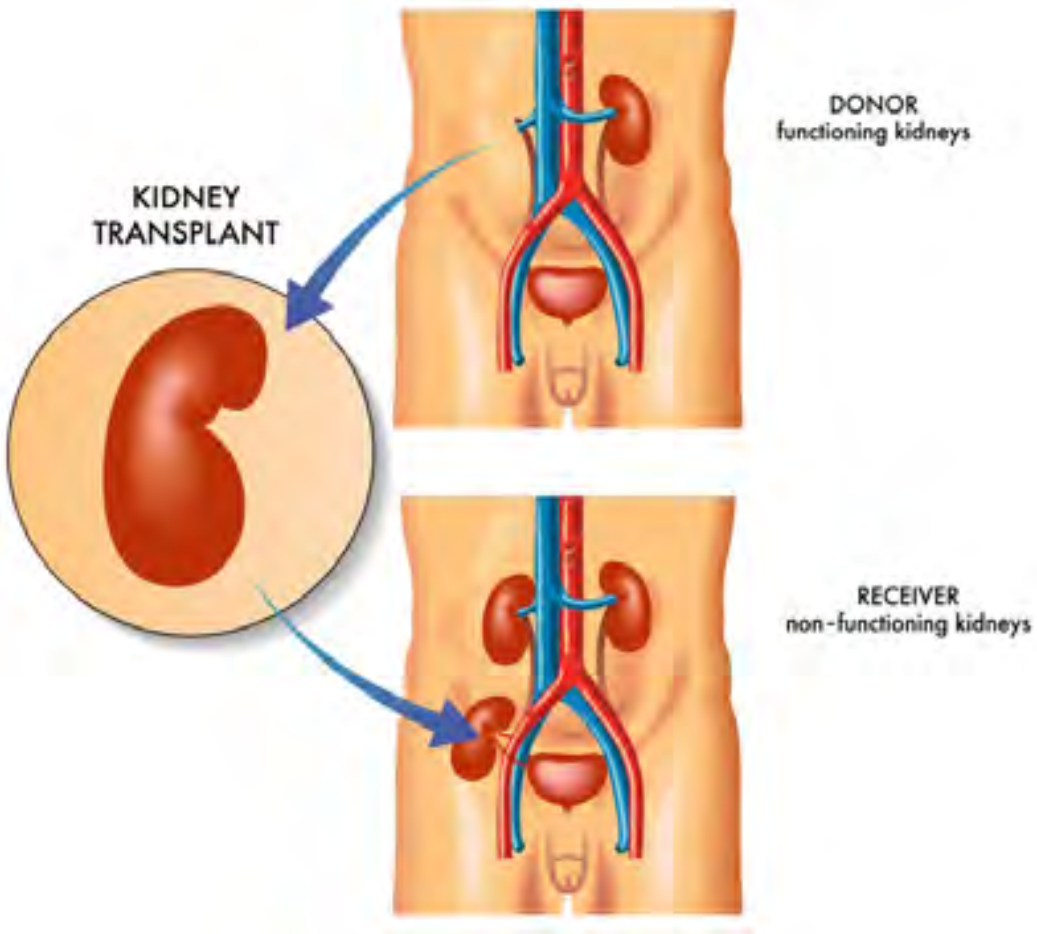


Kidney transplant

Early History



Kidney transplant



- total replacement of renal function
- longer life expectancy with respect to people on dialysis
- good quality of life

Kidney transplant

- Sean Elliott was the first NBA player coming back to play professionally after a kidney transplant.
- Alonzo Mourning received a kidney from a living donor in 2003 and won the NBA finals with Miami Heat in 2006.

Compatibility

There are three tests to evaluate compatibility between recipient and donor (living or deceased):

- ABO blood type test
- Comparison of HLA (Human Leucocite Antigen)
- Screen for antibodies

These factors can affect the possibility of donation, and/or making it more dangerous

PRA

The **PRA** test is an index to show easiness to find a compatible donor. The PRA measures the level of antibodies in the recipients blood:

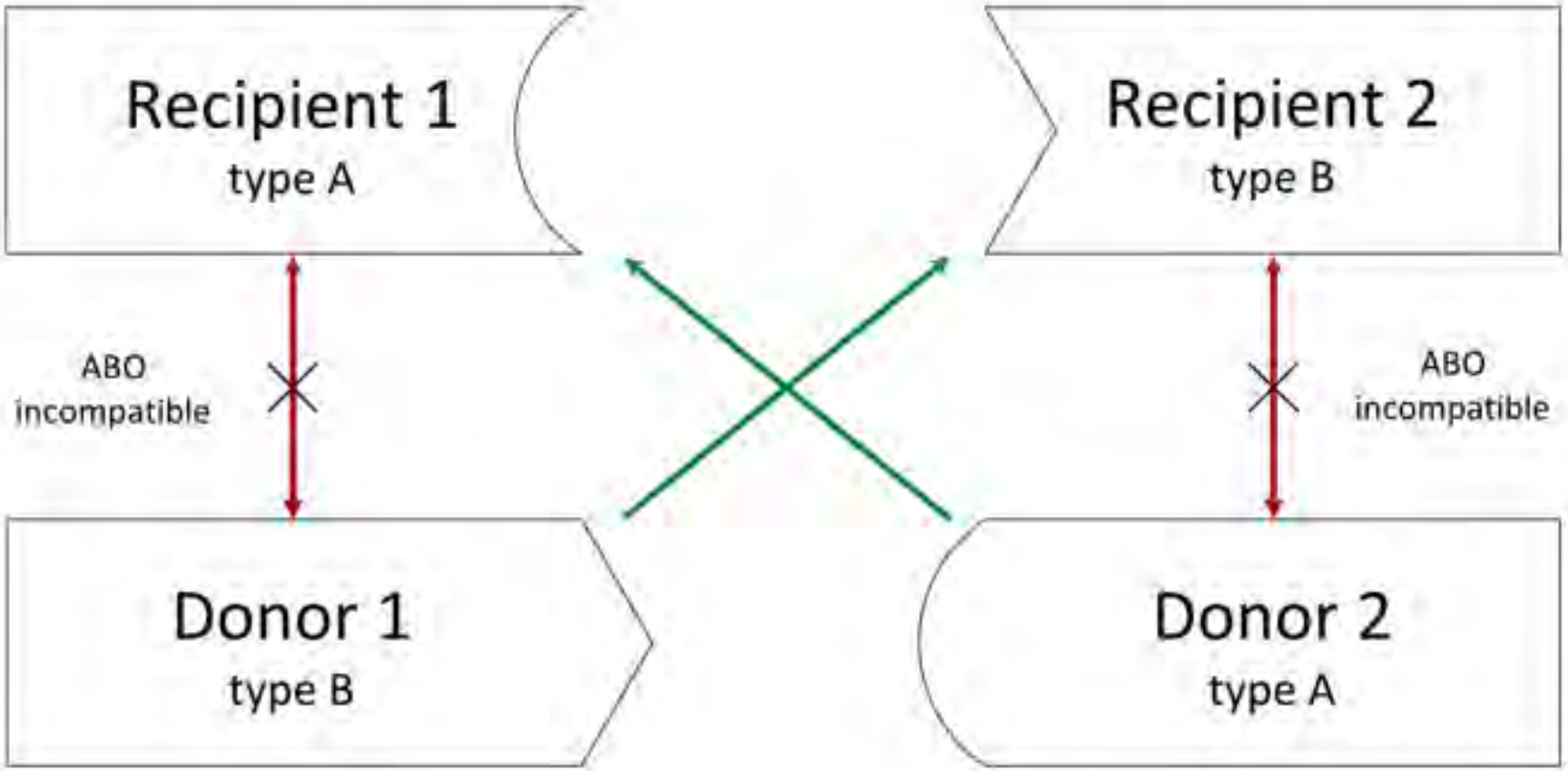
- LOW PRA: <10%
- MEDIUM PRA: 10-80%
- HIGH PRA: > 80% (**highly sensitized** patients)

