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A study of the relationship between improved patient knowledge and compliance with antibiotic use

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A study on the relationship between improved patient knowledge and compliance with antibiotic use

A research report submitted by

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In partial fulfilment of the requirements for the degree

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MSc(Med) Pharmacotherapy

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Declaration

I, Cathatina Colette Beukes, hereby declare that "A study on the relationship between improved patient knowledge and compliance with antibiotic use" and the research results on which the research report is based, is original, except where acknowledgements indicate otherwise.

The research report is submitted for the degree Masters of Science Medical in Pharmacotherapy at the University of the Witwatersrand.

No part of this research report has been submitted for any other degree or examination, at this or any other tertiary institution.

Signed:_____ Date:_____

Acknowledgements

- I thank God Almighty for giving me the strength and opportunity to complete this course, and for opening the doors to a bright future.

- I am grateful for the guidance and insight given by my supervisor, Prof Andries Gous, throughout the course of this study.

- To my husband, Hugo, thank you for the support and patience during my post-graduate studies.

Abstract

Background: Antibiotic resistance is fast becoming a major health challenge. Patients need to be educated on the origin of this medical crisis and need to change their attitude toward antibiotic use. Health professionals need to help patients improve antibiotic compliance and identify problem areas.

Objectives: The aim of this study was to determine whether a better understanding of resistance formation and patient education on responsible use of antibiotics will improve patient compliance towards antibiotic use. To achieve the aim of the study we determined the patient's compliance on antibiotic use by the self-pill count feedback method. We further determined whether the provision of more antibiotic information to the patient correlated to better compliance and other reasons for non-compliance were also recorded. We also compared the findings of the study with findings from other similar antibiotic compliance studies.

Methodology: The study was conducted at a private hospital in Gauteng. Patients receiving antibiotic prescriptions were divided into two groups. Group A received a leaflet with their antibiotic prescription with information on how to use antibiotics responsibly. Group B did not receive any additional information on antibiotic use. Both these groups were contacted via e-mail and asked to complete a survey to test their knowledge and attitude towards antibiotics.

Results: A total of 79 patients participated in the study. Group A with 39 participants and Group B with 40 participants completed the questionnaire and reported on their antibiotic usage and knowledge.

Group Aa, who was provided additional information on antibiotic use and read through the brochure, showed a better compliance to the antibiotic regimen prescribed. When compared to Group Ab, who received additional information on antibiotic use and did not read through the brochure, and Group B, who received no additional information on antibiotic use, a much higher percentage of Group Aa was able to give valid reasons as to why one should complete an antibiotic course. 78% of Group Aa intended to change their future behaviour with regards

to left-over antibiotics. These patients are committed to being completely compliant in future. This group showed a 100% change in attitude when it comes to pressurizing medical practitioners into prescribing antibiotics for minor illness, colds and flu.

The majority of Group Aa admitted to learning something by reading the leaflet handed to them and also showed most interest in wanting more antibiotic information from their pharmacist in future. Participants gave various reasons for not being compliant. Most patients stopped taking their antibiotics as soon as they felt better.

Participants from Group Aa showed most willingness to learn more about antibiotic use with females and children making out the largest portion of the group. Male participants tended to be less eager to learn more about responsible antibiotic use.

The child group that received leaflets with their medication had a 28.21% response rate and the group without leaflets had a 28.57% response rate. There is therefore no significant difference between the two groups.

Conclusion: The main objective of the study was to determine whether a better understanding to antibiotic resistance will lead to better compliance. The hypothesis $\mathbf{H = M_a > M_b}$, where M_a represents Group A and M_b represents Group B of the study, proved to be true. Participants from Group A showed a better understanding of the formation of antibiotic resistance. This group intended to change their negative behaviour and showed a higher compliance rate than Group B.

List of tables

Table page

Table 4.1 Participant demographics 33

Table 4.2 Antibiotic compliance distribution 34

Table 4.3 Antibiotic compliance related to prescribed course periods 35

Table 4.4 Participants who do not put pressure on doctors to prescribe antibiotics in viral infections 46

Table 4.5 Participants changes to future antibiotic use 48

Table 4.6 Lessons learned by Group Aa. 49

Table 4.7 Participants' willingness to learn more about responsible antibiotic use 50

List of figures

Figure

Figure 4.1 Participant response rate 27

Figure 4.2 Gender distribution among patients 29

Figure 4.3 Patient age distribution 30

Figure 4.4 The percentage of responding patients per age group and gender who received the antibiotic leaflet. 31

Figure 4.5 The percentage of responding patients per age group and gender who did not receive the antibiotic leaflet 32

Figure 4.6 Demographic overview of participants 34

Figure 4.7 Reported reasons for patient non-compliance 37

Figure 4.8 Participant knowledge regarding antibiotic resistance 39

Figure 4.9 Reported reasons for completing antibiotic courses 40

Figure 4.10 Participants kept left-over antibiotics for future use 42

Figure 4.11 Participants threw away left-over antibiotics 43

Figure 4.12 Participants gave left-over antibiotics to someone in need of antibiotics 44

Figure 4.13 Participants always complete an antibiotic course 45

Figure 4.14 Pressure from participants to get antibiotics prescriptions for viral infections 47

Figure 4.15 Overview on participants' willingness to learn more about responsible antibiotic use 51

Figure 4.16 Proportion of participating child participants compared to non-responders 52

List of appendices

Appendix A: Patient cover letter and electronic survey 62

Appendix B: Leaflet on responsible antibiotic use: Antibiotics: Use them wisely 65

Appendix C: Ethics Committee Letter of approval 67

Appendix D: Hospital Pharmacy Letter of approval 68

Table of Contents

Declaration ii

Acknowledgements iii

Abstract iv

List of tables vi

List of figures vi

List of appendices vii

Chapter 1: Introduction 1

1.1 Background 1
1.2 Statement of the problem 3
1.3 Antibiotic resistance 3
1.4 Antibiotic non-compliance and reasons for non-compliance 4
1.5 Patient education 5
1.6 Combating antibiotic resistance 6
1.7 Aim of the study 7
1.8 Objectives of the study 8

Chapter 2: Literature review 9

2.1 Patient related factors and non-compliance 9
2.1 Past studies on antibiotic non-compliance 10
2.1 Past studies on patient attitudes to antibiotics 15
2.1 Role of the Pharmacist 18
2.1 Patient Education 19

Chapter 3: Methodology 21

3.1 Study design 21
3.2 Study setting 21
3.3 Study method 21
3.4 Study population 22
3.5 Research hypothesis 24
3.6 Data collection methods 24
3.7 Data analysis 26
3.8 Ethical considerations 26

Chapter 4: Results and discussion 27

4.1 Patient population 27

4.2 Survey responses 34
4.2.1 Participant antibiotic compliance 34
4.2.2 Participant knowledge on antibiotic resistance 39
4.2.3 Participant attitude toward antibiotics 41
4.2.3.1 Left-over antibiotics 41
4.2.3.2 Pressuring doctors for antibiotic prescriptions 46

4.2.3.3 Participants' willingness to change their attitude towards antibiotic use 47

4.2.3.4 Participant willingness to learn more about responsible antibiotic use 50

4.3 Child prescription responses 52

Chapter 5: Recommendations 53

Chapter 6: Limitations 56

Chapter 7: Conclusion 57

References 59

Chapter 1: Introduction and statement of the problem

1.1 Background

Stokowski (2010) wrote that the word "antibiotic" has always been a symbol of the miracles of modern medicine. Perhaps a bit ordinary these days compared with robotic surgery or capsule endoscopy, but in a different time, antibiotics literally changed the world. It began in 1928 when bacteriologist Alexander Fleming serendipitously realized that the growth of *Streptococcus aureus* was inhibited in a petri dish contaminated by mould. Within a few years we had sulfa drugs; rapidly followed by more effective beta-lactams, chloramphenicol, tetracycline, and by 1950, the aminoglycosides.

In the past 70 years, antibiotics have been critical in the fight against infectious disease caused by bacteria and other microbes. However, disease-causing microbes that have become resistant to antibiotic drug therapy are an increasing public health problem. Wound infections, gonorrhea, tuberculosis, pneumonia, septicemia and childhood infections are but a few of the diseases that have become hard to treat with antibiotics. One part of the problem is that bacteria and other microbes that cause infections are remarkably resilient and have developed several ways to resist antibiotics and other antimicrobial drugs. Another part of the problem is due to increasing use, and misuse, of existing antibiotics in human and veterinary medicine and in agriculture. The problem of antimicrobial resistance stems primarily from antibiotic usage (Todar 2004).

Hippocrates described the importance of patient compliance over 2000 years ago. Hippocrates advised a physician, "…to be alert to the faults of the patient which make them lie about their taking of the medicines prescribed and when things go wrong, refuse to confess that they have not been taking their medicines" (Murphy 2007).

Patient may follow prescription orders in different ways. Some will follow instructions to the letter, some patients will follow some of the instructions for some time and others will not follow any instruction.

Compliance or the lack thereof affects us all. One of the most understated problems in the delivery of health services is patient non-compliance, its occurrence and impact on the health services and its associated outcomes if allowed to continue without intervention (Fincham 2007).

Compliance and adherence relate to the medicine-taking behaviour of the patient. This can be estimated using prescription claims records, pharmacy dispensing data, validated survey instruments or electronic pill counters, as well as direct measures such as serum concentration levels of medication taken by the patient (Bell *et al* 2007).

Despite doctors' expectations, non-compliance is common in short-term antibiotic therapy of respiratory tract infections. This phenomenon has profound practical implications. It leads to ineffective management, the deterioration of patients' health, hospital admissions, additional costs and the emergence of antibiotic-resistant micro-organisms (Kardas 2002).

Non-compliance is defined as any deviation by a patient from a doctor's instructions. Non-compliance with medications is particularly important in clinical practice. This form of non-compliance has been found to be associated with treatment failure and all its consequences, namely: deterioration of patients' health, the need for additional consultations, the use of extra drugs, additional hospital admissions as well as an increase in direct and indirect costs of the management of the treated condition (Kardas 2002).

In the case of antibiotic therapy, the right choice of medication, taking into account the pathogen's susceptibilities and appropriate dosage are especially important. The misuse of antibiotics for viral infections and the excessive use of broad spectrum antibiotics in place of narrower spectrum antibiotics have been well-documented throughout the world (Kardas 2002).

1.2 Statement of the problem

Working in a pharmacy one often find that patients recognise antibiotics being dispensed to them, stating that they do not need a whole course as they still have some at home from a previous prescription filling. At times patients would call the pharmacy, having gone through the medicine-cabinet, wanting to know what conditions they can use left-over antibiotics for.

In these conversations one has come to realise that patients do not have an understanding of why they need to finish antibiotic courses and how antibiotic resistance develops.

The problem of antibiotic resistance is related to antibiotic misuse, for instance antibiotic use in the case of viral infections. It also stems from antibiotic overuse due to patients pressuring medical practitioners for antibiotic prescriptions in minor infections as well as medical practitioners prescribing ineffective antibiotics and ineffective doses of antibiotics.

It is evident that patients need to be educated on responsible antibiotic use. We are facing a huge health problem when it comes to antibiotic use and resistance development. I believe that we can make a difference in the use of antibiotics by educating patients on the use of antibiotics and antibiotic resistance.

1.3 Antibiotic resistance

Sir Alexander Flemming said "The greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and from them to other until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save." (Noreddin n.d). This was already the beginning of antibiotic resistance formation.

Antibiotics are responsible for huge advances in medicine, however, their use selects for resistant bacteria and once selected, these bacteria can transfer their resistant genes to new generations, resulting in reduced future efficacy and decreased sensitivity of antibiotics. There are currently resistant strains of nearly all bacteria (Jackson *et al*. 2006).

The emergence of antibiotic resistance is an evolutionary process that is based on selection for organisms that have enhanced ability to survive doses of antibiotics that would have previously been lethal (Cowen 2008). Antibiotics like penicillin and erythromycin, which used to be one-time miracle cures are now less effective because bacteria have become more resistant (Pearson 2007). Antibiotics themselves act as a selective pressure that allows the growth of resistant bacteria within a population and inhibits susceptible bacteria (Levy 1994).

An alarming increase in resistance of bacteria that cause community acquired infections has been documented. In a recent study, 25% of bacterial pneumonia cases were shown to be resistant to penicillin, and an additional 25% of cases were resistant to more than one antibiotic (Todar 2004).

Resolving or lowering the incidence of the problem of antibiotic resistance is considered to be an international public health challenge (Jacson *et al*. 2006). Inappropriate prescribing of antibiotics and non-compliance to antibiotic prescription regimens are the most important human attributes to antibiotic resistance formation.

Inappropriate prescribing of antibiotics has been attributed to a number of causes including: patients who insist on antibiotics, physicians who prescribe antibiotics as they feel they do not have time to explain why they are not necessary and medical practitioners who do not know in which case to prescribe antibiotics or else are overly cautious for medical legal reasons (Arnold & Straus 2005).

A third of people for example believe that antibiotics are effective for the common cold and 22% of people do not finish a course of antibiotics primarily due to that fact that they feel better (varying from 10% to 44% depending on the country) (Todar 2004).

1.4 Antibiotic non-compliance and reasons for non-compliance

Studies in the United States of America (USA) have shown that patient adherence to a prescribed antibiotic regimen is as little as 50%. Non-adherence increase medical expenses and costs the USA as much as $100 billion annually (Brown & Goff 2005).

Patients take their prescribed antibiotic course only until they feel better, and then stop. They save the rest of their medication in case they or their family members have a similar illness in the future. Non-adherence to antibiotic regimens has an effect beyond each individual patient's therapeutic outcome. It has a very important effect on resistance patterns. A study has shown that poor adherence to the prescribed antibiotic regimen is also one of the major factors influencing treatment failure not relate$ to resistance (Brown & Goff 2005).

Compliance depends on many factors, and in different studies different values of compliance are obtained.

1.5 Patient Education

Concordance refers to the nature of the interaction between the clinician and the patient. A greater interaction between the healthcare practitioner and the patient ensures a better understanding of why compliance to the treatment-plan in important (Bell *et al.* 2007).

In 1999 the Department of Health in the United Kingdom launched a National Public Awareness Campaign on antibiotic resistance. The public information campaign aimed to support health professionals by reducing patients' expectations for an antibiotic prescription, by raising awareness and provide education about the problem of antibiotic resistance, to increase understanding about the appropriate use of antibiotics and to increase understanding about when antibiotics will be effective or necessary. The campaign was personalized by the creation of *Andybiotic*, a character symbolizing antibiotics in animated form, and expressing the words *'Don't wear me out'* to introduce the topic of sensible use of antibiotics. The campaign included posters in general practice surgeries and public places, and patient information leaflets given to patients instead of an antibiotic prescription (McNulty *et al.* 2007).

To inform ongoing publicity campaigns, to which The Specialist Advisory Committee on Antimicrobial Resistance (SACAR) was committed, in 2003 the Department of Health funded a large antibiotic survey of British households. The aims of the survey were to:

- Determine the publics' awareness of good antibiotic use and relate this to household characteristics.
- Identify respondent characteristics that explain variation in attitudes to antibiotics.
- Determine the impact of the *Andybiotic* campaigns.

1.6 Combating antibiotic resistance

The following are recommendations to combat the development of antibiotic resistance in bacteria and other micro-organisms (Todar 2004).

- Search for new antibiotics. To combat the occurrence of resistant bacteria, biotechnology and pharmaceutical companies must constantly research, develop and test new antimicrobials in order to maintain a pool of effective drugs on the market.

- Stop the use of antibiotics as growth-promoting substances in farm animals. Of major concern is the use of antibiotics as feed additives given to farm animals to promote animal growth and to prevent infections rather than cure infections. The use of such antibiotics contributes to the emergence of antibiotic-resistant bacteria that threaten human health and decreases the effectiveness of the same antibiotics used to combat human infections.

- Use the right antibiotic in an infectious situation as determined by antibiotic sensitivity testing, when possible.

