ANNALS PLANTATION

ISSN 1425-9524
© Ann Transplant, 2016; 21: 1-11
DOI: 10.12659/AOT.895664

Received: 2015.08.15
Accepted: 2015.09.01
Published: 2016.01.05

Multinational Evaluation of Mycophenolic Acid, Tacrolimus, Cyclosporin, Sirolimus, and Everolimus Utilization

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Departmental funding only

Background: Increasing immunosuppressant utilization and expenditure is a worldwide challenge as more people successfully live with transplanted organs. Our aims were to characterize utilization of mycophenolate, tacrolimus, cyclosporin, sirolimus, and everolimus in Australian transplant recipients from 2007 to 2013; to identify specific patterns of usage; and to compare Australian utilization with Norwegian, Danish, Swedish, and the Netherlands use.

Material/Methods: Australian utilization and expenditure data were captured through national Pharmaceutical Benefits Scheme and Highly Specialized Drug administrative databases. Norwegian, Danish, Swedish, and the Netherlands utilization were retrieved from their healthcare databases. Utilization was compared as defined daily dose per 1000 population per day (DDD/1000 population/day). Data on kidney transplant recipients, the predominant patient group prescribed these medicines, were obtained from international transplant registries.

Results: From 2007–2013 Australian utilization of mycophenolic acid, tacrolimus and everolimus increased 2.7-fold, 2.2-fold, and 2.3-fold, respectively. Use of cyclosporin and sirolimus decreased 20% and 30%, respectively. Australian utilization was significantly lower than European utilization (2013) but was increasing at a faster rate. Total Australian expenditure increased approximately AUD$30 million over the study period to almost AUD$100 million in 2013. Kidney transplantation rates increased across each country over this time, with Australia having the lowest rate.

Conclusions: Immunosuppressant usage and subsequent expenditure are rising in Australia and Northern Europe. With increased numbers of people living with transplants, and the observed growth potential predicted from Northern European data, this class of medicines can be expected to continue consuming an increasing share of Australian pharmaceutical expenditure into the future.

MeSH Keywords: Drug Utilization • Immunosuppressive Agents • Kidney Transplantation • Pharmacoepidemiology

Full-text PDF: http://www.annalsoftransplantation.com/abstract/index/idArt/895664

Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]

Background

Transplant recipients require life-long immunosuppressant therapy to treat and prevent rejection events that would otherwise jeopardise the performance and longevity of their newly acquired graft [1,2]. Immunosuppressant medicines are used in 3 treatment stages; induction, as maintenance therapy and for acute treatment of organ rejection [3]. Community costs are highest for long-term maintenance immunosuppressant therapy, following hospital discharge after transplantation [4]. The kidney is the most common solid organ transplanted; in Australia over 9000 people currently live with a functioning kidney allograft, with over 800 further kidney transplant operations per annum [5]. Increasing rates of utilization and expenditure on immunosuppressants present a worldwide challenge.

Advances in maintenance immunosuppression have led to reductions in acute rejection rates and improvements to short-term patient survival over the past 2 decades [6,7]. In contrast, the evaluation of long-term graft survival has been difficult to interpret with contradictory data being reported [8–10]. The goal of maintenance immunosuppressant therapy is to maximize long-term allograft survival while minimizing acute rejection, drug toxicity and over-immunosuppression leading to infections and certain types of cancer [11]. The immunosuppressant agents, mycophenolic acid, tacrolimus, cyclosporin, sirolimus and everolimus, used in various combinations, often with corticosteroids (prednisone or prednisolone), form the basis of contemporary maintenance therapy for transplant recipients [11,12]. Each of these agents receives public subsidy in Australia through the national Pharmaceutical Benefits Scheme (PBS) for the prevention and/or treatment of renal allograft rejection following transplantation, while some are also subsidized for other less commonly transplanted organs or for the management of certain autoimmune conditions [13]. Dispensing of these medicines is also publically subsidized in Northern European countries such as Norway, Denmark, Sweden, and the Netherlands. With reasonably similar economic conditions, health care systems and scope of prescribing, these 5 countries prove good comparison data for international pharmacoepidemiologic research.

To date, there has only been a single paper investigating the epidemiology and economics associated with usage of maintenance immunosuppression in Australia [14]. This 2009 study compared mycophenolic acid utilization in Australia and Northern Europe to develop a rational baseline for projections of future utilization and costs [14].

The aim of the present study is to examine the utilization of mycophenolic acid, tacrolimus, cyclosporin, sirolimus and everolimus in Australian transplant recipients, and to compare and contrast Australian data with the publically subsidized utilization data from Norwegian, Swedish, Danish, and the Netherlands.

