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CENTRE for Clinical Epidemiology and Evaluation

Informing policymaking on epitope/eplet matching in kidney transplantation: Public deliberation and economic modelling

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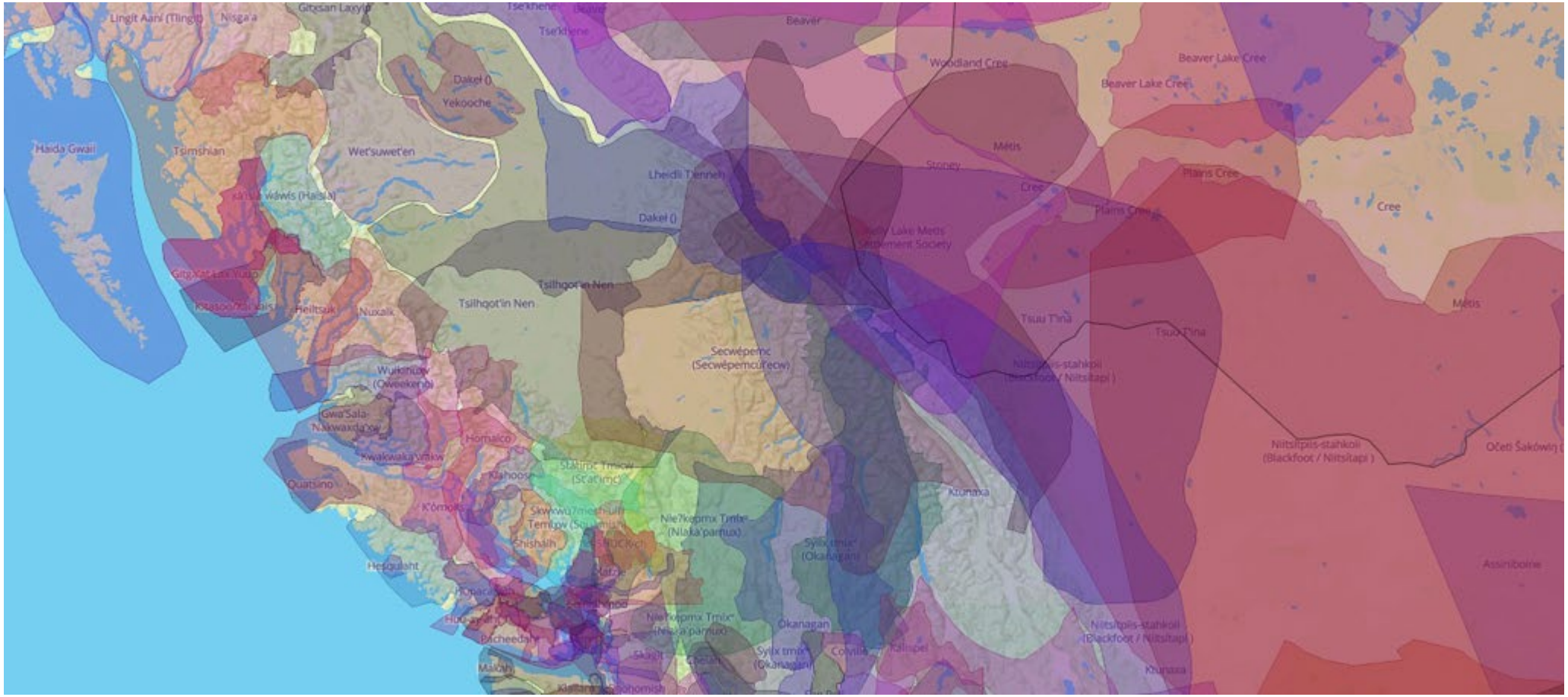
https://native-land.ca/



We acknowledge that this event takes place on the traditional and unceded shared territories of the xʷməθkʷəy̓əm (Musqueam), Skxwú7mesh (Squamish) & səlilwətaʔɬ (Tsleil-Waututh) Nations.

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Disclaimer

- No conflicts of interest to declare
- Large team contributed to planning and development of this work

