ADHERENCE TO ZINC SUPPLEMENTATION GUIDELINES IN THE MANAGEMENT OF ACUTE DIARRHOEA IN HOSPITALIZED CHILDREN

Mini-dissertation for the partial fulfilment of the degree, MSc. Dietetics, in the Department of Nutrition and Dietetics, Faculty of Health Sciences, University of the Free State

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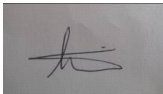**Study leader:** Dr Ronette Lategan

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January 2016

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SUMMARY

The aim of this research study was to determine adherence to zinc supplementation as part of the treatment guidelines for diarrhoea in infants and children at a tertiary hospital in the Eastern Cape, South Africa. Zinc supplements are recommended by the World Health Organization (WHO) and United Nations Children's Fund (UNICEF) to be given to all children experiencing diarrhoea, as zinc is a proven treatment, known to reduce the severity and duration of diarrhoea. Permission to conduct the study was obtained from the management of the tertiary hospital, as well as the Ethics Committee of the Faculty of Health Sciences, University of the Free State. In this study the researcher gathered information from the case folders of infants and children admitted to the general medical paediatric ward (GMPW) for diarrhoea between 1 January 2013 and 31 December 2013. From statistics obtained from the Department of Information Technology at the hospital, it was determined that 385 infants and children under five years of age were admitted to the ward, and of these, 290 cases were included in the study. The study was a retrospective, prescription audit and all information was obtained from case folders, specifically the prescription charts and medical notes. General patient information, prescription information and medical information was collected from the case folders. Data were captured by the researcher in duplicate and compared and verified electronically. Statistical analysis was performed by the Department of Biostatistics, University of the Free State. Descriptive statistics were mainly used and medians and percentiles where calculated for continuous data, and frequencies and percentages for categorical data.

This study reported poor adherence levels to treatment guidelines for zinc supplementation in children with diarrhoea at a tertiary hospital in the Eastern Cape, South Africa. The researcher recommends the need to perform training among health care professionals to increase awareness and improve implementation of zinc supplementation guidelines. Continued monitoring and surveillance were also recommended to ensure sustainability of implementation. It is also recommended that the hospital develop an institutional policy that incorporates zinc supplementation guidelines as part of the management of diarrhoea in hospitalized children.

OPSOMMING

Die doel van hierdie navorsingstudie was om vas te stel of daar aan die behandelingriglyne vir diarree voldoen word onder babas en jong kinders by 'n tersiêre hospitaal in die Oos-Kaap, Suid-Afrika. Sinksupplementasie word deur die Wêreld Gesondheidsorganisasie (WGO) en UNICEF aanbeveel vir alle kinders met diarree, aangesien sinksupplementasie bewys is as effektiewe behandeling om die ernstigheid en duur van diarree te verminder. Toestemming om hierdie studie uit te voer, is verkry vanaf die bestuur van die tersiêre hospitaal, sowel as die Etiekkomitee van die Fakulteit Gesondheidswetenskappe, Universiteit van die Vrystaat. In hierdie studie het die navorser inligting ingesamel uit die gevalsleêrs van babas en jong kinders wat tot die algemene mediese pediatriese saal met diarree opgeneem is tussen 1 Januarie 2013 en 31 Desember 2013. Uit statistiek bekom van die Departement Inligtingtegnologie by die hospitaal, is vasgestel dat 385 babas en kinders onder vyf jaar van ouderdom tot die saal toegelaat is en van hierdie is 290 gevalle by die studie ingesluit. Die studie was 'n retrospektiewe voorskrifoudit. Alle data is uit gevalsleêrs bekom, veral uit die voorskrifkaarte en mediese notas. Algemene pasiëntinligting, voorskrifinligting en mediese inligting is uit die gevalsleêrs bekom. Data is deur die navorser in duplikaat versamel en elektronies vergelyk en geverifieer. Statistiese ontleding is deur die Departement Biostatistiek, Universiteit van die Vrystaat uitgevoer. Beskrywendestatistiek is hoofsaaklik gebruik en mediane en persentiele is bereken vir kontinue data en frekwensies en persentasies vir kategoriese data.

Hierdie studie rapporteer swak nakoming van behandelingriglyne vir sinksupplementasie onder kinders met diarree by 'n tersiêre hospitaal in die Oos-Kaap, Suid-Afrika. Die studie beveel opleiding onder professionele gesondheidsorgwerkers aan om bewustheid en implementasie van sinksupplementasieriglyne te verbeter. Voordurende monitering en waarneming word ook aanbeveel om volhoubaarheid van enige vordering wat met implementering gemaak word te verseker. Daar word ook aanbeveel dat die hospitaalbeleid sinksupplementasie riglyne insluit, by behandelingsriglyne vir diarree in gehospitaliseerde kinders.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
CPIP	Child Problem Identification Programme
E. coli	Escherichia Coli
DHIS	District Health Information System
GAPPD	Global Action Plan for the Prevention and Control
GIT	Gastrointestinal Tract
GMPW	General Medical Paediatric Ward
HCF	Health Care Facility
HIV	Human Immunodeficiency Virus
IMCI	Integrated Management of Childhood Illness
LRTI	Lower Respiratory Tract Infection
MDG	Millennium Development Goal
MUAC	Mid-upper Arm Circumference
NFCS	National Food Consumption Survey
ORS	Oral Rehydration Salts
ORT	Oral Rehydration Therapy
POPD	Paediatric Out-patient Department
RDA	Recommended Dietary Allowance
RR	Relative Risk
SD	Standard Deviation
SDG	Sustainable Development Goal
TB	Tuberculosis
UNICEF	United Nations Children's Emergency Fund
WHO	World Health Organization
WGO	Wêreld Gesondheidsorganisasie

CHAPTER 1: INTRODUCTION

1.1. OVERVIEW AND MOTIVATION

Child mortality rates globally have been steadily improving since the 1970's when an estimated 17.6 million deaths were reported (Rajaratnam et al., 2010:1988). In 2013 mortality rates among children under five years of age had decreased to 6.3 million (Liu et al., 2015:430; Wang et al., 2014:1). Despite the overall improvements in child mortality rates, diarrhoea still remains a leading cause of death globally among children younger than five years of age, killing more children than acquired immune deficiency syndrome (AIDS), measles and malaria combined (Liu et al., 2015:432; UNICEF & WHO, 2009:2). This burden translates roughly to one in 10 child deaths or a total of half a million deaths in predominantly low to middle income countries, with Africa and Asia accounting for 80% of these deaths (Liu et al., 2015:432; Chola et al., 2015:1; Black et al., 2010:1969; White Johansson & Wardlaw, 2009:5).

Diarrhoea is easily preventable and treatable and much has been done over the years to reduce the number of diarrhoea-associated deaths (WHO & UNICEF, 2013:11; Bhutta et al., 2013:1417; White Johansson & Wardlaw, 2009:5; Forsberg et al., 2007:43). However, diarrhoeal diseases are still a global burden in children younger than five years of age, with an estimated 2.5 billion cases reported yearly. This translates to approximately 2.9 diarrhoeal episodes per child per year (Bhutta et al., 2013:1417; Lazzerini & Ronfani, 2013:5; White Johansson & Wardlaw, 2009:5).

In South Africa the burden of diarrhoea is very similar to that of the rest of the world; in 1998 diarrhoea was the 10th leading cause of death among children younger than five years of age. By 2004 and 2005, diarrhoea had became the 3rd leading cause of death (Steyn, 2009:31). Data compiled by Statistics South Africa and the Medical Research Council of South Africa, both indicate that diarrhoea is now the leading cause of death in children under five years in South Africa, accounting for 14% of total deaths in 2014 (Statistics South Africa, 2015: 35; Nannan et al., 2012:iv).

According to the World Health Organization (WHO) diarrhoea is defined as three or more watery or loose stools per day. However, any abnormal increase in the frequency of stools may be noted as diarrhoea. In the majority of cases a diarrhoeal episode is mild. However, acute cases can cause severe fluid losses which may lead to dehydration, electrolyte disturbances and if not treated promptly, death (UNICEF & WHO, 2009:10; White Johansson & Wardlaw, 2009:9).

In a report compiled jointly by United Nations Children's Emergency Fund (UNICEF) and WHO, childhood diarrhoea can be classified into four groups: firstly, acute (watery) diarrhoea with symptoms including large fluid losses and rapid dehydration; secondly, bloody diarrhoea, also known as dysentery where visible traces of blood are found in the stools; thirdly, persistent diarrhoea which occurs for a minimum of 14 days with or without blood in the stools and lastly diarrhoea associated with malnutrition (UNICEF & WHO, 2009:10; White Johansson & Wardlaw, 2009:10).

The causes of diarrhoea vary and often include gastrointestinal infections caused by bacteria, viruses and parasites, however only certain pathogens cause severe cases of acute diarrhoea necessitating medical management. The main causes of acute infectious diarrhoea in children are the Rotavirus and pathogenic *Escherichia coli (E. coli)* (UNICEF & WHO, 2009:2; Thapar & Sanderson, 2004:646).