Crossover exchange

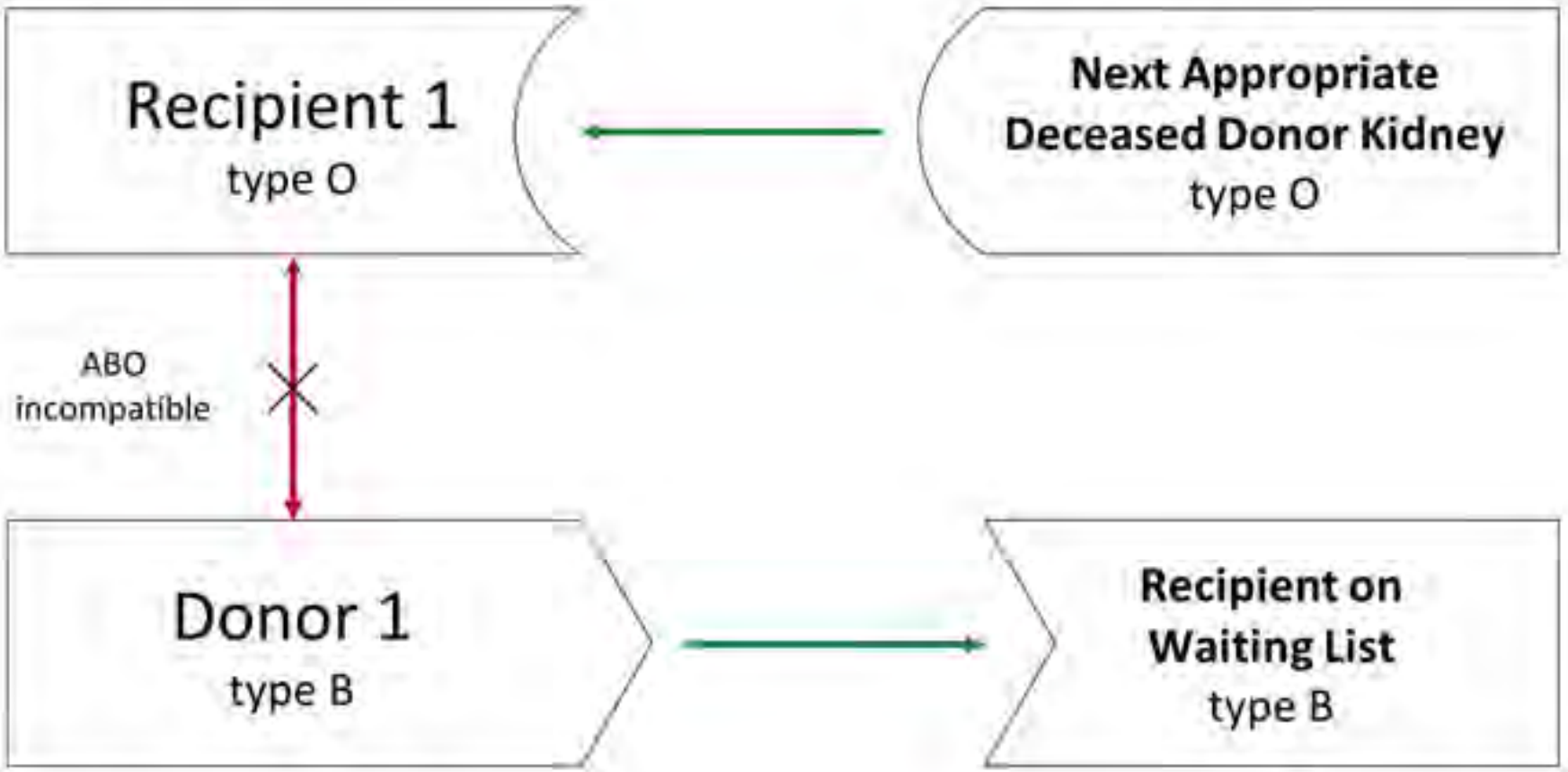
The idea of exchange of donors between patients was introduced by Rapaport in 1986;

This can be done in several ways.