Material and Methods

Data source

Australian records relating to PBS dispensing and expenditure were collected from the administrative database, Medicare Australia Item Statistics [15]. Specific item codes associated with the various forms, strengths and types of subsidy for each studied drug (Appendix 1) were entered into the database and a utilization report generated providing the number and cost of PBS prescriptions dispensed per month between 2007 and 2013 [13]. Due to division in state and federal government responsibilities in health care provision and changes in funding models over the study period, *all* hospital utilization and expenditure information prior to 2014 were not fully characterized using PBS item statistics alone [13,15]. To capture hospital-specific utilization and expenditure, the highly specialized drug (HSD) national expenditure reports (public and private hospitals) [16,17] were used. Mid-year data on population in Australia were obtained from the Australian Bureau of Statistics [18]. Data on utilization for each immunosuppressant in Norway, Denmark, Sweden and the Netherlands were obtained from their respective healthcare databases [19–22]. Data in these archives were available as either daily defined dose (DDD) or DDD/1000 population/day [23]. Mid-year data on population size in each of these countries were obtained from their respective government databases [24–27]. Australian, Norwegian, Danish, and the Netherlands immunosuppressant utilization data were obtained from both the community and hospital settings. Swedish data were only available for community pharmacy dispensing.

Information relating to all allograft transplant operations performed per year, number of renal transplants currently functional in the community and rates of renal transplantation per million population was gathered from Australian Transplant Registries [5,28,29] while international renal transplantation figures were obtained from the International Registry of Organ Donation and Transplantation (IRODaT) maintained on behalf of Scanditransplant and Eurotransplant [30].

Data analysis

Australian PBS and HSD data relating to the utilization of mycophenolic acid, tacrolimus, cyclosporin, sirolimus and everolimus were collated as number of prescriptions dispensed per month from 2007 to 2013. To allow international comparison and analysis these data were converted to DDDs. The DDD (2014) for mycophenolate mofetil was 2000mg, tacrolimus 5 mg,

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cyclosporin 250 mg, sirolimus 3 mg and everolimus 1.5 mg [23]. The DDD for mycophenolate was listed as the mofetil salt and to adjust this to enable aggregation of all different salt forms as mycophenolic acid this was multiplied by 0.739 (DDD for mycophenolic acid 1478mg). DDD for all formulations for each drug were then added together. DDD/1000 population/day was calculated for each year. In short, the number of dispensings was multiplied by the pack size and strength of each individual dosage form (tablet, capsule and suspension) to obtain total milligrams per year. Milligram per year were then divided by the DDD for each immunosuppressant and finally divided by the Australian population, in thousands, and multiplied by the number of days in each respective year. A similar process was applied to HSD reporting where information on the number of dispensings per quarter for each specific PBS item code was available between 2007 and 2013. These were multiplied by pack size and strength, divided by appropriate DDD and finally adjusted for population size and days in a year. In both PBS and HSD databases, data relating to the use of mycophenolate sodium for use in lupus nephritis, recognized by separate item numbers, were excluded to enable transplantation-specific utilization to be calculated.

To calculate the total DDD/1000 population/day for each immunosuppressant in Australia, both PBS and HSD sources were summed. Because of the ongoing changes to hospital and public subsidy over the study period, the PBS utilization data were corrected to exclude all hospital HSD-related PBS item codes, as these were already captured by HSD reporting. This ensured no "double counting" in the overall results. Total expenditure was calculated similarly to utilization. PBS and HSD reporting were summated, again removing HSD-related PBS item codes from PBS item statistic reports to avoid "double counting".

Sensitivity analysis was performed for 2 possible limitations:

a. Including Australian data relating to mycophenolate sodium dispensing in lupus nephritis to estimate any impact if this indication were included in the international data.
b. Using a DDD of 2g for mycophenolic acid formulations to study the influence this may have had on the comparisons to international use, as international data may not have accounted for the mofetil salt adjustment of 0.739.

Differences in utilization between the Northern European countries and Australia were evaluated with descriptive analyses. Chi squared analyses were performed, testing the null hypothesis that there was no difference in utilization between Australia and each of the other countries (2013). Statistical significance was $p<0.05$ (VassarStats online clinical research Chi Square calculator [31]). Linear regression analysis (Microsoft Office: Excel®) was used to calculate the rate of change over time in utilization of the 5 immunosuppressant agents combined in Australia and the Northern European countries.

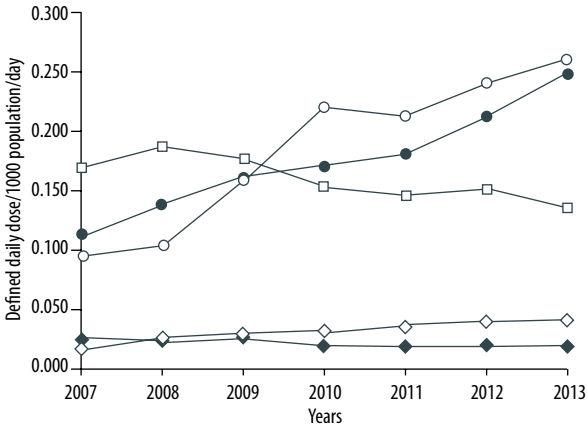

Figure 1. Utilization of mycophenolic acid (○), tacrolimus (●), cyclosporin (□), sirolimus (◆) and everolimus (◇) in Australia between 2007 and 2013.