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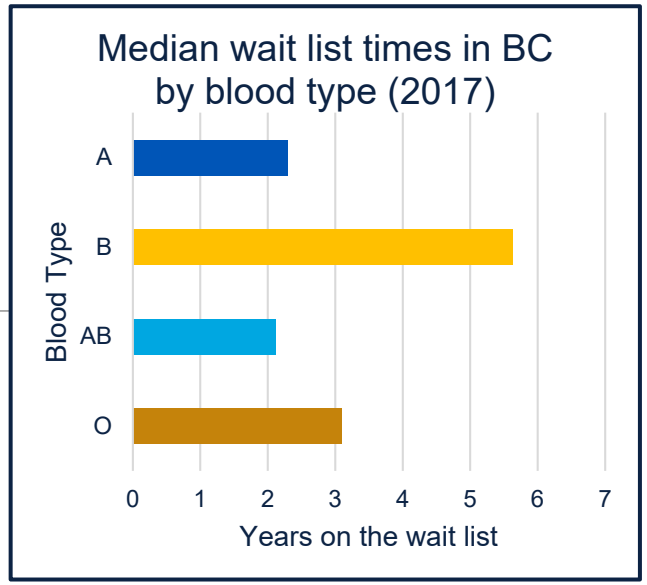
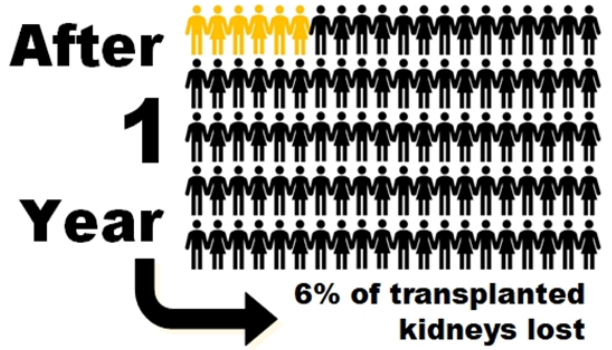
Deceased donor allocation

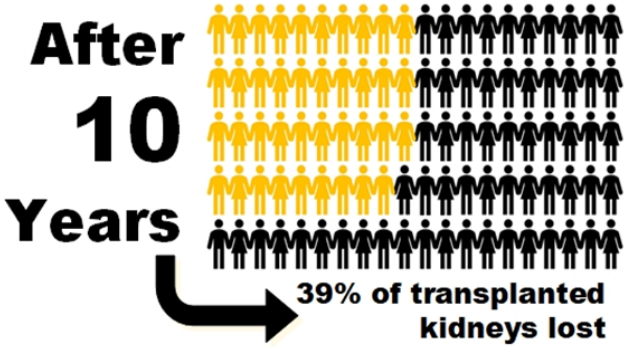


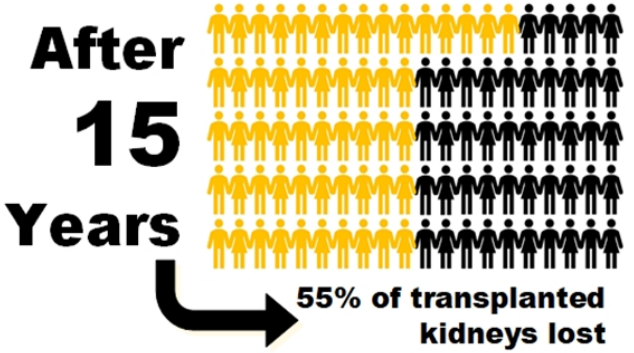
- Supply-demand imbalance for kidneys
- Deceased donor allocation decisions based on…
  - social justice (e.g., waiting time, age)
  - medical need (e.g., medical urgency, blood group compatibility)
- Median wait time in Canada is ~4 years, but varies by…
  - population density differences
  - number of donors
  - characteristics of waitlist candidates (e.g., less common blood types)

Kidney rejection

- Immune system recognizes the transplanted kidney as foreign and attacks it
- Severe graft rejection occurs in up to 30% of kidney transplant recipients
  - Mismatched genes between donors and recipients
  - Some drugs may work better for different genes