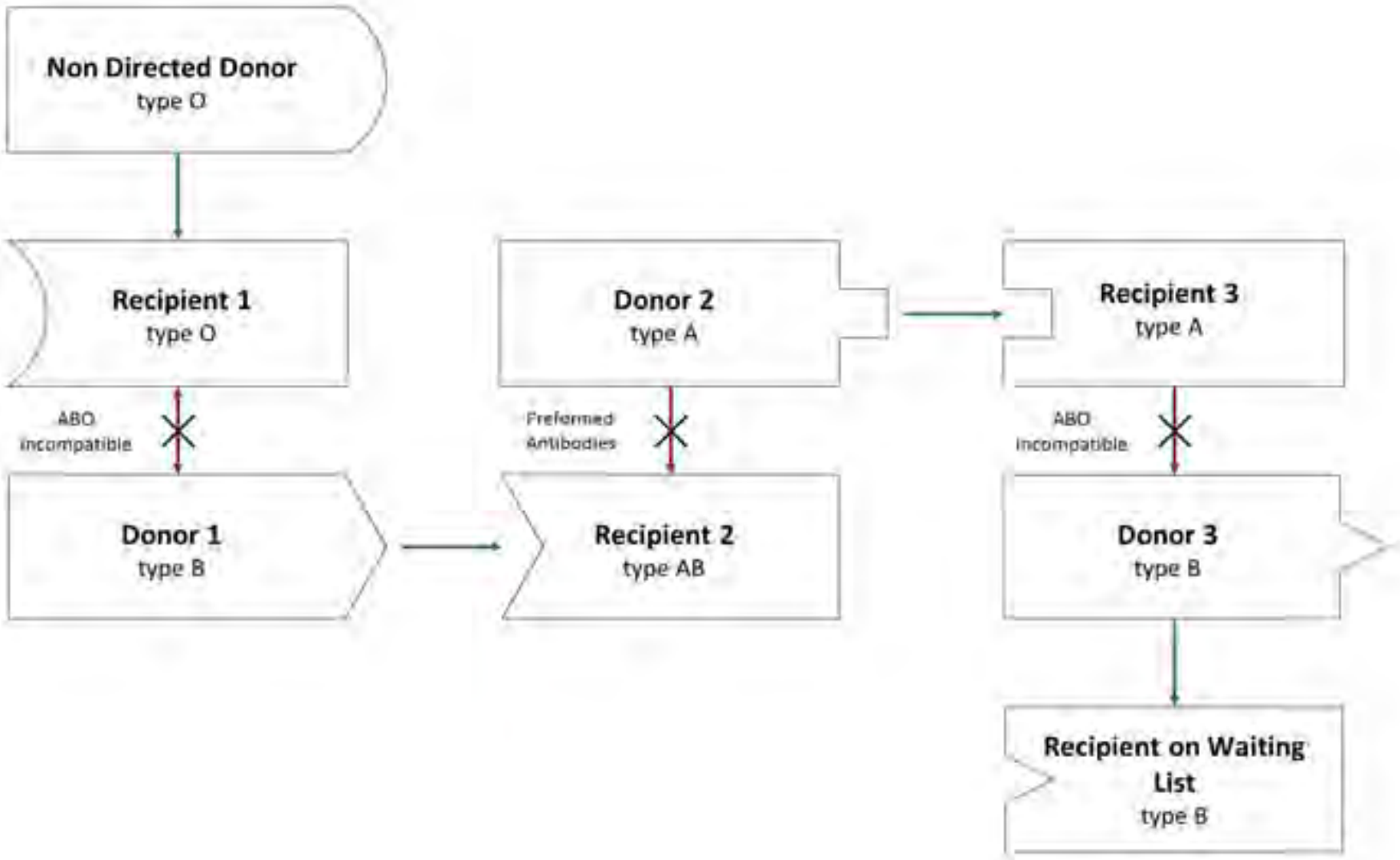
"Conventional" Kidney Exchange



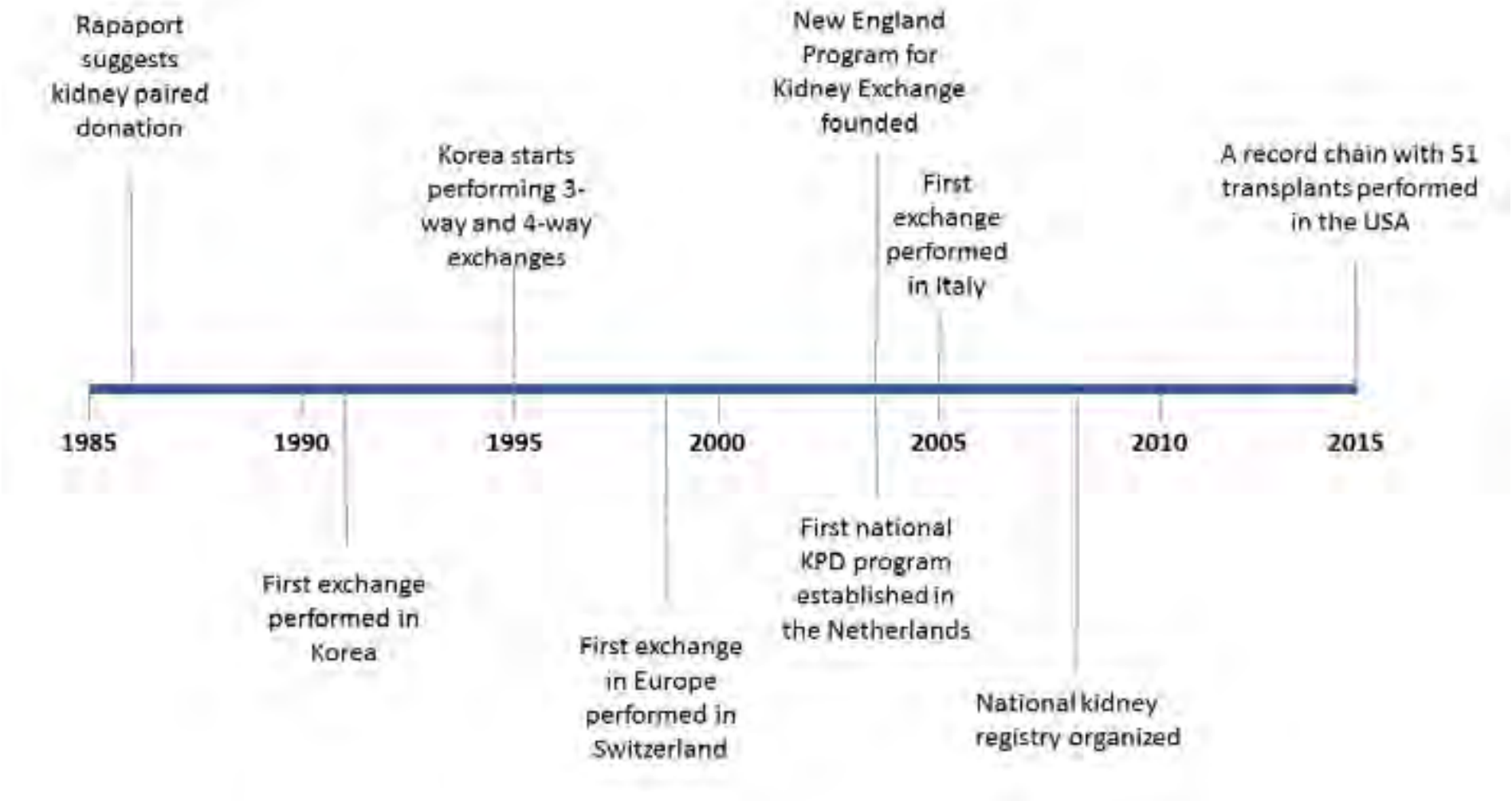
List Exchange



Chain


Non Directed Donor
type O
Recipient 1
type O
ABO
incompatible
Donor 1
type B
Donor 2
type A
Preformed
Antibodies
Recipient 2
type AB
Recipient 3
type A
ABO
incompatible
Donor 3
type B
Recipient on Waiting
List
type B

