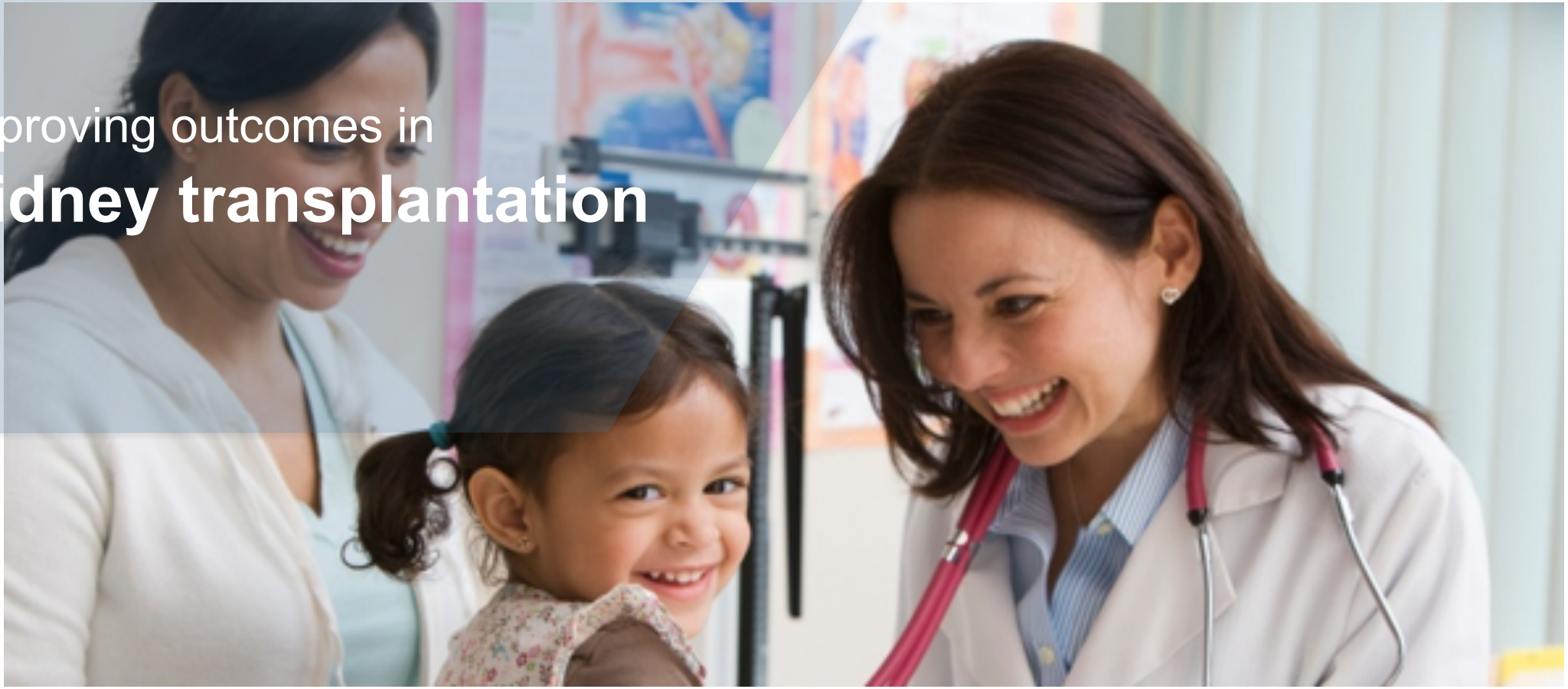
Improving outcomes in

Kidney transplantation



Kidney function and failure

Causes, consequences and treatment options

- Kidneys are vital organs essential for life. They serve both as filters and as factories to maintain normal metabolism and health. Both functions are sensitive to injury and failure.