Due to the large number of diarrhoeal cases reported, it is not surprising that the financial and societal burden is substantial. These costs include medical management costs, as well as societal costs such as transport and absenteeism of caregivers with the resultant loss of income (Guarino et al., 2012:18). In response to this formidable burden of disease, the WHO initiated the Diarrhoeal Diseases Control Programme which was launched in 1982. This programme's chief mandate was to decrease mortality in children with diarrhoea. In order to meet this mandate, international guidelines and implementation strategies were created by a collaborative team at the WHO, in partnership with UNICEF and other stakeholders. The medical curricula focused on oral rehydration solutions, health worker training and public education, with guidelines continually evolving throughout the mid 80's and early 90's. This eventually became part of what is known today as the programme for the Integrated Management of Childhood Illness (IMCI) (Forsberg et al., 2007:42).

The current international goals for the management of diarrhoea are a progression of these initial guidelines, making use of evolving medical research to lower the total impact of the disease by reducing the incidence, co-morbidity and mortality (Guarino et al., 2012:18). The treatment goals and intervention strategies for the treatment of diarrhoea have been clearly combined by the Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD). A single protocol was developed based on scientifically proven strategies and frameworks with the aim to improve implementation and sustainability of interventions. The intervention strategies, outcome goals and treatment guidelines for diarrhoea found in the GAPPD were developed jointly by the WHO and UNICEF, and are based on the guidelines in the IMCI handbook. In these guidelines zinc supplementation is promoted as part of the universal treatment of diarrhoea in childhood (WHO & UNICEF, 2013:11; Guarino et al., 2012:19; UNICEF & WHO, 2009:2; WHO, 2005:14). The use of zinc supplementation in the management of diarrhoea has been reported in numerous clinical trials to have a beneficial impact on the body's immune system as well as the structure and function of the gastrointestinal tract (GIT). The functions of zinc aid in the recovery of the epithelium in cases of diarrhoea and zinc supplementation is now acknowledged to reduce the severity and duration of childhood diarrhoea as well as reducing recurrent diarrhoeal episodes (WHO, 2006:4; Thapar & Sanderson, 2004: 648).

The therapeutic dosage recommended by the WHO and UNICEF is 10 mg of elemental zinc per day for children younger than six months and 20 mg for children older than six months of age. This includes zinc supplementation for all children suffering from diarrhoea (for 10-14 days), including children infected with the human immunodeficiency virus (HIV). Zinc is recommended to be given in the form of water-soluble compounds such as zinc sulphate, zinc acetate or gluconate (Guarino et al., 2012:19; WHO, 2010:2; Lazzerini & Ronfani, 2008:3; WHO, 2005:14). These guidelines are based on a number of published safety and efficacy trials, which show these dosages to be safe and efficacious in children with diarrhoea. Although larger dosages of up to 70 mg given twice a week was found to have no toxic effects, there appears to be no benefit to give dosages higher than the guidelines (Hassan et al., 2012:2).

Child health and mortality rates in South Africa have been highlighted and prioritized over the last 15 years, after the South African government committed to implement the Millennium Development Goals (MDGs) set out by the United Nations in September 2000. The MDGs focused on addressing infant and child mortality rates by aiming to reduce preventable deaths due to diarrhoeal diseases by two thirds by 2015. Improving access to clean, sustainable water sources and sanitation were included in these goals (Liu et al., 2015:430; Wang et al., 2014:1; Lehohla, 2013:61; Rajaratnam et al., 2010:1988: Black et al., 2010: 1969). Although progress was made with the MDGs, the targets for reducing child mortality rates were only met by a handful of countries. At a United Nations conference in Brazil in 2012, member states developed 17 new Sustainable Development Goals (SDGs) to direct policy and set targets for the next 15 years leading up to 2030. The targets include the reduction of preventable childhood deaths to 25 deaths in 1 000 live births in infants and children younger than five years of age, to improve access to clean, safe water and sanitation and to improve access to appropriate nutrition for vulnerable population groups (Liu et al., 2015:430).

Since the initial commitment in 2000, South Africa has developed and initiated strategies to improve childhood survival. These strategies focus on the effective implementation and coverage of health and societal interventions as well as accurate data collection in the form of monitoring and surveillance. This includes the implementation of the IMCI programme, as well as the WHO standard treatment guidelines for the management of diarrhoea in children younger than five years of age (National Essential Medicines List Committee, 2013:26; National Essential Drugs List Committee, 2006:32; Harper et al., 2013a:357).

Diarrhoea is a continued threat to mortality rates in children under five years of age in low to middle income countries and very few studies have been conducted to monitor adherence of health professionals to the standard treatment guidelines for the management of diarrhoea. It is therefore necessary to conduct audits, similar to this study to assess whether the protocols and standard treatment guidelines for the management of diarrhoea are being effectively implemented at health care facilities (HCF). The motivation for this study was to contribute to the monitoring and surveillance of implementation of guidelines and to give a clearer picture as to where

more training and support is needed.

The aim of this study was to explore adherence to WHO treatment guidelines for zinc supplementation in the management of childhood diarrhoea, by health care professionals at a tertiary hospital.

1.2. DESCRIPTION OF THE STUDY AREA

The setting for this study is a tertiary hospital situated in the Eastern Cape province of South Africa. It is a 900 bed hospital which receives referrals from the Northern and Eastern parts of the Eastern Cape, where there are limited HCFs. The areas serviced by the hospital are classified as urban and peri-urban; however the broader catchment area can vary vastly from urban to rural (Harper et al., 2013b:1).

Children that are referred to this tertiary hospital come from various surrounding primary health care centres, clinics and hospitals where there is no access to paediatric specialists. The children are assessed at the hospital's casualty department or paediatric out-patient department (POPD) and, depending on the severity of the condition the child will be assessed as either an out-patient or admitted for in-patient treatment. There are no set admission criteria for children at the hospital, including for those who present with diarrhoea. The decision to admit a child is left to the professional judgement of medical staff and availability of hospital bed space. Children who present with diarrhoea to the hospital are first clinically assessed for shock and dehydration using the assessment guidelines in the Eastern Cape Handbook of Child and Maternal Health (Harper et al., 2013a:357) or the Standard Treatment Guidelines and Essential Medicines list for South Africa (National Essential Medicines List Committee, 2013:26). It is not a simple task to assess shock and dehydration in children, with many co-morbidities, including malnutrition, complicating assessment. It is therefore necessary to complete a rigorous initial assessment, with numerous reassessments, relying on the expertise of medical staff to determine the severity of the condition of the child (National Essential Medicines List Committee, 2013:26; National Essential Drugs List Committee, 2006:32; Harper et al., 2013a:357).

Specialized paediatric wards at the hospital, include a general medical paediatric ward (GMPW), a paediatric oncology ward, two neonatal nurseries, a surgical

paediatric ward and a neonatal/paediatric intensive care unit. The hospital's GMPW has 28 beds this restricted capacity as well as high demand has led to the ward having one of the highest patient turn-over rates in the hospital. The majority of patient care is managed by intern doctors and a medical officer or registrar, with consultants conducting daily ward rounds. In 2011 there were three paediatrician specialists, four registrar doctors, five medical officers and six intern doctors at the hospital to manage the paediatric wards and outpatient department (excluding the paediatric surgery ward) (Harper et al., 2013b:1). With high patient turn-over and demand for hospital space, it is always a concern that patients could fall through the cracks and do not receive the correct treatment for the appropriate length of time.

1.3.   PROBLEM STATEMENT

Zinc supplementation for the treatment of diarrhoea is a relatively easily implemented and inexpensive intervention that through numerous clinical trials has shown beneficial results in reducing the severity and duration of diarrhoeal episodes in children younger than five years of age (Mayo-Wilson et al., 2014:7; Harper et al., 2013a:357). Despite the availability of supporting data for the use of zinc in the management of childhood diarrhoea, as well as the longstanding WHO and UNICEF treatment guidelines, actual adherence and administration levels of zinc appear to be low in low to middle income countries (Omuemu et al., 2012: 69).

Unfortunately there is limited data concerning the awareness and adherence levels amongst health care professionals in implementing zinc supplementation in the management of childhood diarrhoea in South Africa and therefore we have to rely on data from other low to middle income countries.

Two such prescriber awareness and adherence studies were conducted in Nigeria and India respectively, both demonstrated low levels of adherence to standard treatment guidelines. This was found not only in lower level prescribers but also in specialist paediatricians (Omuemu et al., 2012: 69; Pathak et al., 2011:1). In Nigeria only one in three medical staff prescribed zinc in the treatment of diarrhoea and although in the majority of cases the dosage was correct, fewer than half prescribed it for the correct period of time (Omuemu et al., 2012: 71). In India, Pathak et al. (2011:1), reported that in 843 prescriptions for diarrhoea assessed, only six were found to have the recommended zinc treatment.

Health care professionals treating the diarrhoeal episodes in this study population have access to guidelines for the treatment of childhood diarrhoea in the Eastern Cape Handbook of Child and Maternal Health, as well as the Standard Treatment Guidelines and Essential Medicines list for South Africa. Although slight differences are evident in these guidelines when compared to the WHO guidelines, they are still firmly based on the WHO guidelines (National Essential Medicines List Committee, 2013:26; Harper et al., 2013a:130). Zinc supplementation guidelines for the treatment of diarrhoea have been accessible at the Hospital since 2006 according to the Eastern Cape Handbook of Child and Maternal Health (Boon et al., 2006:113). However, to date no monitoring or surveillance has been conducted at the hospital to ascertain the adherence to zinc supplementation guidelines in children younger than five years of age. The information obtained from this research would be useful to indicate if the treatment guidelines for zinc supplementation are being followed and to assess possible gaps in the treatment process. The research will also indicate if training is needed for medical staff about the importance of zinc supplementation in the management of childhood diarrhoea.