History


Rapaport suggests kidney paired donation
Korea starts performing 3-way and 4-way exchanges
New England Program for Kidney Exchange founded
First exchange performed in Italy
A record chain with 51 transplants performed in the USA
1985
1990
1995
2000
2005
2010
2015
First exchange performed in Korea
First exchange in Europe performed in Switzerland
First national KPD program established in the Netherlands
National kidney registry organized

Pairwise exchange

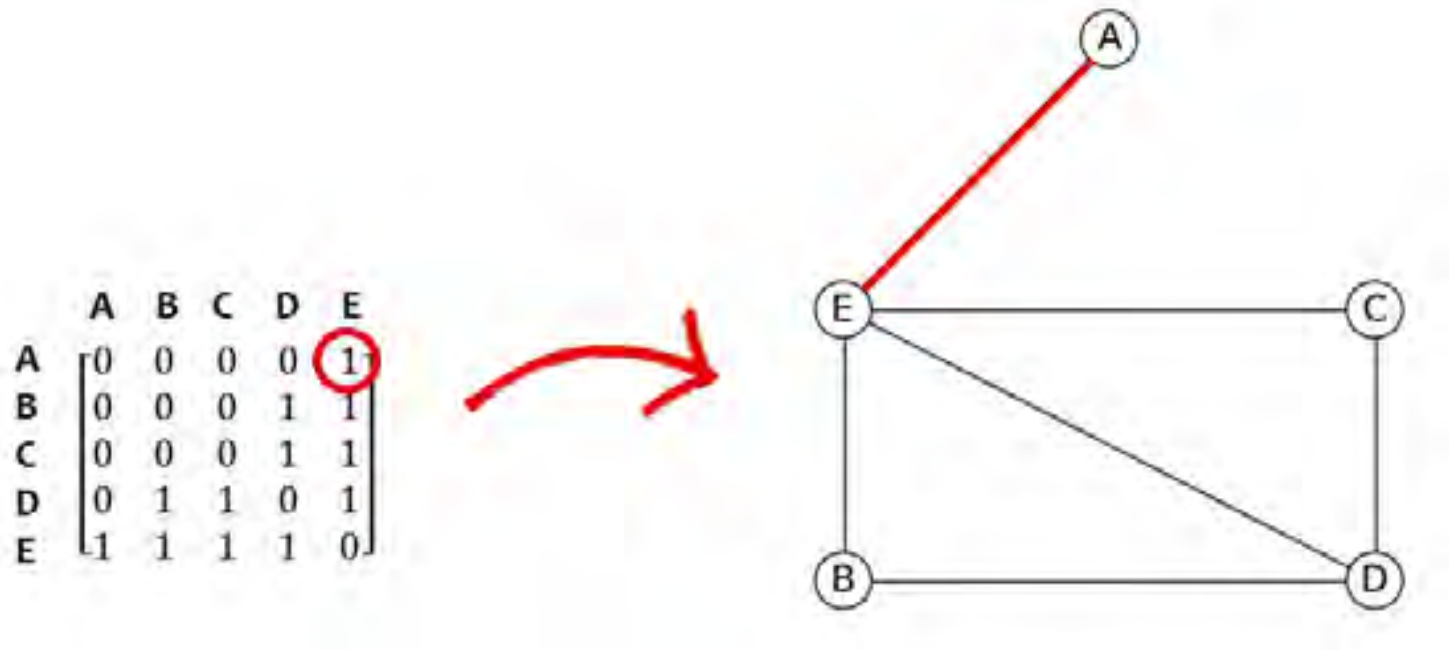
Characteristics of the model

The simplest method is the so called pairwise exchange. Features:

- Only two patients and their donors;
- Patient preferences: indifference among all compatible donors which are strictly better than the associated donor, strictly better of all other incompatible donors

Compatibility matrix and graph

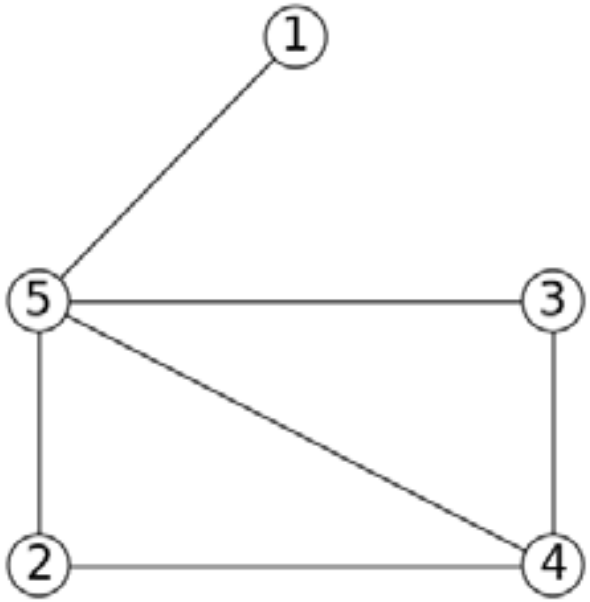
- In the compatibility matrix 1 means that the two patient-donor pairs are mutually compatible
  - for example: the entry AE=1 means that a kidney exchange between couple A e and couple E is possible
- Edges in the graph have the same meaning



