The effectiveness of using pictograms and text on medication labels at primary healthcare facilities in Cape Town

by

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A thesis submitted in fulfillment of the requirements for the degree of M. Pharm

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South Africa

2019

ABSTRACT

Background

Medication labels are often the only information available to patients after obtaining medication from the pharmacy or other healthcare practitioners. Inappropriately designed medicine labelling contributes to poor interpretation and improper use, which could adversely affect patient health outcomes. In developing countries, pictograms (pictures representing words or phrases), on medicine labels tend to support patients' ability to read, understand and recall information.

Objective

This comparative study examined low-literate participants' interpretation of 'text-and-pictogram' instructions versus 'routine text-only' instructions relative to the intended medicine use instructions on an oral rehydration (OR) dry mixture sachet in public sector Community Health Centres (CHCs) in Cape Town.

Method

CHCs, (n=4) from Tygerberg (Cape Town) sub-district were recruited. Two trained data collectors recruited participants from the paediatric section's waiting area. Participants were either shown an OR medicine label containing both "text-and-pictograms" (experimental group) and one containing "routine text-only" (control group) instructions. Data regarding understanding of six instructions for use on the medicine label were recorded. Responses were scored according to a 3-point Likert scale and compared for each question, to calculate which of the experimental or control group answered better. Responses to the questions to explain the observed deviation between the participant interpretation of the label and the intended message of the label, was noted. Responses were recorded and transcribed. Open-ended questions regarding label interpretation and preference were thematically analysed.

Results

A total of 132 participants were recruited of which 67 were allocated to the experimental group and 65 were allocated to the control group. Most of the participants were female (92,67%). The average age of the participants was 28 years.

From the six questions that compared the understanding of the experimental and control participants, two contained pictograms that could aid understanding of the experimental group. One of these questions showed a statistically significant association between the experimental and control groups in understanding (P = 0.000). A sub analysis investigating text was done to determine trends in the accurate interpretation of text on the medicine labels. This analysis showed that larger font size, text surrounded by white space and bold font tended to increase readability and understanding of medicine instructions on the labels.

The majority of experimental participants found the pictograms on the label helpful to their understanding of the medicine instructions. Almost two-thirds of the experimental group (64,00%) indicated that they did not find it difficult to understand the "text-and-pictogram" label, compared to a third of the control group (32,00%) response to the "routine text-only" label. About a third (33,00%) of control participants reported that the reason they did not understand the medicine instructions was that they could not find it on the label (poor readability). The most common suggestion by both groups (36,00%) on how to improve understanding of medicine labels was to add pictures to it.

Conclusion

Text-and- pictogram medicine information was interpreted better than text only medicine labels in terms of interpreting a single pictogram. The use of large font size, bold text and white space had a positive impact on the identification of text on medicine labels. Pictograms may be an effective tool to aid understanding of medicine use instructions. Medicine labels with pictograms that are explained to patients should be encouraged for medicines dispensed at CHCs.

DECLARATION

I declare that this thesis that I now submit for assessment for the program of study leading to the degree Master of Pharmacy has not been submitted for the purpose of a degree at this or any other university. It is entirely my own work and has not been taken from the work of others. All sources I have used or quoted have been specified and approved by complete references.

I agree to deposit this thesis in the University of Western Cape's library repository and/or allow this institution to do so on my behalf, subject to South African Copyright Legislation and the University of Western Cape's conditions of use and acknowledgement.

Signed……………………………………………… Dated…………………………..

DEDICATION

This dissertation is dedicated to my husband who encouraged me to pursue my dreams and complete this masters degree.

ACKNOWLEDGEMENTS

I want to thank the Lord Almighty God for this opportunity to further my studies. I can do all things in Him who strengthens me.

Thank you to my supervisor, Dr. M. van Huyssteen and co-supervisor Prof. A. Bheekie, who guided and inspired me in this process. Your continued support, encouragement and advice throughout my time of studies, will forever be etched in my memory. I am greatful for the priviledge to have worked with you.

LIST OF ABBREVIATIONS

AMA	American Medical Association
ARV	Antiretroviral
CHC	Community Health Centre
CMI	Consumer medicines information
EC	European Commission
FIP	International Pharmaceutical Federation
GCP	Good Clinical Practice
HIV	Human Immunodeficiency Virus
HSD	Honestly significant differences
LCS	Living Conditions Survey
MEDIC	Medicine
OR	Oral Rehydration
PICTOG	Pictogram
PIL	Patient information leaflet
REALM	Rapid Estimate of Adult Literacy in Medicine
SAHPRA	South African Health Products Regulatory Authority
UBPL	upper-bound poverty line
UNESCO	United Nations Educational, Scientific and Cultural Organization
US	United States of America
USP	United States Pharmacopeia
USP-DI	Unites States Pharmacopoeia-Drug Information
UWC	University of the Western Cape
WHO	World Health Organisation

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Chapter 1: Introduction

1.1 Background

Medication errors can be defined as a failure in the treatment process that leads to, or has the potential to cause harm to the patient (Aronson, 2009). Medication errors can arise through an incorrect prescription, discrepancies between prescribed and dispensed medication regimens, poor adherence and lack of patient education (Pouliot *et al.*, 2018). An examination of all United States of America (USA) death certificates spanning a period from 1979 to 2006 showed that, of 62 million death certificates, almost a quarter-million deaths occurred in a hospital setting due to medication errors (Phillips and Barker, 2010). Similarly, inappropriate use of prescribed medications due to low literacy or lack of understanding of medication use instructions can result in similar consequences, which are largely preventable (Kheir *et al.*, 2014).

Patient literacy refers to the ability to read or write and is viewed as a key outcome of education by the United Nations Educational, Scientific and Cultural Organization (UNESCO) in the UNESCO 2006 Education for All Global Monitoring Report (UNESCO, 2006). Medication literacy is the degree to which individuals can obtain, comprehend, communicate, calculate and process patient-specific information about their medications to make informed medication and health decisions in order to safely and effectively use their medications, regardless of the mode by which the content is delivered, e.g. written, oral and visual (Pouliot *et al.*, 2018). Health literacy is defined as the degree to which individuals can obtain, process, understand, and communicate about health-related information which is needed to make informed health decisions (Berkman *et al.*, 2010).

According to the UNESCO 2019 Global Education Monitoring Report, the global adult literacy rate in 2017 was 86,00%, with the sub-Saharan Africa literacy rate at only 65,00% (UNESCO, 2019). Low patient literacy, in turn, is associated with ineffective use of medicine (Banstola, 2012), poor health outcomes, reduced adherence to drug therapy and increased hospitalizations and healthcare cost (Wasserman *et al.*, 2010).

Medication literacy has become a major topic of discussion and research interest since a report on health literacy was released by the American Medical Association (AMA) in 1999 (Montagne, 2013). However, patient understanding and recall of medication information is not a new focus of research. The AMA has shown that patient understanding and recall are related to how easy it is to read and understand medication information materials, and patient proficiency in these areas is typically fair to poor (Montagne, 2013). This situation becomes worse when there is low health literacy (Barros *et al.*, 2014).

For effective medical treatment of disease, it is important to be able to interpret and understand medicine information. People with low literacy, who are not able to interpret and understand medicine information have poorer rates of health service use and poorer health outcomes than people with higher health literacy (Berkman *et al.*, 2011). They have a poorer ability to demonstrate taking medications properly and interpret medication labels and health messages (Berkman *et al.*, 2011).

Information pertaining to medication can be presented to the patient verbally (e.g. during the counseling process) and / or in a written format (e.g. via the medication label and / or other written resources). It is important that this information is presented in a way that is easily understood by the patient, as the patient will be better inclined to appreciate the need for adhering to the treatment. One of the risk factors that may predispose patients to non-adherence is the low retention of verbal information from patient counselling. Recalling of treatment information is a prerequisite for patients' adherence (Linn *et al.*, 2013).

The International Pharmaceutical Federation (FIP) is in official relations with the World Health Organization (WHO) (Barros *et al.*, 2014). They have highlighted the promise of the use of pictograms by developing a program that provides information on pictograms in an effort to offer healthcare professionals a way of communicating medication instructions to patients in cases where language barriers occur (Kheir *et al.*, 2014). Pictograms are United States Pharmacopeia (USP) pictograms are standardized graphic images which were created to convey precautions, medication instructions and / or warnings to patients (USP, 2019). Pictograms are most effective when accompanied by verbal instructions (Kheir *et al.*, 2014).

1.2 Problem statement

Problem statement

With the shortage of health care professionals at the CHCs in South Africa, effectively less resource and time is spent on patient counselling (WHO, 2008). With limited medicine information conveyed to the patient during counselling, understanding the information on the medicine label thus becomes critical to the safe and effective use of medication (Kheir *et al.*, 2014; Davis *et al.*, 2006). However, written patient information is often too complicated to understand and this problem is exacerbated in low-literacy patients (Kheir *et al.*, 2014; Thompson *et al.*, 2010).

1.3 Motivation and rationale for study

In the past ten years (2008 to 2018*)*, the South African unemployment rate has increased from 21,50% to almost 28,00% (Statistics South Africa, 2008; Statistics South Africa, 2019a), with the unemployment rate in Cape Town at 23,90% (Statistics South Africa, 2011). According to the Living Conditions Survey (LCS) 2014 / 2015 approximately half (49,20%) of the adult population in South Africa were living below the upper-bound poverty line (UBPL) (Statistics South Africa, 2019b). In Cape Town, nearly 47,00% of the households live on less than R 3 200 per month (Statistics South Africa, 2011). Poverty forces people to live in environments that make them sick and where they do not have decent shelter, clean water or adequate sanitation, resulting in ill-health (WHO, 2019).

With the issues of poverty in South Africa, comes a very high disease burden with one of the world's largest population of people living with infection of the human immunodeficiency virus (HIV) (Statistics South Africa, 2018). In the underserved communities, communicable diseases like diarrhoea is one of the leading causes of death in children ages 0 to 4 years (Statistics South Africa, 2016). According to South Africa's under-five mortality report, diarrhoeal disease accounted for the highest (21,00%) single cause of death registered during 2007 (Nannan *et al.*, 2012). Oral rehydration (OR) treatment is mainstay therapy for diarrhoeal disease (National Department of Health, 2017). An OR solution can be made by dissolving sugar and salt in clean water (National Department of Health, 2017). At the local primary healthcare level, carers for children with diarrhoea receive OR sachets with instructions on how the dry ingredients could be reconstituted in the home.

South Africa, in common with many developing countries still has significant literacy problems with an adult literacy rate (age 35 to 64) of 79,30% (Statistics South Africa, 2017). Because medicine labelling is being viewed as a major cause of medication taken incorrectly and adverse health outcomes, healthcare centres have turned their attention to supporting patients' ability to read and understand health information by improving the quality of medicine labelling with incorporating pictograms (Kheir *et al.*, 2014). Pictograms, which are pictorial symbols for a word or phrase, can replace written instructions and can be used to represent information about medication, doses, precautions, and warnings (Banstola, 2012) and in lower middle-income economy countries like India, they support patients' ability to understand information (Joshi and Kothiyal, 2011) and adhere to the medicine regimen (Braich *et al.*, 2011). The benefits of including pictures in medicines information have been reported by Mansoor and Dowse within South Africa and internationally by Joshi and Kothiyal, Braich and colleagues, and Houts and colleagues (Houts *et al.*, 2006; Mansoor and Dowse, 2007; Joshi and Kothiyal, 2011; Braich *et al.*, 2011). Most of the South African studies tested the use of pictograms on the medicine label and patient information leaflet (PIL) with isiXhosa and other South African language groups as the target research groups. South Africa is a country with many different cultures and 11 official languages and one cannot generalize the use of pictograms in different cultural populations (Kanji *et al.*, 2018).

In Cape Town, with the majority of the population speaking Afrikaans (34,90%), isiXhosa (29,20%) and English (27,80%), (Statistics South Africa, 2011) the information on the OR dry mixture pack issued by the CHCs, is usually written in English and Afrikaans. Patients' understanding of medicine labels is based on their language, however in government healthcare facilities, medicine instructions in English and Afrikaans may not necessarily match the patient's preference. This poses a further problem if the patient has limited literacy skills. Therefore, culturally sensitive pictograms may serve as a useful aid to promote understanding of medicine use, independent of language.

Pictograms have the benefits of a positive influence on comprehension and acceptability of information, (Dowse *et al.*, 2011) constitute a more "universal language" than text, minimize the amount of reading, clarify information and improve adherence to prescribed regimens (Kheir *et al.*, 2014) .

1.4 Primary aim and objectives

The primary aim of this study was to compare the difference in interpretation of OR medication labels with "text-and-pictogram" instructions, with labels containing "routine text-only" instructions, among patients attending public sector CHCs in Cape Town. In order to reach this goal, the following objectives needed to be achieved:

1. Conduct a literature review about the benefits and use of pictograms in pharmaceutical care of underserved patients.
2. Compare participant interpretation of "text and-pictogram" versus "routine text-only" medication labels relative to the intended medicine use instructions on OR pre-packed dry ingredients.

1.5 Research questions

1. What does the literature say regarding the use of pictograms to aid patients in their understanding of medicine information?

2. How might pictograms assist participants attending CHCs understand the information of the medicine label?

1.6 Methodology

The research methodology and procedures that were followed in the study are presented in chapter three. This chapter includes details of the study setting, sampling, data collection, data analysis and ethical considerations.

1.7 Summary of chapters

The current thesis comprises five more chapters presented as follows:

Chapter 2 examines nine intervention studies which were conducted in English among low literacy patients, and focused on the use of pictograms, (with or without text or verbal counselling) on medicine labels, PILs and other forms of presentation.

Chapter 3 outlines the methodology and procedures followed during the data collection and analysis phases of this study.

Chapter 4 presents the results of the research findings. It includes demographic and socio-economic information of the participants, responses to questions regarding the label, responses to questions asked to explain observed deviation between participant interpretation of the label and intended message of the label, and two sub-analyses.

Chapter 5 presents the discussion of the study findings.

Chapter 6 concludes the study findings and makes recommendations for practice and further research.

Chapter 2: Systematic Literature Review

2.1 Introduction

Studies show that 40,00% to 80,00% of verbal explanations provided by healthcare practitioners to patients about the use of medicines, is forgotten immediately (Kessels, 2003). Patients are reliant on tangible visual aids to recall medicine information instructions. Medicine labels and PILs serve as communication tools, especially when patients have minimum contact with healthcare professionals. Written medication information on labels and PILs is often difficult to read and understand due to the technical nature of the language that is used (Wallace *et al.*, 2008). Literacy is defined as the ability to read and write and illiteracy is defined as inability to read or write, by the Oxford dictionary (Oxford Dictionaries, 2019). Low literacy is a low level of ability to read and write.

Patients' inability to either remember medication information or to read the medication label due to low literacy, leads to inappropriate use of medicine, a decrease in treatment adherence and increases in hospitilisations and healthcare costs (Kheir *et al.*, 2014). Pictograms are simple, clear graphic symbols, (Dowse and Ehlers, 1998) representing words or phrases (Oxford Dictionaries, 2020). Pictogram intervention studies among low literacy populations, showed that pictograms were recalled better than written messages (Dowse and Ehlers, 2004), improved understanding of medicine instructions (Dowse *et al.*, 2011), and were effective in addressing nonadherence among patients (Advani *et al.*, 2013; Braich *et al.*, 2011). Pictograms can convey their intended message to vulnerable patients, including those who are illiterate, the elderly or those who are visually impaired (Dowse and Ehlers, 1998). Pictograms can also be utilized in situations where there are language differences (Sorfleet *et al.*, 2009).

This review is aimed at assessing the outcomes of pictogram intervention studies on medicine labels, PILs or other medicine information materials, conducted among low literacy patients, which tested the difference in understanding, adherence to, recalling and finding the instructions to the medication regimen.

2.2 Method

2.2.1. Inclusion criteria and exclusion criteria

2.2.1.1 Inclusion criteria

Intervention studies that were conducted in English among low literacy patients, were considered for the review. The level of literacy was determined from the number of years of school education or highest level of school education that the participant completed. The interventions focused on the use of pictograms, (with or without text or verbal counselling) on medicine labels, PILs or other materials of presentation, offered to the target groups.

2.2.1.2 Exclusion criteria

Studies published before 2003 were excluded, as the focus was on reviewing current research. Studies conducted with all literacy levels including tertiary level students as participants were excluded as these studies did not satisfy the criteria of low literacy, which was set at the highest level of secondary or school education that was completed. Studies which addressed health literacy, were not considered, as the focus of this study was on low literacy.

2.2.2 Study selection

The Cochrane general guidelines for conducting a systematic review were followed (Higgins and Altman, 2008). Searches were done between February and April 2016. Databases that were searched included Ebscohost CINAHL, Science Direct, Sabinet, Pubmed, Cochrane and Medline. The keywords "PICTOG* and MEDIC* label" were used as search terms.

2.2.3 Review process

2.2.3.1 Data extraction

All the study titles and abstracts were screened by one reviewer. Thirty-nine studies were identified through the search. The articles were manually sorted and after the exclusion process, nine studies were found to meet the inclusion criteria. The articles that appeared in more than one of the databases were only counted and used once (Figure 2.1). The data extraction form documented the studies'; authors, year of publication, geographical location, setting of the study, language of participants, testing groups, administration of pictograms, the purpose of the pictograms, number of pictograms evaluated, origin of pictograms, the number, age and literacy level of participants, presentation form, preference/acceptability of pictograms and outcomes measures (Appendix A Table A.1).