- Stop unnecessary antibiotic prescriptions. Unnecessary antibiotic prescriptions have been identified as causes for an enhanced rate of resistance development. Unnecessary prescriptions of antibiotics are made when antibiotics are prescribed for viral infections (antibiotics have no effect on viruses). This gives the opportunity for indigenous bacteria (normal flora) to acquire resistance that can be passed on to pathogens.

- Finish antibiotic prescriptions. Unfinished antibiotic prescriptions may leave some bacteria alive or may expose them to sub-inhibitory concentrations of antibiotics for a prolonged period of time. *Mycobacterium tuberculosis* is a slow growing bacteria which infects the lung and causes tuberculosis. This disease kills more adults than any other infectious disease. Due to the slow growing nature of the infection, treatment programs last for months or even years. This has led to many cases on unfinished prescriptions and 5% of strains now observed are completely resistant to all known treatments and hence incurable.

- Large scale public health education efforts are underway to stress the importance of finishing prescriptions. Indeed, in many places, failure to finish tuberculosis prescriptions can result in jail time.

In the pharmaceutical industry, past and current strategies to combat resistance have not been effective. Pharmaceutical companies are seeking new, less costly strategies to develop antibiotics. Several countries such as the UK have regulations concerning the use of antibiotics in animal feed.

1.7 Aim of the study

The aim of this study was to determine whether a better understanding of resistance formation and patient education on responsible use of antibiotics will improve patient compliance towards antibiotic use.

1.8 Objectives of the study

To achieve the aim of the study we determined the patient's compliance on antibiotic use by the self-pill count feedback, determined whether the more antibiotic information to the patient correlated to better compliance and recorded any other reasons for non-compliance. We also compared the findings of the study with findings from other similar antibiotic compliance studies.

Chapter 2: Literature review

Medication non-compliance may occur at different points in a patient's decision-making process. It may take place at the start of therapy if a patient does not fill a prescription, or it may occur after therapy has started when the patient fails to follow the instructions.

Patients' compliance with medication is a prerequisite for effective drug therapy. Antibiotic non-compliance is a major public health problem that imposes a considerable financial burden on the health care system.

2.1 Patient related factors and non-compliance

Patient characteristics have been the focus of numerous investigations of compliance. Non-compliance can be of an initial, intentional or unintentional type or of premature discontinuation. Initial non-compliance rates of about 13 to 25 percent are reported where the prescription never reached the pharmacy for filling. The variations in patient compliance are a function of methodological and contextual factors in compliance research. It is important to research the enabling patient attributes, which is the first step to designing effective interventions (Fincham 2007).

Socioeconomic status has not consistently been found to be an independent predictor of compliance. Some factors that are reported significant are: poor socioeconomic status, poverty, illiteracy, low level of education, unemployment, lack of effective social support networks, unstable living conditions, distance from treatment centre, high cost of transportation, high cost of medication, changing environment situations as well as culture and lay beliefs about illness and treatment. Income specifically and not general socioeconomic status has a positive and significant effect on patient compliance (Fincham 2007).

Patient related factors affecting compliance are forgetfulness, psychosocial stress, misunderstanding and non-acceptance of the disease, disbelief in the diagnosis, lack of perception of the risks related to the disease, misunderstanding of the treatment instructions, lack of acceptance of monitoring, low treatment expectations, lack of self perceived need for treatment, lack of perceived effect of treatment, negative beliefs regarding the effect of treatment, anxieties about possible adverse effects, low motivation, inadequate knowledge of treatment, low attendance at counselling, frustration with health care providers, fear of dependence and over complexity of the regimen (Fincham 2007)

2.2 Past studies on antibiotic non-compliance

A large, country-wide German study recently assessed compliance rates among children treated with antibiotics for various infections. A urine test confirmed the presence of antibiotic in 69.5% patients (Kardas 2002).

Brown and Goff (2005) found that the length of the antibiotic course as well as the frequency of the dosage intervals influence adherence. It was also found that income, social class, occupation and educational background did not determine adherence. The classic scenario is that patients take their prescribed antibiotic course only until they feel better, and then stop.

A major factor influencing compliance is the frequency of doses. Numerous studies show that the less frequent the doses, the higher the compliance. A review of over 100 studies by Greenberg (1984) i.e. before the era of electronic measurement, confirmed this tendency. The average compliance was 73% for once daily dosing regimens, 70% for twice daily dosing, 52% for three times daily dosing and 42% for four times a day regimens. The difference between compliance with once daily and twice daily dosing regimens was not significant, but more frequent dosing was associated with significantly worse compliance rates (Kardas 2002).

A literature review performed recently took into account only the studies that used electronic devices for compliance measurement. The 76 publications available to date were analysed.

Compliance decreased with increased complexity of regimen and was 79% ± 14% for once daily dosing, 69% ± 15% for twice daily dosing, 65% ± 16% for three times daily dosing and 51% ± 20% for four times a day dosing. The difference in compliance between once daily and twice daily dosing was not statistically significant (Claxton *et al.* 2001).

The highest compliance during antibiotic therapy is also associated with once daily dosing; with more frequent dosing compliance decreases. However, compliance rates observed in antibiotic treatment of respiratory tract infections tends to be much better than those observed with other medications. In the case of a once daily antibiotic regimen, compliance reaches values approaching 100% (Kardas 2002).

More frequent dosing is generally associated with worse compliance in antibiotic therapy. When patients were randomly prescribed antibiotics with the dosage in the range 1–3 doses per day, increasing complexity of the regimen significantly decreased the probability that the patient would not miss any doses of the course. Based on the data collected for short-term antibiotic therapy, increasing the number of doses to be taken daily by one increased the probability of a patient being non-compliant by 72% (Cockburn *et al.* 1987).

Cook *et al.* (1996) showed that, for twice daily and three times daily Augmentin®, the compliance rate was 90% and 87%, respectively. During a 5-day treatment for respiratory tract infections, at least one dose was missed by 34% of patients in a twice daily regimen, and by 76.5% of patients taking the medication three times a day. Electronic measurement revealed that 70% of patients taking trimethoprim twice daily for respiratory tract infection therapy were fully compliant, compared with only 39% of patients taking cephalexin four times a day. When antibiotic suspensions for children were given twice daily, compliance was higher than with thrice daily regimens. Of the patients taking antibiotics four times a day for a 5-day therapy, none took all of the recommended doses.

More than 50% of interviewees in a Pan-European study (Branthwaite & Pechère 1996) admitted to pressuring their general practitioners to prescribe antibiotics believing that they should be prescribed for most respiratory tract infections. The majority of patients waited 2-3 days before consulting their doctor and over 80% of respondents expected symptoms to

improve after 3 days of treatment. This provided evidence for poor compliance, with most patients stopping after 3 days because they felt better.

Compliance depends also on the length of treatment. This general rule is confirmed in antibiotic therapy for respiratory tract infections. Better compliance was observed for regimens shorter than 7 days duration compared with longer ones. In a study assessing compliance during treatment with penicillin for streptococcal infections by tablet count, on the third day of treatment 44% of children were fully compliant, on the sixth day 29% and on the ninth day only 18%. In another study of children taking oral penicillin for ß-haemolytic streptococcal infection, 81% of patients were taking the antibiotic on the fifth day, but only 56% on the ninth day. Similar results were achieved by Schrag *et al.* (2001), who studied children aged 6–59 months treated for pneumococcal infection with amoxicillin 90 mg/kg/day for 5 days or with 40 mg/kg/day for 10 days. Compliance in this study was significantly better at 82% for the shorter therapy compared with the longer course with only 74% compliance. Among children receiving antibiotic for the longer period, compliance was significantly higher (79%) for days 0–5 compared with days 6–10 (57%).

There are other factors influencing compliance associated with the convenience of therapy. In a study that investigated the relationship between compliance and the form of medication in children aged between 2 months and 5 years, given for pneumonia, the results were as follows: by the fourth day, 82% of patients taking a syrup continued to take their antibiotics, compared with 71% and 55% of patients who took their medication in the form of sachets and tablets, respectively. Compliance had a strong link to the parents' impression of the ease or difficulty of administering the drug (Ellerbeck *et al.*1995).

Favre *et al.* (1997) found the most common mistake is the omission of single doses of antibiotics. Some patients take additional doses of antibiotics, especially at the beginning of the treatment. This may be associated with severity of the symptoms and the patients' desire to get better promptly. A premature halt in taking medication is also characteristic in antibiotic treatment. One reason behind it could be symptomatic relief occurring before the recommended treatment time elapsed, especially in cases of milder infections. Another reason could be the occurrence of adverse effects, which force patients to stop therapy. Large and difficult-to-swallow pills or the unpleasant flavour of a suspension may also lead to non-

compliance. Another type of mistake is caused by changes to the dosing regimen. Some patients decrease the frequency of their doses, for example twice a day instead of three times a day.

Some patients who are prescribed antibiotics do not file the prescription with a pharmacist. They believe that antibiotics may be harmful to the gastrointestinal tract or the immune system. These patients want to see whether the infection resolves without treatment, and so delay the start of the therapy. In the case of antibiotic treatment, as with other therapies, conscious omission of single doses of the medication takes place. The reasons frequently given by patients include fear of interactions with alcohol or other medications (Kardas 2002).

A major factor influencing compliance is the frequency of doses. Numerous studies show that the less frequent the doses, the higher the compliance. Compliance decreased with increased complexity of regimen. Compliance depends also on the length of treatment. Better compliance was observed for regimens shorter than 7 day duration compared to longer than 7 days. There are other factors influencing compliance associated with the convenience of therapy. Compliance was significantly associated with the parents' impression of the ease or difficulty of administering the drug (Kardas 2002).

In some studies the influence of other factors on compliance has been noticed. Compliance was higher if the infection was localized to the lower respiratory tract or the patients thought that they had a severe disease. It has also been observed that compliance depended on the length of time for which the general practitioner had been practising; patients treated by younger doctors being significantly more compliant. In another study, it was found that compliance in the case of children taking penicillin was higher if the GP had been looking after that family for no more than 4 years. On the other hand, non-compliance is associated with poor communication between doctor and patient. It was shown that compliance with antibiotic therapy improved if the patient thought that he knew the prescribing doctor well. In a study performed in Mexico, Reyes *et al.* (1997) showed that patients were more likely to be non-compliant if they did not know the name of the prescriber.

Mistakes involving the administration of antibiotics at times other than those recommended are common. Several studies showed that compliance in taking antibiotics was very high but complying with the correct dosing times was much lower (Kardas 2002).

Unlike Fincham (2007), numerous studies have shown that compliance did not depend on patients' age, gender, marital status, education, income or social class. Similar findings were discovered in the case of antibiotic therapy, where again compliance did not depend on patients' gender, marital status or education. Likewise, the degree of non-compliance during antibiotic therapy was not related to the cost of the medication to the patient or to whether or not the medication was free of charge (Kardas 2002).

Compliance depends on many factors, and in different studies different values of compliance are obtained.

Fincham (2007) found the following to be factors affecting compliance:

- Satisfaction with care: The more the care provided in a patient centred approach, the greater the patient satisfaction and likelihood of compliance.
- Communication: Communication must be seen as the key component for increasing compliance.
- Age: The age of patients have been shown to positively affect, negatively affect or have no affect on compliance. The majority of studies have shown no significant correlation between age and compliance.
- Gender: Gender has not been shown to be a reliable predictor of compliance.
- Cost: Compliance has been shown to be negatively affected by the high cost of medication.
- Knowledge of the disease: Knowledge on the causation, prognosis and cure possibilities of a particular disease have been shown to positively affect patient compliance.
- Income: Income has been directly related to patient compliance and could be linked to the cost of medication.

- Continuity of physician-patient relationship: The presence of a continuous physician-patient relationship has been shown to have a positive influence on patient compliance.
- Medication errors: Medication errors proved to have a negative effect on patients and their compliance

2.3 Past studies on patient attitudes to antibiotics

A study was carried out to determine patient perceptions of respiratory tract infections and attitudes to taking antibiotics, thus helping doctors to have a better understanding of their patients and their requirements. Telephone interviews were conducted in the United Kingdom, Belgium, France, Italy, Spain and Turkey using standardized questionnaires directed at patients who had taken an antibiotic or given one to their child for a respiratory tract infection within the previous 12 months. Pressure on general practitioners to prescribe antibiotics was highlighted by over 50% of interviewees' believing that they should be prescribed for most respiratory tract infections. Although interviewees were positive about antibiotics, with over 75% judging them to be effective and to speed recovery, some ambivalence was shown. Most patients waited 2-3 days before consulting their doctor to see if their symptoms would improve and over 80% of respondents expected symptoms to improve after 3 days' treatment. This provided a natural watershed for compliance, with most defaulters stopping after 3 days because they felt better. Second only to fewer side-effects, patients ranked shorter and more convenient dosage alongside efficacy as the improvements most sought in antibiotic therapy (Branthwaite & Pechère 1996).

A household survey in Britain in 2003 found that 79% of respondents were aware that 'antibiotic resistance is a problem in British hospitals', 38% of respondents did not know that antibiotics do not work against most coughs or colds and 43% did not know that 'antibiotics can kill the bacteria that normally live on the skin and in the gut'. Respondents with lower educational qualifications were less knowledgeable about antibiotics. During this study, in a multivariable analysis, better knowledge of antibiotics was not associated with being less likely to be prescribed any in the last year, but was independently associated with being more

likely to finish a course of antibiotic as prescribed. Being more knowledgeable on antibiotics was also associated with being more likely to take antibiotics without a doctor's instructions. In women, better knowledge was associated with being more likely to give an antibiotic to someone else that was not prescribed for them. The study has shown that there was no simple relationship between increased knowledge and more prudent antibiotic use (McNulty *et al.* 2007).

Patients who were prescribed antibiotics immediately for a sore throat stated that they were more likely to consult a health professional to request antibiotics the next time they developed a sore throat. Presumably patients believe that antibiotics aided their recovery, and therefore need to attend the surgery for antibiotics the next time they get the same condition. Clinicians report that they often prescribe antibiotics because they perceive that patients want antibiotics (Kardas 2002).

General practice consultation data indicate that young women have a higher consultation rate than other groups of patients. In a bid to reduce the patient expectation for antibiotics, in the autumn of 1999, the British Department of Health (DH) launched a National Public Awareness Campaign on antibiotic resistance targeted particularly at these young women and mothers. The public information campaign aimed to support health professionals by reducing expectations for an antibiotic prescription, by raising awareness about the problem of antibiotic resistance, to increase understanding about the appropriate use of antibiotics and, in particular, to increase understanding about when antibiotics will not do any good. An unpublished 1999 DH survey showed that immediately after the campaign there was more public awareness of antibiotic resistance and the public were less likely to expect to receive antibiotics from their GP. Therefore, the campaign was repeated in the spring of 2002 (McNulty *et al.* 2007).

In the McNulty *et al.* (2007) survey, respondents were asked whether they agreed or disagreed with 11 statements about antibiotic use, antibiotic resistance and activity. The respondents mostly knew that overuse of antibiotics increased resistance, and that antibiotic resistance is increasing. Only 8% of respondents did not agree with the statement that 'If taken too often antibiotics are less likely to work in the future', 16% did not agree that 'Bacteria are becoming resistant to antibiotics' and only 19% did not agree that 'antibiotic resistant bacteria

could infect me or my family'. Respondents also knew the principles of prudent antibiotic use, as only 3% did not agree with the statement 'A course of antibiotics should always be completed' and the same percentage did not agree that 'Antibiotics should not be taken unnecessarily' (McNulty *et al*. 2007).

Thirty-two percent of respondents incorrectly agreed that 'Antibiotics work on most coughs and colds' and 43% agreed with the statement that 'Antibiotics can kill viruses'. This indicates that there is a substantial group of the British public who believe that antibiotics will be of value when they have a cough or cold and are therefore still likely to request antibiotics from clinicians when they have these conditions. The survey also revealed a lack of understanding about the differences in activity of antibiotics against bacteria and viruses. In fact a fifth of respondents did not agree with the statement 'Antibiotics can kill bacteria'. In any future antibiotic educational campaigns, it will be important to explain the difference between viruses and bacteria, or discuss the need for antibiotics in relation to the severity of infection or syndrome, rather than the type of microbe responsible (McNulty *et al*. 2007).

