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Economic Evaluation of Screening for Polyomavirus Infection in Kidney Transplant Recipients: A Cost-Utility Analysis

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Background: Screening for polyomavirus infection after kidney transplantation is recommended by clinical practice guidelines, but cost-effectiveness of this strategy is uncertain. The aim of this study was to estimate the incremental costs and benefits of routine screening for polyomavirus infection compared with no screening in kidney transplant recipients. **Methods:** Probabilistic Markov models were constructed to compare the health and economic benefits of routine screening for polyomavirus infection using real-time polymerase chain reaction assay. A series of 1-way and probabilistic sensitivity analyses were conducted to define the most influential variables in the model. **Results:** Monthly screening for 6 mo followed by 3 monthly screenings until 12 mo after transplant was dominant (lower costs and improved outcomes). Compared with no screening, the incremental benefits of screening were 0.294 life-years saved and 0.232 quality-adjusted life-years saved. Total savings from screening were \$6986 Australian dollars (\$5057 US dollars). The cost-effectiveness ratios were most sensitive to the costs of transplantation and dialysis, age of transplantation, prevalence of viremia, and probability of death in patients with a history of polyomavirus-associated nephropathy. Probabilistic sensitivity analysis indicated that screening (compared with no screening) was the dominant strategy across all plausible ranges of transition probabilities. **Conclusions:** Screening for polyomavirus infections 1 year following transplantation appears to save money, improves survival, and improves quality of life in kidney transplant recipients.

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mmunosuppression following kidney transplantation minimizes the risk of acute rejection and is needed to maintain long-term graft survival. However, prolonged suppression of the immune system increases the risk of opportunistic infections and reactivation of latent pathogenic viruses, such as polyomavirus infections.¹ When unrecognized and untreated, polyomavirus BK (BKPyV) infection can result in nephropathy, ureteric strictures, premature graft loss, and return to dialysis.² Viremia (BKPyV-DNAemia) is common during the

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first year after transplantation, affecting approximately 15% of transplant recipients, while 3% to 5% develop polyomavirus-associated nephropathy (PyVAN).³

The primary treatment strategy for identified polyomavirus infections is immunosuppression reduction. Conventional immunosuppression reduction approach may include judicious reduction or elimination of calcineurin inhibitors and antiproliferative agents or conversion to less potent immunosuppression therapy such as changing from tacrolimus to

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Data sharing: The authors are willing to share the statistical codes and program upon requests.

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cyclosporine. These changes allow immune reconstitution during the period of viremia and facilitate viral clearance before it progresses to nephropathy and graft dysfunction.⁴⁻⁸ Once PyVAN is established, the risk of allograft loss is over 50% in 5 y.⁹ The slow evolution of viremia to PyVAN over a typical time frame of 12 to 18 mo allows early reduction of immunosuppression therapies and a window of opportunity to prevent the development of advanced stage PyVAN, provided the infection is promptly identified.¹⁰

Current recommendation by the American Society of Transplantation suggests routine screening for BKPyV-DNAemia monthly through month 9 and then every 3 mo until 2 y post-transplant and stepwise reduction in immunosuppression when the plasma BKPyV-DNAemia is greater than 1000 copies/mL for 3 wk or more.11 The Kidney Disease Improving Global Outcomes guideline recommends screening with quantitative nucleic acid tests monthly for the first 3 to 6 months, followed 3 monthly up until the end of the first posttransplant year.¹² However, the evidence that underpins these recommendations is limited to observational data. No randomized controlled trials have been conducted to detect an improvement in graft function and survival or have assessed the potential harms associated with routine screening, including the development of de novo donor-specific antibodies (dnDSA) and rejection from immunosuppression reduction. Therefore, the best evidence to support or refute routine screening is reliant on the estimates derived from decision analytical modeling. A single published economic evaluation of screening for BKPyV-DNAemia indicates that routine screening is effective and cost-saving, but previous work did not account for retransplantation and the impact of immunosuppression reduction on the risk of dnDSA development.13 The aims of the study were to estimate the health care costs and benefits of screening for BKPyV, compared with no screening in contemporary kidney transplant practices, and to define the key variables that influenced the cost-effectiveness of routine screening.

MATERIALS AND METHODS

This study was reported according to the Consolidated Health Economic Evaluation Reporting Standards Statement.¹⁴ The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.¹⁵

Using a third-party payer's perspective, 2 deterministic and probabilistic Markov models were developed to simulate the natural history of BKPyV infection in a hypothetical cohort of kidney transplant recipients (n = 10000). We structured the models to include all the potential consequences of the infection, from viremia to the development of PyVAN, the downstream consequences of acute rejection, and the occurrence of dnDSA, graft loss, and death. The models were populated by collating and synthesizing all the relevant evidence (clinical, costs, and utilities) as input parameters. Uncertainties within the parameter estimates were assessed using 1-way and probabilistic sensitivity analyses. Costs and benefits were incorporated into each of these health states with the expected outcomes calculated by adding all the costs and effects across the states and weighting according to the time the patient is expected to be in each state. Although the models had no memory as to where and when the transplant recipients originated from and the timing of such transition, we had addressed this limitation by incorporated time dependency into the transition probabilities.16

Structure of the Model

The state transition diagram of the model is shown in Figure 1. The starting age for the base model was 45 y (median age of transplantation in the United States and Australia). This model assumed monthly screening for BKPyV using real-time quantitative polymerase chain reaction (RT-PCR) assay until month 6 and then 3 monthly until 12 mo post-transplant. This strategy was chosen because the median time to the diagnosis of polyomavirus infection is 9.5 mo and consistent with the



FIGURE 1. State transition diagram of the screen and no-screen arm. BK VAN, BK virus-associated nephropathy.

Kidney Disease Improving Global Outcomes recommendations.¹⁷ Of those who developed BKPyV-DNAemia, over 85% were diagnosed within the first 12 mo after transplantation.¹⁸ In the no-screening arm, we assumed no transplant recipients received screening. In the screening arm, BKPyV was identified through routine screening, and in some cases, PyVAN was confirmed with a graft biopsy. False-negative results were defined as patients with BKPyV infections (BKPyV-DNAemia and PyVAN) but were not detected on routine screening. False-positive results were defined as patients with positive BKPyV-DNAemia who never developed clinical nephropathy in the absence of immunosuppression reduction. In the noscreening arm, no transplant recipients received screening, and PyVAN was diagnosed when there was allograft dysfunction and confirmed histologically with biopsies.

Screening allows early recognition of the disease (in this case, viremia) by using the reliable RT-PCR testing. Using published data and estimates from registries, we estimated the probability of viremia as the prevalence of detectable viremia during the first year of transplantation. We then estimated the true and false positive and negative rates based on the test performance estimates of the RT-PCT assay reported in the literature. Through early detection of viremia, this then allowed intervention (reduction in immunosuppression) to prevent the progression of viremia to PyVAN. We have also accounted for the detrimental consequences of immunosuppression reduction including acute rejection and the potential risk of graft loss associated with acute rejection.

The trees (Figure 2A and B; Figure S1A and B, SDC, http:// links.lww.com/TXD/A417), beginning with the decision node (blue boxes), are read from left to right. Screening and no screening are the two alternatives. Events stemming from the chance nodes (represented by green boxes) were assigned with single probabilities such that the total probability of all events originating from a chance node sums up to 1. Information of the probability of response to interventions, quality of life (QoL) implications, and costs were then used to populate the model. The expected values of health outcomes and costs of the different branches in the tree were then calculated. This process was repeated for all options to calculate the expected outcomes and costs of screening and no screening, which were then used to calculate the incremental cost-effectiveness ratio (ICER) of screening compared with no screening.

For patients diagnosed with BKPyV infections, stepwise reduction in immunosuppression was the first step. In general, immunosuppression reduction included a 25% to 50% reduction in antimetabolites and calcineurin inhibitors, followed by complete withdrawal of antimetabolites in patients who did not respond to immunosuppression reduction. Adjuvant therapies including intravenous immunoglobulin were considered in a proportion of patients (10%) with persistent infections.8 Cidofovir and quinolones were not included in the modeling, given the lack of clinical benefits.19 Transplant recipients with BKPyV infections could progress through one of these transition states: acute rejection with or without development of dnDSA, no acute rejection/dnDSA, or stable graft function without dnDSA during the first year post-transplant. Individuals could experience graft loss, death, or remain alive at the end of year one.

Transplant recipients who experienced graft loss could remain alive on dialysis, receive another transplant, or die on dialysis. Those who remained alive at the end of the year could either survive with a functioning graft, die, or experience allograft loss. Those who experienced graft loss could return to dialysis. The model also assumed a small proportion of patients with allograft loss chose not to proceed with any form of kidney replacement therapy. A proportion of patients on dialysis would withdraw from dialysis each year (and opted for palliative and conservative management) and die during the concurrent year. We also assumed that all transplant maintenance costs were similar across the screening and no-screening arms. At the end of each cycle, the model accrued the effectiveness and costs for each patient in the assigned health state. Cumulative benefits and costs were calculated after all patients were deceased.

Sensitivity Analyses

Assumptions were tested over a range of plausible values to assess the robustness of the uncertainties in the model's parameter estimates using sensitivity analyses. Using 1-way sensitivity analyses, we identified the influential variables within the model. In addition to the baseline variables, we also tested the impact of discontinuing all antimetabolites or maintaining a reduced immunosuppression regimen until year 2 after the diagnosis of polyomavirus infections in the screening arm, on the overall cost-benefit ratios. Probabilistic sensitivity analysis was also undertaken. We assigned a distribution to each model parameter and sampled from that distribution using Monte Carlo simulation and estimated the expected value of the screening and no-screening arms. We used the log-normal distributions for relative risks and gamma distributions for costs and randomly sampled over 10000 iterations for each variable of interest.

Input Parameters for the Model

Clinical Data

A comprehensive literature search was conducted to identify the best available data on the clinical events that occurred after transplantation in patients with and without BKPyV infections (Table 1; Table S1, SDC, http://links.lww.com/ TXD/A417). Annual transition probabilities of the following variables in the patients with or without a history of PyVAN were sourced from transplant registries: probability of allograft loss and return to dialysis, death, and retransplantation. Other probabilities such as the annual incidence of acute rejection, development of dnDSA, utilities-based QoL, and test performance characteristics of the RT-PCR assays were sourced from published literature.²⁰⁻²⁷

Costs Data

Unit costs for screening, biopsy monitoring, treatment, and management strategies were estimated using a topdown approach and sourced from the published literature and country-specific costing agencies such as the Australian Refined Diagnosis Related Groups.²⁸ All costs were reported in 2020 Australian dollars (AUD) but also presented in US dollars in the base-case and sensitivity analyses. The impact of variability in the cost schedule was also tested in the sensitivity analyses.

Model Outcomes

The model outcomes included the total costs and health outcomes (expressed in life-years [LYs] and quality-adjusted В



*AR – acute rejection, DSA – donor specific antibodies *positive for viremia and negative for viremia



FIGURE 2. Markov model comparing screening and no screening for BKPyV A, Decision tree for the screened arm. B, Decision tree for the no-screen arm. AR, acute rejection; DSA, donor-specific antibody; PyVAN, polyomavirus-associated nephropathy.

LYs [QALYs]) and the incremental costs and health benefits of screening for BKPyV infections compared with no screening. The ICER of screening compared with no screening was calculated using the following formula: *ICER* = (*CostNew* - *CostComparator*)(*EffectivenessNew* - *Effectiv enessComparator*). Future costs and benefits were discounted using a discount rate of 5% per annum, and half-cycle corrections were employed. We used TreeAge Pro Healthcare 2021 (TreeAge software; Williamstown, MA) and SAS 9.4 to develop and analyze the model. This study used only published data and existing collection of registry records that only contain

TABLE 1.