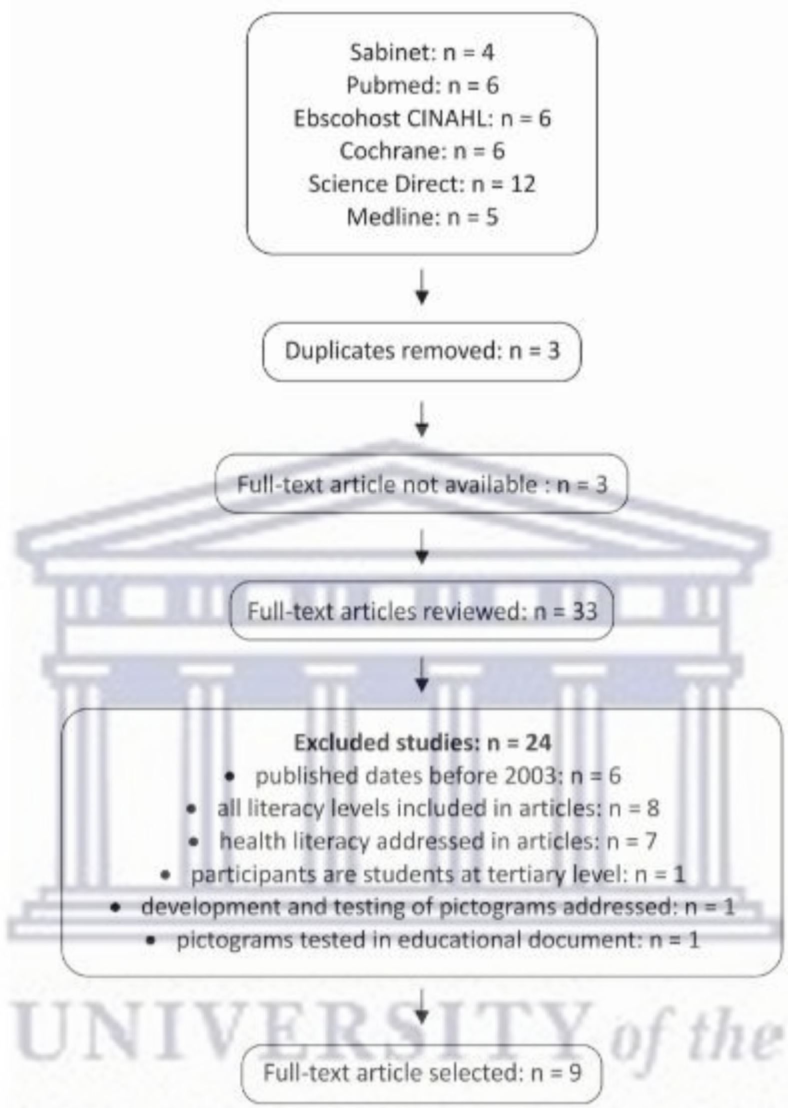

Figure 2.1 Review and Selection Process for the selected Review Articles

2.2.3.2 Assessment of bias

The risk of bias was assessed using the tool developed by the Cochrane collaboration (Higgins *et al.*, 2008). Two reviewers assessed the study bias independently using the following seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting. No other sources of bias were considered. Outcomes of the assessment were compared, discussed and discrepancies cleared up until an agreement was reached. The outcome is presented in Appendix B, Table B.1. It was concluded that, even in the presence of the potential biases, the interventions in the nine studies which tested the use of pictograms on the medicine label / PIL, were effective.

2.3 Results

The experimental studies reviewed were not sufficiently similar for a meta-analysis to be appropriate, therefore a narrative synthesis of results was used in this review (Mays *et al.*, 2005). The following variables were used to compare the information extracted from the nine articles for the review through the selection process in Figure 2.1.

1. Geographical location and study setting.
2. Participant demographics: inclusion criteria, literacy level, and language.
3. Study design: sampling process, study groups' sizes and number of pictograms.
4. Participatory / non-participatory development of pictograms: origin / development of pictograms and participation of the study group in the design of the pictograms.
5. Pictogram administration, types of interventions (inclusion of text and / or verbal and / or pictograms instructions), presentation form, acceptability of form.
6. Purpose of the study / measurements: understanding, adherence to, recalling and finding the instructions to the medicine regimen in the text?
7. Pictogram preference / acceptability of type of presentation.
8. Cross-sectional outcomes: understanding of instructions and ability to locate instructions.
9. Longitudinal outcomes: understanding and recall of information and in adherence to the prescribed regimen.

10. Location of follow-up.

2.3.1 Overview of the included studies

The studies ranged from the use of pictograms which represented general medicine use instructions e.g. "take with meals", studies A, D and I (Joshi and Kothiyal, 2011; Kheir *et al.*, 2014; Dowse and Ehlers, 2004), a demonstration for the use of a medical device used in asthma, study A, (Joshi and Kothiyal, 2011), medicine information for the medicine methotrexate, study B (Thompson *et al.*, 2010), medicine information for an antiretroviral (ARV) regimen for stavudine, lamivudine and efavirenz, study C, (Dowse *et al.*, 2011) medicine information for the use of nystatin suspension study E, (Mansoor and Dowse, 2003) a combination regimen of either tobramycin-dexamethasone or moxifloxacin-prednisolone eye drops study F, (Braich *et al.*, 2011) short-term prescription regimens for the antibiotics amoxicillin (capsules and suspension), phenoxymethylpenicillin tablets and co-trimoxazole tablets, study G (Dowse and Ehlers, 2005) and chronic co-trimoxazole therapy information, study H (Mansoor and Dowse, 2006).

2.3.1.1 The geographic location and setting of the studies

The selected studies were conducted in Africa, Asia, North America and the Middle East. Five of the nine studies were conducted in Africa (C, E, G, H, I), two in Asia (A, F), one in the Middle East (D) and one in North America (B). The African studies were all conducted in South Africa – in a small rural town (n = 4) and one across three selected geographical regions for eight different language groups. Both studies from Asia were in cities located across India, namely Dehradun, Chennai, Rampur, and Tanda Urmar. The study (D) in the Middle East was conducted in Qatar (city – Doha). The last study (B) was conducted by making use of a national consumer marketing database in Canada, North America.

Study settings included hospitals (A, F, I), clinics (C, D, E, F, H, I), an outpatient day hospital (G), and the homes of patients (C). For study I, some of the interviews were also conducted at taxi ranks, at roadside farm stalls and on farms. The location for the interviews of the participants who were recruited through the consumer database (B) was not recorded.

2.3.1.2 Participant demographics – inclusion criteria, literacy level and language

Patients attending the outpatient department of the hospital, were invited to participate in the study (A). Participants who had no prior knowledge of methotrexate were selected from a consumer-marketing database (B). Patients who had not received any counselling about HIV and were not on ARV therapy were recruited by nurses at the clinic and by community health workers (C). Participants were invited from the two major contracting companies that supplied workers to Qatar Petroleum – any participant was free to join or withdraw at any time (D). The selection criteria for the study groups participants were not specified for study E. Study participants were selected from a pool of patients referred for cataract surgery at free vision-screening outreach camps across India (F). Participants were eligible for the study if they were prescribed one of the antibiotics, amoxicillin (capsules and suspension), phenoxymethylpenicillin tablets or co-trimoxazole tablets, or were caregivers who were responsible for the administration of one of these antibiotics. Participants were not included in the study if they had been prescribed or had been responsible for administering one of these antibiotics in the last three months prior to the study (G). Outpatients at the CHC, who were on chronic co-trimoxazole therapy were included in the study (H). Participants were selected from various sectors of the community, for example hospital outpatients, domestic workers, farm workers, informal traders and unemployed people (I).

Participants were reported to be illiterate (A), received up to ten years of schooling (C, G), maximum seven years of schooling (E, I), schooling up to grade eleven (B), an average of 6,1 years of formal education (D), education below grade ten level (F) and the highest level of grade twelve (H).

In the North American study, at least 87,00% spoke English (B). In six of the studies, English was not the first language for the participants. In the South African studies, most of the participants could speak isiXhosa (C, E, G, H, I) or one or more of seven other African languages (I). The languages among migrant participants included Malayalam, Nepali, Urdu, Tagalog and Bengali (D). The languages of the participants from the two studies done in India were not recorded (A, F).

2.3.1.3 Study design – sampling process, study groups' sizes and number of pictograms

The studies were cross-sectional (C, D, E, I), longitudinal (G, H) or a combination of cross-sectional and longitudinal (A, B, F) in design. The number of participants for each study ranged from 39 to 304 participants, with an average sample size of 134 participants. For a single group of 200 participants, ten pictograms were randomly chosen, with the tenth pictogram specifically chosen keeping in mind the prevalence of asthma in Dehradun (where the study population was from) and poor usage of inhalers in this population (A). In a single blind, randomized trial with 100 participants, participants were allocated to a group that either received a prose-based information sheet (n = 48) or a pictogram-based information sheet (n = 52). The number of pictograms was not specified (B). In a single study group of 39 participants, 20 pictograms were tested (C). In a randomized controlled trial with 123 participants, 11 pictograms were tested (D). Participants were allocated to three groups – Group A (n = 40), Group B (n = 47) and Group C (n = 36). For 60 participants who were randomly allocated to either an experimental (n = 30) or a control group (n = 30), the number of pictograms were not specified for the study (E). In a single-blinded, randomized controlled trial with three groups (one control and two experimental) and 75 participants in each group, the number of pictograms were not specified (F). Pictograms were tested on 87 participants who were randomly allocated to an experimental (n = 46) or a control group (n = 41). The number of pictograms were not specified (G). A total of 120 participants were randomly allocated to experimental group A (n = 40), experimental group B (n = 40) and a control group (n = 40) with the number of pictograms not specified (H). A single group of 304 participants were randomly showed two sets of 23 pictograms each (I).

2.3.1.4 Origin / development of pictograms

In study A, nine pictograms were sourced from the United States Pharmacopoeia-Drug Information (USP-DI) and one pictogram that demonstrated the use of an inhaler was selected from a source that was not mentioned in the study. In two of the studies, pictograms were developed through collaboration with the target population (B, D) while in three other studies, most of the pictograms were previously developed and evaluated in the target population (C, E, G). One study compared a set of pictograms from the USP-DI and a second set of corresponding pictograms that were previously developed locally (I). Another study included pictograms that were designed using information collected from the Australian consumer medicines information (CMI), USP-DI, various fact sheets, medicine information sheets, monographs and package inserts (H). In one of the studies, the origin of pictograms used was not recorded (F).

2.3.1.5 Pictogram administration, types of interventions, presentation form, acceptability of form.

A verbal explanation accompanied the pictogram presentation in study A. Participants were first asked to interpret the meaning of the pictograms without a prior explanation, then asked again to interpret the meaning of the pictograms after the pictograms were explained (A). A text-and-pictograms presentation was evaluated in one study (C). Text-only and text-and-pictograms presentations were compared in four of the studies (B, E, G, H). In one of these studies (H), a third group which received no tangible or verbal information was included in the study. In another study with three different groups, Group A received standard text medicine labels with verbal instructions, Group B received pictogram-only medicine labels with no text or verbal instructions and Group C received pictogram medicine labels and verbal instructions (D). In study F, the two experimental and one control group received instructions through a tape recording. In addition to the tape recorder instructions, the two experimental groups' education was accompanied by pictograms – one of the experimental groups was given the pictograms to take home. The last study evaluated both USP and locally developed pictograms in a single study group (I).

Pictograms were presented on PIL's (B, C, H), medicine labels (D, G, I) and both a PIL and medicine label (E). The presentation form was not recorded for two studies (A, F).

Preference for the type of presentation was investigated in five studies (B, C, E, G, I). Participants found the pictogram PIL visually more appealing and useful, easier to read and the preferred presentation to receive compared to the text-only presentation (B). In another study where a text-and-pictograms PIL without a control text-only PIL was tested, all the participants endorsed the inclusion of pictograms for readability and as an aid to understand and recall information (C). In one study, all participants, felt that pictograms on the medicine label helped them to understand the instructions better (E) and preference for the pictogram presentation was expressed by all except for one participant. In the same study, participants preferred the physical appearance of the text-and-pictogram PIL when compared to the text-only PIL and they believed that the presence of pictograms would enhance their understanding of the information. In two of the studies all participants were positive about the pictograms on the labels and felt that it would be an aid in recalling of instructions (G, I). Preference for the type of presentation was not recorded in four of the studies (A, D, F, H).

2.3.1.6 Purpose of study and measurements

Understanding of selected pictograms was measured in two studies (A, D) e.g. could the participant correctly interpret the meaning of the pictogram "do not take with alcohol" or "instill one drop in the eye". In one for the studies immediate versus delayed free and cued recall was compared – understanding of instructions and utility of the presentation form was also measured in this study (B). Examples of the test material were not presented in study B. Participants' ability to locate information on the PIL and explain their understanding of the required information, was tested in two studies (C, E) e.g. "take one tablet at night" or "fill the dropper up to the 1 ml mark". In one of these studies (E), understanding was also tested for the label presentation e.g. "swirl medicine around in the mouth before swallowing". Adherence was measured in one study (H), e.g. "you must use your medicine until the bottle is empty". Both understanding of and adherence to instructions was tested in two studies (F, G) e.g. “allow the drop to settle by gravity into the lower cul-de-sac before releasing the eyelid” and “ take 5 ml 3 times a day”. The difference in patient interpretations between selected USP-DI and locally developed pictograms was tested e.g. “do not store near heat or in sunlight” (I).

2.3.1.7 Outcomes – cross-sectional

In the Indian study with nine USP-DI pictograms with general medicine use instructions and one pictogram specific for asthma patients, (A), the percentage of participants correctly understanding each of the 10 pictograms ranged between 12,00% and 65,00% before explanation and between 52,50% and 88,50% after explanation of the same pictograms. There was no indication that statistical significance was tested for in this study.

In the North American methotrexate study (B), both groups on which the text-only and locally developed text-and-pictograms PILs were tested, scored 80,00% for understanding. There was no statistically significant difference in immediate free recall between the two groups – both groups scored between 17,00% and 23,00%. There was also no statistically significant difference in immediate cued recall between the two groups: both groups scored between 32,00% and 66,00%. However, the participants who read PIL with pictograms found it significantly more appealing (Mann–Whitney U = 851, P = 0,004) and were significantly more comfortable knowing when to call the doctor than the participants who read the text-based PIL (Mann–Whitney U = 998,5 and P = 0,03).

In the African study where a PIL with mostly locally developed pictograms presentation was evaluated (C), correctly understanding the instructions on the PIL for the ARV regimen was between 17,90% and 97,40% and the average understanding was 60,40%. Study C had a single testing group with a text-and-pictograms presentation on a PIL. The number of correct responses for both locating and understanding of the leaflet were added to calculate the overall understanding of the leaflet. The relationship of overall understanding of the leaflet with variables such as gender, education and age was compared by using a One-way ANOVA and t-tests at the 5,00% level of significance. Statistical significance was found in the association between education with overall understanding of the leaflet (P = 0,009). Understanding increased from 44,00% (< Grade 3) to 55,50% (Grades 4 to 7) to 68,40% (Grades 8 to 10). The association of gender with overall understanding tended towards significance (P = 0,05), with females obtaining a higher percentage than males. Age (18 – 49 years = 89,7%, and older than 50 years = 10,3%) did not significantly affect understanding, but there was a trend of increased understanding as age decreased.

In the study conducted in the Middle East (D), pictograms for general medicine instructions on a label were developed with the collaboration of the target population and understanding each of the 11 pictograms was measured on a Likert scale. One-way ANOVA and Chi-square tests were used to compare differences in comprehension between the three groups and to assess differences between group variables with statistical significance set at a P-value < 0,05. Significant differences in the average level of understanding of the medicine instructions between the three groups, verbal-and-text, pictograms-only and verbal-and-pictograms, for 10 of 11 medicine instruction labels was found ($P \leq 0{,}05$). For 10 of the 11 medicine instructions, the verbal-and-pictograms group consistently scored higher than the verbal-and-text group, while the verbal-and-text group had higher scores than the pictograms-only group for 8 of the 11 labels. No statistically significant differences were found between participants in the three intervention groups in their socio-demographic characteristics and self-assessed literacy in English and Arabic languages (P-values for continuous data were calculated using one-way ANOVA test and P-values for categorical data were calculated using Chi-square test).

In the African study a simple, understandable medicine label and PIL for Nystatin suspension was designed, developed, and evaluated in the target population (E). In study E, the European Commission (EC) guideline was used in assessing understandability of the PILs. At least 80,00% of the participants should answer each question correctly – they should locate the appropriate information and be able to explain it in their own words. Differences in understanding of the text-and-pictograms and text-only labels and PILs were determined using χ^2 analysis with the level of significance set at 5,00%. No significance was found between the two groups for four of the six questions asked about the nystatin suspension medicine label. Question 3 was answered correctly by all the participants in both groups, for questions 1 P = 0,313, question 5 P = 0,076 and for question 6 P = 0,076. Pictograms on the medicine label significantly enhanced understanding of the information describing how the medicine should be taken (question 2, P = 0,000), and the times at which it should be taken (question 4, P = 0,000). The EC guideline target was achieved for 9 of the 11 questions for the PIL containing text-and-pictograms compared with 8 for the text-only PIL. The information was located equally well by both groups, but understanding of the text-and-pictogram PIL was superior to the text-only PIL. Significantly more participants in the text-and-pictogram group displayed a high level of understanding when compared with the control group (P = 0,005).

In the Indian study (F), pictograms were evaluated for understanding and adherence to postoperative cataract eye drop regimens (F), and consisted of a control group with verbal presentations (group 1), an experimental group with verbal-and-pictogram presentations (group 2) and a second experimental group with verbal-and-pictogram presentations and pictograms taken home (group 3). The 6 questions of the exam could yield a maximum of 10 points and the following results for understanding instructions on the day of the operation were recorded: the verbal-only group scored 8,68, the verbal-with-pictograms group scored 8,88, and the verbal-with-pictograms and pictograms-taken-home group scored 8,85. The first test at the clinic showed no significant difference in mean scores among the three groups.

The African study compared USP-DI pictograms with locally developed pictograms (I). Chi-square tests were used to test for differences in interpretation and preference between the USP and local pictograms. Chi-square tests and regression analysis were used to assess the influence of the standard of education on the interpretation of symbols. The level of significance was set at the 1,00% level. The local pictograms yielded a significantly higher percentage of correct interpretations (p < 0,01) in 16 of the 23 pictograms. Local images were preferred over the USP pictograms in all 23 cases, with significance (P < 0,01) in 22 of the 23 cases. There was no significant difference in the standard of education among the groups. However, the standard of education significantly influenced the interpretation of 23 of the 46 pictograms (both USP and local). The two groups with the lowest level of education (no formal schooling and grades 1 to 4), interpreted a similar percentage of the images correctly (18,60% and 19,70%, respectively) with interpretation increasing substantially in participants in the grades 5 to 7 group, who interpreted an average of 61,70% of the images correctly. In the assessment for preference of colour, no significant differences were noted between the language groups.

2.3.1.8 Outcomes – longitudinal

To monitor if the initial outcome of the study repeated itself, some studies included follow-up measurements (A, B, F). In two studies assessment was conducted only at follow-up and not at the first meeting at the clinics (G, H).

In the Indian study with nine USP-DI pictograms with general medicine use instructions and one pictogram specific for asthma (A), 164 out of 200 (82,00%) participants reported back for the follow-up, which was in accordance with their prescription schedule. The percentage of participants correctly understanding each of the pictograms varied between 34,15% and 87,81%. There was no indication that statistical significance was tested for in this study.

Delayed free and cued recall was measured after seven days in the North American methotrexate study (B) and 76 out of 100 (76,00%) participants were available for a second interview. There were no differences in delayed free recall and cued recall between the text-only and text-and-pictograms PILs after one week. Immediate free recall, ranging between 17,00 and 23,00%, fell lower to 7,00 – 16,00% after one week and immediate cued recall fell from a range of 32,00 – 66,00% to a range of 28,00 – 62,00% after one week. Yet, when participants viewed both pamphlets together, they found the pictogram PIL visually more appealing (86,00%, Z = 3,60 and

P < 0,001), easier to read (61,00%, Z = 3,38 and P = 0,001), more useful (77,00%, Z = 4,24 and P < 0,001), and the one they would rather receive (75,00%, Z = 4,14 and P < 0,001).