Those less knowledgeable about antibiotics were typically less well educated. For each of the 11 statements, respondents with no formal qualifications were about twice more likely to respond incorrectly than respondents with a degree level of education. In an analysis, lower educational qualifications were the greatest determinant of lack of knowledge about antibiotics. Other subgroups less knowledgeable about antibiotics were the young (16–24 years) and the old (>75 years). The study results indicate that educational campaigns aimed at improving knowledge about antibiotics should be targeted at these less knowledgeable groups (McNulty *et al*. 2007).

The majority of respondents prescribed an antibiotic in the last year completed the course; however, 11.3% reported that they did not finish their last antibiotic course as prescribed. When asked why they did not finish the course, 65% reported that it was because they felt better or forgot to take them. Two per cent did not start the course at all, and the same percentage reported that the antibiotics did not work. 19% stopped them because of side effects. Interestingly, 87% of respondents who did not complete their last course also said that a course of antibiotic should always be completed. This suggests that most of those who did not complete their course did so knowing that they should have done (McNulty *et al*. 2007).

Almost 16% reported that they have kept an antibiotic in the past; 31% in case they needed them again and 8% in case the same infection recurred. Respondents who reported keeping left-over antibiotics tended to be younger (12% of 16–24 year olds kept left-over antibiotics from their last course, compared to 2% of all those over 55 years old

This reported behaviour about compliance with prescribed antibiotics concurred with the antibiotic audit, in which it was found that 4.3% of those prescribed an antibiotic in the last year had a residual antibiotic in the household which had been prescribed for them in the last year. Of the 6983 households, 19% had an antibiotic or antifungal. Of all antibiotics, almost half were not currently in use, 31% were reported by respondents to be left-over and 18% were kept for standby use. Almost half of left-over antibiotics had more than half of the original prescription remaining and 38% were prescribed more than 1 year earlier (McNulty *et al.* 2007).

Almost 5% of respondents reported that they had at some time in the past taken an antibiotic without advice from a doctor, nurse or dentist. Many of these antibiotics were taken for respiratory infections and 49% were taken for the same infection for which they were originally prescribed. Being more educated and being more knowledgeable about antibiotics were independently associated with keeping left-over antibiotics and taking antibiotics without advice (McNulty *et al.* 2007).

2.4 Role of the Pharmacist

Compliance can be a problem which may go undetected. It is a complex problem affected by various factors. Antibiotic compliance can be improved with the help of a pharmacist.

When non-compliance is recognized, the pharmacist is in a good position to offer support to the patient. The approach should be to attempt to remove obvious barriers to compliance. Compliance will most likely increase when a concordant approach is adopted. However, for the pharmacist to provide advice that is consistent with the treatment-plan of the physician, mechanisms will have to be developed for the sharing of information. Depending on the nature of the problem, counselling by the pharmacist may assist in improving compliance. At

other times input from the whole health-care team may be required to influence patient compliance (Winfield & Richards, 2004).

In the McNulty *et al.* (2007) survey it was found that to ensure maximum compliance, patients should receive adequate information on adverse effects and their influence on the treatment. Patients should be educated on antibiotic resistance, antibiotic spectrums as well as the length of treatment.

2.5 Patient Education

In 2003 the Department of Health (DH) survey, respondents were shown the Andybiotic Campaign patient information leaflet from a survey done in 1999 and asked if they had seen the leaflet or seen or heard anything about the Andybiotic Campaign. Penetration of this campaign was poor, as only a fifth of English respondents and only 25% of respondents who had been prescribed an antibiotic in the past year, had seen or heard of the campaign. This is disappointing as the campaign was concentrated in General Practitioner surgeries. The 1999 campaign was accompanied by DH public statements and advertising, but the later campaigns were lower key and restricted by financial constraints. Experience with social marketing for other health issues such as alcohol and driving shows that campaigns must be sustained over several years and include television slots to have a prolonged impact (McNulty *et al.* 2007).

Although a third of the public still believe that antibiotics work against coughs and colds, simply getting the public to believe otherwise may not be enough to reduce the level of prescribing. We have shown that those with a greater knowledge about antibiotics are no less likely to be prescribed an antibiotic. And in respect of how the public use the antibiotics they are prescribed, sometimes increased knowledge is associated with more prudent use or higher chances to self-medicate (McNulty *et al.* 2007).

Greater knowledge about antibiotics was associated with a greater tendency to keep left-over antibiotics and use them without advice from a clinician. Unnecessary use of left-over antibiotics may increase antibiotic resistance in the community's commensal flora by exerting

a selective pressure in the gut, skin and upper respiratory tract, favouring bacteria resistant to the antibiotics. This audit showed that 10% of households have access to left-over or standby antibiotics or anti-fungals. Perhaps, the easiest way to reduce the use of left-over antibiotics is to shorten the course of antibiotics prescribed to 3 or 5 days. A recent International survey showed that respondents living in countries that dispensed antibiotics in set pack sizes were more likely to have left-over antibiotics and use them without advice than respondents living in countries where antibiotic courses were dispensed according to the number of days stated by the clinician (Kardas *et al*. 2002).

Chapter 3: Methodology

3.1 Study design

The design of the study was retrospective and mainly quantitative. Some qualitative aspects were investigated with regards to reasons for non-compliance and the effect that the educational facet of the study had on the patient's view on antibiotic non-compliance.

3.2 Study setting

The study was conducted at a private hospital pharmacy in Pretoria, South Africa. The hospital is located in a wealthy, educated community. Although the pharmacy caters for the local community, patients from all walks of life and other areas visit the hospital.

Patients from foreign countries, mining towns and Workers Compensation dependants are discharged from the hospital with to take out (TTO) medication and consult doctors at their rooms at the hospital. All of these patients collect antibiotic prescriptions from the hospital pharmacy.

3.3 Study Method

Patients receiving antibiotic prescriptions from the study site were identified to form part of the research study. Two study groups were formed. Group A received their antibiotics with additional information on the responsible use of antibiotics and Group B only received their antibiotics and no additional information on antibiotic use. The additional information was handed to the patient in the form of an antibiotic information leaflet.

There were no costs involved in selecting these groups. As part of routine dispensing practice, proper patient counselling was provided to both groups. Patient counselling included information on the length of the antibiotic course and that the course should be completed. Pharmacist spent a moment to explain the necessity to read through the information leaflet handed to Group A.

Pharmacists then collected the patient's e-mail address as patients were sent a cover-letter with an e-mail survey. Electronic surveys have very little costs to consider and are a fast way to reach the patient and get the response.

3.4 Study population

Sampling method:

The selection of the two groups took place in the following manner:

Group A:

Every first and third week of the months of October 2009 to July 2010, excluding the month of December 2009, an information leaflet was handed out to various patients who received oral antibiotics at the pharmacy. The patient's attention was drawn to the content of the leaflet and the patient was asked to read the leaflet on their own time. The patient was then asked for an e-mail address. Copies of these prescriptions with the e-mail addresses were collected. Patients were contacted via e-mail a week after the antibiotics have been collected.

Group A were asked to participate in an electronic survey by completing a questionnaire concerning their antibiotic course and their knowledge on antibiotic use **(Annexure A and Annexure B)**.

Group B:

During every second and fourth week for the months of October 2009 to July 2010, excluding the month of December 2009, patients who received antibiotics from the pharmacy were asked for their e-mail addresses. No additional information leaflet regarding responsible antibiotic use was given to these patients. Copies of these prescriptions together with the e-mail addresses were also collected.

Group B were asked to participate in an e-mail survey by completing the questionnaire concerning their antibiotic course and knowledge on antibiotic use.

All patients who received oral antibiotics with an e-mail address yielded candidates for the survey.

Pharmacists handing out the information and collecting e-mail addresses were asked to do so without bias, including all patients from all possible backgrounds. Patients were not told about the study until they were contacted via e-mail to complete the questionnaire. This was so that patients' adherence could be measured against the influence of the educational leaflet that they have or have not received, and not the knowledge that they would be contacted in connection with their antibiotic course. Informing the patient beforehand about the possibility that they would be contacted might have influenced their antibiotic use.

All antibiotics prescribed as immediate doses were excluded.

Prescriptions for oral antibiotic courses were used for data collection. This excluded antibiotic treatment of Tuberculosis treatment and malaria prophylaxis.

Participants were contacted via e-mail and asked to partake in an electronic survey. The patients were assured of their confidentiality and purposes of the survey.

A cover letter was sent with the questionnaire survey. Participants gave consent on completing the questionnaire and resending the response to the researcher.

Parents or guardians responded to the survey on prescriptions for their children.

3.5 Research hypothesis

The research hypothesis states that patients who receive better education regarding responsible antibiotic use will be more compliant in the use of this medication group. Compliance to the prescribed antibiotic regimen was measured by means of patient's self-pill-count and completion of the antibiotic course.

$$\mathbf{H = M_a > M_b}$$

Where M_a represents Group A and M_b represents Group B of the study.

The groups (*n*) were selected without bias in both categories. A group of 274 patients were contacted of which 79 patients responded to the survey. This group of 79 participants was used for the study. This resulted in 39 participants representing group A and 40 participants representing Group B.

Patients' responses to the survey questions were compared first between the two groups and secondly compared to other studies.

3.6 Data collection methods

The electronic survey was sent to patients from whom an e-mail address had been collected.

The questions were formulated according to a model established during the literature study. The questionnaire comprised of dichotomous questions, multiple-choice questions and open-ended questions. Participants were expected to self-report on whether they have finished their antibiotic course or how much of the course was left-over. They were asked to report on their knowledge of antibiotics before and after they have read the information leaflet and the influence that will have on future antibiotic use. Participants also reported on possible reasons for non-compliance.

The questionnaire focused on the different levels of knowledge of antibiotics resistance development between the groups

All patient responses during the study period were entered into a data collection file. This file was constructed in Microsoft Office Word 2003. The file contained the following information:

- A unique subject number assigned to each patient who responded to the electronic survey.
- The patient prescription without patient details together with the participant's response was copied into the collection file under each assigned subject number.

The subject number was used to represent the patient in order to maintain patient confidentiality. Only the researcher had access to the patient's details.

The copy of the patient's prescription with the corresponding subject number was used to collect more of the patient's personal information. Hospital discharge prescriptions have patient details on, or the retail pharmacy system (UNISOLVE) contains such details. These systems were reviewed to determine patient gender and age.

The e-mail consisted of a cover letter and a questionnaire.

The cover letter explained that the response to the questionnaire would be used for research. The patient was assured of patient confidentiality and that consent to partake in the study would be given by responding to the electronic survey.

The questionnaire collected the following information:

- Whether the patient completed the antibiotic course.
- Whether the antibiotic course was completed in the prescribed time frame.
- Possible causes there might be for non-compliance.
- Whether the patient knows why he/she should complete an antibiotic course.
- What the patient do with left-over antibiotics.
- Patient views on common colds, flu and antibiotic use.

- Whether the patient received a brochure on antibiotic use and whether the patient read the brochure.
- What did the patient learn by reading the brochure?
- Would the patient prefer to receive more information on antibiotic use from their pharmacist?

A data sheet was designed in Microsoft Office Excel 2003, consolidating the information collected for each subject in the same format as the electronic survey. The data sheet contained data collected from Group A separate from Group B.

3.7 Data analysis

All collected data were analysed in a very simple form. The data were sorted into two groups, representing Group A and Group B. Responses for the two groups were compared.

Open-ended question responses that were similar were group together, to be compared to other responses.

3.8 Ethical considerations

An application for approval to conduct the study was submitted for review and was granted by the Human Research Ethics Committee at the University of the Witwatersrand **(Annexure C)**.

Approval from Pretoria East Hospital Pharmacy for collection of data were obtained **(Annexure D)**.

Consent was given by each participant for the information to be used in a research study, by responding to the electronic survey. They were informed that the data collected would be used for research and that their information would be kept confidential.

Chapter 4: Results and discussion

4.1 Patient population

A total of 274 patients were contacted in connection with the study via e-mail. All of these patients received antibiotics from the study site and provided the pharmacy with an e-mail address.

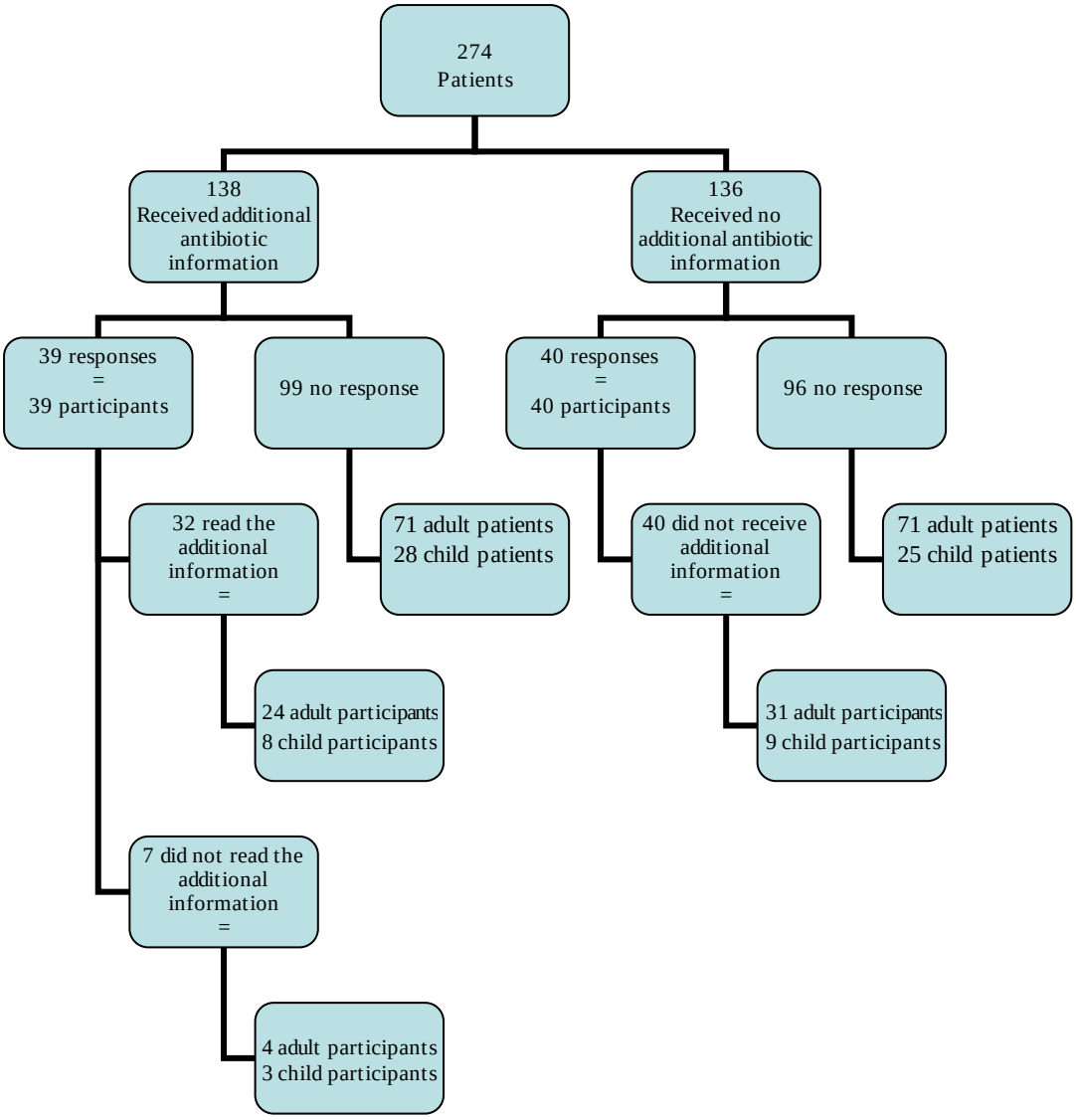

Figure 4.1: Participant response rate

Figure 4.1 shows the total amount of patients contacted during the study with a final 79 participants that made up the study population. The electronic survey study had a response rate of 28.83%.