Clinical, costs, and utilities data for the model

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5y 0.70, 78-0.60, 776-0.60, 776-0.60, 776-0.60, 776-0.60, 776-0.60, 776-0.60, 776-0.60, 776-0.60, 076, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.69-0.70, 0.75-0.60, 0.75-0.70, 0.80, 0.08-0.00, 775-84, 0.34, 0.03-0.36, 0.75, 0.73-0.70, 0.80, 0.08-0.01, 0.75-0.80, 0.75, 0.73-0.70, 0.90, 0.08-0.01, 0.75, 0.73-0.70, 0.90, 0.08-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.90, 0.88-0.01, 0.75, 0.73-0.70, 0.75, 0.		25-44	0.87 (0.87–0.88)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		65-74	0.79 (0.78–0.80)	
5 y 38-6 0.57 (0.33-0.62) 35,36 25-44 0.85 (0.33-0.62) 25-44 0.85 (0.83-0.86) 35,36 25-44 0.85 (0.83-0.86) 35,36 35,36 25-44 0.85 (0.83-0.86) 35,36 45-54 0.89 (0.83-0.86) 35,36 75-84 0.49 (0.83-0.86) 35,36 75-84 0.89 (0.83-0.86) 35,36 75-84 0.89 (0.83-0.86) 35,36 75 y 0.90 (0.83-0.81) 35,36 75 y 0.90 (0.83-0.81) 35,36 75 y 0.90 (0.83-0.81) 35,36 75 y 0.90 (0.88-0.91) 35,36 75 y 0.90 (0.88-0.91) 35,36 75 y 0.90 (0.88-0.91) 35,36 75 y 0.90 (0.98-0.01) 35,36 75 y 0.90 (0.98-0.02) 35,36 75 y 0.90 (0.98-0.91) 35,36 75 y 0.90 (0.92-0.91) 35,36 75 y 0.90 (0.92-0.91) 35,36 75 y 0.90 (0.92-0.91) <		75–84	0.71 (0.69–0.72)	
5 y 18-24 0.49 (0.92-0.95) 35.36 45-64 0.84 (0.68-0.60) 65-74 0.88 (0.88-0.80) 65 Transplant survival 285 0.18 (0.15-0.23) 75-94 0.34 (0.33-0.36) 285 Transplant survival 285 0.19 (0.15-0.23) 75-94 0.39 (0.88-0.91) 75 Transplant survival 0.97 (0.97-0.98) 50 (0.15-0.26) 75 73-30.77 75 To y 0.97 (0.97-0.98) 50 (0.88-0.91) 75 73-30.77 75 75 To y 0.97 (0.97-0.98) 50 (0.97-0.98) 75 73-30.77 75		≥85	0.57 (0.53-0.62)	
25-44 0.98 (0.89-0.70) 65-74 0.89 (0.88-0.90) 75-84 0.34 (0.33-0.36) 285 0.18 (0.15-0.23) Transplant survival 35.36 First yaar 0.97 (0.97-0.96) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.90 (0.88-0.91) 10 y 0.76 (0.74-0.77) 15 y 0.90 (0.88-0.91) 10 y 0.76 (0.74-0.77) 15 y 0.98 (0.94-0.97) 15 y 0.98 (0.94-0.97) 10 y 0.88 (0.86-0.89) 10 y 0.88 (0.86-0.89) 15 y 0.88 (0.86-0.89) 15 y 0.88 (0.86-0.89) 15 y 0.80 (0.97-0.98)	5 y	18–24	0.94 (0.92–0.95)	35,36
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		25-44	0.85 (0.83–0.86)	
75-44 0.34 (0.38-0.39) 285 0.18 (0.15-0.2) Transplant survival 35,36 Pattern survival deceased door transplant 0.97 (0.97-0.89) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.64 (0.61-0.66) First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.64 (0.61-0.66) First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.76 (0.74-0.79) 7 hot year 0.98 (0.88-0.91) 10 y 0.76 (0.74-0.79) 15 y 0.88 (0.88-0.81) 10 y 0.76 (0.74-0.79) 15 y 0.88 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.88 (0.87-0.99) 5 y 0.26 (0.24-0.51) 7 first year 0.88 (0.87-0.99) 5 y 0.26 (0.24-0.51) 10 y 0.75 (0.72-0.77) 10 y		45-64	0.94 (0.69–0.70)	
Dramb Dramb Transplant survival 285 0.18 (0.157-0.23) Transplant survival 35,36 35,36 First year 0.57 (0.37-0.39) 0.05 (0.38-0.31) 10 y 0.75 (0.73-0.77) 0.59 5 y 0.00 (0.48-0.31) 0.04 (0.61-0.66) Graft survival: deceased donor transplant 35,36 35,36 First year 0.37 (0.37-0.39) 35,36 5 y 0.09 (0.88-0.91) 35,36 5 y 0.99 (0.98-0.10) 35,36 First year 0.99 (0.98-0.91) 35,36 First year 0.99 (0.98-0.91) 35,36 First year 0.98 (0.97-0.99) 35 5 y 0.99 (0.88-0.91) 35,36 First year 0.216 35,36 First year 0.216 35,36 S y 0.99 (0.98-0.91) 35,36 S		00-74	0.89 (0.88–0.90)	
Transplant survival Score Score Score Score Patient survival: deceased donor transplant 0.97 (0.97-0.98) Score Score 5 y 0.03 (0.88-0.91) Score Score Score 15 y 0.64 (0.61-0.660) Score <		>85	0.18 (0.15–0.23)	
Painet survival: deceased donor transplant 35,36 First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.64 (0.61-0.66) Graft survival: deceased donor transplant 0.97 (0.97-0.98) First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.90 (0.88-0.91) 15 y 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 15 y 0.94 (0.46-0.51) 70 y 0.94 (0.46-0.51) 90 (0.98-0.00) 0.80 (0.86-0.89) 5 y 0.96 (0.94-0.97) 10 y 0.88 (0.86-0.89) 15 y 0.76 (0.74-0.79) 5 y 0.88 (0.88-0.89) 5 y 0.88 (0.88-0.91) 10 y 0.76 (0.74-0.79) 5 y 0.76 (0.74-0.79) 5 y 0.89 (0.88-0.01) 5 y 0.50 (0.52-0.58) First year 0.216 Deceased donor 2.216 De	Transplant survival	200	0.10 (0.10 0.20)	
First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.64 (0.61-0.66) Graft survia: deceased donor transplant 9.97 (0.97-0.98) First year 0.97 (0.97-0.98) 5 y 0.920 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.930 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.940 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.940 (0.94-0.97) 10 y 0.88 (0.88-0.89) 10 y 0.88 (0.88-0.89) 10 y 0.88 (0.88-0.89) 10 y 0.88 (0.88-0.19) 10 y 0.75 (0.73-0.77) 15 y 0.88 (0.89-0.19) 10 y 0.75 (0.73-0.77) 15 y 0.89 (0.97-0.99) 5 y 0.89 (0.97-0.90) 5 y 0.75 (0.73-0.77) 10 y 0.75 (0.73-0.77) 10 y 0.75 (0.73-0.77) 10 y 0.75 (0.73-0.77) 10 y 0.75	Patient survival: deceased donor transplant			35,36
5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.64 (0.61-0.66) Graft survival: deceased donor transplant 35.36 First year 0.97 (0.97-0.98) 5 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.91 (0.88-0.91) Patient survival: living donor transplant 53.36 First year 0.99 (0.89-1.00) 5 y 0.96 (0.94-0.97) 10 y 0.76 (0.74-0.79) 5 y 0.98 (0.87-0.99) 6raft survival: living donor transplant 9.98 (0.87-0.91) 7 rest year 0.98 (0.87-0.91) 5 y 0.99 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.76 (0.74-0.79) 5 y 0.99 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.75 (0.73-0.77) 15 y 0.21 (0.73 (0.77)	First year		0.97 (0.97-0.98)	
10 y 0.75 (0.73-0.77) 35,36 First year 0.97 (0.97-0.98) 35,36 First year 0.99 (0.88-0.91) 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 35,36 First year 0.99 (0.98-0.91) 35,36 Patient survival: living donor transplant 35,36 35,36 First year 0.99 (0.98-0.91) 35,36 First year 0.99 (0.98-0.97) 36 5 y 0.96 (0.94-0.97) 35,36 15 y 0.98 (0.87-0.99) 35,36 First year 0.98 (0.87-0.99) 36 5 y 0.89 (0.88-0.89-0.91) 35,36 First year 0.98 (0.87-0.99) 35 5 y 0.38 (0.86-0.91) 35,36 10 y 0.75 (0.73-0.77) 35 10 y 0.55 (0.52-0.58) 35,36 Carlat rejection 15 y 35,36 Probability of graft figication: first 6 mo 35,36 35,36 Living donor 15 y 35,36 35,36 Subsequent grafts 0.20	5 y		0.90 (0.88–0.91)	
15 y 0.01 (0.01 - 0.00) Graft survival: deceased donor transplant 5.36 First year 0.97 (0.87 - 0.8) 5 y 0.90 (0.88 - 0.91) 10 y 0.75 (0.73 - 0.7) 15 y 0.48 (0.46 - 0.51) Patient survival: living donor transplant 35,36 First year 0.99 (0.98 - 1.00) 5 y 0.96 (0.94 - 0.97) 10 y 0.98 (0.96 - 0.89) 10 y 0.98 (0.97 - 0.99) 5 y 0.98 (0.97 - 0.99) 5 y 0.88 (0.86 - 0.89) 10 y 0.76 (0.74 - 0.79) 5 y 0.89 (0.97 - 0.99) 5 y 0.89 (0.97 - 0.91)	10 y		0.75 (0.73–0.77)	
Charls survived: Solution Solution Solution First year 0.97 (0.97-0.98) 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 0.48 (0.46-0.51) Patient survival: living donor transplant 0.99 (0.98-0.00) 5 y First year 0.99 (0.98-0.00) 5 y 0.96 (0.94-0.97) 10 y 0.98 (0.94-0.97) 0.96 (0.94-0.97) 0.96 (0.94-0.97) 10 y 0.98 (0.96-0.89) 15 y 0.98 (0.97-0.99) 15 y 0.98 (0.97-0.99) 5 y 0.98 (0.97-0.99) 15 y 0.76 (0.74-0.79) 35,36 First year 0.98 (0.97-0.99) 5 y 0.89 (0.88-0.81) 10 y 0.75 (0.73-0.77) 0.55 35,36 First year 0.98 (0.97-0.99) 5 y 0.89 (0.88-0.81) 0.10 10 y 0.75 (0.73-0.77) 0.55 (0.52-0.58) 5.36 Graft rejection: first 6 mo 1.107 20 5.36 Living donor First year 0.20 7 Probability of acute rejection: subsequent years 0.20 20	ID y Graft survival: deceased deper transplant		0.64 (0.61–0.66)	25.26
Tarky part 0.90 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.48 (0.46-0.51) Patient survival: living donor transplant 35,36 First year 0.99 (0.98-1.00) 5 y 0.96 (0.94-0.97) 10 y 0.88 (0.86-0.89) 15 y 0.76 (0.74-0.79) 6 raft survival: living donor transplant 9.88 (0.86-0.89) 15 y 0.76 (0.74-0.79) 6 raft survival: living donor transplant 0.99 (0.88-0.91) 10 y 0.88 (0.86-0.89) 15 y 0.99 (0.88-0.91) 10 y 0.89 (0.87-0.99) 5 y 0.99 (0.88-0.91) 10 y 0.55 (0.52-0.58) Graft rejection 35,36 First year 0.191 Subsequent grafts 0.216 Deceased donor 35,36 First graft 0.216 Deceased donor 37 First graft 0.20 Probability of acute rejection: first 12 mo 0.216 Deceased donor 37 Probability of acute rejection wi	First year		0.97 (0.97–0.98)	55,50
10y 0.75 (0.73 - 0.77) 15y 0.48 (0.46 - 0.51) Patient survival: living donor transplant 35,36 First year 0.99 (0.98 - 1.00) 5y 0.36 (0.94 - 0.97) 10y 0.36 (0.94 - 0.97) 10y 0.36 (0.74 - 0.79) 15y 0.36 (0.74 - 0.79) Graft survival: living donor transplant 35,36 First year 0.98 (0.97 - 0.99) 5y 0.59 (0.73 - 0.77) 15y 0.59 (0.73 - 0.77) 10y 0.75 (0.73 - 0.77) 15y 0.59 (0.52 - 0.58) Graft rejection 35,36 Living donor 35,36 Living donor 35,36 Living donor 35,36 Living donor 35,36 Subsequent grafts 0.216 Deceased donor 10 First graft 0.185 Subsequent grafts 0.20 Probability of acute rejection: subsequent years 0.04 Acute rejection with BK infection 0.215 21 Probability of acute	5 v		0.90 (0.88–0.91)	
15 y 0.48 (0.46-0.51) Patient survival: living donor transplant 35,36 First year 0.99 (0.98-1.00) 5 y 0.96 (0.44-0.97) 10 y 0.98 (0.86-0.89) 15 y 0.76 (0.74-0.79) Graft survival: living donor transplant 35,36 First year 0.98 (0.97-0.99) 5 y 0.98 (0.88-0.91) 10 y 0.75 (0.73-0.77) 10 y 0.75 (0.73-0.77) 15 y 0.59 (0.52-0.58) Graft rejection 35,36 Probability of graft rejection: first 6 mo 35,36 Probability of acute rejection: first 16 mo 0.191 Subsequent grafts 0.216 Deceased donor 37 First yraft 0.185 Subsequent grafts 0.20 Probability of acute rejection: subsequent years 0.04 38 Acute rejection and DSA 21 7 Probability of acute rejection with BK infection 0.215 21 Probability of acute rejection with NM Wirmia 0.34 22 Probability of acute rejection with NM PVAN 0.66 23 <	10 y		0.75 (0.73–0.77)	
Patient survival: living donor transplant 35,36 First year 0.99 (0.98–1.00) 10 y 0.88 (0.86–0.89) 15 y 0.76 (0.74–0.79) 6 raft survival: living donor transplant 35,36 First year 0.98 (0.97–0.99) 5 y 0.89 (0.88–0.91) 10 y 0.75 (0.73–0.77) 15 y 0.55 (0.52–0.58) Graft survival: living donor 35,36 Probability of graft rejection: first 6 mo 35,36 Living donor 35,36 First year 0.98 (0.87–0.99) 5 y 0.55 (0.52–0.58) Graft rejection 35,36 Probability of graft rejection: first 6 mo 35,36 Living donor 35,36 First graft 0.191 Subsequent grafts 0.216 Deceased donor 20 First graft 0.185 Subsequent grafts 0.20 Probability of acute rejection: subsequent years 0.04 38 Acute rejection and DSA 21 Probability of acute rejection with BSA in pati	15 y		0.48 (0.46-0.51)	
First year 0.99 (0.98-1.00) 5 y 0.96 (0.94-0.97) 10 y 0.88 (0.86-0.89) 15 y 0.76 (0.74-0.79) Graft survival: living donor transplant 35,36 First year 0.98 (0.97-0.99) 5 y 0.89 (0.86-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.55 (0.52-0.58) Graft rejection 35,36 First graft 0.191 Subsequent grafts 0.216 Deceased donor	Patient survival: living donor transplant			35,36