1.4. AIM AND OBJECTIVES OF THE STUDY

1.4.1. AIM
The main aim of this study was to determine adherence levels of health care professionals to treatment guidelines for zinc supplementation, in the management of acute diarrhoea in children birth to five years, admitted to the GMPW at a tertiary hospital between 1 January 2013 and 31 December 2013.

1.4.2. OBJECTIVES
In order to achieve the aim of this research study, four objectives were created, namely: to determine the general characteristics of cases admitted for diarrhoea; to collect information on the diarrhoeal episodes; to collect information on zinc prescriptions; and, to identify any barriers to prescribing and administering of zinc supplementation as noted by medical staff in the case folders.

1.5. STRUCTURE OF THE DISSERTATION
This dissertation is divided into five chapters. Chapter 1 introduces the topic being researched giving an overview and motivation, a description of the study area and

problem statement. Included in this chapter are the main aim and objectives as well as the structure of the dissertation.

Chapter 2 is a literature review elaborating on the background and prevalence of diarrhoea, the different classifications of diarrhoea, the aetiology of diarrhoea and the management of diarrhoea. This chapter also includes a detailed description of zinc including as a treatment for diarrhoea.

Chapter 3 explains the study methodology including the study design and population as well as the sampling method used. The study population and sampling include the inclusion and exclusion criteria for this study. The study processes will also be explained in this chapter this will include: the study variables and operational definitions, measurement techniques, study procedures and data collection. Lastly topics such as validity and reliability, practical implementation of the study, the statistical analysis used to interpret the results and ethical considerations will also be addressed in this chapter.

Chapter 4 is written in the format of an article as approved by the University of the Free State. The article condenses the main points of this dissertation, outlined in a format specific to the author instructions of the journal to which it will be submitted. The article is about the adherence levels to zinc supplementation guidelines in the management of acute diarrhoea in hospitalized children. The article includes two abstracts, an introduction, methodology, results, discussion, limitations and a conclusion.

Chapter 5 will discuss the conclusions and recommendations of the study; this will include the research significance and limitations of the study.

CHAPTER 2: LITERATURE REVIEW

2.1. INTRODUCTION

In 2012, 6.6 million children younger than five years of age died from diarrhoea - a preventable disease, which amounted to a daily death toll of 1 400 children. The mortality rate due to diarrhoea is more than the collective deaths from AIDS, measles and malaria, with 80% of these deaths being in low to middle income countries in Africa, Asia and South America (Pinzón-Róndon et al., 2015:1; Bhutta et al., 2013:1417; UNICEF & WHO, 2009:5).

Intervention programmes to control the burden of diarrhoea, combined with nutrition promotion interventions, if implemented correctly will save millions of young lives (Pinzón-Róndon et al., 2015:1). The recommended interventions and supportive management already exist to control diarrhoea and they are simple and cost-effective. It, however, requires a concerted and sustained promotion, implementation and surveillance of the proven interventions (Pinzón-Róndon et al., 2015:1; WHO & UNICEF, 2013:5).

This literature review expands on the topic of diarrhoea including information defining the illness, causes and management guidelines. The management of diarrhoea will include a summary of the medical management but will focus on zinc and zinc supplementation.

2.2. DEFINITION AND CLASSIFICATIONS OF DIARRHOEA

Diarrhoea comes from the Greek word meaning to "'flow through''. This aptly describes what happens in the body when diarrhoea is present, namely the unusually swift movement of luminal contents through the GIT (Whyte & Jenkins, 2012:443). The WHO defines diarrhoea as the passage of three or more unusually watery or loose stools in a 24 hour period; however, it is the change in consistency of the stools that is of the utmost importance and not just the frequency of the stools when defining diarrhoea. Therefore any abnormal changes in consistency or increase in the frequency of stools can be noted as diarrhoea (WHO & UNICEF, 2013:10; White Johansson & Wardlaw, 2009:9; WHO, 2005:3; Thapar & Sanderson, 2004:264). In practice, mothers will usually know when their children are experiencing changes in stool consistency and frequency and when diarrhoea is present. It is helpful to use this information when diagnosing and classifying

diarrhoea (WHO, 2005:4; Thapar & Sanderson, 2004:264).

UNICEF and WHO jointly classify diarrhoea into four clinical forms namely:

- Acute watery diarrhoea – duration varies from a few hours to multiple days, with symptoms including large fluid losses, rapid dehydration and weight loss;
- acute bloody diarrhoea (dysentery) - Visible traces of blood are found in the stools, which indicates damage to the intestinal mucosa and if untreated can lead to dehydration, sepsis and malnutrition;
- persistent diarrhoea – this diarrhoea occurs for a minimum of 14 days with or without blood in the stools, it may cause dehydration, malnutrition and concomitant infections; and,
- diarrhoea accompanying malnutrition – this diarrhoea may add to vitamin and mineral deficiencies, cause dehydration, sepsis and ultimately heart failure (White Johansson & Wardlaw, 2009:10; UNICEF & WHO, 2009:10; WHO, 2005:4; Thapar & Sanderson, 2004:264).

2.3.   THE PATHOPHYSIOLOGY AND AETIOLOGY OF DIARRHOEA

2.3.1. PATHOPHYSIOLOGY OF DIARRHOEA

The digestive and absorptive capability of the human digestive tract is vast. Eight to nine litres of fluid will enter the proximal small intestine daily, yet a typical stool will only yield 100 to 200 ml of fluid. Of the eight to nine litres of intestinal fluids only two litres come from the ingestion of food and liquids, while the rest come from internal secretions such as gastric juices, pancreatic enzymes and bile secretions. These secretions combine with food to form what is known as chyme (Whyte & Jenkins, 2012:443; Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264).

The tonicity of duodenal chyme is heavily dependent on the type of foods ingested, but generally chyme is hypertonic because of the osmotically active ions and molecules in food (Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264). From the duodenum the chyme moves with peristalsis into the jejunum which is the most permeable part of the GIT and the osmolality of the intestinal lumen thus changes quickly as the particles of food are absorbed (Whyte & Jenkins, 2012:443). Once the chyme reaches the ileum, the majority of the dietary fat, carbohydrates and protein will be absorbed and the tonicity of the chyme changes to the osmolality of plasma.

The volume of ileal chyme, after absorption, will reduce to a total of one litre a day before entering the large intestine, where further fluid and electrolyte absorption occurs. If the small intestine is unable to absorb the bulk of the nutrients, electrolytes and fluid from the chyme or if the absorptive capacity of the small intestine is surpassed, the large intestine will be inundated with chyme. In healthy individuals the large intestine is capable of absorbing up to five litres of fluid. If this is surpassed by additional volumes of fluid, diarrhoea will ensue (Whyte & Jenkins, 2012:443; Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264).

In order to maintain fluid and electrolyte balance in the human body, absorption and secretion occur constantly along the length of the GIT. These functions are performed under the regulatory control of numerous factor, controlling stool frequency and volume. In healthy individuals these complex factors will ensure that adsorption will outweigh secretion or losses. Regulatory factors occur on a cellular level allowing the absorption of substrates from the intestinal lumen across the intestinal wall into the blood. The three absorption pathways are namely; active transport, diffusion and solvent drag also known as bulk transport (Whyte & Jenkins, 2012:443; Spruill & Wade, 2008:618).

Sodium specifically is absorbed and secreted both with active transport and diffusion; it is diffused from a higher concentration in the chyme to the epithelial cells and actively transported from the epithelium into the blood. As this occurs hydrogen ions are secreted out of the epithelial cells into the chyme, which then combines to ultimately produce carbon dioxide and water (Whyte & Jenkins, 2012:443; Spruill & Wade, 2008:618).

The coupled or linked pathways of active transport of fluid and electrolytes in the intestines rely on certain osmotically active molecules, like ions, monosaccharides (e.g. glucose, galactose) and amino acids. These are all derived from the digestion of nutrients. As these molecules are actively transported across the intestinal wall, osmotic pressure is produced pulling electrolytes and water along with the molecules. This linked absorption between the nutrients, fluid and electrolytes reduces the presence of hydrophilic and osmotically active substances in the intestinal lumen (Whyte & Jenkins, 2012:444; Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264). This mechanism is a major contributor to the absorption of

ions, especially sodium from the lumen. In turn sodium then assists the coupled active transport of amino acids and glucose from the epithelial cells from the intestinal wall into the blood (Spruill & Wade, 2008:618).

Another factor which influences absorption and secretion is GIT motility. Hormones and neural pathways control intestinal muscle function and peristaltic movements and thereby control how long chyme is in contact with the epithelial cells. Hormones such as angiotensin, vasopressin, glucocorticoids, aldosterone and their regulatory feedback neurotransmitters, in conjunction with the kidneys control ion absorption and secretion (Whyte & Jenkins, 2012:444; Spruill & Wade, 2008:618).

