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EFFECTIVENESS OF TEXT MESSAGE REMINDERS ON IMPROVING OUT-PATIENTS' ADHERENCE TO ANTIBIOTIC THERAPY AT THE TEMA GENERAL HOSPITAL

BY

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DECLARATION

I, TAY KAFUI AMENYO KOBLA hereby declare that this proposal is a result of my independent work. References to other works have been duly acknowledged. I further declare that this proposal has not been submitted for award of any degree in this institution and other universities elsewhere.

…… ……..

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SUPERVISOR

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Not that we are sufficient of ourselves to think anything as of ourselves; but our sufficiency

is of God.

I am grateful to the Almighty God, my Creator for the continuous gift of life and strength.

Thanks to my entire family, who have remained steadfast in prayer and support throughout the course of this program. I also wish to acknowledge the immense guidance and contribution of my supervisor Dr. Priscilla Nortey.

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DEFINITION OF TERMS

Adherence

The extent to which a patient's behaviour corresponds to agreed recommendations from a healthcare professional

Antibiotic

A type of antimicrobial agent used in the treatment and prevention of bacterial infections

Frequency of dosing

The number of times a drug is taken in a day

Medication regimen

A systematic plan of medication intake.

Non-adherence to medication

A situation where an individual's behaviour does not correspond to agreed recommendations from a health professional.

Out-Patient

A patient who attends a hospital for treatment without staying overnight

Text message

An electronic communication sent and received by mobile phone

LIST OF ABBREVIATIONS

8-MMAS	8-Item Morisky Medication Adherence Scale
AOR	Adjusted Odds Ratio
CI	Confidence interval
COR	Crude Odds Ratio
GHS	Ghana Health Service
GITI	Gastro-Intestinal Tract Infection
IVR	Interactive Voice Response
LRTI	Lower Respiratory Tract Infection
MAQ	Medication Adherence Questionnaire
MEMS	Medication Events Monitoring System
OPD	Out-Patient Department
prn	pre nata
SD	Standard Deviation
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infection
WHO	World Health Organization

ABSTRACT

Background: Medication adherence directly influences the attainment of treatment goals. In spite of this, approximately 50% of patients do not adhere to prescribed medication regimen. Poor adherence to medicines is a global health challenge that needs attention as it leads to increased healthcare costs, poor clinical outcomes, increased morbidity and mortality. Text message reminders have been found to be a useful tool for improving adherence to medicines in several parts of the world. However in Ghana, little is known about the effectiveness of text message reminders on improving adherence to antibiotics.

Objective: To assess the effectiveness of text message reminders on improving out-patients' adherence to antibiotic therapy in the Tema general hospital

Method: The study was carried out at the Pharmacy Department of Tema General Hospital. Two hundred and four adult out patients who visited the hospital and were given one or more antibiotics for a maximum of 7 days to treat various infections were enrolled into the study. The participants were randomly assigned to two groups; those who received text message reminders and those who received no text message reminders. Participants' levels of adherence were assessed through telephone interviews a day after the expected date for completing their antibiotic therapy.

Results: Eighteen of the participants were lost to follow up and of the remaining 186, 85 of the received text message reminders. Sixty-two and half percent of participants who received text message reminders were adherent whereas only 45.5% of participants who did not receive text message reminders were adherent and the difference in adherence

was statically significant. The text message reminders increased the odds of adherence (OR 1.9, 95% CI [1.05-3.68], p value 0.024).

Conclusion: The results of the study suggest that text message reminders are effective in improving out-patient adherence to antibiotics. Further study should be conducted to assess the design and deployment of text message reminders to help optimize its effect on adherence

CHAPTER ONE

INTRODUCTION

1.1 Background

Adherence is defined by the WHO as "the extent to which an individual's behaviour corresponds to agreed recommendations of a healthcare provider"(Burkhart & Sabaté, 2003). Adherence to medicines directly influences the attainment of treatment goals (R. Haynes, McDonald, Garg, & Montague, 2002). In spite of this, it is estimated that approximately 50% of patients have poor adherence to prescribed medication regimen (Burkhart & Sabaté, 2003).

Poor adherence leads to increased healthcare costs, poor clinical outcomes, increased morbidity and mortality (Cooper, Hall, Penland, Krueger, & May, 2009). The consequence of poor adherence to short term antibiotic therapy does not only affect the individual but can affect the whole population. This is because poor adherence to antibiotics could lead to the emergence of antibiotic resistance (Sorensen et al., 2009).

A myriad of methods have been used to improve adherence including patient counselling, use of technology, reduced pill burden and many others. One of the technological methods that has been utilized to increase adherence is the use of text message reminders (Park, 2013). This study therefore seeks to investigate the effectiveness of text message reminders on improving adherence to short term antibiotic therapy in OPD patients at Tema General Hospital.

1.2 Problem Statement

Antibiotics are a vital class of medicines used in the treatment and prevention of infections. Since their discovery, they have helped save lives and kept a lot of infections under control (Dougherty & Pucci, 2014). The full benefits of antibiotics however are only realized when patients adhere fully. Ideally adherence to antibiotics requires that patients take the recommended dose of their prescribed antibiotic at the right time and for the right duration. Anything outside this is considered poor adherence to antibiotics (Kardas, 2002).

Globally, adherence to antibiotics has been found to be low (Weiss, 2012). Fernandes et al. reported non-adherence rates to be 57.7% in a multi-center study across the globe (Fernandes et al., 2014). In Africa 36.2% of patients receive antibiotics from health facilities for the treatment of various infections. However, adherence to antibiotic therapy in many African countries including Ghana remains low (Vialle-Valentin, LeCates, Zhang, Desta, & Ross-Degnan, 2012).

The problem of non-adherence to medicines in general persists seriously in Ghana even though very little data on adherence to medicines exist. Adherence to antibiotics has been found to be low. Donkor et al., reported that adherence rates amongst the elite in Accra to be between 50.8-58.8% which is low and therefore there is the need for measures to be taken in order to improve adherence to antibiotics (Donkor, Tetteh-Quarcoo, Nartey & Agyemang, 2012).

The effects of poor adherence to antibiotics include treatment failure, increased morbidity as well as mortality and increased healthcare costs. Several cases of antibiotic resistance

have been reported in many hospitals in Ghana (Gyansa-Lutterodt, 2013) and this has serious public health implications.

Text message reminders have been found to improve medication adherence in several studies (Sarkar, Sivashankar, & Seshadri, 2015). However, in Ghana little is known about the effectiveness of text message reminders on adherence to antibiotic therapy amongst out-patients in Ghanaian hospitals.

1.3 Justification

Strategies for improving adherence to antibiotic therapy are needed. Improving adherence to antibiotics will help reduce treatment failure, healthcare costs, morbidity and mortality. It will also help reduce the development of antibiotic resistance since non-adherence to antibiotics is one of the main factors that bring about the development of antibiotic resistance. Improving adherence to antibiotic therapy is therefore very critical. This study is therefore needed to assess the effectiveness of one of such adherence improvement strategies. Successful outcomes from this study will demonstrate the usefulness of mobile phones in supporting and improving adherence to antibiotics in Ghana and hence reduce the problems associated with non-adherence to antibiotics.

1.4 Conceptual Framework

The variables to be considered in this study have been compressed in this conceptual framework. The conceptual framework categorizes the variables that influence adherence into demographic factors, treatment factors, disease factors and the interventions such as text message reminders, counseling during dispensing etc. This study assumes that demographic factors such as age, educational level and sex have direct influence on

adherence to antibiotic therapy and disease type as some diseases may be related to a person's age, sex or educational level. Age for instance has been found to influence adherence rates amongst patients. The older a patient is, the more adherent they are to the therapy. Also lower educational level has a negative correlation with patient's adherence to medicines (Catz et al, 1999). Reminders such as text messages dispensing instructions and adherence counselling have been shown to positively correlate with medication adherence (Raifman, Lanthorn, Rokicki, & Fink, 2014). Disease factors may influence the type of antibiotic chosen, frequency and duration of therapy. On the other hand, the treatment regimen may also influence patient adherence.

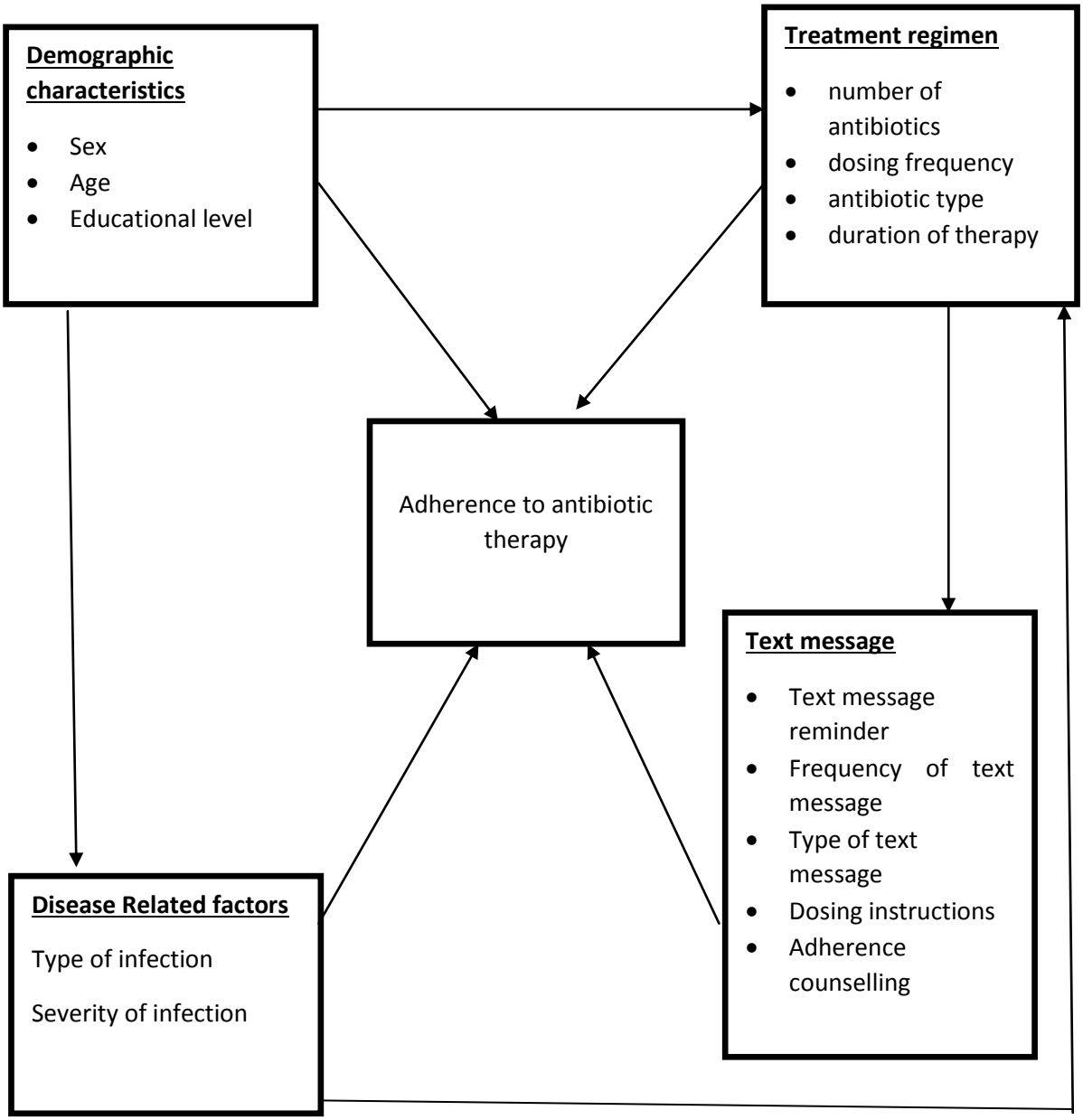

fig. 1 conceptual framework of factors that may influence adherence to antibiotics