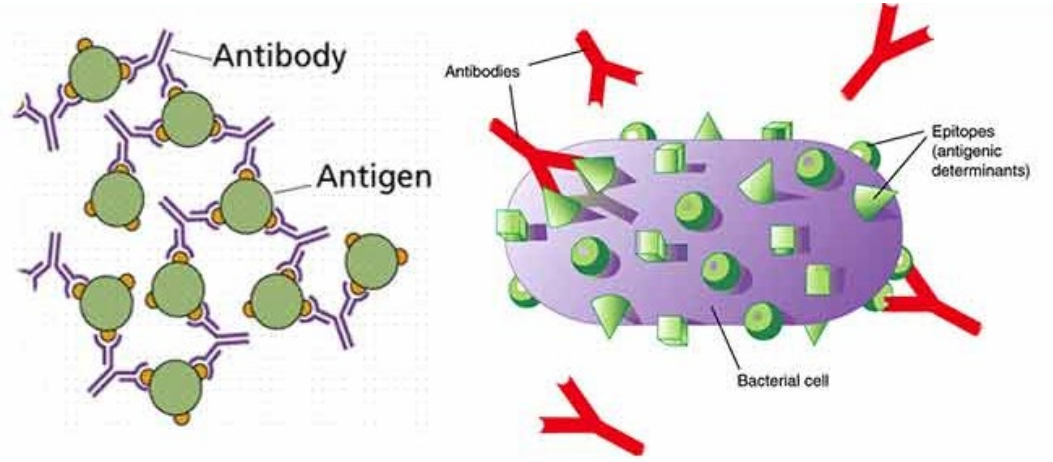


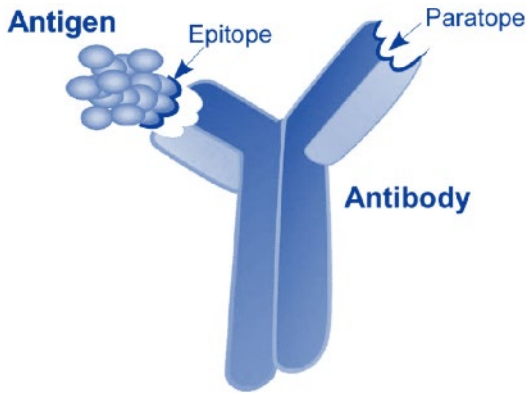




https://microbiologyinfo.com/differences-between-antigen-and-antibody/

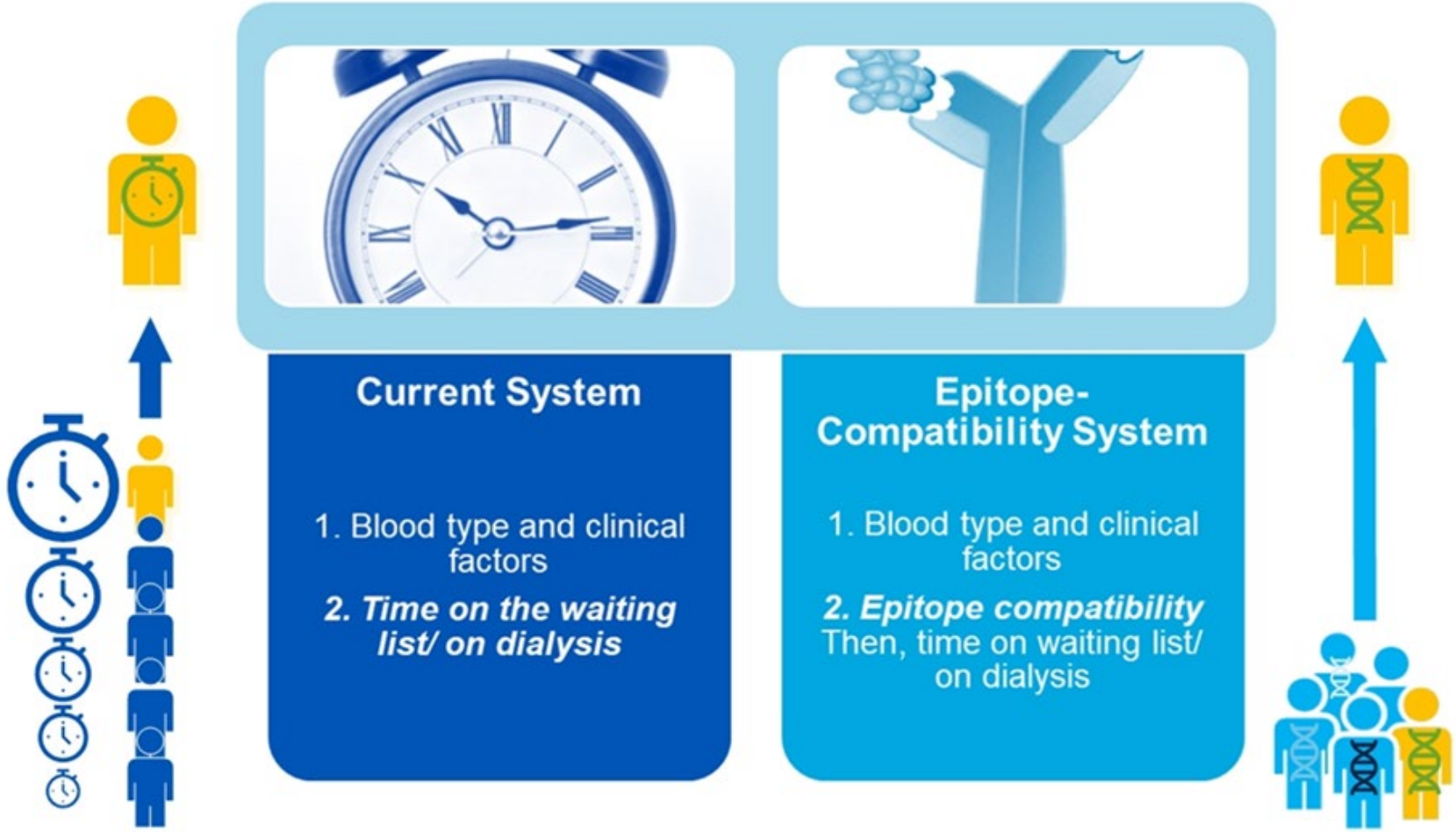
What is epitope compatibility?