In the Indian study for postoperative cataract eye drop regimens, (F), understanding was tested when followed-up on post-operative days 7 and 28. Only 138 out of 225 (61,33%) participants arrived with their prescribed eye drops on day 28 of follow-up. The six questions of the exam could yield a maximum of ten points. Results were as follows for understanding of instructions postoperative day 7: (group 1) verbal-only group scored 5,77, (group 2) verbal-with-pictograms group scored 7,33 and (group 3) verbal-with-pictograms, and pictograms-taken-home group scored 7,62. A post hoc comparisons using Tukey's honestly significant differences (HSD) found no significant differences between mean test scores of group 2 and 3 (P = 0,577), however, statistical significance was found in the test scores between groups 2 and 1 and between groups 3 and 1 (P < 0,001). Greater amounts of medicine consumption were significantly related to higher test scores (P < 0,001).

Results were as follows for understanding of instructions postoperative day 28: verbal-only group scored 4,37, verbal-with-pictograms group scored 5,44 and verbal-with-pictograms, and pictograms-taken-home group scored 7,17. For the third test, significant differences in mean test scores between all three treatment groups was found. The second experimental group scored significantly higher than the first experimental group and the control group (P < 0,001). The first experimental group also scored significantly higher that the control group (P = 0,004). Adherence was tested on day 28 by measuring the percentage of eye drops consumed. Of the 138 participants, 46 (33,33%) participants consumed 30,00% or less, 17 (12,32%) consumed between 31,00% and 50,00%, 21 (15,22%) consumed between 51,00% and 70,00%, 36 (26,09%) consumed between 71,00% and 91,00% and 18 (13,04%) consumed 91,00% or more of the drops. The percentage of eye drops consumed was also significant (P < 0,001). Statistical significance was found in the mean test scores with respect to patient parameters for percentage of topical drops used after 28 days (P < 0,001) and education (P < 0,001). However, when included in the model along with percentage usage of topical drops, education was no longer significant. Education also did not significantly improve the R-squared value, leaving treatment group and the percentage of eye drops consumed as the statistically significant factors.

Understanding and adherence was measured three to five days after dispensing of a short course of antibiotics to patients in one of the African studies (G). The number of patients assessed in the follow-up was not recorded. Average understanding in the text-only and text-and-pictograms groups was 69,50% and 95,20% and average adherence in the text-only and text-and-pictograms groups was 71,50% and 89,60%, when measured during home visits. In study G, Chi-square tests were used to test for differences in the understanding of medicine instructions and adherence between the experimental and control groups and for significant differences in demographic characteristics between the two groups. Significant differences between the experimental and control groups were found for both adherence and understanding of the instructions ($P < 0,01$). No statistical significance was found for the demographic characteristics between the two groups. The influence of literacy on adherence and understanding was investigated using correlation analysis, with the level of significance set at 1,00%. In the pooled results for the experimental and control, significant correlation was found between literacy and understanding ($r = 0,5595$ and $P = 0,00$) and literacy and adherence ($r = 0,5782$ and $P = 0,00$). However, the strong association was noted in the control group, with the association much weaker in the experimental group. Similar results were generated from the regression analysis between literacy and adherence, with a non-significant association between literacy and adherence in the experimental group and a significant association in the control group. These results suggest that pictograms reduced the reliance on literacy skills to understand and adhere to medicine instructions.

In another African study, follow-up of patients on chronic co-trimoxazole therapy was conducted about 14 days after the medication was dispensed (H). The number of patients assessed in the follow-up was not recorded. Overall mean percentage adherence between self-report and tablet count was measured and was found to be 67,70% when no PIL was used, 73,60% when the complex PIL was used and 88,30% when a simple PIL with pictograms was used. In study H, statistical significance was tested for between the control group (no PIL), group A (text-only PIL) and group B (PIL with text-and-pictograms). A significant difference was found in adherence between group B and the control group ($P < 0,05$) for self-report, with group B reporting a higher percentage adherence. A significant difference was also found in adherence between group B (text- and pictograms) and both the control group and group A ($P < 0,05$) for tablet count, with the text-and-pictogram groups' mean percentage adherence significantly higher than the two other groups. Demographic correlation with literacy was not reported in this study. It was not recorded if follow-up was done for studies C, D, E, and I.

2.3.1.9 Location of follow-up

Participants reported back to the study site for follow-up (A), they were followed-up by contacting them after seven days (B), follow-up was at the participant's home (G) and at the participant's home or the clinic (H). One study did not report the location of the follow-up (F).

2.4 Discussion

The studies in this review tested the use of pictograms on medicine labels, PILs and / or other medicine information materials e.g. card board cards, as a medium to communicate medicine use instructions. This discussion will describe the effectiveness of pictograms on medicine information material in terms of overcoming problems such as language barriers and low literacy. It will further describe how the effectiveness of pictograms can be enhanced if it is administered with proper verbal explanations and if it is developed with the target audience.

Most studies that compared different groups of participants either assigned pictogram-and-text versus text only information materials, reported that pictograms significantly increased either understanding, adherence and / or ability to locate information on the study materials (D, E, F, G, H) except for study B. The cross-sectional studies highlighted the effect of pictograms on understanding of information on the label (D, E) and understanding of and locating information on the PIL (E). The longitudinal studies tested adherence to medicine instructions on the PIL (H) and understanding and adherence to medicine instructions on the label (G). Three of the studies were a combination of cross sectional and longitudinal studies and tested understanding of medicine information, with the presentation form not recorded (A), understanding and recall of medicine information on the PIL (B) and understanding and adherence to medicine instructions, with the presentation form not recorded (F).

In the cross-sectional studies, pictograms had a positive effect on understanding of information on the label (D, E) and on the PIL (E). In the longitudinal studies, the presence of pictograms contributed positively to understanding and adherence of information on the label (G) and adherence on the PIL (H). In the first combined cross-sectional and longitudinal study where presentation forms were not recorded (A), 1% of the patients were able to interpret all the pictograms correctly before explanation of their meaning. In the North American methotrexate study (B), no benefit was found in the use of pictograms in the domains of free recall, cued recall or understanding of information on the PIL, immediately or during follow-up after one week. In the last of the combined cross-sectional and longitudinal studies where the presentation form was not recorded (F), pictograms did not prove to have any benefit at the first test at the hospital or clinic in the study for postoperative cataract regimens. The importance of using an effective tool, in this case pictograms to communicate the message so that the participant can carry out the medicine instructions correctly is evident in all the studies. Similarly, other literature has shown that patients are more likely to read and understand information which was presented in picture format and that they preferred patient information presented in pictogram format (Mbuagbaw and Ndongmanji, 2012). In five of the studies in our review participants indicated their preference for pictograms (B, C, E, G, I). All five these studies, included locally developed pictograms. Study I which also included USP pictograms.

The benefits of using pictograms in low literate patient populations were specifically tested for in studies in this review (A, B, C, D, E, F, G, H, I). The studies' participants' education ranged from illiterate to grade 12. Low literacy presents a significant barrier to successfully understand medicines information that is needed for adherence (Davis *et al.*, 2006). Patients with literacy problems cannot read the details in prescriptions, medicine labels or PILs and they also find it difficult to scan a portion of information to identify a single piece that they need (Dowse *et al.*, 2011). In two of the studies (C, E), the ability to find information in the text was tested. In study C, participants struggled with finding the detail in the PIL text for information that was not accompanied by a pictogram and that was not surrounded by white space. Text that was most frequently understood correctly, was in a position either directly below or next to each pictogram. This supports Mayer's "Spatial Contiguity Principle", which states that, when corresponding words and pictures are near each other on the page, learners do not have to use cognitive resources to visually search the page or screen, and learners are more likely to be able to hold them both in working memory at the same time (Moreno and Mayer, 1999). In study E, locating and understanding information on the text-and-pictogram PIL was significantly enhanced with the presence of pictograms, short, easy-to-read and highlighted headings, bullet points, broken paragraphs, larger print size and bigger spaces between paragraphs. However, participants found words like "nystatin," "itchiness," "oral thrush," "blotches," and "allergies," challenging to read and these words were merely ignored. This caused disruptions in the reading process and subsequently a lack of understanding of the entire sentence.

In studies where correlation analysis were carried out between literacy levels and study outcomes (G, I), literacy influenced the outcomes in the control groups but not in the experimental groups in study G, and in study I, literacy influenced the outcomes in both the control and experimental groups. This confirms other research that the level of literacy has an impact on the interpretation of pictograms (Zargarzadeh and Ahamdi, 2017; Dowse and Ehlers, 2003). Patients with lower levels of literacy have greater difficulty in interpreting pictograms correctly than patients with higher levels of literacy (Zargarzadeh and Ahamdi, 2017). Other studies agree that patients with very low literacy skills can be helped with pictures to take home as reminders, (Houts *et al.*, 2006) as pictograms could serve as a cue of how to take medication and allows for better memory retention (Braich *et al.*, 2011).

In contrast, study (B) found no benefit in pictograms aiding understanding or recall of the medicine information. The authors suggested that the reason for this finding could be that the PIL was simple, structured and readable, and, the participants' literacy levels were higher than expected and most could read English. In non-first language English speaking populations, pictograms have been identified to be important tools to overcome communication barriers caused by language differences (Dowse and Ehlers, 2004). Study D reported that pictograms assisted in cases where language barriers exist (Kheir *et al.*, 2014). Indeed, most of the studies that showed successful results from this review included participants who were not first language English speakers. Accordingly, Dowse and colleagues (2011) recommend caution in terms of generalising findings of pictogram studies to other language groups (Dowse *et al.*, 2011). This was partially illustrated by study B, which concluded that the benefit of pictograms was negated by the participants' good understanding of the English language, and reading skills of the participants (Thompson et al., 2010). Literature agrees that in terms of preference, patients prefer medicine information in their home language (Mwingira and Dowse, 2007). Effective communication between healthcare providers and patients to ensure comprehension of their treatment is difficult, and this problem is compounded when healthcare providers and patients speak different languages.

A critical link between language and culture should not be overlooked in healthcare (Johnstone and Kanitsaki, 2006). The different language groups in South Africa also reflect different cultures and traditions, and it cannot be assumed that the same pictogram would be interpreted the same by the different language and cultural groups (Dowse and Ehlers, 2004). In the selected studies, pictograms were tested on a wide variety of language and cultural groups. In study A, the authors recommended that pictograms should be culture-specific to avoid possible ambiguity in pictogram interpretation (Joshi and Kothiyal, 2011). Study C suggested that culture and language are important population characteristics to consider when designing medicine information materials

(Dowse *et al.*, 2011). Older studies concluded that culturally non-specific pictograms fail their purpose (Dowse and Ehlers, 1998). A recent study in Portugal, amongst Hindu cultural minorities, testing 15 USP-DI pictograms and 15 from the FIP, confirmed that pictograms need to be culturally specific for patients to understand their meaning (Kanji *et al.*, 2018). In another study where universal healthcare pictograms were tested in the US, South Korea and Turkey, results showed that the understanding of pictograms varied significantly in the different countries and that cultural aspects are important to consider in the design and development stages (Lee *et al.*, 2014). Silhouetting, faceless faces and colour are interpreted differently and often negatively in some cultures and testing pictograms in the target population, could avoid negative responses (Montagne, 2013). Only one of the selected studies assessed preference for colour by different cultural groups (I) and in this study respondents did not attach cultural importance to the use or avoidance of any particular colour. No information on culture and language was reported in studies E, F, G and H.

One way in which to negate the influence of culture on the interpretation of pictograms is to develop the pictograms with the target audience. In studies B, C, D, E, G and I the pictograms were all or almost all developed with the aid of the target population. Study I was specifically designed to test for differences in understanding between locally developed pictograms versus USP pictograms and found the local pictograms were significantly better interpreted than the USP pictograms. Studies C and E endorsed the involvement of the end-user in the development of the pictograms. A recommendation from study C was that the pictograms should be also tested in the target population, and the feedback from such a process should be used for further refinement of the leaflet. Both studies demonstrate that end-user involvement in the design of pictograms result in the production of improved PILs for low-literate patients.

Most of the studies were done in Africa (n=5), a continent that still struggles with low literacy and the majority of the studies were conducted at clinics or hospitals where it is relatively easy to interview participants who visit the doctor and / or receive their medication. In one study, which investigated the influence of input from the target population on the design and interpretation of pharmaceutical pictograms, interviews were also conducted in historical focal areas for the different language groups which were identified in various regions in South Africa. Within each of these major focal regions, three different geographical locations were chosen as interview sites so that any potential bias associated with the use of only one area was minimized. Within these focal regions, interviewees were selected from various sectors of the community, including unemployed people, domestic workers, informal traders and farm workers at taxi ranks and roadside farm stalls and on farms (I). More culturally-based interventions on design and interpretation of pictograms are needed to ascertain different cultural groups' interpretation of pictograms.

In addition to the development of pictograms with the target audience, another aspect that tended to be associated with the more effective interpretation of pictograms included verbal explanation of pictograms by healthcare personnel. After explanation of the meaning of pictograms, 9,50% of patients managed to interpret the meaning of all 10 pictograms, compared to 1,00% before explanation (A). The understanding of information of the study group with pictograms accompanied with a verbal explanation, were superior to that of the groups with pictograms only and text-with pictograms (D). In study F, the explanation of pictograms in the clinic proved to be beneficial for understanding of information after a one-week period. When compared to the studies in this systematic review, recent and older research also confirmed that pharmaceutical pictograms are valuable if verbal and written instructions are combined (Ngoh and Shepherd, 1997; Kanji *et al.*, 2018). In addition, pictograms could potentially aid in shortening counselling time by increasing understanding for the low literate patient (Dowse and Ehlers, 2004). This was specifically shown in study A, where participants were described as illiterate (A) and study D, where participants had an average duration of formal education of 6,1 years (D). It therefore seems that education and literacy are not important for understanding of the meaning of pictograms when pictograms are explained to participants.

2.5 Study limitations

Although the participant's first point of reference would be the medicine label, many of the studies included a PIL. Due to more space available on the PIL relative to the medicine label, important information regarding warnings can therefore also be communicated to the participant. Both the medicine label and the PIL are valuable forms of presentation to communicate medicine instructions through pictograms. However, two studies (A, F) did not record the presentation form. Since pharmaceutical pictograms were presented to low-literate patients in all the studies, the term "label" in the search terminology, was representative of any presentation form which was used to offer the pictograms to the participants.

The concept of low literacy was differently defined across studies and included various terms such as "schooling", "formal education", "highest level of qualification" and "grade level". The criteria for the target group "low literacy patient" therefore varied as studies were conducted over three continents and four countries. The criteria for low literacy could vary across countries and future research could aim to be more specific in the definition of "low literacy". Participants in study B were primarily selected on their literacy levels and therefore included participants who were not prescribed methotrexate – this could have lowered the motivation to read and remember the information, consequently affecting the outcome. Most of the individuals (78,00%) were at the high school level in the health literacy scores, as measured by the Rapid Estimate of Adult Literacy in Medicine (REALM). This was much higher than anticipated by the researchers and the large majority was English speaking.

Patient literacy was assessed using the REALM test in study B. None of the other studies recorded the use of the REALM test. Participants had a choice of completing a literacy test in either isiXhosa or English in study G and an English literacy test was conducted in study I. Study D reports the self-assessment test of English and Arabic comprehension as a study limitation by the participants, since this is liable to errors. It was not recorded in studies A and C, E, F and H if patient literacy tests were conducted.

Sample sizes were generally small. Randomization was specified in only two studies. Randomized controlled trials require large sample sizes to adequately address the questions that were posed and could therefore not be carried out in all studies. In two of the studies, the interviewers were blinded to the knowledge of the intervention (B, F). In the other studies, the interviewers were not blinded (D, G), or it was unclear if they were blinded (E, H). In some of the studies the participants were not blinded (B, F, G) and in others, it was unclear if they were blinded (E, H). In one study, the participants were not blinded to the knowledge of the intervention, but the outcome of the study was unlikely to be influenced by this (D). One study was a single-group study (A) testing pictograms in a group and another was a focus-group discussion study (C) and study I was a qualitative study. There were therefore no control groups in these studies.

The pictograms used in the studies were not described well or included in the methodology sections. In three of the studies, it was not mentioned in the methodology that pictograms, when shown to the participants, were accompanied by text (A, F, I). However, in the figures where pictograms were presented in study A and I, the pictograms were presented with accompanying text. In the figure in which the pictograms were presented in the study F, mention was made of minor instructions in the participants native language, which accompanied the pictograms.

In study F, all three participant groups also received the standard protocol of the respective clinics, in addition to the postoperative education that was part of the study. The standard protocol included a verbal description of dosing frequency and an occasional demonstration of medication administration and could have aided in reinforcing information that the participant received as part of the study protocol, and thereby influencing results.

In three of the five longitudinal studies, the participants were either poorly followed-up (A), were not available for follow-up (B) or did not bring their medication containers to the final visit to measure volume an indication of adherence (F).

Only one of the studies assessed the effect of colour on the interpretation of pictograms (I). No other studies assessed the appearance of the pictograms on interpretation of pictograms.

2.6 Conclusion

The evidence in the reviewed articles suggests a positive impact of using pictograms on medicine information materials as an intervention for understanding, adhering to and/or recalling the medicine regimen in the text for low literate patients. Pictograms were found as effective tools to communicate medicine instructions to patients with limited literacy and across different languages. The inclusion of pictograms on the materials was also preferred by participants in comparison to text only. Two factors that tended to increase the efficacy of pictograms included development of the pictograms with the target audience to accommodate cultural aspects, and, prior verbal explanation of the meaning of the pictograms to participants.

Factors that limit the generalisability of the findings of this review include small sample sizes and variation of study designs in terms of, number and description of pictograms used, administration and origin of pictograms with respect to the target population, defining and measuring literacy levels of participants and the effect of language and culture on the interpretation of pictograms. Further studies investigating pictograms should consider the foregoing aspects to improve the quality of evidence on pictograms in low literate populations.

Policy makers seem to take a broad and pragmatic view of the information gathered when they set priorities (Mays *et al.*, 2005). While the long-term focus of policy makers should be on achieving education for all, many low-literate patients are still at risk of not understanding medicine instructions. Policy makers should take responsibility to address the case of the low-literate in our society and find solutions to help them cope in an environment where information is mostly available in a format which requires reading skills. Pictograms is a solution which could further be explored by policy makers to aid in understanding of medicine information for the low-literate in our society.