1.5 Main Objective

To assess the effectiveness of text message reminders on improving out-patients' adherence to antibiotic therapy in the Tema general hospital

1.6 Specific Objectives

1. To compare the adherence levels to antibiotics amongst text message reminder groups and no text message groups
2. To determine the effect of being on medicine(s) for chronic condition(s) on adherence to antibiotics.
3. To assess the opinion of participants' in the text message group on helpfulness of text message reminders.

CHAPTER TWO

LITERATURE REVIEW

2.1 Medication Adherence

Pharmacotherapy is the most used health intervention globally as most diseases are managed and prevented using medicines. These medicines however only produce the desired clinical outcomes in patients who take them appropriately. Some patients fail to adhere to their prescribed medicines and hence do not get the full benefits of the drugs (Burkhart & Sabaté, 2003). The degree to which a patient's behavior corresponds to agreed recommendations of a healthcare provider is termed adherence (Burkhart & Sabaté, 2003).

The terms compliance and adherence are often used interchangeably even though the two are not the same. Compliance is defined as the degree to which a person's medication-taking behaviour corresponds to the healthcare provider's medical advice (Aronson, 2007). The use of the term adherence is usually preferred over compliance because it involves an interaction and collaboration between the patient and the care giver (Nichols-English & Poirier, n.d.).

Poor adherence to medicines is a global health challenge that leads to poor clinical outcomes. In 2003 the WHO reported adherence to medicines as generally low and was found to be around 50% (Burkhart & Sabaté, 2003). Patients with acute conditions have higher adherence rates compared with people with chronic conditions. One study found adherence medicine use among chronically ill patients to be low and it worsened after the first six months of therapy (R. B. Haynes, McDonald, & Garg, 2002, Jackevicius, Mamdani, & Tu, n.d., Cramer et al., 2003). Another study found 57.7% of patients

receiving antibiotics not adhering to treatment (Fernandes et al., 2014). Adherence rates amongst patients receiving antibiotics for a respiratory infection, showed only 30.7% adhered with the prescribed antibiotic (Llor et al., 2013).

The effects of poor adherence include poor clinical outcomes, increased morbidity and mortality rates and increased health costs (Brown & Bussell, 2011). Poor adherence to chronic therapies seriously decreases the effectiveness of treatment. As a result, adherence has become a public health issue from both the perspective of patient quality of life and the economics of health. Poor medication adherence has been found to account for between one-third and two-thirds of medicine related hospitalizations (Osterberg & Blaschke, 2005). With respect to infectious diseases, poor adherence to antibiotics could also lead to the emergence of bacterial resistance. The leftover antibiotics at home as a result of poor adherence, may induce self-medication. This may result in the irrational use of antibiotics and thereby leading to the emergence of bacterial resistance (Vrijens & Urquhart, 2005).

2.3 Factors affecting medication adherence

Several factors affect patients' adherence to medicines. These factors can be classified into patient-related, socioeconomic, condition-related, provider-patient/health care system and therapy related factors (Kalogianni, 2011). Below is an elaboration of these factors.

- **Social/economic**: Adherence to medicines is better when people have family support, caregivers or friends to help with medication schedule (Kalogianni, 2011). Some of the factors associated with decreased adherence rates are

unstable living environments, limited healthcare access, unavailability of financial resources, medication cost, and stressful work schedules. Socioeconomic status however cannot be considered a strong predictor of poor adherence to medication because in a met-analysis, the evidence supporting this view remains theoretical (Alsabbagh et al., 2014). In another study, evidence for the effect of education was considered unclear (Mathes, Jaschinski, & Pieper, 2014). Several studies that reported effect direction of educational status however showed a positive influence on adherence (Oosterom-Calo et al., 2013; Broekmans, Dobbels, Milisen, Morlion, & Vanderschueren, 2009).

- **Provider-patient/health care system**: In the health care system one of the most critical factors influencing adherence is the patient-doctor relationship. (Kalogianni, 2011). The relationship between the doctor and the patient has a positive impact on adherence when there is encouragement and reinforcement from the doctor. Some of the factors that can also contribute to poor adherence include insufficient communication with respect to the benefits, instructions for use, and side effects of medications. This is usually common in older adults with memory problems (Vermeire, Hearnshaw, Van Royen, & Denekens, 2001). In other studies, it was found that co-payments and cost of medicines have a negative influence on medication adherence (Sinnott, Buckley, O′Riordan, Bradley, & Whelton, 2013;Vermeire et al., 2001).
- **Condition-related**: In chronic illnesses, where there is long term use, the adherence to treatment regimen often decreases significantly with time and

this is because patients usually do not take their medicines when there are no symptoms. (Kalogianni, 2011). It is important to educate the patient to have an understanding of their illness and the consequences of not treating. However, it has been shown that the adherence to medication in some chronic malignant pain patients is not influenced by the duration of disease. (Pasma, van't Spijker, Hazes, Busschbach, & Luime, 2013).

- **Therapy-related**: The intricacies of the treatment plan, including the number of medicines and required doses per day as well as therapy duration, may affect adherence rates. Treatment regimens that cause some inconvenience or interference with a patient's normal life has been found to decrease adherence rates. Furthermore, treatment related adverse reactions have also been found to be related with decreased adherence rates (Kalogianni, 2011). In one primary study involving Parkinson disease patients, it was shown that the effect of frequency of intake was negative (Daley, Myint, Gray, & Deane, 2012). A negative effect on adherence has also been shown in most of the studies that have reviewed intake of different medications. (Daley et al., 2012;Oosterom-Calo et al., 2013). However, a positive effect direction on adherence has been shown in patients taking oral anticancer agents especially when they take medications at meal time. (Mathes et al., 2014).

- **Patient-related factors**: Some of the factors that increase the risk for poor adherence in especially older adults are physical impairments and cognitive limitations. Also important patient related factors that affect adherence are

lack of disease knowledge and the reasons medication is needed, low self-efficacy, substance abuse and lack of motivation. (Kalogianni, 2011). In other studies, patient related factors that affect adherence also include age, sex, level of education, religion, marital status, fear of disclosure and feeling depressed, hopeless, or overwhelmed and forgetting to take medication at the specified time (Starace et al., 2002).

2.4 Measuring medication adherence

According to WHO, measurement of medication adherence has been categorized generally into two, namely subjective and objective measurements. (Burkhart & Sabaté, 2003)

Subjective measurements are basically measurements requiring patient's or provider's assessment of their medication-taking pattern. The rate of adherence is measured by patients' own report and healthcare professionals' evaluation. (Velligan et al., 2007). One of the most common limitations associated with subjective measurements is underreporting of non-adherence by patients in order to avoid disapprobation from their healthcare professionals (Vik, Maxwell, & Hogan, 2004).

Objective measurements use methods such as electronic monitoring, pill counts, biochemical measures secondary and database analysis. These are usually thought to be an more accurate than subjective methods (Vermeire et al., 2001). As a result of this, objective methods should be used to prove and correlate the measures based on subjective methods. However a meta-analysis on medication adherence outcomes stated that employing a multi-subjective-measure method may show higher sensitivity but not

accuracy compared to using one objective measure (Dew et al., 2009). In summary, methods based on both subjective and objective measures have their positives and negatives and hence for effective measurement of adherence they should be used in combination. Below is a further discussion of the details of objective and subjective methods of measuring adherence rates.

Objective Measurements

Direct measures have been observed to be the method of measuring adherence with the highest accuracy and can be used to provide physical proof that the patient has adhered to their prescribed medication, they however have many setbacks in respect of their use. They reveal a Yes/No finding without exposing any non-adherence pattern or what causes it (Farmer, 1999). These tests are sometimes very intrusive and may cause anxiety in patients.

When using these methods, drug metabolism should be considered. For instance, drugs used for managing neuroleptic and psychiatric conditions may have traces in blood that can be detected even long after the patient has stopped taking the medication. Plasma concentrations of drugs vary after different people take the same dose of the same drug because individuals different physiological states and metabolic rates. More so, there are difficulties sometimes in quantification of the plasma levels of some drugs. For example, a biological marker such as riboflavin, is simply non-quantitative for detection (Diaz et al., 2001). Furthermore, the accuracy of the assay can be influenced by drug-drug interactions as well as drug-food interactions. Therefore, in psychiatric patients and those under multiple drug regimen, these direct methods are generally unsuitable even when they are on hospital admission.

In cases where patients only take the medication just before the upcoming tests, bias can be introduced. White coat adherence (Osterberg & Blaschke, 2005) is a one phenomenon that needs to be considered in studies using direct measures or healthcare professionals' visits. This is usually reported as the "improved patient adherence to treatment around clinic visits" (Modi, Ingerski, Rausch, Glauser, & Drotar, 2012). Modi et al., found an average adherence rate of 88% before clinic visit. They also showed that adherence rates after the clinic visit reduced to 86%. However adherence rates decreased significantly to 67% after a month (Modi et al., 2012).

Medication Events Monitoring System (MEMS)

Over several decades, a variety of models have been designed but the basic principle of the medication events monitoring system (MEMS) is that a microprocessor embedded would record the time and date whenever the medicine is taken from the pill container and the assumption is that a specific dose has been taken by the patient at that particular time (Svarstad, Chewning, Sleath, & Claesson, 1999).