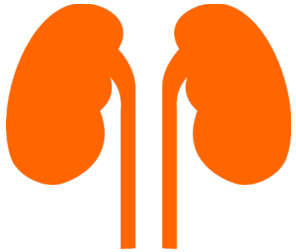
- **Epitope compatibility:** comparing specific immune system molecules between kidney donors and recipients
  - Some epitope mismatches cause antibodies to develop
  - Could reduce kidney rejection
  - Will change order candidates are offered kidneys and waiting time

How would epitope compatibility change kidney allocation?



Importance of public perspective

- Kidney failure is common
- Organ donation hinges on public trust
- **Equity-efficiency trade-offs** from epitope compatibility-based allocation (benefits & risks to changing the criteria)

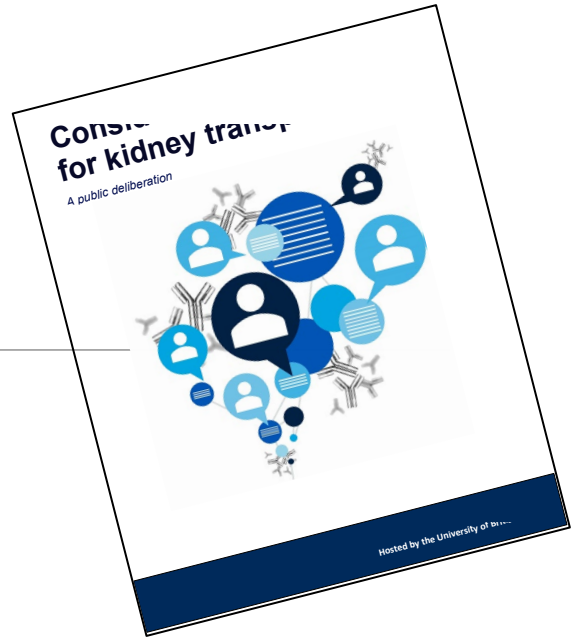


Topic: *How do we establish **a trustworthy process** for the distribution of kidneys for transplantation, given this new science (i.e., targeted epitope compatibility)?*

