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Interprovincial organ sharing national data report:

Highly Sensitized Patient Program

2013–2018

Organs & Tissues for Life

Permission for use of data

A glossary of terms can be found in Appendix 1.

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For more information, please contact:

Organ and Tissue Donation and Transplantation
Canadian Blood Services
1800 Alta Vista Drive
Ottawa, ON K1G 4J5
Canada

Email: transplantregistry@blood.ca

This report is accessible online at

https://professionaleducation.blood.ca

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Table of Contents

Report development

Annual data reports are developed to provide a comprehensive set of results on critical metrics for the national patient programs National Organ Waitlist (NOW), Highly Sensitized Patient (HSP), Kidney Paired Donation (KPD). These reports are shared with our partners, key stakeholders, the donation and transplantation community, and the general public.

Data sources

Data has been extracted from the Canadian Transplant Registry (CTR). This is the information technology system developed and maintained by Canadian Blood Services in which transplant candidate data is stored and matching algorithms are run. Additional data has also been provided directly by provincial organ and tissue donation and transplant programs and provincial human leukocyte antigen (HLA) laboratories.

Unless otherwise stated, data in this report covers the period of 2013-2018, from the initiation of the HSP program (started in November of 2013) to the end of 2018.

Acknowledgements

Canadian Blood Services acknowledges, with gratitude, the commitment of the Kidney Transplant Advisory Committee, the Living Donation Advisory Committee, the National HLA Advisory Committee, the Heart Transplant Advisory Committee, the Liver Transplant Advisory Committee, the Organ Donation and Transplantation Expert Advisory Committee, and all those whose advice supports the continued growth and achievements of Canadian Blood Services' interprovincial organ sharing programs.

Most importantly, through this report we sincerely acknowledge the generosity of the organ donors, their families and their loved who gave so selflessly to provide hope to transplant candidates across the country.

Foreword from Canadian Blood Services
Amber Appleby, RN, BScN, MM

Director, Organ and Tissue Donation and Transplantation

Canadian Blood Services manages and operates national programs that support interprovincial sharing of organs and the national technology platform essential to the success of these programs.

The Highly Sensitized Patient (HSP) program was established by Canadian Blood Services in collaboration with provincial and territorial governments and organ donation and transplantation programs across the country to increase transplant opportunities for patients needing very specific matches from deceased kidney donors. Through this program, this group of patients now has access to a larger national donor pool, increasing the chance of a match.

Digital technology is transforming the way healthcare services are delivered in Canada. The Highly Sensitized Patient program is supported by the Canadian Transplant Registry (CTR), a sophisticated technology platform operated by Canadian Blood Services. The CTR matches available donor organs with potential waitlist recipients anywhere in the country. This national web-based technology is currently used by more than 400 health professionals coast-to-coast.

Prior to the establishment of the HSP program, kidneys from deceased donors stayed within the province of origin — now, when a deceased donor anywhere in Canada has two eligible kidneys, one kidney is provided through the CTR to the HSP program for matching to potential recipients across the country. Kidneys are shared between provinces using the CTR platform, which tracks all HSP matches, offers and transplants.

This year we are pleased to share individual reports for each of the interprovincial organ sharing programs, which is an evolution from previous reporting that combined annual data for the National Organ Waitlist (NOW), the Kidney Paired Donation (KPD) program, and the HSP program. These new individual data reports also offer greater insights into the growth of each program by reporting on longer periods of data collected.

Collaboration is an essential component of a high-performing organ donation and transplantation system and Canadian Blood Services is committed to working together with provincial organ donation organizations and other system stakeholders to continue to lead national data collection, collation and reporting on HSP program activity.

Canadian Blood Services remains focused on working to deliver a better future for Canadian patients. Together, we are Canada's lifeline.

Amber Appleby, RN, BScN, MM
Director, Organ and Tissue Donation and Transplantation
Canadian Blood Services

Executive summary

Canadian Blood Services currently operates three interprovincial organ sharing programs that serve to maximize transplant access for patients most in need. These include the National Organ Waitlist (NOW), the Kidney Paired Donation (KPD) program and the Highly Sensitized Patients (HSP) program. These programs are operated on the Canadian Transplant Registry (CTR) web-platform, which is maintained by Canadian Blood Services.

The HSP program was initiated in the Fall of 2013 and has become a cornerstone of Canadian Blood Services' contribution to the organ donation and transplantation system in Canada. It provides access to deceased donors on a national scale for kidney transplant candidates who have significantly reduced access to compatible donors due to their immunological profile.

The data in the following report has been extracted from the CTR and covers the period of 2013–2018, from the initiation of the HSP program (started in November of 2013) until December of 2018.

Key success factor: Interprovincial organ sharing

Interprovincial cooperation continues to be crucial to the success of the HSP program. At the end of 2018, the HSP program facilitated 499 transplants, 297 of which being interprovincial transplants. The proportion of interprovincial transplants facilitated through the HSP program is increasing year over year, with 68 per cent of transplants facilitated in 2018 involving a donor and recipient from programs in different provinces.

Hardest to match transplant candidates

The vast majority of active transplant candidates registered in the HSP program at any given time are in the hardest to match group. These are candidates whose calculated Panel Reactive Antibody (cPRA) rating suggests that they would be a match with fewer than one donor in 100 (cPRA 100%). In most cases, transplant candidates with a cPRA 100% can be expected to match 0.1 per cent of donors or fewer. To date, only 15 per cent of cPRA 100% transplant candidates who have participated in this program received a transplant through the program, primarily due to the difficulties in finding a compatible donor. To address these difficulties, the HSP program policy regarding organ allocation was amended in 2016 to prioritize HSP transplant candidates in the highest cPRA categories, which resulted in a significant increase in transplants for these hard to match candidates. Of the 240 transplants facilitated by the HSP program prior to the implementation of the revised allocation policy, only 51 were to cPRA 100% patients, while 74 transplants were facilitated through the program to cPRA 100% patients in the first 240 transplants that followed the policy's implementation. This represents a 47 per cent increase in the number of cPRA 100% patients receiving transplants. cPRA 99% patients who were also given priority access to compatible donors benefited from this policy shift as well.

Fewer future transplants possible

Despite these advancements, current results suggest that fewer transplants may be possible through the HSP program in the future, especially for the hardest to match transplant candidates (cPRA 99% and 100% patients). This is due to a confluence of factors, including the increasing proportion of cPRA 100% transplant candidates (the hardest to match) in the candidate pool.

New measures and operational metrics

In addition to ongoing monitoring and reporting, proactive measures to enhance transplant opportunities are currently being considered, with select measures (such as incorporating new antibody crossing options and transitioning to more precise compatibility measurements) potentially being implemented in the future. As a complement to ongoing improvements, current operational metrics are extremely positive, including low rates of immunological problems that would prevent proposed transplants from proceeding and infrequent cases in which transplants are not able to be completed to the intended recipient. A major achievement for the HSP program is the low number of unexpected positive crossmatches. Transplant outcome results are also high, with both graft survival and patient survival being within expected ranges for deceased donor transplants.

Program overview

Canadian Transplant Registry activity – Highly Sensitized Patients

Overview of key program performance metrics

Candidates active on waitlist:	
cPRA 99%-100% candidates	448
cPRA 95%-98% candidates	23
Total candidates active on waitlist	471
Total donors with HSP allocation run	**3,895**

HSP program transplants:	
Interprovincial transplants	297
Intraprovincial transplants	202
Total HSP program transplants completed	499

New developments and other recent issues

Two major changes were made to the HSP program within the CTR based on a program evaluation process and modelling that occurred in 2015. One adjusted the ranking methodology and one discontinued the use of import thresholds. Both changes were made to ensure that the growing population of cPRA 99% and cPRA 100% patients have maximum access to all transplant opportunities.

This transplant candidate population in the HSP program continues to grow and new strategies are being explored to decrease waiting time for these individuals. Strategies currently under consideration include providing options for transplant programs to identify select antibodies in a candidate's profile that could potentially be crossed in order to expand the number of compatible donors, and increasing the precision with which cPRA categories are determined.

Analysis and evaluation of recent policy changes

Prioritization of hardest-to-match patients

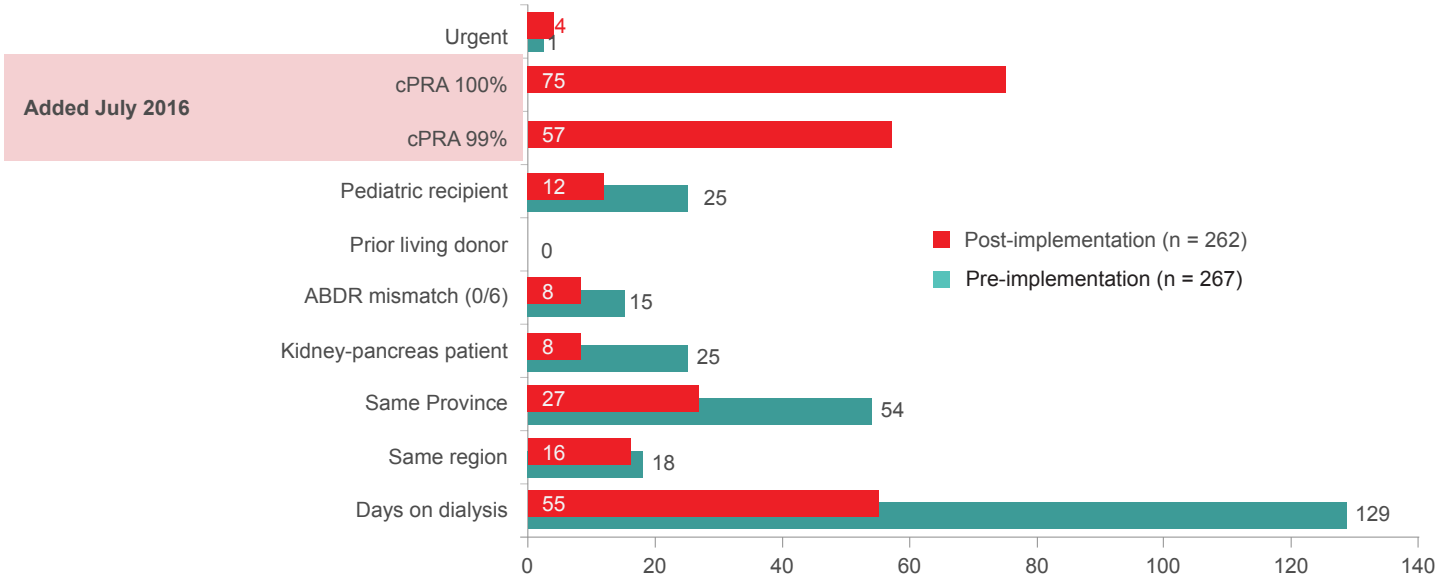
The Kidney Transplant Advisory Committee (KTAC) began a re-evaluation of operational elements of the HSP program in April 2015 as part of ongoing system performance review. Canadian Blood Services provided data, modelling and missed opportunity analysis for the evaluation. In situations where a donor matched multiple transplant candidates, there were multiple instances where the kidney was allocated to a transplant candidate with cPRA ≤ 98% over a cPRA >98% patient, as the allocation rules in effect at that time did not include cPRA as a consideration.

The KTAC recommended a change to the allocation rules of the HSP program within the CTR to incorporate the prioritization of cPRA 99% and cPRA 100% patients in cases where multiple transplant candidates match a given donor, in consideration of the difficulty in finding a match for candidates with cPRA >98%. This recommendation was endorsed and was implemented in the CTR as of July 15, 2016.

Impact

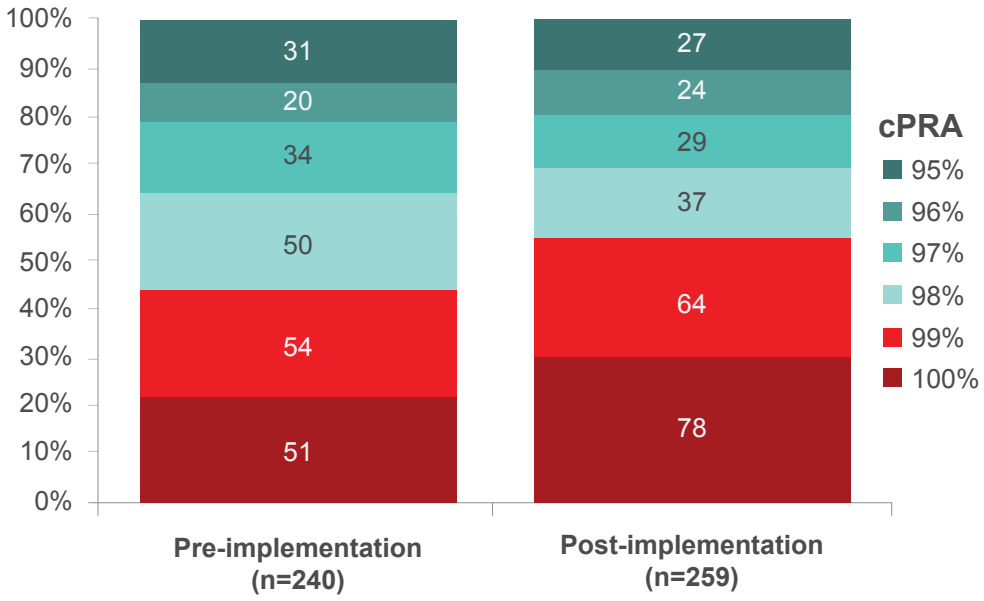
Since the policy was implemented, the cPRA criteria were used to adjudicate between recipients in 50 per cent of cases in which multiple recipients matched the same donor. In situations where none of the matching recipients were cPRA 99%-100% or medically urgent cases, the usage of ranking attributes since the implementation of cPRA-based prioritization reflected the same pattern as was observed prior to the policy coming into effect.

Attributes used to determine candidate rankings in multiple-match cases



Following implementation, the proportion of transplants to cPRA 100% patients rose from 21 per cent to 30 per cent, and the proportion of transplants to cPRA 99% patients rose from 23 per cent to 25 per cent. Overall, the relative proportions of transplants to cPRA 100%, cPRA 99% and cPRA 95%-98% patients changed significantly following the implementation of the prioritization criteria ($\chi^2 = 7.071$, df = 2, $p < 0.05$).

Transplants by cPRA prior to and following implementation of cPRA allocation criteria



Interpretation

The policy appears to have achieved the objective of providing better access to transplant for those transplant candidates in the highest sensitization categories. The impact on access to transplant for cPRA 100% patients is particularly notable.

Discontinuation of provincial import limits

During the evaluation, the second observation made by KTAC related to the interprovincial import and export thresholds designed to ensure import and export balance between provinces. The data analysis and simulation models showed smaller provinces were “on hold for HSP” due to import threshold restrictions for a combined 705 days. In this case, KTAC recommended the removal of all import thresholds but agreed to maintain export thresholds as a safeguard for transplant activity in net-exporting provinces.