This measure is objective and has been highly accurate in several studies over the years (Svarstad et al., 1999). It assists in determining whether the low adherence is intermittent or regular. It also helps identify any other unusual pattern of medication taking. In addition, when there is a situation of partial adherence it is able to give an idea of the number of daily doses taken or missed. Based on these features, MEMS is somewhat more beneficial than both biochemical and self-report measures (Farmer, 1999). It is used in most cases as a reference standard for assessing the validity of other adherence measures. Furthermore, using methods such as pill count comes with a higher likelihood of deception since the patient may open the bottle each day at the particular time and

dispose off the medication (if they want to) in order to ensure same "adherence" pattern is recorded (Diaz et al., 2001)

One drawback of MEMS is that, the bulk nature of the container can be an impedance for patients and make them fail to carry their medicines when they are outside their homes. Again, this can make patients move their medicines into another container and defeat the purpose of MEMS (Diaz et al., 2001). Furthermore, the container itself may serve as reminder to the patient that they are being monitored. This has been found to cause anxiety, somatic complaints and stress in some cases (Farmer, 1999).

Pill Count

This is an indirect and objective measure. Between two clinic visits, the number of dosage units that the patient may have taken is counted. The adherence ratio is computed by comparing the total number of dosage units dispensed to the individual initially with the units taken by the individual at the end of the period (Vik et al., 2004).This method is simple and has a low cost. As a result, it is more popular in comparison with other methods. However, it is not without limitations.

To begin with, it can be employed for as a measure of adherence to several formulations, including but not limited to tablets, actuated inhaler and capsules. This approach however is not feasible in estimating adherence rates in patients who have been asked to take their medication as and when necessary (prn) or those taking medicines without discrete dosages (Vik et al., 2004).

Moreover, underestimation of adherence occurs frequently, since the equation used in this method has the denominator being the dispensed date without considering the

possibility of having leftover medication. It is a usual practice especially for patients with chronic conditions to refill the medicines before it actually runs out (Vik et al., 2004). Moreover, in this case, the threshold value to distinguish between adherence and non-adherence, is usually arbitrarily generated (Farmer, 1999). This can result in disparities in determining patient's adherence rates measured among different studies also measuring adherence.

Both pill count and MEMs operate based on a similar principle and that is the removal of the dosage unit translates to actual taking of the medicine. However comparative studies done for pill count and MEMS showed that with pill count, medication-taking patterns are not generated as MEMs does. Removal of the required number of units from a medication container does not directly translate into the patient adhering with the dosing regimen (van Onzenoort et al., 2010;Lee et al., 1996). Another drawback with the pill count besides its inability to describe the pattern of adherence is the inability to describe its causes (Farmer, 1999).

Pill count has been shown to have a more accuracy comparatively to other methods which are subjective. That notwithstanding, pill count been replaced by MEMS as a reference standard for validating other methods of assessing adherence in the 1990's (Farmer, 1999).

Questionnaires and Scales

These approaches are subjective and were initially constructed to reduce the drawbacks of other subjective measures by standardizing adherence measurements to a particular drug regimen (Farmer, 1999). Validation of such questionnaires are done generally using

other measures, both objective and subjective, and with several versions to allow for a variety of disease conditions. Patients or their caretakers usually fill these self-report questionnaires. However, patients with low literacy may have difficulties completing these questionnaires (Nguyen, Caze, & Cottrell, 2014).

Nguyen et al. in a systematic review, evaluated 43 self-report adherence scales that were validated (Nguyen et al., 2014). 40 of these 43 self-report scales measured the degree of execution of a dosing regimen, including the commencement, execution, and discontinuance stages. They grouped the scales into 5 main groups. The first being those that assessed only medication-taking behaviors and the second group being those that assessed only barriers to adherence. The third, fourth and fifth groups were respectively those that assessed both medication-taking behavior and adherence barriers, both barriers to and beliefs associated with adherence and only beliefs associated with medication adherence and

Other scales, like the 8-item Morisky Medication Adherence Scale (MMAS), Medication Adherence Questionnaire (MAQ) and the Brief Medication Questionnaire, assess adherence by ranking the level of adherence rather than setting an absolute threshold for adherence. Researcher's expertise or clinical outcomes can be used to determine the rationale for the adherence ranking.

Eight-Item Morisky Medication Adherence Scale (MMAS-8)

The 8-item MMAS (MMAS-8) was created by Morisky et al.in 2008. It is made up of eight questions with first seven requiring Yes/No answers. The eighth question is a 5-point Likert like answer. Medication-taking behaviours, including those associated with

underutilization, such as forgetfulness is assessed. As a result, adherence barriers can be detected more clearly (Tan, Patel, & Chang, 2014). Ninety three percent sensitivity and fifty three percent specificity were recorded while validating in "very low income minority patients treated for hypertension seeking routine care in a clinic setting" (Morisky, Ang, Krousel-Wood, & Ward, 2008). MMAS was also validated with high validity and reliability in patients with other long-term disease conditions (Tan et al., 2014). As a result, it is amongst the most popular self-report measure for adherence to medication.

Together with information on blood pressure control, MMAS must be able to help detect medication non-adherence and aid in controlling blood pressure (Morisky et al., 2008). As a result, it is proposed to serve as a screening tool for some pre-tested diseases in the clinic setting.

2.5 Medication adherence improvement strategies

Medication adherence improvement strategies may be broadly categorized into 5 groups namely behavioural interventions, integrated care, educational, risk communication, self-management interventions and packaging and every day reminders (Costa et al., 2015). Below is an elaboration on these interventions:

Behavioral interventions

The main aim of behavioral interventions is to transform patients' behavior especially relating to daily life. In the case of medication adherence, the objective is to change patients' attitude toward treatment (NICE, 2007). Interventions are defined by cognitive–behavioral methods and treatments concentrated on impaired emotions, cognizance and

behaviors with the aim to improve healthy lifestyles and bring about positive modifications toward treatment and symptoms (Clarkesmith, Pattison, & Lane, 2013).

Interventions aimed at changing behaviour to enhance medication adherence have shown conflicting results (Nieuwlaat et al., 2008). Interventions that integrate multiple components are most effective but are not without the limitations of being quite expensive and not being easy to execute in daily clinical practice (Nieuwlaat et al., 2008). As a result, there is an expanding interest in the development of effective interventions aimed at behavioral changes, especially for the elderly for whom behavioral counseling is given directly to patients by health care staff. These health care staff are specially equipped in cognitive behavioral techniques, despite the professions. Behavioral and counseling components are incorporated and combined in more well explained interventions. Home visits and follow-up telephone calls seem to have a positive impact, especially in conjunction with educational components. It provides planning and support with integrated before and after discharge interventions that help improve adherence (Garcia-Caballos, Ramos-Diaz, Jimenez-Moleon, & Bueno-Cavanillas, 2010;Mistiaen, Francke, & Poot, 2007).

Educational interventions

Educating patients has become an important component of medicine in recent times. In various studies patient education has been shown to improve medication adherence (Holman, 2004).

Education of patients must be done by health care staff in order to improve adherence to medicines. Adequately explaining to patients how they should take their medicine and

addressing with individuals any issues of unwillingness to take their medicines and discussing their knowledge and beliefs with respect to their own health and related therapies (Ratanawongsa et al., 2013).

Information and communication with respect to medicinal treatment and diseases are important. Therefore, the thinking that directs strategies to increase adherence should not only concentrate on individuals but also on the whole health care system. Progressively this approach is being accepted. In order to realized improved adherence, the provision of information to the individuals about issues bordering around their conditions and falls in therapy is critical.

Integrated care interventions

In several studies, integrated care has been defined as a group of techniques and organizational models that improve alignment, collaboration and connectivity among health care staff at various levels including financing, administrative and health provider (Costa et al., 2015). Ouwens et al. in a review, threw more light on the following as being among the most common factors encountered when implementing integrated care interventions: multi-sectoral nature of the health care providers team; multi-sectoral clinical pathways and responses, health care staff education, self-management support and patient education (Ouwens, Wollersheim, Hermens, Hulscher, & Grol, 2005).

The objective of integrated care interventions is to increase quality of care. It also aims to increase health care gratifications and cost-effectiveness for providers and patients who have complicated health issues (Leutz, 1999). Although using integrated care has several benefits, it has been proven to be a difficult task. This is partly as a result of the complex

nature of various health care systems. As a result, health care providers occasionally find it daunting to coordinate their efforts in providing unsegregated care plans for patients. To successfully implement integrated care intervention and achieve excellent quality of care, collaboration and coordination amongst healthcare staff is necessary (Glouberman & Mintzberg, 2001). Stakeholders who are usually enlisted to have a discourse on adherence improvement strategies for patients involve the doctors, pharmacists and health insurers. (Glouberman & Mintzberg, 2001). Several studies have shown that the likelihood of hospitalization as well as length of stay in the hospital can be dereased when integrated care plans are implemented by multi-disciplinary teams (Kesteloot, 1999). In addition, the coordination by members of the team is very critical to the success of an intervention and may affect the efficiency of any treatment strategy of this type (Büla et al., 1995).

Self-management interventions

Chronic disease prevalence has over the years increased and this has raised some concerns to policy formulators and providers of health care. Hence the decision to invest the more resources to manage such patients (Richard & Shea, 2011).Wilkinson and Whitehead (Wilkinson & Whitehead, 2009) define self-management as:

"the ability of the individual, in conjugation with family, community, and health professionals, to manage symptoms, treatments, lifestyle changes, and psychosocial, cultural, and spiritual consequences of chronic disease".

Self-management considers a variety of ideas including self-care, adherence, patient education, self-monitoring, collaborative care and health behavior change. The intention

is to keep patients informed about their own pathological conditions in order to stimulate them to play a more active rather than passive role in managing these conditions (Richard & Shea, 2011). Lifestyle choices, self-monitoring, access to records and adherence to medication are all care areas that are directly under patients' control (Wilkinson & Whitehead, 2009). In self-management interventions, the use of technological devices is increasing in comparison with physical meetings. Telephone support/counseling alone, telemedicine, tele-care monitoring, cell phones/text messaging and internet-based interactive computer-operated communication on health are all examples of technology based self-management interventions.

Risk communication interventions

Risk, defined as the discerned likelihood or susceptibility to harm is an important construct in many descriptive postulates of health behavior (Shreck, Gonzalez, Cohen, & Walker, 2014). It is a central aspect of deliberate non-adherence to medicines (Lehane, McCarthy, Collender, Deasy, & O'Sullivan, 2013). Literature on adherence, have shown that patients' behavior and in this case, medication taking may be affected by the person's perception of the risk related with the behavior and the corresponding positive or negative results. Effective conveyance of risk by health care staff is therefore essential to ensure that information about benefits and risks are conveyed correctly to empower patients make informed decisions. The complexity of risk perception is multidimensional in nature and as such must be looked from both affective and cognitive perspectives (Lehane et al., 2013). Clinicians' perception of risk and that of patients have often been contradictory (Lehane et al., 2013). Considering the importance of this

phenomenon on the possible change of medication adherence behavior, interventions to improve risk communication are the critical (Walker, Mertz, Kalten, & Flynn, 2003).