Public deliberations

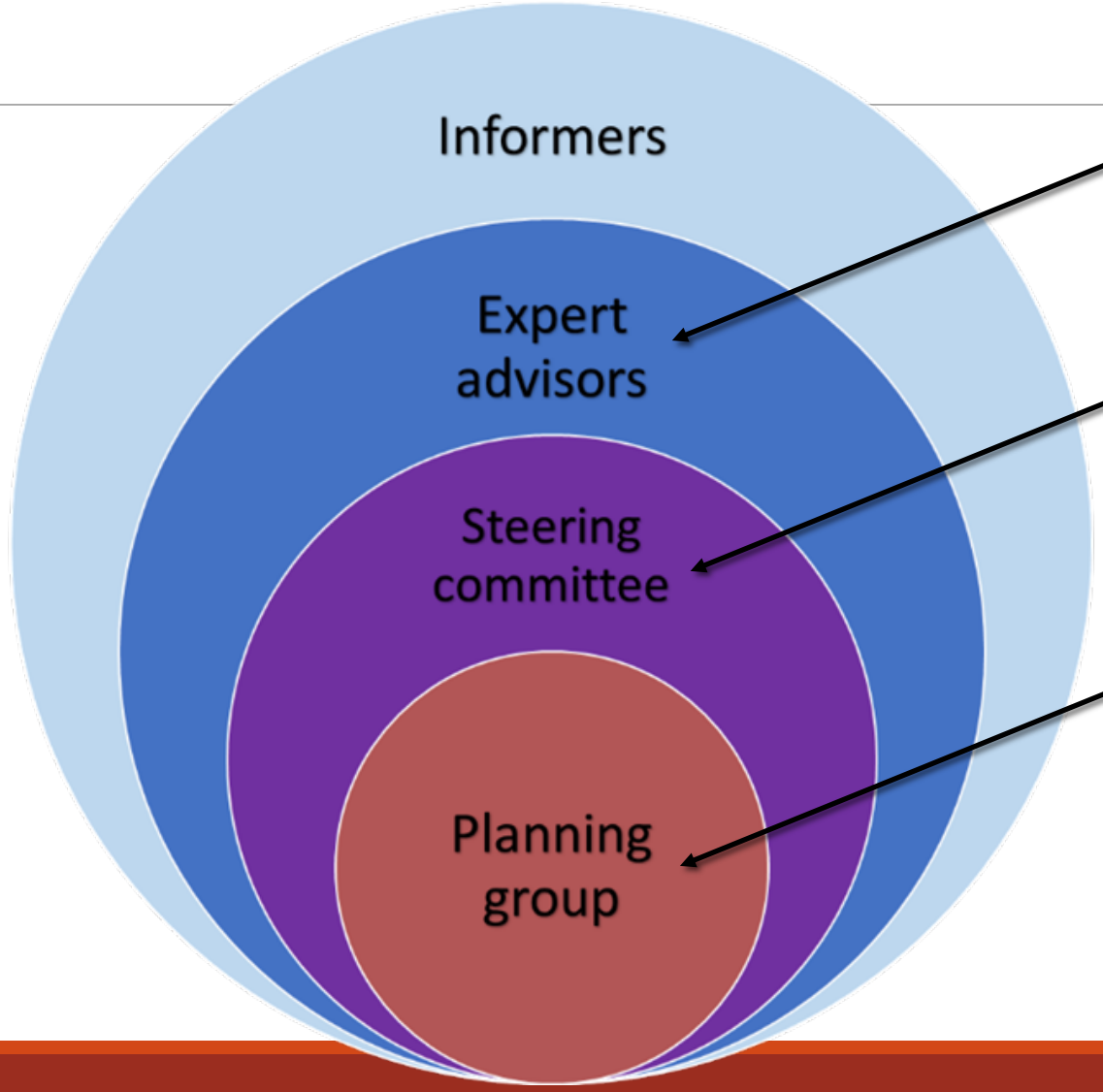
- Community discussion on **substantial and complex problems**
- Used when **evidence and values** are important
- Used when people **need time** to understand and consider the relevant issues
- **Enables better decision-making** by examining the **potential implications of decisions** amongst general population

Key attributes



- Provide **background information**:
  - Information booklet
  - Expert speaker presentations
- Facilitated **small & large group discussions**:
  - Small group of **25–30 members of the public**
  - Focussed policy-informed questions to answer
  - ‘Scenarios’ provided to elicit deliberation on questions
- Form **recommendations**:
  - Voted on (for, against, abstain)
  - Reasons/justification included

Deliberation planning & development



Clinical experts, Indigenous Knowledge Keeper, 14 Patient Advisors

Research team + “Policy receptor” groups

Research team, clinical & methodological experts, 4 patient advisors

Deliberation session details (Nov-De

Online	Duration	Who	Focus
Session 1	2 hours	All participants	• Expert speakers • Overview of deliberation
Session 2	2 hours	Small groups x4 (6-8 participants)	• 'Hopes and concerns' for deliberation • Relationship building

Session 3	2 hours	All participants	• Discuss deliberation questic
			  • Explore views/beliefs
			  • Form & vote on recomr

Session 4	2 hours	All participants	
Session 5	2 hours	Policy Panel (4) + All participants	• Review & discuss recomme • Ask participants for clarifica

EXPERT SPEAKERS

1. **Indigenous knowledge keeper**
2. **Nephrologist**
3. **Bioethicist**
4. **Patients** (x2)

POLICY PANEL MEMBERS

1. **BC Transplant**
2. **Trillium Gift of Life**
3. **Transplant Quebec**
4. **Canadian Blood Services**

