Transplant International

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

A survey to determine the views of renal transplant patients on generic substitution in the UK

Mubarak N. Al Ameri,[1] Clare Whittaker,[2] Arthur Tucker,[1] Magdi Yaqoob[1,2] and Atholl Johnston[1]

1 Clinical Pharmacology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, UK

2 Barts and The London, Royal London Hospital, Renal Transplant Clinic, Whitechapel, London, UK

Keywords

clinical outcomes, generic medicines, generic substitution, patients' opinions, professionals' roles on generic substitution.

Correspondence

Mubarak N. Al Ameri, Clinical Pharmacology, Barts and The London, Charterhouse Square, London, EC1M 6BQ, UK. Tel.: +44-20-7882 3413; fax: +44-20-7882 3408; e-mail: m.al-ameri@qmul.ac.uk

Conflicts of Interest

The authors have declared no conflicts of interest.

Received: 3 March 2011
Revision requested: 23 March 2011
Accepted: 16 April 2011
Published online: 16 May 2011

doi:10.1111/j.1432-2277.2011.01268.x

Summary

Rising healthcare costs promote the generic substitution among patients because it is identifiable costs. A key concern is that patients should be involved in the decision of switching. The aim of this study was to examine renal transplant patients' views on generic substitution in the UK. A total of 163 renal patients were surveyed using 36 multiple-choice questions at Barts and The London Renal Transplant Clinic, in the UK. Transplant recipients over 18 years, able to read and write English and willing to fill in the questionnaire were targeted; 84% of patients were conscious of the availability of generic medicines, 70% understood the terms ''generic'' and ''branded'' in relation to medicines and 54% were aware of generic substitution practice. However, 75% did not know if they were taking generics and 84% felt that generics are not equivalent or only equivalent sometimes and they were uncertain that generics had the same quality as branded medicines. Moreover, many patients admitted that they would not accept the generic substitution of ciclosporin when become available in the UK. A number of factors such as patients' education, knowledge, severity of the disease, efficacy of generic medicines and patients' involvement in decisions regarding their health appear to drive patients' attitudes towards generic substitution.

Introduction

Rising healthcare costs have received significant attention in both the public and political arenas [1,2]. Most policy makers are looking to limit their health expenditure while, optimistically, maintaining or improving the quality of care. It is often easier to intervene on the expenditure of medications because their costs are easily identified. It is already proven that substitution of generic medicines can result in substantial savings [3–5]. As a result, the preference for promoting generic substitution among patients was reported in many countries [6,7]. For example, in the UK and other European countries, the cost-saving benefits of promoting generic substitution are considerable [4,5,8]. Furthermore, last year the Department of Health (DH) in England considered and then abandoned the idea of automatic generic substitution of medicines by pharmacists [2,9].

Switching to a cheaper medicine usually has two forms: *generic* and *therapeutic*. *Generic substitution* refers to switching between a branded product and a generic or a branded generic version of the same medicine (such as for ciclosporin switching from Neoral® to Deximune) [10]. *Therapeutic substitution* means switching between medicines either within the same class (such as for statins switching from atorvastatin to simvastatin) or from different classes [such as an angiotensin converting enzyme (ACE) inhibitor for an angiotensin receptor blocker (ARB)], the clinical effect of which is considered to be broadly equivalent [11]. Generic and therapeutic substitutions have raised concerns about whether they serve the interests of patients or simply the target of reducing

healthcare related costs. But some authors and general practitioners are now questioning the quality of some cheaper medicines [11–19]. Without consulting patients, and thus obtaining their consent to treatment, many healthcare providers including the British NHS have been promoting drug substitution in an attempt to contain their costs [20,21]. Despite the UK's National Health Service espousing ''evidence based medicine'', this has been done without any attempt to determine the extent, if any, of long-term savings (drug substitution may involve spending or costs in addition to the simple product acquisition costs). It has also been done without any consideration of the potential for adverse consequences which may arise [22].

Although there are few published articles to evaluate patients' views on drug substitution, some have shown that drug substitution can be problematic [14,23]. For example, a survey of patients in the UK has shown that over 20% reported that they would be very or extremely concerned if their prescription was changed, even with their doctor's approval. Of these, 40% felt that the new drug was less effective than the branded drug and 30% experienced more or different side effects [24]. In another British study, 46% of patients stated that they were dissatisfied when faced with generic substitution [25].

This article is not against generic prescribing or substitution, but it is concerned with the effective prescribing, and public (patients) engagement, in the process and its perceived transparency. This study evaluates renal transplant patients' current understanding, opinions and experiences concerning branded and generic medicines and how they consider this may be better managed by healthcare professionals. These are important factors in the acceptance of generic substitution and in obtaining valid and legal consent from patients.

Methods

This study was approved by the Ethics Committee of the East London & The City REC Alpha (REC number 10/H0704/16).