Packaging and daily reminders

The use of patient reminders helps greatly to improve the health of people by reminding them to take their drugs or to program medical appointments and screenings (Kendall et al., 2014). The different types of reminders include phone call reminders, pagers, text messages, interactive voice response (IVR) systems, medication boxes, video telephone calls or personalized blisters (West, Fenerty, Feldman, Kaplan, & Davis, 2012). Some studies have demonstrated that often most patients are non-adherent with their medicines as required and some of them fail to remember to refill or take their medication in most instances. Several studies have been conducted to investigate a variety of tools aimed at increasing medication adherence. A pilot study was done by Reidel et al to determine whether an IVR can help improve mediation adherence. In this study, the automated IVR system called the patients and reminded them of taking their medicines or refilling their prescribed medicines after information about their demographic, mobile phone and medicines had been inputted in an IVR system. The study reported that the system was unsuccessful in improving adherence to medications. This failure was attributed to technical such as incorrect call time etc. (Reidel, Tamblyn, Patel, & Huang, 2008).

Text message reminders as a tool for improving adherence

One of the ways to deliver electronic reminders in practice is through Mobile telephone text messaging. The technology has been in existence for some time now and can therefore be conveyed to any mobile phone. Mobile telephones usage is increasing astronomically and in one study, there were about seven billion mobile phone users as at

the end of 2014, approximately the world's population (Thakkar et al., 2016). This technology is widely used by individuals within every socioeconomic class (Koivusilta, Lintonen, & Rimpelä, 2007), age groups and continents (Goggin, 2006).

The use of text messages in recent times as a prompt and support in a variety of health programs has increased. Several analyses have demonstrated positive benefits of text message reminders. However till date only narrative analyses of text messages and other electronic interventions such as text messages, beepers, audiovisual reminders and pagers have been issued to date**.** So far no meta-analysis have been published on the effect of text message reminders and other electronic interventions have been published (Kannisto, Koivunen, & Välimäki, 2014)(Tao, Xie, Wang, & Wang, 2015)

CHAPTER THREE

METHOD

3.1 Study Design

Cross-sectional study design was used for this study

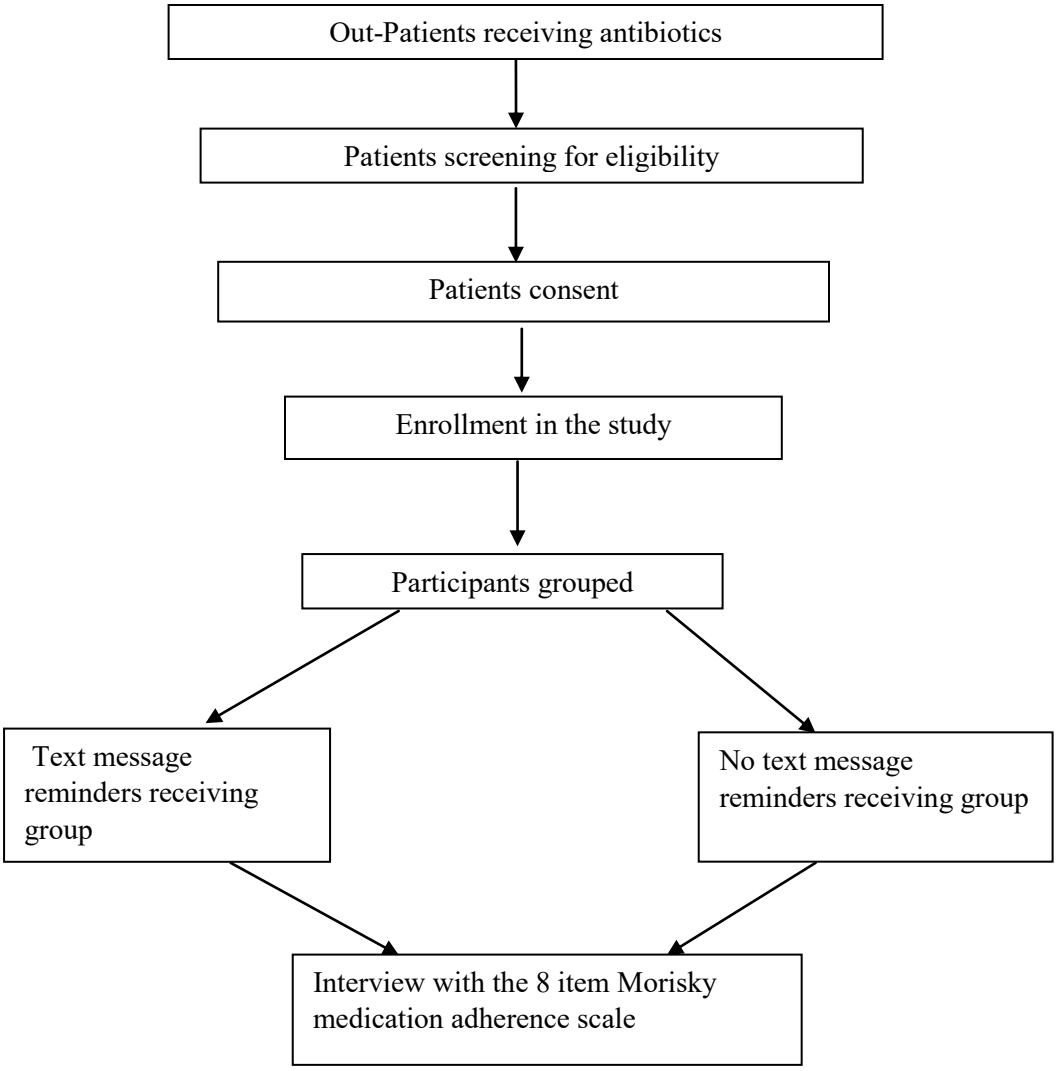

Fig 2. Schematic diagram of study design

The study was carried out at the pharmacy department of Tema General Hospital. The study participants were out patients who were dispensed one or more antibiotics for a

maximum duration of 7 days. The study was carried out over a period of 6 weeks and quantitative methods were used for data collection. Participants were randomly assigned to two groups; those who were to receive text message reminders and those who were to receive no text message reminders. Patients within the text message group received text messages reminding them to take their antibiotic whilst those within the no text message group received no text message reminders. Text messages were sent twice daily to all participants within the text message receiving group who were to take their antibiotics more than once in a day. The messages were sent at 7am and 7pm daily. For participants within the text message receiving group whose medication required a once daily dosing, text message reminders were only sent once daily at 7am. Participants within the text message receiving group received text message reminders for the duration of their antibiotic therapy.

3.2 Study Location

The study was carried out at the Pharmacy Department of the Tema General Hospital in Tema. Tema is a metropolis in the Greater Accra Region of Ghana. The population of Tema was projected to be at 345622 in 2018 according to the 2010 population census (Ghana Statistical Service, 2013). The literacy rate of Tema is high (91%) making it suitable for the study because most patients/care givers are likely to be able to read text messages (Ghana Statistical Service, 2013). Also, about 76.5% of the population of Tema uses mobile phones making text message reminders more accessible to most patients.

Tema General Hospital is the largest government hospital in the Tema metropolis and serves the population of Tema and other surrounding communities. It has a 300 bed capacity and has a heavy OPD clinic which sees about 300 out-patients daily (District

Analytic Report, 2014). About 30 percent of these out-patients come with infections for which antibiotics are prescribed making this study site suitable for this study since the target population of antibiotic users can be reached (Tema General Hospital Annual report, 2017).

The hospital has seven main departments and these are; the dental, ophthalmic, medicine, surgery, obstetrics and gynaecology, pharmacy and diagnostics departments. The pharmacy department of the hospital offers pharmaceutical care services to patients who patronize the facility. The pharmacy is well stocked with various types of drugs including antibiotics. Data from the pharmacy tally cards also suggest a high consumption of antibiotics suggesting the target population can be obtained in this facility. The department has four outlets including the OPD pharmacy, diabetic clinic pharmacy, in-patient pharmacy and ART pharmacy. However, the OPD pharmacy is the largest amongst all the pharmacy units. This makes the OPD pharmacy suitable for this study.

3.3 Study Population

Participants of this study were out patients receiving antibiotics for a maximum of seven days from the OPD pharmacy.

Inclusion Criteria

- Individuals aged 18 years and above
- Out-patients
- Individuals who use mobile phones with text messaging
- Individuals who could read
- Individuals who have been dispensed at least one antibiotic

Exclusion Criteria

- Patients who did not administer their own drugs
- In patients
- Patients receiving antibiotics for more than seven days

3.4 Study Variables

The dependent variable that was measured in this study was adherence to antibiotics amongst participants. This was measured using the 8 item Morisky adherence scale. Independent variables considered in this study included demographic factors, disease related factors, treatment regimen and the text message reminders.

Dependent Variables

- Adherence was measured as a dichotomous variable (Adherent and Non-adherent).

Independent Variables

- Demographic factors: Age, Sex, Educational level, marital status.
- Type of disease: The disease being treated.eg. Upper respiratory tract infections, lower respiratory tract infections, urinary tract infections, gastrointestinal tract infections, sexually transmitted infections etc.
- Treatment Regimen: Number of prescribed antibiotics, dosing frequency of antibiotics, antibiotic type, duration of therapy.
- Text message reminders: Receipt of text message reminder, frequency of text message, type of text.

Table 3-1.Table showing variable type and the scale of measurement

	Variable name	Type of variable	Scale of measurement
Dependent variable	Adherence	Categorical	Non-adherent (<6) Adherent (>=6)
Independent variables	Age	Continuous	Years
	Sex	Categorical	Male/female
	Educational level	Ordinal	No education Primary level Secondary level Tertiary level Postgraduate level
	Marital status	Categorical	Single Married Divorced Widow/widower
	Type of disease	Nominal	URTI, LRTI, UTI, GITI etc.
	Text message	Categorical	Yes No
	Treatment regimen		
	Number of antibiotics	Continuous	
	Dosing frequency	Categorical	Twice daily Thrice daily Four times daily Others
	Type of antibiotic	Nominal	
	Duration of therapy	Categorical	1-3 days 4 days 5 days 6 days 7 days

3.5 Text Message Reminder

The message contained in the text message that was sent to participants was ***"please remember to take your antibiotic as prescribed".*** This simple message was designed based on similar studies which deployed similar messages to serve as a reminder for patients to take their antibiotics and helped improve adherence to medicines (Raifman et al., 2014). However, the message was slightly modified to specify antibiotics for the purpose of this study. The M-notify application software which is an internet based platform used for sending text messages was used in deploying the text messages to participants. The time and duration for sending messages were entered into the software and so the messages were sent automatically once participants' phone numbers were uploaded into the application. Participants within the text message group who had a more than once daily dosing antibiotic, received this message twice daily whilst those who had a once daily dosing antibiotic received the message once in a day. The first at 7am and second at 7 pm. These served as reminders for all participants within the text message group irrespective of the dosing frequency of antibiotic received.