Impact

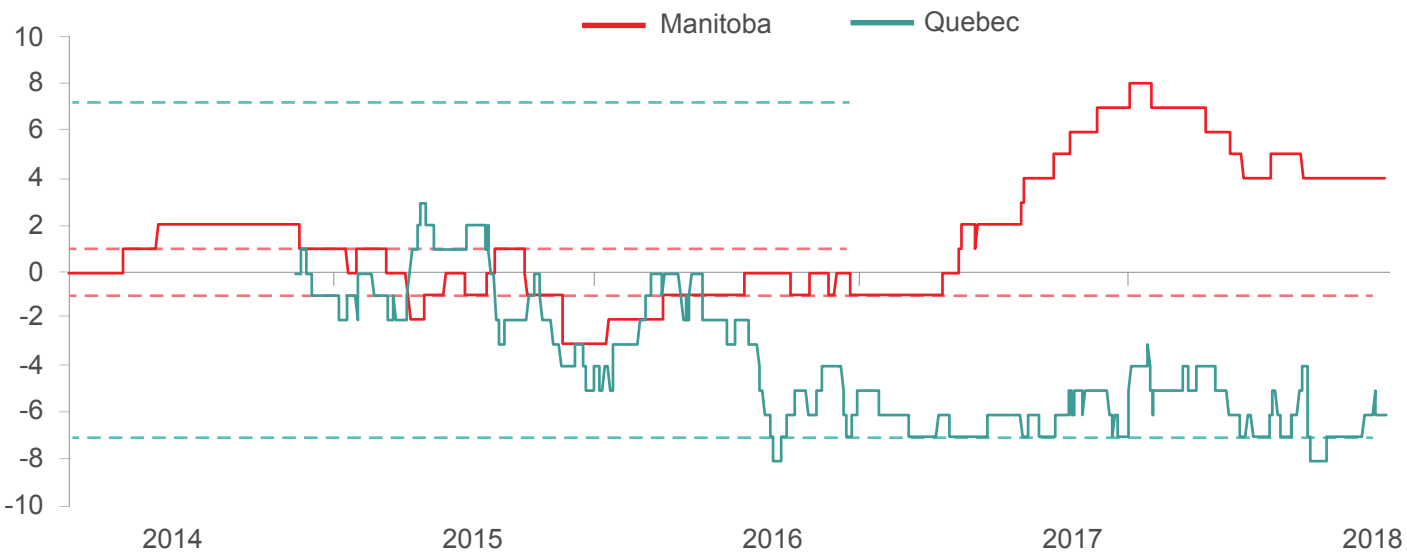
Only Manitoba and the Atlantic region appear to have consistently remained with a net positive balance that exceeds the previous import threshold level, with British Columbia evidencing wider variation than was previously the case, but still oscillating around a point of balance in import and export credits.

In the case of Manitoba, the HSP program has facilitated 11 interprovincial transplants to Manitoba recipients in the period since the import thresholds were removed, six of which were from Ontario or Quebec donors. Similarly, the Atlantic region received interprovincial transplants through the HSP program exclusively from Ontario and Quebec, with 13 interprovincial transplants facilitated to Atlantic recipients since the removal of import thresholds.

Although net-exporting provinces such as Ontario and Quebec were not prevented from receiving interprovincial offers by the import thresholds, and were therefore not directly impacted by their discontinuation, their credit balance was indirectly affected as the consequences of the change manifested in the system as a whole.

Specifically, while both provinces were historically net exporters, they maintained a credit balance that rarely reached their respective export thresholds; however, when the discontinuation of the provincial import thresholds enabled other provinces such as Manitoba and the Atlantic region to carry increasingly positive credit balances (predominantly as a result of importing from Ontario and Quebec), the corollary was that the net negative balances of these larger provinces increased to the point of regularly hitting and remaining at the export threshold.

Provincial net credit balance over time: Manitoba and Quebec



Positive values indicate a greater number of import credits than export credits.
Dashed lines show provincial threshold limits.

What would have happened if the import thresholds had remained cannot be definitively known; however, of the 24 interprovincial HSP transplants from Ontario and Quebec donors to Manitoba and Atlantic recipients, 14 were cases in which the donor only matched with one HSP transplant candidate, suggesting that no HSP candidate would have benefitted from these transplants if the import limits were still in effect.

Interpretation

It was anticipated that discontinuing the import thresholds could have a system-wide impact, since the interprovincial balancing credits are (with limited exceptions) a zero-sum closed system. Consistent with this expectation, removal of import thresholds was conducive to certain programs transitioning to (or exacerbating) net importing, with other programs showing a corresponding increase in their degree of net exporting while remaining within program parameters or continuing to fluctuate as normal based on organ exchange patterns. In this sense, the policy change can be understood to have a positive impact consistent with expectations.

Nevertheless, the systemic changes have negative consequences as well. As provinces such as Manitoba and the Atlantic region increased their net balance by taking in more interprovincial transplants from the system than they contributed, the net exporting provinces supplying these transplants (which were previously carrying credit balances within their export threshold) began to reach and stay at their export threshold levels.

When at their export limits, donors that would otherwise be accessible to all programs nationally are no longer required to be made available; as such, these provinces that were continuously making all their qualifying donors available to recipients throughout Canada will no longer be required to do so. This translates to decreased access to available donors system-wide, including reducing access for provinces whose net balance did not depart from their normal credit patterns following the policy change.

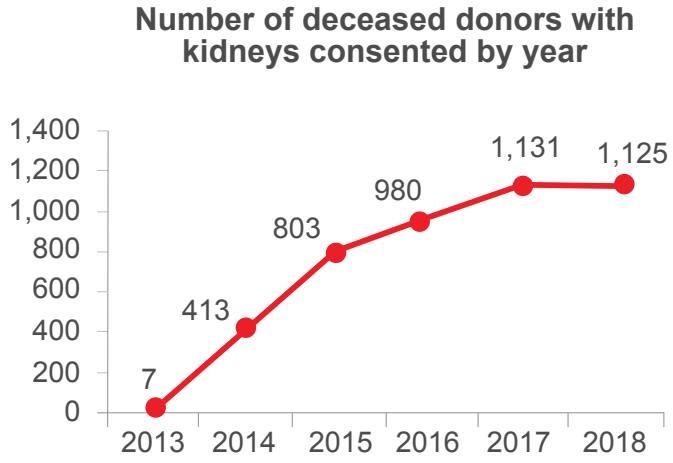
Deceased donors in HSP program

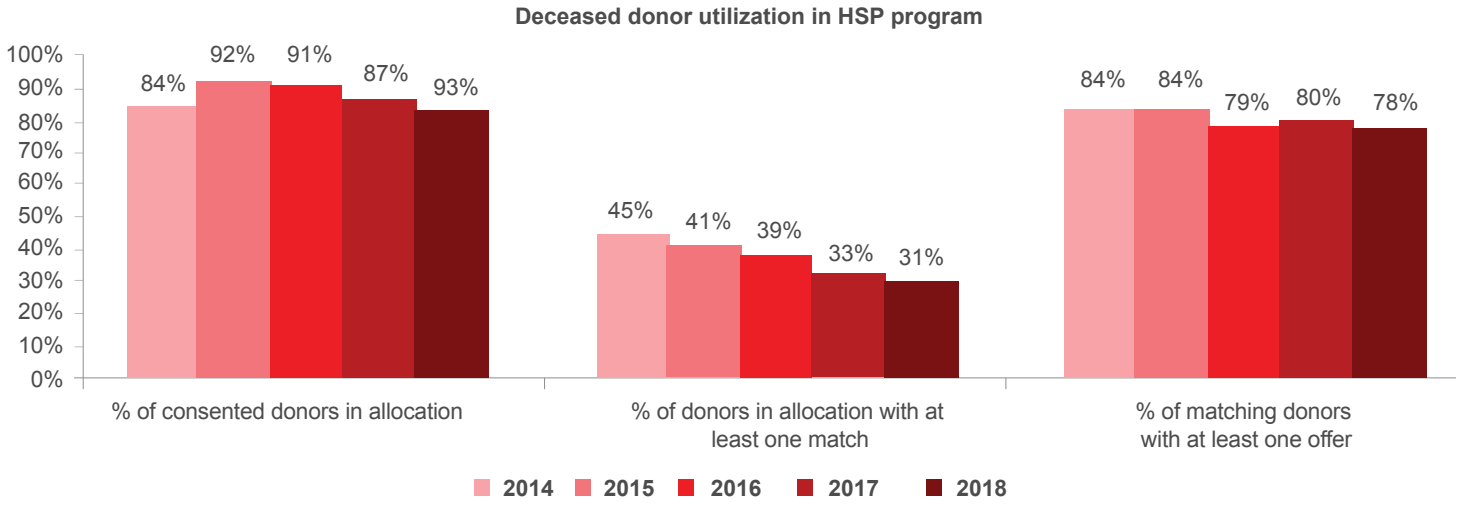
Donor availability and utilization

The HSP program has facilitated donations to highly sensitized patients at a consistent rate, with approximately nine donations per month (Standard Deviation (SD) = 2.8) from June of 2014 to the end of 2018. This is largely a product of two factors which, up to this point, have been well-balanced: increasing donor availability and decreasing donor utilization rates.

With respect to donor availability, the HSP program has seen considerable increases in the number of donors being entered into the Canadian Transplant Registry (CTR) from year to year in the past, with the number of consented donors in 2017 (1,131) being nearly triple the number available in 2014 (413). The total consented donors in 2018 (1,125) was roughly equivalent to the 2017 total, which suggests that donor availability seems to be plateauing.

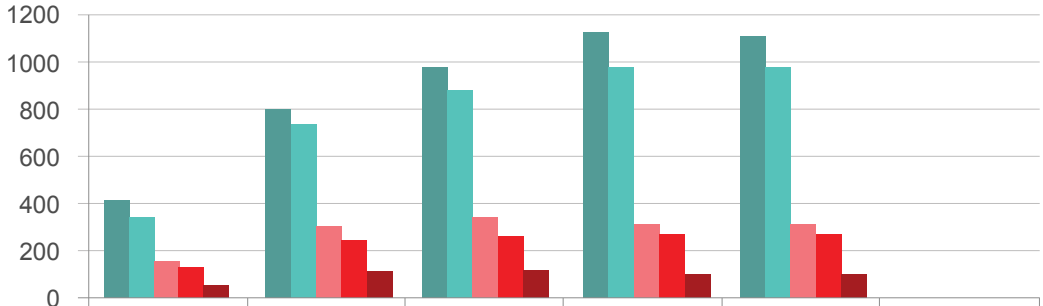
In contrast to this pattern of increasing donor availability, the rates at which donors progress through the phases of the HSP program donation process have been decreasing from year to year. Proportionally fewer consented donors are being entered into the organ allocation process to identify potential matches, with the allocation being run on 92 per cent of consented donors in 2015 to 83 per cent of consented donors in 2018. Similarly, the proportion of donors who match one or more recipients has steadily decreased from 45 per cent of those against whom the allocation was run in 2015 to 31 per cent in 2018, and the proportion of matching donors where one or more offers was made decreased from 84 per cent in 2014 to 78 per cent in 2018.





While 15 per cent of donors participating in the allocation process proceeded to donate in both 2014 and 2015, the equivalent rates in 2017 and 2018 has been nine per cent in both cases. For reference, if the consenting donors in 2018 had proceeded through the phases at equivalent rates, approximately 170 donations would have been facilitated by HSP in 2018 rather than just more than 100 as actually observed.

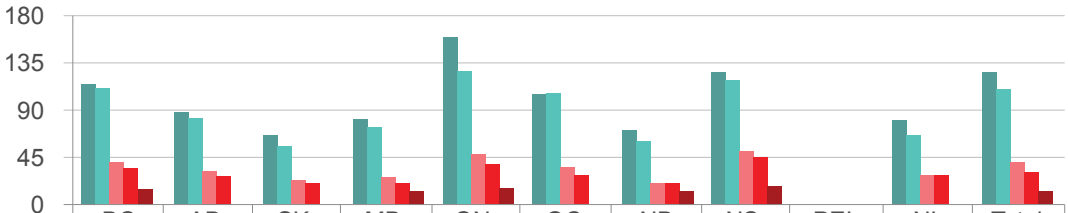
Donation tracking over time by donor registration date



	2014*	2015	2016	2017	2018	Total
Donors with kidneys consented	420	803	980	1,131	1,125	4,459
Donors for which allocation was run	353	738	887	981	936	3,895
Donors with at least one match	161	304	344	324	287	1,420
Donors with at least one offer	136	254	271	260	224	1,145
Donors with at least one HSP donation	63	119	111	100	104	497

Donors with kidneys consented = Number of donors consented for kidney donation and eligible to be included in an HSP allocation run
Donors for which allocation was run = Number of donors participating in the HSP program for which allocation was run
Donors with at least one match = Number of donors with one or more HSP matches identified
Donors with at least one offer = Number of donors for which one or more offers was made to transplant candidates as a result of the HSP program
Donors with at least one donation = Number of donor cases from which one or more kidneys were donated to patients, as a result of the HSP program. Non-intended recipient donations are excluded.
*Includes results from November-December 2013.

Donation tracking by ODO province of donor, per million population (PMP)



	BC	AB	SK	MB	ON	QC	NB	NS	PEI	NL	Total
Donors with kidneys consented	106.7	80.9	63.7	77.7	162.5	101.2	68.8	119.8		76.1	120.3
Donors for which allocation was run	102.1	77.7	52.5	69.5	129.4	100.4	58.4	113.5		62.8	105.1
Donors with at least one match	37.8	29.6	23.2	24.4	46.9	34.6	20.8	49.0		28.6	38.3
Donors with at least one offer	31.4	25.5	19.8	21.4	36.7	26.5	20.8	44.8		28.6	30.9
Donors with at least one HSP donation	12.9	9.2	11.2	14.1	16.4	11.0	14.3	17.7		9.5	13.4

Donors with kidneys consented = Number of donors consented for kidney donation and eligible to be included in an HSP allocation run
Donors for which allocation was run = Number of donors participating in the HSP program for which allocation was run
Donors with at least one match = Number of donors with one or more HSP matches identified
Donors with at least one offer = Number of donors for which one or more offers was made to transplant candidates as a result of the HSP program
Donors with at least one HSP donation = Number of donor cases from which one or more kidneys were donated to transplant candidates, as a result of the HSP program. Non-intended recipient donations are excluded.
Population values used in rate calculations based on Oct. 1, 2018 estimates from *Statistics Canada. Table 17-10-0009-01 Population estimates*, quarterly, available online at **https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901.** Extraction date: Feb. 15, 2019. In keeping with standard practice by the Canadian Institute for Health Information and the Canadian Organ Replacement Register, the population of YT has been included in calculating the rate for BC, and the population for NU and NT have been included in calculating the rate for AB.

Given its large population relative to other Canadian provinces, it is unsurprising that close to half (48 per cent) of the deceased donors entered into the HSP program's allocation process come from Ontario; however, even relative to its population, Ontario has contributed donors at a higher rate than the other provinces. Nova Scotia has the second highest rates for donor participation in the HSP program relative to its population and has even surpassed Ontario's rates for donors who are matched, donors for whom an offer is generated, and actual donations.

Despite interprovincial differences in donors entering and progressing through the HSP program's processes, there seem to be some anomalies of interest. The two donation programs operating in Alberta have collectively contributed approximately eight per cent of the donors progressing through the HSP process, which is on par with the province comprising approximately 12 per cent of the national population; however, Alberta has the lowest rate for donors making a donation through the program to a highly sensitized patient (other than Prince Edward Island) despite the province having the fifth highest rate for donors who match HSP candidates. Newfoundland and Labrador similarly has the fourth highest rate for donors for whom offers are generated, yet the lowest actual donation rate after Alberta and Prince Edward Island.