A total of 163 transplant recipients treated at Barts and The London Renal Transplant Clinic, in the UK, were included in a quantitative survey. A questionnaire was used as a tool to obtain the required information. The aim and the protocol of the study were explained and discussed with the medical professionals in a weekly Renal Clinic meeting. Patients were recruited by reception and nursing staff as patients booked in for clinic visit over a period of 6 months (from May 1st until November 1st, 2010). Adult patients over 18 years, able to read and write English, and willing to fill in the questionnaire were targeted. The questionnaire consisted of 36 multiple-choice closed questions. After reviewing the information sheet which contained a short introduction about generic medicines and substitution, patients consented by choosing to fill in the questionnaire. This survey was related to all medication and not immunosuppressant agents alone. The data from the questionnaire were collected and analysed using Microsoft Office Excel 2007 and Minitab 16 (Minitab Inc, Pennsylvania, PA, USA) statistical software. Results of all questions put to patients in the survey are reported and expressed as % [95% confidence intervals (CI)]. The missing values are not included in the calculations of percentages; the total number (n) of respondents for each question is given in parentheses after each question.

The survey's short introduction to the topic for the patients was as follows

Brands and 'generic' versions exist in all areas of life. For example, Heinz Baked Beans versus supermarket own brand beans. Where medicines are concerned, the original brands are introduced by the pharmaceutical companies who researched and developed them. Subsequently, at a later date, other manufacturers introduce generic versions, which they can produce generally at a lower price.

The subject of switching patients from branded to generic medicines has become a subject of debate for patients and healthcare providers alike. Indeed, many healthcare providers have been promoting switches to generic medicines in an attempt to save money. The following questionnaire is designed to evaluate your understanding, opinions and experiences concerning branded and generic medicines and how you consider this may have been managed by healthcare professionals.

Results

According to the study protocol, a minimum of 100 patients were intended to be surveyed. However, nurses and receptionists in the participating clinic were able to recruit a total of 163 patients. It was difficult to enrol a higher number of patients during the regular clinic hours because of time constraints. Renal transplant recipients were specified in this survey because any small changes in the medicinal effect can negatively impact on their clinical outcome.

A total of 87 (53%) male and 76 (47%) female patients with an average age of 48 years [range (18–81), median 47] participated in the study. The majority [96% (95% CI 91–98)] of participating patients confirmed that they had undergone a kidney transplant more than a year ago. In addition, more than two-thirds were taking more than seven medications [44% (95% CI 36–52) were taking between 7 and 9 medications and 27% (95% CI 20–35)

were taking more than nine medications]. In addition, 74/147 participants [50.34% (95% CI 42–59)] were highly educated (graduated from college, university or postgraduate) and 73/147 participants [49.66% (95% CI 41–58)] were less educated (graduated from secondary school, vocational training or sixth forms) (Table 1).

The questionnaire was divided into three sections as follows: patients' general knowledge of generic medicines and substitution

Although 75% (95% CI 67–82) of participated patients did not know and were unsure of taking generic medicines, 84% (95% CI 76–89) of them felt that generics are not equivalent or only equivalent sometimes and they were uncertain that generics had the same quality as branded medicines. Nevertheless, 81% (95% CI 74–87) of patients were unaware and uncertain that a generic form of ciclosporin, an immunosuppressant agent, is available in the UK and only 23% (95% CI 16–31) admitted that they would accept the generic substitution of ciclosporin when become available (Table 2).

Findings in this survey marked the effect of educational attainment on patients' acceptance of generic substitution. A total of 69 highly educated patients (graduated from college, university or postgraduate) responded to a question evaluating their awareness of generic substitution practice. Of these 51 [74% (95% CI 62–84)] had reported that they were aware of the substitution practice. On the other hand, from a total of 67 less educated patients (graduated from secondary school, vocational training or sixth forms) who responded to the same question, 39 [58% (95% CI 46–70)] were aware of the generic substitution practice ($P = 0.013$), Fig. 1.

Moreover, a total of 64 highly educated renal patients responded to a question evaluating their potential acceptance of generic substitution of ciclosporin. Of these 18 [28% (95% CI 18–41)] confirmed that they would refuse the substitution of ciclosporin. On the other hand, from a total of 60 less educated renal patients who responded to the same question, 29 [48% (95% CI 35–62)] confirmed that they would refuse generic substitution of ciclosporin ($P = 0.056$), Fig. 2.

Patients' attitudes towards generic medicines and substitution

According to the survey, most patients (67%, 95% CI 53–79) receiving generic medicines were dissatisfied or uncertain about their satisfaction concerning generic medicines and more than half (55%, 95% CI 41–67) had experienced noticeable differences between the branded and the

Table 1. Demographics of the participated patients ($n = 163$).