3.6 Sampling Procedure

Due to the fact that sample frame for out-patients receiving antibiotic therapy may be practically difficult before commencement of the study, a purposive sampling method was used to recruit study participants based on the inclusion criteria set for the study and given consent. The population for this study was every patient dispensed one or more antibiotics at the pharmacy. Research assistants were positioned at the 3 dispensing windows at the pharmacy and so had access to patient prescriptions and were signaled by the dispenser when the medicines dispensed included an antibiotic. The research

assistants then recruited patients into the study based on the eligibility criteria set. Recruitment of participants was done from the 13th to 22nd of June, 2018 between the hours of 8am and 2:30pm. Each day during the data collection period, eligible patients were given the opportunity to read consent form and those who agreed to be included in the study gave their consent by signing the consent form. After signing the consent form, they were then interviewed using a questionnaire to collect basic demographic data. Recruited participants were assigned randomly to two groups i.e. the text message reminder and no text message reminder using the graph pad software to randomly pick the I.D numbers of the participants to be put in the text message group. This was done until the minimum sample size of 200 was achieved.

3.7 Sample size

Sample size was estimated based on previous study by Strandbygaard et al., showed adherence rate to be 60% in the no text message group and that of the text message group to be 80% (Strandbygaard, Thomsen, & Backer, 2010). A power of 80% at an alpha level 0.05 was inputted in the formula below.

$$n = [z_{\alpha/2}\sqrt{2p^*q^*} + z_{\beta}\sqrt{(p_1q_1 + p_2q_2)}]^2 / \Delta^2$$

n = sample size for one sample

$z_{\alpha/2}$ = z value for a two-sided test corresponding to the chosen alpha

z_{β} = z value for a one-sided test for the chosen β

p_1 = estimated proportion for first population

p_2 = estimated proportion for second population

p^* = mean estimated proportion $(p_1 + p_2)/2$

Δ = difference being measured

Inputting the above into the equation, the minimum sample for each group will be 81. Adjusting for 20% non-response and loss to follow up increased the sample size of each group to 100 and hence a total of 200 participants.

3.8 Data Collection tools

Two types of questionnaires were used in to collecting data. The first one was used to collect patient information (demographic data, type of disease, antibiotics etc.) and the second was the 8-item Morisky adherence scale which was used to assess adherence. Both questionnaires are attached in the appendix.

3.9 Data Collection

Each participant was interviewed a by trained research assistant using the questionnaire (Appendix 3) to collect demographic data. Treatment regimen data was filled out in the questionnaire by research assistants as well at the point of recruitment from patient folder and prescription. Information collected each day was entered into excel and patients randomly assigned to groups that same day. Follow up interviews were conducted via telephone a day after the expected date of completion of treatment. This was done using the 8-item Morisky medication adherence scale. Data cleaning was done to remove all duplicate records as a result of double entries and also to help identify errors in data records that must be removed manually

3.10 Adherence

Adherence was measured using the 8 item Morisky adherence scale attached in appendix 3. This is a self-reporting assessment scale. The scale is articulated to escape a yes saying bias. The response choice is yes or no for question 1 through to question 7 and question 8

has a 5 point Likert response scale. A "No" response scores 1 and a "yes" response scores 0 except for question 5 in which a "yes" response scores 1 and "No" response scores 0. The total score of the patient was calculated and ranges from 0 to 8. The tool ranks adherence to medicines as high if patient a scored , medium adherence to medicines if a patient scored 6 or 7 and low adherence if the patient scored below 6. However, for the purpose of this study, adherence was measured as a binary variable and hence participants' total scores were dichotomized with a score of 6 or more representing medication adherence and a score below 6 representing medication non-adherence.

Telephone follow up

Participants in both text message and no text groups were followed up to assess medication adherence by telephone calls. The telephone calls were made for each participant a day after the expected date of completion of his or her antibiotic therapy. Up to 3 calls were made to a participant who could not be reached over 3 days before the participant was considered lost to follow up. The maximum duration of follow up calls was 13 minutes.

3.11 Data Processing and analysis

The data collected each day of the study period was screened and coded before entry. Data was entered using Microsoft Excel 2013. It also helped identify missing values and help ensured no errors were made. The dataset was then imported to STATA software version 15.0 for analysis.

3.12 Statistical analysis

The data collected was analyzed using STATA Version 15.0. Demographic characteristics of participants as well as treatment related factors were described using descriptive statistics. The association between categorical independent variables and adherence was analyzed using cross-tabulation and the significance tested using Chi-squared tests. Crude and adjusted odds ratios (COR/ AOR) at 95% confidence interval (CI) were estimated to determine the strength of association between text message reminders and antibiotic adherence. A *p*-value less than 0.05 will be considered statistically significant. Associations between dependent variable (adherence to antibiotics) and independent variable (text message reminders) as well as other independent variables were analyzed using multiple logistic regression model. A backward stepwise selection method was used to fit the model. The results and analyzed data were presented in a form of frequencies, tables, charts, means, standard deviation, graphs and percentages.

3.13 Data Strategy / Data Protection

Questionnaires were locked in a cabinet. Data entered in the computer were be coded and stored securely in a folder. The data on the computer was only accessible to principal investigator.

3.14 Quality Control

Pre-testing / pilot Study: The software for sending text messages, M-notify, was pretested by selecting 10 participants from Tema General Hospital to validate the accuracy of the software for deploying the text messages and also the questionnaires designed for the study. Participants were interviewed by telephone to find out if they

received the text messages at the right time and for the duration for which they were sent as a means of assessing the validity of the software. This pretesting was done to eliminate wrong questions and make both questionnaires and test-message sending software reliable before using them for the actual study.

3.15 Training of Research Assistants

Six intern pharmacists at the Tema General Hospital were used as research assistants in this study. An orientation and training was done for research assistants one week before the study commenced. Research assistants were taken through all aspects of the study including recruitment, data collection and entry. After the data entry, the data set were cleaned before analysis was run.

3.16 Ethical Consideration / Issues

Ethical approval was obtained from the Ghana Health Service Review Committee before the study commenced. The research proposal was sent to the committee and application fee paid.

Participants' consent was sought before recruitment into the study. Data collected was only used for research and academic purposes. Confidentiality was ensured by making sure participants' identity and contact details were kept anonymous when the results were presented or published. Filled questionnaires were kept securely in a cabinet and only accessible to principal investigator. Softcopies of data collected were coded and stored in a locked file on a computer with passwords only accessible to principal investigator.

3.17 Voluntary Withdrawal

Participants were at liberty to withdraw from the study at any time without any penalties.

3.18 Compensation

No material or financial benefits was given to participants before or after patients had been recruited.

3.19 Declaration of conflict of interest

The principal investigator had no conflict of interest in this study.

3.20 Dissemination of findings

The results of this research was submitted to the School of Public Health in partial fulfilment

of the requirements for the award of a Master of Public Health Degree. The findings will also be written for publication in a journal.

CHAPTER FOUR

4.1 RESULTS

A total of 204 outpatients aged 18 to 79 years from the Tema General Hospital OPD Pharmacy who were prescribed antibiotics for 3 to 7 days and who consented were recruited into the study. Participants were recruited from the 13th to 22nd June, 2018. Eighteen participants were lost to follow up after 3 follow up telephone calls were unsuccessful over 3 days after the intended day of completion of antibiotic therapy. The response rate was 91% and therefore, the analysis for adherence was done on 186 participants who responded to the follow up calls.

4.2 Demographic and socio –economic characteristics of participants.

The mean age of participants was 42.8 years (SD 17). As shown in Table 4-1, there was no significant difference between the groups for the mean age, educational level, marital status, employment status and participants taking medicines for chronic conditions, (*p* >0.05). There was barely a significant difference in the sex distribution among the groups (*p* = 0.052).

Majority of the participants (68%) were females, married (57.8%) and had up to JHS/secondary school education. Only twenty-eight percent (58/204) of participants were taking medicines for chronic conditions.

Table 1: Demographic and Socioeconomic Characteristics of Participants at baseline

VARIABLE	TOTAL	NO TEXT MESSAGE	TEXT MESSAGE	P VALUE
Age mean (SD)	42.8(17)	44.2 (16)	41.3(17)	0.2209
Sex n (%)				
Male	65 (32)	27 (25.7)	38 (38.4)	0.052
Female	139 (68)	78 (74.3)	61 (61.6)	
Educational level n (%)				0.636
No Education	6 (2.9)	3 (2.9)	3 (3)	
Primary/Elementary	60 (29.4)	32 (30.5)	28 (28.3)	
JHS/Secondary	84 (41.2)	39 (37.1)	45 (45.5)	
Tertiary	54 (26.5)	31 (29.5)	23 (23.2)	
Marital Status n (%)				0.591
Single	76 (37.3)	39 (37.1)	37 (37.4)	
Married	118 (57.84)	60 (57.1)	58 (58.6)	
Separated/Divorced	5 (2.5)	4 (3.81)	1 (1)	
Widow/widower	5 (2.5)	2 (1.9)	3 (3)	
Employment Status n (%)				0.624
Unemployment	28 (13.7)	14 (13.3)	14 (14.1)	
Part-time employed	16 (7.8)	11 (10.5)	5 (5.1)	
Full-time employed	113 (55.4)	56 (53.3)	57 (57.6)	
Student	18 (8.8)	8 (7.6)	10 (10.1)	
Retired	29 (14.2)	16 (15.2)	13 (13.1)	
Participants taking medicines for chronic condition(s) n (%)				0.328
No	146 (71.6)	72 (68.6)	74 (74.8)	
Yes	58 (28.4)	33 (31.4)	25 (25.2)	

4.3 Disease and treatment related factors

Antibiotic and infection categories across the text message receiving group as well as no text message receiving groups are shown in Table 4-2 below. There were no significant differences between both text message receiving and no text message groups for duration of treatment, number of antibiotics and dosing frequency ($p > 0.05$). However, there was significant difference between the two groups for category of infection ($p = 0.034$) and type of antibiotic ($p = 0.012$).