Results

Utilization of all formulations of mycophenolic acid, tacrolimus, cyclosporin, sirolimus and everolimus in Australia between 2007 and 2013 is shown in Figure 1. Mycophenolic acid showed a 175% or 2.7-fold increase from 0.095 DDD/1000 population/day in 2007 to 0.260 DDD/1000 population/day in 2013. Tacrolimus increased from 0.113 DDD/1000 population/day in 2007 to 0.248 DDD/1000 population/day in 2013, a 2.2-fold or 120% increase in utilization. Cyclosporin utilization decreased by approximately 20% from 0.169 DDD/1000 population/day in 2007 to 0.135 DDD/1000 population/day in 2013. Sirolimus utilization similarly decreased by 30% from 0.025 DDD/1000 population/day in 2007 to 0.018 DDD/1000 population/day in 2013. Lastly, everolimus utilization increased by 2.3-fold from 0.018 DDD/1000 population/day in 2007 to 0.041 DDD/1000 population/day in 2013.

When considering the specific formulations of mycophenolic acid and tacrolimus individually, utilization of enteric-coated mycophenolate sodium increased from approximately 18% of total mycophenolic acid consumption in 2007 to 27% of total mycophenolic acid consumption in 2013, taking market share from the mycophenolate mofetil formulation. Similarly usage of extended-release tacrolimus, first dispensed in December 2010, has grown continually such that it now accounts for 10% of the total tacrolimus consumption in 2013.

Dispensing and provision of these 5 medicines in Australia can be through community pharmacies or public and private hospitals. Between 2007 and 2013 approximately 25% of total supply was via community pharmacies, through general public subsidization, while 70% and 5% was via public and private hospitals, respectively, through the HSD scheme.

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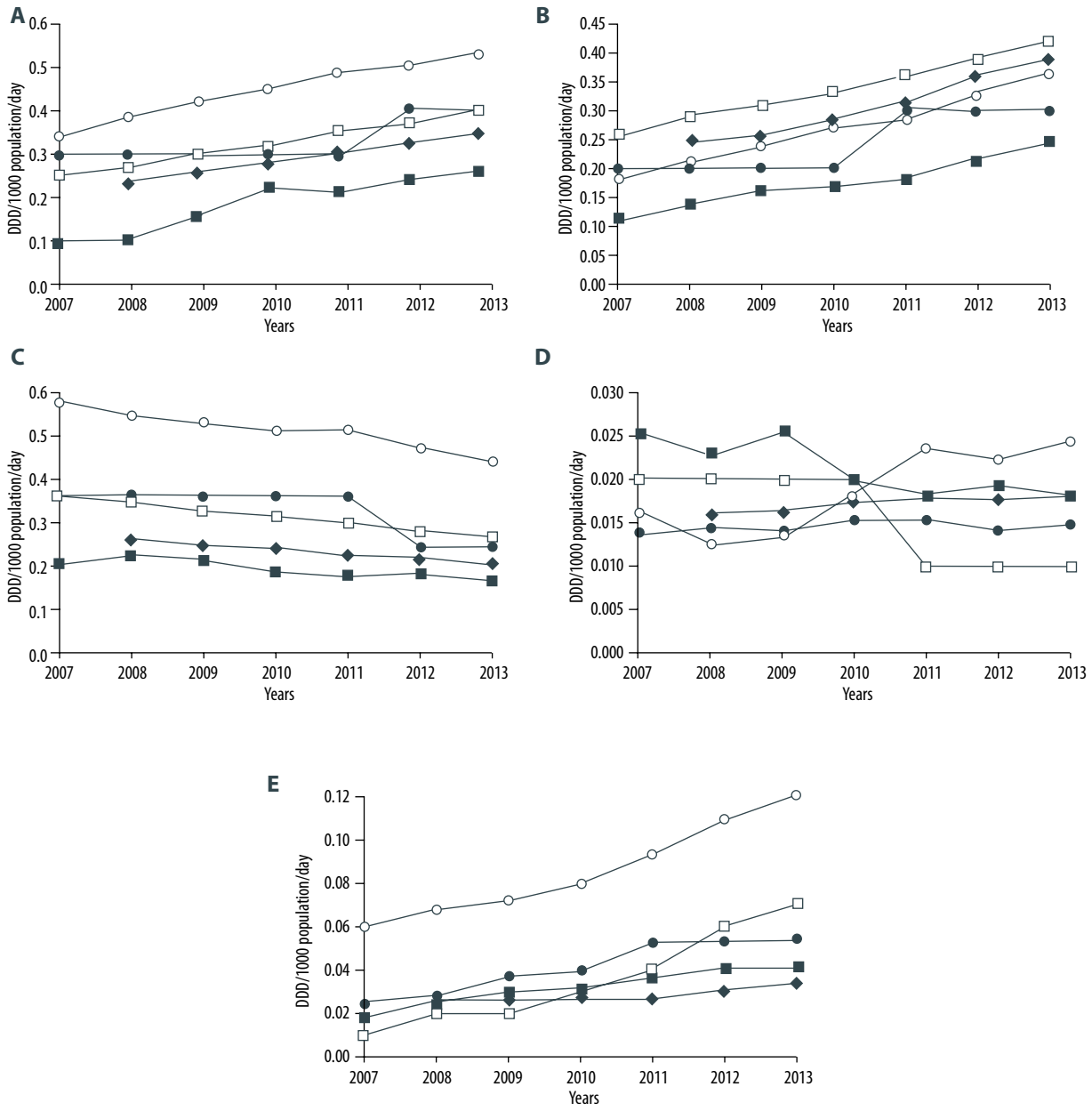