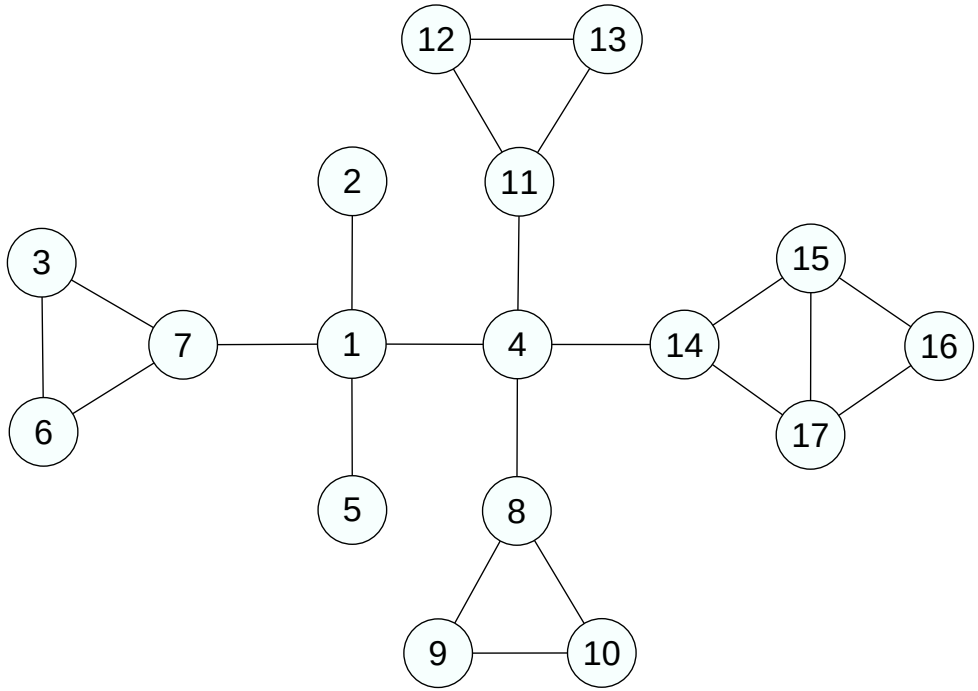
Efficient matching

1. A matching is efficient if it is not possible to add another edge to it to build a bigger matching
2. There can be more than one efficient matching;
3. All efficient matchings have the same number of transplanted patients.

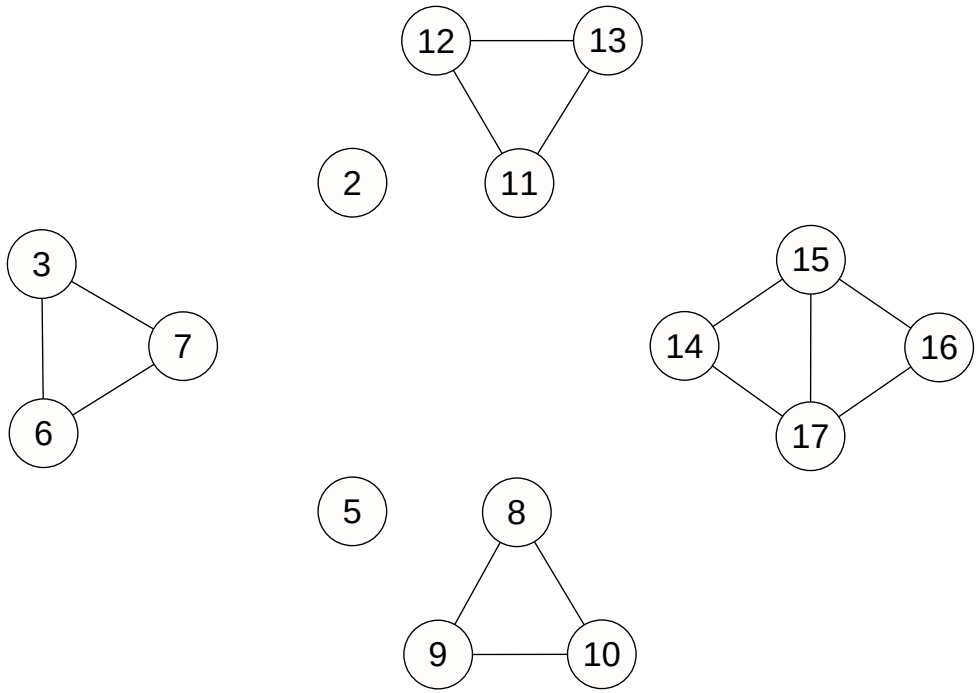
Example: priority mechanism



$$\text{STEP } 0 = \{(1,5)(2,4);(1,5)(3,4);$$
$$(2,5)(3,4);(2,4)(3,5)\}$$
$$\text{STEP } 1 = \{(1,5)(2,4);(1,5)(3,4)\}$$
$$\text{STEP } 2 = \{(1,5)(2,4)\}$$

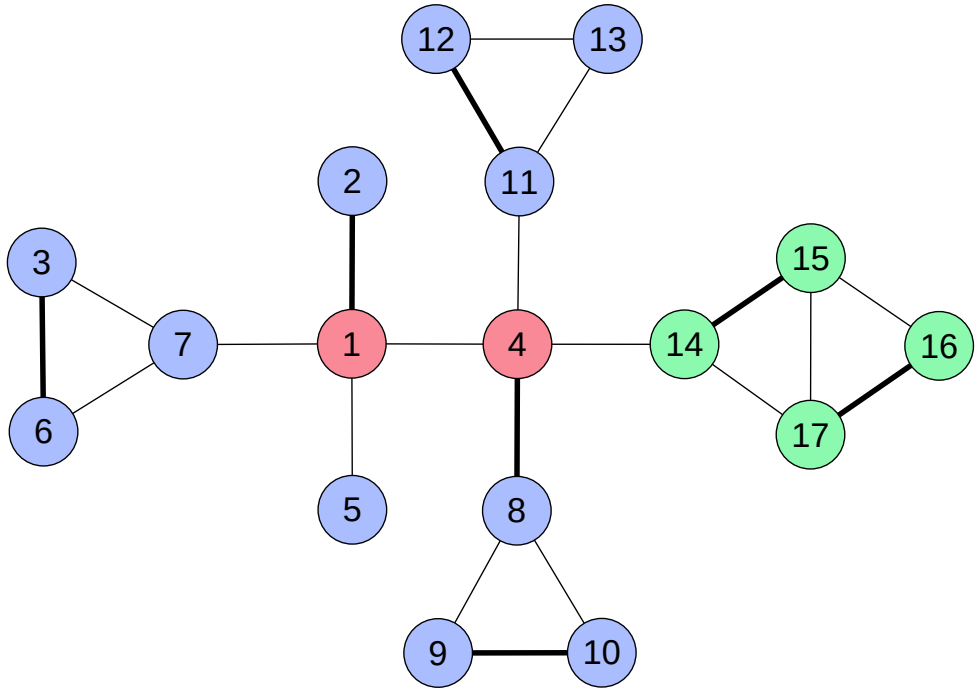


- Identify those patients who would receive a transplant in any maximal matching (overdemanded)
- remove them from the graph



The reduced graph has

- some odd components (underdemanded)
- some even components (perfectly matched)



UNDERDEMANDED OVERDEMANDED PERFECTLY MATCHED

- perfectly matched patients are matched with each other
- each overdemanded is matched to an underdemanded (priority ordering)
- the remaining underdemanded are matched with each other (priority ordering)