Diarrhoea occurs when the processes that regulate the homeostasis of fluid and electrolyte absorption are disrupted and sway towards secretion. This can be due to an alteration in the active transport of ions (by reduced sodium absorption from the intestines or due to increased secretion of chloride electrolytes into the intestines) (Whyte & Jenkins, 2012:445; Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264). It can also be due to a variation in GIT motility, a rise in the osmolality of the intestinal lumen or an increase in epithelial hydrostatic pressure. These physiological disruptions to fluid and electrolyte homeostasis are summarized in four physiological causes of diarrhoea namely: secretory, osmotic, exudative and altered GIT motility (Whyte & Jenkins, 2012:445; Spruill & Wade, 2008:618).

Secretory diarrhoea is caused by various agents which, either increase intestinal secretions or reduce the absorptive capabilities of the small intestine or a combination of both. This type of diarrhoea generally has substantially increased stool volumes (greater than one litre a day). Stool volumes or frequency are also not affected by food in this type of diarrhoea. Some causes of this diarrhoea include rotavirus, bacterial toxins, large amounts of bile salts and laxatives (Whyte & Jenkins, 2012:445; Thapar & Sanderson, 2004:264).

Osmotic diarrhoea occurs when osmotically active substances are inadequately absorbed leading to an increase in the osmotic pressure in the intestinal lumen. Some causes of this diarrhoea include malabsorption syndromes such as lactose intolerance. When the specific food or substance is avoided, the diarrhoea stops (Whyte & Jenkins, 2012:444; Spruill & Wade, 2008:618).

Exudative diarrhoea is caused by damage to the epithelial tissue leading to reduced absorption. It also leads to an increase in the discharge of mucous, proteins and blood from the damaged tissue into the intestinal lumen. This is most often caused by inflammatory diseases and results in high stool volumes irrespective of food intake (Spruill & Wade, 2008:618).

Lastly, changes in GIT motility can cause diarrhoea; both increased and decreased motility can cause diarrhoea. With increased peristaltic movements and motility, intestinal chyme can rapidly and prematurely void into the large intestine. This rapid emptying can lead to insufficient and inadequate absorption of nutrients, electrolytes and fluid as well as overloading the large intestine with chyme beyond its absorptive capabilities. Some causes include intestinal resection and certain medications which alter gastric motility i.e. metoclopramide and certain laxatives. Alternately, reduced gastric motility may cause increased faecal bacterial growth, which can alter the natural micro biota of the intestines and can lead to bacterial overgrowth and cause subsequent diarrhoea (Whyte & Jenkins, 2012:445; Spruill & Wade, 2008:618).

In some cases the physiological causes of diarrhoea precipitate each other and are present at the same time in an individual. For example, in diarrhoea which is caused by the rotavirus, the virus attacks mature enterocytes reducing the number of cells that can perform absorption leaving predominately immature cryptal cells, which in turn increases secretion. The destruction of enterocytes and the subsequent loss of brush border enzymes worsen the malabsorption of nutrients, fluid and electrolytes, thereby increasing the volume of osmotically active substances in the intestinal lumen. This in turn encourages peristalsis and motility and further stool losses (Spruill & Wade, 2008:618; Thapar & Sanderson, 2004:264).

With this increased loss of fluid and electrolytes in the stools, a deficit may develop if these losses are not replenished, this is known as dehydration. The fluid and electrolyte losses vary depending on the type and severity of diarrhoea and fluid losses can range from between five ml/kg, which is considered normal, up to 200 ml/kg. Electrolyte losses of sodium, potassium and chloride in children with severe dehydration are similar and can each amount to 70-110 mmol/L in fluid lost. Fluid and electrolyte deficits can be caused by all forms of diarrhoea and a variety of aetiologies. However, dehydration is most predominantly found in diarrhoeal cases

triggered by the rotavirus, *E. coli* and Cholera infections (during outbreaks) (WHO, 2005:4).

2.3.2. AETIOLOGY OF DIARRHOEA

The causes of diarrhoea are numerous and vary according to the different categories of diarrhoea. In humans, fluid and electrolyte homeostasis is maintained so tightly that any slight variation of intestinal contents can cause diarrhoea (Whyte & Jenkins, 2012:444; Thapar & Sanderson, 2004:646).

Possible causes of acute diarrhoea include gastrointestinal infections such as bacteria, viruses and parasites. The pathogen profile causing diarrhoea in children across the world is similar, with 16 common pathogens identified in 65% of children with acute diarrhoea irrespective of country of origin (UNICEF & WHO, 2009:2; Thapar & Sanderson, 2004:646).

The most common infectious causes of acute diarrhoea in children are the rotavirus and pathogenic *E. coli*. Rotavirus is responsible for approximately 70-80% of diarrhoeal episodes in low to middle income countries and 40% of all diarrhoeal disease admissions to hospital in higher income countries (Fatima et al., 2014:12). Other pathogens implicated as causes of diarrhoea include bacteria such as *Campylobacter, Salmonella,* and *Vibrio cholerae* (during outbreaks). In certain situations parasites cause diarrhoea such as the protozoa, *Cryptosporidium* and *Giardia* which are commonly found in HIV infected patients (Whyte & Jenkins, 2012:445; Guarino et al., 2012:17; White Johansson & Wardlaw, 2009:9; UNICEF & WHO, 2009:2; Steyn, 2009:31; Thapar & Sanderson, 2004:646). Gastrointestinal infections causing acute diarrhoea are mainly spread through contaminated water and food sources or through personal contact due to inadequate hygiene (UNICEF & WHO, 2009:2; Steyn, 2009:32). In total 88% of global diarrhoeal deaths can be attributed to contaminated water sources, poor sanitation facilities and inadequate hygiene, with over 99% of these deaths occurring in low to middle income countries (Pengpid & Peltzer, 2012:149). In some parts of South Africa, diarrhoea presents more frequently in the summer months, due to the increased growth of pathogens in food and water as a result of warm and humid weather conditions (Steyn, 2009:32). However in temperate environments, rotavirus epidemics generally present in the winter months (Thapar & Sanderson, 2004:646).

Unlike acute diarrhoea, persistent diarrhoea may be caused by a number of compounding factors including the infections stated above, as well as tuberculosis (TB), *clostridium dificile*, malnutrition, food intolerances or allergies, malabsorption and the HIV itself (Lazzerini & Ronfani, 2008:3; Thapar & Sanderson, 2004:646). Certain medications can also disturb and increase gastric motility, causing diarrhoea. The main cause of drug related diarrhoea are antibiotics which cause gastric irritation and can destroy beneficial micro biota, leading to opportunistic infections (Thapar & Sanderson, 2004:646).

Although there are a number of different causes responsible for the development of diarrhoea, often the cause of the diarrhoea does not alter the case management. One of the exceptions to this is dysentery, where cause specific treatment is necessary. The most common cause of dysentery is a parasite known as *Shigella* and it is responsible for 15% of deaths due to diarrhoea in children birth to five years (Guarino et al., 2012:17; White Johansson & Wardlaw, 2009:9; UNICEF & WHO, 2009:2; Thapar & Sanderson, 2004).

2.3.3. MALNUTRITION AND DIARRHOEA

The WHO (2005:6), has identified diarrhoea not only as a disease of fluid and electrolyte imbalances but also a nutritional disease. Those children that succumb to diarrhoea, regardless of proper management, are generally malnourished and malnutrition is known to be a negative prognostic indicator in childhood diarrhoea. It is a vicious cycle where diarrhoea causes a worsening of the child's nutritional status by further weight loss due to increased nutrient losses, as well as decreased nutrient intake and absorption. Malnutrition in turn puts the child at risk for more frequent and prolonged diarrhoeal episodes, which is evident in up to 40% of diarrhoea associated deaths. This double burden is most evident in low to middle income countries where four out of five children are underweight for age which translates to 129 million children globally. Research on the incidence of stunting indicates that 40% of children younger than five years of age are classified as stunted in Africa and nearly 50% in South Asia. This recurrent cycle of diarrhoea and undernutrition leads to higher mortality rates seen amongst children younger than five years of age (WHO & UNICEF, 2009:2; Thapar & Sanderson, 2004:647). Fortunately prevention and proper management of diarrhoea, especially during the first six months of age including adequate nutrition will help to lower the prevalence of stunting and

undernutrition as a whole (WHO & UNICEF, 2009:14).

Many of the problems linked with diarrhoea and malnutrition occur due to the physical changes to the structure of the GIT associated with malnutrition, known as 'leaky gut' as well as impaired immunity due to macro and micronutrient deficiencies (Thapar & Sanderson, 2004:647).

2.4.   MANAGEMENT OF DIARRHOEA

The MDGs were a set of developmental goals agreed upon by the United Nation's member states including South Africa at the Millenium summit held in 2000. These goals were created to improve the lives of millions of people around the world in various sectors including health, nutrition and socio-economically. The baseline data for these specific goals was the year 1990 and the target date by which to achieve the goals was set at 2015. Two of these goals broadly incorporated and promoted the reduction of the burden of childhood diarrhoea, namely: the fourth MDG goal which aimed to reduce overall mortality rates in children younger than five years of age, by improving all-cause mortality rates including diarrhoea and; the seventh goal which targeted the burden of diarrhoea, by aiming to halve the number of people that did not have access to safe, clean water and basic hygiene and sanitation. The progress that has been made to achieve these goals has gone a long way to improve the lives of many, but still more progress is needed. A sustained and targeted approach, with an acceleration of key interventions was needed (Wang et al., 2014:1; Lehohla, 2013:61; WHO & UNICEF, 2013:10; Rajaratnam et al., 2010:1988: Black et al., 2010: 1969). This was addressed by the development of 17 new SDGs which focus on alleviating poverty and reducing preventable deaths in vulnerable populations. These targets build on the progress made from the MDGs, with more focused goals aiming beyond 2015 (Liu et al., 2015:430).