Table 2: Comparison of Treatment Related factors in Text message and No text message groups at baseline

Variable	Total n (%)	No Text message group n (%)	Text message group n (%)	*P* value
Category of infection				0.034
Dental infection	14 (6.9)	6 (5.7)	8 (8.1)	
Gastro-Intestinal Infection	52 (25.5)	28 (26.7)	24 (24.2)	
Lower Respiratory Tract Infection	8 (3.9)	5 (4.8)	3 (3.0)	
Sexually Transmitted Infection	14 (6.9)	11 (10.5)	3 (3.0)	
Skin Infection	16 (7.8)	13 (12.4)	3 (3.0)	
Upper Respiratory Tract Infection	78 (38.2)	35 (33.3)	43 (43.4)	
Urinary Tract Infection	12 (5.9)	5 (4.8)	7 (7.1)	
Ear Infection	9 (4.4)	2 (1.9)	7 (7.1)	
Eye Infection	1 (0.5)	0 (0.0)	1 (1.0)	
Duration of treatment				0.186
3 days	21 (10.3)	10 (9.5)	11 (11.1)	
5 days	77 (37.8)	34 (32.4)	43 (43.4)	
6 days	2 (1)	2 (1.9)	0 (0.0)	
7 days	104 (51)	59 (56.2)	45 (45.5)	
Number of antibiotics				0.352
1	167 (81.9)	84 (80)	83 (83.8)	
2	35 (17.2)	19 (18.1)	16 (16.2)	
3	2 (1)	2 (1.9)	0 (0.0)	
Dosing Frequency				0.184
Once daily	20 (9.8)	10 (9.5)	10 (10.1)	
Twice daily	130 (63.7)	69 (65.7)	61 (61.6)	
Thrice daily	42 (20.6)	17 (16.2)	25 (25.3)	
4 times daily	12 (5.9)	9 (8.6)	3 (3.0)	

Nine types of infections were recorded as the reason for antibiotic treatment amongst study participants. The most common infection recorded amongst participants was upper respiratory tract infection accounting for 38.2% (78/204). 43.4% (43/99) of the participants within the text message receiving group had upper respiratory tract infection, whilst 33.35 (35/105) within the no text message receiving group had upper respiratory tract infection. Fig 4.1 gives a graphical representation of the distribution of infections amongst participants.

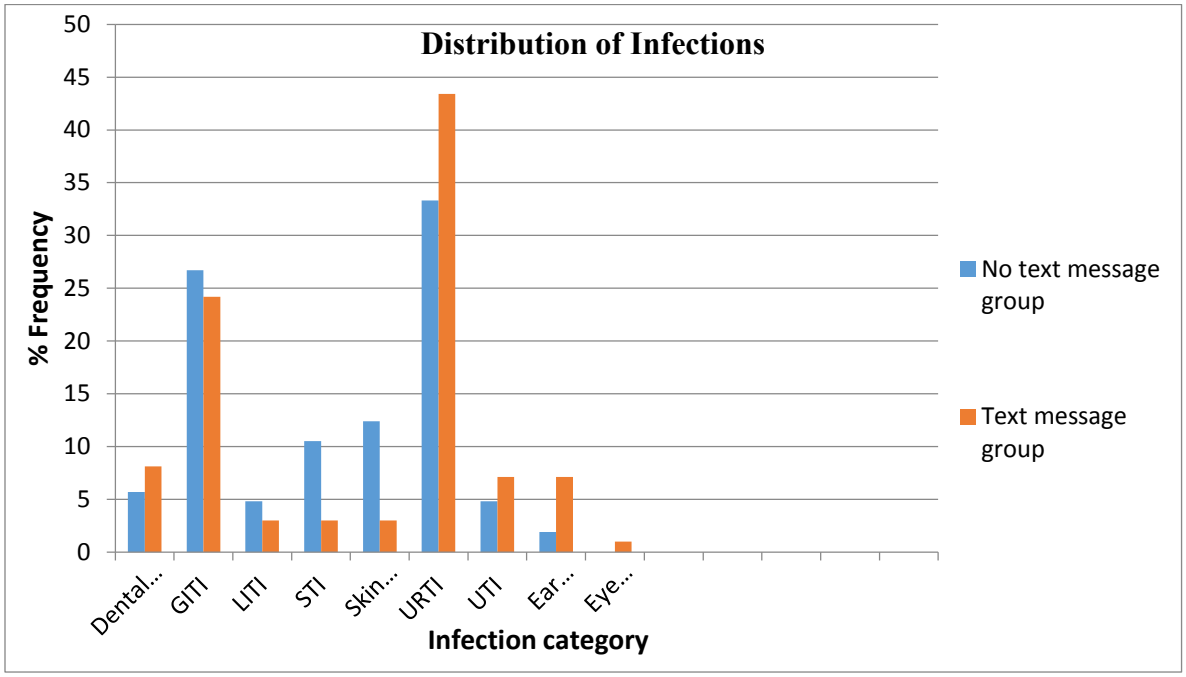

Fig.4-1 Distribution of infections in both Text message and no text message groups

As shown in Table 4-3, 7 different antibiotics were dispensed singly to participants with the most common dispensed single antibiotic being co – amoxicillin 25% (5/204) followed by cefuroxime 24% (49/204). Most participants 81.9% (167/204) received one antibiotic.

Ten different combinations of these antibiotics were also dispensed to participants with the most common combination being doxycycline and ciprofloxacin combination 4.4% (9/204). Dosing of antibiotic(s) was predominantly twice daily 63.7% (130/204) and this was same in both groups.

Table 3: Distribution of antibiotics in Text message and No text message groups at baseline

Variable	Total n (%)	Number of different pills	No Text message	Text message	P value
Antibiotic					0.012
Amoxicillin	10 (4.9)	1	4 (3.81)	6 (6.06)	
Azithromycin	22(10.8)	1	10 (9.5)	12 (12.1)	
Cefuroxime	49 (24.0)	1	20 (19.1)	29 (29.3)	
Ciprofloxacin	15 (7.4)	1	10 (9.5)	5 (5.1)	
Clindamycin	7 (3.4)	1	7 (6.7)	0 (0.0)	
Co-amoxicillin	51 (25)	1	25 (23.8)	26 (26.3)	
Doxycycline	4 (2)	1	4(3.8)	0 (0.0)	
Metronidazole	9 (4.4)	1	4 (3.8)	5 (5.1)	
Amoxicillin & metronidazole	7 (3.4)	2	1 (1)	6 (6.1)	
Azithromycin & cefuroxime	2 (2)	2	2 (1.9)	0 (0.0)	
Azithromycin & co-amoxicillin	5 (2.5)	2	1 (1)	4 (4.0)	
Azithromycin & flucloxacillin	1 (0.5)	2	1 (1)	0 (0.0)	
Ciprofloxacin & clindamycin	4 (2)	2	2 (1.9)	2 (2)	
Ciprofloxaxin & Doxycycline	9 (4.4)	2	8 (7.6)	1 (1)	
Ciprofloxacin, doxycycline & metronidazole	2 (1)	3	2 (1.9)	0 (0.0)	
Ciprofloxacin & metronidazole	1 (0.5)	2	0 (0.0)	1 (1)	
Co-amoxicillin & metronidazole	4 (2.0)	2	3 (3)	1 (1)	
Doxycycline & metronidazole	2 (1.0)	2	1 (1)	1 (1)	

Non-Adherent= Morisky adherence score of <6

Fifty-one percent (104/204), representing majority of the antibiotics were prescribed for a 7-day duration. Majority of the participants within the text message receiving group 45.5% (45/99) were prescribed antibiotics for 7 days and 56.2% (45/105) of the no text message receiving group were prescribed antibiotics for 7 days.

4.4 Adherence Outcome

The 8 item Morisky adherence scale ranks adherence to medicines as high if a patient scored 8, medium adherence to medicines if a patient scored 6 or 7 and low adherence if the patient scored below 6. However, for the purpose of this study, adherence was measured as a binary variable and hence participants' total scores were dichotomized with a score of 6 or more representing medication adherence and a score below 6 representing medication non-adherence. Table 4-4 summarizes the adherence outcome amongst study participants in both text message and no text message groups. The proportion of participants adherent i.e those who scored 6 and above amongst study participants was 54% (95% CI; 38.9-53.2%). The adherence rate amongst the text message group was 62.5% whereas that of the no text message group was 45.9% and this difference was statistically significant (p = 0.024).

Table 4: Adherence outcome in text message and No text message groups

Variable	Total n (%)	No Text message group n (%)	Text message group n (%)	P value
Adherence				0.024
Adherent	100 (54.0)	45(45.9)	55(62.5)	
Non-Adherent	88 (46.0)	53(54.1)	33(37.5)	

[1]

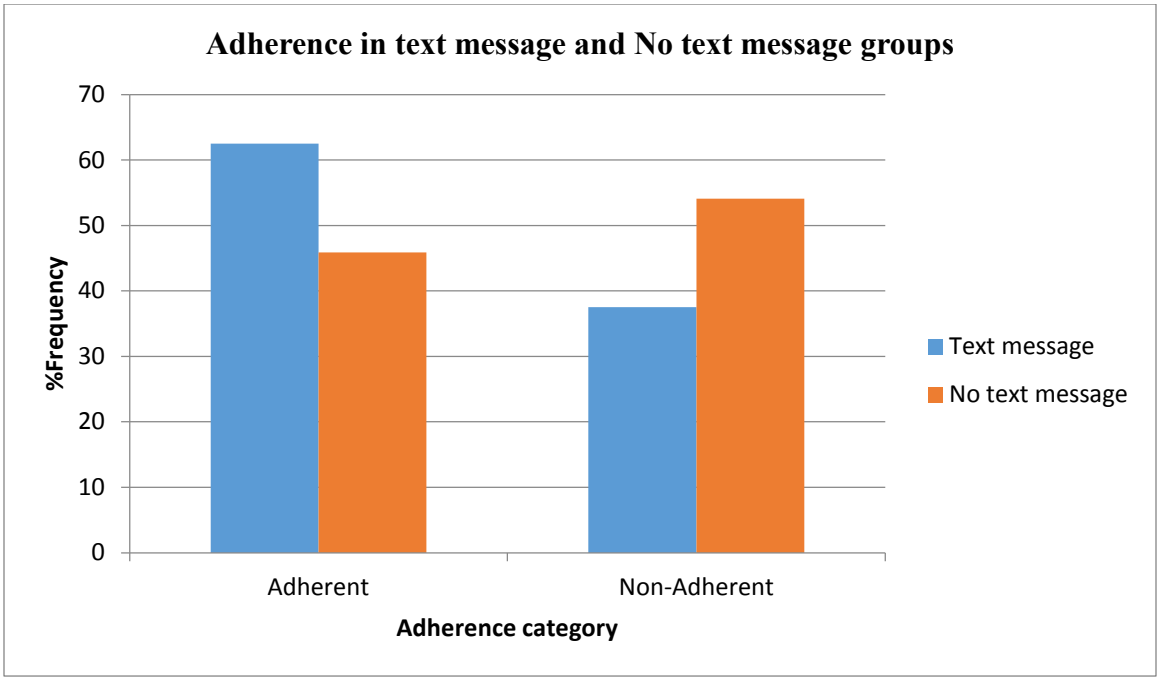

Fig. 4-4. A chat comparing Adherence rate in text message and no text message groups.