Figure 2. International comparison of utilization for (**A**) mycophenolic acid, (**B**) tacrolimus, (**C**) cyclosporin, (**D**) sirolimus, and (**E**) everolimus between Norway (○), Denmark (●), Sweden (□), The Netherlands (◆), and Australia (■).

Figure 2 displays the comparisons between Australia, Norway, Denmark, Sweden and the Netherlands for each of the 5 immunosuppressants. Patterns of utilization are similar across each of the 5 nations (i.e., rising usage of mycophenolic acid, tacrolimus and everolimus, falling usage of cyclosporin and sirolimus) while Norwegian utilization was consistently higher than the other 4 countries. In 2013, utilization of mycophenolate, tacrolimus and cyclosporin was significantly higher for each European country compared to Australia (Chi-squared analyses; $p<0.001$ for each medication). While sirolimus and everolimus use was lower in Australia compared to each European country, these differences were not statistically significant. Australian utilization (all 5 medications combined) was found to be growing faster than Denmark, at similar rates to Sweden and the Netherlands and slower than Norway (0.009, 0.005, 0.009, 0.009 and 0.01 DDD/1000 population/day per year, respectively). Overall Australian utilization was growing slightly faster than total Northern European utilization (0.009 verses 0.007 DDD/1000 population/day per year).

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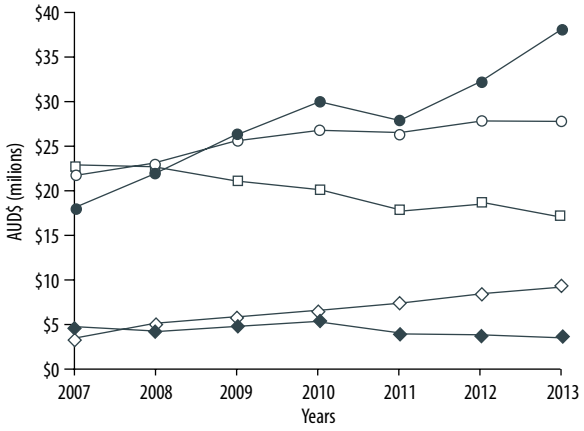

Figure 3. Total cost of mycophenolic acid (○), tacrolimus (●), cyclosporin (■), sirolimus (◆), and everolimus (◇) to the Australian government through community and hospital subsidization.

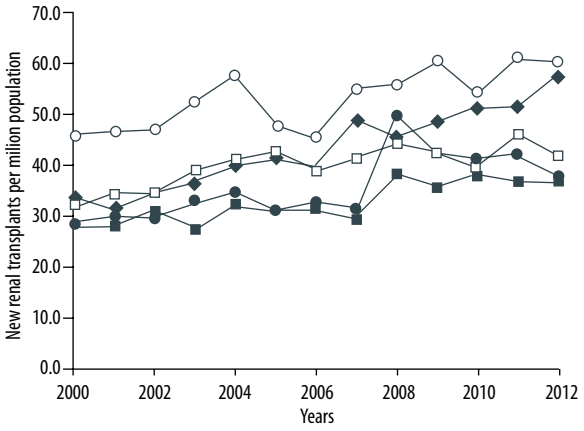

Figure 5. Number of new renal transplants per million population per year in Denmark (●), Norway (○), Sweden (□), the Netherlands (◆), and Australia (■) between 2000 and 2012.