Recommendations for practice may focus on reaching out to patients with pictographic reminder messages on cell phones. Favourable patient compliance outcome has been reported in a study that focused on the use of daily cell phone messages to remind patients to take their medication (Strandbygaard et al., 2010). Some messages e.g. “do not crush” are difficult to convey with static images, and cell phones represent the potential to animate this message (Wolpin *et al*., 2016). The aid of pictographic messages on cell phones could enable community healthcare workers to engage meaningfully with patients, which could help to reduce the burden on healthcare professionals at CHCs. Cell phone technology and the advantages offered by this technology in the health setting is a topic worth exploring.

Chapter 3: Methodology

3.1 Introduction

Chapter 3 outlines the methodologies and procedures used for data collection and analysis. An overview is given of the study setting, sampling and data collection procedure, analysis of the data and ethical considerations.

3.2 Methodology

This research study was explorative in design and a combination of quantitative and qualitative data was collected, by administering a semi-structured questionnaire to the participants attending CHCs.

3.2.1 Study setting

The research was conducted in public sector CHCs in the Cape Flats of the Cape Town Metropole in the Western Province of South Africa. This underserved, poverty stricken area has serious social problems including a high rate of unemployment and health related problems (South African History, 2011). An outline of the demographics, educational levels and living conditions of the Cape Town population are provided below.

The population in Cape Town is predominantly Coloured (42,40%) and Black African (38.60%) (Statistics South Africa, 2011). The percentage of people aged 20 years and older with no schooling is 1,80%, 5,30% has grade 5 or less, 29,80% completed grade 12 and 16,60% completed education higher than grade 12 (Statistics South Africa, 2011). Cape Town has an unemployment rate of 23,90% of the labour force (aged 15 to 64 years) and about half of the households (47,00%) have a monthly income of R 3 200 or less (Statistics South Africa, 2011). Having to share such a low income between members of a household, the poor are often hungry, are exploited, have a lack of access to clean water, sanitation and

schools, are vulnerable to crisis and homelessness and have particular difficulties in accessing healthcare due to transport costs (Woolard, 2002).
Approximately 95,00% of households have their refuse removed once a week by the local authority or a private company, 88,02% of households have access to a flushing toilet connected to the public sewer system, 78,40% do not live in a formal dwelling and 75,00% percent has access to piped water inside a dwelling (Statistics South Africa, 2011).

This study was linked to the service learning program at the School of Pharmacy at the University of the Western Cape (UWC) (University of the Western Cape, 2016). First year pharmacy students pre-packed a sugar and salt mixture according to standard operating procedures (University of the Western Cape, 2016) and the labeled sachets were subsequently distributed to the CHCs which served as student learning sites for the service learning program. The pre-packs were labeled with 'text-and-pictogram' instructions for use (University of the Western Cape, 2016) i.e. the experimental pack in this study.

3.2.2 Sampling

The CHCs were selected through purposive sampling, including all sites where the OR dry mixture sachet was distributed to via the Service-Learning in Pharmacy program. The study population included any patient attending a selected CHC on the day of data collection. Participants were selected by convenience sampling and we selected an arbitrary number of 60 participants for the experimental ('text-and-pictogram' instructions) and control groups ('routine text-only' instructions), to allow for statistical analysis. Participants were eligible for the study if they were older than 18 years of age and spoke English, Afrikaans and / or Xhosa. Exclusion criteria were: (1) severely impaired vision (2) hearing problems (3) too ill to participate in the survey and 4) non-English, non-Afrikaans and / or non-Xhosa speaking.

3.2.3 Data collection

Data collection was performed via semi-structured interviews. Two data collectors conducted the interviews. The researcher trained the data collectors in a standardised way of interacting with participants during the interview process. This entailed greeting the patient, asking permission to share the information sheet and in using the interview guide (Appendix E) to conduct the interview.

The data collector approached potential participants while they were waiting for an appointment at the CHC and introduced herself in a language that the participant could understand. An invitation to take part in the study was extended to each potential participant by reading the information from the study information sheet (see Appendix C). Following the agreement to take part in the study, the participant was asked to sign the consent form (see Appendix D). At each facility the study participants were sequentially allocated to either one of the two groups: a control group who received a 'routine text-only' or an experimental group who received a 'text-and-pictogram' OR dry mixture sachet.

The interview was structured into three parts; demographics and socio-economic information, questions about the preparation and use of the medicine which required reading of the content from the label and explanatory questions about how participants experienced interpreting the label. The first part of the questionnaire collected demographic data such as gender, marital status, residence, age, home language, educational level and the ability to read time from a digital watch.

In the second part of the interview, participants in the experimental group were shown the 'text-and-pictogram' medication label (Figures 3.1 and 3.2) and the control group was shown the 'routine text-only' medicine label that was dispensed at the CHC (Figures 3.3 and 3.4). The medicine labels were not explained to the participants prior to asking them the following questions, because the routine practice at facilities was being simulated. The six questions about the preparation and use of the medicines included:

1. What is the name of the medicine?
2. What should the medicine be used for?
3. How should this medicine be prepared for use?
4. How much of the medicine should be taken?
5. When / how often and for how long should the medicine be taken?
6. When should this medicine be thrown away?

Figures 3.1, 3.2, 3. 3 and 3.4 shows the actual size of the medicine labels and the arrows to indicate where the answers to the questions above were located on the labels.

Part three of the interview involved explaining to participants the intended message of the medication label and the following questions were asked to probe more about the reasons for participants' understanding of the medicine information and preferences for the label allocated to them:

- Which instructions were easy to understand?
- Which instructions were difficult to understand?
- What do you think could be the reason why you did not understand the instructions?
- Where the pictograms on the label helpful or hindering to your understanding of the medication instructions? (Only for those participants in the experimental group.)
- What do you think might help you interpret medication labels better? (Only for those participants in the control group.)
- To conclude the interview, participants were asked for any suggestions to aid him / her understand the medicine label better.

3.2.4 Data analysis

The interviews were audio recorded and transcribed verbatim. Data collectors also made notes on the data collection sheet. Descriptive statistics were used to describe the demographics of the participants such as gender, marital status, age, home language and educational level, and socio-economic status such as employment, monthly income and type of residence. The Mann-Whitney U-test and Chi-Square test were used to determine if there was a significant difference or associations between selected demographic variables of participants of the experimental and control groups, respectively. The Mann-Whitney U-test was used for the continuous variable such as age and the Chi-Square test was used for categorical variables such as level of education, language and the ability to read time.

The participants' responses to the six questions that comprised the second part of the questionnaire regarding the preparation and use of OR medicine were categorized according to a three point Likert Scale, where (1) was not aligned with the information appearing on the label (way off, not even close), (2) neutral (recognized some of the information), and, (3) fully aligned with the information appearing on the label. Table 3.1 summarises the answers as they appeared on the label of the OR sachets. The primary outcomes were correct interpretation of the information according to the intended medicine use instructions on the medication label presented to the participants. Figures 3.1, 3.2, 3.3 and 3.4 represent the labels that the participants were presented with during the data collection process. The scoring allocation for the six questions on the preparation and use of OR dry mixture are detailed in Appendix F, Table F.1. The Chi-Square test was used to determine if there were any significant association between the accuracy of responses of the experimental and control group participants. The association characteristics that were tested included not aligned, partially aligned or fully aligned with the answer appearing on the respective label, i.e. did being in the control group make these participants more likely to be fully aligned with the correct answer than being associated with the experimental group. A P-value of less or equal to 0.05 was considered statistically significant.

IBM SPSS version 25 was used to perform all statistical analyses. For the Chi-Square test the results were also shown as bar charts.

Table 3.1: Summary of the information that appeared on the experimental and control labels in response to the six medication preparation and use questions.

Question	**Experimental label**	**Control label**
What is the name of the medicine?	Oral Rehydration Mixture.	Trade name.*
What should the medicine be used for?	For prevention of dehydration during diarrhea (front and back).	For rehydration (front). Powder for oral rehydration therapy (back). For the treatment of electrolyte and fluid depletion associated with diarrhoea (back).
How should this medicine be prepared for use?	Boil 2 liters of water and cool. Pour water in a clean 1 liter bottle. Add dry ingredients to clean water (also depicted in three sequential pictograms).	Dissolve one sachet in a liter of previously boiled and cooled water.
How much of the medicine should be taken?	Drink ½ cup after every watery stool (accompanied by one pictogram).	Administer the solution in frequent small volumes to compensate for electrolyte and fluid imbalance.
When/how often and for how long should the medicine be taken?	Drink after every watery stool / take when you have diarrhoea (derived from the indication for use, “for	Take when you have diarrhoea, take after a loose stool and take until the diarrhoea clears up (derived

	prevention of dehydration during diarrhoea"). Take until the diarrhoea clears up (derived from "for prevention of dehydration during diarrhoea"). Take no longer than 24 hours (derived from "do not keep mixture for more than 24 hours".	from "for the treatment of electrolyte and fluid depletion associated with diarrhoea"). Take when you have an electrolyte and fluid imbalance, take frequent small volumes, discard unused mixture after 24 hours (derived from "administer the solution in frequent small volumes to compensate for electrolyte and fluid imbalance" and "discard unused solution after 24 hours.")
When should this medicine be thrown away?	Do not keep mixture for more than 24 hours.	Discard unused solution after 24 hours.

1186 **Trade name not revealed for confidentiality purposes*

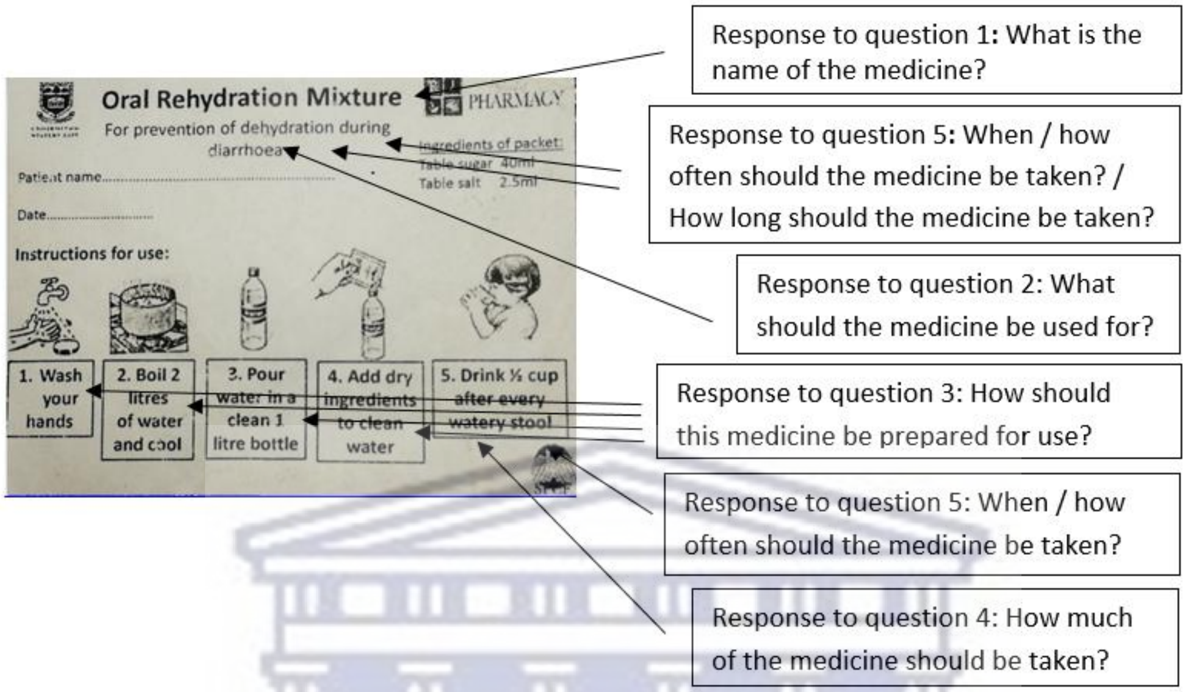

Figure 3.1: The OR dry mixture label mounted on the front of the experimental group (n = 67) sachet, packed by UWC pharmacy students during compounding sessions, with the exact sizes of the pack presented (length = 5,5 cm, width = 7,5 cm).

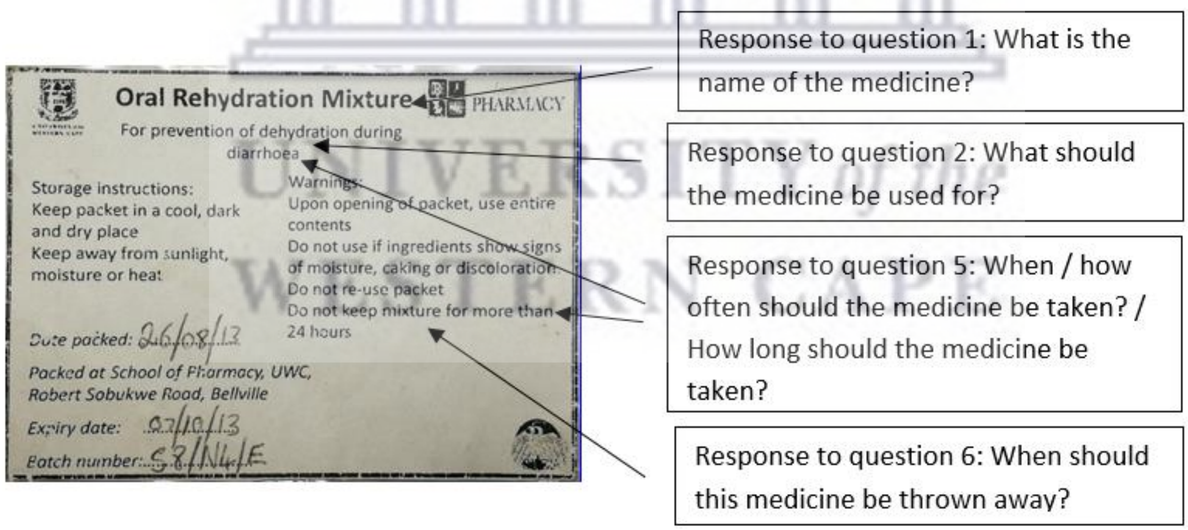

Figure 3.2: The OR dry mixture label mounted on the back of the experimental group (n = 67) sachet, packed by UWC pharmacy students during compounding sessions, with the exact sizes of the pack presented (length = 5,5 cm, width = 7,5 cm).

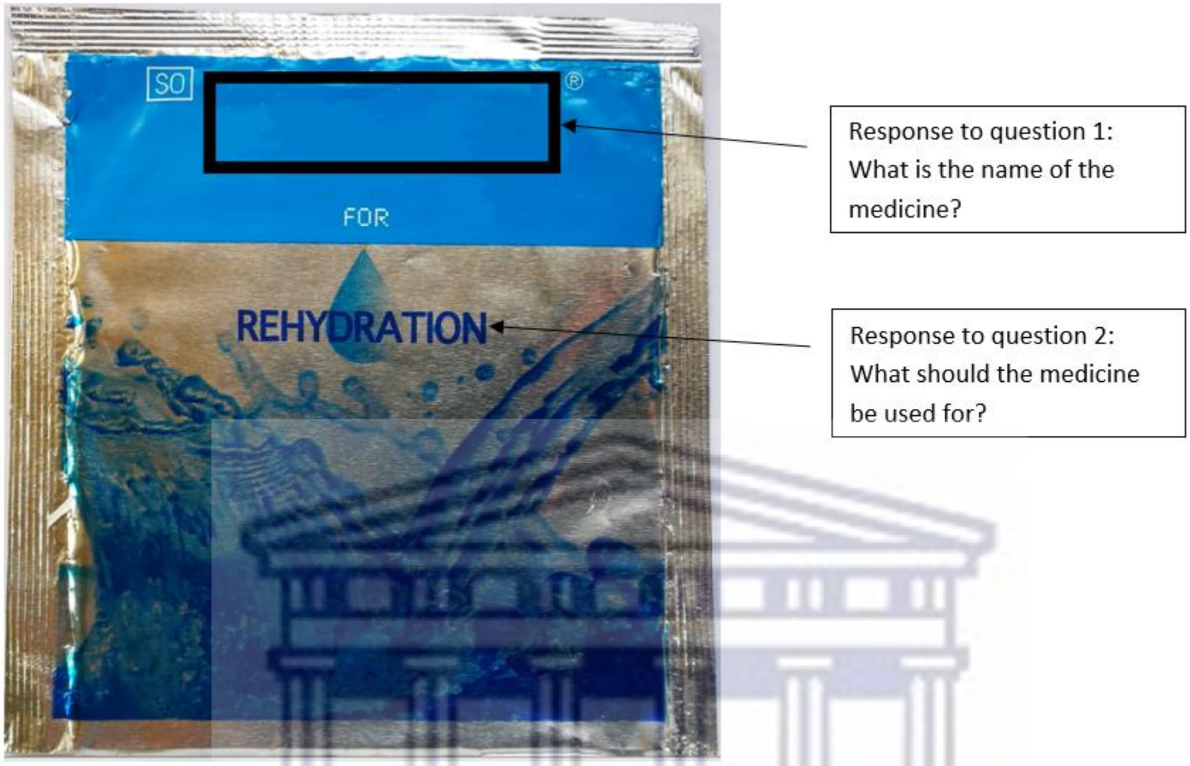

Figure 3.3: Front of the OR dry mixture label of the control group (n = 65) sachet that is routinely dispensed at the CHCs, with the exact sizes of the pack presented (length = 10,5 cm, width = 10,0 cm).
** For protection of the third party, the names of the product and manufacturer are blocked out.*

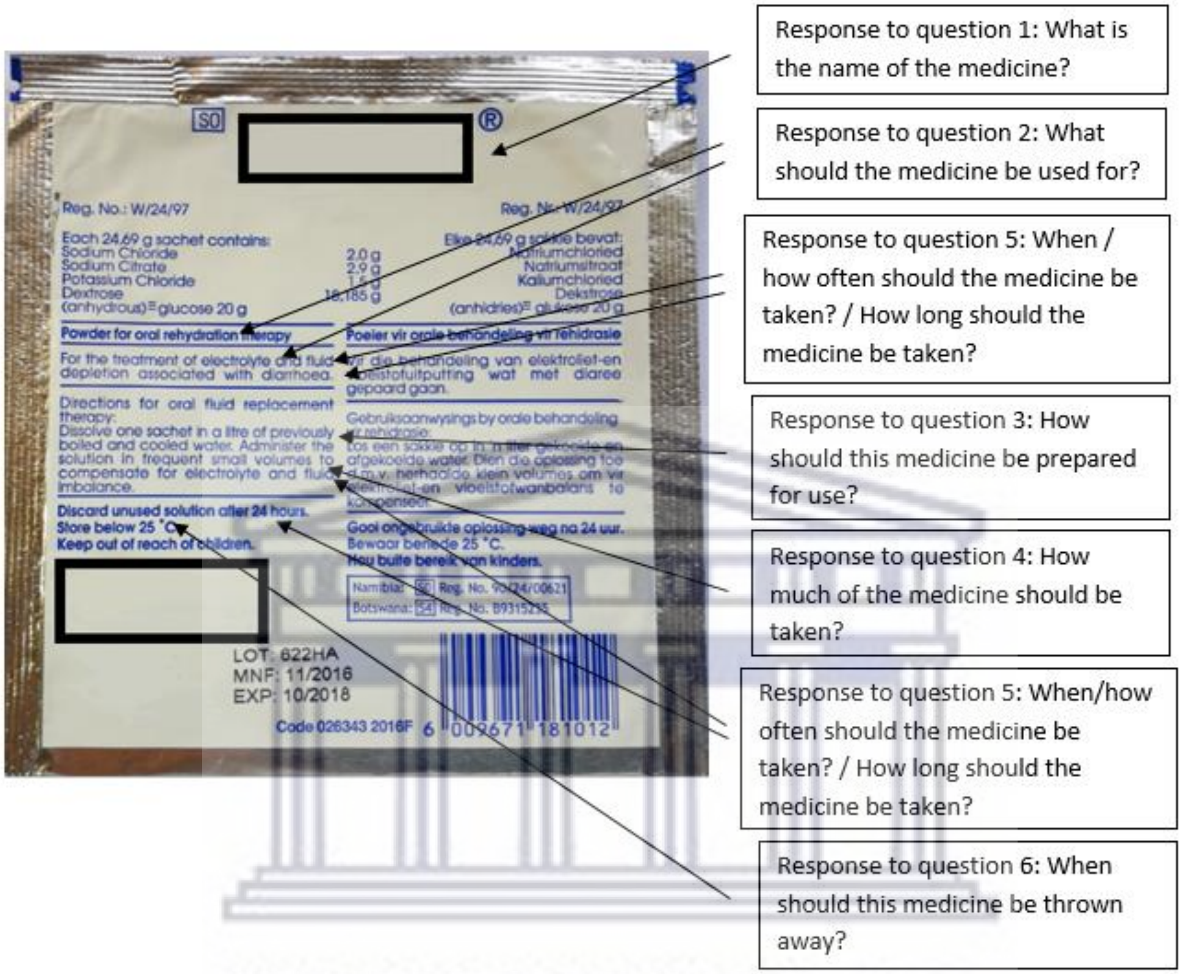

Figure 3.4: Back of the OR dry mixture label of the control group (n = 65) sachet that is routinely dispensed at the CHCs, with the exact sizes of the pack presented (length = 10,5 cm, width = 10,0 cm). ** For protection of the third party, the names of the product and manufacturer are blocked out.*

Participants' responses to the explanatory questions in part three of the interview were thematically analysed.