Top trading cycles and chains

Preferences

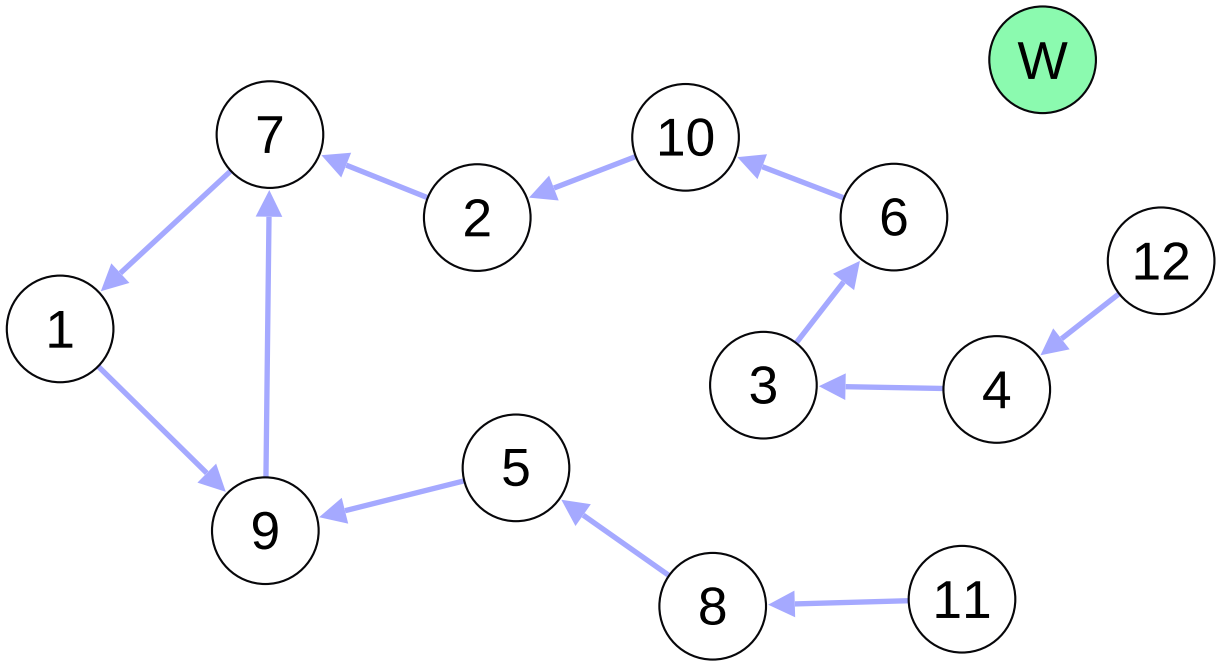
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
D9	D7	D6	D3	D9	D10	D1	D5	D7	D2	D8	D4
D4	D10	D3	D9	D3	W	D9	D3	W	D3	D1	D12
D1	W		D11	D8		D7	D11		W	D5	
			W	D2			D8			W	
				D5							

$$p = patient(recipient); d = donor; w = waitinglist$$

Preferences of patient 1:

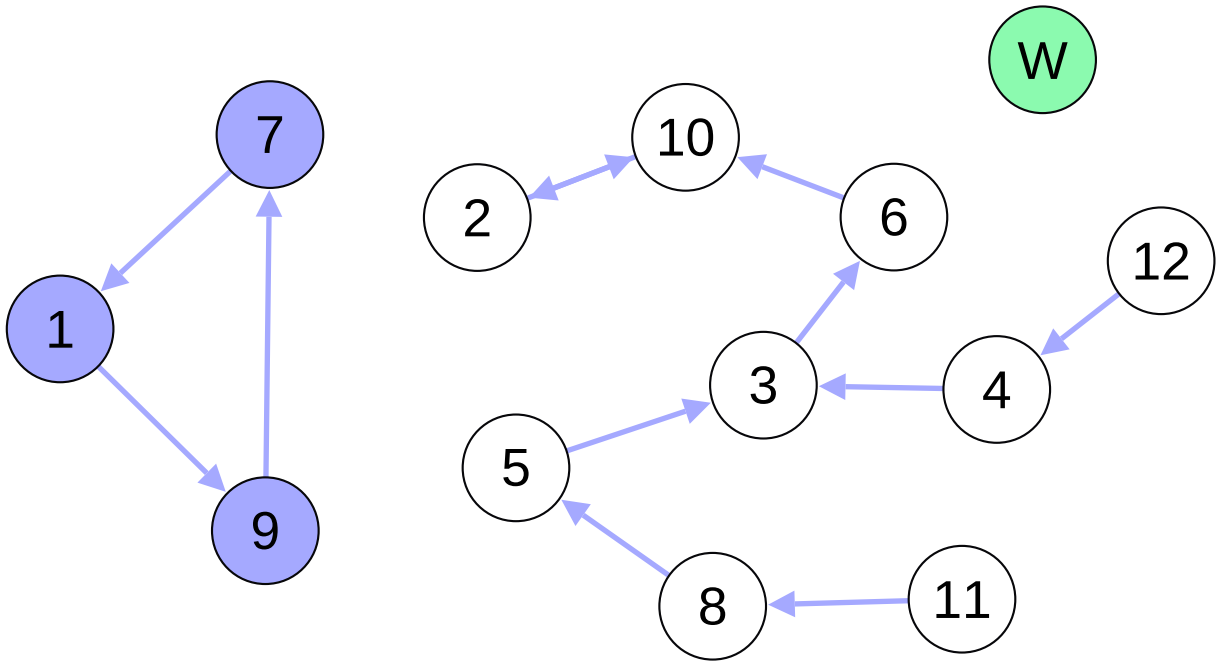
1. donor of patient 9
2. donor of patient 4
3. her own donor (there are no other compatible donors)