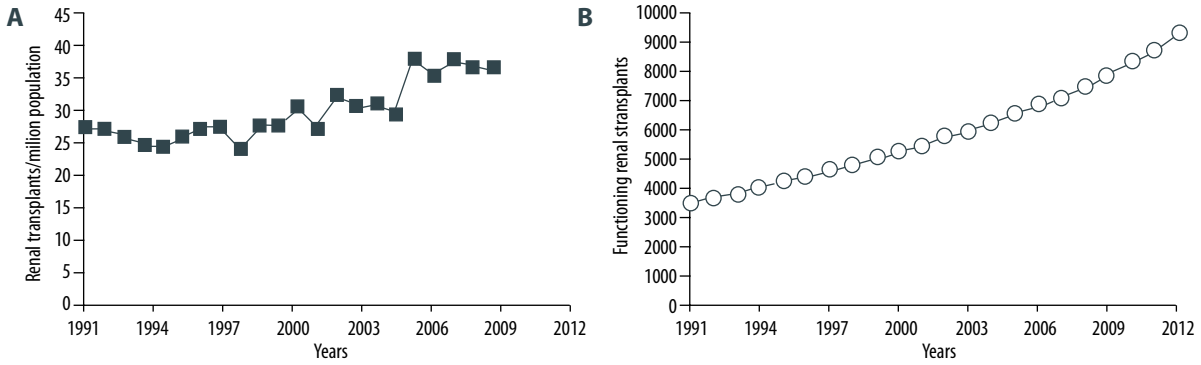

Figure 4. (**A**) Number of renal transplant operations in Australia per million population 1991–2012 and (**B**) number of functioning renal allografts in the Australian community 1991–2012.

Australian public subsidy for the maintenance immunosuppressants is represented in Figure 3. Combining total community and hospital expenditure the immunosuppressant with the highest cost to the Australian government was tacrolimus at AUD$40 million in 2013. Second was mycophenolic acid with a financial outlay of AUD$30 million in 2013. Third was everolimus with government reimbursement increasing from AUD$3 million in 2007 to just over AUD$9 million in 2013. These represent increases of 110%, 30% and 180%, respectively. Conversely, cyclosporin expenditure decreased 25% from AUD$23 million in 2007 to AUD$17 million in 2013. Sirolimus expenditure decreased by AUD$1 million over the study period (20% decrease). Dispensing and subsidization of these 5 medicines in Australia can be through community pharmacies or public and private hospitals. Community pharmacies accounted for approximately 25% of subsidized costs from 2007 to 2013 whereas subsidy through the HSD scheme to public and private hospitals accounted for 70% and 5%, respectively, between 2007 and 2013. Overall, public funding of the 5 studied immunosuppressants has increased from AUD$70 million in 2007 to almost AUD$100 million in 2013, a 1.4-fold increase.

Kidney transplantation accounted for 61% of all solid organs transplanted in Australia in 2012 while liver, lung, heart and pancreas transplantation contributed 19%, 11%, 6% and 2%, respectively [5,28,29]. Figure 4 shows the number of renal transplant operations per million population and the number of people living with a functioning renal allograft between 1991 and 2012 in Australia. The rates of both have continually increased over this period.

Figure 5 displays the number of new kidney transplants conducted in Australia, Denmark, Norway, Sweden and the Netherlands per million population 2007–2012. Kidney transplant rates increased across all countries, however Norway and the Netherlands had more transplants per million population

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with 60 and 57.5, respectively, compared to Australia, Denmark and Sweden with 36.7, 37.6 and 41.8, respectively.

Sensitivity analyses showed inclusion of PBS item codes pertaining to the use of mycophenolate in lupus nephritis (Appendix 1) increased overall Australian utilization figures by 2% whereas using the DDD for the mofetil salt of mycophenolate, rather than the corrected DDD for mycophenolic acid contributed a 9% drop.

Discussion

This study for the first time documents the increasing use of maintenance immunosuppressive medications, contrasting different countries which have publicly funded subsidy for these medications. Immunosuppressant usage and subsequent expenditure are rising in Australia and Northern Europe. The number of transplant operations performed each year and the number of people living with a functioning renal allograft in the community is rising. With the current ageing population [32,33] and increasing rates of hypertension and type II diabetes [32]; new techniques such as ABO incompatible live donor transplantation and HLA desensitization providing avenues to increase organ availability [34,35]; and improvements in post-transplant care it is expected that the number of people requiring a transplant and those living with a functional allograft will continue increasing into the future. This will have future implications for the pharmaceutical budgets of these countries.