Demographics	Number of responders	Percentages of responders	95% confidence intervals
Gender ($n^* = 163$)			
Male	87	53	(45–61)
Female	76	47	(39–55)
Age distribution ($n^* = 163$)			
39 years or less	44	27	(20–34)
40–49 years	46	28	(21–36)
50–59 years	47	29	(22–36)
60 years or more	26	16	(11–22)
Number of medications taken daily ($n^* = 154$)			
1–3 medications	1	1	(0.02–4)
4–6 medications	43	28	(21–36)
7–9 medications	68	44	(36–52)
>9 medications	42	27	(20–35)
The time of organ transplant ($n^* = 154$)			
Less than a year ago	5	3	(1–7)
More than a year ago	147	96	(91–98)
No transplantation	2	1	(0.02–4)
The level of education ($n^* = 147$)			
Secondary school	60	41	(33–49)
Vocational training	4	3	(1–7)
Sixth form	9	6	(3–11)
College	39	26	(20–34)
University	22	15	(10–22)
Postgraduate	13	9	(5–15)

*The total number of patients responded to the question.

Table 2. Questions and responses evaluating renal patients' general knowledge of generic medicines and substitution.

Questions	Answers	Number of responders	Percentages of responders	95% confidence intervals
Were you aware that there are different forms of the same medicine available, produced by different manufacturers? (*n** = 160)	Yes	134	84	(77–89)
	No	13	8	(4–13)
	Uncertain	13	8	(4–13)
Do you understand the terms ''generic'' and ''branded'' in relation to medicines? (*n** = 142)	Yes	99	70	(61–77)
	No	33	23	(17–31)
	Uncertain	10	7	(3–13)
Are you aware of the practice of generic substitution? (*n** = 146)	Yes	79	54	(46–62)
	No	50	34	(27–43)
	Uncertain	17	12	(7–18)
Do you know if you are currently taking any generic prescription medications? (*n** = 147)	Yes	37	25	(18–33)
	No	52	35	(28–44)
	Uncertain	58	40	(32–48)
Were you aware that a generic form of ciclosporin is available in the UK? (*n** = 150)	Yes	28	19	(13–26)
	No	108	72	(64–79)
	Uncertain	14	9	(5–15)
Would you agree to switch your current branded ciclosporin to a generic form to save the NHS money? (*n** = 135)	Agree	31	23	(16–31)
	Disagree	50	37	(29–46)
	Uncertain	54	40	(32–49)
Do you think that generic medicines are equivalent and have the same quality as the branded medicines? (*n** = 146)	Agree-always	24	16	(11–23)
	Disagree-always	10	7	(3–12)
	Yes-sometimes	50	34	(27–43)
	Uncertain	62	43	(34–51)

*The total number of patients responded to the question.

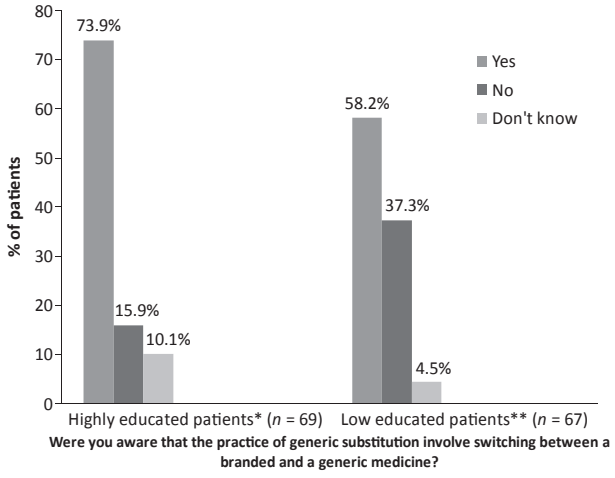

Figure 1 The relationship between the renal patients' level of education and the awareness of generic substitution (*Graduated from college, university or postgraduate, **Graduated from secondary school, vocational training or sixth form).

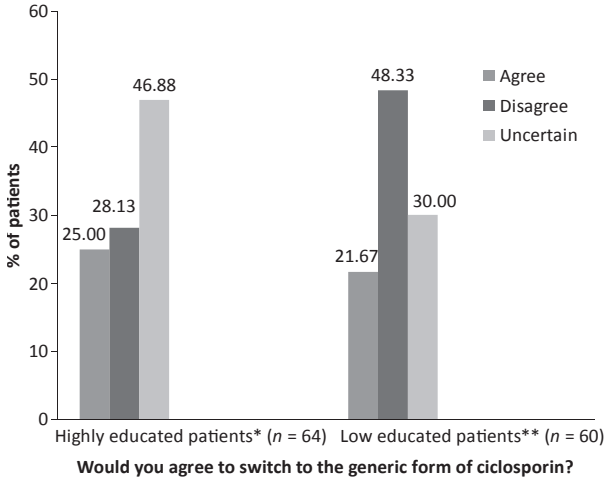

Figure 2 The relationship between the renal patients' level of education and the acceptance of generic substitution of ciclosporin (*Graduated from college, university or postgraduate, **Graduated from secondary school, vocational training or sixth form).

generic medicines and were uncertain about these differences. Of these, 76% (95% CI 62–86) were uncertain about the consequence of theses differences and admitted that adapting to these differences was a problem. In addition, 55% (95% CI 41–67) of participants felt that the generic medicines might affect their medications regime adherence. Nevertheless, 79% (95% CI 71–85) wished to be always notified when switching their medicines (Table 3).