5 y 0.96 (0.94–0.97) 10 y 0.88 (0.86–0.89) 15 y 0.76 (0.74–0.79) Graft survival: living donor transplant 35,36 First year 0.98 (0.97–0.99) 5 y 0.89 (0.88–0.91) 10 y 0.75 (0.73–0.77) 15 y 0.55 (0.52–0.58) Graft rejection 35,36 First year 0.191 Subsequent grafts 0.191 Subsequent grafts 0.216 Deceased donor	First year		0.99 (0.98–1.00)	
10 y 0.00 (0.00-0.09) 15 y 0.76 (0.74-0.79) Graft survival: living donor transplant 35,36 First year 0.98 (0.97-0.99) 5 y 0.89 (0.88-0.91) 10 y 0.75 (0.73-0.77) 15 y 0.55 (0.52-0.58) Graft rejection 35,36 Probability of graft rejection: first 6 mo 35,36 Living donor 35,36 First graft 0.191 Subsequent grafts 0.216 Deceased donor 7 First graft 0.185 Subsequent grafts 0.20 Probability of acute rejection: first 12 mo 0.214 Probability of acute rejection with BK infection 0.215 Probability of acute rejection with BK infection 0.215 Probability of acute rejection with bigh viremia 0.34 Probability of acute rejection with bigh inpatients with PyVAN 0.16 Probability of acute rejection with DSA in patients with PyVAN 0.19 Probability of acute rejection with DSA in patients with PyVAN 0.19 Probability of no acute rejection with DSA in patients with PyVAN<	5 y 10 y		0.96(0.94-0.97)	
Graft survival: living donor transplant35,36First year0.98 (0.97–0.99)5 y0.89 (0.88–0.91)10 y0.75 (0.73–0.77)15 y0.55 (0.52–0.58)Graft rejection35,36Probability of graft rejection: first 6 mo35,36Living donor0.191Subsequent grafts0.216Deceased donor0.216First graft0.185Subsequent grafts0.20Probability of acute rejection: sits 12 mo0.214Probability of acute rejection with BK infection0.215Probability of acute rejection with high viremia0.34Probability of acute rejection with byVAN0.19Probability of acute rejection with DSA in patients with PyVAN0.19Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with acute rejection with PyVAN0.1 </td <td>15 v</td> <td></td> <td>0.76 (0.74–0.79)</td> <td></td>	15 v		0.76 (0.74–0.79)	
First year 0.98 (0.97–0.99) 5 y 0.89 (0.88–0.91) 10 y 0.75 (0.73–0.77) 15 y 0.55 (0.52–0.58) Graft rejection 35,36 Living donor 35,36 First graft 0.191 Subsequent grafts 0.216 Deceased donor	Graft survival: living donor transplant			35.36
5 y 0.89 (0.88–0.91) 10 y 0.75 (0.73–0.77) 15 y 0.55 (0.52–0.58) Graft rejection 35,36 Living donor 35,36 First graft 0.191 Subsequent grafts 0.216 Deceased donor 1 First graft 0.185 Subsequent grafts 0.20 Probability of acute rejection: first 12 mo 0.214 Probability of acute rejection: subsequent years 0.04 Acute rejection and DSA 21 Probability of acute rejection with BK infection 0.215 21 Probability of acute rejection with BK infection 0.34 22 Probability of acute rejection with bg viremia 0.17 22 Probability of acute rejection with bg viremia 0.23 23 Probability of acute rejection with DSA in patients with PyVAN 0.19 24,25 Probability of no acute rejection with DSA in patients with PyVAN 0.13 21,39	First year		0.98 (0.97-0.99)	,
10 y 0.75 (0.73-0.77) 15 y 0.55 (0.52-0.58) Graft rejection 35,36 Probability of graft rejection: first 6 mo 35,36 Living donor 0.191 First graft 0.191 Subsequent grafts 0.216 Deceased donor 0.20 First graft 0.185 Subsequent grafts 0.20 Probability of acute rejection: first 12 mo 0.20 Probability of acute rejection: subsequent years 0.04 38 Acute rejection and DSA 1 2 Probability of acute rejection with BK infection 0.215 21 Probability of acute rejection with by viremia 0.34 22 Probability of acute rejection with by NaN 0.06 23 Probability of acute rejection with DSA in patients with PyVAN 0.1 21,39 Probability of no acute rejection with DSA in patients with PyVAN 0.65 21,39	5 y		0.89 (0.88–0.91)	
15 y0.55 (0.52–0.58)Graft rejection35,36Probability of graft rejection: first 6 mo35,36Living donor0.191Subsequent grafts0.216Deceased donor0.185First graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.214Probability of acute rejection with bK infection0.215Probability of acute rejection with high viremia0.34Probability of acute rejection with high viremia0.17Probability of acute rejection but no DSA in patients with PyVAN0.19Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.21,39	10 y		0.75 (0.73–0.77)	
Grant rejection35,36Probability of graft rejection: first 6 mo35,36Living donor0.191Subsequent grafts0.216Deceased donor0.185First graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.214Probability of acute rejection: subsequent years0.04Acute rejection and DSA0.215Probability of acute rejection with BK infection0.215Probability of acute rejection with ligh viremia0.34Probability of acute rejection with low viremia0.17Probability of acute rejection but no DSA in patients with PyVAN0.19Probability of acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.65Probability of no acute rejection and no DSA in patients with PyVAN0.65	15 y Cyster existence		0.55 (0.52–0.58)	
First graft0.191Subsequent grafts0.216Deceased donor0.20First graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.214Probability of acute rejection: subsequent years0.04Acute rejection and DSA0.215Probability of acute rejection with BK infection0.215Probability of acute rejection with BK infection0.215Probability of acute rejection with bK infection0.217Probability of acute rejection with bK infection0.217Probability of acute rejection with bK infection0.215Probability of acute rejection with bK infection0.215Probability of acute rejection with bK infection0.215Probability of acute rejection with bK infection0.217Probability of acute rejection with DSA in patients with PyVAN0.06Probability of acute rejection with DSA in patients with PyVAN0.19Probability of no acute rejection but has DSA in patients with PyVAN0.1Probability of no acute rejection but has DSA in patients with PyVAN0.1Probability of no acute rejection but has DSA in patients with PyVAN0.1Probability of no acute rejection but has DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.65Probability of no acute rejection and no DSA in patients with PyVAN0.65	Gran rejection			25.26
First graft0.191Subsequent grafts0.216Deceased donor0.185First graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.214Probability of acute rejection: subsequent years0.04Acute rejection and DSA0.215Probability of acute rejection with BK infection0.215Probability of acute rejection with BK infection0.215Probability of acute rejection with bigh viremia0.34Probability of acute rejection with low viremia0.17Probability of acute rejection with DSA in patients with PyVAN0.06Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with as DSA in patients with PyVAN0.1Probability of no acute rejection with no DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with DSA in patients with PyVAN0.1Probability of no acute rejection with no DSA in patients with PyVAN0.1Probability of no acute rejection with no DSA in patients with PyVAN0.1Probability of no acute rejection with no DSA in patients with PyVAN0.1Probability of no acute rejection with no DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.65Probability of no acute rejection and no DSA in patients with PyVAN0.65	Living donor			55,50
Subsequent grafts0.216Deceased donor	First graft		0.191	
Deceased donorFirst graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.214Probability of acute rejection: subsequent years0.04Acute rejection and DSA38Probability of acute rejection with BK infection0.215Probability of acute rejection with BK infection0.34Probability of acute rejection with high viremia0.34Probability of acute rejection with low viremia0.17Probability of acute rejection with DSA in patients with PyVAN0.06Probability of acute rejection with DSA in patients with PyVAN0.19Probability of no acute rejection but no DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.1Probability of no acute rejection and no DSA in patients with PyVAN0.13Probability of no acute rejection and no DSA in patients with PyVAN0.15	Subsequent grafts		0.216	
First graft0.185Subsequent grafts0.20Probability of acute rejection: first 12 mo0.21437Probability of acute rejection: subsequent years0.0438Acute rejection and DSA721Probability of acute rejection with BK infection0.21521Probability of acute rejection with BK infection0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection with DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but no DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Deceased donor			
Subsequent grafts0.20Probability of acute rejection: first 12 mo0.21437Probability of acute rejection: subsequent years0.0438Acute rejection and DSA0.21521Probability of acute rejection with BK infection0.21521Probability of acute rejection with high viremia0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but no DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	First graft		0.185	
Probability of acute rejection: Irfst 12 mo0.21437Probability of acute rejection: subsequent years0.0438Acute rejection and DSA0.21521Probability of acute rejection with BK infection0.21521Probability of acute rejection with high viremia0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Subsequent grafts		0.20	07
Acute rejection and DSA0.0438Probability of acute rejection with BK infection0.21521Probability of acute rejection with high viremia0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection: first 12 mo		0.214	37
Probability of acute rejection with BK infection0.21521Probability of acute rejection with high viremia0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but na DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Acute rejection and DSA		0.04	30
Probability of acute rejection with high viremia0.3422Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but no DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection with BK infection		0.215	21
Probability of acute rejection with low viremia0.1722Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection with high viremia		0.34	22
Probability of acute rejection but no DSA in patients with PyVAN0.0623Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection with low viremia		0.17	22
Probability of acute rejection with DSA in patients with PyVAN0.1924,25Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection but no DSA in patients with PyVAN		0.06	23
Probability of no acute rejection but has DSA in patients with PyVAN0.121,39Probability of no acute rejection and no DSA in patients with PyVAN0.6521,39	Probability of acute rejection with DSA in patients with PyVAN		0.19	24,25
Probability of no acute rejection and no DSA in patients with PyVAN 0.65 21,39	Probability of no acute rejection but has DSA in patients with PyVAN		0.1	21,39
	Probability of no acute rejection and no DSA in patients with PyVAN		0.65	21,39