All the Northern European countries in this study had higher utilization of the maintenance immunosuppressant medications than Australia. Australia has an opt-in system for organ donation requiring citizens to nominate themselves as organ donors [34]. Internationally, The Netherlands and Denmark have a similar opt-in system [30] but both still have higher rates of transplantation than Australia [30]. Norway and Sweden have an opt-out system for organ donation and everybody is considered as a potential organ donor unless they specify otherwise [30]. These differing policies may be one of the underlying factors contributing to the larger number of transplants per head of population in these countries compared to Australia, and hence higher immunosuppressant use. The specific patterns of utilization in Australia and Northern Europe show that mycophenolic acid, tacrolimus and everolimus utilization had an increasing and steady uptake. This practice is supported by literature evidence that a mycophenolic acid/tacrolimus regimen offers patients an increased length and quality of life when compared to the previously common azathioprine/cyclosporine regimen [11]. As tacrolimus can cause nephrotoxicity and subsequent rejection, everolimus substitution has shown promise as an alternative for the long-term management of rejection combined with mycophenolic acid [36]. Everolimus substitution is considered most clinically appropriate between 12 and 72 months post-transplant [37–40]. This evidence aligns well with the observed results and provides insight into the evolving practice of prescribers being shaped by the current literature. Similarly, cyclosporin and sirolimus utilization is decreasing, also supported by current evidence. Tacrolimus has been identified as a clinically and pharmacoeconomically superior calcineurin inhibitor thus a majority of new transplant recipients should receive tacrolimus [41]. Nevertheless there are no data to suggest that switching from cyclosporin to tacrolimus after stabilization has benefits on long-term outcomes so patients already stabilized on cyclosporin generally remain on it [42–44]. This is consistent with utilization patterns seen in this study, with cyclosporin utilization decreasing gradually over time, not dropping off completely. Sirolimus appears to be in a similar situation as everolimus use has been shown to be clinically non-inferior with a more tolerable side effect profile and it appears to be the preferred mammalian target of rapamycin inhibitor (mTOR) [37].

Australian utilization was significantly lower for mycophenolate, tacrolimus, and cyclosporin compared to the 4 European nations ($P<0.001$). Linear regression, investigating changes over time, showed Australian utilization of these 5 medications growing at a slightly faster rate than total Northern European utilization. Using Northern European utilization as a projection for growth, it is postulated that Australia is lagging by roughly 5 years, probably due to lower transplant rates [30,45]; i.e., Australian utilization in 2013 is comparable to Northern European utilization in around 2008. Australia has had many public campaigns to try to increase organ donation [46]. With the potential for growth, Australia could bridge the gap with Northern Europe in future years, and it is important that it is realized that entails an increase in overall government expenditure probably in line with that experienced in recent years in Northern European countries.

Australian government expenditure on maintenance immunosuppressants has already climbed rapidly to almost AUD$100 million in 2013. Similar to utilization, government expenditure on mycophenolic acid, tacrolimus and everolimus increased over the study period. The opposite was recorded for cyclosporin and sirolimus. Several initiatives recently enacted by the Australian government, as well as cheaper generic availability of pharmaceuticals after patent expiry, have introduced cost-savings measures and these introduce uncertainty about future pricing structures and PBS expenditures. However, by considering the increasing number of kidney transplant operations, functioning kidney transplants in the community and potential for widening of the subsidized indications, particularly for mycophenolate [47–49], tacrolimus [50] and everolimus [51–53], immunosuppressant expenditure will continue to rise into the future. It is not likely that generic formulations

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will decrease costs by the amount needed to offset increased utilization. It is also important to consider the wider scope of health expenditure, not just the government outlay on prescription medicines. Tacrolimus has been demonstrated to be a cost-effective option compared to cyclosporin and although a more expensive drug in direct costs, indirect cost-savings such as reduced hospital stay, longer graft functioning and improved patient quality of life provide benefits [54–56]. Similarly, mTOR introduction to the immunosuppressive regime through substitution or minimization strategies, although expensive, has been estimated to provide a cost-saving role to the overall treatment of these patients [36]. It is through pharmacoeconomic analysis the true price of these medicines can be understood and displayed in a holistic manner not just with a focus on drug acquisition costs [57].

This study did not include other therapies used in the management of rejection in renal transplant patients including azathioprine, corticosteroids and the biological monoclonal antibodies. Azathioprine has now been largely replaced by mycophenolic acid in maintenance regimens and is mainly used for indications other than rejection prevention [5]. Similarly usage of oral corticosteroids (prednis(ol)one) in transplant recipients specifically cannot be identified in the PBS database as these agents have numerous subsidized indications, all sharing the same PBS item code, and cost of these medicines falls below the PBS co-payment. Biological monoclonal antibodies are very costly treatments sometimes used for induction therapy and the treatment of acute rejection. These agents are not included in long-term maintenance immunosuppressant regimens and thus were not included.

The data relate primarily to kidney transplantation, although use of immunosuppressants in other transplant groups was included to a lesser extent. Kidney transplantation accounted for 61% of all the solid organ transplants in Australia in 2012. Mycophenolate is subsidized by the PBS for the use in cardiac and renal transplantation, tacrolimus for all transplants, cyclosporin for all transplants, sirolimus for cardiac and renal and everolimus for only renal (Appendix 1). The next highest transplant group after renal transplant recipients was liver recipients (19% in 2012), but only tacrolimus and cyclosporin receive subsidy for this indication.