In well-educated populations, response rates can vary from as low as 3% up to 90%. As a rule of thumb, the best response levels are achieved from highly-educated people and people with a particular interest in the subject. According to Sheehan (2001), e-mail response rates may only approximate 25% to 30% without a follow-up e-mail or reinforcements. In this study only 79 out of 273 patients responded to the electronic survey. The response rate of 28.83% correlates well with Sheehan's findings.

The main objective of this study was to determine whether a better understanding of resistance formation and patient education improved patient compliance in antibiotic use. Patient antibiotic compliance was investigated as well as reasons for non-compliance. Results from this study were compared to previous studies done globally.

Adult patients were divided into gender groups. More female patients were approached for the study. More female patients than male patients participated in the study by responding to the survey. A similarly higher percentage of female patients compared to male patients did also not respond to the survey.

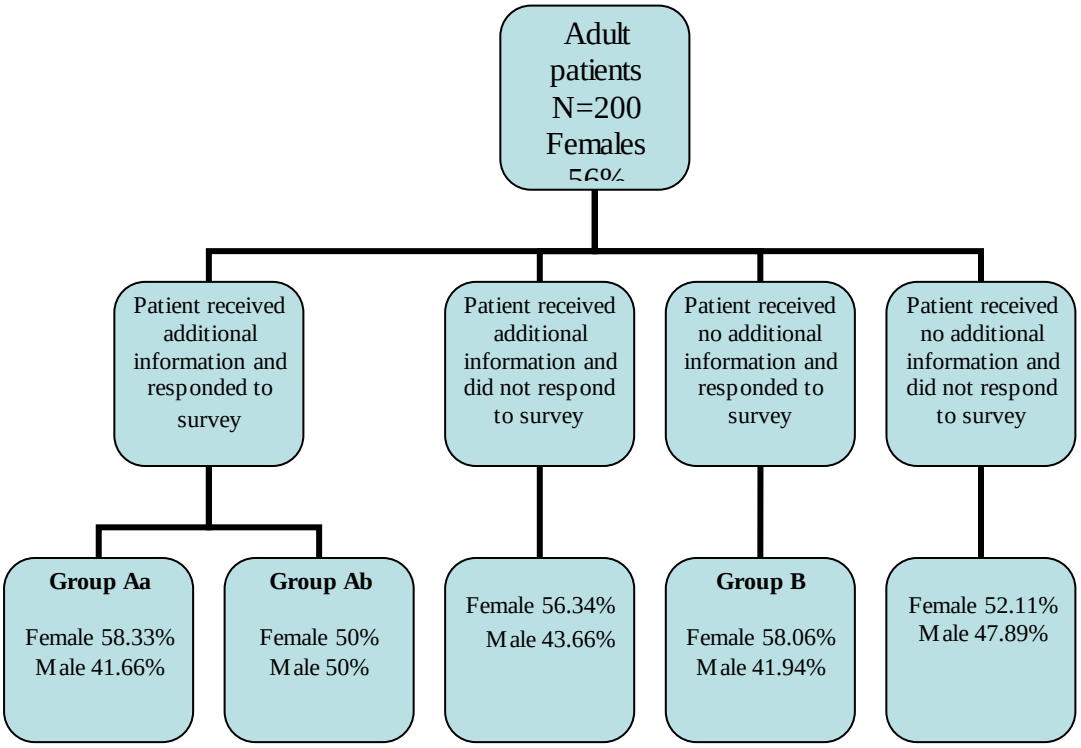

Figure 4.2: Gender distribution among adult patients

The group of 79 participants who responded to the survey consisted of 25 (31.64%) males, 34 (43.03%) females and 20 (25.32%) children. Group A, who received additional antibiotic information, was represented by 39 participants, making up 49.37% of the study population. Group B, who received no additional antibiotic information, had 40 participants with 50.63% of the study population.

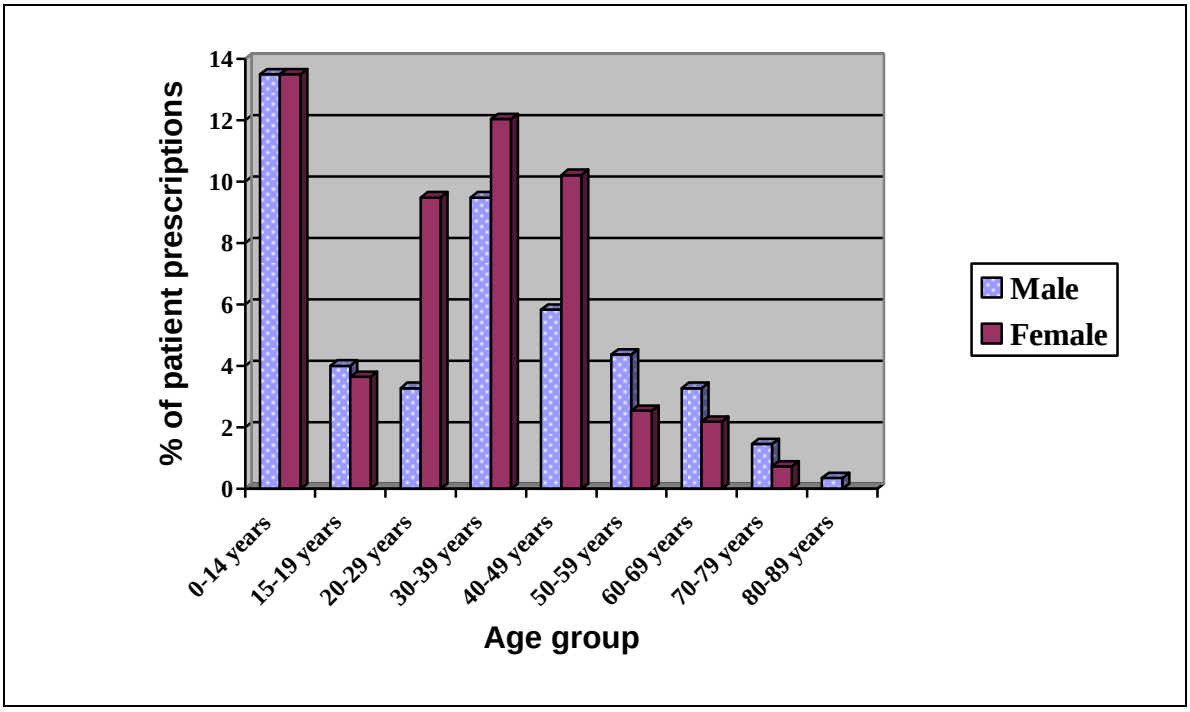

Figure 4.3 Patient age distribution

Considering all patients contacted in connection with the research study, 27% was represented by prescriptions for children (up to 14 years of age) and 73% by prescriptions for adults.

50.36% of the whole patient group consisted of patients aged between 20 and 59 years. The age group distribution is presented in Figure 4.3.

Patients who received an information leaflet and responded to the study formed Group A of the study group. Considering only adult prescriptions, in Group A only female patients between the ages 15 to 29 years responded to the survey. A higher percentage of females in the age group 50-59 years responded the survey than male patients in this age group. Male patients between the ages of 30 and 39 years yielded a higher response rate than female patients. Child prescriptions will be dwelt with at a later stage.

The patient response per age group and gender, who received the antibiotic leaflet, is demonstrated in Figure 4.4.

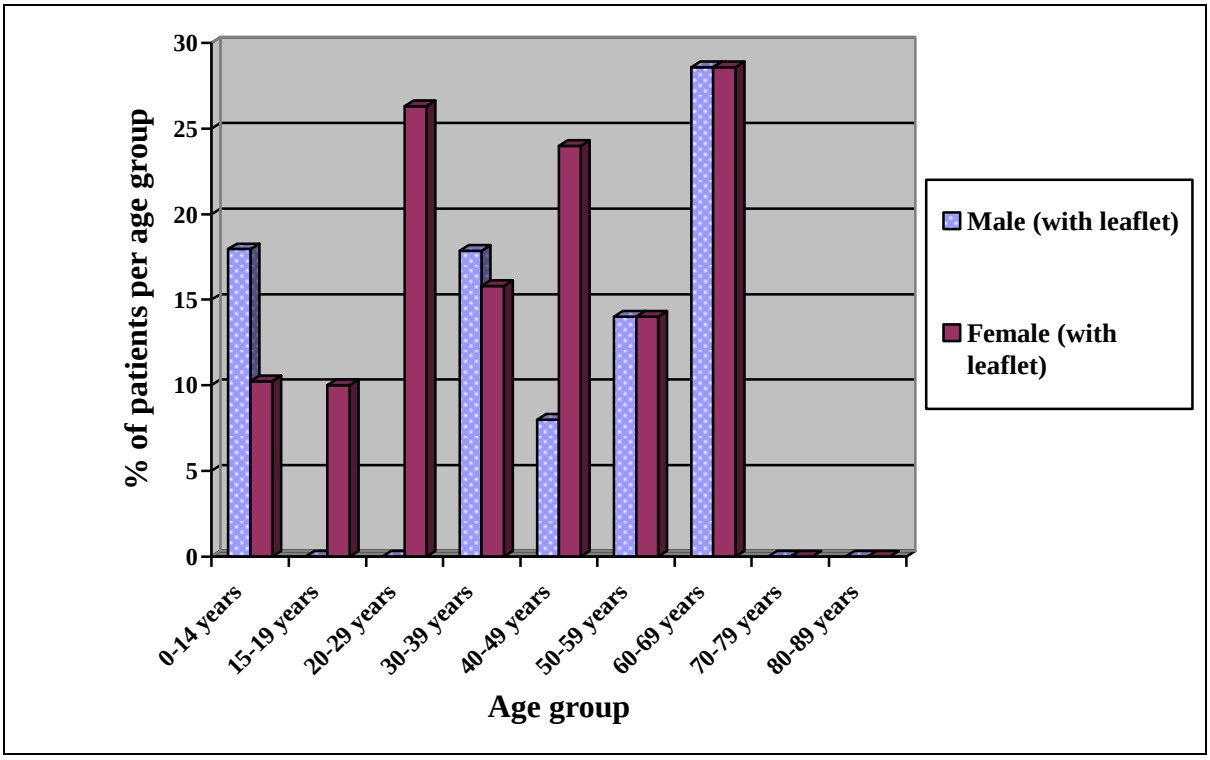

Figure 4.4 The percentage of responding patients per age group and gender who received the antibiotic leaflet. Group A: N = 39

The patient group who did not receive an antibiotic leaflet but responded to the survey formed Group B of the study group. A considerably higher percentage of male patients aged 15 to 19 years responded to the survey compared to Group A. Only female patients aged 20-29 years responded to the survey and formed part of the study group. Male as well as female patients aged 30-39 years responded well to the survey. Participants in the age group 40-49 years demonstrated a similar response to that of Group A with a higher male response between 50 and 59 years in Group B who did not receive any additional reading material concerning antibiotic use.

Figure 4.5 demonstrates the percentage of responding patients per age group and gender who did not receive the antibiotic leaflet.

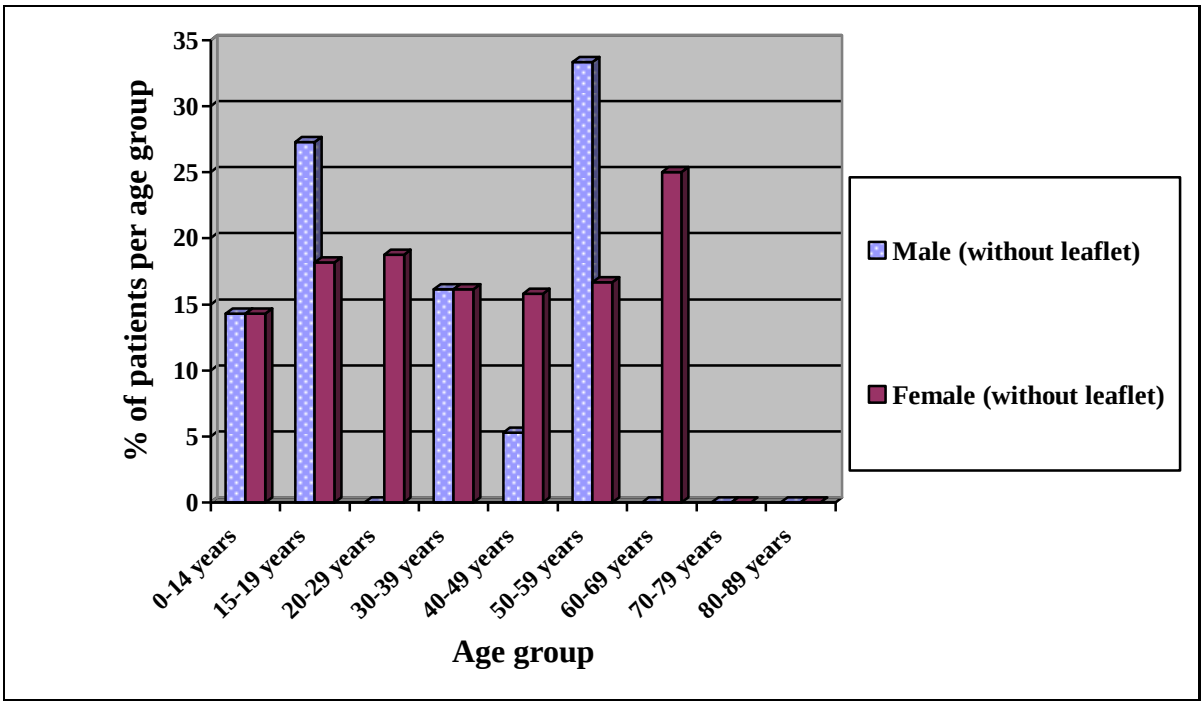

Figure 4.5 The percentage of responding patients per age group and gender who did not receive the antibiotic leaflet. Group B: N = 40

In general the female patients showed a higher response to the survey than male patients. No male patients between the ages of 20 to 29 years showed any interest in the study. More male participants aged 50 to 59 years responded to the electronic survey without having to read a leaflet.

Study group	**Group A** **49.37%**		**Group B** **50.63%**		
N = 79 participants	**39 received a leaflet**		**40 received no leaflet**	**Gender/ age**	**% per gender/ age group**
	Group Aa **82.05%**	**Group Ab** **17.95%**			
	32 read the leaflet	7 didn't read the leaflet			
	9 male	2 male	13 male	25 male	31.64%
	14 female	2 female	18 female	34 female	43.04%
	8 children	3 children	9 children	20 children	25.32%
100%	40.51%	8.86%	50.63%		100%

Table 4.1 Participant demographics

Table 4.1 shows the subdivisions and demographics of the study group. The study population was divided into Group A and Group B, where Group A received a leaflet containing information on responsible antibiotic use and Group B received no additional antibiotic information. Group A was further subdivided into a group that read the leaflet and a group that did not read the leaflet representing Group Aa and Group Ab respectively.