Step 1



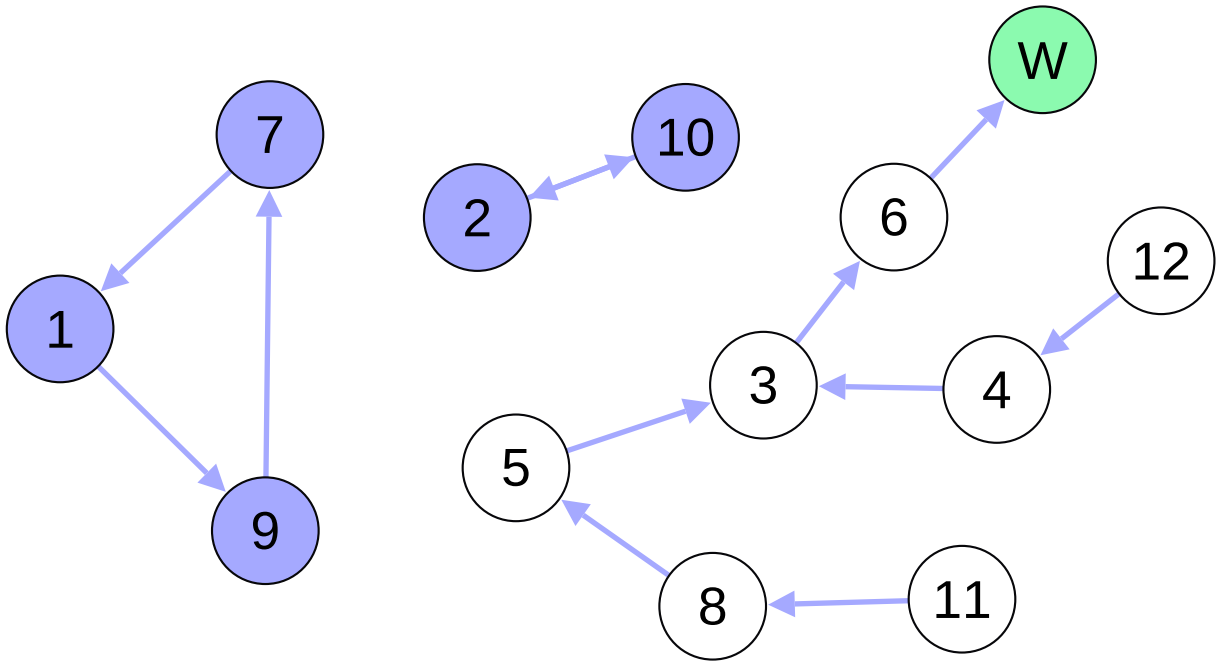
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
D9	D7	D6	D3	D9	D10	D1	D5	D7	D2	D8	D4
D4	D10	D3	D9	D3	W	D9	D3	W	D3	D1	D12
D1	W		D11	D8		D7	D11		W	D5	
			W	D2			D8			W	
				D5							

Step 2



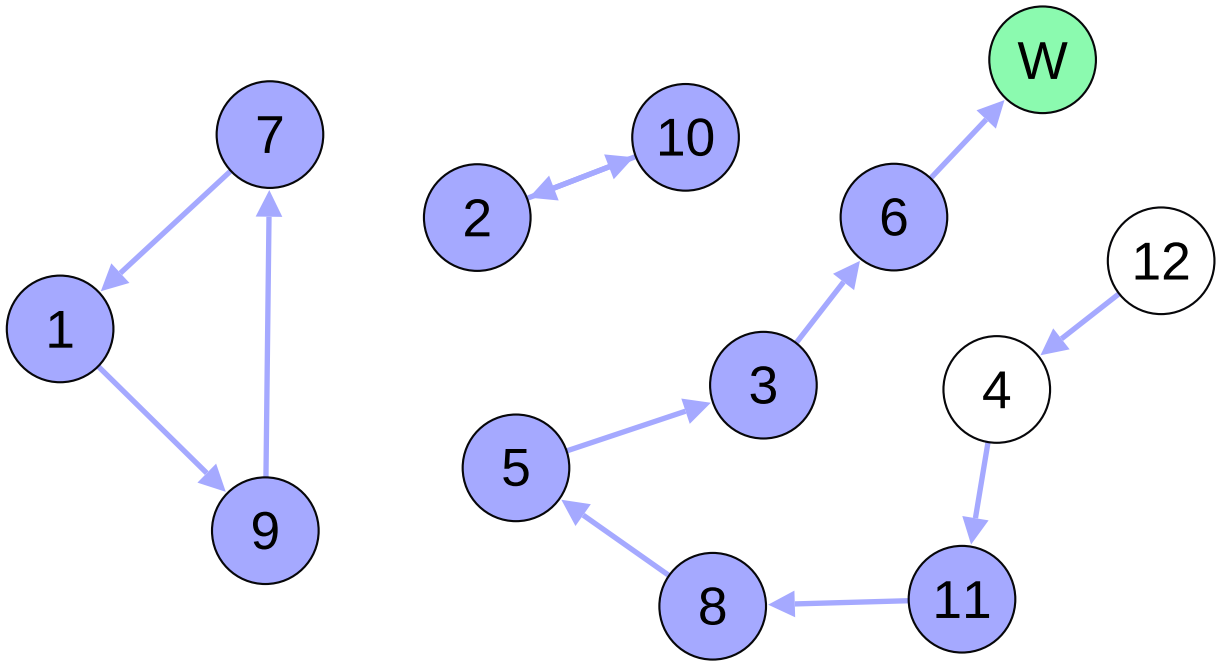
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
D9	D7	D6	D3	D9	D10	D1	D5	D7	D2	D8	D4
D4	D10	D3	D9	D3	W	D9	D3	W	D3	D1	D12
D1	W		D11	D8		D7	D11		W	D5	
			W	D2			D8			W	
				D5							

Step 2



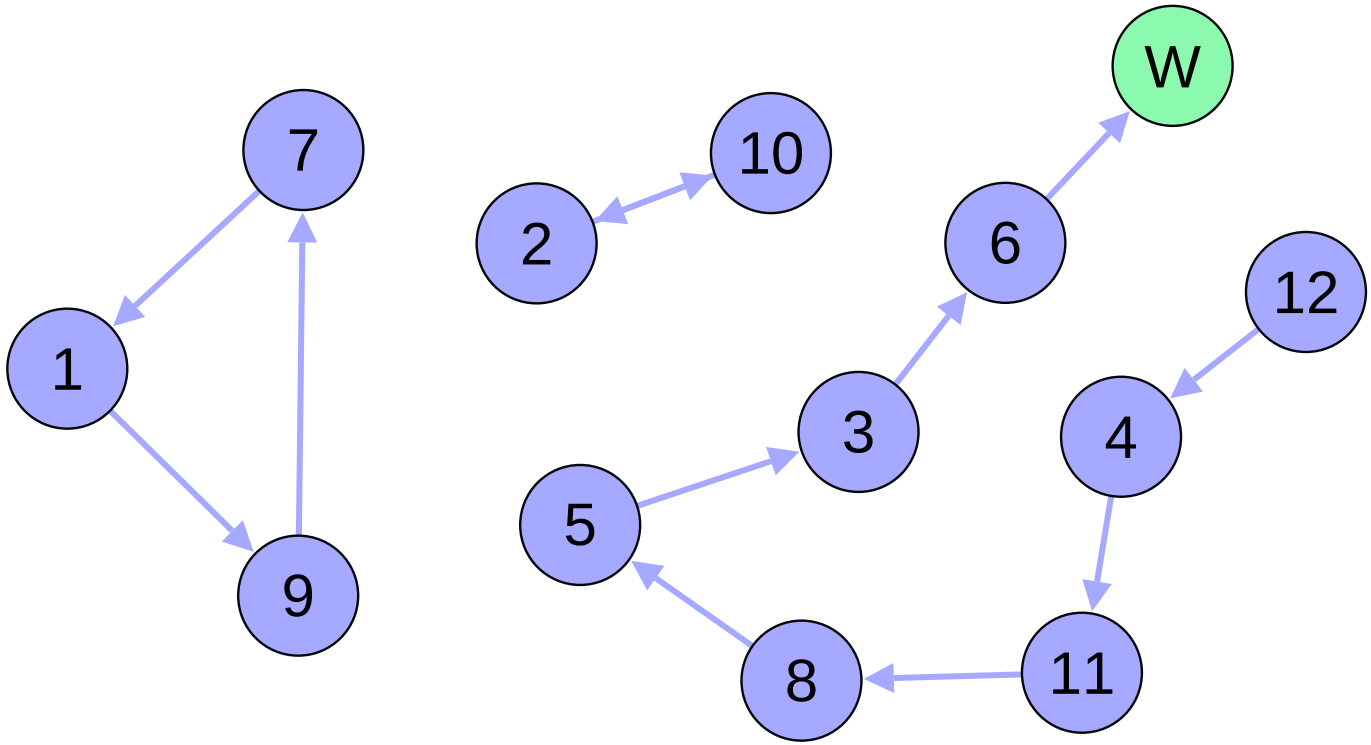
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
D9	D7	D6	D3	D9	D10	D1	D5	D7	D2	D8	D4
D4	D10	D3	D9	D3	W	D9	D3	W	D3	D1	D12
D1	W		D11	D8		D7	D11		W	D5	
			W	D2			D8			W	
				D5							