The severity of the disease is also affecting patients' acceptance of generic substitution. Patients were asked about their potential acceptance of generic substitution if they were diagnosed with mild versus chronic disease,

Table 3. Questions and responses evaluating renal patients' attitudes towards generic medicine and substitution.

Questions	Choices	Number of responders	Percentages of responders	95% confidence intervals
How satisfied are you with the generic alternative that you are taking? (*n** = 55)	Very satisfied	18	33	(21–47)
	Dissatisfied	8	14	(6.5–27)
	Neither very satisfied nor dissatisfied	29	53	(39–66)
Have you experienced any differences in terms of the effectiveness or side effects between the branded and generic medicine? (*n** = 56)	Yes	8	14	(6.4–26)
	No	25	45	(31–59)
	Uncertain	23	41	(28–55)
Do you think adapting to these differences was a concern? (*n** = 57)	Agree	18	32	(20–45)
	Disagree	14	24	(14–38)
	Uncertain	25	44	(31–58)
Do you think that receiving a generic medicine might affect how regularly you take your medicines? (*n** = 148)	Agree	21	14	(9–21)
	Disagree	66	45	(36–53)
	Uncertain	61	41	(33–50)
How much would you favour or oppose a requirement that patients always be notified if their medicine is changed to a generic form? (*n** = 144)	Favour	113	79	(71–85)
	Oppose	6	4	(2–9)
	Neither favour nor oppose	25	17	(12–25)
What were the differences between the branded and generic medicines that you have experienced? (*n** = 52)	Packaging	30	57	(43–71)
	Shape, colour or taste	16	31	(19–45)
	The brand is more effective	3	6	(1–16)
	The generic is more effective	1	2	(0.5–10)
	The brand has more side-effect	0	0	(0–6)
	The generic has more side-effect	1	2	(0.5–10)
	Others	1	2	(0.5–10)

*The total number of patients responded to the question.

irrespective of their renal transplant. According to the survey, more than half of participating patients [55% (95% CI 47–63)] admitted that they would accept generic substitution if they had mild disease compared to 34% (95% CI 27–43) who would do so if had a chronic disease, Fig. 3.

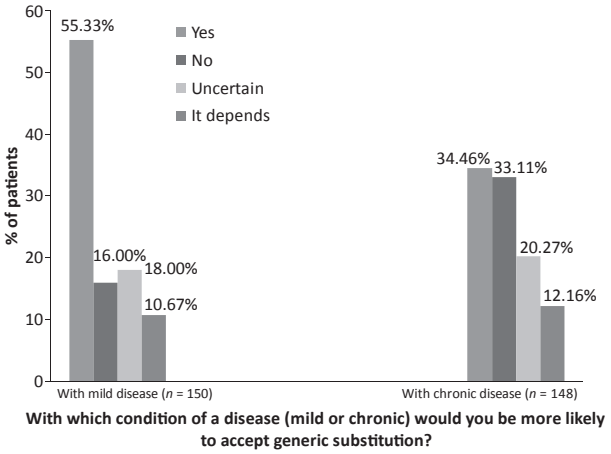

Figure 3 The responses of renal patients when asked about their potential acceptance of generic substitution if they were diagnosed with mild versus chronic disease, irrespective of their renal transplant.

Professionals' roles on generic substitution

A number of patients (34%, 95% CI 26–42) were uncertain if their doctor had changed their medicine to a generic form. Nevertheless, 79% (95% CI 67–88) of patients declared that no background information regarding generic medicines and substitution was provided and more than half [51% (95% CI 42–59)] felt that they had been involved to a small degree or not at all in decisions regarding their healthcare. Moreover, 85% (95% CI 73–93) of patients stated that they were not monitored or uncertain of being monitored after switching to a generic medicine. According to 32% (95% CI 17–51) of patients, pharmacists and the written information were the main source and form of information concerning generic medicines; 48% (95% CI 29–67) of patients were uncertain about the information provided and considered them insufficient. The reasons for switching medicines were not discussed with 69% (95% CI 57–80) of patients; however, 38% (95% CI 21–58) of them believed that general practitioners (GPs) were the professionals who most often discussed the reasons for switching their medicines. When patients were asked about the potential reasons for

promoting generic substitution, many of them (60%, 95% CI 49–69) believed that substitution was promoted mainly to save the NHS money or because of the unavailability of branded medicines. When patients were asked about their communication with healthcare professionals regarding generic medicines, 53% (95% CI 44–61)

Table 4. Questions and responses evaluating healthcare professionals' roles on renal patients' acceptance of generic substitution.