The Australian PBS administrative database primarily documents dispensing of publicly subsidized medicines for the purposes of reimbursement and expenditure analysis. This provides several limitations for research including the assumption that each recorded dispensing was the maximum PBS subsidized quantity. It was also assumed that all use of these medicines was publically subsidized. Private prescription use however is likely to be vanishingly small due to the extremely high prices of these medicines and the ready accessibility of public subsidy for all Australian residents. Transplant recipients requiring rejection prophylaxis fulfil the subsidy restrictions to receive these medicines for a low price.

Sensitivity analyses were conducted to consider the potential impact if mycophenolic acid data pertaining to lupus nephritis use were included in Northern European data (whereas they are separated in Australian data). Inclusion of this information together with the data for transplantation only contributed another 2% to the overall mycophenolic acid utilization in Australia, therefore was not likely to make a major difference if this use was included in Northern Europe. This study assumed that international reporting of mycophenolic acid DDDs and DDD/1000 population/day incorporated the mofetil salt correction factor of 0.739. As it is difficult to ascertain whether these databases accounted for this correction or not, further sensitivity analyses were conducted to assess the impact this would have on results. Sensitivity analyses show that by using the DDD for mycophenolate of 2000mg instead of 1478mg, even the 9% higher apparent utilization which would have resulted would not have been sufficient to explain the difference between Australian and Northern European usage.

Conclusions

There is an increasingly large number of Australians receiving kidney transplant for which they are required to take various combinations of mycophenolic acid, tacrolimus, cyclosporin, sirolimus, and everolimus for the remainder of their lives. Because of this, immunosuppressant utilization and expenditure is rising in Australia. Internationally, this study found significant differences between the utilization of the 5 medicines in Australia and Northern Europe. Trends in utilization were considered and with the growth potential predicted from Northern Europe it can be expected that these medicines will continue consuming an increasing share of Australian pharmaceutical expenditure in years to come. The 5 studied immunosuppressants (mycophenolic acid, tacrolimus, cyclosporin, sirolimus, and everolimus) are high-cost, life-preserving drugs; increasing utilization and expenditure have increased the financial impact felt by Australian and international pharmaceutical budgets.

Statements

The authors declare no sponsorships or funding. The authors have no conflicts of interest

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Appendix 1. ATC codes and PBS item codes for immunosuppressants in Australia.

ATC code	PBS item code	Item description	Qty	Schedule	Authority
L04AA06	8649F	Mycophenolate mofetil 250 mg capsule	300	General	Management of renal and cardiac allograft rejection
	8650G	Mycophenolate mofetil 500 mg tablet	150		
	8651H	Mycophenolate mofetil 1 g/5 mL oral liquid – 165 mL	1		
	6208R	Mycophenolate mofetil 250 mg capsule	600	s100 HSD private	
	6209T	Mycophenolate mofetil 500 mg tablet	300		
	6364Y	Mycophenolate mofetil 1 g/5 mL oral liquid – 165 mL	2		
	9501C	Mycophenolate mofetil 250 mg capsule	600	s100 HSD public	Streamlined – 3355: management of renal rejection and 3356: cardiac rejection
	9502D	Mycophenolate mofetil 500 mg tablet	300		
	9500B	Mycophenolate mofetil 1 g/5 mL oral liquid – 165 mL	2		
	*2150E	Mycophenolate 180 mg tablet: enteric	120	General	WHO Class III, IV or V lupus nephritis
	*2193K	Mycophenolate 360 mg tablet: enteric	120		
	2150E	Mycophenolate 180 mg tablet: enteric	120		Management of renal allograft rejection
	8653K	Mycophenolate 360 mg tablet: enteric	120		
	6369F	Mycophenolate 180 mg tablet: enteric	240	s100 HSD private	Renal allograft rejection prophylaxis and WHO class III, IV or V lupus nephritis
	6370G	Mycophenolate 360 mg tablet: enteric	240		
	9503E	Mycophenolate 180 mg tablet: enteric	240	s100 HSD public	Streamlined – 4084: Prophylaxis of renal rejection and 4095: WHO Class III, IV or V lupus nephritis
	9504F	Mycophenolate 360 mg tablet: enteric	240		
	1836P	Mycophenolate capsule 250 mg	300	General	Management of renal and cardiac allograft rejection
	1837Q	Mycophenolate capsule 250 mg	600	s100 HSD private	
	1839T	Mycophenolate capsule 250 mg	600	s100 HSD public	Streamlined – 3355: management of renal rejection and 3356: cardiac rejection
L04AD02	8646C	Tacrolimus 0.5 mg capsule	100	General	Maintenance of allograft rejection
	8647D	Tacrolimus 1 mg capsule	200		
	8648E	Tacrolimus 5 mg capsule	200		
	6328C	Tacrolimus 0.5 mg capsule	100	s100 HSD private	Initiation and maintenance of allograft rejection
	6216E	Tacrolimus 1 mg Capsule	200		
	6217F	Tacrolimus 5 mg capsule	200		
	9558C	Tacrolimus 0.5 mg capsule	50	s100 HSD public	Streamlined: 3328 – management of allograft rejection
	9560E	Tacrolimus 1 mg capsule	100		
	9561F	Tacrolimus 5 mg capsule	100		
	5299X	Tacrolimus 0.5 mg XR capsule	30	General	Maintenance of allograft rejection
	5300Y	Tacrolimus 1 mg XR capsule	60		
	5451X	Tacrolimus 5 mg XR capsule	60		
	9681M	Tacrolimus 0.5 mg XR capsule	60	s100 HSD private	Initiation and maintenance of allograft rejection
	9682N	Tacrolimus 1 mg XR capsule	120		
	9683P	Tacrolimus 5 mg XR capsule	120		
	9664P	Tacrolimus 0.5 mg XR capsule	30	s100 HSD public	Streamlined: 3328 – management of allograft rejection
	9665Q	Tacrolimus 1 mg XR capsule	60		
	9666R	Tacrolimus 5 mg XR capsule	60		