Clinical, costs, and utilities data for the model

Gent displanding of particulation in alcoances 0.4 39 Probability of particulation in alcoances 0.11 40.41 Probability of particulation in alcoances 0.22 25 Gent loss in patients with particulation in alcoances 0.048 4.20 Probability of particles in patients with particulation in alcoances 0.114 27 Probability of particles after patients with Particulation in alcoances 0.048 4.20 Probability of particles after patients with Particulation in alcoances 0.033 42 Probability of particles after patient sequences 0.033 42 Probability of particles after patient sequences 0.033 42 Probability of particles after patient sequences 0.05 20 Probability of particles after patient sequences 0.25 20 Probability of particles without PARM 0.46 26 Probability of particles from alcoances 0.37 20 Probability of particles from alcoances 0.47 20 Probability of particles from alcoances 0.67 30 Probability of particles from alcoances 0.46 420	Clinical data		Estimates	References
Probable of grid defunction from all causes 0.4 39 Probable of for Name registion is patients with grid defunction 0.22 25 Grid loss in patients with patient definitions 0.057 4.20 Probable of for Name is natients with patient definitions 0.057 4.20 Probable of grid hass in patients with pAWA but no registion 0.058 20 Orbable of grid hass in patients with pAWA but no registion 0.058 20 Orbable of grid hass from all causes 0.147 27 Probable of grid hass from all causes 0.038 20 Orbable of grid hass definitions with PAWA 0.068 20.30 Kinetchn within the first year 0.16-0.30 20 Probable of grid hass definitions with add in 200001 FICR is within the first year 0.36 20 Probable of grid hass from all causes 0.05 35 Recarrence of HK in interaregridination 0.06 36 Probable of grid hass from all causes 20 20 Probable of grid hass from the start part definition of th	Graft dysfunction (no-screen arm)			
Probability of avails with graft defanction 0.11 40.41 Probability of avails enclosin patients with pAVN 0.22 25 Graft ises in patients with pAVN 0.048 4.20 Probability of graft ises in patients with pAVN but no rejection 0.048 4.20 Probability of graft ises in patients with pAVN but no rejection 0.048 4.20 Probability of graft ises ins active rejection 0.038 20 Probability of graft ises sing active rejection 0.03 42 Probability of graft ises sing active rejection 0.046 20.30 Probability of graft ises representation is evalued relevant 0.046 20.30 BK infection within the first year 0.10-0.30 20 Probability of resentation is evalued relevant 0.26 20	Probability of graft dysfunction from all causes		0.4	39
Probability of actions in patients with spart dystanction 0.22 26 Probability of graft loss in patients with PANN and a cute rejection 0.657 4.20 Probability of graft loss in patients with PANN and a cute rejection 0.038 20 Probability of graft loss in patients with PANN 0.038 20 Probability of graft loss in patients with PANN 0.038 20 Probability of graft loss in patients with PANN 0.038 20 Probability of graft loss without PANN 0.038 20 Probability of graft loss without PANN 0.038 20 Probability of graft loss without PANN 0.038 20 Probability of PANN with RS varial less of the seve 0.110-0.30 20 Probability of PANN with RS varial less of the seve 0.25 20 Probability of PANN with RS varial less of the seve 0.31 20 Probability of PANN with RS varial less for RS varial less	Probability of PyVAN in patients with graft dysfunction		0.11	40,41
Grift loss in patients with PVMI of a cube rejection 0.057 4.20 Probability of path loss in patients with PVMI of a cube rejection 0.048 4.20 Grift loss in patients with PVMI of a cube rejection 0.048 4.20 Enditiss in patients with PVMI of a cube rejection 0.038 20 Probability of path loss them cube rejection 0.038 20 Probability of path loss them cube rejection 0.038 20 Probability of path loss them cube rejection 0.03 42 Probability of path loss them cube rejection 0.03 20 Probability of path loss them cube rejection 0.046 20 Probability of path loss them cube rejection 0.26 20 Probability of path loss them cube rejection 0.31 20 Probability of them loss them cube rejection 0.06 26 Probability of them loss them cube rejection 0.06 26 Probability of them loss them cube rejection 0.06 26 Probability of them loss them cube rejection 0.06 26 Probability of them loss them cube rejection 0.06 26 <t< td=""><td>Probability of acute rejection in patients with graft dysfunction</td><td></td><td>0.22</td><td>25</td></t<>	Probability of acute rejection in patients with graft dysfunction		0.22	25
Probability of profits in patients with PVMN and scalar ergection 0.057 4.20 Probability of profits in patients with PVMN to respiciton 0.0468 4.20 Probability of profits so from all causes 0.033 20 Probability of profits so from all causes 0.033 42 Probability of profits so from all causes 0.046 20.30 BK intection within the first year 0.046 20.30 Probability of profits so from all causes 0.10-0.30 20 Probability of profits so from all causes 0.10-0.30 20 Probability of profits so from SK wall kad >10000 0.75 20 Probability of profits So from SK wall kad >10000 0.67 20 Probability of profits So from SK wall kad >10000 0.67 20 Probability of profits So from SK wall kad >10000 0.67 20 Probability of profits So from SK wall kad >10000 0.67 20 Probability of profits So from SK without monitoring 0.46 26 Probability of Profits So from SK without monitoring 0.75 43 Probability of Profits So from SK without moninbring 0.76 43	Graft loss in patients with PyVAN			
Produbility of print loss in patients with PyWA but no rejection0.0484.20Probability of print loss from acid uses0.14.727Probability of print loss from acids rejection0.03820Probability of print loss from acids rejection0.0342Probability of print loss from acids rejection0.04620Probability of print loss from acids rejection0.0620Probability of positive BWCM with the first year0.10-0.3020Probability of positive BW raid acid >10000 PCR 8 + ve0.2520Probability of positive BW raid acid >10000 PCR 8 + ve0.7520Probability of positive BW raid acid >10000 PCR 8 + ve0.7520Probability of positive BW raid acid >10000 PCR 8 + ve0.7520Probability of positive BW raid acid >10000 PCR 8 + ve0.7535Probability of reprint BW raid acid >100000.312020Probability of reprint BW raid acid >100000.452535Recurrence of the acond/subsequent transplant BW0.462626Probability of reprint BW raid acid >1000023535Recurrence of the acond/subsequent transplant BW reprint BW raid Acid >10.483636Year after transplant BW reprint BW raid Acid >10.483636Year after transplant BW reprint BW raid >10.483636Year after transplant BW reprint BW raid >10.483636Year after transplant BW reprint BW raid >10.483636Year after	Probability of graft loss in patients with PyVAN and acute rejection		0.057	4,20
Gart Loss in painfare without PMAN 0.147 27 Probability of yait loss form actus rejection 0.039 20 Probability of yait loss form actus rejection 0.039 20 Probability of yait loss form actus rejection 0.039 20 BK intection within the first year 0.0469 20.30 Probability of poster BK winal act 10000 PDR s-we 0.75 20 Probability of poster BK winal act 10000 PDR s-we 0.75 20 Probability of poster BK winal act 10000 PDR s-we 0.37 20 Probability of poster BK winal act 10000 PDR s-we 0.37 20 Cate depression BK non-screening arm 0.46 26 Probability of poster BK winal act 10000 PDR s-we 0.37 20 Cate depression BK non-screening arm 0.47 26 Probability of poster BK wina back 10000 PDR s-we 0.36 44 Surveor DK Nu hin the second transplant thransplant 1 0.46 26 Probability of poster BK Wind act 10000 PDR s-we 0.36 36 43 Variant fort manaphant thre currence 0.36 0.44 30 <t< td=""><td>Probability of graft loss in patients with PyVAN but no rejection</td><td></td><td>0.048</td><td>4,20</td></t<>	Probability of graft loss in patients with PyVAN but no rejection		0.048	4,20
Probability of part loss for a alter exection0.14727Probability of part loss for a alter exection0.03820Probability of part loss for a alter exection0.03842Bit factorn within the first year0.04620.300Probability of part loss for a alter factorn0.0520Probability of part loss for a alter factorn0.0520Probability of part loss for a loss of loss	Graft loss in patients without PyVAN			,
Probability of part loss from scale rejection0.03320Probability of part loss from scale rejection0.03342Probability of part loss without PyWN0.04620,30BK infection within the first year0.10–0.3020Probability of partive BK Viral load >100001 FPC1 is ve0.10–0.3020Probability of partive BK Viral load >100001 FPC1 is ve0.7520Probability of PyMN with BK Viral load >1000010.8720Probability of PyMN with BK Viral load >1000010.3120Late diagnosis of BK no-screening am0.4626Probability of partines from SK With with rest or motioning0.4626Probability of retransplantation0.17543Probability of retransplantation0.17543Probability of Part loss from SK With with rest rescond 'managenest states43Structured for transplantation10.986 (0.39-1.00)Probability of retransplant with recurrence30.996 (0.88-1.00)Stratt transplant10.996 (0.88-1.00)	Probability of graft loss from all causes		0.147	27
Probability of grint loss without PVAN 0.03 42 Probability of grint loss without PVAN 0.046 20.30 Bt intection within the first year 0.10–0.30 20 Probability of positive BKV all load -10000 IPCN is +ve 0.25 20 Probability of positive BKV and load -10000 IPCN is +ve 0.37 20 Probability of provide BKV and load -10000 0.87 20 Probability of provide BKV and load -10000 0.87 20 Probability of provide BKV and load -10000 0.37 20 Probability of provide BKV and load -10000 0.37 20 Probability of provide BKV and load -10000 0.46 26 Probability of representation 0.46 26 Probability of representation 0.46 26 Probability of representation 0.47 3 Representation of representation 0.43 3 Survival 1 0.985 (9.33–100) 44 Yeas after transplant 1 0.985 (9.33–100) 45 Cards survival 2 0.94 (9.85–100) 44	Probability of graft loss after acute rejection		0.038	20
Probability of path loss within the first year 0.046 20,30 BK intection within the first year 0.10–0.30 20 Probability of positive BK vial loss 1-0000 IPCR is +ve 0.25 20 Probability of positive BK vial loss 1-0000 IPCR is +ve 0.75 20 Probability of PVAN with BK vial loss 1-0000 IPCR is +ve 0.31 20 Late diagnosis of BK ros-screening arm 0.05 35 Probability of PVAN with BK vial loss 1-0000 IPCR is +ve 0.05 35 Probability of retransplantation 0.05 35 Recurrence of BK in retransplantation 0.173 43 Probability of PVAN with BK vial loss cons Users 1 0.985 (0.93-1.00) Start for transplant time scons distansplant with recurrence 0.33 0.985 (0.93-1.00) Vear after transplant 1 0.985 (0.93-1.00) 43 Vear after transplant 1 0.986 (0.88-1.00) - Casts and resource uses, \$ (vLD) 43 800-1500 80 Casts and resource uses, \$ (vLD) 40 90000 2000-1000 Casts and resource uses, \$ (vLD) 433	Probability of graft loss from acute rejection		0.03	42
Bit infection within the first year 0.10-0.30 20 Probability of positive BKVral isked >10000 if PCR is +ve 0.25 20 Probability of positive BKVral isked >10000 if PCR is +ve 0.75 20 Probability of positive BKVral isked >10000 0.87 20 Probability of PXVAW with BK via isked >10000 0.87 20 Probability of positive BKVral isked >10000 0.87 20 Probability of present BK without monitoring 0.46 26 Probability of present BK without monitoring 0.05 35 Recurrence of BK in retransplantation 0.175 43 Probability of retransplantation 0.06 44 Survised of retransplant second busequent ransplants 0.175 43 Probability of Exercise 0.06 44 Survised of retransplant 1 0.985 (9.33-1.00) 44 Survised of retransplant 2 0.94 (0.85-1.00) 45 The safter transplant 1 0.96 (9.3-1.00) 45 Sets and resource uses, S (ALD) 44 40 46 Vears after transplant	Probability of graft loss without PvVAN		0.046	20.30
Probability of positive BX with the first year 0.10–030 20 Probability of positive BX with load <10000 FPCH is +ve	BK infection within the first year			-)
Probability of positive BK viral load >10000 if PCR is +ve 0.25 20 Probability of PVAW with BK viral load >10000 0.87 20 Probability of PVAW with BK viral load >10000 0.87 20 Probability of PVAW with BK viral load >10000 0.87 20 Probability of prostite BK viral load >10000 0.87 20 Probability of prostite BK viral load >10000 0.87 20 Probability of prostite BK viral load >10000 0.46 26 Probability of prostite BK viral load >10000 0.46 26 Probability of transplantation 0.05 35 Recurrence of BK in retransplantation 0.175 43 Virat of retransplant the courrence 0.66 (0.83-1.00) 2 Survial of retransplant 1 0.96 (0.83-1.00) 4 Vears after transplant 1 0.96 (0.83-1.00) 2 Costs on resour	Probability of positive BKPCR within the first year		0.10-0.30	20
Probability of positive BK viral load <10000 HCR is +ve	Probability of positive BK viral load >10000 if PCR is +ve		0.25	20
Probability of PVAN with BK viral lead >100000.8720Probability of prant bas from SK without monitoring0.6120Probability of prant has from SK without monitoring0.6526Probability of prant has from SK without monitoring0.6535Recurrence of HK in retransplantation0.7543Probability of prantsplantation0.0644Survial of retransplantation0.0644Survial of retransplantation0.0644Survial of retransplantation0.986 (0.39-1.00)3Years after transplant10.986 (0.39-1.00)4Years after transplant10.966 (0.38-1.00)4Years after transplant10.966 (0.38-1.00)4	Probability of positive BK viral load <10000 if PCR is +ve		0.75	20
Probabiling of pVMN with BK viral load < 10 000	Probability of PyVAN with BK viral load >10000		0.87	20