3.3 Ethical considerations

Approval for the study was obtained from the Biomedical Research Ethics Committee of UWC (BM/16/3/01). Approval for access to facilities was obtained from the Western Cape Department of Health (WC_2016RP38_657). Permission to conduct the study at the CHCs was obtained from the facility managers of the CHCs.

All participants were provided with a study information sheet (Appendix 3) upon recruitment and signed informed consent (Appendix 4) before starting with the questionnaire. All information was kept confidential by assigning a unique identifier to each participant on the informed consent form and only using this unique identifier on the individual interview outline (Appendix 5). The consent forms and interview collection sheets were stored in separate locations to prevent any identifying information being available during data collection and analysis. All information collected from the patient was locked in a secure location and will be destroyed after the research outputs have been published. There were no risks anticipated for the participants in this study. The participants may have experienced the benefit of better understanding of how to prepare and use OR medication.

3.4 Summary of Chapter 3

The main procedures for data collection in this chapter were outlined and the results are presented in the following chapter.

Chapter 4: Results

4.1 Introduction

This chapter presents the results of the research questions that were asked in the data collection and analyses phases of the study (refer chapter 3). The study was conducted over a three week period in September 2016 at four different CHCs in the Tygerberg sub-district of the Cape Town Metropole. A total number of 132 participants took part in this study of which 67 were allocated to the experimental group and 65 allocated to the control group.

Most of both the experimental (67,00%) and control group (66,00%) participants, were visiting the paediatric clinic for immunization, a check-up, to see the dietician, deworming, a cold / flu injection, weighing the baby or because the baby or child was sick. The remainder of both the experimental (33,00%) and control group (34,00%) participants visited the clinic either for seeking treatment for themselves or collecting chronic medicines. The time taken for each interview varied between 6 and 20 minutes.

4.2 Demographic data

The demographic information obtained from the participants is displayed in Table 4.1. Most (121) participants were female. Over three-quarters (78,03%) of the participants were single or unmarried. The ages of participants ranged from 18 to 59 years, with about half (49,24%) of the participants between 20 to 29 years. Almost two-thirds of the participants (63,63%) reported Afrikaans as their home language. Most (90,15%) of the participants received formal education ranging between grades 7 and 12. Only eight (6,06%) of the participants could not tell the time on a watch (analog and / or digital); of which six had education levels between Grade 7 to 12, and two between Grade 1 to 6.

1252 **Table 4.1:** Demographic information of the participants (n = 132).

	Number	**Percentage**
Groups		
· Experimental	n = 67	50,76%
· Control	n = 65	49,24%
Location (suburb)		
· A	n = 30	22,73%
· B	n = 43	32,57%
· C	n = 18	13,64%
· D	n = 41	31,06%
Gender		
· Male	n = 11	8,33%
· Female	n = 121	92,67%
Marital status		
· Married	n = 26	19,70%
· Unmarried	n = 103	78,03%
· Divorced	n = 3	2,27%
Age range (in years)		
· 18 to 19	n = 11	8,33%
· 20 to 29	n = 65	49,24%
· 30 to 39	n = 41	31,06%
· 40 to 49	n = 11	8,34%
· 50 to 59	n = 4	3,03%
Home language		
· Afrikaans	n = 84	63,63%
· English	n = 7	5,30%
· isiXhosa	n = 37	28,03%

·	Afrikaans, English, isiXhosa and other	n = 4	3,04%
Educational level			
·	Grade 1 to 6	n = 6	4,55%
·	Grade 7 to 12	n = 119	90,15%
·	Tertiary	n = 7	5,30%
Tell the time from a digital watch			
·	Yes	n = 124	93,94%
·	No	n = 8	6,06%

Statistical sub-analyses were performed to determine if there was a significant difference or associations between the experimental and control groups in terms of age (Mann-Whitney U-test), education (Chi-Square test), language (Chi-Square test) and ability to read time (Chi-Square test) – there were no significant differences or associations in numbers between the groups (Table 4.2). As such, the two groups were well matched in terms of these demographics.

Table 4.2: Summary of statistical analyses of the demographic profile for age, education, language and ability to read time, of the experimental group (n = 67) and control group (n = 65) participants.

Variable	**Experimental group**	**Control group**	**P-value**
Age, years (median, range)	28 (18-53)	27 (18-56)	0,321[a]
Education			
Grade 1 to 6	3 (4,50%)	3 (4,60%)	0,941[b]
Grade 7 to 12	60 (89,60%)	59 (90,80%)	0,941[b]
Tertiary	4 (6,00%)	3 (4,60%)	0,941[b]
Language			
Afrikaans	43 (64,20%)	41 (63,10%)	0,734[b]
English	5 (7,50%)	3 (4,60%)	0,734[b]
Other	19 (28,40%)	21 (32,30%)	0,734[b]

Ability to read time			
Yes	62 (92,50%)	62 (95,40%)	0,718[b]
No	5 (7,50%)	3 (4,60%)	0,718[b]

a: P-value calculated from Mann-Whitney U-test.
b: P-value calculated from Chi-Square test

The socio-economic details of the participants are summarized in Table 4.3. Only a third (31,06%) of the participants were employed and over half (55,54%) had some form of income. Over two-thirds of participants lived in a formal dwelling (67,42%), with the majority (78,03%) having access to a tap inside the house. Refuse removal services were available to almost all the participants (96,21%).

Table 4.3: Socio-economic information of the participants (n = 132).

	Number	Percentage
Groups		
· Experimental	n = 67	50,76%
· Control	n = 65	49,24%
Employed		
· Yes	n = 41	31,06%
· No	n = 91	68,94%
Monthly income		
· No income	n = 59	44,70%
· R 1 to R 3 200	n = 48	36,36%
· More than R 3 200	n = 23	17,42%
· Do not know	n = 1	0,76%
· Social grant	n = 1	0,76%
Access to running water – tap inside the house		
· Yes	n = 103	78,03%

· No	n = 29	21,97%
Access to running water – tap outside the house		
· Yes	n = 83	62,88%
· No	n = 14	10,61%
· Missing info	n = 35	26,51%
Refuse removal		
· Yes	n = 127	96,21%
· No	n = 5	3,79%
Residence		
· Formal dwelling	n = 89	67,42%
· Informal dwelling	n = 22	16,67%
· Informal dwelling / shack in a back yard	n = 16	12,12%
· Informal dwelling / shack not in a back yard	n = 5	3,79%
Reason for visiting the clinic		
· Baby the reason for visit to clinic	n = 88	66,67%
· Caregiver the reason for visit to clinic	n = 44	33,33%

4.3 Responses to questions relating to the label

The responses of the six questions relating to the medicine label were scored and divided into three categories, namely: not aligned, partially aligned and fully aligned to the model answer that appeared on each label. These categories were compared to determine if there were any significant associations between the answer being not aligned, partially aligned or fully aligned and being the experimental or control group. A summary of the results is provided in Table 4.4, for the experimental group and Table 4.5, for the control group. The Chi-Square statistical test was used to determine whether there were significant associations (for example did being in the experimental group make participants more likely to have a fully aligned answer?).

Table 4.4: Results of the questions regarding the preparation and use of medication as instructed on the medication label – experimental group (n = 67).

	Question 1	**Question 2**	**Question 3**	**Question 4**	**Question 5**	**Question 6**
Not aligned with intended message	11,90%	9,00%	11,90%	20,90%	23,80%	46,20%
Neutral alignment with intended message	16,40%	3,00%	25,40%	7,50%	44,80%	6,00%
Fully Aligned with intended message	71,70%	88,00%	62,70%	70,10%	29,90%	46,30%
Missing answer	-	-	-	1,50%	1,50%	1,50%
Total	100	100	100	100	100	100

Table 4.5: Results of the questions regarding the preparation and use of medication as instructed on the medication label – control group (n = 65)

	Question 1	**Question 2**	**Question 3**	**Question 4**	**Question 5**	**Question 6**
Not aligned with intended message	7,70%	12,30%	24,60%	60,0%	40,00%	35,40%
Partial alignment with intended message	10,80%	3,10%	16,90%	26,20%	35,40%	3,10%

Fully Aligned with intended message	81,50%	84,60%	58,50%	12,30%	24,60%	61,50%
Missing Answer	-	-	-	1,50%	-	-
Total	100	100	100	100	100	100

4.3.1 What is the name of the medicine?

More participants in the control (81,50%) than the experimental group (71,60%) were fully aligned with the correct answer for the question "what is the name of the medication" (see Figure 4.1). However, no significant association was found in the accuracy of responses between the experimental and control groups (p = 0,407) i.e. being associated with the control group did not make participants more likely to be fully aligned with the correct answer appearing on the label than being associated with the experimental group.

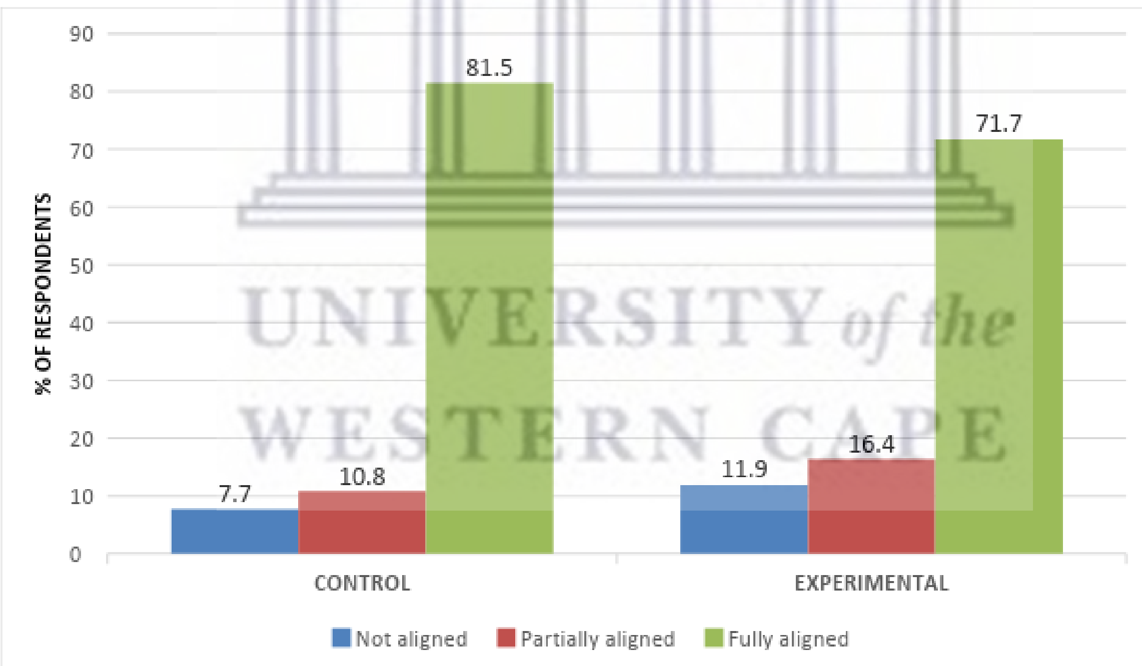

Figure 4.1: Accuracy of responses to the question: "what is the name of the medication" obtained from the experimental group (n = 67) and control group (n = 65) (p= 0,407).

4.3.2 What should the medicine be used for?

For the question “what should the medicine be used for” more participants from the experimental group (88,00%) than the control group (84,60%) were fully aligned with the correct answer (see Figure 4.2). However, no significant association was found in the accuracy of responses between the experimental and control groups (p = 0,820).

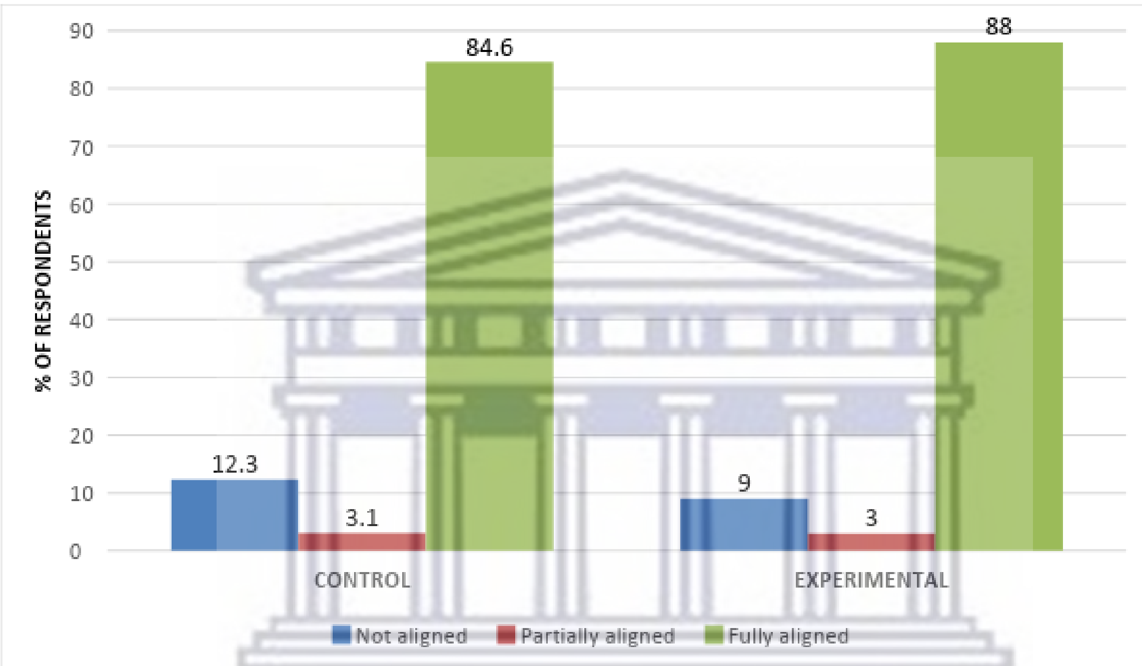

Figure 4.2: Accuracy of responses to the question: “what should the medicine be used for” obtained from the experimental group (n = 67) and control group (n = 65) (p = 0,820)

4.3.3 How should this medicine be prepared for use?

For the question, “how should this medication be prepared for use”, more participants from the experimental (62,70%) than the control group (58,50%) were fully aligned with the correct answer (see Figure 4.3), but no significant association was found (p = 0,127).

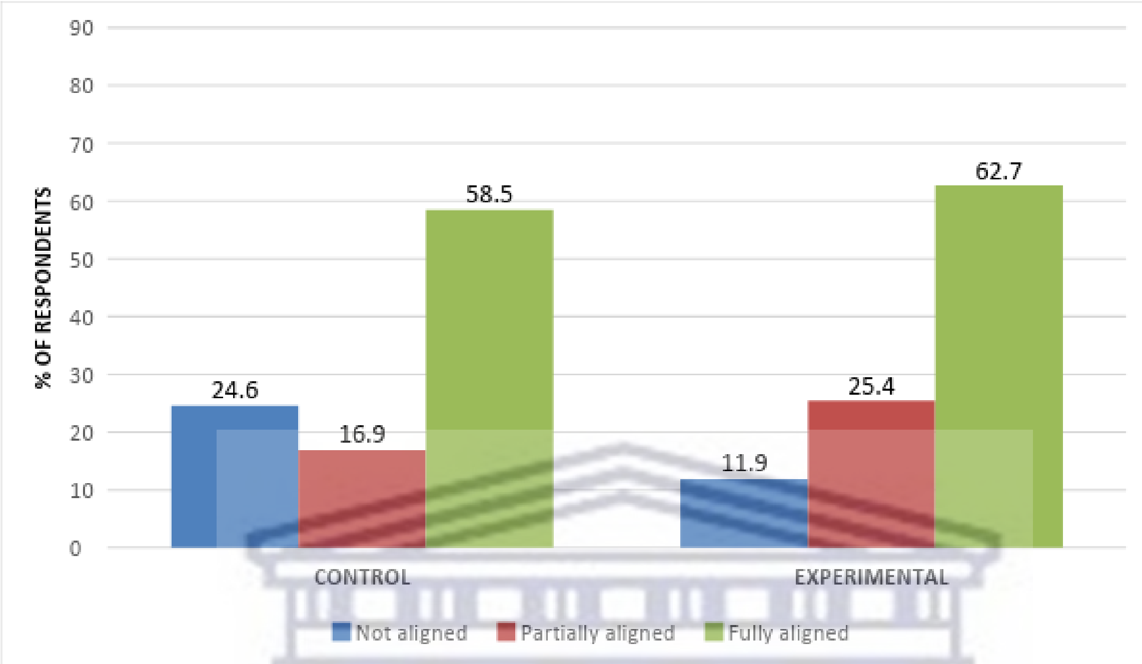

Figure 4.3: Accuracy of responses to the question: "how should this medication be prepared for use" obtained from the experimental group (n = 67) and control group (n = 65) (p = 0,127).