Questions	Choices	Number of responders	Percentages of responders	95% confidence intervals
Has your doctor ever changed your medicine to a generic form? (*n** = 141)	Yes	25	18	(12–25)
	No	68	48	(40–57)
	Uncertain	48	34	(26–42)
Did anyone provide you with background information about your generic medicine? (*n** = 67)	Yes	9	13	(6.3–24)
	No	53	79	(67–88)
	Uncertain	5	8	(2.4–17)
In general, how far do you feel that your doctor involves you in decisions regarding your medications? (*n** = 152)	A lot	75	49	(41–58)
	A bit	45	30	(22–38)
	Not at all	27	18	(12–25)
	Uncertain	5	3	(1–8)
Did your doctor monitor the effect of your medicine after switching you to a generic medicine? (*n** = 58)	Yes	9	15	(7.3–27)
	No	23	40	(27–53)
	Uncertain	26	45	(32–58)
Who provided you with background information about your generic medicine? (*n** = 31)	Specialist	5	16	(24–17)
	Hospital doctor	8	26	(12–45)
	General practitioner	5	16	(24–17)
	Pharmacist	10	32	(17–51)
	Nurse	3	10	(20–26)
	Others	0	0	(0–9)
Did you consider the information provided about your generic medicine to be sufficient? (*n** = 29)	Yes	15	52	(33–70)
	No	3	10	(22–27)
	Uncertain	11	38	(21–58)
Did anyone discuss the reasons for switching your medicine to the generic form? (*n** = 65)	Yes	12	19	(10–30)
	No	45	69	(57–80)
	Uncertain	8	12	(5.4–23)
Who discussed the reasons for switching your medicine to the generic form? (*n** = 29)	Specialist	6	21	(8–40)
	Hospital doctor	8	27	(13–47)
	General practitioner	11	38	(21–58)
	Pharmacist	4	14	(4–32)
	Nurse	0	0	(0–10)
	Others	0	0	(0–10)
Has your doctor ever told you to make sure that you always receive the same brand of any medicine? (*n** = 142)	Yes	60	42	(34–51)
	No	75	53	(44–61)
	Uncertain	7	5	(2–10)
Would you agree to switch your medicine to a generic alternative if your doctor felt that the two medications were interchangeable? (*n** = 72)	Agree	43	60	(47–71)
	Disagree	8	11	(5–21)
	Uncertain	21	29	(19–41)
Which of the following do you think may be potential reasons for switching your medicine to the generic form? (*n** = 96)	Save the NHS money	44	46	(36–56)
	Generics are more effective	5	5	(2–12)
	Generics have the same effectiveness and less costs	34	35	(26–46)
	The branded medicine was not available	13	14	(7–22)
Do you think that you should be consulted about being given generic medicines? (*n** = 142)	Yes-only by GP	15	11	(6–17)
	Yes-only by hospital specialist	45	32	(24–40)
	Agreement of both GP and hospital specialist	70	49	(41–58)
	Do not think that this is necessary	12	8	(4–14)

*The total number of patients responded to the question.

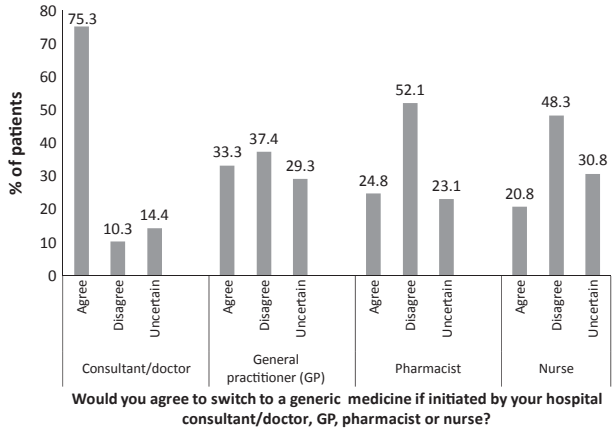

Figure 4 The influence of healthcare professionals on renal patients' acceptance of generic substitution.

reported that their doctors never informed them about whether they should always receive branded or generic medicine. Almost half of participated patients (49%, 95% CI 41–58) believed that they should be consulted about being given generic medicine by their general practitioner (GP) and the hospital specialist, Table 4. Nevertheless, about 75% (95% CI 68–82) of the participating patients agreed to accept generic substitution if it was initiated by a hospital consultant or doctor, Fig. 4.

Discussion

Although the majority of the participating renal patients in this survey reported that they were aware of the term generic medicine and substitution, three quarters of them did not know if they were taking generics and one-third did not know if their medicine was substituted. Most of these patients were uncertain that generics had the same quality as branded medicines. Therefore, many renal patients in the survey were suspicious about their satisfaction concerning generic medicines and; furthermore, they claimed that they would not accept the generic substitution of ciclosporin. These beliefs were marked in patients with less education, chronic diseases and who suspected that the cheaper drug substitution was implemented only to save costs.

The level of education, knowledge, severity of the disease and involving patients in decisions concerning their health played major roles in framing patients' views and acceptance of generic substitution. For example, patients with high level of education were more knowledgeable about their generic medicines and substitution; as a result they were more likely to accept generic substitution of ciclosporin than those with a lower level of education. However, according to the results, there are still some educated patients suspicious about generic medicine and substitution. This suspicion mostly occurred among patients who were not assured, by their healthcare professionals, about the safety and the effectiveness of the prescribed generic medicine [26].