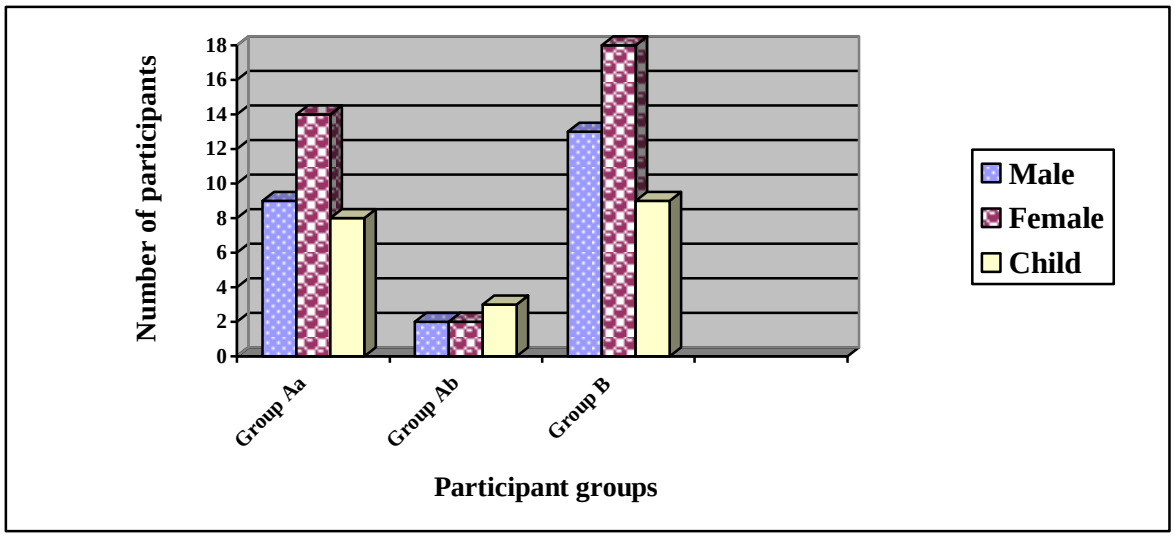

Figure 4.6 Demographic overview of participants

4.2 Survey responses

4.2.1 Participant antibiotic compliance

Question	Sample (N) 79	Yes	%	No	%	Group total
1. Have you finished your antibiotic course?	Group Aa	31	96.88%	1	3.12%	32 (100%)
	Group Ab	5	71.43%	2	28.57%	7 (100%)
	Group B	34	85%	6	15%	40 (100%)
	Total	70	88.61%	9	11.39%	79 (100%)

Table 4.2 Antibiotic compliance distribution

One can consider Group Ab and Group B together as neither read the leaflet containing information on why antibiotic compliance is important. This new group represented 90.91% of the non-compliant patients.

The one patient in Group Aa that was non-compliant admitted to knowing that one should complete an antibiotic course in another part of the survey. The non-compliant group consisted of eight adults and one child with 88.88% represented by adults and 11.11% by children.

Question	**Sample (N) 79**	**Yes**	**%**	**No**	**%**	**Group total**
2. Did you complete the antibiotics in the prescribed time?	Group Aa	30	93.75%	2	6.25%	32 (100%)
	Group Ab	5	71.43%	2	28.87%	7 (100%)
	Group B	33	82.50%	7	17.50%	40 (100%)
	Total	68	86.08%	11	13.92%	79 (100%)

Table 4.3 Antibiotic compliance related to prescribed course periods

All non-compliant participants included participants who did not complete their antibiotic courses at all. Considering Group Ab and Group B together, as neither of these groups read the additional information nor received the information, they represent 81.81% of the non-compliant population. Eleven participants (10 adult and one paediatric prescription) were not compliant. The adult non-compliant group consisted of 70 % female participants and 30% male participants.

Although there is much controversy in the literature regarding gender and compliance, some studies reported that gender was no significant predictor of compliance (Kane & Shaya, 2007). In this study gender groups responded differently depending on the age group.

On a self -pill-count, 86.08% of all the participants reported that they have been compliant to the antibiotic prescription and 13.92% admitted that they were non-compliant.

Participants from Group Ab and Group B accounted for 90.91% of the non-compliant participant group with ten participants from these two groups not completing their courses and only one participant from group Aa. There has been a significant difference between the participants who read the additional antibiotic information and the groups who did not.

The same results were evident with an investigation into the antibiotic compliance when considering the time period of the antibiotic prescription where patients had to complete an antibiotic course within a specific period of time.

In a 1999 United Kingdom survey, 38% of respondents did not know that antibiotics do not work against most coughs or colds, 11.3% reported that they did not finish their last antibiotic course as prescribed. When asked why they did not finish the course, 65% reported that it was because they felt better or forgot to take them. Two per cent did not start the course at all, and the same percentage reported that the antibiotics did not work. 19% stopped them because of side effects (McNulty *et al*.2007).

Compliance decreased with increased complexity of regimen and was 79% ± 14% for once daily dosing, 69% ± 15% for twice daily dosing, decreasing even more with three times daily dosing and four times a day dosing (Claxtont *et al*. 2001). Compliance depends also on the length of treatment. Better compliance was observed for regimens shorter than 7 days duration compared with longer ones (Kardas 2002).

Participants were asked to give reasons for stopping with their antibiotic courses before they have completed the course. Their responses are illustrated in Figure 4.7:

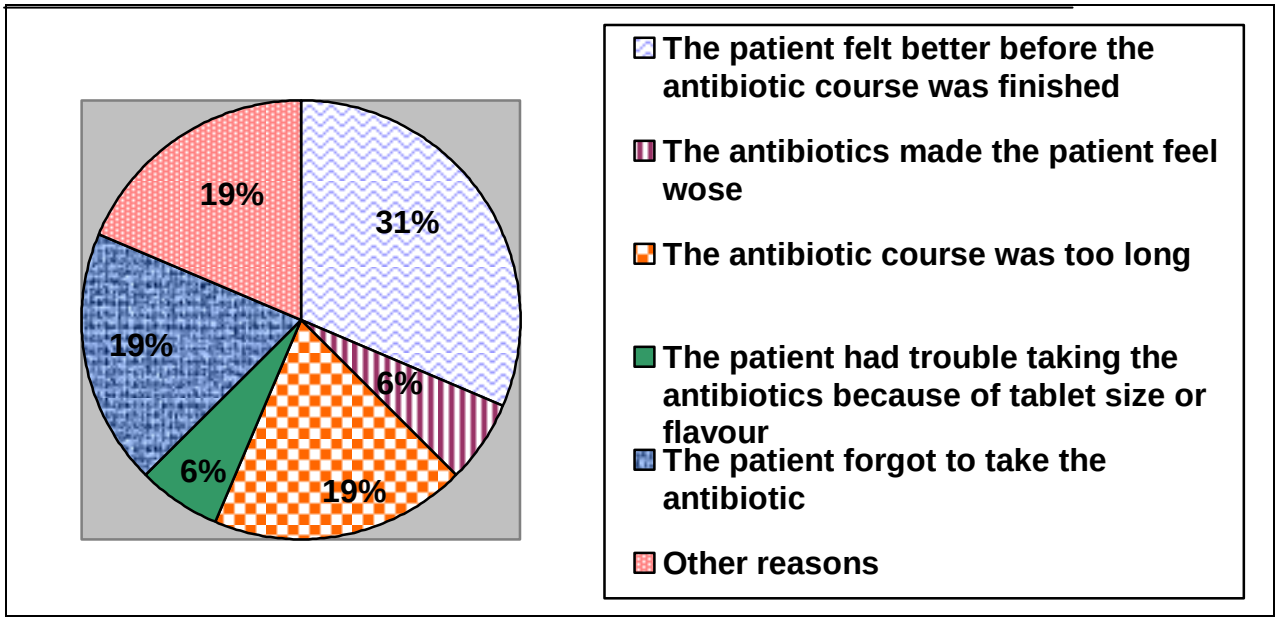

Figure 4.7 Reported reasons for patient non-compliance by non-compliant participants

Question 3: The following might be possible reasons for not finishing the prescribed antibiotics. Choose the most appropriate option.

Reason	Result	Persentage
☐ You felt better before the antibiotic course was finished	**5**	**31%**
☐ The antibiotics made you feel worse	**1**	**6%**
☐ The antibiotic course was too long	**3**	**19%**
☐ You did not know for how long to take your antibiotics	**0**	**0%**
☐ You did not receive the whole antibiotic course	**0**	**0%**
☐ You had trouble taking the antibiotics because of tablet size/flavour	**1**	**6%**
☐ You forgot to take the antibiotic	**3**	**19%**
☐ Other reasons or when answering **Yes** to question **1.**	**3**	**19%**
N = 16		**100%**

The largest portion (31%) of non- compliant participants did not complete the course because they felt better before the end of the course. An equal number of participants said that the course was either too long (19%), they forgot to take the antibiotic (19%) or had other reasons (19%) for not completing the course.

Branthwaite & Pechère (1996) reported that interviewees were positive about antibiotics, with over 75% judging them to be effective and to speed recovery. Over 80% of respondents expected symptoms to improve after 3 days' treatment. This provided a natural watershed for compliance, with most defaulters stopping after 3 days because they felt better.

4.2.2 Participant knowledge on antibiotic resistance

Question 4: Do you know what happens when one does not finish a course of antibiotics? What do you think will happen?

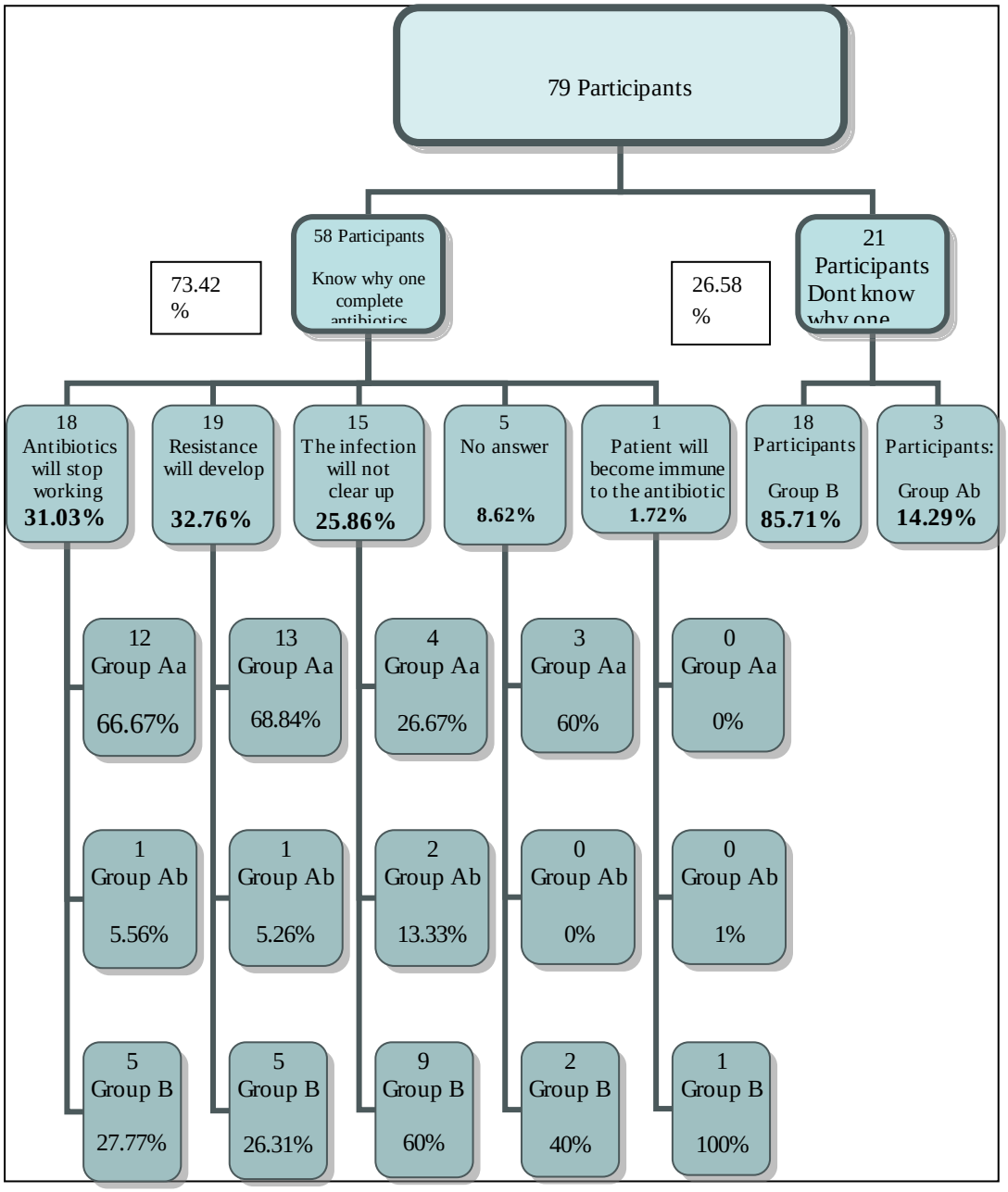

Figure 4.8 Participant knowledge regarding antibiotic resistance

Participants' responses to the question regarding their knowledge on why an antibiotic course should be completed were grouped into similar themes to form five main statements. Another group who admitted knowing that one should complete the course of antibiotics but gave no reason as to why this is the case, formed the sixth statement.

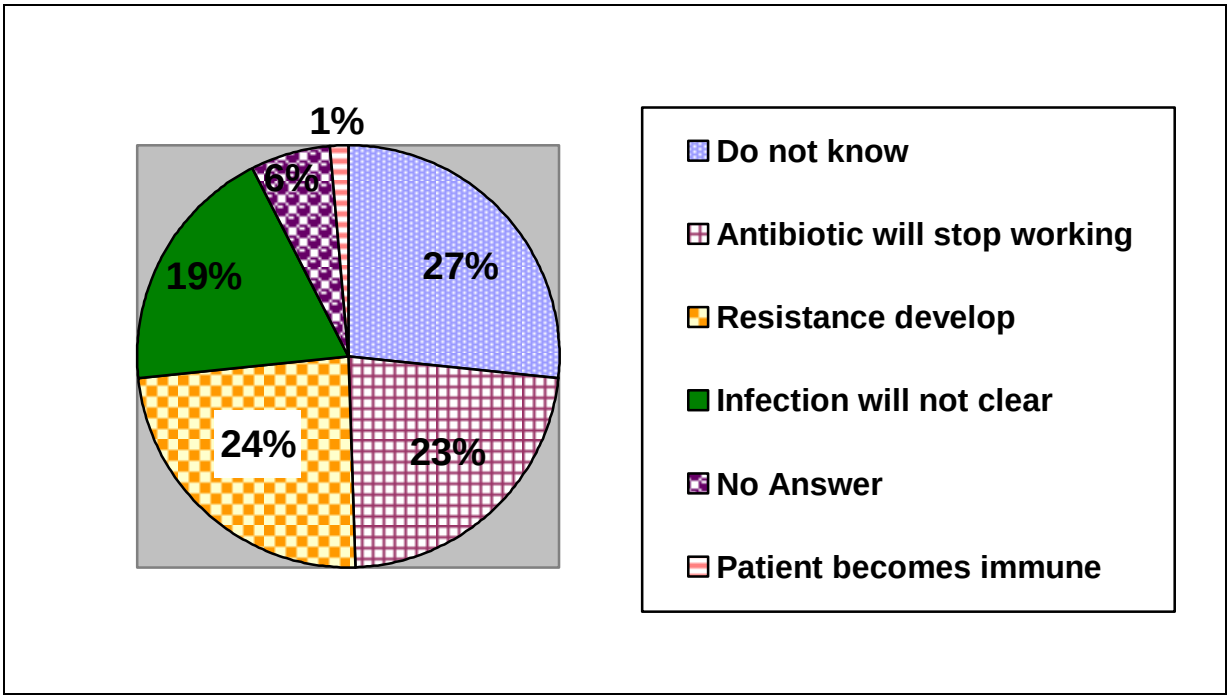

Figure 4.9 Reported reasons for completing antibiotic courses

All participants who did not know the reason for completing antibiotic courses consisted of Group Ab and Group B. Thus 100% of these participants did not receive additional information on responsible antibiotic use.

The participants who gave reasons for completing antibiotic courses consisted of 55.17% represented by Group Aa, 6.90% Group Ab and 37.93% Group B.

Group Aa responded 100% positively. Only 55% of Group B responded positively and 57.14% of Group Ab.

The greatest percentage of participants that knew that one should complete the course of antibiotics to prevent resistance of bacteria to antibiotics, were from Group Aa.