While Alberta and Newfoundland and Labrador have the lowest proportions of HSP registered donors from whom an offer is made actually proceeding to donation (36 per cent and 33 per cent, respectively), Manitoba and New Brunswick have the highest proportions proceeding to donation in Canada (66 per cent and 69 per cent of donors for which an offer is made, respectively).

Donations to non-intended recipients through the HSP program

In addition to the 497 donors who donated to a highly sensitized patient through the HSP program (including two donors from whom both kidneys were donated to highly-sensitized recipients), kidneys were procured from an additional 28 donors through the HSP program that did not result in transplants to highly sensitized patients registered in the program.

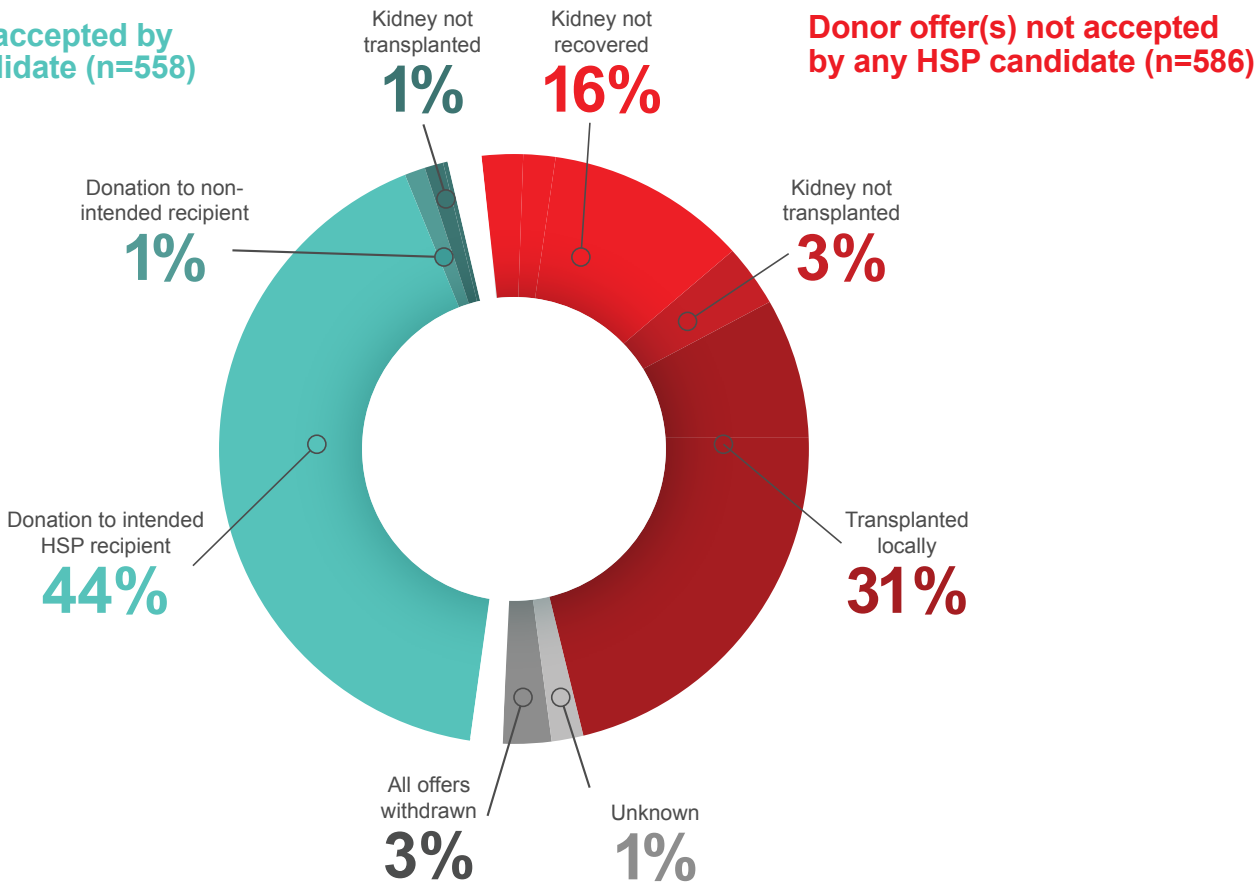
For 12 of these 28 cases, the kidney was not transplanted after being procured; this is typically due to the organ being determined to be medically unsuitable for transplant or otherwise not transplantable after being recovered.

In the remaining 16 cases, while the transplant was not able to proceed to the intended highly sensitized patient as offered, the organ was still able to be transplanted to a non-intended recipient from the local kidney transplant waitlist[1]. Typical reasons for this to occur include cases where the transplant to the intended highly sensitized patient cannot proceed due to a positive crossmatch or cases where the potential recipient is determined to be medically unsuitable to receive the transplant.

Of the 16 donations made to non-intended recipients, 12 resulted in interprovincial transplants, with one of the four intraprovincial transplants to non-intended recipients involving an exchange between Alberta's Human Organ Procurement and Exchange (HOPE) program in Edmonton and the Foothills Medical Centre in Calgary.

Donations that did not result in a transplant to a highly sensitized patient, including donations that were redirected to non-intended recipients, are not included in the reported donation and transplantation results for the HSP program.

Donors with HSP program offers by organ disposition



[1] In the unlikely event that the donor is a match to another local highly sensitized patient, the kidney designated for the HSP program would be offered to that patient. CTR records do not have sufficient information to confirm that this has taken place, and in the majority of cases a non-intended recipient will have a cPRA rating below the highly sensitized range.

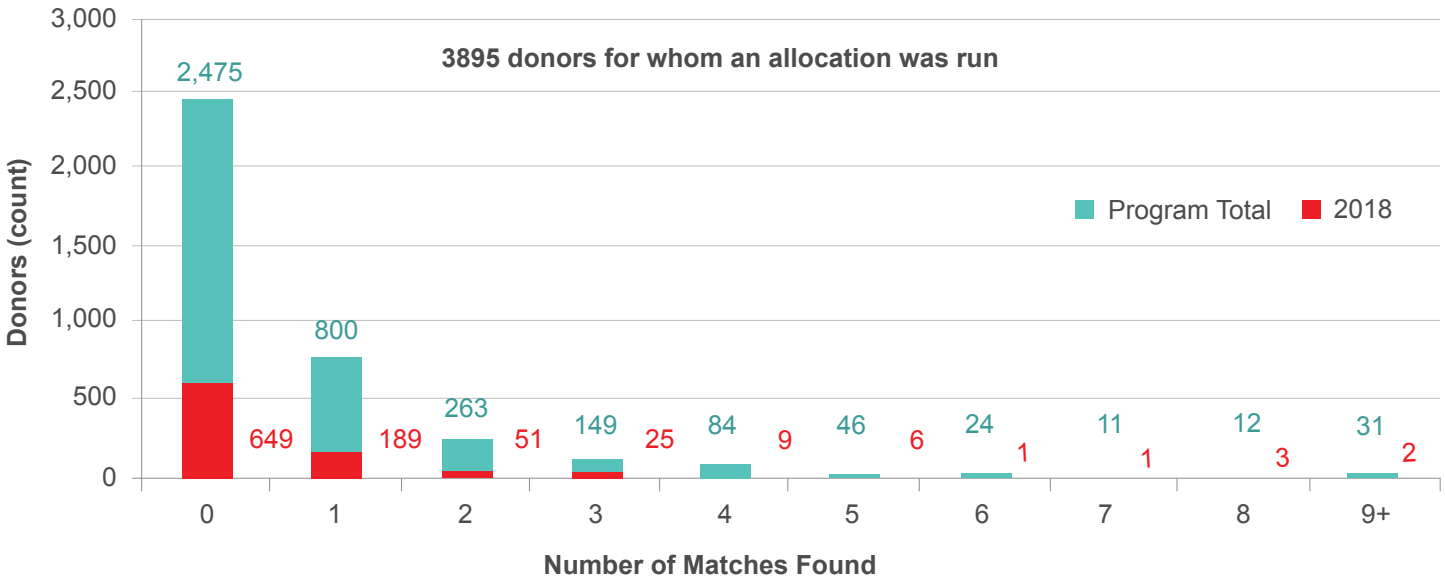
HSP matching and allocation

HSP program allocation

There are four tiers of matching and ranking that the HSP algorithm performs to develop a final listing of potential HSP recipients who are compatible with an available deceased donor organ (see Appendix 3 for details).

- **Step One:** Matching for compatible blood group, using the same compatibility rules as any patient requiring a blood transfusion.
- **Step Two:** HLA compatibility to avoid donor specific antibodies for patients identified as blood group compatible.
- **Step Three:** Further screening of donor suitability based on individual attributes of the potential recipient/donor.
- **Step Four:** If more than one potential recipient is identified, the HSP algorithm uses agreed-upon policies to transparently prioritize recipients based on key medically and logistically relevant factors.

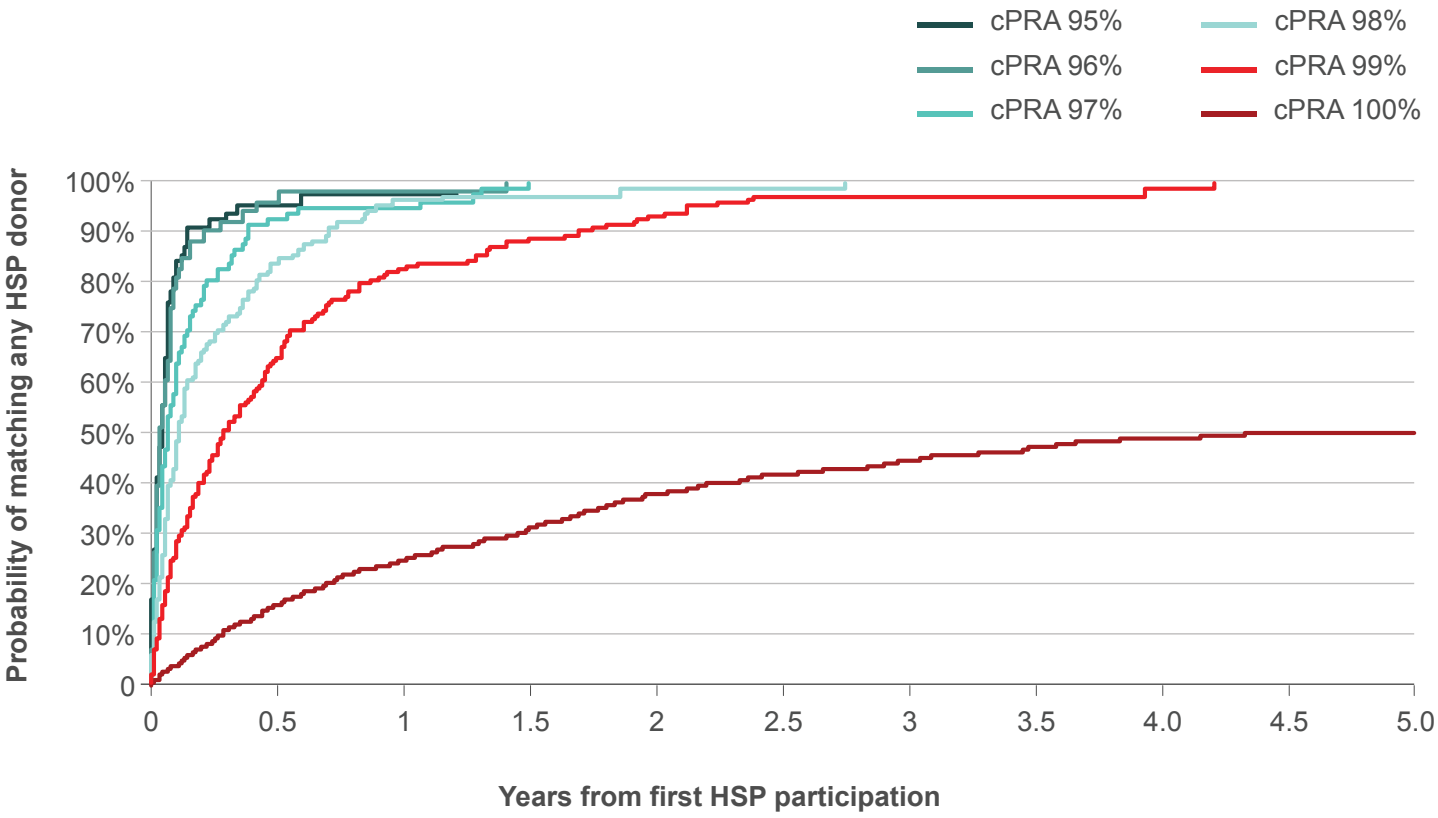
HSP matches found per donor



For transplant candidates in the cPRA 95% to cPRA 98% categories, the probability of finding a compatible donor through the HSP program is generally proportional to their cPRA rating. Although candidates whose cPRA is 100% have a substantially lower probability of matching a deceased donor through the HSP program — and consequently a lower probability of receiving an offer — it is worth noting that the vast majority of these transplant candidates are expected to match fewer than one donor in 1,000. With fewer than 1,000 donors per year being entered into the HSP matching algorithm, this difference in results is to be expected.

Approximate time to 90% match probability	
cPRA 95%	2 months
cPRA 96%	3 months
cPRA 97%	5 months
cPRA 98%	9 months
cPRA 99%	21 months

Probability of candidate matching a donor in the HSP program by cPRA



Values based on Kaplan Meier product limit estimate as calculated for actual results. Accuracy may be impacted by cohort effects. cPRA values based on cPRA at transplant for transplant recipients or most recent cPRA recorded in CTR for other transplant candidates as of the end of 2018.

HSP program offers

For the 1,420 donors whose HSP allocation results indicated that one or more active HSP eligible transplant candidates matched, offers were proposed for 1,145 (81 per cent) of these donors, with an average of 1.13 offers per matching donor. Of the 1,145 donors from whom an offer was proposed, 282 (25 per cent) of these donors resulted in offers being proposed to multiple HSP candidates. Only 15 donors resulted in offers to more than four HSP candidates.

Historically, 33 per cent of offers are accepted, 61 per cent of offers are declined (including offers that were initially accepted but for which the acceptance was subsequently cancelled), and the remaining six per cent of offers are withdrawn; however, in 2018, 39 per cent of offers were accepted and 55 per cent were declined, despite there being fewer offers made than in previous years.