Late degnosis of 9k: no-screening arm 0.46 26 Probability of graft loss from BK without monitoring 0.05 35 Recurrence of BK in retransplantation 0.06 44 Probability of retransplantation 0.06 44 Survial of retransplants derecond/subsequent transplant 0.06 44 Survial of retransplants after previous graft loss 3 0.986 (0.83-1.00) Years after transplant 1 0.986 (0.83-1.00) 3 Years after transplant 1 0.96 (0.88-1.00) 3 Years after transplant 1 0.96 (0.88-1.00) 44 Years after transplant 1 0.96 (0.88-1.00) 2 Zost and resource uses.\$ (AUD) 2 0.94 (0.85-1.00) 2 Access surgery 1043 800-1500 50 Bloosy 607 500-750 50 Death 6000 2000-100000 4 Cartes transplant subsequent years 18864 10000-100000 1 Transplant subsequent years 18864 10000-100000 1	Probability of PvVAN with BK viral load <10 000		0.31	20
Probability of graft loss from BK without monitoring 0.46 26 Probability of retransplantation 0.05 35 Returnee of BK (in retransplantation) 0.175 43 Probability of KWN in the second/subsequent transplants 0.06 44 Survival of retransplants after previous graft loss 3 3 Patient survival 1 0.985 (0.93-1.00) 2 Vears after transplant 1 0.996 (0.83-1.00) 44 Years after transplant 1 0.96 (0.88-1.00) 44 Years after transplant 1 0.96 (0.88-1.00) 44 Years after transplant 1 0.94 (0.85-1.00) 45-50 Access surgery 1043 800-1500 45-50 Biopsy 607 500-750 45-50 Biopsy 607 500-750 45-50 Pertoneal dalysis 5045 45000-100000 45-50 Parametric transplant triat year 51044 40000-100000 45 Transplant: triat year 51044 10000-50000 45 6000-100000	Late diagnosis of BK: no-screening arm			
Probability of retransplantation 0.05 35 Recurrence of IR in retransplantation 7 Probability of RWAN in the second/subsequent transplants 0.06 44 Survival of retransplants after previous graft loss 43 Probability of RWAN in the second/subsequent transplant 1 0.985 (0.39-1.00) Pattert survival 2 0.986 (0.39-1.00) Vers after transplant 1 0.96 (0.88-1.00) Graft survival 1 0.96 (0.88-1.00) Vers after transplant 1 0.96 (0.88-1.00) Z 0.94 (0.85-1.00) 2 Stand resource uses, \$ (AUD) 2 0.94 (0.85-1.00) Costs and resource uses, \$ (AUD) 44 50 Access surgery 1043 800-1500 Biopsy 607 500-750 Death 6000 2000-10000 Center hemodialysis 85 987 60000-120000 Fransplant: subsequent years 18 864 10000-50000 Immunosuppression reduction 4380 2000-500 Immunosuppression reducting (seriest) 29<	Probability of graft loss from BK without monitoring		0.46	26
Recurrence of BK in retransplantation Internation Internation Probability of recurrence in the second/subsequent transplants 0.175 4.3 Probability of Retransplants after previous graft loss	Probability of retransplantation		0.05	35
Probability of recurrence in the second/subsequent transplants 0.175 43 Probability of RVANA in the second transplant with recurrence 0.06 44 Variand of retransplants after previous graft loss 43 Patient survival 1 0.985 (0.93-1.00) 2 0.985 (0.93-1.00) 3 2 0.985 (0.93-1.00) 3 2 0.986 (0.88-1.00) 2 3 0.94 (0.85-1.00) 3 2 0.940 (0.85-1.00) 3 3 0.94 (0.85-1.00) 3 3 0.94 (0.85-1.00) 3 3 0.94 (0.85-1.00) 3 3 0.94 (0.85-1.00) 3 4 5 0.40 (0.85-1.00) 3 0.94 (0.85-1.00) 3 4 5 0.00 Access surgery 1043 800-1500 Biopsy 607 500-750 Pertioneal datysis 5 1044 40000-100000 Transplant: first year 1 1044 40000-100000 Transplant: first year	Recurrence of BK in retransplantation			
Probability of BKVAN in the second transplant with recurrence 0.06 44 Survival of retransplant after previous graft loss 43 Years after transplant 1 0.985 (0.93-1.00) 2 0.985 (0.93-1.00) 3 Graft survival 2 0.94 (0.85-1.00) Graft survival 2 0.94 (0.85-1.00) Zosts and resource uses, \$ (AUD) 2 0.94 (0.85-1.00) Costs and resource uses, \$ (AUD) 45-50 Access surgery 1043 800-1500 Biopsy 607 500-750 Death 6000 20000-10000 Home hemodialysis 70304 50000-100000 Carter hemodialysis 70304 50000-100000 Transplant: furst year 51044 40000-100000 Transplant: subsequent years 18864 10000-50000 Immunosuppression reduction 4380 2000-500 Polymaxirus PCR test: involtoring 762 500-100 Lurinex testing (per test) 6030 5000-10000 Transplant: subsequent yeacrint first year 1600 <td< td=""><td>Probability of recurrence in the second/subsequent transplants</td><td></td><td>0.175</td><td>43</td></td<>	Probability of recurrence in the second/subsequent transplants		0.175	43
Conversion	Probability of BKVAN in the second transplant with recurrence		0.06	44
Patient survival 43 Years after transplant 1 0.985 (0.93-1.00) 2 0.985 (0.93-1.00) 3 0.985 (0.93-1.00) 3 0.985 (0.93-1.00) 44 Years after transplant 1 0.96 (0.88-1.00) 2 0.94 (0.85-1.00) 2 0.94 (0.85-1.00) 3 0.94 (Survival of retransplants after previous graft loss		0.00	
Years after transplant 1 0.985 (0.93–1.00) 2 0.985 (0.93–1.00) 3 0.985 (0.93–1.00) Graft survival 1 0.96 (0.88–1.00) 44 Years after transplant 1 0.96 (0.88–1.00) 2 Access surgery 1043 800–1500 50 Biopsy 607 500–750 50 Death 6000 2000–10000 45–50 Access surgery 1043 800–1500 50 Biopsy 607 500–750 50 Death 6000 2000–10000 45 Home hemodialysis 50 455 45 000–100 000 50 Certer hemodialysis 70 304 50 000–100 000 50 Transplant. subsequent years 18 864 10 000–50 000 1000 Immunosuppression reduction 4380 2000–500 20 Polyomavirus PCR test: instituting for test) 29 20–50 20 Polyomavirus PCR test: instituting tests 18 308 10 000–30 000 10000–30 000 10000–30 0000	Patient survival			43
1 0.986 (0.93-1.00) 3 0.985 (0.93-1.00) Graft survival 4 Years after transplant 1 0.96 (0.88-1.00) 2 0.94 (0.85-1.00) 3 0.94 (0.85-1.00) 2 0.94 (0.85-1.00) 3 0.94 (0.85-1.00) 2 0.94 (0.85-1.00) 3 0.94 (0.85-1.00) Costs and resource uses, \$ (AUD) 45-50 4500-750 Biopsy 607 500-750 Death 6000 2000-10000 Home hemodialysis 50045 45000-10000 Pertoneal dialysis 50045 45000-10000 Transplant: subsequent years 18864 10000-5000 Immunosuppression reduction 4380 2000-5000 Polyomavirus PCR test: initial (per test) 29 20-50 Polyomavirus PCR test: initial (per test) 18864 10000-30000 Treatment of acute rejection: RMR 18308 10000-30000 Treatment of acute rejection: RMR 18308 10000-30000 Treatment of acute rejection: RMR (steroid responsive) 603	Years after transplant	1	0 985 (0 93–1 00)	10
Image: constraint of a cut rejection: TAMR set of the constraint of acut rejection: TAMR set of the constraint the constraint of the consten the consten the constraint of the constraint the constraint		2	0.985 (0.93–1.00)	
Graft survival 44 Years after transplant 1 0.96 (0.88-1.00) 2 0.94 (0.85-1.00) 3 Costs and resource uses, \$(AUD) 45–50 Access surgery 1043 800–1500 Biopsy 607 500–750 Death 6000 2000–10000 Home hemodialysis 50045 45000–100000 Center hemodialysis 70304 50000–100000 Center hemodialysis 70304 50000–100000 Transplant. first year 51044 40000–100000 Transplant. subsequent years 18864 10000–50000 Immunosuppression reduction 4380 2000–5000 Polyomavirus PCR test: initial (per test) 29 20–50 Polyomavirus PCR test: monitoring 762 500–1000 Treatment of acute rejection: TCMR (steroid responsive) 6030 5000–10000 Treatment of acute rejection: TCMR (steroid responsive) 6030 5000–10000 Treatment of acute rejection: TCMR (steroid responsive) 6030 5000–10000 Distributions Prevalence of viremia 9.762 200–50 Probability of		3	0.985 (0.93–1.00)	
Years after transplant 1 0.96 (0.88–1.00) 2 0.94 (0.85–1.00) 3 0.94 (0.85–1.00) 3 0.94 (0.85–1.00) Access surgery 1043 Biopsy 607 Death 6000 Home hemodialysis 50045 Certer hemodialysis 50045 Opposition 2000–10000 Certer hemodialysis 70304 Transplant. Tist year 51044 11 (not suppression reduction 4380 Polyomavirus PCR test: initial (per test) 29 Polyomavirus PCR test: initial (per test) 1600 Treatment of acute rejection: TCMR (steroid responsive) 6030 Treatment of acute rejection: TCMR (steroid responsive) 6030 Discount costs 0.05 0.03–0.08 Distributions 29 20–50 Prevalence of viremia 0.18 (0.001) Normal (mean, SD) Prevalence of viremia 0.18 (0.001) Normal (mean, SD) Probability of graft dysfunction in patients with PyVAN 0.1 (0.05) Normal (mean, SD) Probability of drat dysfunction in patients with PyVAN 0.1 (0.05)	Graft survival	0	0.000 (0.00 1.00)	44
$ \begin{array}{c} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 $	Years after transplant	1	0.96 (0.88–1.00)	
Image: Construct of the second sec		2	0.94 (0.85–1.00)	
Costs and resource uses, $\$$ (AUD)45–50Access surgery1043 $\$00-1500$ Biopsy 607 $500-750$ Death 6000 $2000-10000$ Home hemodialysis 50045 $4500-10000$ Center hemodialysis 50045 $4500-100000$ Center hemodialysis 70304 $5000-100000$ Peritoneal dialysis 70304 $5000-100000$ Transplant: first year 510444 $40000-100000$ Transplant: subsequent years 18864 $10000-50000$ Immunosuppression reduction 43800 $2000-5000$ Polyomavirus PCR test: initial (per test) 29 $20-50$ Polyomavirus PCR test: initial (per test) 1600 $500-2000$ Treatment of acute rejection: ABMR 18308 $10000-30000$ Treatment of acute rejection: TCMR (steroid responsive) 6030 $5000-10000$ Discount costs 0.05 $0.03-0.08$ Distributions $Prevalence of viremia$ $0.18 (0.001)$ Normal (mean, SD)Probability of graft toss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD) $29,30.39$ Probability of retansplantation $0.1 (0.05)$ Normal (mean, SD) $29,30.39$ Probability of death in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30.39$ Probability of retansplantation $0.1 (0.05)$ Normal (mean, SD) $29,30.39$ Probability of retansplantation $0.1 (0.05)$ Normal (mean, SD) $29,30.39$ Probability of retansplantation $0.1 (0.05)$ Normal (mean, SD) </td <td></td> <td>3</td> <td>0.94 (0.85–1.00)</td> <td></td>		3	0.94 (0.85–1.00)	
Control 1043 800–1500 Biopsy 607 500–750 Death 6000 2000–10000 Home hemodialysis 50045 45000–100000 Center hemodialysis 80987 60000–120000 Peritoneal dialysis 70304 50000–120000 Transplant: first year 51044 40000–100000 Transplant: subsequent years 18 864 10000–50000 Immunosuppression reduction 4380 2000–5000 Polyomavirus PCR test: initial (per test) 29 20–50 Polyomavirus PCR test: monitoring 762 500–1000 Luminex testing (per test) 1600 500–2000 Treatment of acute rejection: ABMR 18308 10000–30 000 Treatment of acute rejection: TCMR (steroid responsive) 6030 5000–1000 Discount costs 0.05 0.03–0.08 Distributions Probability of graft dysfunction in patients with PyVAN 0.18 (0.001) Normal (mean, SD) 26 Probability of graft dysfunction in patients with PyVAN 0.19 (0.05) Normal (mean, SD) 29,30,39 Probability of graft dysfunctin in patients with PyVAN 0.2225	Costs and resource uses \$ (ALID)	0	0.01 (0.00 1.00)	45-50
House call product using VFor a to CGOUGOUBiopsy607 $500-750$ Death6000 $2000-10000$ Home hemodialysis 50045 $45000-100000$ Center hemodialysis 85987 $6000-120000$ Peritoneal dialysis 70304 $50000-100000$ Transplant: first year 51044 $40000-100000$ Transplant: subsequent years 18864 $10000-50000$ Immunosuppression reduction 4380 $2000-5000$ Polyomavirus PCR test: intila (per test) 29 $20-50$ Polyomavirus PCR test: monitoring 762 $500-1000$ Luminex testing (per test) 1600 $500-2000$ Treatment of acute rejection: ABMR 18308 $10000-30000$ Treatment of acute rejection: TCMR (steroid responsive) 6030 $5000-10000$ Discount costs 0.05 $0.03-0.08$ Distributions $Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)29,30,39Probability of graft dysfunction in patients with PyVAN0.12005Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.12005Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.225 (0.005)Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.12005Normal (mean, SD)29,30,39Probability of death in patients with PyVAN$	Access surgery	1043	800-1500	10 00
DeathGood2000-10000Home hemodialysis50 04545 000-100 000Center hemodialysis85 98760 000-120 000Peritoneal dialysis70 30450 000-100 000Transplant: first year51 04440 000-100 000Transplant: subsequent years18 86410 000-50 000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)2920-50Polyomavirus PCR test: initial (per test)2920-50Polyomavirus PCR test: initial (per test)1600500-2000Treatment of acute rejection: ABMR18 30810 000-30 000Treatment of acute rejection: TCMR (steroid responsive)60 305000-10 000Treatment of acute rejection: TCMR (steroid responsive)0.0305000-10 000Distributions0.050.03-0.080.03-0.08Prevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of det in patients with PyVAN0.1 (0.05)Normal (mean, SD)Costs of transplanti: subsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ Costs of tiansplanti: ubsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$	Bionsy	607	500-750	
Home hemodialysis5004545000-100000Center hemodialysis8598760000-120000Pertioneal dialysis703045000-100000Transplant: first year5104440000-100000Transplant: subsequent years1886410000-50000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)29 $20-50$ Polyomavirus PCR test: monitoring762 $500-1000$ Luminex testing (per test)1600 $500-2000$ Treatment of acute rejection: ABMR18308 $10000-30000$ Treatment of acute rejection: TCMR (steroid responsive)6030 $5000-10000$ Treatment of acute rejection: TCMR (steroid responsive) 0.33 $30000-50000$ Discount costs0.05 $0.03-0.08$ DistributionsPrevalence of viremia $0.18 (0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of death in patients with PyVAN $0.225 (0.005)$ Normal (mean, SD) $29,30,39$ Probability of death in patients with PyVAN $0.225 (0.005)$ Normal (mean, SD) $29,30,39$ Costs of transplant: subsequent years, ξ (AUD)	Death	6000	2000-10,000	
Center hemodialysis85 98760 000-120 000Peritoneal dialysis70 30450 000-100 000Transplant: first year51 04440 000-100 000Transplant: subsequent years18 86410 000-50 000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)29 $20-50$ Polyomavirus PCR test: monitoring762500-1000Luminex testing (per test)1600500-2000Treatment of acute rejection: ABMR18 30810 000-30 000Treatment of acute rejection: TCMR (steroid responsive)60305000-10 000Treatment of acute rejection: TCMR (steroid resistant)43 33030 000-50 000Treatment of acute rejection: TCMR (steroid resistant)40 322000-10 000Discount costs0.050.03-0.08DistributionsProbability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of death in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of death in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of death in patients with PyVAN0.25 (0.005)Normal (mean, SD)Probability of death in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of death in patients with PyVAN0.25 (0.005)Normal (mean, SD)Probability of death in patients with PyVAN0.20 (0.05)Normal (mean, SD)Probability of death in patients with	Home hemodialvsis	50.045	45,000-100,000	