On testing participants' knowledge of antibiotic resistance, 26.58% (21 participants) did not know why they need to complete an antibiotic course. This entire group consisted of Group Ab and Group B who either did not receive additional information on antibiotics or did not read the brochure. On the other hand 73.42% gave reasons for completing antibiotic courses with the majority represented by Group Aa who read the additional antibiotic information.

4.2.3 Participant attitude toward antibiotics

4.2.3.1 Left-over antibiotics

Participants reported on what they would have done with left-over antibiotics in the past and how they would handle left-over antibiotics in the future based on their new knowledge of antibiotics received in the form of the leaflet.

Question 5: What have you done with left-over antibiotics in the past?

- Kept it for future use
- Threw it away
- Gave it to someone that needed antibiotics

Question 6: What would you do with left-over antibiotics in future?

All of the19 participants in Figure 4.10 used to keep antibiotics for future use. Twenty four percent of all the participants formed part of this group. Participants from Group Aa who read the leaflet on responsible antibiotic use showed a 77.78% positive change by committing to completing antibiotic courses in future.

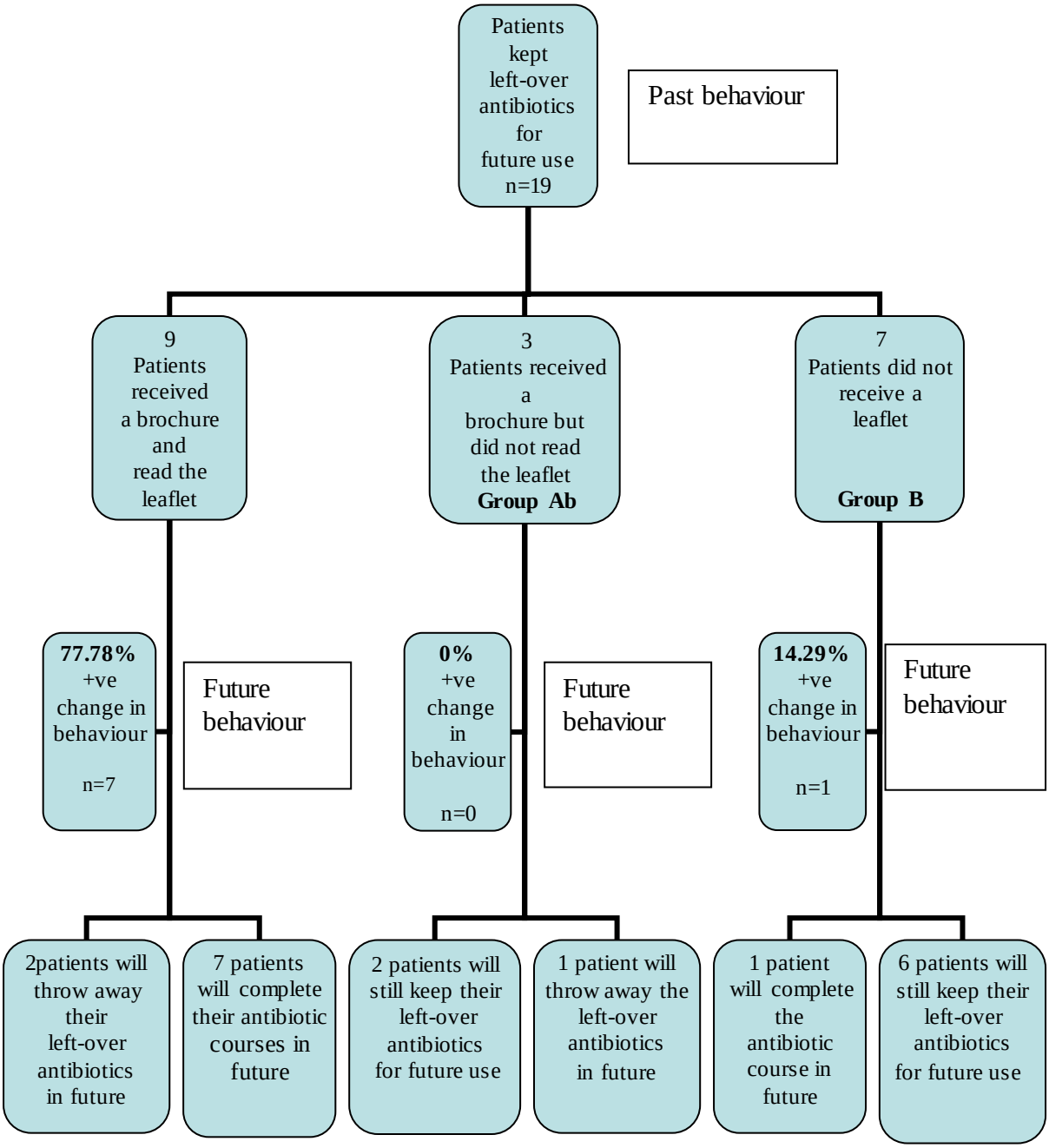

Figure 4.10 Participants kept left-over antibiotics for future use

In the United Kingdom almost 16% reported that they have kept an antibiotic in the past; 31% reported that they needed them again and 8% of case the same infection recurred. Respondents who reported keeping left-over antibiotics tended to be younger (McNulty *et al.* 2007).

Some participants used to throw away unused antibiotics. Their responses are demonstrated in Figure 4.11.

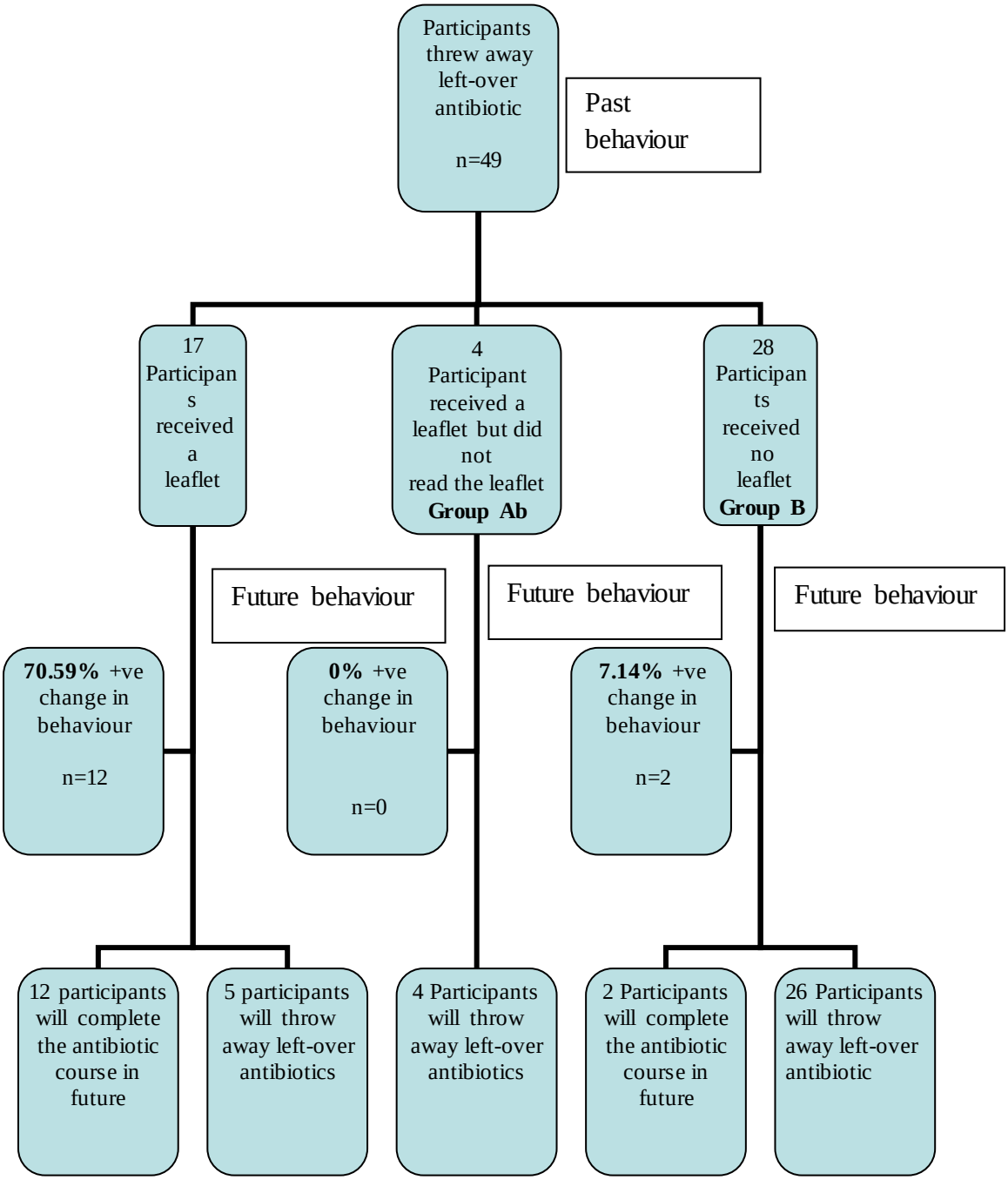

Figure 4.11 Participants threw away left-over antibiotics

A large portion of the participant population threw away left-over antibiotics in the past. A total of 62.03% of the study population admitted to this behaviour. Nearly 70% of Group Aa who used to throw away left-over antibiotics, committed to completing their antibiotic courses in future.

A small portion (3.8%) of the participants used to keep unused antibiotics for someone else who might need it.

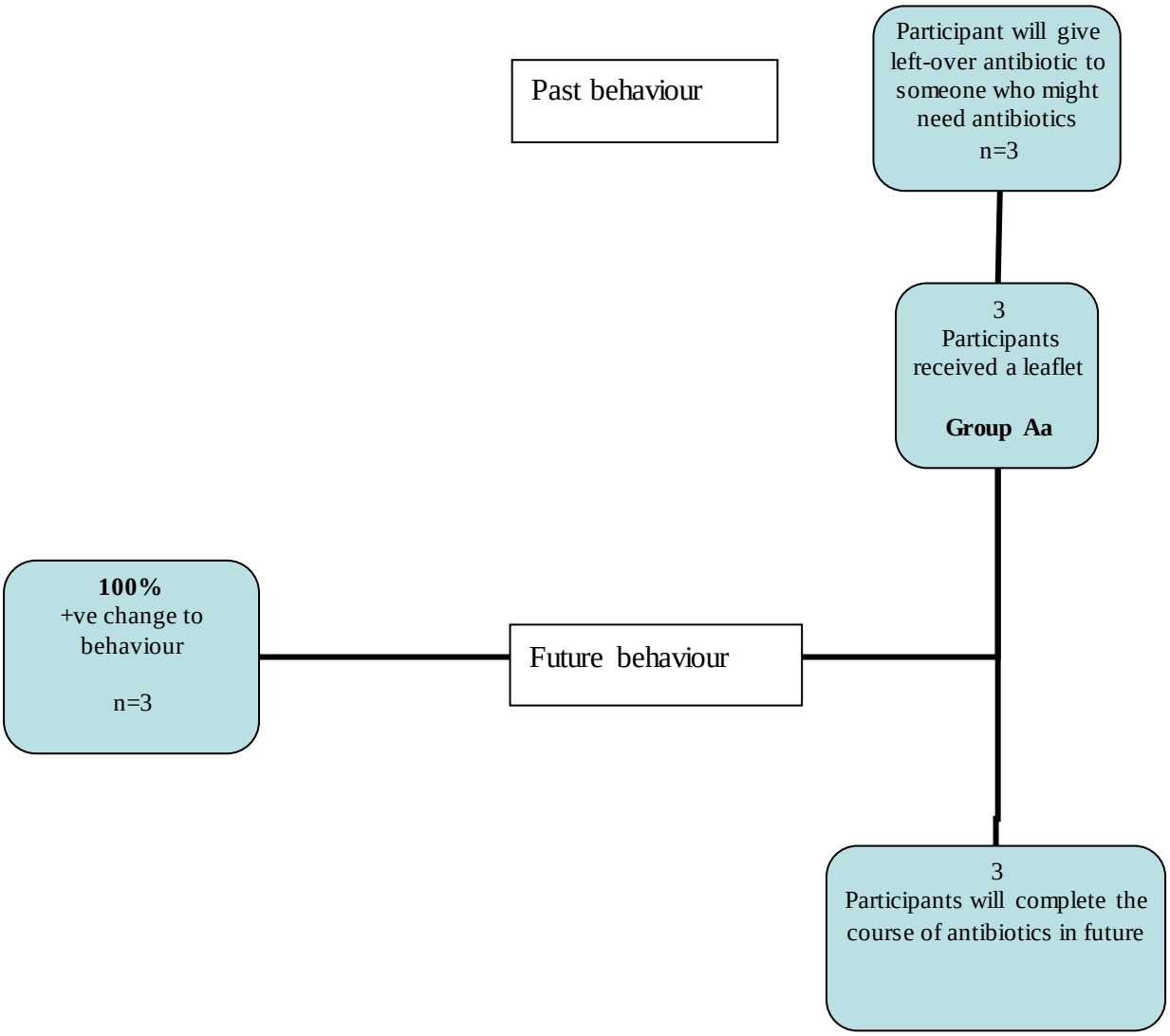

Figure 4.12 Participants gave left-over antibiotics to someone in need of antibiotics

All participants represented in Figure 4.12 showed a 100% improved behaviour concerning antibiotic use.

Although participants only had three options to choose from in the survey question concerning past and future antibiotic use behaviours, 10 participants chose to add another answer by stating that they always complete antibiotic courses. The distribution of participants is shown in Figure 4.13.

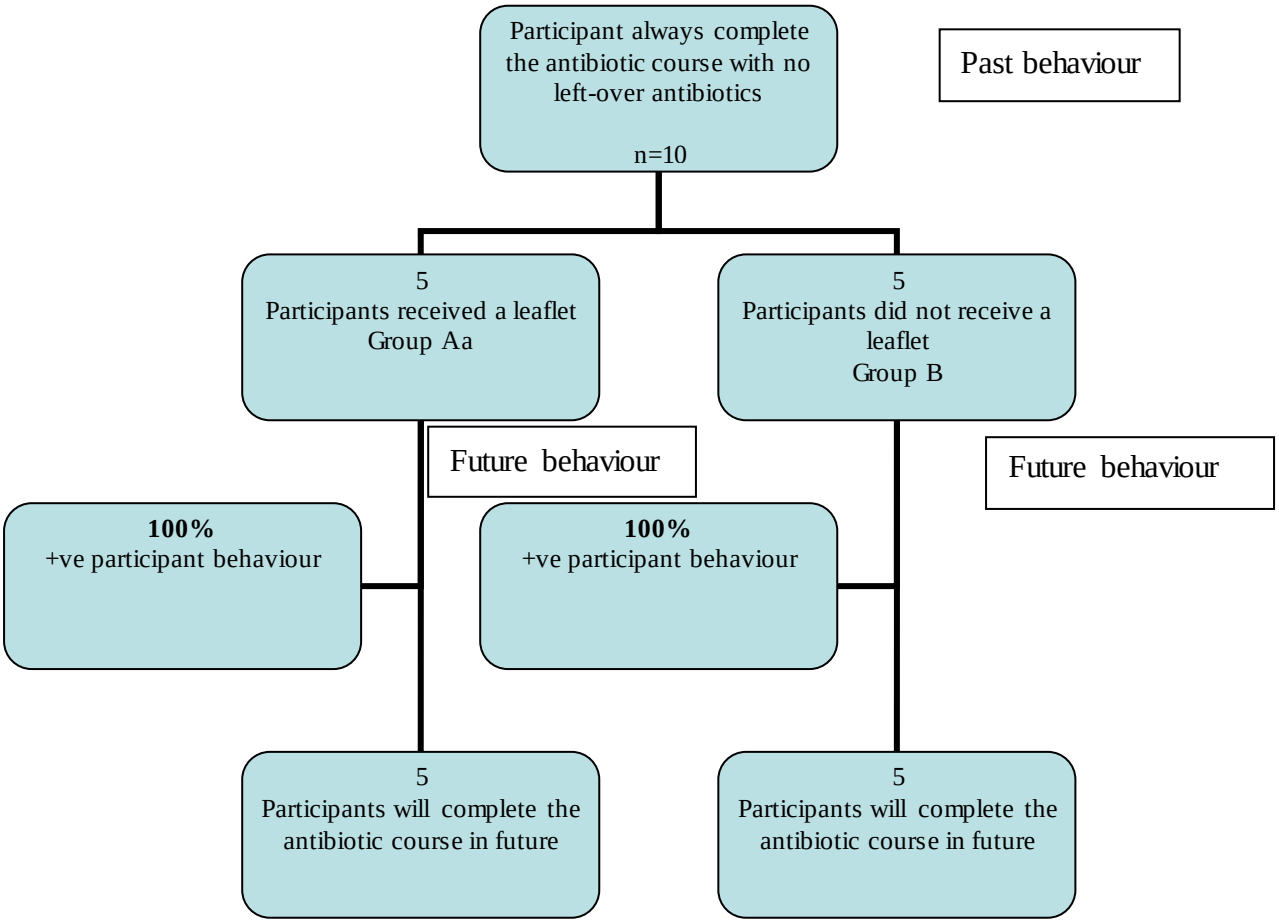

Figure 4.13 Participants always complete an antibiotic course

In conclusion, approximately 78% of Group Aa who used to keep left-over antibiotics for future use will in future complete the course. Nearly 71% of Group Aa who threw away left-over antibiotics will in future complete the course and 100% of Group Aa who kept antibiotics for someone who might need it, will complete the course in future. This shows a 84.38% positive change in Group Aa.