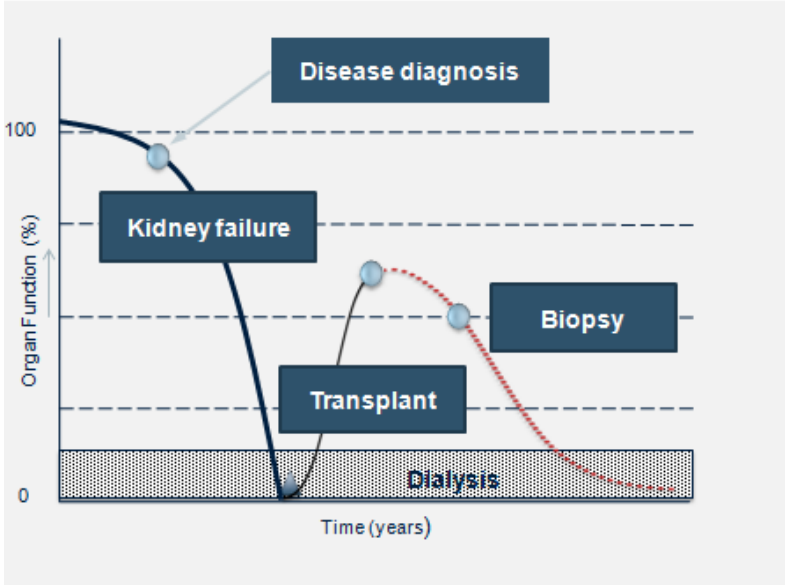
- Kidney disease is now reaching epidemic proportions in all our countries, with a global prevalence approaching 10%. Kidney damage may be due to infection, inflammation, infiltration or secondary to many other diseases.

- Kidney disease has 2 main options for treatment, dialysis or transplantation. While both offer advantages and disadvantages, transplantation is the treatment of choice enabling return to normal health, activity and societal integration with substantial economic savings.

Kidney transplant is the optimal treatment for kidney failure

Transplant offers superb early success

- Rapid recovery and rehabilitation
- normal growth and development (children)
- lower cost < $20,000 vs $90,000 / year (HD)



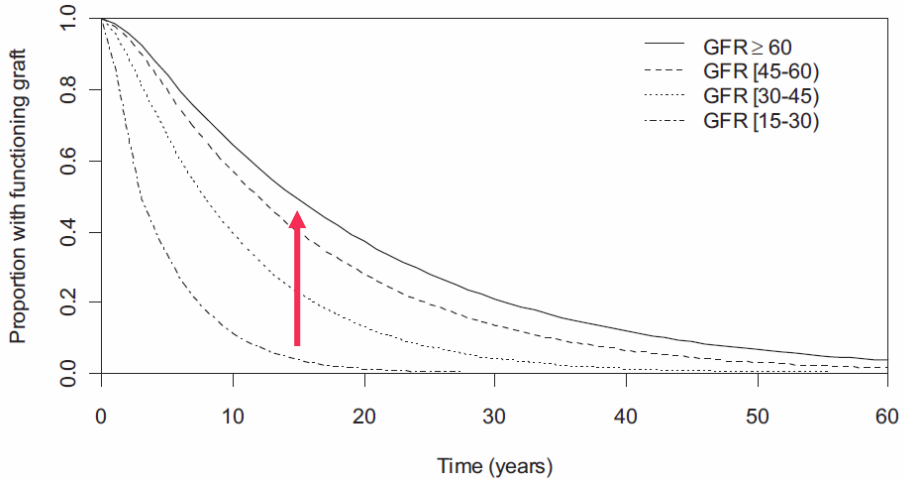
Premature transplant failure is a tragic loss of health and resources

but poor long-term survival

- Few grafts survive beyond 10-20 years
- 500+ patients lose their graft every year
- $1 million incremental lifetime cost of care