Overview of HSP program offers by outcome (unique recipient–donor combinations only)

	2014*	2015	2016	2017	2018	Total
All Offers	193	374	381	359	276	1,583
Withdrawn	10	27	26	16	17	96
Declined	118	222	242	241	153	976
Accepted	65	125	113	102	106	511

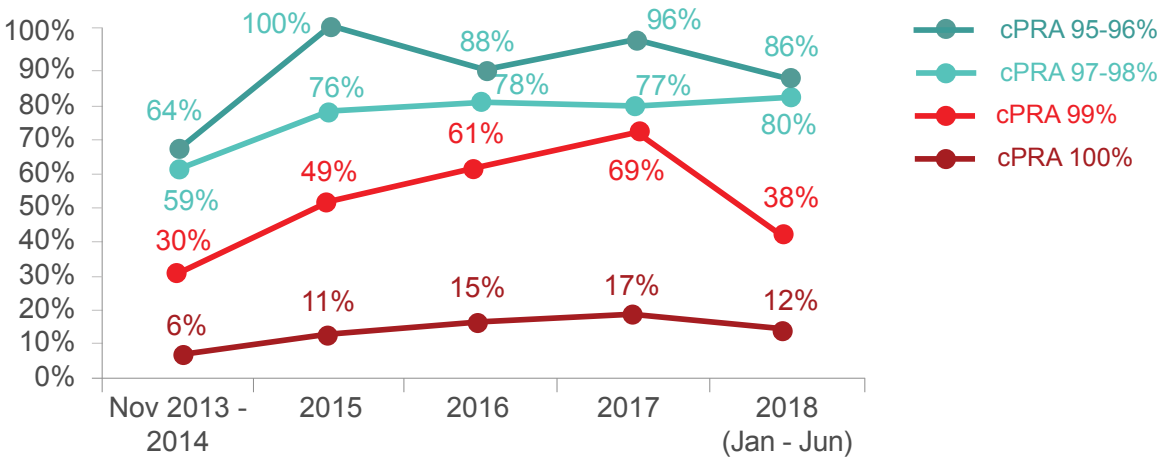
* Includes results from November-December 2013.
Results do not include offers entered in CTR to document non-intended (i.e. non-eligible) recipients of HSP offers in cases where the intended recipient was not able to receive the transplant. For 12 of the 511 accepted offers, the organ was not able to be transplanted.

Since the initiation of the HSP program, three out of four renal transplant candidates with ratings in the range of cPRA 95% to cPRA 98% received an offer through the program within six months of the first date that they were entered in the matching algorithm, with over 80 per cent of those who first participated in the program in January to June of 2018 receiving an offer within six months. Transplant candidates in this range account for approximately one quarter of the total number of candidates who have participated in the program to date and in recent years have accounted for approximately five per cent of the candidates who are actively registered at any given time.

For transplant candidates in the hardest to match categories, the proportion who received an offer within six months following their first inclusion in the HSP matching algorithm had been steadily increasing from year to year; however, results from early 2018 suggest that this trend will not continue, with only 38 per cent of cPRA 99% candidates whose initial participation was in the first half of 2018 receiving an offer within six months, as compared with 69 per cent of candidates whose first participation was in 2017.

The proportion of cPRA 100% candidates receiving an offer within the first six months showed a similar but less extreme decrease, consistent with their substantially lower baseline probability of receiving an offer.

Proportion of candidates who received an offer within six months of entry into the HSP program by cPRA and year of first participation

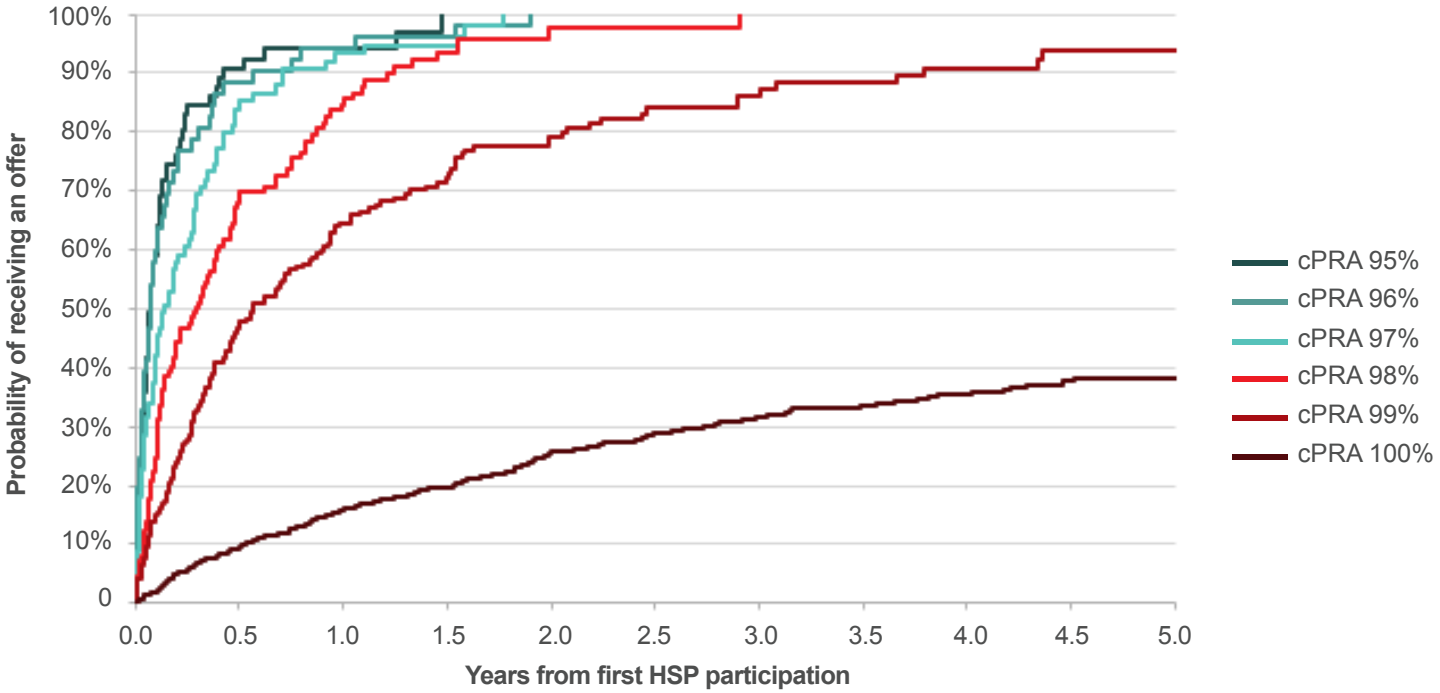


Historically candidates in the cPRA 95% to cPRA 97% range have had a relatively high probability of receiving an offer through the HSP program in a relatively short amount of time, with transplant candidates in the cPRA 98% and cPRA 99% categories having lower but still positive results in accordance with their respective likelihoods of finding a match.

Approximate time to 90% probability of receiving offer

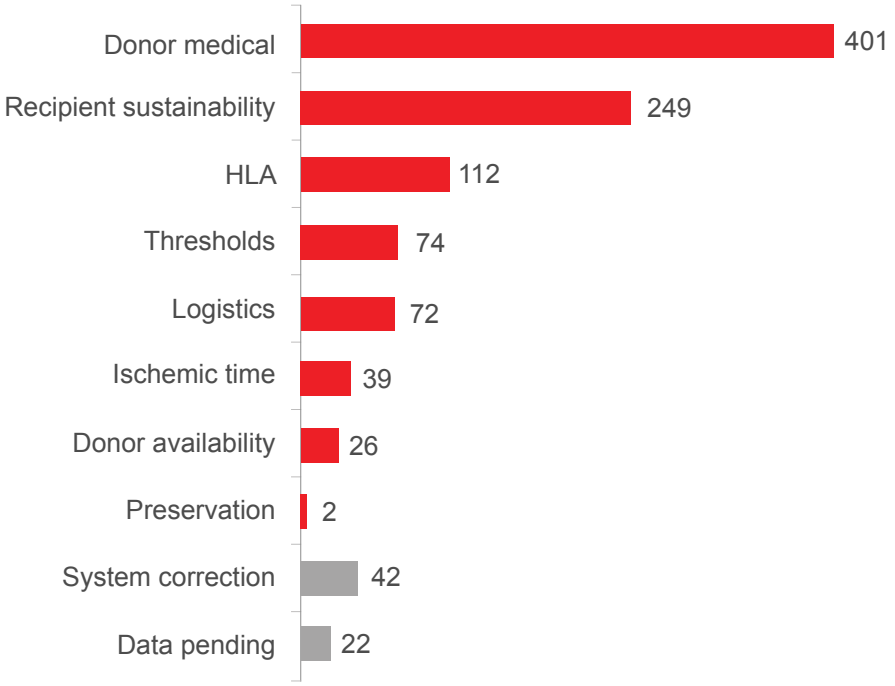
cPRA 95%	5 months
cPRA 96%	7 months
cPRA 97%	9 months
cPRA 98%	14 months
cPRA 99%	46 months

Probability of candidate receiving an offer by cPRA



Values based on Kaplan Meier product limit estimate as calculated for actual results. Accuracy may be impacted by cohort effects. cPRA values based on cPRA at transplant for transplant recipients or most recent cPRA recorded in CTR for other transplant candidates as of the end of 2018.

Offers declined by transplant team by reason



Note: offers may be declined multiple times and for multiple reasons between the same donor and recipient combination. Results reflect counts of unique recipient donor matches that were declined (or for which acceptance was cancelled) in each reason category.

The most common reason for offers to be declined is for donor medical reasons, with donor quality being the reason given most often and donor medical history, and donor age also being common issues. This differs from donor availability, which would include donors with an unstable medical condition or a DCD donor who did not die within time allowed by protocol. Offers may also be declined due to reasons relating to the medical suitability of the organ, including prolonged cold/warm ischemic time or issues regarding preservation (e.g. poor flush).

The vast majority of offers that are unable to proceed due to HLA issues are declined due to director review prior to organ acceptance.[2] Cases in which a proposed HSP registered transplant cannot proceed due to a positive crossmatch result are relatively rare and account for less than one per cent of HSP offers.

Although some offers are declined due to logistics issues, offers are no longer declined due to a province being at import threshold limits with the elimination of the provincial import thresholds.

HLA declines and unexpected positive crossmatches

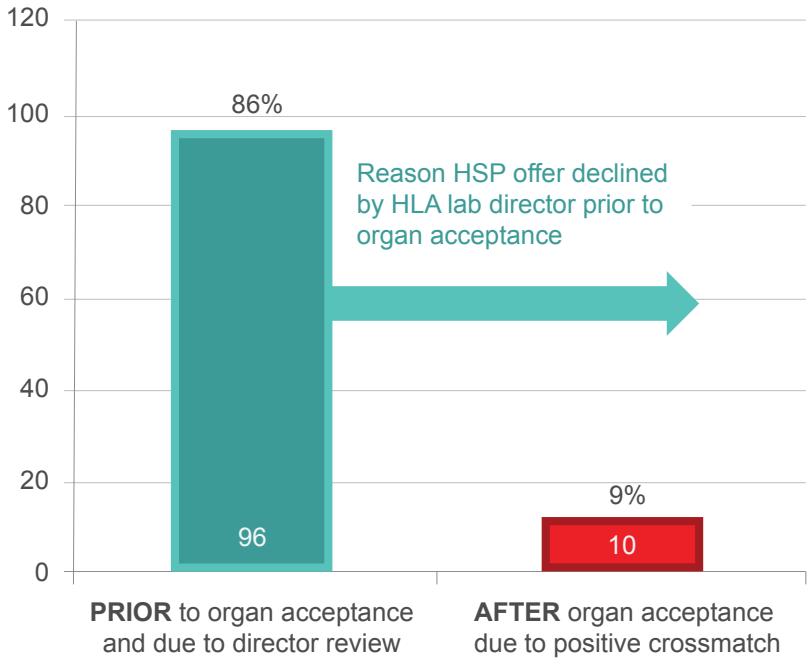
Offers are made to registered HSP program candidates on the basis of a virtual crossmatch test that computes the compatibility of that candidate with a given donor based on HLA information entered in the CTR. Prior to receiving a transplant, actual crossmatch testing is also performed to confirm that the donor and recipient are compatible (i.e. a negative result).

A major achievement for the HSP program is the low number of unexpected positive crossmatches. As of the end of 2018, there have only been 10 cases of an unexpected positive crossmatch out of 1,583 offers between unique donor–recipient combinations. Less than two per cent of accepted offers that would otherwise have resulted in a transplant to an HSP registered recipient had to be redirected to a backup recipient due to an unexpected positive crossmatch.

HLA laboratories review each kidney offer to a highly sensitized patient in order to appropriately adjudicate antibodies that cannot be identified by the automated virtual crossmatch in the CTR. The vast majority of offers declined on the basis of this review presented allele-specific issues.

[2] See *HLA declines and unexpected positive crossmatches* section for further details.

Reason offer declined for known HLA cases



	n	%
Allele specific	78	81%
Allele specific DSA & could not resolve typing to allele	7	7%
Indeterminate	6	6%
VXM positive due to new antibody	3	3%
Other	2	2%

Multiple offers between the same recipient–donor combination are not counted multiple times in the results above.

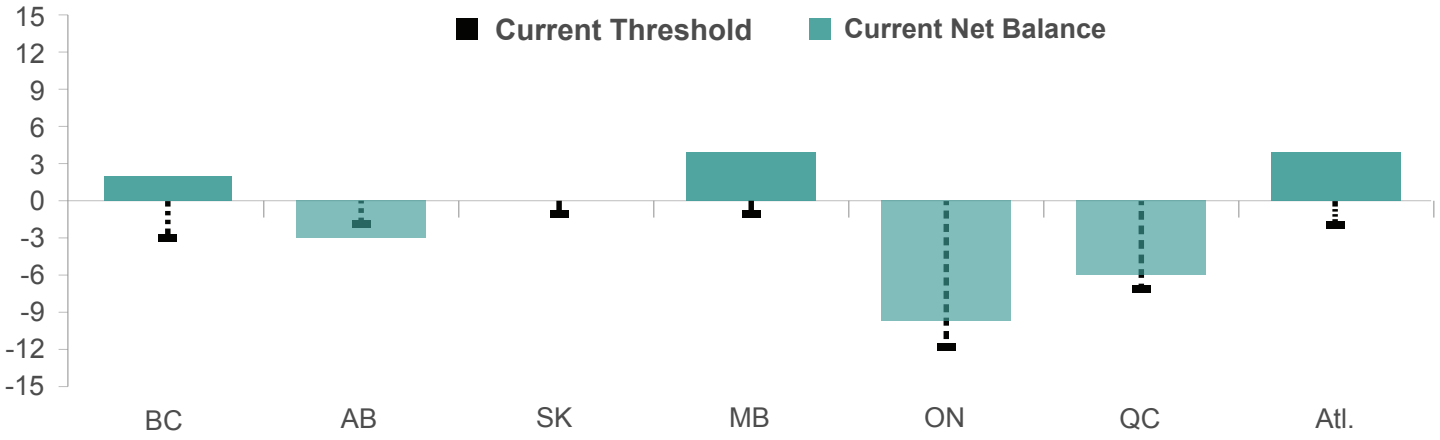
HSP thresholds and general ledger

Provincial thresholds, which are based on the relative deceased donation activity between provinces, are used to ensure protection of provincial local transplant activity (Note: Atlantic Canada operates as a single importing region, as they share a single waitlist managed by the transplant program in Halifax, NS).

Although the thresholds were intended to protect provinces from importing or exporting organs above a certain value, they do not prevent making or receiving offers through the CTR. When at export threshold, a provincial donation program is not required to offer a kidney to an HSP recipient in another province (but may choose to). Similarly, import thresholds were in effect until the end of 2016, under which offers from eligible donors would no longer be mandatory to HSP candidates from provinces that were at or above their import threshold; nevertheless, provincial donation programs still retained the option to make offers to those provinces regardless of this threshold. Several provinces exceeded their import and export thresholds, often based on discussion between offering and receiving programs in the context of patient need.