Deliberation questions

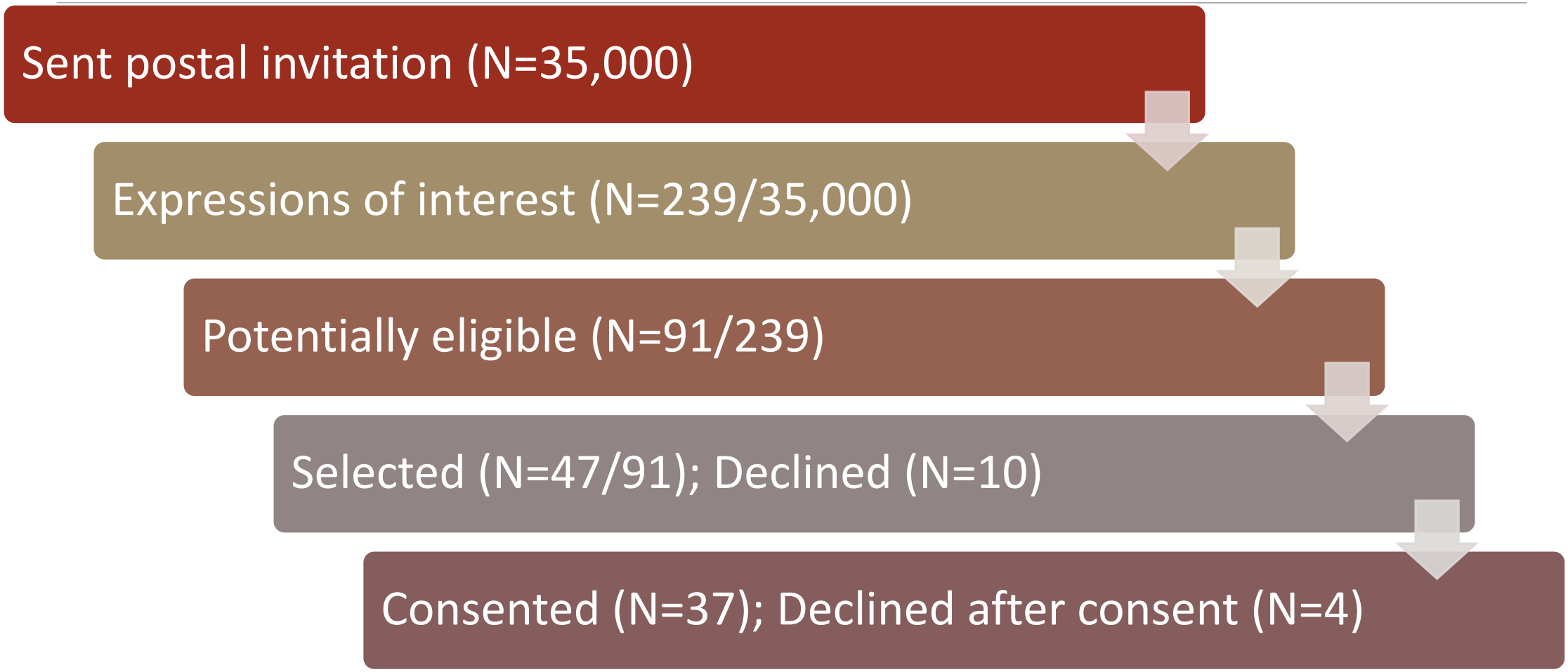
1. *How can epitope compatibility be implemented in a way that is fair for transplant candidates?*
2. *What are important considerations in the way kidney allocation policies and decisions are made?*

Analyses – Two levels

1. Deliberative output: recommendations, votes, and collective reasons for the votes

2. Qualitative analysis: focused on **participants' values and guiding principles**, shared in discussions and recommendations
   - Standard thematic or content analysis *not* appropriate
   - Used line-by-line coding, deductive (ethical principles in healthcare) & inductive (open coding) approaches

Recruitment



* Participants from rural/remote locations (N=4)