With this in mind and the need to accelerate key interventions, the WHO and UNICEF, in conjunction with their partners in 2013, developed the GAPPD. It was established to incorporate and accelerate the progress that was made with the MDG's, IMCI and previous strategies, with specific reference to a combined approach to managing diarrhoea and pneumonia. The GAPPD combined the strategies from the Global Action Plan for the Prevention and Control of Pneumonia as well as the seven point comprehensive control strategy for the prevention and

treatment of diarrhoea set out by UNICEF and the WHO in 2009 (UNICEF & WHO, 2009:2). This action plan includes a framework explicitly detailing intervention guidelines for the protection, prevention and treatment of diarrhoea in children, as well as goals to measure and monitor intervention outcomes. The GAPPD focuses on increasing and sustaining the implementation of scientifically proven interventions for diarrhoea. A summary of these interventions with the relevant reductions in mortality and incidence of diarrhoea are found in Table 2.1 (WHO & UNICEF, 2013:11).

Table 2.1: Diarrhoea prevention and management interventions and associated risks/reductions in mortality and morbidity (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419)

Interventions	Risks/Reductions in mortality and morbidity
1. Protection and prevention of diarrhoea	
Exclusive Breastfeeding for 6 months	If not breast fed there is a 10.5 times higher risk of death from diarrhoea and 165% increase in the incidence of diarrhoea in infants 0-5 months of age. Not exclusively breastfeeding caused a high risk of diarrhoea incidence (RR 1.26-2.65), prevalence (RR 2.15-4.90) and mortality (RR 1.48-14.40) in infants 0-5months of age.
Continued breastfeeding from 6-23 months	If not breast fed there is a 2.8 times higher risk of death from diarrhoea and a 32% increase in incidence of diarrhoea in infants 6-23 months of age. Not breastfeeding lead to a high risk of incidence of diarrhoea (RR 1.32), prevalence (RR 2.07) and mortality (RR 2.18) in infants 6-11 months of age.
Appropriate and adequate complementary feeding among children 6-23 months including sufficient micronutrient intake	Results in a 6% reduction in all causes of child mortality, this includes diarrhoea.
Vitamin A supplementation	Results in a 23% reduction in all child mortality rates, this includes diarrhoea
Rotavirus vaccine	The vaccine was 74% effective against very severe rotavirus infection, 61% in severe infections and reduced hospital admissions due to rotavirus by 47%.

Prevention of HIV transmission in children	Results in a 2% reduction in child mortality rates.
Water, sanitation, and hygiene interventions	Handwashing with soap reduces risk of diarrhoea between 31- 48%. Improved sanitation reduces risk of diarrhoea by 36%. Improved water quantity (a minimum of 25 litres is needed per person) reduces risk of diarrhoea by 17%. Improved water quality through household water treatment and clean, safe storage reduces the risk of diarrhoea between 31 – 52%.
2. Treatment of diarrhoea	
Community-based care management using simple, standardized treatment guidelines to identify and treat diarrhoea	Improved access to treatment for diarrhoea namely; ORS and zinc at community level results in a 93% reduction in mortality rate in children younger than fives years of age.
ORT using the new ORS solution	Results in a 69% reduction of diarrhoea mortality rates with recent coverage statististics, with a 93% reduction expected with 100% coverage.
Zinc Treatment	Results in a 23% reduction of mortality rates due to diarrhoea and between 14-15% reduction in the incidence of diarrhoea. Results in a 23% reduction of hospital admissions due to diarrhoea.
Antimicrobial Treatment	Treatment for *shigella* results in a 82% reduction in clinical failure and a 96% reduction in bacteriological failure. Treatment for cholera results in a 63%

| | reduction in clinical failure and a 75% in bacteriological failure. |
| | Treatment for *cryptosporidiosis* results in a 52% reduction in clinical failure, 38% parasitological failure and has a 76% non-significant reduction in mortality (all cause). |

RR = relative risk; ORS = oral rehydration salt; ORT = oral rehydration therapy

The GAPPD have set out specific goals for the management of diarrhoea. Some of the diarhoea specific goals for management include:

- The reduction of diarrhoea related mortality rates in children younger than five years of age to less than one in 1 000 child births;
- a 75% reduction in the incidence of diarrhoea in children younger than five years of age, compared to the baseline statistics of 2010; and,
- a reduction of 40% in global stunting in children younger than five years of age compared to the baseline statisitics of 2010 (WHO & UNICEF, 2013:9).

In order to achieve these goals the action plan has set out certain coverage targets for interventions for the treatment of childhood diarrhoea. These targets include:

- Obtaining 90% full-dosage coverage of all appropriate vaccines and immunizations, with 80% vaccine coverage per district;
- obtaining 90% access to suitable diarrhoea management, with 80% coverage obtained per district;
- a minimum of 50% coverage of exclusive breastfeeding for the initial six months of life;
- the near eradication of paediatric HIV;
- obtaining access to clean safe water in homes and HCFs;
- obtaining access to sufficient sanitation in homes by 2040 and HCFs by 2030;
- obtaining access to appropriate hand washing facilities with soap and water in homes and universal access to handwashing facilities in homes and HCFs; and,
- obtaining access to energy sources that are not harmful in homes and HCFs (WHO & UNICEF, 2013:9).

Of all the interventions to reduce the burden of diarrhoea, prevention still remains the best solution for managing childhood diarrhoea. Many of the interventions in Table 2.1 focus on reducing the incidence of infectious pathogens that cause the majority of diarrhoeal episodes. By promoting interventions such as exclusive breastfeeding, appropriate complementary nutrition, vaccines, vitamin A supplementation, providing populations with safe, clean water and sanitation facilities as well as promoting hygiene pratices, diarrhoeal episodes can be vastly decreased in vulnerable populations (WHO & UNICEF, 2013:14; Thapar & Sanderson, 2004:649).

The general manangement of a diarrhoeal episode on the other hand is mostly supportive, until which time the infectious agent or the cause has subsided and the mucosa has healed. In most cases of acute diarrhoea the illness is self-limiting and generally dissipates after three to seven days. However, if moderate to severe dehydration is present, along with pyrexia and blood or mucous in the stools, medical intervention is needed (Spruill & Wade, 2005:623). The management of cases aims at avoiding and treating dehydration, preventing and treating nutritional deficiencies and, if warranted, antimicrobial treatment. This is achieved by providing fluid therapy in the form of oral rehydration therapy (ORT), specifically low osmolarity oral rehydration salts (ORS) and treating nutritional deficiencies with zinc supplementation and adequate nutrition during and after diarrhoeal episodes (WHO & UNICEF, 2013:14; Applegate et al., 2013:1; Whyte & Jenkins, 2012:445; Thapar & Sanderson, 2004: 646).

The ultimate goal of both prevention and treatment is the reduction of mortality and co-morbidies due to diarrhoea. The prevemtion and management of diarrhoea is outlined in Table 2.1 and expanded upon in the text below. For the purposes of this literature review, the focus will mainly be on the management of acute diarrhoea.

2.4.1. MEDICAL NUTRITION THERAPY

It is essential that children receive sufficient amounts of macro and micronutrients for the development of strong immune systems. Children that are well nourished have stronger immune systems and are less likely to develop diseases such as diarrhoea, and if they do develop diarrhoea, the severity and duration are often less (WHO & UNICEF, 2013:6; UNICEF & WHO 2009:21).

Exclusive breastfeeding of an infant from birth to six months of age up to two years

and older remains one of the most effective interventions to reduce the incidence and severity of all infections including diarrhoea. It is beneficial for all infants, including those of HIV infected mothers (WHO & UNICEF, 2013:6; Whyte & Jenkins, 2012:445; UNICEF & WHO, 2009:14). Research has shown that breastfeeding an infant during an episode of diarrhoea decreases stool losses as well as fluid therapy requirements. This protective effect is clearly evident from the research which shows a 165% increase in the incidence of diarrhoea and a 10 times higher risk of death due to diarrhoea in non-breastfed infants aged birth to six months (Table 2.1). As part of the management of diarrhoea it is therefore, priority to promote and protect exclusive breastfeeding for the first six months of life, with appropriate complementary feeding and continued breastfeeding after six months (WHO & UNICEF, 2013:6; Bhutta et al., 2013:1418). Breastmilk supplies the infant with everything that they need to develop and thrive; this includes macro and micro nutrients, hormones and antibodies. The benefits of breastfeeding go beyond just the physical and include psychological, social, economic and environmental advantages (Bhutta et al., 2013: 1418; UNICEF & WHO, 2009:14). Despite all the benefits of breastfeeding, according to data from 2012, only 37% of infants, birth to six months of age, were exclusively breastfed (WHO & UNICEF, 2013:6). The rate of exclusive breastfeeding needs to be increased if childhood mortality rates are to be reduced. The best way to do so is through promotional interventions, trials have indicated significant improvements in breastfeeding with a combination of HCF and community based interventions (Bhutta et al., 2013:1418).