Provincial thresholds are reviewed and modified as required by the Kidney Transplant Advisory Committee (KTAC) based on analysis provided by Canadian Blood Services.

General ledger by province[3]

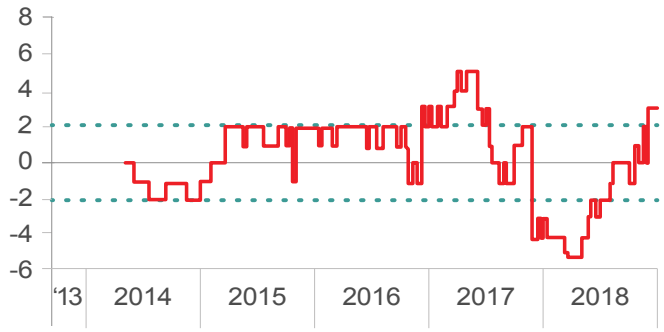


Net Balance	2	-3	0	4	-10	-6	4
Imports	50	34	10	23	100	62	31
Exports	48	37	10	19	110	68	27
In Province	18	12	1	3	134	26	9

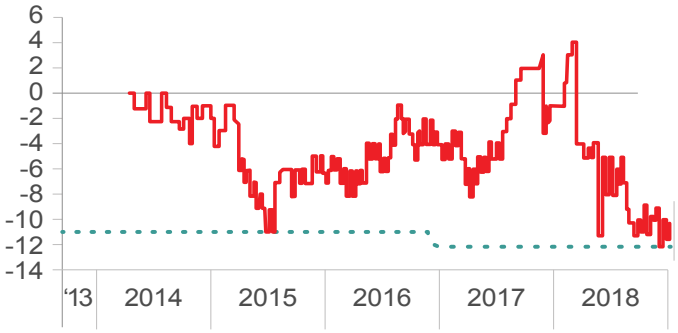
[3] Net Balance: import credits less export credits; Imports: number of kidneys received from out of province and transplanted. Exports: number of kidneys shipped out of province and transplanted. In Province: number of intraprovincial HSP program transplants.

Net balance over time by province

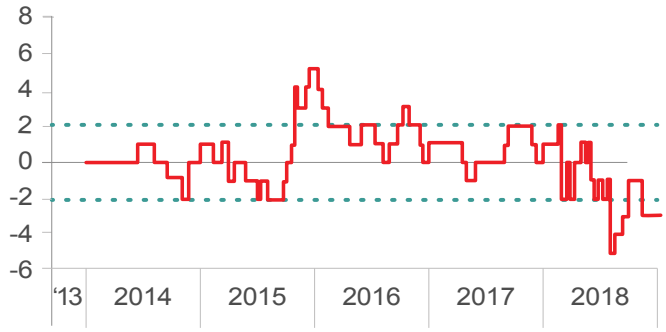
British Columbia



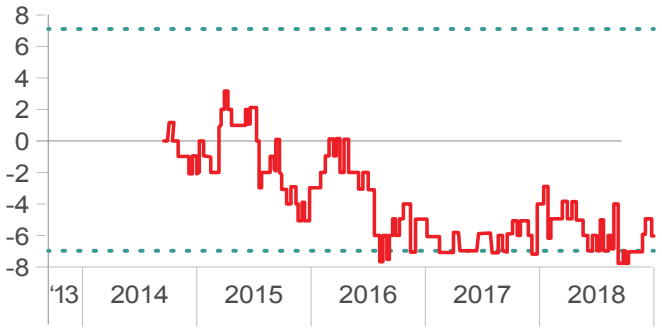
Ontario



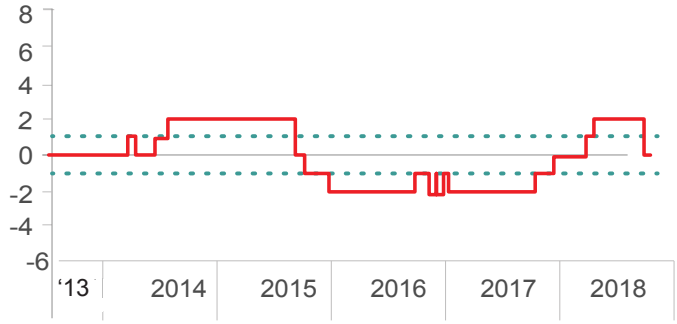
Alberta



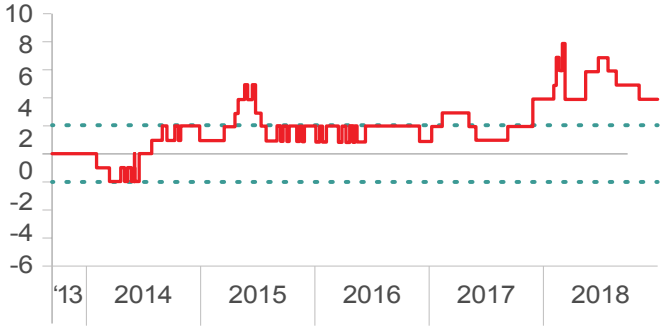
Quebec



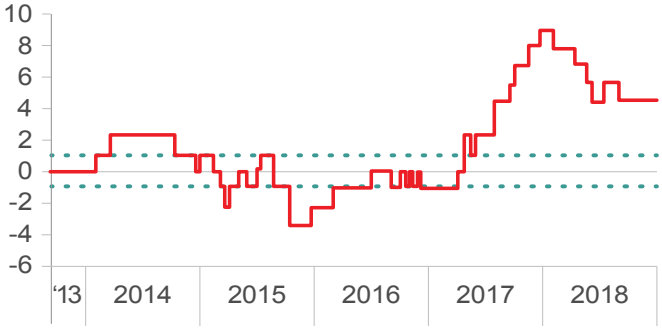
Saskatchewan



Atlantic



Manitoba



Positive values indicate a greater number of import credits than export credits

Dashed lines show provincial threshold limits

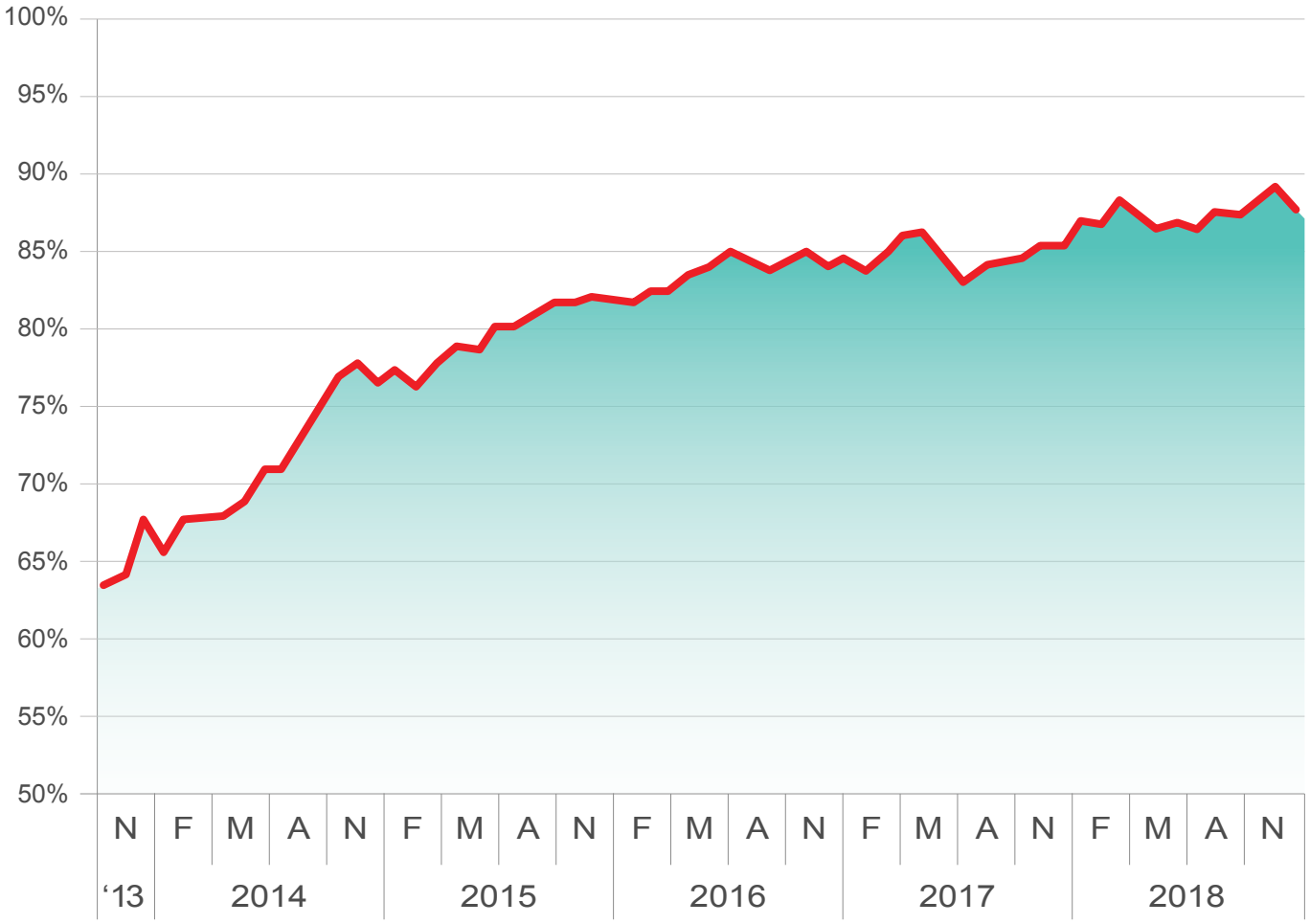
HSP program patients

HSP registered candidates and transplant recipients[4]

Although the number of active HSP program candidates has remained stable in recent years, the proportion of patients in the active candidate pool with a rating of cPRA 99.5% or higher (classified as cPRA 100%) has continued to increase over time. Transplant candidates with cPRA 100% originally made up less than 75 per cent of the candidate pool during the program's first year of operation and recently reached a new high of 89 per cent of the pool in November of 2018. With an increasing proportion of HSP program candidates being in the hardest to match category and no meaningful increase in the overall number of candidates, it is unsurprising that the proportion of donors who found a compatible recipient has similarly decreased over time.

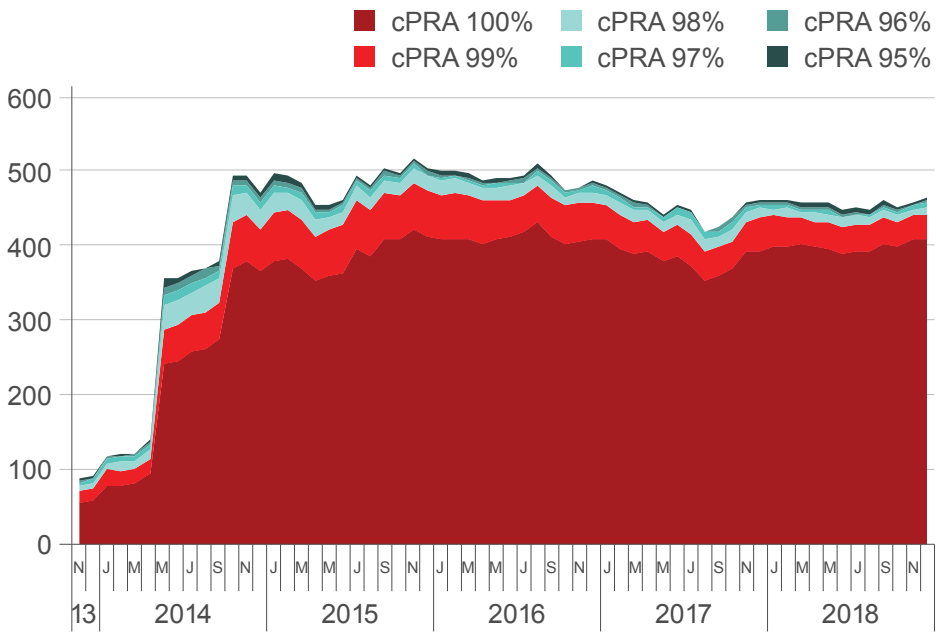
The factors that determine whether a donor will proceed to donation through the HSP program, such as whether a donor matches an active HSP transplant candidate and whether the donor is accepted, are generally limited in the degree to which they can be affected by HSP program policy. Nevertheless, there are several areas that could potentially be explored as options for maximizing access to transplant for highly sensitized patients through the HSP program, such as modifying the standards used to determine compatibility, including exploring willing-to-cross antibody policies.

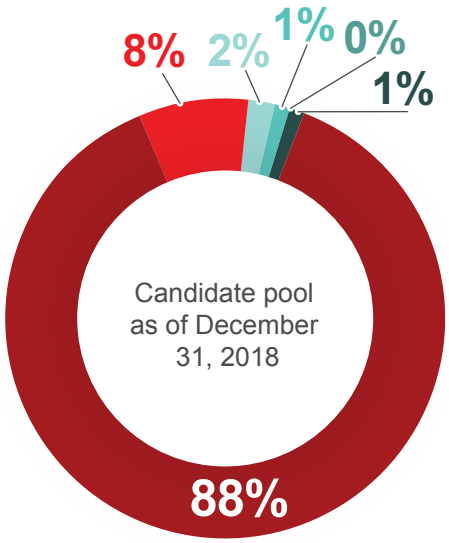
cPRA 100% patients as a proportion of all active candidates over time



[4] cPRA values may change over time. For the results reported here, cPRA results for transplant candidates reflect their cPRA ratings at year-end 2018. Results for transplant recipients are based on their cPRA as calculated at the time of transplant. One candidate whose cPRA changed to be outside the HSP-eligible range immediately prior to transplant is included in the cPRA category (96%) that was their rating at the time they received the HSP program offer leading to transplant.