Value in Health

Levy et al, 2014



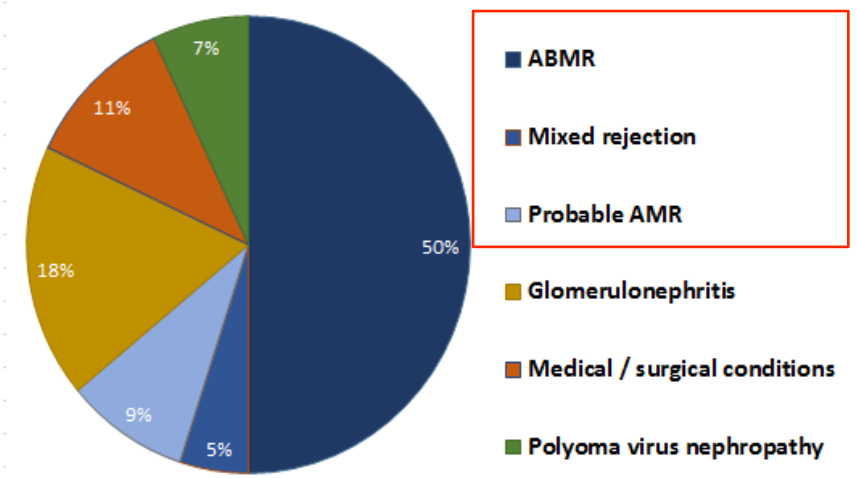
Graft Rejection: the most important cause of failure

Causes of graft failure

- AMR is the cause in 60% of graft losses
- Injury may be slow and silent (sub-clinical)
- treatment is generally ineffective