Step 3



P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
D9	D7	D6	D3	D9	D10	D1	D5	D7	D2	D8	D4
D4	D10	D3	D9	D3	W	D9	D3	W	D3	D1	D12
D1	W		D11	D8		D7	D11		W	D5	
			W	D2			D8			W	
				D5							

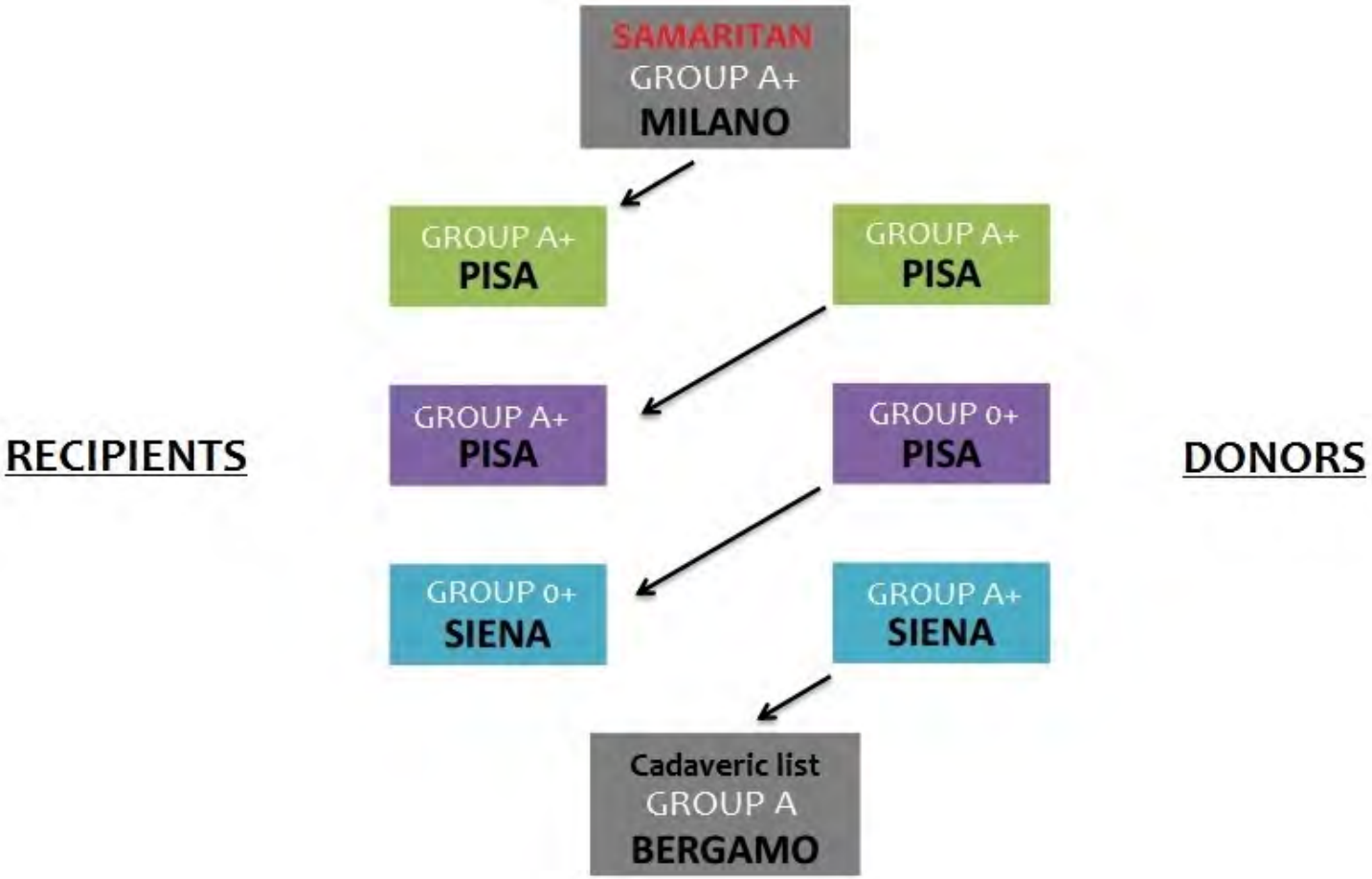
Final matching



Good Samaritan donors

- With Good Samaritan donation, a person donates a kidney to an unknown recipient, starting a chain of transplants
- Chains starting with a samaritan can be very long, since transplant in this case, differently from the case of cycles, need not be contemporary

A chain in Italy in 2016



«60 lives, 30 kidneys, all linked »

One of the longest chain performed in the Usa starting with a samaritan donor (New York Times 2012)

Conclusions: towards the future

1. In November 2019 two chains originated by a deceased donor both involved three patients and their donors, from three different regions: this Program is called Deck protocol and has been invented in Italy;
2. In October 2019 a second crossover exchange has been performed between Spain and Italy, under the Program SAT (South Alliance for Transplant)
3. Up to today in Italy, thanks to 20 crossover chains, 55 transplants have been performed, involving 41 pairs donors/recipients and 8 samaritans.