Active HSP transplant candidates over time by cPRA



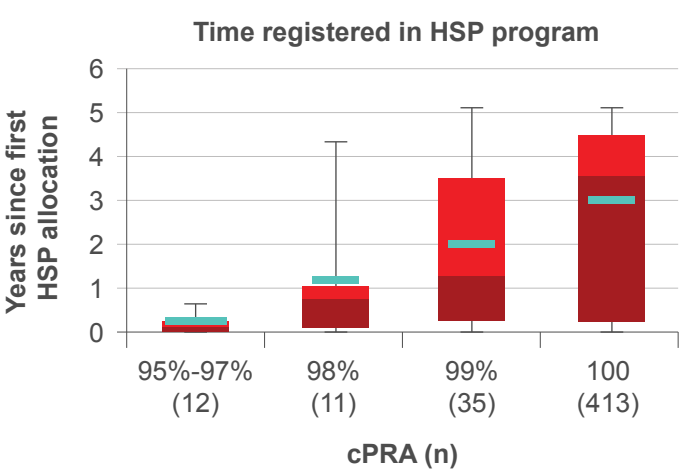


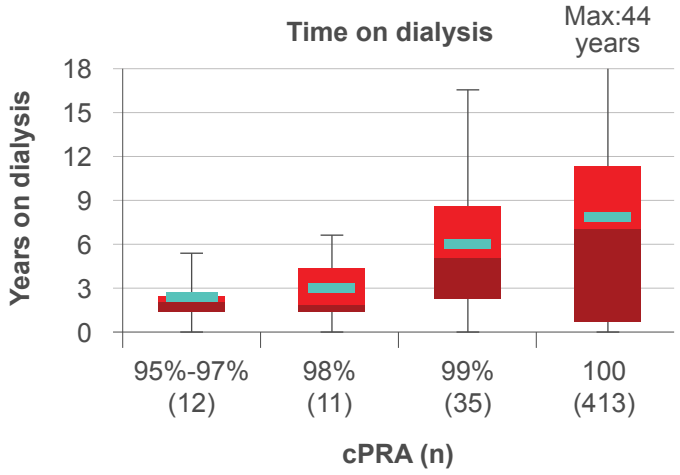
Values shown represent count of active HSP transplant candidates at end of month.
Provincial programs began participating in the HSP from 2013 to 2014 (SK & MB: Oct. 21, 2013; Atlantic provinces: Nov. 4, 2013; AB: January 6 [Edmonton] and April 7 [Calgary], 2014; ON: May 27, 2014; BC: June 12, 2014; QC: October 27, 2014).

The total number of active candidates registered in the HSP program at any given time has been reasonably consistent, with 2018 proving to show even less variation over time than had been typical for the program in the past. The total number of transplant candidates active in the HSP program at the end of 2018 (471) was within four patients of the total at the end of 2017, representing a change of less than one per cent.

There were 184 candidates whose first participation in the HSP allocation process was in 2018, and there were 105 transplants facilitated in that year.

Wait times for active HSP transplant candidates by cPRA





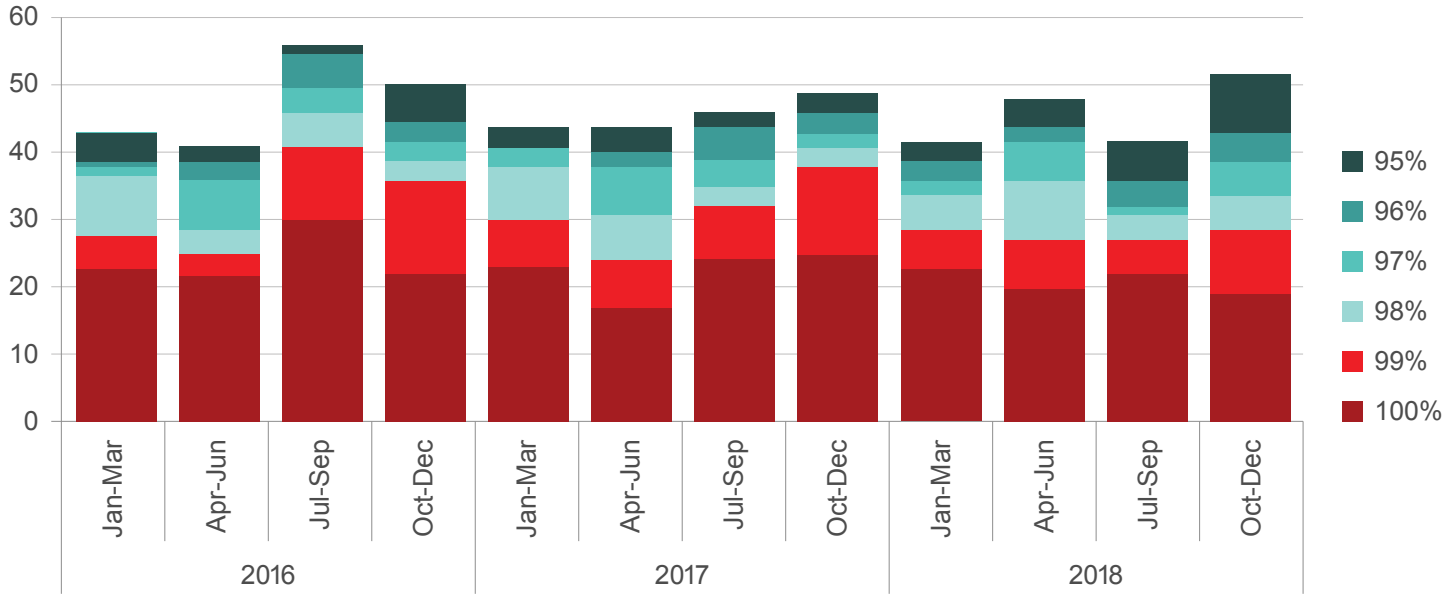
Error bars show range; coloured bars indicate inner quartiles (IQR); black bar represents mean.

Time registered in HSP program measured from time of first HSP allocation to December 31, 2018. Candidates may not have been active in the program for the entire duration. Time on dialysis measured from a transplant candidate's most recent dialysis start date.

Historically, the time waiting for a transplant among active transplant candidates registered in the HSP program is largely dependent on cPRA rating, with transplant candidates having ratings less than cPRA 99% having been active in the CTR and having been on dialysis for only a fraction of the time that is typical among transplant candidates with ratings of cPRA 100%.

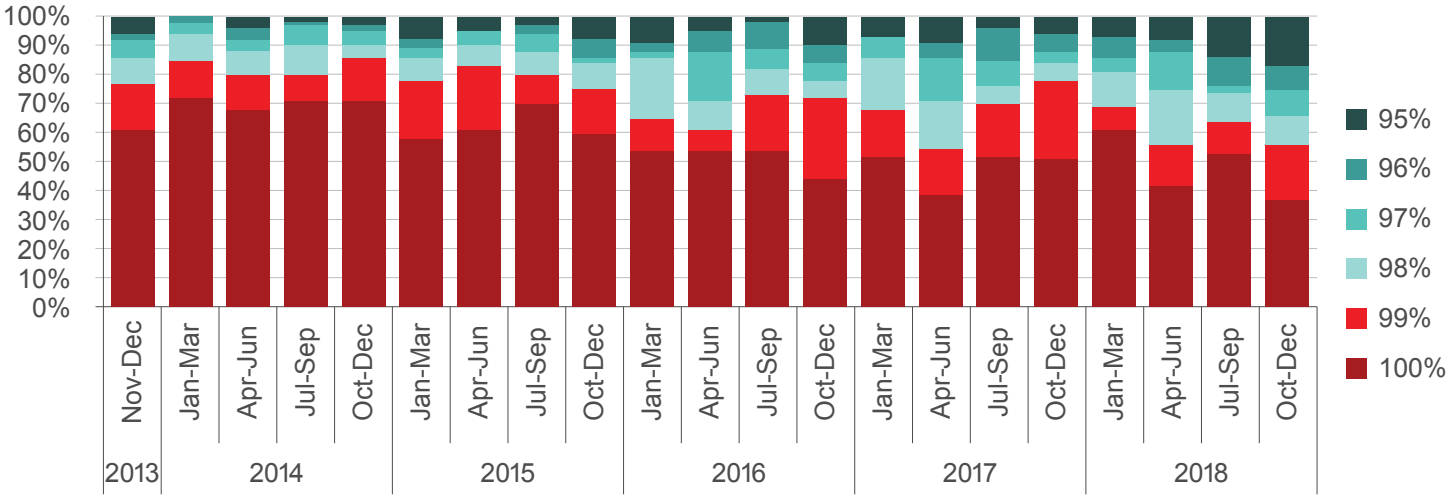
For instance, among candidates with cPRA ratings in the cPRA 95% to cPRA 97% range, all had been registered in the HSP program for eight months or less since their first inclusion in an HSP allocation, while the average time for cPRA 100% candidates was over three years since first inclusion in an allocation. Similarly, while the median time on dialysis for transplant candidates with ratings less than cPRA 99% is approximately two years, the equivalent for cPRA 99% patients is over five years, and approximately seven years for cPRA 100% patients.

New candidates by date first entered in the HSP matching algorithm and cPRA: 2016-2018



The rate at which new transplant candidates participate in the program has been generally stable in recent years. Since the start of 2016, approximately 16 new HSP candidates are included in the matching algorithm per month on average, or 47 per quarter. Prior to this there was an average of 20 new transplant candidates participating per month in 2015.

New candidates by date first entered in the HSP matching algorithm: Proportion by cPRA

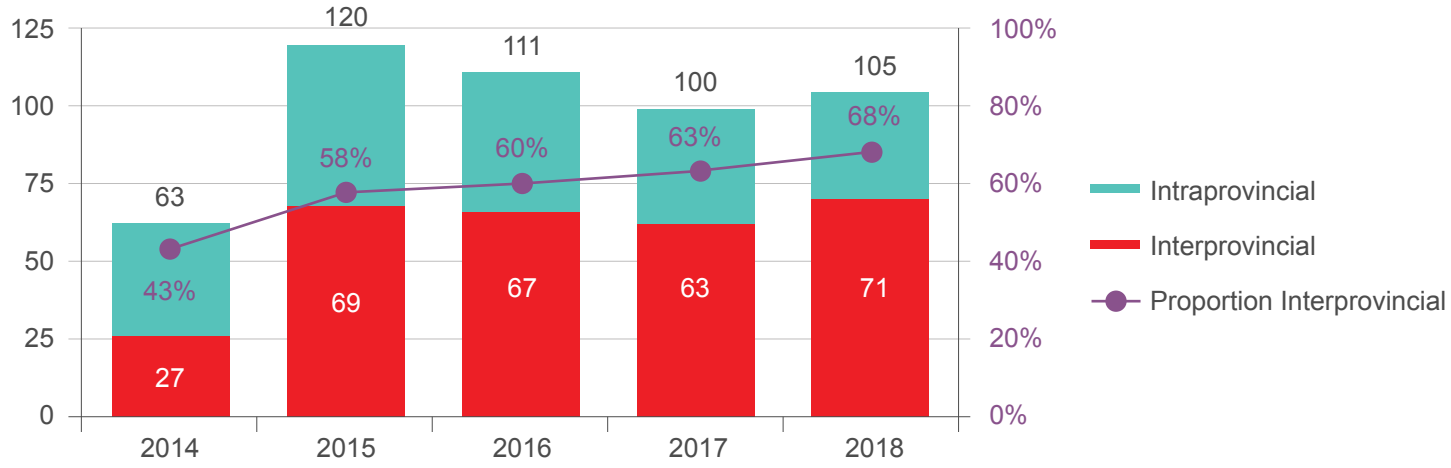


From the time that the HSP program was first initiated in 2013 to the end of 2015, cPRA 100% patients made up approximately one third of those entered into the HSP program's matching algorithm, with cPRA 99%+ patients comprising approximately 80 per cent of candidates who participated in the program at that time. Since then, less than one-third of new candidates have had ratings of cPRA 99% or higher, with less than half of new candidates entered being cPRA 100% patients.

As of the end of 2018, 33 per cent of transplant candidates who were entered into the allocation process received a transplant through the HSP program, and 31 per cent remained active.

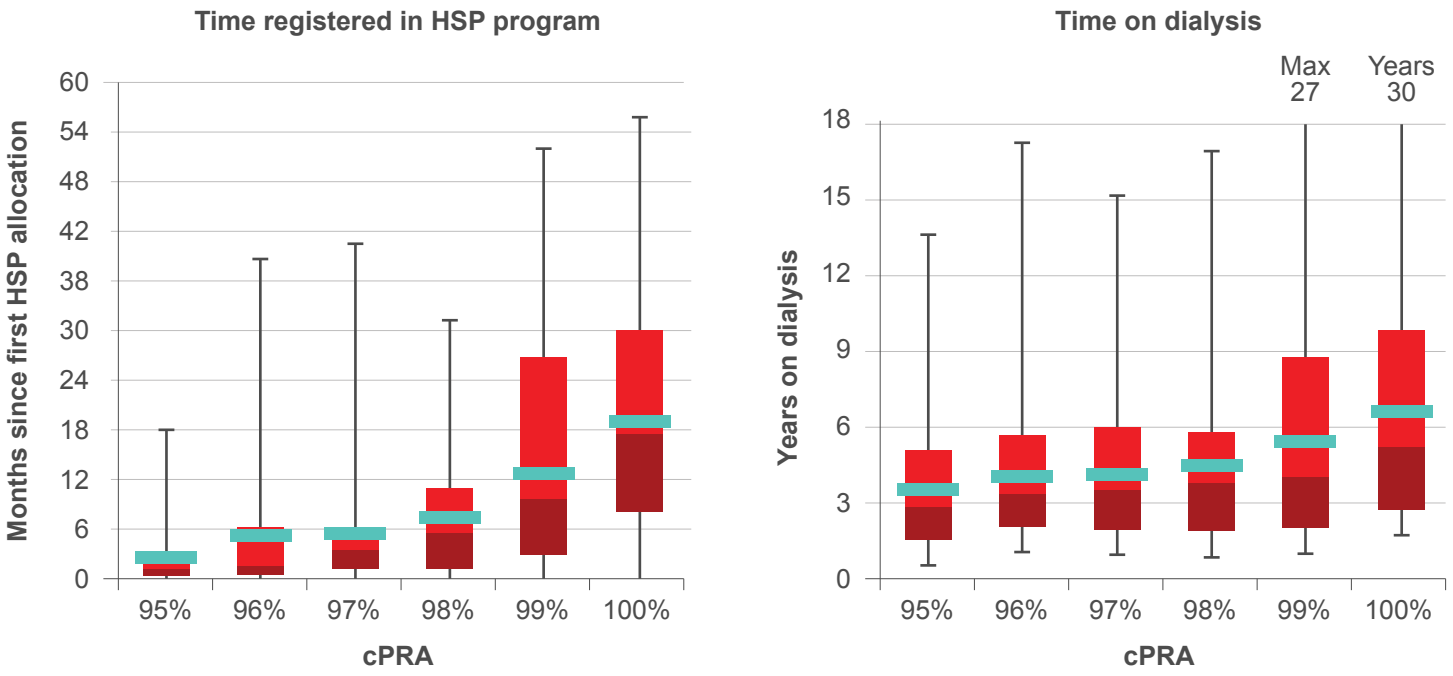
Many transplant candidates receive transplants from their local waitlist, and in some cases through the Kidney Paired Donation (KPD) program, and are removed from the list. They may also be removed from the list for other reasons. Alternatively, transplant candidates may be placed on hold pending a temporary issue that would make them ineligible to receive a transplant.

Interprovincial and intraprovincial HSP transplants over time



Over time the HSP program has seen an increasing proportion of transplants being facilitated between donors and recipients in different provinces, with interprovincial transplants accounting for more than two-thirds of the total transplants facilitated through the HSP program in 2018. Nevertheless, the total number of interprovincial transplants facilitated has remained in the range of 63–71 transplants per year over the 2015–2018 period. As such, the trend toward a higher proportion of transplants being facilitated interprovincially is also attributable to the decrease in intraprovincial transplants from 51 in 2015 to 34 in 2018.