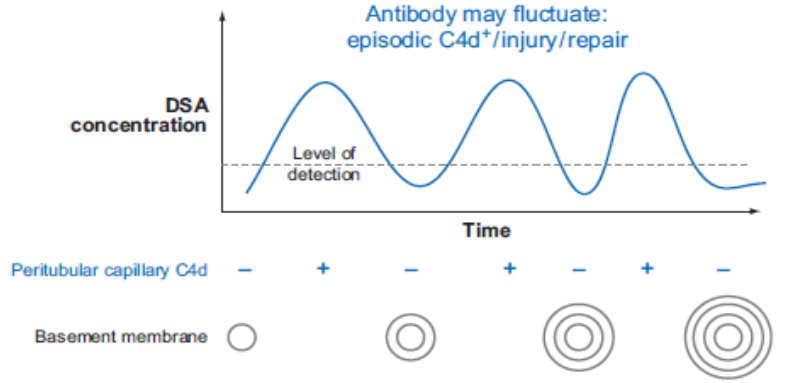
American Journal of Transplantation

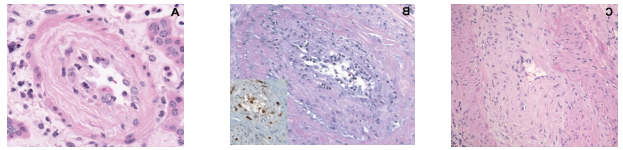
Sellares et al, 2011



Mechanisms of graft injury

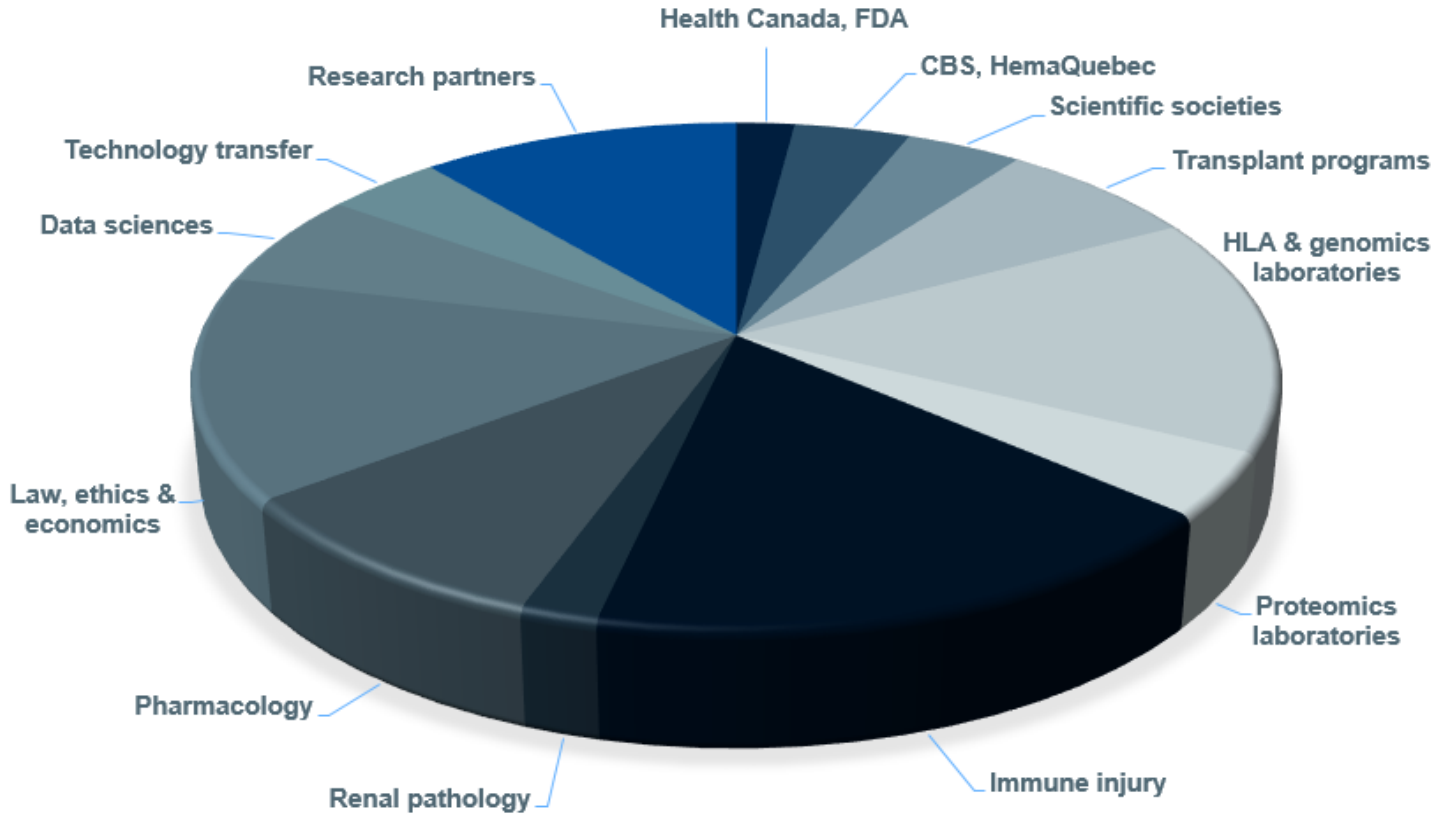
- graft HLA antigens trigger immune response
- T-cells and B-cells are activated and proliferate
- antibodies destroy graft blood vessels & tissues





The Genome Canada Transplant Consortium

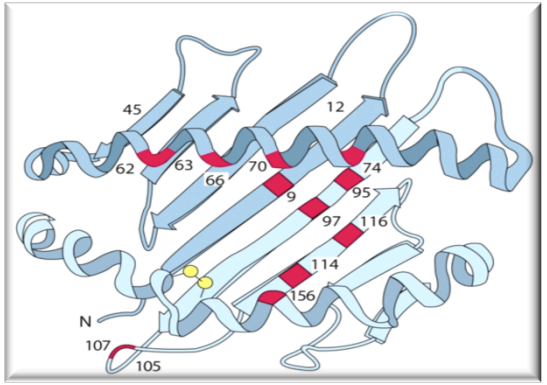
Includes government, academia, healthcare, patients & industry with over 70 investigators and teams in 25 universities across North America and Europe



Precision Medicine Can Prevent this “Failure of Therapy” by:

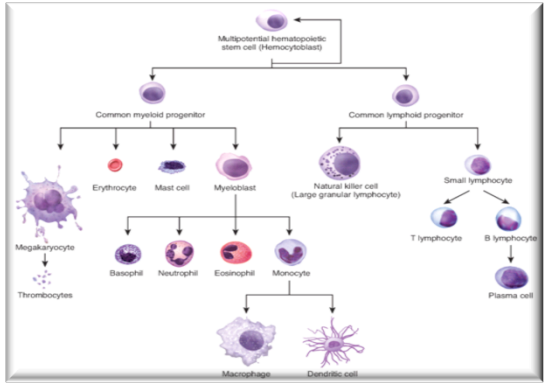
1. Precise matching of donors and recipients