In addition, most patients reported that they were not provided with background information regarding their generic medicine upon substitution and very few reported that they were monitored after substitution. The severity of the disease was also found to play a major role in patients' acceptance of generic substitution. For example, many patients reported that they would be more reluctant to accept generic substitution if they were diagnosed with chronic disease, this is also conformed by other studies [27]. The majority of patients favoured being informed upon switching their medicines and many reported that they would agree to accept generic substitution and adhere to the treatment if they were informed and educated by their healthcare professionals. This explores the clear need for educating patients about generic medicine and substitution, particularly in terms of clarifying the prevalence and processes by which generic substitution occurs and the potential roles of healthcare professionals in successfully introducing generic substitution.

Findings in this study are compatible with those in the existing literature [27–29]. For example, some studies proved that there is a lack of confidence among healthcare professionals in the therapeutic equivalence of all available generic substitutions [28,29]. Small differences in some particular medicines during manufacturing could theoretically result in a risk of significant adverse effects or loss of efficacy [14–16]. Many other studies indicated that patients need to be informed adequately about the equivalence of the branded and the generic medicines otherwise, generic substitution will be challenging [14,23,27,30].

A study examined the economic impact of switching from branded ciclosporin A to its counterpart generic form. The study revealed that the total healthcare costs were significantly higher for patients receiving generic ciclosporin A compared with the branded form. The main driver for the difference was the cost associated with immunosuppressants other than ciclosporin A [31]. Another study reported that patients treated with the branded ciclosporin A had fewer hospitalization days and lower physician costs for inpatient and outpatient procedures. This resulted in lower overall healthcare costs [32]. Moreover, a study compared the effect of valsartan to other cheaper ARBs. It concluded that hypertensive patients who were switched to the cheaper ARB experienced an increase in medication discontinuation, healthcare resource use as well as costs compared with those who were maintained on valsartan treatment [33]. Another study found that switching from atorvastatin to

simvastatin in a primary care setting was associated with a significant increase in morbidity (major cardiovascular events), mortality and in treatment discontinuation compared with patients who did not switch [12]. Random switching among generic versions of the same drug is also not suggested [17,18]. A study reported that indiscriminate switching among generic versions of branded drug could potentially result in 40–60% differences in rate or extent of absorption [34].

Many studies have also concluded that generic substitution caused unexpected and negative effects [35,36]. For example, the increased generic market share in Sweden between 1972 and 1996 was found to be associated with the increase in the number of reported side effects for seven of the 15 medicines studied [37]. Other studies showed differences in the pharmacokinetic profile between branded and generic medicines, disparities that might affect clinical outcomes [38–40]. In addition, a bioequivalence study comparing a generic ciclosporin with its counterpart branded drug Neoral® (Novartis Pharmaceuticals UK Ltd, Surrey, UK) found that the extent and rate of absorption of the former were significantly lower than those of the latter [41]. Similarly, another study compared the biopsy-proven rate of acute rejection (BPAR) at 6 months after kidney transplantation between the branded immunosuppressant drug Neoral® and the branded-generic Gengraf™ (Abbott Laboratories, North Chicago, IL, USA). It found that BPAR was significantly higher in patients who received Gengraf™ [42]. However, The FDA (Food and Drug Administration) considers Gengraf™ to be bioequivalent and interchangeable with Neoral® [43].

The results of this survey show that the research into therapeutic and generic substitution maybe problematical. Health service providers and payers including health insurance companies, in countries outside the NHS system, are promoting generic substitution and not prepared to consider that there may be a problem in that patient outcomes could be detrimentally affected. To do so would reduce the potential savings from these substitutions [31–33] and might lay the providers open to legal redress from patients adversely affected by the substitution policies. They also fail to get patients' valid and legal consent to treatment when they switch treatments without explaining their reasons to the patients. For example, health insurance companies were accused of pressurizing doctors to alter the treatment of patients even if another better method was available [26]. Another example, in the US, it was reported that about one in three doctors admitted withholding information from patients about useful medical services because they are not covered by the patient's health insurance company [44]. Nevertheless, it was revealed that health insurance company offered financial rewards to doctors to prescribe generic medicines [45].

Research by pharmaceutical companies is viewed with suspicion as they have vested interests in demonstrating poor treatment outcomes in patients who have been switched from their products. In addition, pharmaceutical companies run the risk of being seen as indulging in anti-competitive practices by the Office of Fair Trading and risk being subjected to large fines. For example, a Pfizer's study found that major cardiovascular adverse events were recorded with patients switching from atorvastatin to simvastatin compared with others who did not switch [12] and although a number of authors have questioned the results of this study claiming it has major limitations [18,46,47] no one has attempted to repeat the study and refute the findings.