4.2.3.2 Pressuring doctors for antibiotic prescriptions

As part of the survey, participants were tested on their knowledge of antibiotic use in viral infections.

Question 7: Would you ask your doctor for antibiotics when you have a common cold?

Yes

No

Have you asked your doctor for antibiotics when having a common cold in the past?

73% of the study population had never put pressure on a medical practitioner to prescribe antibiotics in a viral infection. Group Aa showed a 31.25% improvement in participant behaviour with 100% of the group intending not using antibiotics in viral infections in future.

N=79	Group	Past	%	Future	%
	Group Aa	22/32	68.75%	32/32	100%
	Group Ab	4/7	57.14%	4/7	57.14%
	Group B	32/40	80%	32/40	80%

Table 4.4 Participants who do not put pressure on doctors to prescribe antibiotics in viral infections

Thirty one percent of Group Aa admitted to pressuring health professionals in the past to supply antibiotics. None of Group Aa will pressure doctors unnecessarily for antibiotics in future, with a 100% positive change in attitude and no change in Group Ab and Group B.

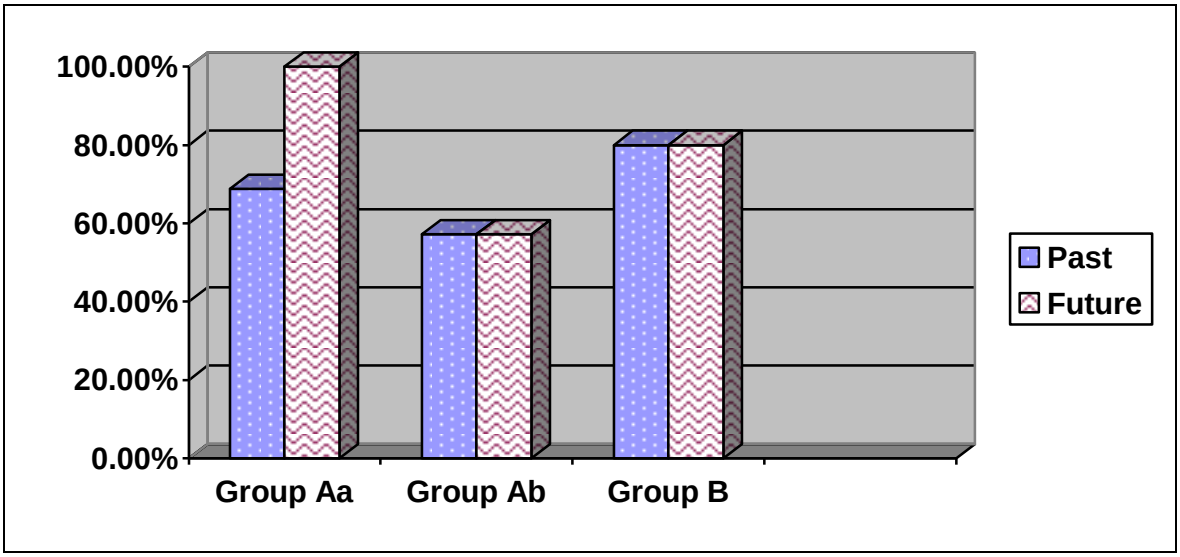

Figure 4.14 Pressure from participants to get antibiotics prescriptions for viral infections

In a global survey, pressure on general practitioners to prescribe antibiotics was highlighted by over 50% of interviewees' believing that they should be prescribed for most respiratory tract infections. Interviewees were positive about antibiotics, with over 75% judging them to be effective and to speed recovery. Over 80% of respondents expected symptoms to improve after 3 days' treatment. This provided a natural watershed for compliance, with most defaulters stopping after 3 days because they felt better. (Branthwaite & Pechère 1996).

4.2.3.3 Participants' willingness to change their attitude towards antibiotic use

Participants were asked to comment on how they might change their behaviour when taking antibiotics in future. Only participants from Group Aa who read the leaflet handed to them, commented. The comments that implicated the same idea were grouped in into statements.

Question 8: In what way would you change your use of antibiotics, if you would change anything?

N =32	Statement #	Statement	
15	Nr. 1	Nothing	Participants did complete course in prescribed time and have not asked for antibiotics from a medical practitioner
10	Nr. 2	One should always complete the course	(1 overlap statement Nr 4 and 1 overlap with Nr 5)
2	Nr. 3	One should only use antibiotics when it is necessary	
4	Nr. 4	One should use antibiotics for bacterial infections and not for viral infections	(1 overlap statement Nr 2)
2	Nr. 5	One should not pressure a medical practitioner for an antibiotic prescription when having a flu	(1 overlap with statement Nr 2)
1			No answer provided

Table 4.5 Participants changes to future antibiotic use

Participants who already showed responsible use of antibiotics chose statement Nr 1, with no changes needed in their antibiotic use. 56.25% of participants in Group Aa gained knowledge and based on that will use antibiotics more responsible in future.

The leaflet was supplied to patients as a tool to enrich their knowledge on responsible antibiotic use. Participants were asked to give feedback on what they have learned by reading the leaflet. Only the participants form Group Aa commented. The comments that implicated the same idea were grouped in into statements.

87.50% of Group Aa learned something by reading the leaflet concerning responsible antibiotic use. 9.38% of Group Aa did not learn anything new and one participant chose the incorrect statement Nr 5.

Question 10: What is the most important lesson you learned by reading the 'Antibiotics: wise-up and take responsibility' brochure?

N =32	Statement #	Statement	
12	Nr. 1	Antibiotics has no effect on viruses and should only be used for bacterial infections, not colds and flu	(1overlap with statement Nr 2)
12	Nr. 2	All bacteria need to be killed by the antibiotic and the course should be completed to reduce antibiotic resistance	(1overlap with statement Nr 1) (2overlap with statement Nr 3)
7	Nr. 3	One should not over use antibiotics	(2 overlap with statement Nr 2)
3	Nr. 4	Nothing learned	
1	Nr. 5	Patients will become immune to antibiotics	

Table 4.6 Lessons learned by Group Aa.

Participants from Group Aa commented on the knowledge that they have gained from the leaflet handed to them. Participants who already showed responsible use of antibiotics chose not to change anything about the way they use antibiotics. Nearly 88 % of participants in Group Aa gained knowledge on not to use antibiotics for viral infections, to complete the course and not to over use antibiotics and based on that will use antibiotics more responsible in future.

McNulty (2007) found that four years after the campaign on antibiotic use in the United Kingdom in 1999 only a fifth of respondents and only 25% of respondents who had been prescribed an antibiotic in the past year, had seen or heard of the campaign. A third of the public still believe that antibiotics work against coughs and colds, and it has been shown that those with a greater knowledge about antibiotics are no less likely to be prescribed an antibiotic. And in respect of how the public use the antibiotics they are prescribed, sometimes

increased knowledge is associated with more prudent use or higher chances to self-medicate. Greater knowledge about antibiotics was associated with a greater tendency to keep left-over antibiotics and use them without advice from a clinician (McNulty *et al*.2007).

Participants in this study responded to the survey within a week or two after they have read the leaflet. The information was still fresh in their memory but one could conclude from McNulty's study that patients will need constant reminders as to how they should use antibiotics responsibly.

4.2.3.4 Participant willingness to learn more about responsible antibiotic use

Question 11: Would you prefer to receive more information on responsible antibiotic use?

Table 4.7 demonstrates the various responses by different groups on their willingness to learn more on how to responsibly use antibiotics

Answer	**Group**	**Gender/Age Group**		
		Female	**Male**	**Children**
Yes	Group Aa	12	7	7
	Group Ab	1	1	3
	Group B	11	8	4
Total: 54 (68.35%)		Total: 24 (70.59%)	Total: 16 (64%)	Total: 14 (70%)
No	Group Aa	2	3	1
	Group Ab	1	1	0
	Group B	7	5	5
Total: 25 (31.64%)		Total: 10 (29.41%)	Total: 9 (36%)	Total: 6 (30%)
Total: 100%		100%	100%	100%

Table 4.7 Participants' willingness to learn more about responsible antibiotic use

Participants from Group Aa showed most willingness to learn more about antibiotic use with females and children making out the largest portion of the group. Male participants tended to be less eager to learn more about responsible antibiotic use. Eighty one persent of Group Aa showed a willingness to learn more about antibiotics. Only 57.50% of Group B showed interest in learning more about responsible antibiotic use.

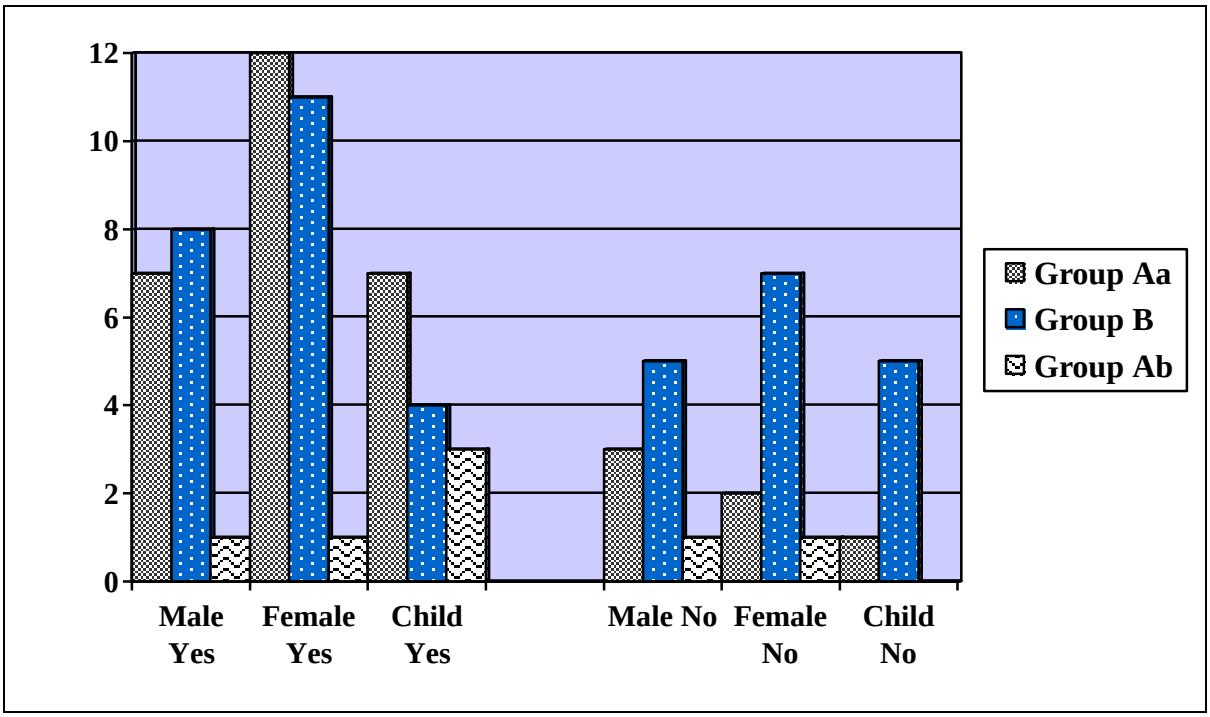

Figure 4.15 Overview on participants' willingness to learn more about responsible antibiotic use

4.3 Child prescription responses

Child prescriptions formed part of the study population. Parents or guardians of these children responded to the survey. The group that received leaflets with their medication had a 28.21% response rate and the group without leaflets had a 28.57% response rate. There is therefore no significant difference between the 2 groups.

Figure 4.16 shows the number of responding child patients compared to the non-responding child patients.

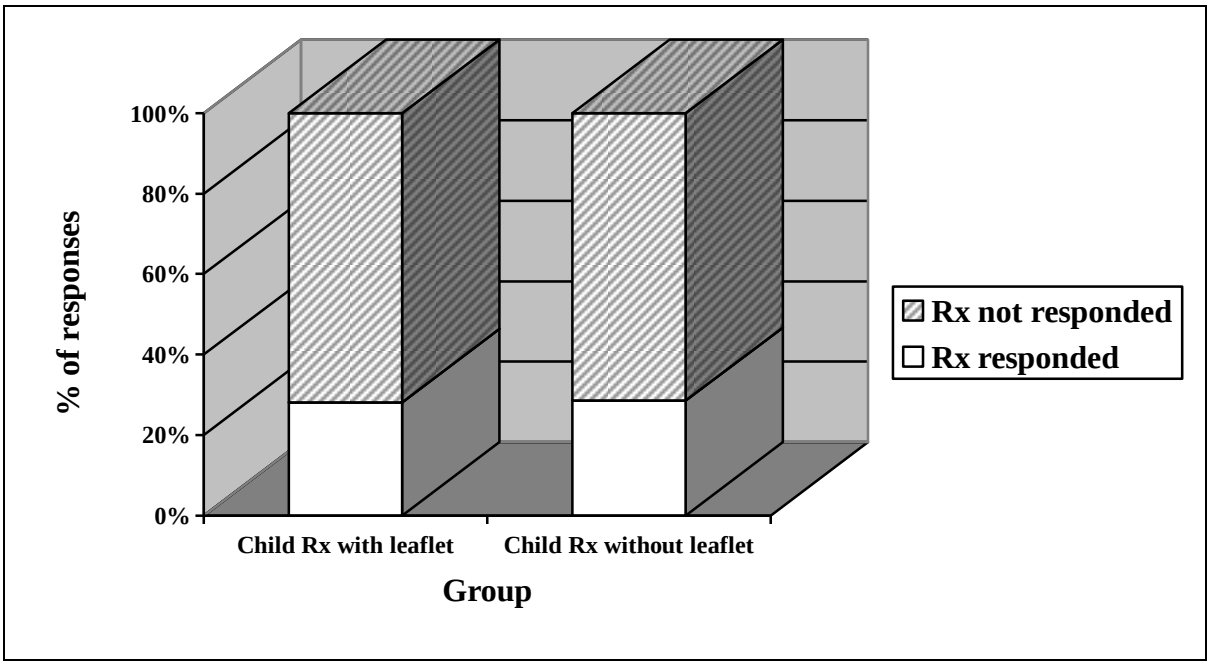

Figure 4.16 Proportion of participating child participants compared to non-responders

Figure 4.15 showed that 70% of adults responding on behalf of a child would prefer to receive additional information regarding antibiotic use from their pharmacist.