- typing HLA genes and define epitopes precisely
- matching donors and recipients for these epitopes
- sharing matched organs efficiently across Canada



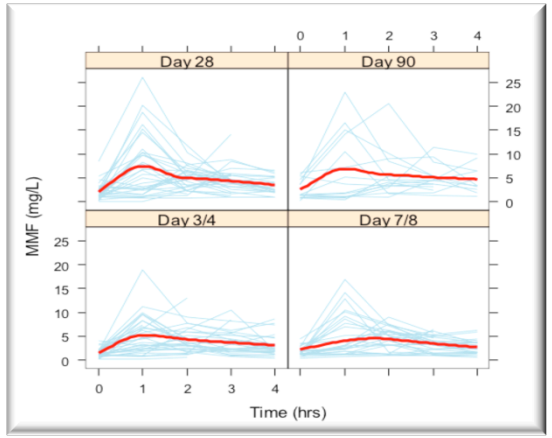
2. Careful monitoring of the immune response

- monitoring immune recovery and competence
- measuring specific response to donor epitopes
- detecting graft injury through non-invasive tests



3. Personalized, informed and responsive therapy

- combining pharmacometric and immune monitoring
- making our current therapy much more effective
- designing innovative and informed therapeutic trials



Personalized treatment to optimize outcomes

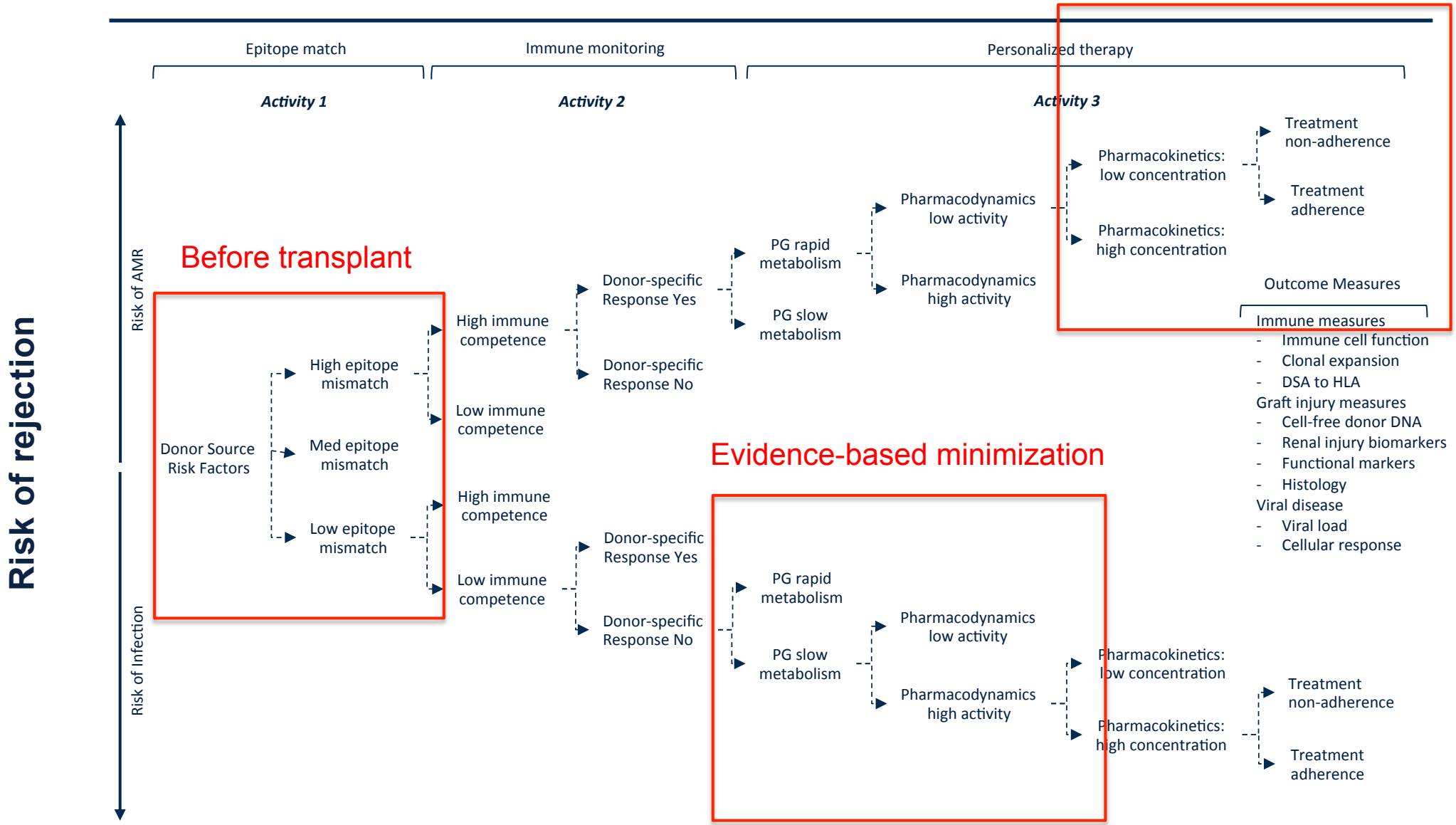
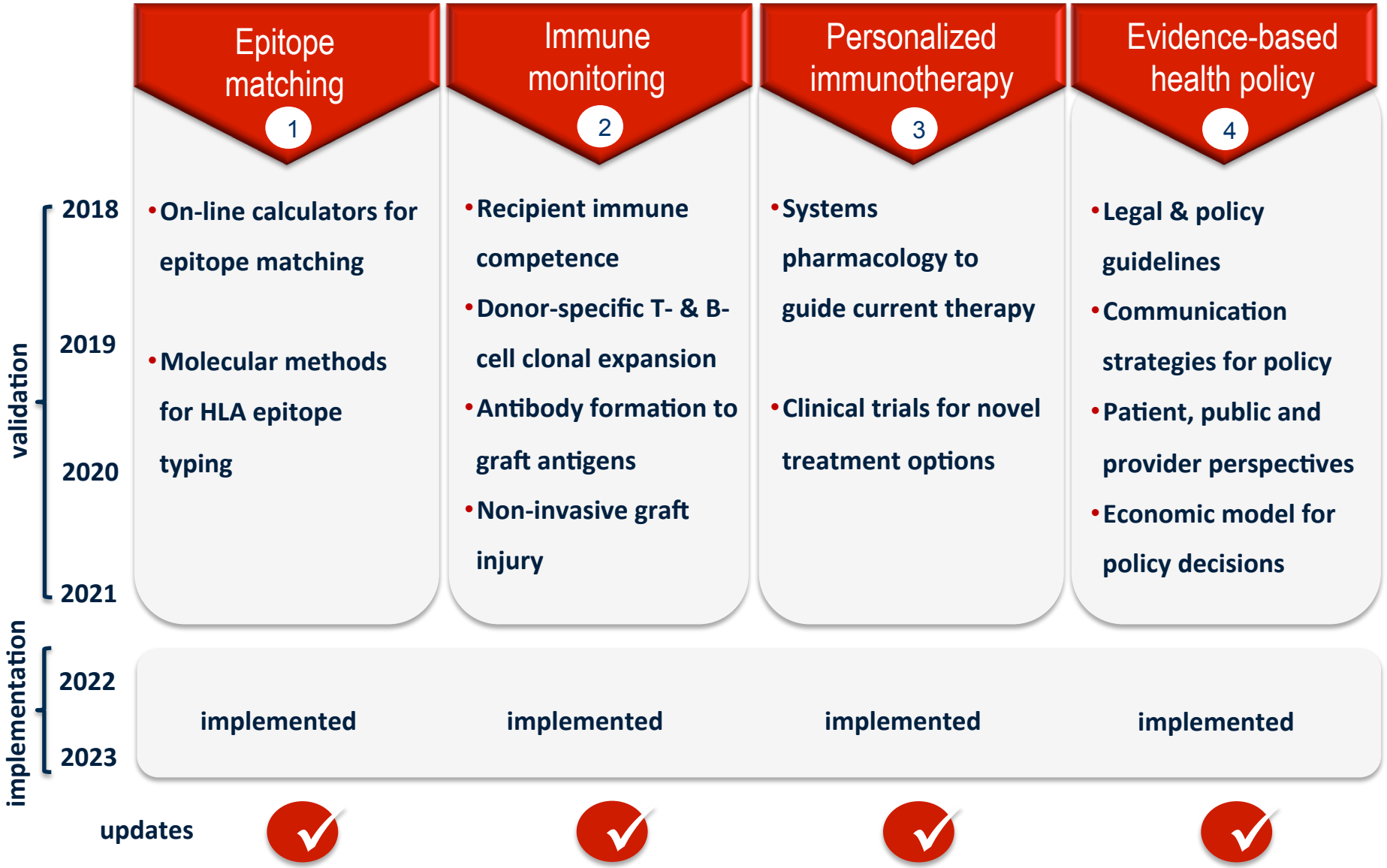
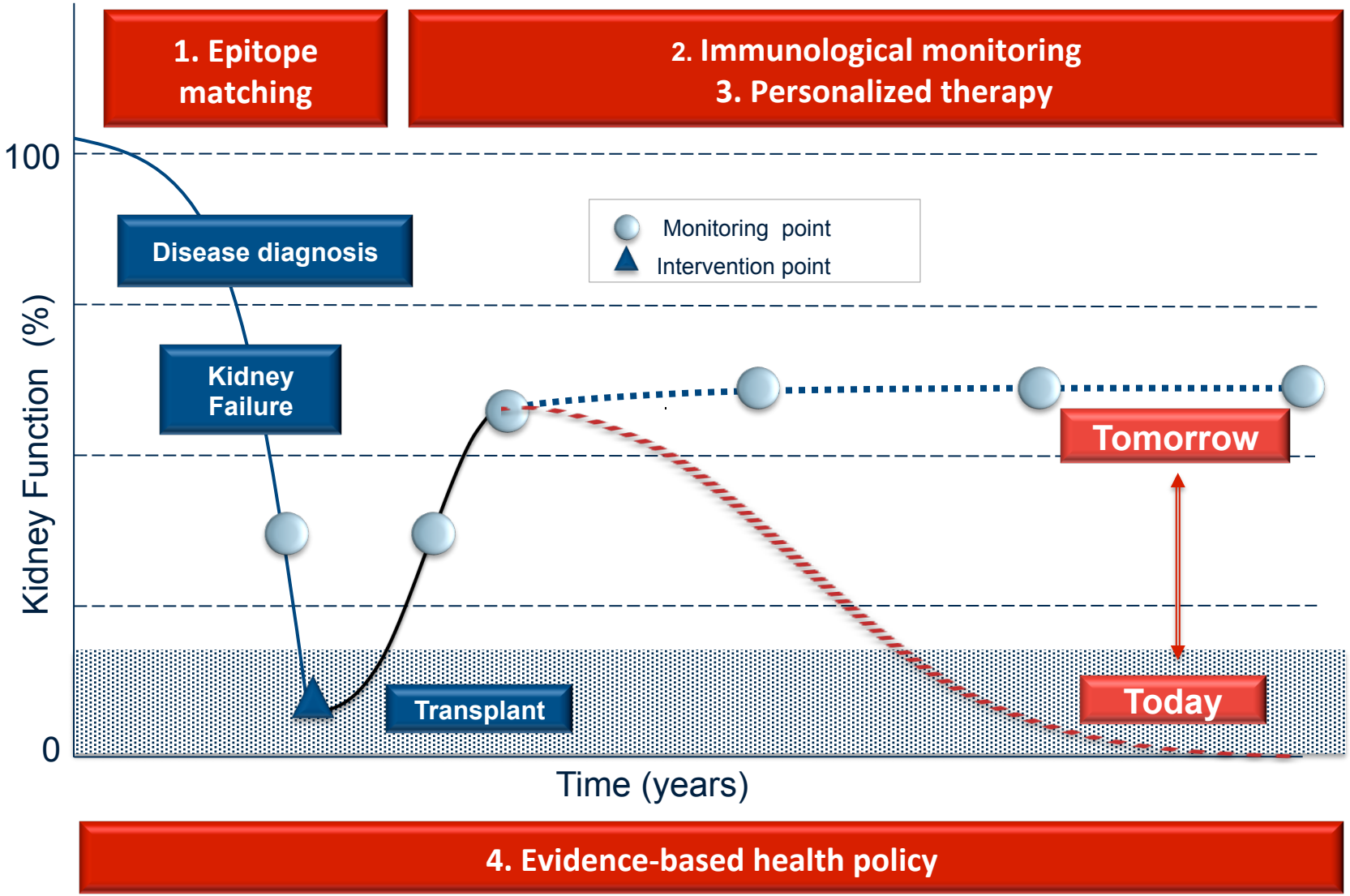