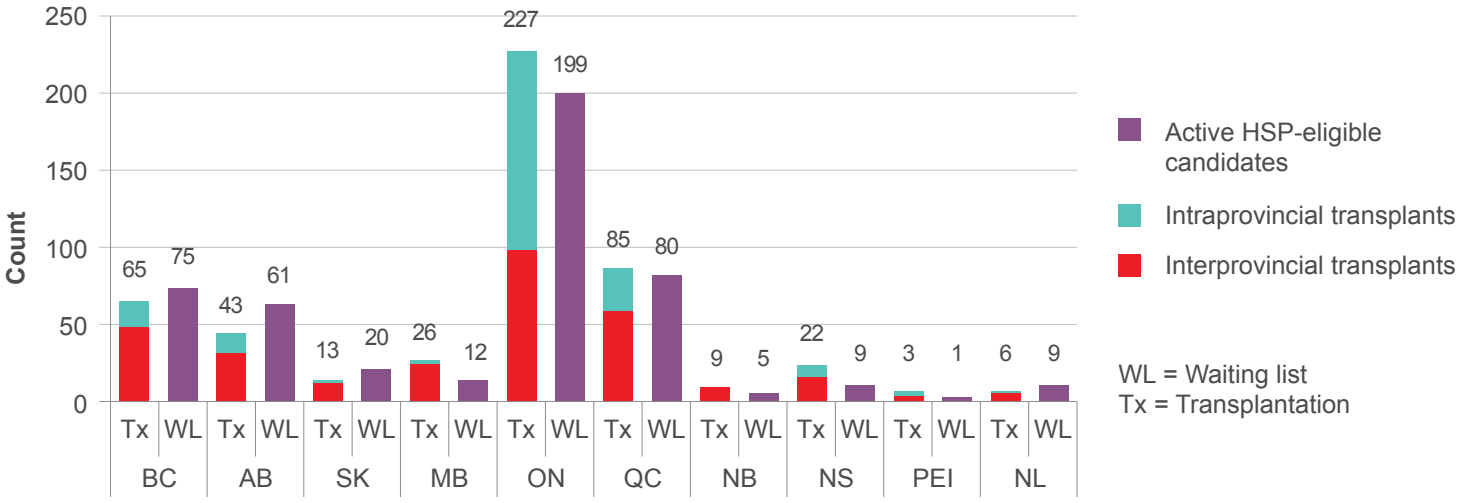
Wait times for HSP transplant recipients by cPRA



Error bars show range; coloured bars indicate inner quartiles (IQR); black bar represents mean.
Time registered in HSP program measured from date of first HSP allocation to date of transplant. Time on dialysis measured from recipient's most recent dialysis start date to the date of transplant. Recipients may not have been active in the program for the entire duration. Three transplant candidates each received two transplants facilitated by the HSP program; each transplant has been counted as separate cases.

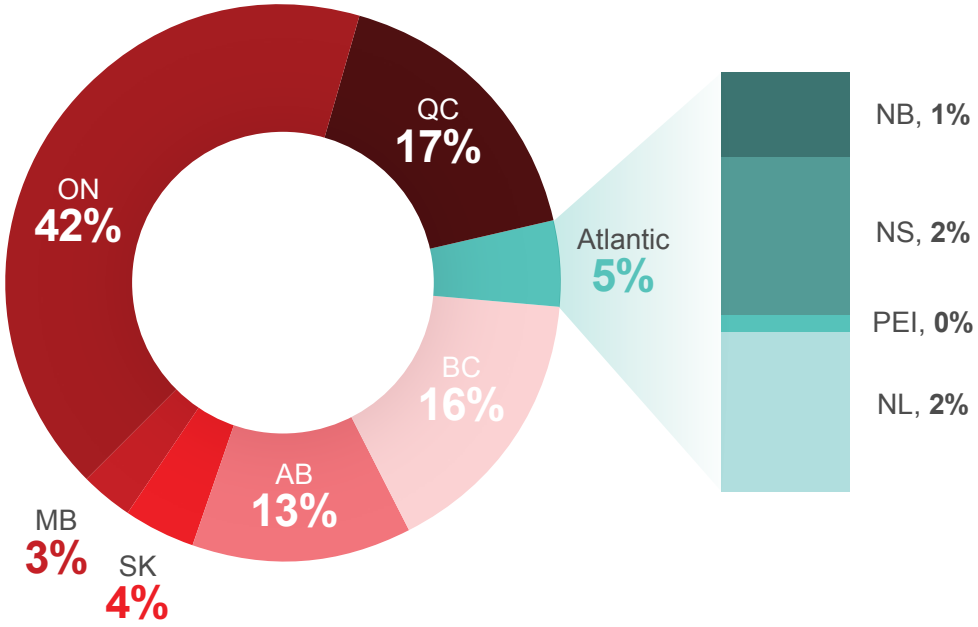
For transplant recipients, the average time from a transplant candidate first being entered into the HSP allocation to receiving a transplant appears to be inversely proportional to their cPRA rating (r = 0.46), with the median wait time among cPRA 100% recipients (17.5 months) being more than 12 times as long as the median wait time among cPRA 95% patients (1.4 months). Time on dialysis prior to transplant evidences a similar pattern, although the association is less pronounced (r = 0.23); the extended periods for which recipients received dialysis prior to the HSP program's existence obscure the relationship to some extent.

HSP program transplants and active candidates by provincial health number province (count)



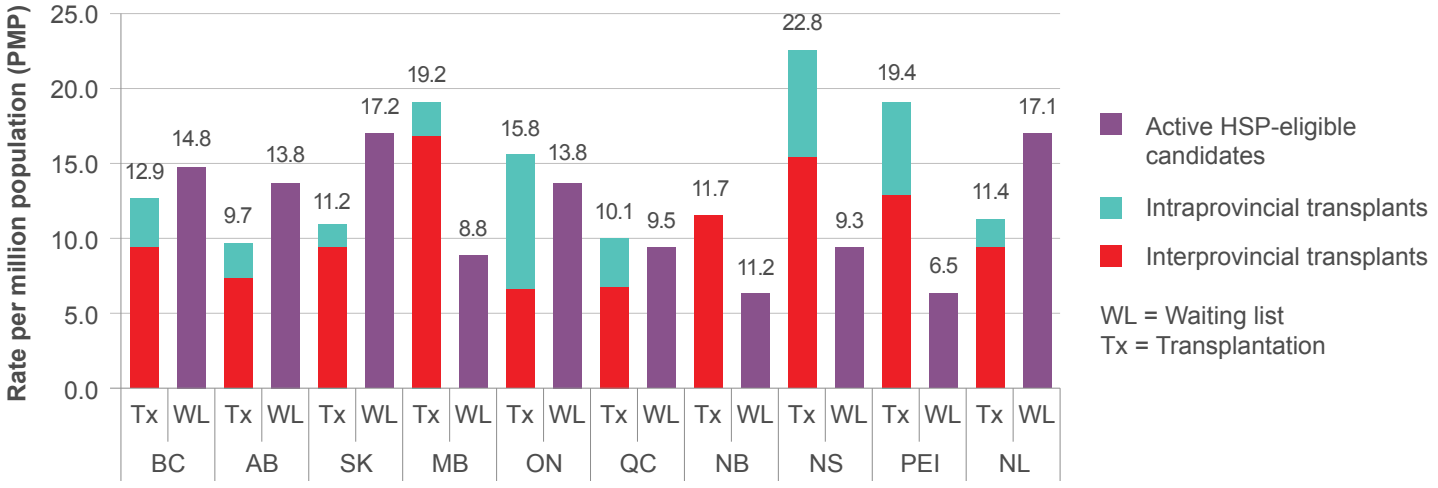
Transplants to recipients in the Atlantic provinces (NB, NS, PE, NL) from Atlantic donors are considered to be intraprovincial transplants.

As has historically been the case, the majority of transplant candidates participating in the HSP program are from Ontario, with 89 per cent of transplants facilitated by the program being received from donors from Ontario, Quebec, British Columbia, or Alberta. At this point in time, the number of transplant candidates currently active in the HSP program is generally comparable to the number of transplant candidates who received transplants through the program for most provinces



HSP program transplants and active candidates by provincial health number province

Rate per million population (PMP)



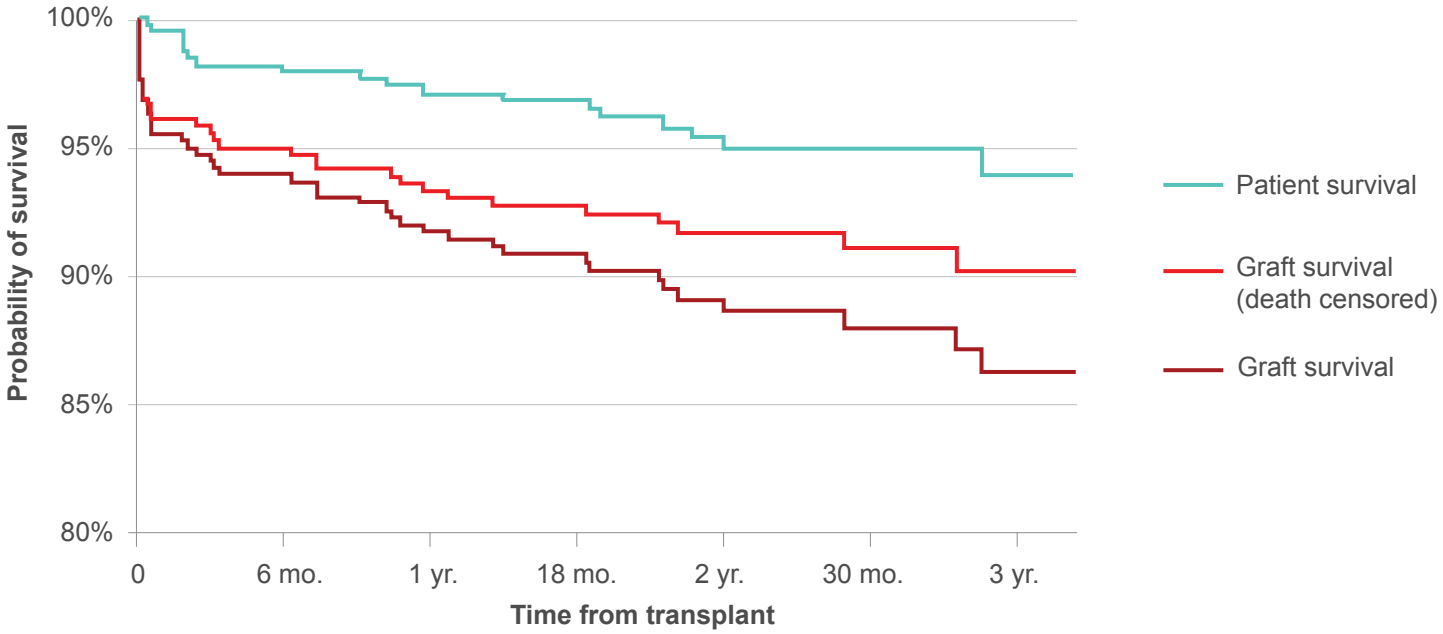
Population values used in rate calculations based on Oct. 1, 2018 estimates from Statistics Canada. Table 17-10-0009-01 Population estimates, quarterly, available online at https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901.
Extraction date: February 15, 2019. In keeping with standard practice by the Canadian Institute for Health Information and the Canadian Organ Replacement Register, the population of YT has been included in calculating the rate for BC, and the population for NU and NT have been included in calculating the rate for AB. Transplants to recipients in the Atlantic provinces (NB, NS, PE, NL) from Atlantic donors are considered to be intraprovincial transplants.

Relative to the national population, 13.4 transplants per million population have been facilitated by the HSP program, with 12.6 active candidates registered in the HSP program per million population nationally.

When comparing rates per million population across provinces, Manitoba, Prince Edward Island, and Nova Scotia have the highest transplant rates (19.2 to 22.8 PMP), while Newfoundland and Saskatchewan have the most active candidates relative to their provincial populations at over 17 candidates per million population.

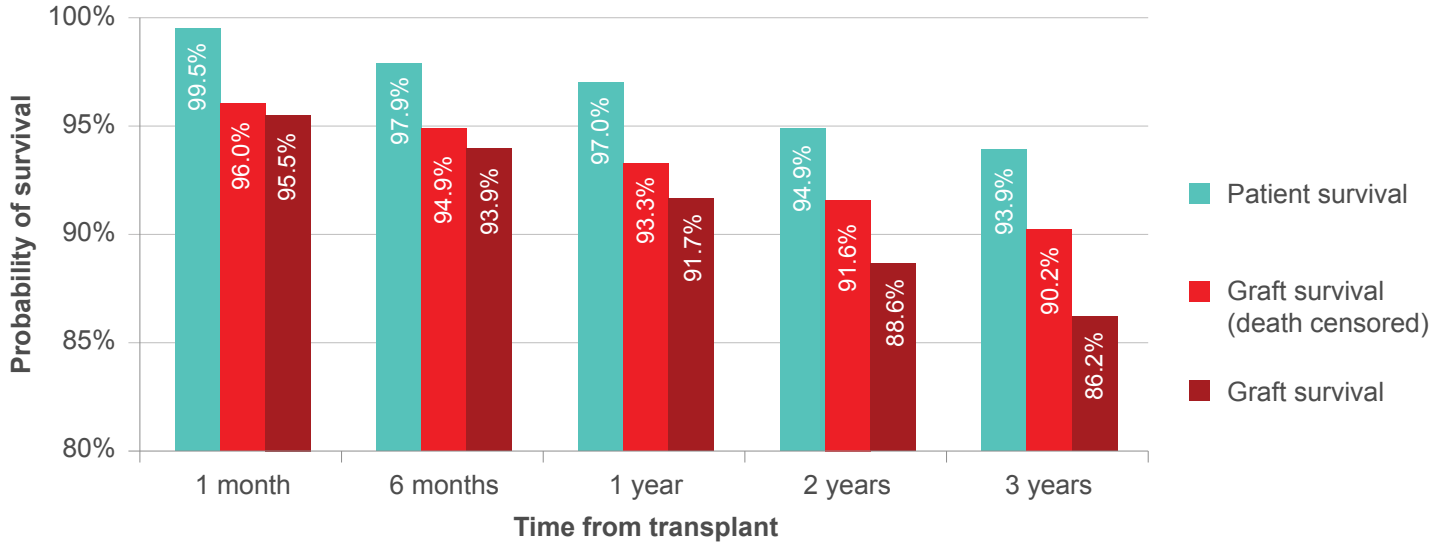
HSP recipient outcomes

Kaplan Meier survival curves for patient survival and graft survival probability over time, 2014 to 2017 transplants



Survival information available for 378 of 394 HSP transplants performed from 2014 to 2017.
"Death censored" graft survival results are based on graft failure only, while overall graft survival rates reflect patient death and/or graft failure.
Chart segment shown to highlight differences.

Overview of patient and graft survival probability at key timepoints



Survival information available for 378 of 394 HSP transplants performed from 2014 to 2017.
"Death censored" graft survival results are based on graft failure only, while overall graft survival rates reflect both patient death and/or graft failure.
Chart segment shown to highlight differences.

Appendix 1: Glossary of terms

ABO (or Blood Group)

A term used interchangeably with "blood group." For example, ABO–O refers to blood group O whereas ABO–B refers to blood group B.

Active

Any donor or candidate record that is ready for matching in the CTR.

Algorithm (or Matching Algorithm)

An automated computer program which is used to determine potentially compatible candidate–donor pairs.

Antibody

A protein molecule produced by the immune system in response to a foreign body (known as an antigen).