4.3.4 How much of the medicine should be taken?

For the question "how much of the medicine should be taken", more participants from the experimental (70,10%) than the control group (12,30%) were fully aligned with the correct answer. Most of the control group participants (60,00%), were not aligned with the correct answer (see Figure 4.4). Chi-square test showed significant association in the responses between experimental and control groups ($p < 0.001$). These associations implied that the experimental group was more likely to have a higher number of participants who were fully aligned than in the control group.

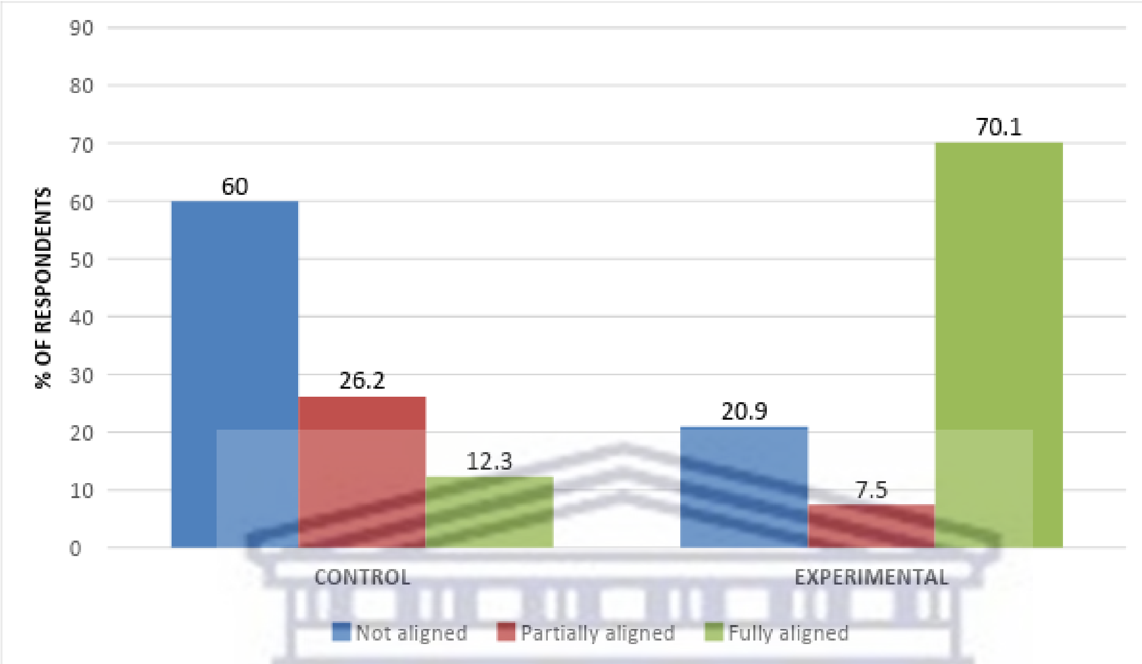

Figure 4.4: Accuracy of responses to the question: "how much of the medicine should be taken" obtained from the experimental group (n = 66) and control group (n = 64) (p = 0,000).

4.3.5 When / how often and for how long should the medicine be taken?

For the question "when / how often and for how long should the medicine be taken", participants from the experimental and the control groups were either not aligned (40.00%) or partially aligned (44.80%) with the correct answer (see Figure 4.5), respectively. In the statistical analysis, no significant association was found between experimental and control groups regarding the responses (p = 0.154).

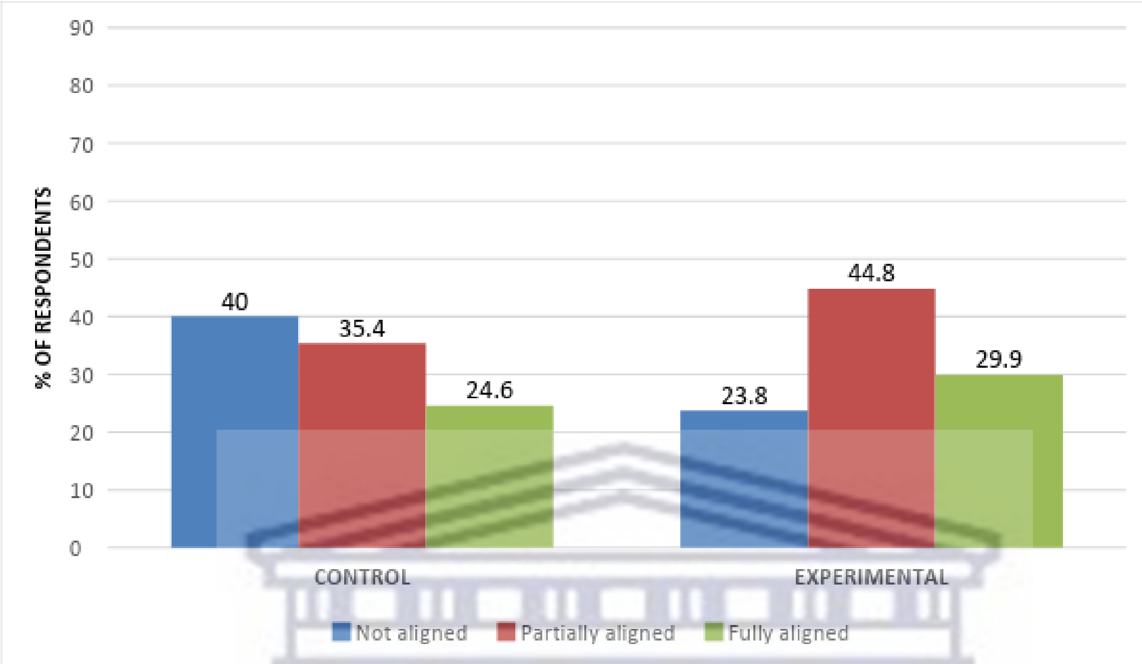

Figure 4.5: Accuracy of responses to the question: "when / how often and for how long should the medicine be taken" obtained from the experimental group (n = 66) and control group (n = 65), (p = 0,154).

4.3.6 When should this medicine be thrown away?

For the question "when should this medicine be thrown away" more participants from the control group (61,50%) than the experimental group (46,30%) were fully aligned with the correct answer (see Figure 4.6). In the statistical analysis, no significant association was found between experimental and control groups regarding the responses (p = 0,225).

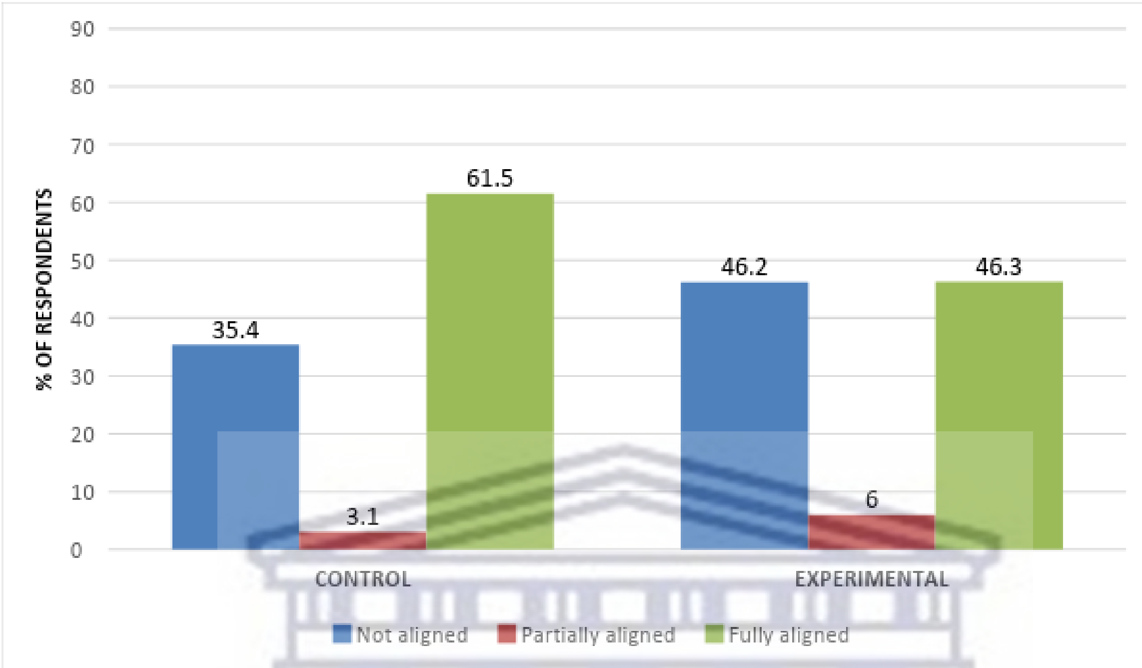

Figure 4.6: Accuracy of responses to the question: "when should this medicine be thrown away" obtained from the experimental group (n = 66) and control group (n = 65), (p = 0,225).

The statistical power of this Chi-Square test was calculated posthoc based on the sample size (n=132) using G*Power version 3.1.9.4. The power was found to be 93% calculated with an effect size of 0,3 (medium), α-value of 0,5 and degrees of freedom of 1.

4.4 Control group sub-analyses – font size, bold / not bold font types and white space

From the primary analysis, it was noted that font size, white space and bold type face could have influenced the accuracy of responses for the "text only" control label. An analysis was completed to determine if these variables could have led to significant differences in the accuracy of the responses. The different font sizes of the instructions on the routine text-only pack were determined by comparison with printed samples of Arial font in different point sizes (a common measure of print size). The fonts on the label and printouts were measured with a ruler (Leat *et al.*, 2014). The font sizes on the control routine text-only medicine label were found to be equivalent to 7 (question 2, 3, 4, 5, 6), 18 (question 2), 35 (question 1) and 55 (question 1) pt Arial. A comparison in responses to questions 1 to 6 with respect to font size was performed using the

Kruskal-Wallis test. This test indicated that there was overall significance ($p < 0,001$) in the responses of the six questions regarding the medicine information on the label. Furthermore, post-hoc analysis was performed using the Mann-Whitney U-test in order to determine specifically where the significance lay. Values were reported as median and range. The results of the Mann-Whitney U-test are summarized in Appendix G Table G.1.

Statistical significance in the difference in the responses was found in each case for the comparison of question 1 with questions 3 ($p = 0,015$), 4 ($p = 0,000$), 5 ($p = 0,000$) and 6 ($p = 0,000$) except for the comparison of question 1 with question 2 ($p = 0,414$), where there was no statistical significant difference. Question 1 was answered better than questions 3, 4, 5 and 6. The bigger difference in font size between the answers to question 1 (font size 35 and 55 pt Arial) and questions 3, 4, 5, and 6 (font size 7 pt Arial), could have contributed to a significant difference in the accuracy of responses. The much smaller difference in font size between the answers to questions 1 (font size 35 and 55 pt Arial) and 2 (font size 18 pt Arial) could have contributed to no significant difference found between the responses of these two questions. Answers to both questions 1 and 2 had white space around it, which also might have improved ease of reading.

Statistical significance in the difference in the responses was found for the comparison of question 2 with the remaining questions 4 ($p = 0,000$), 5 ($p = 0,000$) and 6 ($p = 0,002$), except for the comparison of question 2 with question 3 ($p = 0,120$), where there was no significant difference. Question 2 was answered better than questions 4, 5 and 6. The bigger difference in font size between the answers to question 2 and questions 4, 5 and 6 could have contributed to significant difference in responses in these cases. The white space around the answer to question 2 might have also improved ease of reading.

Statistical significance in the difference in the responses was found in each case for the comparison of question 3 with all the remaining questions, 4 ($p = 0,000$), 5 ($p = 0,000$), and 6 ($p = 0,049$). Question 3 was answered better than questions 4, 5 and 6.

No statistical significance was found in the difference in responses for the comparison of question 4 with question 5 (p = 0,060) which could be attributed to the answers to both questions being the same font size and not bold font type. A significant difference was found in the difference in responses for the comparison of questions 4 and 6 (p = 0,000). Question 6 was answered better than question 4. The only difference between the fonts of the answers to these two questions is that question 6's answer was in bold font type.

Statistical significance in the difference in responses was found for the comparison of questions 5 and 6 (p = 0,001). Question 6 was answered better than question 5. The only difference between the fonts of the answers was that question 5's answers were in either bold or not bold font type and question 6's answer was in all bold font type.

The statistical power of this Mann-Whitney U-test was calculated posthoc based on the sample size (n=65) using G*Power version 3.1.9.4. The power was found to be 70% calculated with an effect size of 0,3 (medium) and α-value of 0,5.

4.5 Responses to questions: observed deviation between participant interpretation of the label and intended message of the label

In response to the question "which instructions were easy to understand", almost half (33/67) of the experimental group stated that everything on the label was easy to understand in contrast to only 18,46% (12/65) of the control group. The experimental group also specified instructions depicted by pictograms (38/67) to be easy to understand. The rest of the experimental group (14/67) participants mentioned instructions relating to text to be easy to understand, including small font text surrounded with white space, pictograms and small font text, pictograms and all text, small font text and large font text. The control group mentioned instructions relating to large font text (26/65), small font text (11/65) and bold font type text (6/65) to be easy to understand. In addition, almost half of the control group (31/65) found the preparation of medication easy to understand.

In response to the question: "Which instructions were difficult to understand?", approximately two thirds (43/67) of the participants in the experimental group indicated that they did not find anything difficult about the text-and-pictogram instructions while approximately one third (22/65) of the control group participants indicated that they did not find anything difficult about the label with routine instructions. The positive effect of a pictogram was evident for the question relating to medicine dosage, where more control participants (15/65) reported this instruction was difficult to understand, when compared to the experimental group (1/67). The most difficult instruction for both the experimental (20/67) and control (16/65) participants, was reported to be related to the indications for use question, question 5, which was in text only on the experimental label.

In response to the question for the reasons why participants thought they might have misunderstood the instructions on the label, a third of the control participants (22/65) indicated that they could not see the information on the medicine label, whereas for the experimental group this did not seem to be a problem (1/67). The second most prevalent reason that both groups (experimental n = 10 and control n = 9) gave was that they did not understand what was written on the label. Other reasons for not understanding the instructions included not being familiar with the medication, difficulty understanding English, difficulty in reading label information and being illiterate.

The majority of participants (63/67) from the experimental group agreed that the pictograms on the label were helpful for them to understand the label. The control participants provided suggestions on what they thought might have helped them understand the routine label better. A quarter of these participants (16/65) indicated that pictures, larger font size (6/65) and more understandable language (6/65) would have helped them to interpret the medicine label better. Other suggestions included inclusion of more languages, more information, and an explanation by the health care provider.

4.6 Participants' suggestions on how to improve medicine labels

The most frequent suggestion from both groups (experimental 31/67; control 17/65) on how to improve medication labels was to add pictures to it. Some participants had no suggestions (experimental 13/67; control 16/65). Participants' responses could be further subdivided into suggestions to improve the readability of the label and using simpler and more explicit language to improve their understanding of the medicine label. In terms of understanding, experimental participants wanted more clarity on when to take the medicine (7/67), more explicitly specified quantities for preparation and dosage (5/67), use simpler language (7/67) and more languages on the label (2/67). In terms of readability, participants suggested bigger font.

In terms of understanding, control participants suggested using different languages on the label (7/65), adding verbal explanations (4/65), more explicit instructions on when to take the medication (2/65), what to use the medicine for and to use simple language. Control group participants also had various suggestions of improving the readability of the medicine label such as moving information to the front of the label (3/65), bigger font (3/65), bigger containers, use arrows to show what to do, information should be in point form, give step by step instructions, and use better contrast between writing and background.

Chapter 5: Discussion

The primary aim of this study was to compare the accuracy of the interpretation of medicine use instructions from two different OR medication labels – the control 'routine text-only' label and an experimental label with 'text-and-pictograms'. The purpose of this study was to mimic normal practices of the dispensing of OR packages at CHCs in Cape Town and determine how well participants understood the instructions for use from the medication label only, as this is often the only information available in healthcare clinics and government hospitals. This discussion section will discuss the results firstly in terms of demographics of the participants and how these are matched with previous pictogram studies, secondly the effect that pictograms and text had on the accuracy of interpretation of participants, and thirdly in terms of text only on the OR medicine labels.

Even though most of our participants were in the educational group of having completed education level between grade 7 and 12 (90,00%), the number of years of formal schooling cannot predict literacy (Remshardt, 2011). With literacy defined as the ability to read and write (Oxford Dictionaries, 2019), health literacy is more than the ability to read or write and involves accurate interpretation of health information and using it for its "best benefit" (Remshardt, 2011). Patients with inadequate literacy also have less health-related knowledge and healthcare workers should mitigate the effects of low literacy by communicating more clearly with patients (DeWalt and Pignone, 2005).

Low literacy or illiteracy is only part of the complicated compliance issue, but if you cannot read or understand medicine information, you are effectively not taking part in the patient healthcare relationship (Remshardt, 2011). There is also an important link between low literacy and a lack of desire to take part in medical decision making (DeWalt *et al.*, 2007). In addition to health and illness challenges, problems with literacy become a "silent disability", a disability which can be targeted with medical information materials at the patient's level of understanding (Conlin and Schumann, 2002).

Most participants were female (92,67%). Women, traditionally, have better health seeking behavior than men and would more frequently seek medical help (O' Brien, *et al.*, 2005). This demographic compares well with the same demographic in studies of the literature review, where eight of the nine studies reported more female than male participants. Most of the participants in our study were in the age group 21 to 29 years. The reason for this could be that our study participants were recruited outside the paediatric clinic, where young mothers between the ages of 21 and 29 years brought their children for a visit to the clinic.

Differences in numbers of participants in the experimental and control groups from the different educational, age and language groups were statistically compared. There were no significant differences or associations in numbers between the groups. In addition, participant ability to tell the time from a watch was noted. The effect of language (Afrikaans, English or isiXhosa) on the understanding of information on the labels was not evaluated.