Figure 1: Epitope match, immune monitoring, personalized therapy and outcome measures incorporated in a systems pharmacology therapeutic model. The figure shows two clonal arms of a probabilistic model relating individual factors and overall risk of AMR or infection

New National Programs to prevent graft loss due to AMR



We will employ these new programs throughout the graft course



Benefits to our patients, to providers and to Canada

To patients

1

- reduced premature graft loss (>50%)
- gain in quality-adjusted life years (10-20%)
- reduced care-giver burden and health costs
- potential for life-long kidney graft survival

To providers

2

- new tools for organ typing and allocation
- new tools for immune monitoring therapy
- tools for other organs, stem cells and immune diseases
- models for evidence-based health policy

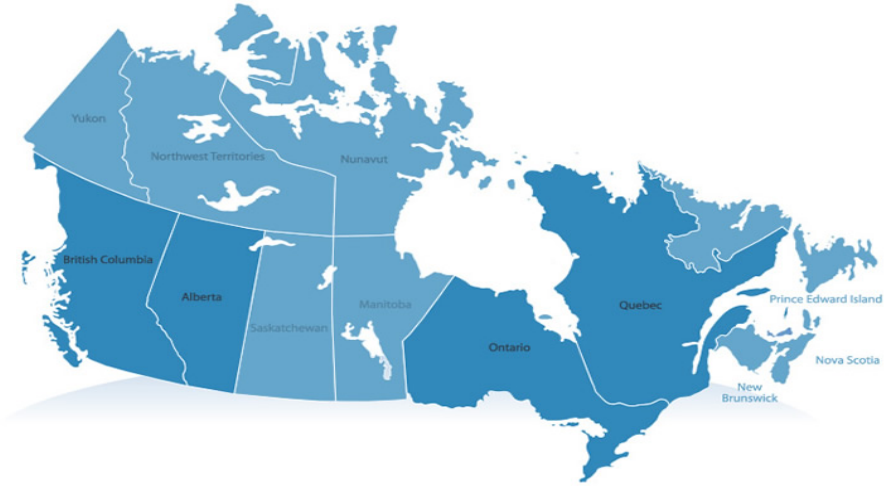
To Canada

3

- reduced costs of renal care ($1 billion / 15 yr)
- major gain in human health and resources
- platform for increased organ access and use
- potential to transform the care of renal failure

National and international transplant programs

Canadian Blood Services Donation and Transplantation Program



Coordinated through national committees and working groups

Provincial programs

- Provincial Transplant Programs
- Organ Procurement Programs
- Provincial Transplant Registries
- Provincial HLA Laboratories
- Provincial Transplant Biobanks

National programs

- Canadian Transplant Registry (CTR)
- National organ waitlist (NOW)
- Canadian cPRA Calculator (*)
- Kidney Paired Exchange (KPD)
- Highly Sensitized Program (HSP)

Support services

- National program coordination
- Strategic planning & operations
- Knowledge translation
- Professional education
- Public education

Activities 1, 2, 3 & 4

The time, team and technologies that will Transform Transplantation!

- prevent rejection, optimize expensive therapy and prolong graft survival
- restore healthy and productive life for patients and their families
- reduce the need for re-transplantation and make more organs available
- extend these benefits to other countries through our global partnerships

I love my new kidney. . and I can keep it for

all my life!