The results of this study suggest that patient decisions about and acceptance of generic substitution are likely to be multi-faceted. A number of factors such as patients' education, knowledge, severity of the disease, efficacy of the generic medicines and patients' involvement in decisions regarding their health appear to drive patients' attitudes towards generic medicines and substitution. A lack of transparency around generic medicines and substitution was clearly marked in the result of this survey. Many patients, with or without experience in generic substitution, were sceptical about generic medicines. This could be related to the prejudice that inexpensive drugs must be inferior quality. Therefore, generic substitution necessitates patient education and additional time to provide more information and reassurance.

Main limitations of the study

Limitations of this study include that the view of generic substitution was mainly assessed from the renal patients' point of view and not that of healthcare professionals. We are not sure if the healthcare professionals were already giving the necessary information about generic medicines and substitution. Another limitation is that this study was conducted to evaluate the attitudes of a specific group of patients (renal transplant recipients) who should be well informed about their medications and may be particularly affected by generic substitution; therefore, generalizing the results to a wider patient population as whole is not appropriate. A similar study is required to evaluate the healthcare professionals' and the general patient population views towards generic medicines and substitution.

Authorship

MA: designed the study, analysed the data and wrote the paper. CW: collected data and revised the paper. AT: designed the study and revised the paper. MY: revised the

paper. AJ: designed the study, analysed the data and revised the paper.

Funding

This survey was funded by the William Harvey Research Institute at Queen Mary University of London and Mubarak Al Ameri was supported by the government of the United Arab Emirates, Abu Dhabi. The authors have no financial or proprietary interest in the subject matter or material discussed.

Acknowledgements

Authors would like to acknowledge the collaboration and commitment of all the medical staff and receptionists in Barts and The London Renal Transplant Clinic, in the UK, without whom the present study would not have been possible. We also thank all participating patients.

References

1. Bloor K, Freemantle N. Lessons from international experience in controlling pharmaceutical expenditure. II: influencing doctors. *BMJ* 1996; **312**: 1525.
2. Department of Health (DH). Consultation on the proposals to implement 'Generic Substitution' in primary care, 2010. Available at: http://tinyurl.com/2f2wlrt (cited January 26, 2010).
3. Haas JS. Potential savings from substitution generic drugs for brand drugs: Medical Expenditures Panel Survey 1997–2000. *Ann Intern Med* 2005; **142**: 891.
4. Tilson L, Bennett K, Barry M. The potential impact of implementing a system of generic substitution on the community drug schemes in Ireland. *Eur J Health Econ* 2005; **6**: 267.
5. Andersson K, Sonesson C, Petzold M, Carlsten A, Lonnroth K. What are the obstacles to generic substitution?. An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden *Pharmacoepidemiol Drug Saf* 2005; **14**: 341.
6. Sagardui-Villamor JK, Lacalle Rodriguez-Labajo M, Casado-Buendia S. Substitution of generic for brand medicines in primary care. Factors associated to refuse the change. *Aten Primaria* 2005; **9**: 489.
7. Igoe G. Generic utilisation on the general medical services scheme in 2001. *Ir Med J* 2003; **96**: 315.
8. Kjoenniksen I, Lindbaek M, Granas AG. Patients' attitudes towards and experiences of generic drug substitution in Norway. *Pharm World Sci* 2006; **28**: 284.
9. Department of Health (DH) Press Release. No plans to implement generic substitution of medicines, 2010. Available at: http://tinyurl.com/4qpuvwx (cited March 2, 2011).
10. Suh DC. Trends of generic substitution in community pharmacies. *Pharm World Sci* 1999; **21**: 260.
11. Kereiakes DJ, Willerson JT. Therapeutic substitution: guilty until proven innocent. *Circulation* 2003; **108**: 2611.
12. Phillips B, Roberts C, Rudolph AE, Morant S, Aziz F, O'Regan CP. Switching statins: the impact on patient outcomes. *Br J Cardiol* 2007; **14**: 280.
13. Snow V, Weiss KB, Mottur-Pilson C. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. *Ann Intern Med* 2003; **138**: 587.
14. Himmel W, Simmenroth-Nayda A, Niebling W, *et al.* What do primary care patients think about generic drugs. *Int J Clin Pharmacol Ther* 2005; **43**: 472.
15. Pocock SJ. The pros and cons of noninferiority trials. *Fundam Clin Pharmacol* 2003; **17**: 483.
16. Garattini S, Bertele V. Non-inferiority trials are unethical because they disregard patients' interests. *Lancet* 2007; **370**: 1875.
17. Alameri M, Epstein M, Johnston A. Generic and therapeutic substitutions: are they always ethical in their own terms? *Pharm World Sci* 2010; **32**: 691.
18. Duerden MG, Hughes DA. Generic and therapeutic substitutions in the UK: are they a good thing? *Br J Clin Pharmacol* 2010; **70**: 335.
19. McGettigan P, McManus J, O'Shea B, Chan R, Feely J. Low rate of generic prescribing in the Republic of Ireland compared to England and Northern Ireland: prescribers' concerns. *Ir Med J* 1997; **90**: 146.
20. National Health Service. Prescriptions dispensed in the community statistics for 1996 to 2006: England The NHS Information Centre, 2006. Available at: http://tinyurl.com/d8yux2 (cited June 11, 2009).
21. Dombrowski C. U.K. drug pricing scheme to allow generic substitution, promote innovation, 2008. Available at: http://tinyurl.com/359hqal (cited June 17, 2009).
22. Duh MS, Paradis PE, Latremouille-Viau D, *et al.* The risks and costs of multiple-generic substitution of topiramate. *Neurology* 2009; **72**: 2122.
23. Meredith P. Bioequivalence and other unresolved issues in generic drug substitution. *Clin Ther* 2003; **25**: 2875.
24. Johnston A. Challenges of therapeutic substitution of drugs for economic reasons: focus on CVD prevention. *Curr Med Res Opin* 2010; **26**: 871.
25. Dowell JS, Snadden D, Dunbar JA. Changing to generic formulary: how one fundholding practice reduced prescribing costs. *BMJ* 1995; **310**: 505.
26. Melchior J. Therapeutic drug substitution raises consumer concerns. Health Care News, 2009. Available at: http://tinyurl.com/6btfbaa (cited March 27, 2011).
27. Decollogny A, Eggli Y, Halfon P, Lufkin TM. Determinants of generic drug substitution in Switzerland. *BMC Health Serv Res* 2011; **11**: 17.
28. Gossell-Williams M. Generic substitutions: a 2005 survey of the acceptance and perceptions of physicians in Jamaica. *West Indian Med J* 2007; **56**: 458.