4.5 Effectiveness of Text message reminders

The multiple logistic regression analyses model which was fitted using the backward stepwise elimination method showed that the text message reminders significantly increased the odds (OR=1.9, 95% CI [1.05-3.68] *p* value 0.024) of adherence. Covariates controlled for in the model are shown in Table 4-4. The odds of adherence amongst the participants who were taking medicines for chronic conditions was 2.2 times (95% CI; [1.02-4.83] *p* value 0.045) that of those who were not taking medicines for chronic conditions and this was found to be statistically significant. For antibiotic type, odds of adherence in reference to azithromycin were found not to be statistically significant ($p > 0.05$).

[1] Adherent = Morisky adherence score of >=6
Non-Adherent= Morisky adherence score of <6

Table 5:Effectiveness of Text message reminders on adherence

Variable	%Adherent	%Non-Adherent	OR (95% CI)	95% CI	*p* value
Text Group					
No Text message group	45.9	54.1	Ref. group		
Text message	62.5	37.5	1.9	1.05-3.68	<0.05
Dosing Frequency					
Once daily	55.6	44.4	Ref. group		
Twice daily	55.8	44.2	1.7	0.12-24.19	0.689
Thrice daily	59.5	40.5	0.2	0.01-4.68	0.322
4 times daily	16.7	83.3	0.02	0.01-0.98	0.049
Chronic Medicine					
No	51.5	48.5	Ref. group		
Yes	60.4	39.6	2.2	1.02-4.83	0.045
Antibiotic					
Azithromycin			Ref. group		
Doxycycline	14.3	85.7	2.7	0.06-133.6	0.615
Clindamycin	55.6	44.4	1.7	0.05-56.6	0.780
Ciprofloxacin	64.2	35.7	1.8	0.11-29.29	0.695
Amoxicillin	57.1	42.9	1.3	0.04-38.89	0.891
Cefuroxime	36.4	63.6	0.1	0.01-1.34	0.083
Co-amoxicillin	55.6	44.4	0.3	0.02-2.92	0.251

4.6 Opinion of participants in the Text message group on the helpfulness of text message reminders.

Sixty-four percent (57/88) of participants within the Text message receiving group said the text message reminders were very helpful in reminding them to take their antibiotics whereas 14.8% (13/88) and 20.4% of the participants responded extremely helpful and somewhat helpful respectively. Table 4-5 shows participants' opinion responses and their 95% confidence intervals.

Table 6: Opinion of participants in Text message group on helpfulness of text message reminders

Participants' response	Percentage (n)	95% CI
Extremely helpful	14.8	8.6-24
Very helpful	64.8	54.1-74.2
Somewhat helpful	20.4	13.2-30.4

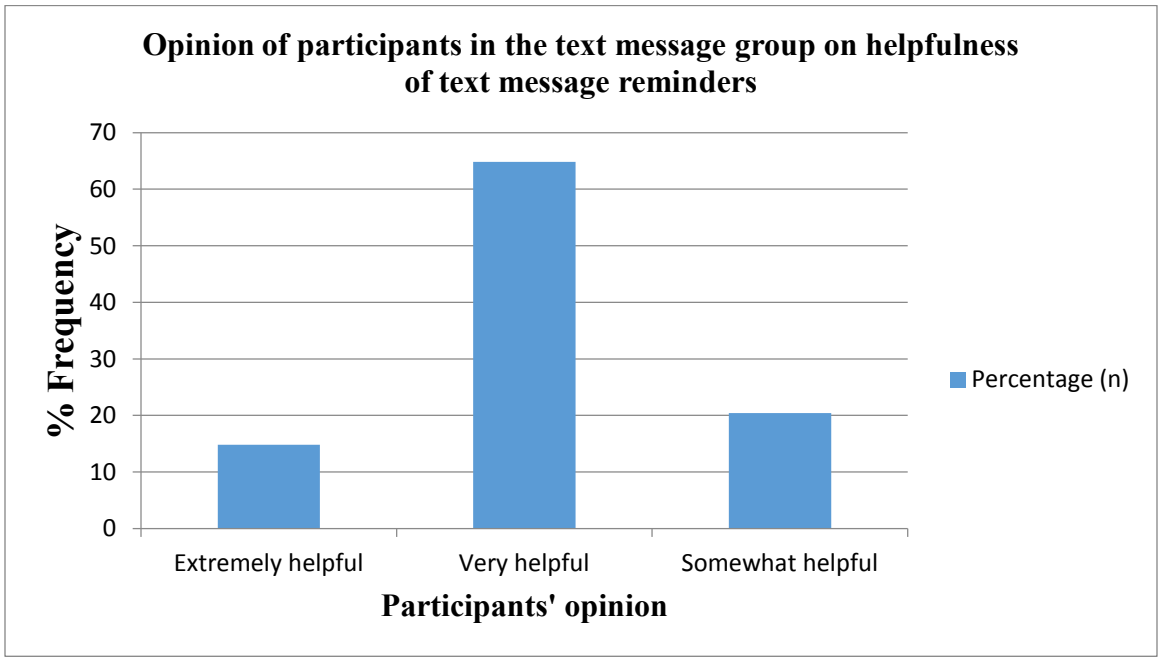

Fig. 4-5. Participants opinion on helpfulness of text message reminders

4.7 Demographic Factors associated with Participants' opinion on Helpfulness of text message reminders

As shown in table 7, demographic factors that had significant associations with participants' opinion on helpfulness of text message reminders were marital status and employment status. Seventy-seven percent of the participants who responded extremely useful were married people and this difference was statistically significant. Similarly, majority of those who responded very helpful 50.9% (29/57) were married. Only 1.8% (1/57) amongst those who responded very helpful were separated/divorced.

Amongst participants who responded extremely helpful, 30.8%(4/13), 53.9%(7/13) and 15.4%(2/13) were unemployed, full-time employed and retired respectively. For those who responded very helpful, 10.5%(6/57), 7%(4/57), 59.7% (34/57), 17.5%(10/57) and 5.3%(3/57) were unemployed, part-time employed, full-time employed, student and retired respectively. 16.7% (3/18), 44.4(8/18) and 38.9(7/18) of participants who responded somewhat helpful were unemployed, full-time employed and retired respectively. Table 6 shows the result of participants' opinion on helpfulness of text message reminders.

Table 7: Demographic factors associated with Participants' Opinion on helpfulness of text message reminders

	% (n)Participants' Opinion on Usefulness of text message reminders			
Variable	Extremely helpful	Very helpful	Somewhat helpful	P Value
Sex				0.397
Male	30.1 (4)	33.3(19)	50 (9)	
Female	69.2 (9)	66.7 (38)	50 (9)	
Marital Status				0.012
Single	23.1 (3)	47.4 (27)	11.1(2)	
Married	76.9 (10)	50.9 (29)	77.8 (14)	
Separated/divorced	0	1.8 (1)	0	
Widow/widower	0	0	11.1(2)	
Employment Status				0.004
Unemployed	30.8(4)	10.5(6)	16.7(3)	
Part-time employed	0	7.0(4)	0()	
Full-time employed	53.9(7)	59.7(34)	44.4(8)	
Student	0	17.5(10)	0	
Retired	15.4(2)	5.3(3)	38.9(7)	
Educational Level				0.629
Primary/Elementary	23.1(3)	29.8 (17)	44.4(8)	
JHS/Secondary	53.8(7)	45.6(26)	44.4(8)	
Tertiary	23.1(1)	24.6(14)	11.2(2))	
Chronic Medicine				0.460
No	76.9(10)	75.4(43)	61.1(11)	
Yes	23.1(3)	24.6(14)	38.9(7)	

CHAPTER FIVE

5.1 DISCUSSION

The results from the study have two main implications with respect to adherence to antibiotics amongst out – patients.

5.1.1 Overall adherence in both groups

Firstly, adherence to antibiotics is low among study participants. The overall adherence in both groups was 54%. There are limited studies on adherence to antibiotics in Ghana but a similar study by Donkor et al., also showed an overall adherence rate of 55%, which is quite consistent with the findings of this study (Donkor, Tetteh-Quarcoo, Nartey, & Agyeman, 2012). Another study by Suffeleto et al., also reported overall adherence rate to be 57% which is also quite consistent with the results of this study (Suffoletto, Calabria, Ross, Callaway, & Yealy, 2012). This low rate of adherence has serious implications on the health of patients and can affect efforts to reduce antibiotic resistance which is an imminent public health problem in Ghana (Raifman et al., 2014).

5.1.2 Effect of text message reminders on adherence to antibiotics

Secondly, the findings of this study show that receiving a simple text message reminder stating “please remember to take your antibiotic”, significantly increases adherence. The study showed that the proportion of participants who were adherent in the text message group was 62.5% compared with 45.9% in the no text message group. The absolute difference in adherence between the two groups was about 16.6% and was found to be statistically significant and hence there is a strong association between adherence to antibiotics and receiving text message reminders. One study done in the U.S in relation to

adherence to antibiotics and text message reminders, showed a difference of 12% in the adherence rates of patients who received text message reminders and those who did not receive text message reminders (Suffoletto et al., 2012). This relatively higher difference observed in our study may be as a result of the fact that the duration of treatment in our study was limited to 7 days compared with longer duration in the afore mentioned. As it is already shown, that longer durations of treatment are somewhat associated with non-adherence compared with shorter duration of treatment and hence the observed difference (Brown & Bussell, 2011, Vlasnik, Aliotta, & DeLor, 2005). Again, it did not include once daily dosing antibiotics which is usually associated with high adherence but this study did. More so, the variety of antibiotics that were looked at in this study were quite different and may have contributed to this difference.