Scientific research has yet to ascertain the ideal nutritional approach to enhance recovery and safeguard nutritional status during an episode of diarrhoea in a child (Bhutta et al., 2013:1420). Irrespective of the questions about which nutritional interventions to use, the priority is always to continue feeding a child during a diarrhoeal episode. Breastfeeding and/or food should never be stopped, reduced or diluted, and the child's normal diet should be maintained if at all possible throughout the episode (WHO & UNICEF, 2013:6; WHO, 2005:11; Thapar & Sanderson, 2004:647). A child's appetite will often be reduced especially in cases of dysentery and if dehydration is present. However the majority of children will regain their appetites once the dehydration has improved. In the case of dysentery the child's appetite will usually be slow to return until the disease resolves (WHO & UNICEF,

2013:6; WHO 2005:11).

The aim of feeding during a diarrhoeal episode is to provide energy dense foods as soon as the child is willing to consume it. In most cases there will be at least partial absorption and digestion of nutrients, despite the diarrhoea. This will help to prevent growth faltering and possible malnutrition, as well as increase the recovery of healthy intestinal function including absorption and digestion. In cases where food is withheld or restricted; the risk of weight loss and malnutrition is increased and the duration of the diarrhoeal episode is lengthened (delaying intestinal recovery time) (WHO & UNICEF, 2013:6; WHO, 2005:11). According to data from the WHO and UNICEF (2013:6) only 33% of children are fed continuously during a diarrhoeal episode. Appropriate food choices should always take into account the child's age, previous diet, food preferences and cultural feeding practices. Food choices can generally be the same as that of a healthy child and research suggests that it is safe and effective in persistent diarrhoea (WHO & UNICEF, 2013:6; WHO, 2005:11; Thapar & Sanderson, 2004:647).

Infants from birth to six months of age should be exclusively breastfed and mothers should be encouraged (Bhutta et al., 2013:1419; WHO, 2005:11) to do so for as long and as frequently as the infant requires. If the infant has received any other foods, it is preferential to decrease those foods and increase breastfeeding. If any other fluids are given to the infant, a cup should be used rather than a bottle to protect breastfeeding and to encourage good hygiene. In cases where the infant is not breastfed, the infant's normal formula (or standard formula) should be mixed according to the manufacturer's mixing instructions and given every three hours with a cup (Whyte & Jenkins, 2012:445; WHO, 2005:11). Specialized infant formulas (e.g. lactose free formulas, semi-elemental formulas) are costly and in most cases of acute diarrhoea unnecessary (WHO, 2005:11).

Only in prolonged diarrhoeal episodes or in rare cases will milk intolerances (e.g. lactose intolerance or cow's milk protein intolerance) be clinically significant. It is of no benefit to routinely test all children with diarrhoea for intolerances. Intolerance tests such as stool pH or faecal reducing substances are over sensitive and will frequently show compromised lactose absorption (WHO, 2005:11). This transient lactose intolerance as well as possible cow's milk protein sensitivity or intolerance is

not uncommon and is known as postenteritis syndrome. It has been evident in 4.3–18.4% of diarrhoeal cases and in 30-50% of children after rotavirus infection and in the majority of cases the GIT will recover. This syndrome is caused by injury to or blunting of the villi in the small intestine by the pathogen, leading to the reduced production and activity of lactase, which is needed for the adequate absorption of lactose. This reduction in the activity of lactase and other disaccharidases leads to impaired absorption of carbohydrates. However it is often not clinically important and self-limiting. The mucosa normally repairs within two to three weeks after a diarrhoeal episode (Whyte & Jenkins, 2012: 445; Dalgic et al., 2011:678; Thapar & Sanderson, 2004:647). It is therefore better to observe and assess a child's clinical response and symptoms. Lactose intolerance only becomes important when there is protracted diarrhoea with increased symptoms; such as stool frequency and volume, deteriorating dehydration and weight loss aggravated by the milk or formula given (WHO 2005:11). Trials that assessed lactose free formula or lactose free diets to manage diarrhoea in children, showed a slight reduction in the duration of diarrhoeal episodes and a 47% decrease in the risk of treatment failure. However, there was no effect on the number or volume of stools or weight gain. Research indicates that children that switched to a normal diet earlier (inclusive of lactose) had improved weight gain and symptoms were not extended or aggravated by the diet (Bhutta et al., 2013:1420; Applegate et al., 2013:1; Thapar & Sanderson, 2004:647).

If a child is older than six months of age or if complementary feeding has already started, the child should receive in addition to breastmilk or formula, a variety of cereals, vegetables, fruit and other food items. Alternately if the child has reached six months and age appropriate foods have not yet been introduced, they should be started as soon as possible, either during or directly after the diarrhoeal episode. Whichever foods are chosen, should be micro and macronutrient dense, easily accessible, sustainable and culturally acceptable. Food items can be made simpler to digest by cooking, plus mashing or grounding. Some suggestions to make food more nutrient dense include adding milk and one to two teaspoons of vegetable oil to cereals. A child with diarrhoea should be given small, frequent feeds every three to four hours. At least six small meals a day are more acceptable than less frequent, larger meals. Nutrient dense foods should continue to be given to the child as well as additional meals for at least two weeks or longer after the episode to regain any

weight lost or to reach an adequate weight-for-height standard deviation (WHO, 2005:11).

A review of trials comparing the use of commercially available feeds or specialized nutritional products with household foods, showed no advantages in the use of commercial products for acute or persistent diarrhoea. This research highlights that household food and locally available produce are as effective as commercial products at managing diarrhoea and are more acceptable to individuals (Bhutta et al., 2013:1420). In some cases oral intake is impaired or inadequate but the GIT is still functioning: in these cases, a nasogastric feeding tube should be inserted and ORT and feeding initiated through the tube. Extraordinary feeding interventions such as parenteral nutrition should only be implemented when all other avenues of feeding have been exhausted and where intestinal failure is present (Thapar & Sanderson, 2004:647).

If a child presents with co-morbidities such as severe acute malnutrition, liver failure or renal failure, specific feeding guidelines need to be followed (WHO & UNICEF, 2009:10; Thapar & Sanderson, 2004:647).

The GIT is a complex system that not only provides nutrients to the rest of the body but also plays host to a multitude of live micro-organisms. These microbes are known as probiotics and form part of the colonization of a healthy GIT. Probiotics form a barrier against pathogens; they moderate exchanges with the environment and are crucial in the creation and regulation of advantageous immune responses associated with the mucosa. In most cases probiotics are symbiotic bacteria but there are a few strains of yeast which form part of beneficial human micro biota. There are countless strains of probiotics but the most common include; *lactobacillus* (e.g. *L. rhamnosus*), *bifidobacterium* (e.g. *B. bifidum*), *streptococcus* (e.g. *Strep. thermophiles*) and the yeast *Saccharomyces boulardi* which is from non-human origin (Farthing et al., 2012:14; Thapar & Sanderson, 2004:649).

A number of meta-analyses have assessed the effectiveness of probiotics as a treatment for diarrhoea and have shown positive results the occurrence and duration of diarrhoeal episodes in patients with acute infectious diarrhoea. These reviews reported a significant decrease in the risk of developing diarrhoea for longer than three days as well as a reduction in stool frequency on the second day with probiotic

use. This could be of benefit in reducing the persistence of diarrhoea in already vulnerable populations such as children with malnutrition. There is also some evidence to indicate that probiotics play a preventative role by decreasing the reoccurrence of diarrhoeal episodes especially where the cause was a viral infection. Specifically probiotics decreased the period of rotaviral shedding and reduced gut permeability (Applegate et al., 2013:1; Dinleyici et al., 2012:871; Allen et al., 2010:36; Szajewska et al., 2007:871). The yeast *Saccharomyces boulardi* also appears to have a beneficial and protective effect against *Clostridium difficile* (Dinleyici et al., 2012:871*).*

More research is needed to show the effectiveness of probiotics compared with current interventions of ORS, feeding and zinc supplementation in the treatment of childhood diarrhoea. Along with effectiveness trials, cost-effective analyses should be conducted on the use of probiotics in childhood diarrhoea to determine accessibility and feasibility of using this intervention in low to middle income countries (Applegate et al., 2013:1). The results of studies using probiotics in the treatment of diarrhoea should be viewed cautiously; firstly due to the studies being partially financed by manufacturers, which then brings into question the validity of the results and secondly, because there are many probiotic formulations on the market and the effectiveness of these products is questionable (Thapar & Sanderson, 2004: 649).

Due to the strong relationship between malnutrition and diarrhoea, as well as increased stool losses and reduced oral intake, vitamin and mineral deficiencies are prevalent in children that develop diarrhoea. Two important micronutrients with a role in the treatment of diarrhoea include vitamin A and zinc. Vitamin A plays a role in the preservation of the epithelial lining of the GIT while the role of zinc will be discussed further in the next section entitled zinc. The benefits of vitamin A supplementation as a single intervention in the treatment of diarrhoea are minor in comparison to that of zinc supplementation. However, data still indicate a 23% reduction in overall childhood mortality rates which includes diarrhoea as indicated in Table 2.1 (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419; Thapar & Sanderson, 2004:648). The Vitamin A supplementation programme forms part of the IMCI guidelines, with approximately 92% of all children receiving two dosages of Vitamin A before the age of five years (WHO & UNICEF, 2013:6).