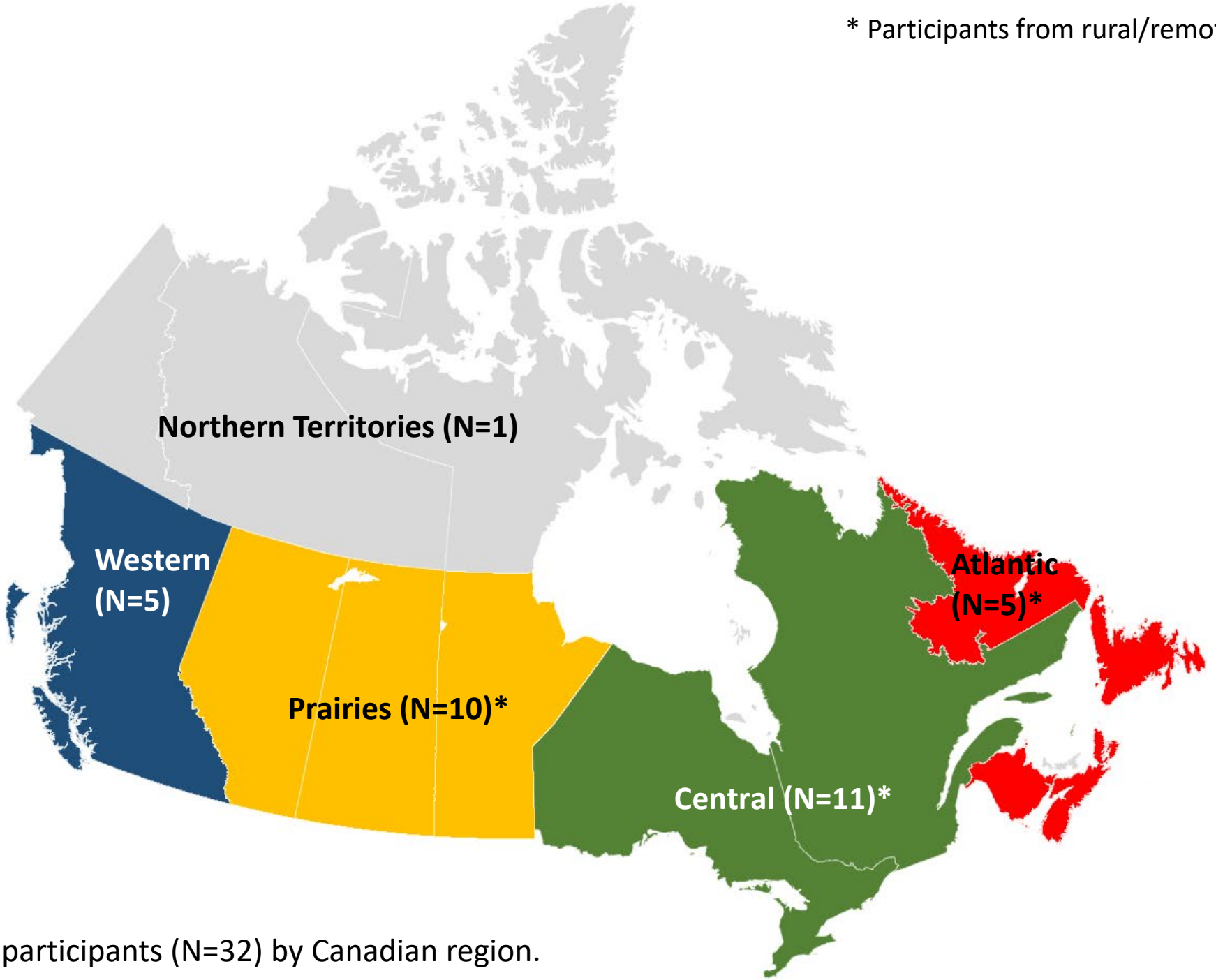


Figure 1. Number of participants (N=32) by Canadian region.

Table 1. Participant characteristics (N=32).

	N (%)
Gender: Female	18 (56)
Ancestry: European	23 (72)
Other	9 (28)
Age group: 18-24 years	4 (13)
25-34	3 (9)
35-49	9 (28)
50-64	10 (31)
65+	6 (19)
Education: High school	3 (9)
College/apprenticeship	4 (13)
Other	25 (78)
Main activity: Working	18 (56)
Retired	8 (25)
Other	6 (19)
Chronic condition present: Yes	8 (25)

Other ethnicities: N (%)

Indigenous	2 (6)
South Asian	1 (3)
East Asian	2 (6)
South/Central American	1 (3)
Arab	3 (9)

Other education: N (%)

Some university	8 (25)
University (BA/BSc level)	11 (34)
University above BA/BSc	6 (19)

Other main activities: N (%)

Looking for work	2 (6)
Going to school	2 (6)
Household work	1 (3)
Long-term illness	1 (3)

Results 1: Recommendations – Question 1

Question 1: *"How can epitope compatibility be implemented in a way that is fair for transplant candidates?"*

Table 2a. Recommendations and distribution of votes for Question 1.

	Recommendations	Y	N	A
Support for adding epitope compatibility	1. Epitope compatibility should be added as an additional criterion (added to the matrix) for transplant candidate selection.	30	0	1
Safeguards and/or flexibility needed	2. Safeguards/flexibility need to be part of epitope compatibility to promote fairness.	28	0	3
	3. When epitope compatibility is being considered, we should also allow people with seriously declining health to receive less- or non-epitope matched kidneys.*	23	3	1
	4. Quality of life should be considered as a priority.	11	12	7
	5. Deteriorating health should be considered as a priority.	20	5	5
	6. Epitope matching should be given high, but not absolute priority in the allocation of kidneys.	29	0	1

* Session went overtime and 4 participants were unable to stay longer and vote.

Recommendations – Question 2

Question 2: "*What are important considerations in the way kidney allocation policies and decisions are made?*"

Table 2b. Recommendations and distribution of votes for Question 2.

	Recommendations	Y	N	A
Transition plan and period	7. There needs to be an ongoing comprehensive education program for the public, beginning with the transition to epitope matching.	27	1	2
	8. There needs to be a transition period and plan before starting the epitope matching system.†	25	0	2
Ongoing monitoring and assessment	9. Assessing epitope compatibility outcomes at least every 5 years and communicate results widely to patients, healthcare professionals, and public, whether successful or not.	29	0	0

† Session went overtime and 3 participants were unable to stay longer and vote.