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Appendix 1 continued. ATC codes and PBS item codes for immunosuppressants in Australia.

ATC code	PBS item code	Item description	Qty	Schedule	Authority
L04AD01	8657P	Cyclosporin 10 mg capsule	120	General	Organ rejection, atopic dermatitis, psoriasis, nephrotic syndrome and severe active RA
	8658Q	Cyclosporin 25 mg capsule	60		
	8659R	Cyclosporin 50 mg capsule	60		
	8660T	Cyclosporin 100 mg capsule	60		
	8661W	Cyclosporin 100 mg/mL suspension	2		
	6232B	Cyclosporin 10 mg capsule	120	s100 HSD private	
	6352H	Cyclosporin 25 mg capsule	120		
	6353J	Cyclosporin 50 mg capsule	120		
	6354K	Cyclosporin 100 mg capsule	120		
	6125J	Cyclosporin 100 mg/mL suspension	4		
	5632K	Cyclosporin 10 mg capsule	120	s100 HSD public	Streamlined: 3328 – organ rejection, 3329 –atopic dermatitis, 3330 – psoriasis, 3331 – nephrotic syndrome & 3332 – severe active RA
	5634M	Cyclosporin 25 mg capsule	120		
	5635N	Cyclosporin 50 mg capsule	120		
	5636P	Cyclosporin 100 mg capsule	120		
	5633L	Cyclosporin 100 mg/mL suspension	4		
L04AA10	8984W	Sirolimus 0.5 mg tablets	100	General	Management of renal allograft rejection
	8724E	Sirolimus 1 mg tablets	100		
	8833X	Sirolimus 2 mg tablets	100		
	8725F	Sirolimus 1 mg/mL suspension	1		
	9748C	Sirolimus 0.5 mg tablets	200	s100 HSD private	
	6436R	Sirolimus 1 mg tablets	200		
	6457W	Sirolimus 2 mg tablets	200		
	6437T	Sirolimus 1 mg/mL suspension	2		
	9747B	Sirolimus 0.5 mg tablets	200	s100 HSD public	Streamlined: 3355 – management of renal allograft rejection
	9549N	Sirolimus 1 mg tablets	200		
	9548M	Sirolimus 2 mg tablets	200		
	9550P	Sirolimus 1 mg/mL suspension	2		
L04AA18	8840G	Everolimus 0.25 mg tablet	60	General	Maintenance therapy following initation and stablisation in renal and cardiac transplant patients
	8841H	Everolimus 0.5mg tablet	60		
	8842J	Everolimus 0.75mg tablet	120		
	9352F	Everolimus 1 mg tablet	120		
	6459Y	Everolimus 0.25 mg tablet	120	s100 HSD private	Management of renal and cardiac allograft rejection
	6460B	Everolimus 0.5 mg tablet	120		
	6461C	Everolimus 0.75 mg tablet	240		
	9582H	Everolimus 1 mg tablet	240		
	5738B	Everolimus 0.25 mg tablet	120	s100 HSD public	Streamlined authority – 3355: Management of renal allograft rejection and 3356: Management of cardiac allograft rejection
	5739C	Everolimus 0.5 mg tablet	120		
	5740D	Everolimus 0.75 mg tablet	240		
	5737Y	Everolimus 1 mg tablet	240		

* Data pertaining to utilisation of mycophenolic acid in lupus nephritis was collected for purposes of sensitivity analysis only.

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