Two questions that directly pertained to the interpretation of pictograms and text on the experimental medicine label, included the pictogram pertaining to dosing of OR solution and four sequential pictograms illustrating the preparation of OR solution. The question "how much of the medicine should be taken" was the only question that showed statistical significance in the results with a P-value of 0,00. The correct answer appeared as a single pictogram of a little boy drinking from a glass with the text "half a cup after each loose stool" underneath it. This was the last pictogram in a series of five pictograms on the front of the experimental label. The positive effects of pictograms was consistent with other studies carried out in South Africa (Dowse and Ehlers, 2005; Mansoor and Dowse, 2003) where text-only medicine information was compared with text-and-pictogram information. One study tested the understanding of medicine pictograms on labels for antibiotics with isiXhosa speaking participants (Dowse and Ehlers, 2005) and the second tested a label and PIL for an antifungal for the mouth with local African population participants, mostly from the Xhosa ethnic group (Mansoor and Dowse, 2003). Both studies reported that the presence of pictograms on medicine labels had a significantly positive influence on the understanding of medicine instructions.

Some of the participants in this study specifically mentioned the picture of the little boy who was shown drinking the medication on the experimental label. In this study, it was not tested how the boy in the picture was perceived by different cultural and language groups. It has been noted in the literature that pictograms developed for specific cultural groups, tend to produce higher levels of comprehension and are more preferred (Dowse and Ehlers, 2001). When creating pictograms, cultural norms of dress, hair, gestures, facial expressions, objects and buildings should be considered (Montagne, 2013). Symbols that are specific to a culture will not translate to other groups (Montagne, 2013). In a Canadian study to determine if linguistically and culturally diverse individuals would interpret pictogram instructions for medicines differently, participants in three different language groups, from the Cantonese-speaking Chinese community, the Punjabi-speaking East Indian community and the Somali-speaking Somali community pointed out that many of the pictograms in the study contained confusing and ambiguous elements (Kassam *et al.*, 2004).

In terms of participants' preferences and understanding of the labels, most of the participants in the experimental group agreed that the pictograms were helpful for aiding their understanding of the medicine label. Almost half of the experimental group participants identified the pictograms to be easy to understand as compared to the rest of the information on the label. This was most evident in the identification of the dosage question where more control participants had difficulty in understanding the text only instructions as compared to the experimental group who hardly mentioned this question to be difficult. Indeed, both control and experimental participants suggested pictograms or pictures as suggestions to understand the medicine label better. In other studies where text-and-pictogram presentations were compared, participants also indicated preference for pictogram presentations (Thompson *et al.*, 2010; Mansoor and Dowse, 2003; Dowse *et al.*, 2011; Dowse and Ehlers, 2005; Dowse and Ehlers, 2004)

It seemed that it was easier for the respondents to find the answer to a question that was presented in one pictogram, compared to finding the answer in four pictograms and text, as in the question relating to the preparation for use. This question required the participants in the experimental group to translate four sequential pictograms and accompanying text of the instructions for use on the front of the experimental pack, into their answer. Although the answer to this question was in pictogram and text format, the experimental participants found it difficult to mention all four steps of the preparation process in their answer. This seems to support literature that states that a logical sequence of the pictograms may be interpreted differently for viewers who struggle to read (Montagne, 2013) and multi-step instructions are confusing to patients (Wolf *et al.*, 2006). In our study group, most of our participants were in the grade 7 to 12 educational level, but adults read three to five grade levels lower than their number of school years completed (Doak *et al.*, 1996). The sequence of pictograms was therefore not interpreted well. No more information could be found in the literature regarding the use of pictogram sequences for a single medicine instruction. In a study which tested a leaflet containing ARV information targeted for low-literate readers, no indication was given how many pictograms illustrated key concepts (Dowse *et al.*, 2011).

In a systematic review which forms part of this study, five of the nine studies reviewed did not specify the number of pictograms which were tested for understanding, adherence to, recalling and finding the instructions to the medication regimen in the text. It was therefore difficult to compare studies in terms of number of pictograms. Only one of the nine studies mentioned the use of a sequence of pictograms to explain a single concept (Braich *et al.*, 2011). A series of illustrated pictograms in study F (Braich *et al.*, 2011) indicted the use of four pictograms to illustrate the application of the medicine (eye drops). The authors did not indicate whether this short series of pictogram instructions was difficult for the participants to understand. More robust studies should be done to assess the patients’ ability to manage more than one pictogram per instruction.

However, even though patients with low-literacy could gain the most from the use of pictograms (Montagne, 2013), it is important to explain them to patients and provide the intended meaning through counseling (Joshi and Kothiyal, 2011; Montagne, 2013). In our study, pictograms were not explained to participants before asking the participant to interpret the pictograms. Yet, in the explanatory questions, some participants suggested that the labels be explained better. The effectiveness of pictograms on understanding of medication instructions is greatly increased when patients are trained on the intended meaning of the pictograms (Montagne, 2013). Prior explanation of the pictograms assists in recall of the medication instructions (Joshi and Kothiyal, 2011) and time should be taken to explain the pictograms to patients (Dowse and Ehlers, 2005).

In addition to the possibility that the sequence of pictograms might have been confusing to participants to mention the preparation of the medication, they could not answer this question significantly more accurately than the control group for which these instructions were in small and more hidden text on the back of the control pack. Indeed, almost half of the control group participants (31/65) reported that they found the instructions for the preparation of medication easy to understand. The reason for this could be a high baseline knowledge of OR solution preparation for both groups due to an ongoing OR awareness program, conducted by the Western Cape Government Department of Health in collaboration with the City of Cape Town. This OR awareness program involves the dispensing of a plastic bottle (Figure 5.1) with instructions of how to prepare the OR solution. The plastic OR solution bottle is dispensed at all the CHCs that participated in this study. The instructions for the preparation of OR solution are printed on the bottle in English, Afrikaans and isiXhosa (P Moosa, personal communication, 16 August 2018). This awareness program could have contributed to a higher level of accurate responses to the preparation of OR solution for the control group, with the result that no significant difference was found between the experimental and control groups. A person's existing medicine knowledge, from doctors, pharmacists, packaging design and other public or private sources, affects safe usage of the medicine regimen (Wilke *et al.*, 2011). With the high prevalence of diarrhoea and in areas where the baseline knowledge is not high, pictograms could assist with understanding and adherence when presented as a single pictogram per instruction.

Instructions written on the OR solution bottle:

- Wash your hands with soap and water.
- Wash bottle and spoon in clean water.
- Measure one liter of clean drinking water.
- Add 8 level teaspoons of sugar.
- Add half a level teaspoon of salt.
- Mix well.
- Give the drink often, a little at a time.

Figure 5.1: Plastic bottle with instructions for a home-made sugar and salt mixture, which the Western Cape Department of Health dispenses to patients at the health care facilities

In terms of the comparison between the experimental and control groups accuracy of responses to the other questions, no significant difference was found in the accuracy of interpretation of text between the experimental and control OR medicine labels. However, a trend was noted between the good responses for both groups for the name and indication of the medicine as compared to the poor responses for dosage, instructions for use and storage instructions. On the experimental pack the name of the medication appeared on the front and back of the medicine pack, in regular font size with all the other information that is legally required to be on the pack. On the control pack the name appeared on the front and back of the pack and stood out clearly in large font size – the only other text on the front of the control pack was the indication for use. The larger font size on both packs seemed to make it easy for the participants to read the product name. Indeed, a study of Bernard *et al*. (2003), where two font sizes were compared, confirmed that a larger 12-point Arial typeface was generally preferred by participants as compared to a smaller 10-point Arial typeface, which was generally read slower (Bernard *et al.*, 2003). In addition to font size, the prominence of the words (in terms of position and bold font) on the pack is also important and improved use of spacing can increase legibility and understanding (Leat *et al.*, 2014; Shrank *et al.*, 2007).

Medicine labels or any form of written patient information is commonly evaluated according to two primary criteria, namely readability and understanding. Readability or legibility relates to the ability of patients to identify / locate /find / acquire specific information on the written document. Readability has been correlated with font size, white space, bold font, among others (Leat *et al.*, 2014; Shrank *et al.*, 2007). Readability is a pre-requisite for understanding of the information. Understanding of health information has been correlated with language and terminology (Berkman *et al*, 2010; Herrera *et al.*, 2019; La Caze, 2018).

The aspect of readability was most notable in the answer to the first two questions (medication name and indication) for both groups. In addition, the control group sub-analysis showed a significantly better correct answer for question 1 and 2 as compared to the other questions. Research with respect to the presentation of the trade name on medicine labels confirms the widespread practice to use large, bold font types and bright colours to give it the most prominence (Prescrire Editorial Staff, 2017; Pons *et al.*, 2019; Lalor, 2011). Although the name was clearly identified in this instance, the large font size in which the trade name was presented on the control pack is not ideal in medication packaging and in promoting medication use. For decades, insufficient prominence has been given on the medicine label to the medication's international non-proprietary name (INN). The result has been that patients find it difficult to identify the composition of their medication, with all the risks that are associated with potentially taking incorrect medication (Prescrire Editorial Staff, 2017). At the healthcare clinics in South Africa, medicines are bought by the state on a tender basis, with subsequent changes in the trade name as new tenders are awarded. This can be confusing to the patient, who would find it difficult to identify the medication that was prescribed for them and could result in them taking twice the proper dose if they take two different brands of the different medicines containing the same active ingredient (Hoffman and Proulx, 2003). Medical aids in South Africa also prefer that retail and hospital pharmacies dispense the lowest cost generic medication to the patient. More prominence should therefore be given to the generic name of the medication, in a large enough font size for the patient to identify.

The name and indication for use of the medicine was printed on the front of the high-gloss, aluminium foil, control medicine pack in large font size which made it easy for the patient to read the information. Reflective foil reduces the visibility of information, but in this case, with the information printed in a dark print in a high contrasting colour, (Pons *et al.*, 2019) the participants recognized the information very well as indicated by the number of participants who were fully aligned to the intended message. Information should rather be printed on non-reflective matt foils (Pons *et al.*, 2019) or non-glossy paper (Leat *et al.*, 2014). The medicine information on the back of the control medicine pack was printed on a white matt finish which covered the glossy aluminium foil.

The statement referring to the indication for use, "For prevention of dehydration during diarrhoea", is stated on the front and back of the experimental pack in regular font size, not bold font type, directly underneath the name of the medicine. On the front of the control pack the indication is stated as "for rehydration" in large font size. On the back of the control pack, "powder for oral rehydration therapy” appears in regular font size and bold font type in the centre of the medicine pack. Underneath this wording, the following sentence appears in regular font size, not bold font type – “for the treatment of electrolyte and fluid depletion associated with diarrhoea”. This position on the back of the control pack is the only place where it is indicated that the medication should be used for dehydration that is associated with diarrhoea. On both the experiment and control packs, the indication for use was in readable, large font size, surrounded with white space and positioned as such that it was easily recognizable amongst the other text and it was clearly visible for the participants in both groups. This all contributed to clear understanding of the information by both the experimental and control groups.

In contrast to the experimental group, question 4, “how much of the medicine should be taken”, was the most poorly answered of all the control group’s questions. For the control group almost a fifth (17,00%) of the participants from this group indicated that they did not see this answer (i.e. poor readability). The correct answer “administer in frequent small volumes” appeared in the centre on the back of the medicine pack in approximately 7 point font size and normal font type amongst other text. To prevent patients from missing important information, the readability of text should also be improved by surrounding it with white space and using larger font sizes (Shrank *et al.*, 2007). An increase in the readability of this information, would have had a positive impact on understanding of the medicine instructions.

The text “administer in frequent small volumes” could be recognized better by patients through the use of simplified language or avoiding medical jargon and unfamiliar words (La Caze, 2018). Understanding of the words used on the medicine label information is critical to safe and effective use of medication (Kheir *et al.*, 2014). Even though most of the participants were in the grade 7 to 12 education group (90,00%), the individuals’ ability to read and understand prescription labels, may have been significantly worse than their general literacy because of unfamiliar vocabulary (difficult words) and concepts (e.g. administer instead of take, frequent instead of often) on the prescription label (Wolf *et al.*, 2007; Lalor, 2011).

Participants in both groups also struggled to find the required text to answer the question, "when / how often and for how long should the medicine be taken". This question comprised of two questions in one. This aspect could be included in future studies when assessing understanding of medicine information by low literate patients. Both parts of the question were also interpretive, with more than one answer which could be found on the label.

For the experimental group, the answer to the question "when should this medicine be thrown away", appeared in regular font size and type, as the last text in the right hand column on the back of the sachet. There is white space directly after the statement "do not keep mixture for more than 24 hours" from which the answer is derived. For the control group the answer appeared in regular font size and bold font type. Bold font type should be used to highlight key information (Aldridge, 2004) and the bold font type could have made it easier for the control group participants to recognize and read the answer and thereby enhance understanding of the information.

Readability and comprehension should be enhanced with the use of larger fonts and white space. In addition, lists, headers, and the use of simple language and logical organization of the information could aid the patient in recognizing and understanding information (Shrank *et al.*, 2007). Adequate font size may be tricky for manufacturers, because OR dry mixture packs are often dispensed without a PIL and therefore, all the information that is legally required to be given to the patient, needs to appear on the medicine label. Manufacturers need to add a substantial amount of information on the label of a single pack to include information such as the indication for use and dosage and directions for use, which will normally appear on the PIL. Inevitably reducing the font size to accommodate the required information makes it difficult for the patient to find the pertinent information.

The South African Health Products Regulatory Authority (SAHPRA) guidelines for PILs state that "pictograms may be used as an additional measure if they make the message clearer to the patient, but be without any element of a promotional nature" (National Department of Health, 2014 p. 5).

Other requirements from this guideline include the use of English and one other official language, the use of bullet points where appropriate, the use of bold font type for the headings, text should be phrased so that it is readily intelligible for the patient, and where a specialised term is used, an explanation should be given (National Department of Health, 2014 p. 5). This guideline thus provides opportunity for industry to implement the use of pictograms and other elements that could assist the low literate patient in understanding medicine information.

Another aspect of pictograms that was not relevant in this study, but that might have had an effect on identification and interpretation of the medicine label is the addition of colour to the label. Colours may have different meanings in different cultures (Montagne, 2013). Background and text colour also have an impact on reading performance (Wu and Yuan, 2003). Future studies could assess culturally appropriate colours and how colour impacts the understanding of pharmaceutical pictograms and text.

5.1 Limitations

This explorative study focused on participants' interpretation of information from an OR dry mixture sachet label. Explorative studies do not generalize well but through explorative studies, general statements and hypotheses can be developed and these can be tested for generality in studies that follow (Mayring, 2007).

A factor that we did not investigate was the dual language on the routinely dispensed medicine pack. As per regulation, the instructions on the routine text-only pack were in two of the official languages, Afrikaans and English and the instructions on the experimental pack were in English only ('text-and-pictogram' instructions). Most of the participants (63,63%) who were recruited for the study, were Afrikaans speaking. The Afrikaans speaking participants in the control group might have had an advantage with instructions on the medicine label in their home language, compared to the Afrikaans speaking participants in the experimental group who did not receive instructions in Afrikaans. The sample sizes were too small to determine if Afrikaans speaking participants preferred reading the control label in their home language. We also did not investigate whether participants who spoke IsiXhosa or another language, might have had a disadvantage to read the Afrikaans on the experimental and Afrikaans and English on the control labels. Language issues hinders equitable and effective delivery of public healthcare (Deumert, 2010) and this is an important factor that should be considered in future research on this topic.

A health literacy test was not administered to the participants. The most commonly used literacy test in a medical setting is the REALM tool. However, validation testing of the REALM in developing countries suggests the use of validated test items in local language for reliable results (Rathnakar *et al.*, 2014).

In this study an existing label with pictograms was used and members of the community were not consulted for the creation of pictograms, therefore pictograms were not necessarily culturally sensitive. Points to take into account when developing pictograms for a target audience, include engaging with participants of the target audience (Montagne, 2013) pilot-testing of pictograms among a small sample of potential users (Kheir *et al.*, 2014) considering the education level of the target group, symbols that are simple and familiar to the target group, pre-testing pictograms in real-life settings, incorporating modifications and retesting of the pictograms until the interpretation errors reach a minimum (Kassam, *et al.*, 2004). Design thinking would be an option to test pictogram prototypes with patients until an acceptable pictogram is identified (Kheir *et al.*, 2014).

Good Clinical Practice (GCP) Guidelines (Department of Health, 2006) states that verbal consent should be obtained in the presence of and countersigned by a literate witness if the participant is illiterate**.** Our Informed Consent Form did not make provision for a witness to countersign. There were no illiterate participants in our study.

The Individual Interview Outline, Study Information Sheet and Informed Consent Form in our study were only available in English. Good Clinical Practice Guidelines (Department of Health, 2006) stipulates that special consideration should be given to groups not having English as a first language. The primary concern was that the written documents (study information sheet and informed consent form) could not be provided to patients in their preferred language. To mitigate this, the trained data collectors in this study could speak Afrikaans and isiXhosa and translated the documents written in English for patients who could not understand English.

Chapter 6: Conclusions and recommendations

The primary aim of this study was to compare the difference in interpretation of OR medication labels with “text-and-pictograms” instructions with labels containing “routine text-only” instructions, among patients attending CHCs in Cape Town. In order to achieve these objectives a literature review was conducted on the benefits of using pictograms in the pharmaceutical care of patients, and compare two groups of participants’ interpretation of two medicine labels, one with text and pictograms and one with routine text only instructions.

6.1 Conclusion

The studies in the literature review indicated that pictograms were beneficial in aiding in understanding of medicine information in low literate patient populations and across languages. Understanding is further enhanced with the aid of a verbal explanation and when pictograms are designed in collaboration with the target population.

This study showed that text-and- pictogram medicine information was interpreted better than text only medicine labels in terms of interpreting a single pictogram. The use of large font size, bold text and white space had a positive impact on the identification of text on medicine labels.

Sequences of pictograms is an important tool that can be used to represent medication messages to low literate patients. With the aid of the target audience, a participative design process with end-user feedback can result in pictogram sequences that are easy to understand and which can potentially increase medicine safety for this vulnerable population.

Visual communication aids like pictograms are effective as a tool to help patients understand medicine label instructions. The use of large font size, bold text and white space has a positive impact on the recognition of important text. This study data provides valuable information on the use of pictograms and text to aid low literate patients to understand medicine information, and should serve to guide future efforts in further research for using a combination of text and pictograms as an aid to understanding medicine labels.

6.2 Recommendations

Since there is limited South African data available on patients' understanding of medication use, adherence rates to prescribed medication regimen, hospitalisation or even death due to non-adherence, it would be recommended that more research needs to be done to understand the effect of poor understanding of the label on medication use.

Pictograms are interpreted differently by different cultures (Montagne, 2013) and future studies in the Western Cape could focus on differences in the accuracy of interpretation of pictograms by different ethnic and language groups.

This study was conducted in clinics located in an urban setting. Further studies in a rural setting will be a useful investigation.