1. Epitope compatibility should be added as an additional criterion (added to the matrix) for transplant candidate selection.

Votes & Reasons for votes:

FOR: N=30

- Uncertainty around effectiveness of epitope matching; may not lead to better kidney health in long term. Additional criteria added to existing system – balanced way to do it.
- Another tool in the kit
- Can closely monitor “perfect match” to gather data; if effective, transition to more of a priority.
- Preserves fairness already inherent in the system; you don’t lose fairness already in system.
- Recommending a dual system in a sense: High risk individuals not overlooked
- We have the science therefore should not disregard it
- Transition stage would feel better for people on waitlist because hybrid.

AGAINST: N=0

ABSTAIN: N=1

- I want to ditch the wait time – it’s the health state that’s important. I would remove the wait time but I am in favor of adding the epitope.

Results 2 – Qualitative analysis

- Two domains of results:
  1. ***Values*** important to participants, reflected in deliberations
  2. ***Operational principles*** required for acceptable implementation of epitope compatibility

Results 2a – Participants' values

- Five values drove much of discussions:
  - Health maximization
  - Protection/Mitigation of Negative Impacts
  - Science/Evidence-based Healthcare
  - Responsibility to Maintain Trust
  - Fairness

- Two additional values influenced voting and recommendations:
  - Efficient Use of Resources
  - Logic/Rationality

Table 3. Sample of values identified in discussions and their definitions

Value	Definition
Health Maximization	Pursuit of the most health benefit for the most people (**utilitarianism**); improving public/population health
Protection/Mitigation of Negative Impacts	The imperative to put in place **strategies to protect the vulnerable**, or against possible **negative effects**
Science/Evidence-based Healthcare	The goal or obligation of using of health interventions that have been **shown to result in benefit** for patients
Efficient Use of Resources	**Moral duty to use scarce health resources** in the best possible way

Value of Fairness

- Recurring point of discussion, multiple contexts, changed over time
  - Not necessarily mean equal treatment (i.e., sometimes it may be fair for someone to receive special consideration)

"*My big concern would be is someone has been **waiting for such a long time and they cannot seem to get that match** […].*" ~Sandy, Session 2

*"I think yes, it's a concern…I mean **I know it's not fair for someone who has an epitope that doesn't match, but life is not fair**…I wouldn't want it to be unfair in the sense that you know give kidneys to women and not give them to men, or vice versa. Or something like that. But if it's because your epitope causes you your problem, well it's not fair for those who have kidney problems, no? Life is not fair."* ~Jacques, Session 2

Results 2b – Operational principles

- Over time, more complex discussions with **values in conflict**
- Moderated how participants' values could be upheld or balanced against one another
- Upheld participants' values and informed recommendations

Ensuring Fairness
(Value)

"…And so, yeah, like, it isn't fair. I agree. It's ***not fair for somebody who's been waiting on the list****. But I think we're just saying for the most critical patients. And that's why I think it'll be important to figure out that rating system… because you're right, like* ***somebody shouldn't be waiting 15 years****, for sure not. But if somebody is in critical, you know,* ***almost about to die, how can we justify****, like I know,* ***Jane is sitting for 10 years, you know, on dialysis, but Jane is still able to have a transplant eventually****."* ~Evelyn, Session 4

Protection/Mitigation
of Negative Impacts
(Value)

Need for Flexibility
(Operational principle)

Results 2b – Operational principles

- Discussed operational principles to guide acceptable implementation of epitope compatibility; needs for:
  - Flexibility
  - A Transition Plan
  - Transparent Communication
  - Accountability

Conclusions

- First study on public's preferences and values for epitope compatibility-based allocation
- 9 recommendations driven by 5 values: *Health Maximization, Protection/Mitigation of Negative Impacts, Fairness, Science/Evidence-based Healthcare, & Responsibility to Maintain Trust in public healthcare systems*
- Conflicts between values resulted in operational principles: *Flexibility, Accountability, Transparent Communication, & need for a Transition Plan*
  - Enabled maintenance or balancing of participants' values against one another
  - Directly drove formation of all recommendations
- Principles required for acceptable implementation of epitope compatibility

Summary & Future implications

- Consensus on adding epitope compatibility
- But, **safeguards and flexibility** needed
  - Division on specifics
- Plan and **transition period** needed in advance
  - Ongoing public education program
- Regular monitoring of outcomes of epitope compatible transplants, publicly shared

Acknowledgements

- All 32 participants!
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