The odds of adhering to antibiotics with people who received text message reminders was 1.9 times that of those who did not receive text reminders and this was statistically significant. Several studies done on other classes of medicines other than antibiotics have also shown significant difference in adherent rates between participants who received text message reminders and those who did not. The text message reminders in these studies varied in frequencies and length with most of them being sent twice daily and once daily. The difference ranged from 8% - 26.1% across different therapeutic classes of medicines and disease conditions, and therefore the difference in adherence rates of 16.6% is consistent with range reported from other studies (Thakkar et al., 2016). As a result of the above findings, text message reminders significantly improved adherence to antibiotics and was found to be effective in improving adherence to antibiotics. Text message reminders therefore have the a great potential of increasing adherence to antibiotics and

will help reduce the consequences of non-adherence with antibiotics amongst patients eg. Increased health costs, treatment failure, increased morbidity and mortality as well as development of antibiotic resistance

5.1.3 Effect of taking medicine(s) for chronic conditions on adherence to antibiotics

With respect to effect of taking medicine(s) on adherence to antibiotics, the study showed a significant association between adherence and taking medicines for chronic conditions. Adherence for participants who responded yes for chronic medicines was found to be 60.4% compared to 51.5% amongst those who responded no to taking medicines for chronic conditions and this was statistically significant. In fact, the odds of adherence in persons taking medicines for chronic conditions was found to be 2.2 times that of participants who were not on chronic medications. The implication of this finding is that the people who are not on any chronic medicines are less likely to adhere to short –term antibiotic therapy compared with people who are already taking medicines for chronic condition. Hence extra efforts should be taken to improve adherence to antibiotics amongst patients not taking medicines for chronic conditions

The higher adherence observed in participants on chronic medicines compared with those who were not, may be due to the fact that people on chronic medicines are used to taking medicines routinely and hence remember to take the antibiotics regularly resulting in the high adherence observed in this group compared with those not taking medicines for any chronic condition. This finding is consistent with other studies which also showed higher adherence in patient who are already on chronic medicines (Brown & Bussell, 2011,Vlasnik et al., 2005).

5.1.4 Opinion of participants on helpfulness of text message reminders on reminding them to take their antibiotic

Another finding worthy of note is the opinion of participants who received the text message reminders on its usefulness in reminders to their antibiotics. Majority (63.8%) of the participants who received the text reminders said they found it to be very useful. The remaining responses were split on somewhat (20.4%) useful and extremely useful (14.8%). This implies that most of the participants who received text message reminders were happy with such a service and hence patients' acceptability of such a service is most likely to be high when such an intervention is implemented. Interestingly, marital status and employment status were the only factors significantly associated with participants' opinion on helpfulness of text message reminders were marital status and employment status.

Amongst participants who responded very helpful, 76.9% were married with only 23.1% being single. Therefore, married people found the text message reminders more helpful in reminding them to take their antibiotics compared to singles and separated / divorced persons. These differences in opinion responses based on marital status was statistically found to be statically significant.

As stated earlier, employment status and participants' opinion on helpfulness of text message reminders were found to have a statistically significant association. Amongst participants who responded extremely helpful, 53.9% of them were full time employed, followed by students (17.5%), unemployed (10.5%), part – time employed (57%) and 5.3% retired. The full – time employed participants may have found the text message reminders extremely helpful more than the other groups as a result of the fact that they

have a busy schedule and which could mean a higher to tendency not for forget to take their medicines. As a result, they are in a better position to appreciate the helpfulness this intervention compared with the others. There incorporating text message reminders services for patients taking antibiotics will help improve adherence to antibiotics especially amongst the full-time employed.

5.2 Limitations of the study

Firstly, the main outcome variable of the study which was adherence was measured based on self – report questionnaires, which may either overestimate or underestimate the true adherence rates even though the 8 – item morisky adherence questionnaires have been validated and found very useful. Again social desirability bias cannot be over ruled and this could underestimate the non – adherence rates observed in this study since the main means of measuring adherence was subjective.

Secondly it is also worth mentioning that effect of text message reminders as an intervention for improving antibiotics adherence studied in this study cannot generalized for vulnerable groups such as children, pregnant women and persons with a disability.

The study had some imbalances across the groups even though participants were assigned to groups randomly. For instance, the different proportion of infection types across the groups could have influenced adherence to the antibiotics.

CHAPTER SIX

6.1 CONCLUSION

This study suggests that text message reminders significantly increase adherence to antibiotics in OPD patients. The difference in adherence between the text message and no text message groups was statistically significant.

Patients who take medicine(s) for chronic conditions are more adherent to antibiotics than those who are not on chronic medicines. The adherence rate in persons on chronic medicines was 60.4% and that of those not on chronic medicines was 51.5% and this difference is statistically significant.

Majority (64.8%) of participants in the text message group found the text message very helpful in reminding them to take their antibiotics and hence high acceptability of patients for text message reminders.

6.2 RECOMMENDATIONS

Policy

- Ghana Health Service (GHS) should develop policies on improving medication adherence which considers incorporating text message reminder services in its facilities to help improve out – patients' adherence to antibiotics.
- Healthcare professionals such as pharmacists, doctors should intensify education on the need for patients to adhere fully to antibiotics through the media and other forms of communication.

Research

- Pilot studies should be done by the Ghana Health Service in other parts of the country especially in the rural areas to see how feasible text message reminders can be incorporated within healthcare system in Ghana.
- Further studies are needed to help develop the most effective text message reminder and frequency that improves adherence to antibiotics.
- Further studies should be done to determine how best text message reminders can be automated and deployed to optimize its effect on improving adherence to antibiotics

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APPENDICES

Appendix 1: Informed Consent Form for Participants

Effectiveness of text message reminders on improving out-patients' adherence to antibiotic therapy at the Tema general hospital

Informed Consent

Participant's Name: ……. Date:

Introduction

The aim of this study is to determine the effectiveness of text message reminders on improving patients' adherence to antibiotic therapy at the Tema general hospital. This study will be conducted over a period of 6 weeks

There will be no discomfort associated with this study. **There will also be no potential risks to participants except time lost in filling the questionnaires. Participants will not receive any direct benefits except that outcomes from the study may help improve policy and overall health of the public**. However, you reserve the right to withdraw from the study at any point in the study.

Highest form of confidentiality concerning any information given towards this study will be maintained at all times. Your identity will be kept anonymous when the results are

presented or published. All participants involved in the study will be referred to as "Subjects".

Problems or Question

If you have any problem or question about this study, you can contact the investigator

Tay Kafui Amenyo Kobla (0201425379) in the Department of Epidemiology, School of

Public Health, and University of Ghana **as well as the Administrative secretary (Ms. Hannah Frimpong) of the Ghana Health Service Ethical Review Committee on 0302681109 or 0243235225/0507041223**

Consent

I have read or have had someone read to me, the entire explanation of this study and have been given the opportunity to discuss any questions. I understand the nature, risk and benefits of this study and that I may withdraw at any time from the study. I have also received a copy of this informed consent document. I hereby consent to take part in this study.

Participant's Signature: Date Signed

…….. …….

Investigator's Signature Date Signed

…….. ……

Appendix 2:Participant Questionnaire

SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF GHANA

Effectiveness of text message reminders on improving out-patients' adherence on antibiotic therapy at the Tema general hospital

PARTICIPANT QUESTIONNAIRE

Instruction; Circle the relevant option and write in the space provided on the right.

Introduction

I am with a team of researchers from the School of Public Health, University of Ghana. We are looking at how to improve patient adherence to antibiotic therapy with text message reminders. We will ask you a few questions. We assure you that information collected will be kept confidential. General findings will be made available to relevant authorities for the purpose of making important decisions and conclusions. The interview will last about 10 minutes.

Date of interview (dd/mm/yyyy): DATE __ / / ___//_____

1. Name of subject:

2. Patient phone number:

Demographic

3. Sex:

Male (1) Female (2)

4. Age (at last birthday): [ ]

5. Marital status:

a. Single [1] b. Married [2] c. Separated/Divorced [3] d. Widow/Widower [4]

6. What is your highest educational level?

a. No Education b. Primary/Elementary c. Secondary d. Tertiary e. Others

If other please specify……..

7. Employment Status

a. Unemployed

b. Part-time employed

c. Full-time employed

d. Student

e. Retired

7. Are you on any daily routine medicines ?

a. Yes b. No

if yes specify the number……

8. Diagnosed condition

a. Upper Respiratory Tract infection (URTI)

b. Lower Respiratory Tract Infection (LRTI)

c. Gastrointestinal Tract Infection (GITI)

d. Skin Infection

e. Sexually transmitted Infection (STI)

f. Other (Please specify)

…….

Treatment Related

9. Prescribed antibiotic(s)

i. ……

ii. ……

iii. ……..

iv. ……

10. Dosing frequency per day

a. once b. twice c. thrice d. 4 times b. others

Specify…….

11.Duration of treatment ……..

12. Total number of tablets/capsules dispensed per antibiotic in question 8

i.……

ii……

iii……...

iv…….

Apendix 3: Adherence Questionnaire

EEFECTIVENESS OF TEXT MESSAGE REMINDERS ON IMPROVING OUT-PATIENTS'S ADHERENCE TO ANTIBIOTIC THERAPY

Adherence Questionnaire

Instruction; Circle the relevant option and write in the space provided on the right.

Introduction

I am with a team of researchers from the School of Public Health, University of Ghana. We are looking at how to improve patient adherence to antibiotic therapy with text message reminders. We will ask you a few questions. We assure you that information collected will be kept confidential. General findings will be made available to relevant authorities for the purpose of making important decisions and conclusions. The interview will last about 10 minutes.

Date of interview (dd/mm/yyyy): DATE __ / / ___//_____

8 item Morisky medication adherence scale (MMAS-8) Questionnaire

1. Do you sometimes forget to take your antibiotic?	1. YES 2. NO
2. Thinking over the past week, were there any days when you did not take your antibiotic?	1. YES 2. NO
3. Have you ever cut back or stopped taking your antibiotic without telling your doctor because you felt worse when you took it?	1. YES 2. NO
4. When you travel or leave home, do you sometimes forget to bring along your antibiotic?	1. YES 2. NO
5. Did you take your antibiotic yesterday?	1. YES 2. NO
6. When you feel like your symptoms are under control, do you sometimes stop taking your antibiotic?	1. YES 2. NO
7. Taking an antibiotic is a real inconvenience for some people, do you ever feel hustled about sticking to your treatment plan?	1. YES 2. NO
8. How often do you have difficulty remembering to take your antibiotics?	1. Never / Rarely 2. Once in a while 3. Sometimes 4. Usually 5. All the time

9. How tablets/capsules per dispensed antibiotic do you have left?.....
10. Did you experience any side effect(s) whilst taking the antibiotic(s)?
    1. YES 2. NO

Only for text message reminder receiving group

1. Was there a day you didn't receive the text message reminders for your antibiotic(s) in a day……
    a. Yes
    b. No
2. Was a day you didn't you read the text message reminders ……
    a. Yes
    b. No
3. How helpful were the text message reminders in helping you remember to you're your antibiotic(s) ……
    a. Extremely helpful
    b. Very helpful
    c. Somewhat helpful
    d. Slightly helpful
    e. Not helpful