Another topic well worth exploring in future studies in the Western Cape, is the effect that explaining pictograms to patients have on the understanding and recalling of medicines instructions. Patients with low literacy are at risk of poor health and possible adverse events if they do not understand their medication information. Even though pictograms assist with patient understanding of medicine use, it is important to explain it to patients to ensure maximal efficacy.

Cell phone technology has the potential to aid in increasing medicine safety and improving health outcomes by sending daily reminders in pictogram format to low literate patients. We live in an era of smart phones and the advantage it offers is well worth exploring.

More robust studies should be done to assess the patients' ability to manage more than one pictogram in the situation where a medicine instruction includes a sequence of pictograms**.**

To prevent the use of confusing and ambiguous elements being used in pictograms, best practice would be to develop pictograms with the aid of the target population. With SAHPRA allowing the use of pictograms, the challenge remains for industry to introduce and implement culturally sensitive pictograms into routine practice.

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APPENDICES

Appendix A Table A.1: Data extraction form - Systematic Review

Appendix B Table B.1 Summary of the assessment of bias in the Systematic Review

Appendix C: Study Information Sheet

UNIVERSITY of the WESTERN CAPE

Dr Mea van Huyssteen
Pharmacy building, First floor Room F6
School of Pharmacy, University of the Western Cape
Robert Sobukwe Road, Bellville, 7535
Tel: (021) 959 2864

Ms Jeanne Heyns
39 Hawkins Avenue
Epping Industria 1, 7460
Tel: (021) 507 4844

The effectiveness of using pictograms and text on medication labels at primary healthcare facilities in Cape Town

Invitation

You are being asked to take part in a research study on the understanding that patients have of the medicine label. The study will be conducted by Jeanne Heyns, a Master's Degree student at the School of Pharmacy at the University of the Western Cape. The supervisor of the study is Dr Mea van Huyssteen.

Before you make a decision on whether you would like to take part in this study, I would like to tell you a bit more about this study and answer all the questions that you may have. If you would like to participate in the study, I will ask you to sign a consent form. A copy of this study information sheet will be given to you for your own records. You may decide to stop being a part of the research study at any time without explanation. You have the right to ask that any data you have supplied to that point be withdrawn / destroyed. There are no negative consequences if you choose not to take part in this study.

Purpose

The aim of the study is to evaluate the use of pictograms on medication labels in CHCs of the Cape Metropole, and establish how well the pictogram conveys its meaning and if there is any benefit for the patient to use pictograms. The study is for patients with no education or patients who have completed some or all 7 grades of primary school education. I would also like to compile recommendations or ways to improve medication labels for patients.

Procedures

Interviews will be conducted at the CHCs by the research pharmacist. Participant will be asked specific questions about the medicine label to determine their understanding of the instructions on the medicine label.

Participants' Rights

You will not be identified in any way. You have the right to withdraw from the study at any time without an explanation. You have the right to have all your questions about this study material answered.

Risks and Benefits

There is no risk for you in this study. You may experience the benefit of better understanding of how to take your medication.

Confidentiality

The data I collect will not contain any personal information. Your name will not be mentioned in any of the study reports. Study material will be kept in a secure location under lock and key. Only the research team will have access to this material and it will be destroyed after the research output has been published.

Voluntary Participations

If you would like to take part in the study you will be asked to sign the consent form. Participating in this study will not cost you any money and you will not be paid for your participation. We will only take about 10 minutes of your time.

Contact Information

I will be glad to answer your questions about this research study at any time. If you have any questions now, you may ask them. Alternatively you can contact me at:

39 Hawkins Avenue
Epping Industria 1, 7460
Tel: (021) 507 4844
E-mail: jeanne.a.heyns@gsk.com

or

Dr Mea van Huyssteen
Pharmacy building, First floor Room F6
School of Pharmacy, University of the Western Cape
Robert Sobukwe Road, Bellville, 7535
Tel: (021) 959 2864
Email: mvanhuyssteen@uwc.ac.za

The committees giving ethical approval for this study is the UWC Faculty board Research and Ethics Committee and the UWC Senate Research Committee. If you have any problems or questions about this study you can also contact the Ethics committee directly at telephone number 021 959 3170.

Appendix D: Informed Consent Form

UNIVERSITY *of the* WESTERN CAPE

Dr Mea van Huyssteen
Pharmacy building, First floor Room F6,
School of Pharmacy, University of the Western Cape,
Robert Sobukwe Road, Bellville, 7535
Tel: (021) 959 2864

Ms Jeanne Heyns
39 Hawkins Avenue,
Epping Industria 1, 7460
Tel: (021) 507 4844

Informed consent for patients who are invited to participate in the research project titled:

The effectiveness of using pictograms and text on medication labels at primary healthcare facilities in Cape Town

Date: ________________________________

Name of participant: ____

Unique identifier assigned to participant: ______________________________

Name of person taking consent: ____________________________________

I have been invited to participate in research about understanding of the medicine label, by patients.

I have read the information that follows / the information that follows has been read to me in a language that I understand and I understand the objectives of the study.

I have been provided with a study information sheet and I was given the opportunity to ask questions about it. The questions I asked have been answered to my satisfaction.

I understand that I can withdraw from the study at any time.

I understand that the information that I provide will not be a test of how clever I am, but will be valuable to the researcher to understand where improvements can be made on how to provide information regarding the medication.

I understand that my name will not be mentioned with any of the information I provide.

I understand that all information I provide will be kept secure by the researchers.

I hereby give voluntarily consent to be a participant in this study.

Print Name of Participant: ___________________

Signature of Participant: ____________________

Date: _____________________ dd/mm/yyyy

Statement by the researcher / person taking consent:

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the information sheet. I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily. A copy of this Informed Consent Form has been provided to the participant.

Print Name of Researcher / person taking the consent: _________________________

Signature of Researcher / person taking the consent: ___________________________

Date: _____________________ dd/mm/yyyy

Appendix E: Individual Interview Outline

Dr Mea van Huyssteen
Pharmacy building, First floor Room F6
School of Pharmacy, University of the Western Cape
Robert Sobukwe Road, Bellville, 7535
Tel: (021) 959 2864
Ms Jeanne Heyns
39 Hawkins Avenue
Epping Industria 1, 7460
Tel: (021) 507 4844

The effectiveness of using pictograms and text on medication labels at primary healthcare facilities in Cape Town

Unique Identifier: ________________________________

Name of interviewer: ____________________________

Date: ____

Location (facility name): __________________________

Duration of interview (in minutes): __________________

Introduction

Good day, my name is [________________]. I would like to find out more about your understanding of how to take your medication. Your name will not be mentioned with any of the information that you share with me. The results of all the interviews will be used to learn more about what patients understand on how to use their medication and will be recorded in the write-up of a research study. The information that you provide will not be a test of how clever you are, but will be valuable to us for understanding where we can improve on how we provide information regarding your medication.

Interviewer instructions

- Provided informed consent and other background information.
- Asked interviewee for permission to record the interview.
- Collected the following relevant information during the introduction phase.

Gender: Male ☐

Female ☐

Marital status: Married ☐

Single ☐

Divorced ☐

Residence: Formal dwelling ☐

Informal Dwelling / shack in backyard ☐

Informal Dwelling / shack NOT in backyard ☐

Other ☐

Age: ____________________

Home language: Afrikaans ☐

English ☐

Educational level: No Schooling ☐

Grade 1 - 3 ☐

Grade 1 - 6 ☐

Grade 7 - 12 ☐

Tertiary ☐

Reason for visiting the CHC: ____

Are you able to tell me what the time is by looking at this watch: Yes ☐

No ☐

Are you employed: Yes ☐

No ☐

Monthly income: No income ☐

R 1 to R 3 200 ☐

More than R 3 200 ☐

Access to running water from a tap inside your house: Yes ☐

No ☐

Access to running water from a tap outside your house: Yes ☐

No ☐

Refuse removal: Never ☐

Yes ☐

If the answer to any of the below questions was "yes" except for the last question, the patient will not be able to take part in the study:

- Do you have problems with your eye sight so that you have difficulty seeing pictures on a paper?

  Yes ☐ No ☐
- Do you have trouble hearing?

  Yes ☐ No ☐
- Do you feel that you are too ill take part in this study?

  Yes ☐ No ☐
- Can you speak English / Afrikaans / isiXhosa?

  Yes ☐ No ☐

Research Questions

Allocate participant to: Control group ('routine instructions')

Experimental group ('text and pictogram')

Present the allocated medication label to the patient and ask the following questions:

- What is the name of the medication?
- Model answer: Oral Rehydration Mixture
- What should the medicine be used for?
- Model answer: diarrhoea

- How should this medication be prepared for use?
- Model answer: boil and cool one liter of water, add the contents of the packet to the cooled water and mix until all crystals are dissolved.
- How much of the medicine should be taken?
- Model answer: Half a cup after each loose stool
- When/how often and for how long should the medicine be taken?
- Model answer: Half a cup of the solution after each loose stool until diarrhea resolves, or if 24 hours elapse after making up the solution
- When should this medication be thrown away?
- Model answer: Within 24 hours of the time it was made up

The responses are recorded and on the basis of the answers the patient is categorized according to the Likert Scale as follows:

1. Not aligned with intended message (way off the model answer, not even close)
2. Partially aligned with intended message (some aspects of the model answer)
3. Fully aligned with intended message (the model answer)

Explain to the patient the intended message of the medication label. The following set of questions is asked to establish the patients' perception of the labeling practices and their opinion of the respective medication label:

- Which instructions were easy to understand?
- Which instructions were difficult to understand?

- What do you think could be the reason why you did not understand the instructions?
- (Only for those in the experimental group). Were the pictograms on the label helpful or hindering to your understanding of the medication instructions?
- (Only for those in the control group). What do you think might help you interpret medication labels better?

The patient is asked for any suggestions that could help him/her understand the medicine label better:

____

____

Interviewer script

Thank you very much for taking the time to look at the labels and answer the questions. The results of this study will be available soon. If you would like to know what the results are, please contact the research pharmacist at the following contact details:

Jeanne Heyns
39 Hawkins Avenue
Epping Industria 1, 7460
Tel: (021) 507 4844

Appendix F Table F.1: Participant responses to Question 1 to 6, scored according to a Likert scale in relation to the intended therapeutic message on the medication label

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
Question 1: What is the name of the medicine?	Oral Rehydration Mixture.	3: "Oral Rehydration Mixture".	Name of medication** for rehydration / powder for oral rehydration therapy, for the treatment of electrolyte and fluid depletion associated with diarrhoea.	3: "Name of the medication**" / "name of the medication** for rehydration".
		2: E.g. "mix for rehydration".		2: E.g. "electrolyte powder"/ "for rehydration".
		1: E.g. "I don't know" / "diarrhoea".		1: E.g. "glucose water".

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
Question 2: What should the medicine be used for?	For prevention of dehydration during diarrhoea.	3: E.g. "For prevention of dehydration during diarrhoea" / "for diarrhoea" / "for dehydration".	For rehydration / powder for oral rehydration therapy/for the treatment of electrolyte and fluid depletion associated with diarrhoea.	3: "Oral rehydration therapy" / "for rehydration" / "for diarrhoea".
		2: E.g. "for prevention of diarhhoea".		2. E.g. "for the stomach".
		1: E.g. "to keep the blood and body clean".		1: E.g. "if the child cannot take in food".

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
Question 3: How should this medicine be prepared for use?	Boil 2 liters of water and cool, pour water in a clean 1-liter bottle and add dry ingredients to clean water.	3: All four elements of the model answer is mentioned, "boil the water, cool the water, use 1 liter of water and add dry ingredients/content of sachet to the water".	Dissolve one sachet in a liter of previously boiled and cooled water.	3: All four elements of the model answer is mentioned, e.g. "boil the water, cool the water, use 1 liter of water and dissolve one sachet in water".
		2: At least three of the elements of the model answer is mentioned, e.g. "boil 2 liters of water and cool, pour water in a clean bottle and add this powder to clean water".		2: At least three of the elements of the model answer is mentioned, e.g. "use a liter of boiled and cooled water".

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
		1: One or two elements of the model answer is mentioned e.g. “boil water and add mixture”, or “throw in a bottle”.		1: One or two elements of the model answer is mentioned e.g. “boil a liter of water” or “use one scoop”.
Question 4: How much of the medicine should be taken?	Drink half a cup after every watery stool.	3: E.g. “half a cup after each loose stool” / ”half a cup”	Administer the solution in frequent small volumes.	3: E.g. “frequent small volumes”/”small volumes”.
		2: E.g. “half a cup daily”		2: E.g. “the contents of the sachet”.
		1: E.g. “two cups”.		1: E.g. “a glass two times an hour”.

	There are two possible answers to the first part of the question "when/how often should the medicine be taken?": - Drink after every watery stool. Or - Take when you have diarrhoea (derived from "for prevention of dehydration during diarrhoea"). There are two possible answers to the second	3: Both parts of the model answer is mentioned e.g. "take after every loose stool and discard unused solution after 24 hours" or "take after diarrhoea and stop when the stool is not watery".	There are two possible answers to the first part of the question "when/how often should the medicine be taken?": - Administer the solution in frequent small volumes. Or - Take when you have diarrhoea (derived from the indication for use, "for the treatment of electrolyte and fluid depletion associated with diarrhoea").	3: Both parts of the model answer is mentioned e.g. "take frequently and discard unused solution after 24 hours" or "take after diarrhoea until diarrhoea has stopped".

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
	part of the question for how long should the medicine be taken?": If interpreted as "how long to take the medicine for intended	2: One part of the model answer is mentioned e.g. "when the packet is open, you should use it all and not keep it for longer than 24 hours" or "use it until the diarrhoea stops"	There are two possible answers to the second part of the question "for how long should the medicine be taken?":	2: One part of the model answer is mentioned e.g. "discard unused solution after 24 hours" or take "until the diarrhoea has cleared up".

Question 5: When / how often and for how long should the medicine be taken?	use", the answer would be: - Take until diarrhoea has cleared up (derived from the indication for use "for prevention of dehydration during diarrhoea"). If interpreted as "how long to take the medicine before it should be discarded?": - Take for no longer than 24 hours (derived from instruction "do not	1: E.g. "use for one week".	If interpreted as "how long to take medicine for intended use", the answer would be: - Take until the diarrhoea has cleared up (derived from the indication for use, "for the treatment of electrolyte and fluid depletion associated with diarrhoea"). If interpreted as "how long to take the medicine before it should be discarded?": - Take for no longer than 24 hours (derived from the instruction "discard	1: E.g. "take a spoon 3 times a day until you finish it".

Questions	Model answer: experimental group	Scoring* on Likert scale: experimental group	Model answer: control group	Scoring* on Likert scale: control group
	keep mixture for more than 24 hours”).		unused solution after 24 hours”).	
Question 6: When should this medicine be thrown away?	Do not keep mixture for more than 24 hours.	3: E.g. “24 hours” or “1 day”.	Discard unused solution after 24 hours.	3: E.g. “24 hours” or “1 day”.
		2: E.g. “when the diarrhoea has cleared up”.		2: E.g. “a day or two”.
		1: E.g. “2 – 3 weeks”.		1: E.g. “7 days”.

*A score of 3 was allocated for the model answer, a score of 2 was allocated for part of the model answer and a score of 1 was allocated if the participant did not know the answer or the answer was not in line with the intended message.
**For protection of the third party, the name of the product is not mentioned.

Appendix G Table G.1: Summary of statistical analyses for font size (control group)

Question	Possible answer to questions	Font size* and position	Font type	White space Y / N	Median and Range	Font size legibility score and statistical significance (P-value**)
<u>Question 1:</u> What is the name* of the medication? (Name of the product).**	1. Trade name	1. 55 pt (FP) and / or 35 pt (BP)	1. Bold	1. Y	3 (1 to 3)	<u>Between Q 1 and Q 2</u> Not significant (P = 0,414) <u>Between Q 1 and Q 3</u> Significant (P = 0,015)
<u>Question 2:</u> What should the medicine be used for? (Indication for use).	1. For rehydration 2. Powder for oral rehydration therapy	1. 18 pt (FP) 2. 7 pt (BP) 3. 7 pt (BP)	1. Bold 2. Bold 3. Not bold	1. Y 2. N 3. N	3 (1 to 3)	<u>Between Q 1 and Q 4</u> Significant (P = 0,000) <u>Between Q 1 and Q 5</u> Significant (P = 0,000)

	3. For the treatment of electrolyte and fluid depletion associated with diarrhoea					<u>Between Q 1 and Q 6</u> Significant (P = 0,000) <u>Between Q 2 and Q 3</u> Not significant (P = 0,120) <u>Between Q 2 and Q 4</u> Significant (P = 0,000) <u>Between Q 2 and Q 5</u> Significant (P = 0,000) <u>Between Q 2 and Q 6</u> Significant (P = 0,002) <u>Between Q 3 and Q 4</u>
<u>Question 3:</u> How should this medication be prepared for use? (Preparation of medication for use).	1. Dissolve one sachet in previously boiled and cooled water	1. 7 pt (BP)	1. Not bold	1. N	3 (1 to 3)	

<u>Question 4:</u> **How much of the medicine should be taken? (Medication dosage).**	1. Frequent small volumes	1. 7 pt (BP)	1. Not bold	1. N	1 (1 to 3)	Significant (P = 0,000) <u>Between Q 3 and Q 5</u> Significant (P = 0,000) <u>Between Q 3 and Q 6</u> Significant (P = 0,049) <u>Between Q 4 and Q 5</u> Not significant (P = 0,060) <u>Between Q 4 and Q 6</u> Significant (P = 0,000) <u>Between Q 5 and Q 6</u> Significant (P = 0,001)
<u>Question 5:</u> **When / how often and for how long should the medicine be taken? (Frequency and duration of use).**	• When / how often should the medicine be taken? 1. Administer the solution in frequent small volumes 2. Take when you have	1. 7 pt (BP) 2. 7 pt (BP) 3. 7 pt (BP) 4. 7 pt (BP)	1. Not bold 2. Not bold 3. Not bold 4. Bold	1. N 2. N 3. N 4. N	2 (1 to 3)	

	diarrhoea (derived from "for the treatment of electrolyte and fluid depletion associated with diarrhoea") • How long should the medicine be taken? 3. Take until the diarrhoea has cleared up (derived from					

	"for the treatment of electrolyte and fluid depletion associated with diarrhoea") 4. Take for no longer than 24 hours (derived from "discard unused solution after 24 hours")					

<u>Question 6:</u> When should this medicine be thrown away? (Expiry of medication).	1. Discard unused solution after 24 hours.	1. 7 pt (BP)	1. Bold	2. N	3 (1 to 3)	

* The font sizes are estimates in font type Arial
** P-values calculated from the Mann-Whitney test
*** For protection of the third party, the name of the product is not mentioned