29. Berg MJ, Gross RA, Haskins LS, Zingaro WM, Tomaszewski KJ. Generic substitution in the treatment of epilepsy: patient and physician perceptions. *Epilepsy Behav* 2008; **13**: 693.
30. Meredith PA. Generic drugs: therapeutic equivalence. *Drug Saf* 1996; **15**: 233.
31. Helderman JH, Kang N, Legorreta AP, Chen JY. Healthcare costs in renal transplant recipients using branded versus generic ciclosporin. *Appl Health Econ Health Policy* 2010; **8**: 61.
32. Kingma I, Ludwin D, Dandavino R, *et al.* Economic analysis of Neoral in de novo renal transplant patients in Canada. *Clin Transplant* 1997; **11**: 42.
33. Signorovitch J, Zhang J, Wu EQ, *et al.* Economic impact of switching from valsartan to other angiotensin receptor blockers in patients with hypertension. *Curr Med Res Opin* 2010; **26**: 849.
34. Colaizzi JL, Lowenthal DT. Critical therapeutic categories: a contraindication to generic substitution? *Clin Ther* 1986; **8**: 370.
35. Berg MJ, Gross RA, Tomaszewski KJ, Zingaro WM, Haskins LS. Generic substitution in the treatment of epilepsy: case evidence of breakthrough seizures. *Neurology* 2008; **71**: 525.
36. Richton-Hewett S, Foster E, Apstein CS. Medical and economic consequences of a blinded oral anticoagulant brand change at a municipal hospital. *Arch Intern Med* 1988; **148**: 806.
37. Hellstrom J, Rudholm N. Side effects of generic competition? *Eur J Health Econ* 2004; **5**: 203.
38. Kovarik JM, Noe A, Wang Y, Mueller I, DeNucci G, Schmouder RL. Differentiation of innovator versus generic cyclosporine via a drug interaction on sirolimus. *Eur J Clin Pharmacol* 2006; **62**: 361.
39. Qazi YA, Forrest A, Tornatore K, Venuto RC. The clinical impact of 1:1 conversion from Neoral to a generic cyclosporine (Gengraf) in renal transplant recipients with stable graft function. *Clin Transplant* 2006; **20**: 313.
40. Roza A, Tomlanovich S, Merion R, *et al.* Conversion of stable renal allograft recipients to a bioequivalent cyclosporine formulation. *Transplantation* 2002; **74**: 1013.
41. Hibberd AD, Trevillian PR, Roger SD, *et al.* Assessment of the bioequivalence of a generic cyclosporine A by a randomized controlled trial in stable renal recipients. *Transplantation* 2006; **81**: 711.
42. Taber DJ, Baillie GM, Ashcraft EE, *et al.* Does bioequivalence between modified cyclosporine formulations translate into equal outcomes? *Transplantation* 2005; **80**: 1633.
43. Food and Drug Administration (FDA). Approved drug products with therapeutic equivalence evaluations, 2009. Available at: http://tinyurl.com/y92ahby (cited February 1, 2010).
44. Gottlieb S One in three doctors don't tell patients about services they can't have. *BMJ* 2003; **327**: 123. Available at: http://tinyurl.com/6j2t2mo (cited February 3, 2011).
45. Sheldon T. Dutch insurance company will pay doctors to prescribe cheap drugs. *BMJ* 2006; **332**: 254. Available at: http://tinyurl.com/6knx7aq (cited March 27, 2011).
46. Goldsmith D, Duerden M. Statins: to switch or not to switch? *Prescriber* 2008; **19**: 35.
47. Moon JC, Bogle RG. Switching statins. *BMJ* 2006; **332**: 1344.