Peritoneal dialysis70 30450 000-100 000Transplant: first year51 04440 000-100 000Transplant: subsequent years18 86410 000-50 000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)2920-50Polyomavirus PCR test: monitoring762500-1000Luminex testing (per test)1600500-2000Treatment of acute rejection: ABMR18 30810 000-30 000Treatment of acute rejection: TCMR (steroid responsive)60305000-10 000Treatment of acute rejection: TCMR (steroid responsive)60305000-10 000Treatment of acute rejection: TCMR (steroid resistant)43 33030 000-50 000Treatment of acute rejection: TCMR (steroid resistant)40322000-10 000Discount costs0.050.03-0.080.05DistributionsProbability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)29, 30,39Probability of death in patients with PyVAN0.225 (0.005)Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18 864 (0.85) γ (α , λ)29Costs of dialysis: after allograft loss, \$ (AUD)113 932 (0.85) γ (α , λ)	Center hemodialysis	85987	60,000-120,000	
Transplant: first year5104440000-100000Transplant: first year5104440000-100000Transplant: subsequent years1886410000-50000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)2920-50Polyomavirus PCR test: monitoring762500-1000Luminex testing (per test)1600500-2000Treatment of acute rejection: ABMR1830810000-30000Treatment of acute rejection: TCMR (steroid responsive)60305000-10000Treatment of acute rejection: TCMR (steroid resistant)4333030 000-50 000Treatment of acute rejection: TCMR (steroid resistant)403222000-10 000Discount costs0.050.03-0.08DistributionsPrevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft toss in the no-screen arm0.46 (0.05)Normal (mean, SD)29,30,39Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.225 (0.005)Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ 29Costs of dialysis; return to dialysis after allograft loss, \$ (AUD)113932 (0.85) $\gamma (\alpha, \lambda)$	Peritoneal dialysis	70.304	50,000-100,000	
Transplant:Subsequent years18 86410000-50000Immunosuppression reduction4380 $2000-5000$ Polyomavirus PCR test:initial (per test)29 $20-50$ Polyomavirus PCR test:monitoring762 $500-1000$ Luminex testing (per test)1600 $500-2000$ Treatment of acute rejection: ABMR18 308 $10000-30000$ Treatment of acute rejection:TCMR (steroid responsive) 6030 $5000-10000$ Treatment of acute rejection:TCMR (steroid responsive) 6030 $5000-10000$ Treatment of acute rejection:TCMR (steroid resistant) 43330 $30000-50000$ Treatment using IVIG 0.05 $0.03-0.08$ Discount costs 0.05 $0.03-0.08$ Distributions26Prevalence of viremia $0.18 (0.001)$ Normal (mean, SD)29,30,39Probability of graft loss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD)29,30,39Probability of retransplantation $0.1 (0.05)$ Normal (mean, SD)29,30,39Probability of retransplantation $0.12 (0.05)$ Normal (mean, SD)29Costs of transplant:subsequent years, $\$$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ Costs of dialysis; return to dialysis after allocraft loss, $\$$ (AUD)113393 (0.85) $\gamma (\alpha, \lambda)$	Transplant: first vear	51 044	40,000–1,00,000	
Insupart of constraints100011000000000Immunosuppression reduction43802000-5000Polyomavirus PCR test: initial (per test)2920-50Polyomavirus PCR test: monitoring762500-1000Luminex testing (per test)1600500-2000Treatment of acute rejection: ABMR1830810 000-30 000Treatment of acute rejection: TCMR (steroid responsive)60305000-10 000Treatment of acute rejection: TCMR (steroid resistant)4333030 000-50 000Treatment of acute rejection: TCMR (steroid resistant)43322000-10 000Discount costs0.050.03-0.08DistributionsPrevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)29,30,39Probability of retransplantation0.1 (0.05)Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.1 (0.05)Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ 29Costs of dialysis: return to dialysis after allograft loss, \$ (AUD)113932 (0.85) $\gamma (\alpha, \lambda)$	Transplant: subsequent years	18864	10,000-50,000	
Initial constraint2920-50Polyomavirus PCR test: initial (per test)762 $500-1000$ Luminex testing (per test)1600 $500-2000$ Treatment of acute rejection: ABMR18308 $10000-30000$ Treatment of acute rejection: TCMR (steroid responsive) 6030 $5000-10000$ Treatment of acute rejection: TCMR (steroid resistant) 43330 $30000-50000$ Treatment of acute rejection: TCMR (steroid resistant) 4032 $2000-10000$ Discount costs 0.05 $0.03-0.08$ DistributionsPrevalence of viremia $0.18 (0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD)Probability of deth in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD)Probability of deth in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD)Costs of transplant: subsequent years, \$ (AUD) $113932 (0.85)$ $\gamma (\alpha, \lambda)$ Costs of dialysis; return to dialysis after allograft loss, \$ (AUD) $113932 (0.85)$ $\gamma (\alpha, \lambda)$		4380	2000-5000	
Polyomatrice for text multar generatoryZeroLeroPolyomatrice for text monitoring762 $500-1000$ Luminex testing (per test)1600 $500-2000$ Treatment of acute rejection: ABMR18308 $10000-30000$ Treatment of acute rejection: TCMR (steroid responsive) 6030 $5000-10000$ Treatment of acute rejection: TCMR (steroid resistant) 43330 $30000-50000$ Treatment using IVIG 4032 $2000-10000$ Discount costs 0.05 $0.03-0.08$ DistributionsPrevalence of viremia $0.18(0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46(0.05)$ Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN $0.1(0.05)$ Normal (mean, SD)Probability of etransplantation $0.1(0.05)$ Normal (mean, SD)Probability of etransplantation $0.1(0.05)$ Normal (mean, SD)Probability of otransplant subsequent years, \$ (AUD) $18864(0.85)$ $\gamma(\alpha, \lambda)$ Costs of tiansplant subsequent years, \$ (AUD) $113932(0.85)$ $\gamma(\alpha, \lambda)$	Polyomavirus PCB test: initial (per test)	29	20-50	
Luminex testing (per test)160500–200Treatment of acute rejection: ABMR1830810000–30000Treatment of acute rejection: TCMR (steroid responsive)60305000–10000Treatment of acute rejection: TCMR (steroid resistant)43330 $30000-50000$ Treatment of acute rejection: TCMR (steroid resistant)4032 $2000-10000$ Discount costs0.05 $0.03-0.08$ DistributionsPrevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)Probability of retransplantation0.1 (0.05)Normal (mean, SD)Probability of death in patients with PyVAN0.0225 (0.005)Normal (mean, SD)Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ Costs of dialysis: return to dialysis after allograft loss, \$ (AUD)113932 (0.85) $\gamma (\alpha, \lambda)$	Polyomavirus PCR test: monitoring	762	500-1000	
Treatment of acute rejection: ABMR1830810 000–30 000Treatment of acute rejection: TCMR (steroid responsive)6030 $5000-10 000$ Treatment of acute rejection: TCMR (steroid resistant)43 330 $30 000-50 000$ Treatment using IVIG4032 $2000-10 000$ Discount costs0.05 $0.03-0.08$ DistributionsPrevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)26Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)29,30,39Probability of death in patients with PyVAN0.0225 (0.005)Normal (mean, SD)43Probability of death in patients with PyVAN0.1864 (0.85) γ (α , λ)29Costs of dialysis: return to dialysis after allograft loss, \$ (AUD)113932 (0.85) γ (α , λ)	Luminex testing (ner test)	1600	500-2000	
Treatment of acute rejection: TCMR (steroid responsive)60305000-10 000Treatment of acute rejection: TCMR (steroid resistant)43 330 $30 000-50 000$ Treatment using IVIG4032 $2000-10 000$ Discount costs 0.05 $0.03-0.08$ Distributions $Vermal$ $0.18 (0.001)$ Normal (mean, SD)Prevalence of viremia $0.46 (0.05)$ Normal (mean, SD) 26 Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of retransplantation $0.12 (0.05)$ Normal (mean, SD) 43 Probability of death in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD) 29 Costs of transplant: subsequent years, \$ (AUD) $18864 (0.85)$ $\gamma (\alpha, \lambda)$ $\gamma (\alpha, \lambda)$	Treatment of acute rejection: ABMR	18308	10,000-30,000	
Treatment of acute rejection: TCMR (steroid resistant)43 330 $30000-50000$ Treatment using IVIG4032 $2000-10000$ Discount costs 0.05 $0.03-0.08$ Distributions V V Prevalence of viremia $0.18(0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46(0.05)$ Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN $0.1(0.05)$ Normal (mean, SD)Probability of retransplantation $0.1(0.05)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.0225(0.005)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.0225(0.005)$ Normal (mean, SD)Costs of transplant: subsequent years, \$ (AUD) $18864(0.85)$ $\gamma(\alpha, \lambda)$ Costs of dialysis: return to dialysis after allograft loss, \$ (AUD) $113932(0.85)$ $\gamma(\alpha, \lambda)$	Treatment of acute rejection: TCMR (steroid responsive)	6030	5000-10,000	
Treatment using IVIG4032 $2000-10000$ Discount costs 0.05 $0.03-0.08$ Distributions $0.18(0.001)$ Normal (mean, SD)Prevalence of viremia $0.18(0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46(0.05)$ Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN $0.1(0.05)$ Normal (mean, SD)Probability of retransplantation $0.1(0.05)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.0225(0.005)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.0225(0.005)$ Normal (mean, SD)Costs of transplant: subsequent years, \$ (AUD) $18864(0.85)$ $\gamma(\alpha, \lambda)$ Costs of dialysis: return to dialysis after allograft loss, \$ (AUD) $113932(0.85)$ $\gamma(\alpha, \lambda)$	Treatment of acute rejection: TCMR (steroid resistant)	43,330	30,000-50,000	
Discount costs0.050.03–0.08DistributionsPrevalence of viremia0.18 (0.001)Normal (mean, SD)Probability of graft loss in the no-screen arm0.46 (0.05)Normal (mean, SD)26Probability of graft dysfunction in patients with PyVAN0.1 (0.05)Normal (mean, SD)29,30,39Probability of retransplantation0.11 (0.05)Normal (mean, SD)43Probability of death in patients with PyVAN0.0225 (0.005)Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) γ (α, λ) γ (α, λ)	Treatment using IVIG	4032	2000-10.000	
Distributions 0.18 (0.001) Normal (mean, SD) Prevalence of viremia 0.18 (0.001) Normal (mean, SD) Probability of graft loss in the no-screen arm 0.46 (0.05) Normal (mean, SD) 26 Probability of graft dysfunction in patients with PyVAN 0.1 (0.05) Normal (mean, SD) 29,30,39 Probability of retransplantation 0.1 (0.05) Normal (mean, SD) 43 Probability of death in patients with PyVAN 0.0225 (0.005) Normal (mean, SD) 29 Costs of transplant: subsequent years, \$ (AUD) 18864 (0.85) γ (α , λ) γ (α , λ)	Discount costs	0.05	0.03-0.08	
Prevalence of viremia $0.18 (0.001)$ Normal (mean, SD)Probability of graft loss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD)Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD)Probability of retransplantation $0.1 (0.05)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD)Probability of death in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD)Costs of transplant: subsequent years, \$ (AUD) $18864 (0.85)$ $\gamma (\alpha, \lambda)$ Costs of dialysis: return to dialysis after allograft loss, \$ (AUD) $113932 (0.85)$ $\gamma (\alpha, \lambda)$	Distributions	0.00		
Probability of graft loss in the no-screen arm $0.46 (0.05)$ Normal (mean, SD) 26 Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of retransplantation $0.1 (0.05)$ Normal (mean, SD) 43 Probability of death in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD) 29 Costs of transplant: subsequent years, \$ (AUD) $18864 (0.85)$ $\gamma (\alpha, \lambda)$ $\gamma (\alpha, \lambda)$	Prevalence of viremia	0.18 (0.001)	Normal (mean, SD)	
Probability of graft dysfunction in patients with PyVAN $0.1 (0.05)$ Normal (mean, SD) $29,30,39$ Probability of retransplantation $0.1 (0.05)$ Normal (mean, SD) 43 Probability of death in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD) 29 Costs of transplant: subsequent years, \$ (AUD) $18864 (0.85)$ $\gamma (\alpha, \lambda)$ $\gamma (\alpha, \lambda)$	Probability of graft loss in the no-screen arm	0.46 (0.05)	Normal (mean, SD)	26
Probability of retransplantation0.1 (0.05)Normal (mean, SD)43Probability of death in patients with PyVAN0.0225 (0.005)Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) γ (α , λ)Costs of dialysis: return to dialysis after allograft loss, \$ (AUD)113932 (0.85) γ (α , λ)	Probability of graft dysfunction in natients with PvVAN	0.1 (0.05)	Normal (mean, SD)	29 30 39
Probability of death in patients with PyVAN $0.0225 (0.005)$ Normal (mean, SD)29Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) $\gamma (\alpha, \lambda)$ Costs of dialysis: return to dialysis after allograft loss, \$ (AUD)113.932 (0.85) $\gamma (\alpha, \lambda)$	Probability of retransplantation	0.1 (0.05)	Normal (mean, SD)	43
Costs of transplant: subsequent years, \$ (AUD)18864 (0.85) γ (α , λ)Costs of dialysis: return to dialysis after allograft loss. \$ (AUD)113.932 (0.85) γ (α , λ)	Probability of death in patients with Pv/AN	0.0225 (0.005)	Normal (mean, SD)	29
Costs of dialysis: return to dialysis after allograft loss. (AUD) 113.932 (0.85) $\gamma(\alpha, \lambda)$	Costs of transplant: subsequent years. \$ (AUD)	18864 (0.85)	$\gamma(\alpha, \lambda)$	20
	Costs of dialvsis: return to dialvsis after allograft loss \$ (ALID)	113,932 (0.85)	$\gamma(\alpha, \lambda)$	