Antigen (ABDR Antigen or HLA Antigen)

An HLA protein on a cell surface (such as those on a donor kidney) that can cause the recipient immune system to react and injure or reject the organ. Antigens help determine donor/recipient compatibility.

Blood Group

See ABO.

Calculated Panel Reactive Antibody (cPRA)

A population-based estimate of the percentage of donors that will be incompatible with a given candidate due to the presence of antibodies.

Canadian Transplant Registry (CTR)

A web-based database for interprovincial listing of donors and potential recipients and for allocating the donor organs to the recipients. The CTR is operated by Canadian Blood Services and supports the Kidney Paired Donation (KPD) program, the Highly Sensitized Patient (HSP) program for high-cPRA kidney transplant candidates and the National Organ Waitlist (NOW) for non-renal transplant candidates.

Candidate (or Transplant Candidate)

A patient who needs a solid organ transplant and who is registered in the Canadian Transplant Registry (CTR).

Compatible Match

A transplant candidate and donor whose ABO and HLA types are compatible for transplantation.

Crossmatch

A test performed in an HLA laboratory to determine the HLA compatibility between a candidate and a potential donor. When the result of a crossmatch test is positive, it indicates that the HLA profiles of the donor and the recipient indicate that they would not be a compatible match.

Donation after circulatory death (DCD)

An option for organ donation for patients with severe brain injuries once a decision has been made to remove all life-sustaining treatments. DCD requires that the heart has permanently stopped beating.

Donor

A person, either living or deceased, who provides cells, tissues, or organs for transplantation.

Donor-Specific Antibodies (DSA)

Recipient HLA antibody or antibodies against a given donor's antigens.

Graft

A transplanted organ, tissue, or cells. In the case of CTR renal registries (including HSP), a transplanted kidney.

Interquartile Range (IQR)

A statistical measure of dispersion (variability) based on dividing a data set into quartiles.

Human Leukocyte Antigen (HLA)

The antigens on the donor cells' surface that may cause the recipient's immune system to react and reject a transplanted organ. See also antigen, above. HLA antigens are named in groups, or loci, and identified as: A, B, Cw, DR, DRw, DQA, DQ, DPA, and DP.

HLA Crossmatch

A test performed in an HLA laboratory to determine the HLA compatibility between a candidate and a potential donor.

Kidney Transplant Advisory Committee (KTAC)

The committee provides expert guidance to the development, operation and evolution of the national Kidney Paired Donation program (KPD) and Highly Sensitized Patient program (HSP) with the goal of increasing kidney transplantation in Canada.

Matching Algorithm

See Algorithm.

Organ Donation Organization (ODO)

The source establishment responsible for the processing and safety assessment of donated organs from donors.

Rejection

An immunological response to the transplanted organ in which the recipient's immune system (antibodies) attempts to destroy the graft, resulting in decreased function. A rejection episode does not necessarily result in graft loss.

Appendix 1: (cont.)

Virtual Crossmatch (VXM)

A comparison between candidate antibodies and donor antigens. A positive VXM means that the candidate has antibody(ies) to the donor's antigen(s) and could result in injury or rejection of the transplanted organ. A negative VXM means that the candidate's antigens match the donor's antigens with a corresponding lower risk of organ injury and rejection.

Waitlist

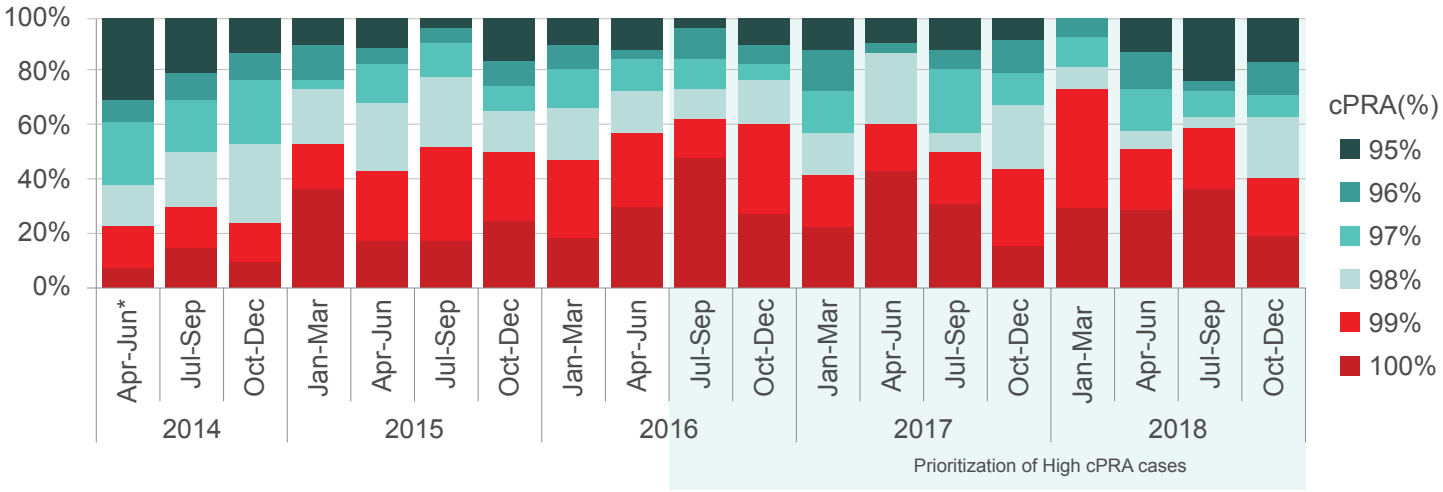
A list of patients who are qualified and registered by a transplant program and who are waiting to receive an organ transplant.

Appendix 2: Additional data for HSP program

HSP transplants by blood group of donor and recipient

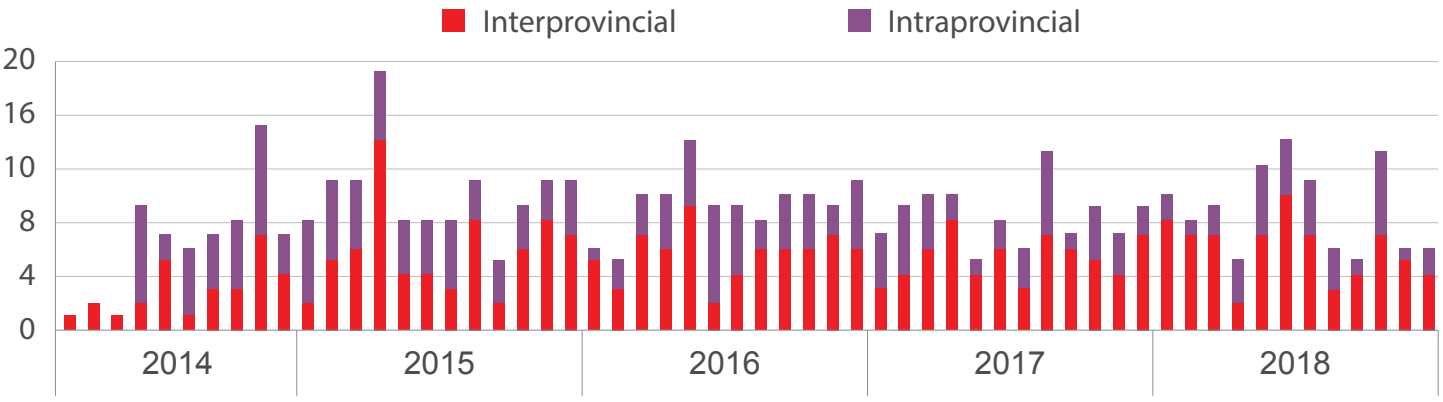
		Recipient blood group				
		A	AB	B	O	Total
Donor blood group	A	106	11	--	--	117
	AB	--	1	--	--	1
	B	--	6	28	--	34
	O	88	11	50	198	347
	Total	194	29	78	198	499

Transplants by cPRA over time



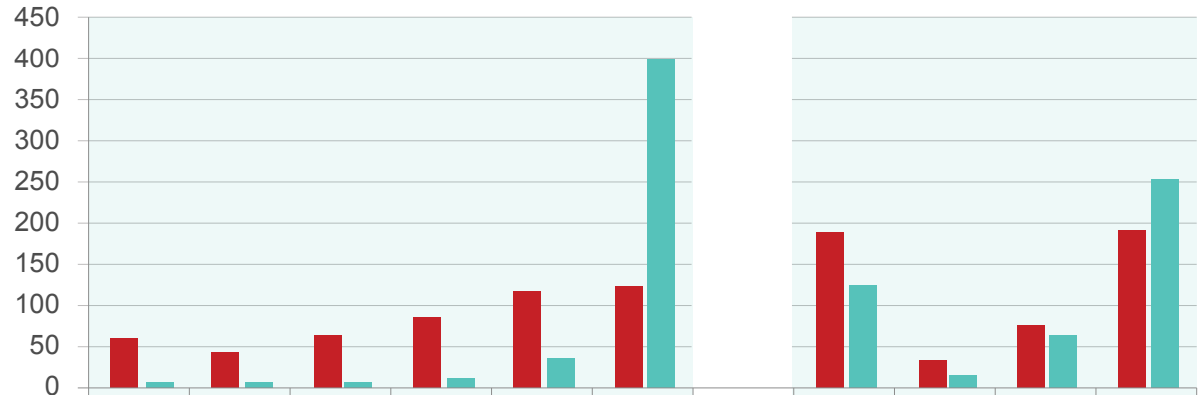
* Includes on transplant from March 2014. Results based on date of transplant and cPRA at transplant, with the exception of one case in which cPRA changed after acceptance to be outside of HSP range. Transplants to non-intended recipients are excluded.

Interprovincial and intraprovincial HSP transplants by month



Appendix 2: (cont.)

Transplants and active candidates by cPRA and blood group (ABO)



	cPRA						Total	Blood group (ABO)			
	95%	96%	97%	98%	99%	100%		A	AB	B	O
Transplant recipients	54	44	63	87	118	29	499	194	29	78	198
Active candidates	5	2	5	11	35	413	471	129	15	66	261

Donations by ODO province and year

	2014	2015	2016	2017	2018	All years
BC	6	9	17	23	10	**65**
AB	7	7	7	6	13	**40**
SK	2	2	2	3	4	**13**
MB	2	9	4	1	4	**20**
ON	37	58	44	47	50	**236**
QC	3	27	31	13	18	**92**
Atl.	6	8	6	7	6	**33**
National	**63**	**120**	**111**	**100**	**105**	**499**

Transplants by transplant centre province and year

	2014	2015	2016	2017	2018	All years
BC	6	9	17	23	10	**65**
AB	7	7	7	6	13	**40**
SK	2	2	2	3	4	**13**
MB	2	9	4	1	4	**20**
ON	37	58	44	47	50	**236**
QC	3	27	31	13	18	**92**
Atl.	6	8	6	7	6	**33**
National	**63**	**120**	**111**	**100**	**105**	**499**

Appendix 2: Additional data for HSP program (cont.

Offers declined by reason (unique donor–recipient combinations only)

Offers may be declined multiple times and for multiple reasons between the same donor and recipient combination. Results reflect counts of unique recipient–donor matches that were declined (or for which acceptance was cancelled) in each reason category.

Donor Medical	401*
Abnormal test results	27
ABO identical donor preferred	3
Donor age	64
Donor medical history	79
Donor quality	171
Donor size	12
Donor social history	8
High medical risk	14
Organ anatomical damage or defect	8
Organ declined on visualization in OR	4
Organ not as described	9
Organ test results unacceptable	16
Organ test results unavailable	3
Positive serology	3

Recipient Suitability	249*
Multi-organ placement	13
No suitable recipient	17
Recipient deceased	1
Recipient medically unsuitable	75
Recipient refused	21
Recipient unavailable	23
Selected incorrect recipient	100

Logistics	72*
No recovery team available	5
Surgeon unavailable	3
Technical problem in OR	2
Transportation logistics	63

*Category totals reflect declines for any reason within category between unique recipient–donor combinations.

Donor Availability	26	**Thresholds**	74
Preservation	2	**System Correction**	42
Prolonged Ischemic Time	39	**Data Pending**	22

HLA	112
AFTER organ acceptance due to positive crossmatch	10
PRIOR to organ acceptance and due to director review	96
Data Pending	6

Appendix 3: HSP matching algorithm

There are four tiers of matching and ranking that the HSP algorithm performs to develop a final listing of potential HSP recipients who are compatible with an available deceased donor organ.

- **Tier One:** Matching is first done on blood group, using the same compatibility rules as any patient requiring a blood transfusion.
- **Tier Two:** The second step checks HLA compatibility for patients identified as blood group compatible. Recipient's "unacceptable HLA antigens" are compared to a donor's HLA antigens to identify recipients that are unlikely to have a positive crossmatch to the donor (virtual crossmatch). In this step, potential donor–recipient matches are excluded when the donor has HLA antigens that have been listed in the recipient's record as being incompatible.
- **Tier Three:** Further screening of donors based on individual attributes of the patient or the clinical direction of a local program occurs at this step. This involves filters based on donor age, donor infectious disease status, and whether or not the proposed donor was declared dead using donation after cardio-circulatory death (DCD).
- **Tier Four:** At this point, it is quite common for a donor to have only one or sometimes no matches. However, for cases with two or more potential candidates that are blood group, HLA, and patient-filter matches, the HSP algorithm uses agreed upon policies to rank order the remaining matches based on key medically and logistically relevant factors.

All four of the tiers are examined annually by clinical experts advising Canadian Blood Services on the operations and policies of the HSP program. As policy changes are proposed and endorsed by the national community (including physicians, donation professionals, laboratory professionals, and administrators), these matching and ranking rules used by the Canadian Transplant Registry are updated accordingly.

Tier one: Blood group matching

Blood Group (ABO) Compatibility	
If donor blood group is	**Then recipient blood group can be**
O	Any (O, A, B, AB)
A	A, AB
B	B, AB
AB	AB

Tier two: HLA compatibility

HLA compatibility to avoid donor specific antibodies for patients identified as blood group compatible.

Tier three: Patient and transplant program-specific filters

- Accept a donor to specified maximum age:
  - <45, <55, <65, no restrictions)
- Accept a donor above a specified minimum age:
  - (>10, >11, >12, >13, >14, >15, >16, >17, >18, no restriction)
- Accept a donor who has tested positive for Hepatitis B core antibody
- Accept a donor who has tested positive for Hepatitis C
- Accept a DCD (donation after cardio-circulatory death) donor

Tier four: Ranking attributes for cases in which a donor matches multiple recipients

Matching/Ranking Attribute	Rank
Medical urgency (requires prior approval of KTAC sub-committee)	**1**
Recipient cPRA is 100%	**2**
Recipient cPRA is 99%	**3**
Pediatric recipient (≤19 years of age)	**4**
Recipient is a prior living donor	**5**
HLA match: The HLA typing for the donor and recipient indicates a zero out of six (0/6) mismatch for ABDR antigens	**6**
Kidney–pancreas patients	**7**
The donor and recipients are in the same province	**8**
The donor and recipient are in the same region: • West region: BC, AB, SK, MB • East region: ON, QC, ATL	**9**
Time on dialysis (number of days starting at the most recent initiation of dialysis)	**10**