2.4.2. MEDICAL MANAGEMENT

The medical management of diarrhoea incorporates two lines of management, namely, the prevention and protection of children against infections causing acute diarrhoea and if that fails, the therapeutic treatment of related symptoms and causes (Kee et al., 2015: 218; Spruill & Wade, 2008:619).

Preventative interventions for the management of diarrhoea are very important in lowering the incidence of diarrhoea in children younger than five years of age. One way of reducing the burden of diarrhoea is to immunize children against some of the infections that cause diarrhoea, namely rotavirus and measles (Kee et al., 2015:218; WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419).

Rotavirus is responsible for 100 million diarrhoeal episodes, accounting for 40% of all diarrhoea-related hospital admissions. This motivated the development and introduction of a vaccine (UNICEF & WHO, 2009:14). This vaccine is needed in areas with the highest number of diarrhoeal cases such as Africa and South Asia and thus the WHO has recommended that this vaccine be implemented along with the other guidelines for managing diarrhoea (Table 2.1) (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419).

Measles is an often self-limiting, acute viral infection and is not one of the main causes of diarrhoea in children. However in some cases, where the child is immune compromised or malnourished, the child may develop complications, such as diarrhoea and this contributes to the large number of deaths associated with measles. The measles vaccination regimen is recommended as part of the IMCI vaccination programme in children younger than five years of age and is important for the prevention of measles as well as associated co-morbidities (UNICEF & WHO, 2009:14).

In more affluent regions of the world children that present with acute infectious diarrhoea will most likely only develop mild or moderate fluid deficits, which in many instances would only require oral fluids and continued feeding. This is not the case in countries where malnutrition and infectious diarrhoea are more prevalent, causing severe electrolyte and fluid losses (UNICEF & WHO, 2009:16; Thapar & Sanderson, 2004: 646). Dehydration is assessed clinically according to the presenting signs and symptoms and these determine the degree of dehydration or fluid deficit. During the

initial period of dehydration, no signs or symptoms are obvious, however as dehydration progresses symptoms begin to present (such as thirst, agitation or restlessness, reduced skin turgor, sunken eyes and in the case of infants, a sunken fontanelle). In severe cases of dehydration, the signs and symptoms become more prominent and eventually, if not treated, hypovolaemic shock may present. This will include loss of consciousness, oliguria or anuria, cool and clammy extremities, a quick and weak pulse (possibly undetectable radial pulse), an undetectable or low blood pressure and peripheral cyanosis. Dehydration needs prompt intervention in order to prevent progression and possible death (WHO, 2005:4).

One of the greatest medical innovations of the 20th century was the development of ORT. This simple intervention which stemmed from the developing world has saved millions of lives worldwide and has become the golden standard for rehydration of children with diarrhoea. This breakthrough came in the 1960's and 1970's, when it was observed that despite the cause of the infectious diarrhoea, coupled transport of sodium and glucose or other electrolytes continued (WHO, 2005:2). Based on the findings of a number of trials, the WHO decided to endorse ORS solutions as an intervention to be used in all types of diarrhoea for all age groups. Implementation rates of ORT increased from zero in 1979 to 80% in 1995, simultaneously mortality rates in children younger than five years of age due to diarrhoea fell by two million (WHO & UNICEF, 2009:16; Thapar & Sanderson, 2004:646). Researchers came to the conclusion that ORT significantly reduced mortality rates (WHO & UNICEF, 2013:15). It was, however, difficult to determine the individual impact of this treatment as other new treatments were also initiated in combination with ORT. The other interventions that were originally recommended together with ORT were continued feeding, breastfeeding promotion, access to clean water, as well as the use of antimicrobial medication in the treatment of dysentery. These interventions could also have caused those initial mortality rate reductions (Thapar & Sanderson, 2004:646).

Oral rehydration therapy solutions consist of precise amounts of water to which certain concentrations of glucose, sodium, potassium, chloride and an alkali are added. The alkali used is generally bicarbonate or citrate. The specific concentrations of the electrolytes were determined to be equal molar concentrations of sodium and glucose to ensure coupled transport is promoted along with other

electrolytes and alkali. The osmolarity of the first ORT that was used in cholera epidemics in India was 31 mOsm/L, with a 90 mmol/L concentration of sodium (WHO & UNICEF, 2013:15; WHO & UNICEF, 2009:16; Thapar & Sanderson, 2004:646). There were some concerns especially from the European community that the electrolyte concentration was too high for all forms of acute infectious diarrhoea and for all population groups. Consequently the European Society of Paediatric Gastroenterology and Nutrition developed a reduced concentration ORT formulation (Thapar & Sanderson, 2004:646). A meta-analysis performed in 1984 on children admitted to hospital with diarrhoea concluded that the use of the reduced osmolarity ORS solution significantly decreased stool output, vomiting and decreased the necessity for intravenous fluids to a greater extent than the older solution, with no difference in hyponatremia found between the two solutions (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1420; WHO & UNICEF, 2009:16; Thapar & Sanderson, 2004: 646).

A new ORS solution was recommended by the WHO in 2004, also known as 'low-osmolarity ORS'. It was developed to make ORT more acceptable to caregivers as well as more effective for the treatment of all forms of diarrhoea and for the majority of age groups (UNICEF & WHO, 2009:16; Thapar & Sanderson, 2004: 647). As the name indicates, the solution has a slightly lower sodium concentration of 75 mmol/L than the previous solution; however, it is still not as low as the European recommendations of 60 mmol/L. The WHO has recommended ranges of concentrations which they deem to be safe and effective for use as ORT (Whyte & Jenkins, 2012: 445; Thapar & Sanderson, 2004:647). However, the impact of the new lower osmolarity ORS solution is reported to have resulted in a 69% reduction of diarrhoea mortality rates (Bhutta et al., 2013:1420) and improves recovery and outcomes compared with the previous solution. The new ORT when compared with the old solution lowered stool losses and vomiting by 20-30% and decreased the need for intravenous fluids by 33% in children suffering from diarrhoea. Because of the large impact of ORT, the WHO and UNICEF have recommended that ORT be made available and accessible to as many children as possible (UNICEF & WHO, 2009:16). Rehydration solutions should be accessible and administration should ideally begin at home, when diarrhoeal symptoms first present and be given by a caregiver (UNICEF & WHO, 2009:16). Other fluids also used in ORT are household

solutions and cereal-based drinks, e.g. a thin gruel made from rice, maize or potato. Both have shown effectiveness in treating dehydration in children with large diarrhoeal outputs. The search for the optimum ORS solution continues, with research being performed on the use of non-absorbable starches along with standard ORT (UNICEF & WHO, 2009:16). Some evidence suggests that it does reduce the fluid volume in the stool and decreases duration of diarrhoea (UNICEF & WHO, 2009:16; Thapar & Sanderson, 2004:647). Although many other oral fluids can be used to rehydrate a child suffering from dehydration, the most effective treatment still remains the new ORT (UNICEF & WHO, 2009:16).

The main concern with ORT is the poor implementation and coverage of this treatment intervention. Research from South Asia showed current implementation levels to be below 20% in the region, while the WHO and UNICEF (2013:6) suggest that globally only 33% of children with diarrhoea will receive ORT. The implementation of inappropriate rehydration methods and solutions is still a widespread problem, primarily being the unnecessary use of intravenous fluids (Panchal et al., 2013:336; Weru, 2013:5). The recommended fluid management of dehydration in diarrhoea is the use of ORT orally or if it is not possible, via a nasogastric tube (WHO & UNICEF, 2009:10). This is appropriate even in the cases of severe dehydration. Intravenous fluids are only recommended if the patient has hypovolaemia or shock, but once resolved, ORT should be initiated as quickly as possible. ORT has been found to be as effective at treating dehydration as intravenous fluids and less invasive. If intravenous fluids are used for resuscitation or fluid maintenance it is imperative that serum electrolytes be checked regularly. The goal of fluid therapy is to rehydrate the child in the initial four hour period after presenting with dehydration and thereafter to continue on maintenance fluids until the diarrhoea has stopped. Dehydrated children that present with co-morbidities, such as severe acute malnutrition need to be treated cautiously according to specific guidelines (WHO & UNICEF, 2009:10; Thapar & Sanderson, 2004:647).

"Antidiarrhoeal" medication and anti-emetics are not recommended for the treatment of acute infectious diarrhoea and vomiting in children, as the use of these medications can lead to possible toxic side effects and have shown no benefit. These drugs do not reduce the incidence of dehydration, nor have an effect on nutritional status, which are the goals of diarrhoea management (Spruill & Wade,

2008:619; WHO, 2005:5). Some of the potential side effects can be fatal in children (Spruill & Wade, 2008:619). These medications also detract focus from beneficial treatment interventions such as ORT, continued feeding, and zinc supplementation (WHO, 2005:5). This message has been widely propagated, yet antidiarrhoeal drugs are still being prescribed for children (Panchal et al., 2013:24; Weru, 2013:5). Some examples of drugs that fall into these categories include loperamide, opiates, bismuth subsalicylate, kaolin, smectite, and anticholinergic medications used as anti-emetics (Spruill & Wade, 2008:619; WHO, 2005:5; Thapar & Sanderson, 2004:648).