AUD, Australian dollars; ABMR, antibody mediated rejection; BKVAN, BK virus-associated nephropathy; DSA, donor-specific antibody; PCR, polymerase chain reaction; PyVAN, polyomavirus-associated nephropathy; TCMR, T-cell mediated rejection.

nonidentifiable data and therefore was exempted from the Human Research Ethics Committee review.

RESULTS

Base Case

Assuming a starting age of 45 y, a cycle length of 1 y, with the model terminating after all recipients were deceased, the estimated total costs of posttransplant care were \$350947 AUD (\$254017 US dollars) in the screened arm, compared with \$357933 AUD (\$259090 US dollars) for the no-screening arm, resulting in 11.59 LYs and 8.416 QALYs in the screening arm and 11.296 LYs and 8.184 QALYs for no screening. The incremental benefits for screening were 0.294 LYs saved and 0.232 QALYs, with screening dominant and resulting in savings of \$6986 AUD (\$5057 US dollars). The Markov state cumulative probabilities of death and survival with a functioning graft for both the screen and no-screen arms after 50 cycles are shown in Figure S2 (SDC, http://links.lww.com/TXD/A417).

Sensitivity Analyses

The most influential variables identified in the model were the costs of transplantation (maintenance immunosuppression and management after year one post-transplant), starting age of transplantation, costs of dialysis after allograft loss, probability of death in patients with a history of PyVAN, prevalence of BKPyV-DNAemia, and the probability of graft loss in patients without PyVAN and acute rejection. The extent of the variability associated with these variables on the incremental health outcomes and costs is shown in the tornado diagram (Figure 3) and Table 2. For example, if the age of transplantation is decreased from 70 y (higher values, represented by shades of black) to 18 y (lower values, represented by shades of gray), then the incremental benefits of screening would increase from 0.201 to 0.236 QALYs. However, the total savings from screening would reduce from \$7884 to \$6844, as younger recipients would incur greater resources used over their lifetime compared with the older counterparts. The overall ICER was reduced from -\$39294/QALY to -\$28933/ QALY, suggesting screening in younger recipients would save less money but acquire slightly more health benefits over time (Figure S3, SDC, http://links.lww.com/TXD/A417).