Child participants showed 95% antibiotic compliance. It is thought that these children showed a high compliance rate because of an adult giving their medication according to the prescriber's orders. Parents are often more concerned about a small child's health than their own and might explain why they follow the doctor's orders to the letter.

Chapter 5: Recommendations

Future campaigns that are aimed at reducing the level of prescribing antibiotics unnecessarily should be focused towards those more likely to be prescribed an antibiotic. In this study women aged between 20 and 50 years as well as child prescriptions made out a large portion of the study group.

We should examine and consider modifying consultation behaviours of prescribers and other behavioural components involved in patients expectations for antibiotics. This should include delayed antibiotic prescriptions.

We could focus the message that antibiotics should be completed and not stored for future use towards the higher educated, young women who are more likely to store and take antibiotics without advice.

Some reports recommend that the public should be educated about the value of their normal flora. Normal flora did not feature in this survey although various participants indicated that they would prefer more information on probiotic use together with antibiotics. In the McNulty (2007) study, 42% of respondents did not agree with the statement 'Bacteria that normally live on the skin and in the gut are good for your health' and 43% of respondents did not agree that 'Antibiotics can kill bacteria that normally live on the skin and gut'.

Campaigns on the responsible use of antibiotics need to become a everyday practice for all health practitioners. Experience with social marketing for other health issues such as alcohol and driving shows that campaigns must be sustained over several years and have to be highlighted continuously.

More campaigns can be run in South Africa to emphasize responsible antibiotic use, focusing on healthcare professionals and the public. Campaigns to fight antibiotic resistance should be supported by government and be institutionalised by the Minister of Health. There are two suggestions: First, education and awareness of this issue must increase among the medical community. Second, political, and scientific forces must work together to recognize the scope of the problem and develop solutions.

Strategies to address antimicrobial resistance should be introduced that would strengthen antimicrobial resistance surveillance, help with prevention and control, and research efforts, and it should enhance the collection of critical information on the use of antibiotics in humans and animals.

Many private hospitals focus on antibiotic stewardship programmes with in-patients. Extending this practice to out-patients as well could have a huge effect on the way practitioners write antibiotic prescriptions for patients with less severe infections.

Pharmacists play a very important role in educating the patient, and should use the opportunity to give out-patients proper advice and information regarding the use of antibiotics. Pharmacists could explain to the patient why it is important to complete the antibiotic course or hand out information to patients regarding responsible antibiotic use.

When non-compliance is recognised, the pharmacist is in a good position to offer support to the patient. The approach should be to attempt to remove obvious barriers to compliance. A concordant approach should be adopted. However, for the pharmacist to provide advice that is consistent with the treatment-plan of the physician, pharmacists should be recognised as part of the healthcare team and be involved in the treatment-plan of a patient. Depending on the nature of the problem, counselling by the pharmacist may assist in improving compliance.

Many studies suggest that the easiest way to reduce the use of left-over antibiotics and improve compliance is to shorten the course of antibiotics prescribed to 3 or 5 days. Female patient compliance might be increased by focussing on shorter courses or fewer dosage intervals.

It is necessary to create a changed mindset in clinicians' and patients' beliefs about the expectations for and effectiveness of antibiotics for minor illness, to be able to control and decrease the unnecessary use of antibiotics (McNulty *et al.* 2007).

Turnidge (1998) wrote that it is generally agreed that the best way to reduce the selective pressure of antibiotics is to reduce usage. Australia and Hungary have shown that this is possible, but finding effective ways to do this is not simple. A coordinated cooperative effort between the professionals, patients, and regulators is required. The elements of this

coordinated approach include education, regulatory measures, public health measures, surveillance, and further research.

Education of both professionals and the public is a key component to change. There have been many efforts over the years to improve rational use of antibiotics though education. Techniques such as the development of consensus guidelines; promotion of rational prescribing methods, including better use of diagnostics; promotion of shorter treatment courses where these have been shown to be equally effective; and the use of delayed prescribing (prescription is written but filled only if the condition worsens) have been used extensively. Additional techniques—such as rotational usage in an individual patient or in a practice, the use of different antibiotic classes in different conditions to spread selective pressure, and a stronger emphasis on narrow spectrum agents—need to be considered. None of these techniques will be effective, however, until the public becomes better educated about infectious diseases and the role of antibiotics, including such simple distinctions as the difference between viruses and bacteria. Ideally, this should start in secondary school as part of health education and biology courses. Patients should also be educated at the time of consultation, and the message that antibiotics are not useful in many common infections should be reinforced. Brochures and other educational material handed out at the time of consultation can help in this process. The risks of prescribing antibiotics when they are not needed must be emphasised, such as the side effects and potential for picking up resistant organisms and spreading them to others. This "green" message will be easier to sell now that the public is more aware of personal health and environmental issues. When antibiotics are prescribed, increased attention must be given to ensuring compliance and patients' understanding through such instruments as consumer product information leaflets (Turnidge 1998).

Chapter 6: Limitations

Various areas of the study could be seen as limitations to the study results.

The questionnaire was only completed by patients with access to e-mail. This group of participants were from one pharmacy in the private sector only. Although the hospital service patients from all backgrounds, the majority of patients might be seen as educated and from a higher income group. This should not influence the study results as the focus of the study is on the influence of extra information on antibiotic use and not on the influence of different backgrounds of patients on antibiotic use.

Pharmacists who had to give out the leaflet concerning the responsible use of antibiotics, had to do so without bias but work under pressure and often forgot to give out leaflets or gave it to more approachable customers.

Participants often give information that they think might be acceptable to the researcher.

Child prescriptions that formed part of the study had an adult responding on behalf of the child. The child prescription group was still kept segregated from the adult group to test for any difference in compliance between the groups.

Non-response bias due to a low response rate of 29% affects both the reliability and validity of survey study findings.

Fincham (2008) found that e-mail surveys incorporating multimode approaches may yield response rates as high as 70%. Allowing for differing methods of returning surveys (e-mail and/or mailed options; eg, multimode) will aid those respondents who prefer to print out a survey instrument and respond via mail. This mixed-mode approach, combining both mailed and e-mailed survey instruments with an Internet-based response mechanism, also is an approach to help reduce the problem of coverage error in administration of surveys.

Chapter 7: Conclusion.

The main objective of the study was to determine whether a better understanding of responsible antibiotic use will lead to better compliance. The hypothesis $\mathbf{H = M_a > M_b}$, where M_a represents Group A and M_b represents Group B of the study, proved to be true. The hypothesis state that Group A (M_a) will be more influenced by the additional antibiotic information than Group B (M_b).

Group Aa showed a better compliance to the antibiotic regimen prescribed. When compared to Group Ab and Group B, a much higher percentage of this group was able to give valid reasons as to why one should complete an antibiotic course.

78% of Group Aa intended to change their future behaviour with regards to left-over antibiotics. These patients are committed to being completely compliant in future. This group showed a 100% change in attitude when it comes to pressurizing medical practitioners into prescribing antibiotics for minor illness, colds and flu.

The majority of Group Aa admitted to learning something by reading the leaflet handed to them and also showed most interest in wanting more antibiotic information from their pharmacist in future.

Participants gave various reasons for not being compliant. Most patients stopped taking their antibiotics as soon as they felt better.

Participants from Group Aa showed most willingness to learn more about antibiotic use with females and children making out the largest portion of the group. Male participants tended to be less eager to learn more about responsible antibiotic use.

The child group that received leaflets with their medication had a 28.21% response rate and the group without leaflets had a 28.57% response rate. There is therefore no significant difference between the 2 groups.

The study suggests that handing out information leaflets has an effect on patients' understanding of antibiotic resistance and compliance. This might not be the case for all age

groups, for instance, young adult males. This age group might need another approach. Male patients in their middle-ages also showed response to the e-mail; but not very good response to the leaflet handed to them. This age group might be reached by sending antibiotic information by e-mail and not handed out to them.

It is my conclusion that the additional information given to patients at the pharmacy level can make a great impact in the patient's view of when and how antibiotics should be used.

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Appendix A

Dear Pretoria East Hospital Pharmacy Patient,

We would like to follow-up on the use of your antibiotics received at our pharmacy on _____. A questionnaire survey has been compiled to measure patients' adherence to antibiotic prescription instructions and also the information received from the pharmacist or assistant that issued your prescribed antibiotics.

We would appreciate it if you could take 3 minutes to answer the 11 questions. This survey aims to determine how we can improve our service to patients and ensure that patients receive the necessary information regarding the medication they need to take.

All patient information will be kept confidential and will only be used for the purposes of the study. No names are asked in this questionnaire and all data will be saved anonymously.

Your consent to partake in this study will be given by completing the questionnaire below and returning it to the sender. Your participation would be greatly appreciated.

Please first answer the questions, next 'copy' the text with the given answers. Click on the 'reply' button, then 'paste' the completed questionnaire before clicking on the 'send' button.

1. Have you finished you antibiotic course?

- Yes
- No

If you answered 'No', please specify how many of the tablets or how much of the suspension do you have left over?

2. Did you finish the antibiotics in the prescribed time?

- Yes
- No

3. The following might be possible reasons for not finishing the prescribed antibiotics. Choose the most appropriate option.

- ☐ You felt better before the antibiotic course was finished
- ☐ The antibiotics made you feel worse
- ☐ The antibiotic course was too long
- ☐ You did not know for how long to take your antibiotics
- ☐ You did not receive the whole antibiotic course
- ☐ You had trouble taking the antibiotics because of tablet size or flavour
- ☐ You forgot to take the antibiotic
- ☐ Other reasons or when answering **Yes** to question **1.**

Please explain when choosing 'Other reasons':

4. Do you know what happens when one does not finish a course of antibiotics?

- ○ Yes
- ○ No

If your answer is 'Yes', what do you think would happen?

5. What have you done with left-over antibiotics in the past?

- ○ Kept it for future use
- ○ Threw it away
- ○ Gave it to someone that needed antibiotics

6. What would you do with left-over antibiotics in future?

7. Would you ask your doctor for antibiotics when you have a common cold?

- ○ Yes
- ○ No

Have you asked your doctor for antibiotics when having a common cold in the past?

8. Did you receive an 'Antibiotics: wise-up and take responsibility' brochure from your pharmacist?

Did you read the brochure? (answer from drop-down menu)

- Yes
- No

9. What is the most important lesson you learned by reading the 'Antibiotics: wise-up and take responsibility' brochure?

10. In what way would you change your use of antibiotics, if you would change anything?

11. Would you prefer to receive more information on responsible antibiotic use?

- Yes
- No

Appendix B

Antibiotics: Wise-up and take responsibility

Antibiotics are the first line of defence against many infections, however, overusing or misusing antibiotics can cause treatment failure in future.

What are antibiotics?

Antibiotics are used for treating many less serious to life-threatening diseases caused by bacterial infections. Taking antibiotics when you don't need to, can lead to antibiotic-resistance. Antibiotics are only effective against bacterial infections, certain fungal infections and some kinds of parasites. Most infections result from either bacteria or viruses. **Antibiotics are not effective against viral infections!**

Common bacterial infections cause severe upper-respiratory-tract infections e.g. pneumonia, wound and skin infections and urinary tract infections.

Common colds, influenza, most ear infections and stomach flu are caused by viral infections. These can be treated by anti-viral drugs or by treating the symptoms.

How does antibiotic resistance develop?

Penicillin was introduced in the first part of the 20th century and since then scientists have developed many more antibiotics to help stop the spread of infectious disease. Antibiotics have saved millions of lives but because of frequent use, often for conditions or infections that aren't caused by bacteria, the bacteria have become resistant to many commonly used antibiotics.
Resistance develops when an antibiotic fails to kill all of the bacteria it targets. The surviving bacteria adapt and become more resistant to that particular drug. Doctors then needs to prescribe stronger antibiotics, but the bacteria quickly learn to defend themselves against the more potent drugs as well, creating a cycle in which increasingly powerful drugs are required to treat infections.
Experts are working to develop new antibiotics and to keep pace with antibiotic-resistant strains of bacteria, but bacteria adapt quickly. Antibiotic-resistant bacteria continue to be a global health concern and using antibiotics wisely is an important part of preventing the development of resistance.

Consequences of antibiotic resistance

As an increasing amount of bacteria become resistant to first line treatments, the consequences become severe. Illnesses last longer, and the risk of complications and death increases. The inability to properly treat a particular infection leads to longer periods in which a person is contagious and able to spread the resistant bacterial strains to others.
Because of first line treatment failures, doctors have to resort to less-conventional antibiotics, many of which are much more costly and have more side-effects.
Many other factors need to be considered, including the increased costs associated with prolonged illnesses, direct expense for additional laboratory tests, treatments and hospitalization, and the indirect costs from loss of income or time away from family.

Safeguard effective antibiotics: What you can do

Finishing your prescribed course of antibiotics is utmost importance.

Using antibiotics too often or incorrectly is a major cause of the increase in resistant bacteria. Here are some things you can do to promote proper use of antibiotics:

- **Understand when antibiotics should be used.** Don't expect to take antibiotics every time you're sick. Antibiotics are effective in treating bacterial infections, but they're not useful against viral infections, such as colds, acute bronchitis, or the flu. And even some common minor bacterial ailments, such as mild ear infections, don't benefit much from antibiotics.
- **Don't pressure your doctor for antibiotics if you have a viral illness.** Talk to your doctor about ways to relieve the symptoms of your viral infection.
- **Take antibiotics exactly as prescribed.** Follow your doctor's instructions when taking prescribed medication, including how many times a day and for how long. Never stop treatment a few days early if you start feeling better — a complete course of antibiotics is needed to kill all of the harmful bacteria. A shortened course of antibiotics often only kills the most vulnerable bacteria, while allowing relatively resistant bacteria to survive.

- **Never take antibiotics without a prescription.** You might be tempted to use leftover medication the next time you get sick. This might be the incorrect antibiotic for you infection and an incomplete course.

- **Protect yourself from infection in the first place.** Good hygiene can go a long way in preventing infection. Wash your hands thoroughly with soap and water, especially after using the toilet, changing a diaper or handling raw meat or poultry. Keep food preparation areas clean.

Antibiotic resistance is a pressing, global health problem. Nearly all bacterial infections are becoming resistant to commonly used antibiotics. When you abuse antibiotics, the resistant micro-organisms that you help create can cause new and hard-to-treat infections. That's why the decisions you make about antibiotic use — unlike almost any other medicine you take — extend far beyond your reach. Responsible antibiotic use protects the health of your family, neighbours and ultimately the global community.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mrs CC Beukes

CLEARANCE CERTIFICATE	**M090533**
PROJECT	A Study on the Relationship between Improved Patient Knowledge and Compliance with Antibiotic use
INVESTIGATORS	Mrs CC Beukes.
DEPARTMENT	Department of Pharmacy & Pharmacology
DATE CONSIDERED	09.05.29
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 2009/09/03 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof AGS Gous

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Tel: +27 (0) 12 422 2424
Fax: +27 (0) 12 422 2628
Cnr Garsfontein and Netcare Roads, Moreleta Park, South Africa
Private Bag X 997, Pretoria, 0001, South Africa
www.netcare.co.za

28 April 2009

Mrs CC Beukes

LETTER OF PERMISSION TO CONDUCT RESEARCH IN A NETCARE FACILITY

Pharmacy Manager 2IC:

RESEARCH IN PRETORIA EAST HOSPITAL PHARMACY

I hereby would like to inform you that your application to conduct research on "**A study on the relationship between improved patient knowledge and compliance with antibiotic use**" at Pretoria East Hospital Pharmacy has been approved, subject to the following:

i. All information with regards to Netcare will be treated as confidential.
ii. Netcare's name will not be mentioned without written consent from the Academic Board of Netcare.
iii. A copy of the research will be provided to Netcare once it is finally approved by the tertiary institution, or once complete.
iv. All legal requirements with regards to patient rights and confidentiality will be complied with.

Yours Faithfully

Christine Jansen van Vuuren
Pharmacy Manager 2IC