If the costs of transplantation in subsequent years in both the screen and no-screen arms for patients with and without prior polyomavirus infections were increased from \$15000 AUD (\$11100 US dollars) to \$60000 AUD (\$44400 US dollars), then screening (compared with no screening) would vary from being cost-savings to incurring additional costs of \$8578 AUD (\$11737 US dollars). However, the ICER remained below the willingnessto-pay threshold of \$50000 per LYs saved or QALYs. In this model, if the annual probability of death in patients with PyVAN was twice that of those without PyVAN, the incremental benefits of screening increased from 0.263 to 0.301 QALYs gained. If the probability of other causes of graft loss unrelated to PyVAN was reduced from 0.05 to 0.02 (ie, the probability of other competing causes of graft loss was reduced), then the incremental benefits of screening would increase from 0.171 to 0.276 QALYs. If the costs of return to dialysis (after allograft loss) were increased from a base rate of \$50000 AUD (\$37000 US dollars) to over \$120000 AUD (\$87000 US dollars) per annum, savings from screening



FIGURE 3. Tornado diagram showing the influential variables on the incremental cost-effectiveness ratios of the base model. EV, expected value; HD, hemodialysis; PyVAN, polyomavirus-associated nephropathy; QALY, quality-adjusted life-years.

TABLE 2.

One-way sensitivity analyses

	Benefits (no						
	Costs (screen), \$	Costs (no screen), \$	Benefits (screen),	screen),	Incremental costs, \$	Incremental benefits,	ICER,
Variables	AUD	AUD	QALYS	QALYS	AUD	QALYS	(\$/UALYS)
Costs of trans	splantation: subsequent	t years (assuming recipie	nts returned to standard i	mmunosuppressio	n after year 1), \$ (AUD)		
15000	315980	324 558	8.48	8.243	-8578	0.236	-36319
37 500	534706	533127	8.48	8.243	-1579	0.236	6689
48750	644069	637 411	8.48	8.243	6659	0.236	28139
60 000	753 433	741 695	8.48	8.243	11737	0.236	49697
Prevalence of	f viremia in the screene	ed arm					
0.05	353741	360 376	8.49	8.243	-6635	0.247	-26869
0.15	353 550	360 376	8.48	8.243	-6825	0.237	-28 850
0.2	353 458	360 376	8.475	8.243	-6921	0.231	-29908
0.3	353 359	360 376	8.47	8.243	-7016	0.226	-31013
Probability of	death in recipients with	n PyVAN					
0.01	353836	362213	8.488	8.287	8376	0.201	-41708
0.035	353248	358883	8.472	8.208	5635	0.263	-21 393
0.0475	352954	357647	8.463	8.179	4692	0.285	-16490
0.06	352660	356606	8.455	8.154	3945	0.301	-13104
Costs of dialy	sis						
50 000	292346	292755	8.48	8.243	410	0.236	-1734
85 000	325 848	329775	8.48	8.243	3926	0.236	-16624
102500	342 600	348284	8.48	8.243	5685	0.236	-24070
120000	359351	366794	8.48	8.243	7443	0.236	-31 515
Probability of	graft loss in recipients	without PyVAN and acute	e rejection				
0.02	342 572	349721	8.98	8.704	7149	0.276	-25936
0.035	358 342	365 034	8.26	8.042	6691	0.218	-30640
0.043	364 837	371 333	7.962	7.768	6495	0.194	-33517
0.05	370613	376931	7.696	7.525	6317	0.171	-36 853
Age of transp	lantation, y						
18	353 543	360 376	8.48	8.243	6833	0.236	-28933
44	351 186	358160	8.422	8.19	6973	0.232	-30063
57	345657	352898	8.285	8.062	7240	0.223	-32407
70	328 496	336380	7.862	7.662	7884	0.201	-39294
Costs of trans the initial of	splantation in recipients diagnosis), \$ (AUD)	s with prior PyVAN in the s	screen arm (assuming red	cipients remained o	on reduced immunosuppres	sion in up to year 2 after	
8000	352738	357 989	8.48	8.243	5251	0.236	-22233
13432	353140	357 989	8.48	8.243	4848	0.236	-20529
16148	353341	357 989	8.48	8.243	4647	0.236	-19678
18864	353 542	357 989	8.48	8.243	4446	0.236	-18826
Costs of trans	splantation in recipients	s with prior PyVAN in the r	no-screen arm (assuming	recipients remain	ed on reduced immunosupp	ression over the life cours	е
9000	353144	356360	8.48	8,243	3216	0.236	-13618
14500	353144	358 599	8.48	8.243	5455	0.236	-23 099
17 250	353144	359719	8 48	8 243	6575	0.236	-27 839

AUD, Australian dollars; ICER, incremental cost-effectiveness ratio; PyVAN, polyomavirus-associated nephropathy; QALY, quality-adjusted life-years.

8.48

would increase from around \$410 AUD (\$300 US dollars) to approximately \$7500 AUD (\$5500 US dollars). The model was also sensitive to the costs of a reduced immunosuppression regimen in patients with a history of PyVAN, with additional savings of around \$5250 (compared with no screening) if the antimetabolites were discontinued or decreased up to 2 y after the initial diagnosis in the screening arm.

360838

Probabilistic Sensitivity Analyses

353144

20 0 00

The scatter plot shown in Figure 4 shows the incremental costs and health outcomes and the uncertainties surrounding plausible range of mean parameter estimates in the screening and no-screening arms. The x-axis represents the incremental gains in QALYs, and the y-axis represents the incremental costs

of screening compared with no screening. The scatter plot is located at the lower southeast quadrant of the cost-effectiveness plan, indicating screening is effective and cost-saving, compared with no screening (ie, dominant). Figure 5A and B shows the predicted probabilities that screening (compared with no screening) being cost-saving and effective is 100%, indicating that screening for BKPyV-DNAemia always dominated the no-screening strategy and across clinically relevant ranges and scenarios.

0.236

-32579

7694

DISCUSSION

8.243

This economic evaluation, derived from the best available evidence, demonstrates that universal screening for polyomavirus infections using RT-PCR to detect viremia within the



FIGURE 4. Probabilistic sensitivity analyses showing the incremental cost-effectiveness ratios (ICERs) of screening vs no screening. AUD, Australian dollars; QALY, quality-adjusted life-years.

first 12 mo post-transplant results in meaningful improvement in survival and QoL (0.2–0.3 LY/QALYs) and is costsaving compared with no screening. In health economic terms, this means that screening is dominant (cost-savings and more cost-effective) compared with no screening. The extent of the survival benefits is dependent on the prevalence of viremia after transplant, age of transplantation, the survival probability of patients with PyVAN, and the annual incidence of allograft loss in recipients without a history of acute rejection and polyomavirus infections. The economic benefits of screening are influenced by the costs of transplantation after the first year. If viremia is cleared by reduced immunosuppression and the lowered costs of immunosuppression are maintained in subsequent years, screening could save up to \$5200 AUD, compared with no screening.

One of the major difficulties in the management of polyomavirus infection is the balance between over- and underimmunosuppression.²⁹ Immunosuppression reduction remains the primary therapy for patients with polyomavirus infections. Defining the optimal immunosuppression therapy to avoid reactivation of the virus and at the same time preventing acute rejection and dnDSA development is the ultimate challenge, as these two events will eventually lead to kidney damage, allograft dysfunction, and subsequent graft loss.³⁰ In our sensitivity analyses, we assumed a proportion of patients would remain on reduced immunosuppression even if they had cleared the viruses. The cost estimates of immunosuppression reduction greatly influenced cost-savings in both the screening and no-screening arms. However, uncertainties exist whether reduction in immunosuppression load will translate into longer term health benefits. Our study was

built on previous research that has also considered the impact of reduced immunosuppression on the cost-benefit ratio of screening. Prior modeled analyses, using data from the United Network of Organ Sharing and the US Renal Data System databases also reported considerable savings of approximately \$2000 US dollars with screening (compared with no screening), driven largely from immunosuppression reduction in the screened arm. In a scenario that the antimetabolites were ceased completely, the savings will further increase.¹³ In this current analysis using contemporary data, we have shown that the net benefits and savings from screening were considerably higher than the previous analysis.¹³

Our predictions show that screening incurred the greatest cost-savings if the underlying prevalence of PyVAN is high (>25%). This finding is expected because as the total number of patients with PyVAN increases, the overall costs of screening will be shared and offset by a greater number of individuals who may benefit from early intervention to prevent graft loss. However, even with a background prevalence viremia rate of only 5%, costs are reduced by approximately \$6800 AUD. In contrast to the previous analyses,¹³ the absolute gains in the effectiveness of screening observed in the current model were reduced with higher prevalence of viremia. The prior model had assumed that immunosuppression reduction is effective in reducing the risk of developing advanced disease such as polyomavirus-associated nephropathy without the added risk of acute rejection, which improves allograft outcomes at a population level. However, in the current analyses, the model reflected the clinical scenario in which a proportion of patients managed with reduced immunosuppression developed acute rejection and allograft dysfunction from



FIGURE 5. A, Predicted probabilities that screening (compared with no screening) is effective. B, Predicted probabilities that screening (compared with no screening) is cost-saving. QALY, quality-adjusted life-years; AUD, Australian dollars.

immunosuppression reduction. Therefore, the gains in health outcomes achieved through early detection and immunosuppression reduction were counterbalanced by the morbidity associated with a higher risk of acute rejection and subsequent graft loss. The model was also dependent on the inherent differences in the probability of death between patients with a history of PyVAN in the screening and no-screening groups. Apart from an increased risk of allograft loss in transplant recipients with PyVAN, progressive decline in allograft function over time may have contributed to the increased risk of death from other causes including other infections and cancer. Our study findings highlighted the critical importance of detecting the disease during the sojourn time, the time of the presymptomatic health status (early viremic state) before progression to graft dysfunction.

This study has several potential limitations. Our cost-effectiveness and cost-utility results are sensitive to some model inputs. However, many of these estimates, such as the prevalence of disease, the probability of death, and allograft loss attributed to PyVAN, are imprecise and may differ considerably between different sites and transplant units. Furthermore, many of these inputs such as costs and the impact of maintenance immunosuppression and medications after transplantation may change over time. It is also important to note that routine screening is not without harms. In this analysis, we had assumed a 1.5-fold increased risk of acute rejection and a 2-fold increase in the risk of dnDSA in patients with screened detected viremia, owing to the reduction in immunosuppression. However, if the risk of allograft loss associated with PvVAN was increased in the no-screening arm, then screening would incur greater benefits, and the relative harms associated with screening may be reduced, rendering screening more attractive and desirable than no screening. There may be reasons to suggest that the frequency of screening and screening intervals for polyomavirus infection should vary according to the risk factors for polyomavirus infections.³¹ Patients with risk factors such as use of T cell-depleting agents as induction therapy, prior acute rejection episodes, and human antigen leukocyte incompatibility may benefit from more frequent screening to increase the probability of detecting viremia early.³² In this model, we did not assess whether these additional risk factors combined with screening frequency influence cost-effectiveness. The present analysis also assumed that immunosuppression reduction strategies, cessation of antimetabolites, and the use of adjuvant therapies such as intravenous immunoglobulins are effective management strategies for BKPyV-DNAemia and PyVAN. However, none of these strategies have been assessed in randomized trials. We also have not considered patients' preferences and perspectives in the analyses. Routine screening in the form of a regular blood test may pose added burden on our patients, as well as the fear and potential harms of false-positive or negative results, the implications of reduced immunosuppression, and the downstream consequences of acute rejection and allograft dysfunction.

In conclusion, using the best available existing data, routine screening for BKPyV-DNAemia using RT-PCR is cost-saving, improves survival, and improves overall QoL in kidney transplant recipients across all settings and assumptions, compared with no screening. Our findings support universal screening for all kidney transplant recipients for polyomavirus infections during the first 12 mo after transplantation, when the net immunosuppression load is at the highest level.

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