Antibiotics or antimicrobials are not generally prescribed in cases of acute infectious diarrhoea, only in certain cases of bacterial diarrhoea and dysentery. It is difficult to differentiate between infectious causes of diarrhoea that will respond to antimicrobials and thus these medications should not be routinely used (Bhutta et al., 2013:1421; Spruill & Wade, 2008:619). The use of antimicrobials can be costly, and there are risks of side effects or adverse reactions and the progression to antibiotic resistance. Antimicrobial use requires, knowledge of the infection causing the diarrhoea, responsiveness of specific organisms to antimicrobials and the sensitivity and resistance patterns of the specific antimicrobials recommended for the treatment of the infectious agent. Examples of antibiotics used with proven effectiveness in reducing diarrhoea mortality rates due to bacterial infections include: ciprofloxacin, ceftriaxone and, pivmecillinam. In cases of cholera, WHO recommends that the primary intervention is rehydration, with only severe cases receiving antimicrobials. In cases of dysentery caused by *shigella*, antimicrobials are useful and a variety can be used depending on resistance patterns and guidelines for that area. One commonly used drug is nalidixic acid, which has been associated with the increased occurrence of quinolone resistance. Another cause for diarrhoea which is sometimes treated with antimicrobials is *cryptosporidium*, this parasite contributes mostly to mortality rates in children with HIV. However anti-protozoal medications are rarely used only in severe cases (Bhutta et al., 2013:1421; WHO, 2005:5; Thapar & Sanderson, 2004:648).

2.5.   ZINC

2.5.1. THE BACKGROUND AND FUNCTION OF ZINC

Zinc is an essential trace element and micronutrient, second only to iron according to the amount found in the human body. Zinc's role in human health became recognized in the 1960's, yet still there remain many unanswered questions about the mechanism of its functions and interactions in the body (Basnet et al., 2014: 163).

In 1961 a 21 year old Iranian subsistence farmer presented with a new syndrome including dwarfism, hypogonadism and anaemia. He was eating a diet of unleavened bread, potatoes and milk (Prasad et al.,1963:537). Shortly after this, Egyptian youths who were eating a similar diet to the Iranian farmer of unleavened bread and beans, were observed with the same syndrome. In both cases, iron supplementation resolved the anaemia but did not resolve any of the other symptoms. It was only when a zinc supplement or animal-protein source was given, that growth and the hypogonadism improved. Studies only later showed that it was a primary zinc deficiency secondary to inadequate intake that caused the set of symptoms. Since these early discoveries curiosity over zinc's properties and functions have spiked with more research being conducted (Roohani et al., 2013:144; Prasad, 2008:353).

Zinc performs many functions in the human body, of which some are not clearly understood. However, its known functions include the synthesis of numerous proteins and enzymes as well as cell growth, and differentiation. Zinc also acts as a pro- antioxidant and an anti-inflammatory (Liberato et al., 2014:181). Zinc acts primarily in association with over 300 enzymes as an intracellular ion and is vital for the adequate functioning of the human immune system (Gallagher, 2008:122; Lazzerini & Ronfani, 2008:2; Overbeck et al., 2008:15).

Zinc has an effect on many areas of the human immune system, including both cell-mediated and humoral (anti-body mediated) immunity (Wintergerst et al., 2006:88). Zinc affects the proper development, differentiation and functioning of both types of immunity (Overbeck et al., 2008:15).

Innate immunity, also referred to as non-specific immunity, is the first line of defence in the body and includes components of both cell-mediated as well as humoral

immunity. This initial physical and chemical barrier to pathogens is directly affected by zinc concentrations. Zinc acts as an anti-oxidant and controls the permeability of cell membranes, as well as preventing free-radical damage caused to healthy tissue by the inflammatory processes (Hassan et al., 2012:2; Prasad, 2008:354). If zinc concentrations are lowered, it affects cellular mediators of innate immunity. Those functions affected include phagocytosis by macrophages, neutrophil and natural killer cells activity, development and activation of T-cell lymphocytes, cytokine production and complement activity. These factors increase the permeability of cell membranes, specifically those of the GIT and increase the risk of infection (Hassan et al., 2012:2; Wintergerst et al., 2006:88).

In addition to its role in immunity, zinc also plays a role in the growth and sexual maturity of children. Several nucleoproteins which contain zinc are involved in the replication and gene expression of enzymes necessary for growth. One specific enzyme which is slowed by zinc deficiency is insulin-like growth factor one, along with the cellular responsiveness of the body to this hormone (Hassan et al., 2012:2).

2.5.2. ABSORPTION, METABOLISM AND EXCRETION OF ZINC

Zinc, when consumed, is absorbed in the small intestine through poorly understood mechanisms. Two absorption pathways which have been identified, include: a saturable carrier mediated transport mechanism which functions best when concentrations of zinc in the GIT are low; and, a transport mechanism which requires a concentration gradient (a passive absorption pathway, whereby zinc moves from a high concentration in the lumen to a low concentration into the epithelium, during periods of high zinc intake) (Gallagher, 2008:121; IZINCG, 2004:S96).

It is challenging to determine the percentage of zinc absorbed in the small intestine, as zinc is not only absorbed in the GIT but also secreted. When fasting respondents were given oral zinc solutions, approximately 70% of the zinc consumed was absorbed. However, in a varied diet, absorption will be less effective, depending on the zinc content as well as other influencing dietary factors (Gallagher, 2008:122). Certain dietary components that have an influence on zinc absorption in the GIT include phytates, which have a large influence in reducing zinc absorption especially in diets rich in cereal or wholegrain foods. Copper and cadmium also influence zinc absorption as they both use the same transport proteins and thus reduce absorption

of zinc through competition. There are concerns that iron, folic acid (in cases of low zinc intake and high dosage folic acid supplementation) and dietary fibre may also reduce zinc absorption, while calcium is known to decrease absorption and homeostasis. Alternately, glucose, lactose, protein and red wine improve zinc absorption (Roohani et al., 2013:146; Gallagher, 2008:122; IZINCG, 2004:S96). Protein (animal and soy sources of protein) sources increase absorption, as zinc forms chelates with the amino acids which are more absorbable in the lumen. It is approximated that in a varied diet 33% of dietary zinc will be absorbed. Zinc status also influences absorption; those deficient in zinc will have increased absorption while those with an adequate zinc status will have reduced absorption. The absorption of zinc occurs in the duodenum and jejunum in the small intestine (Roohani et al., 2013:146; Gallagher, 2008:122).

When zinc is ingested it becomes a free ion near the brush border where it follows the respective transport pathways into the enterocytes. At the brush border, zinc ions bind to carrier proteins like metallothionein (zip transporter) (Gallagher, 2008:121). These transport proteins, through trans-cellular transport the zinc through the cytosol of the cell to the cell border to exit the cell into the blood. Active transport is then used to move the zinc from the cell into the blood. This is due to the lower concentration of zinc in the cytosol compared to blood (Roohani et al., 2013:146; Gallagher, 2008:121).

From the epithelium, zinc is absorbed straight into the portal system and goes directly to the liver, and from there transported to the rest of the body through the systemic circulation. The majority of serum zinc, approximately 70%, is bound to albumin in the blood. Any changes in serum albumin levels will also have an impact on serum zinc levels. Serum zinc only accounts for 0.1% of the body's zinc, but serum zinc is promptly used if needed by the rest of the body (Roohani et al., 2013:146; Gallagher, 2008:121).

There are at least 15 zip transporters that mediate transport of zinc across the brush border into the cells and 10 zinc transporters which facilitate cellular movement and active transport. The expression and centration of these zinc transporters in the cells is tightly regulated by the levels of zinc in the body, and will respond to changes in dietary intake of zinc, deficiencies and surplus as well as other stimuli such as

hormones and cytokines (Roohani et al., 2013:146; Gallagher, 2008:121).

Half of all the zinc excreted from the body is excreted from the GIT. It is secreted from intestinal cells as well as through bile, however, a large proportion will be reabsorbed depending on the bodies zinc needs and GIT function (Gallagher, 2008:121). This is necessary for the control of zinc homeostasis in the body. Zinc is also excreted through urine, sweat, hair and skin. Approximately one to three milligram per day will be lost via the GIT and 0.5 mg per day via urine, these values were based on healthy adults with sufficient dietary intake of zinc, and amounts will possibly vary in other population groups (Roohani et al., 2013:146; Gallagher, 2008:121; IZINCG, 2004:S96).

2.5.3. ASSESSING ZINC STATUS

When developing intervention programmes, it is of utmost importance to determine parameters and outcome indicators. The same applies to nutritional interventions; methods are needed to determine the nutritional status of populations, to determine not only baseline status but also any changes that may occur. Unfortunately there is no single biochemical, nutritional or clinical indicator of zinc deficiencies in humans (Willoughby & Bowen, 2014:581; Roohani et al., 2013:153).

In combination with other investigations, dietary intake assessments can be a useful tool for evaluating the risk of zinc deficiency in children. However, it should not be used as a solitary indicator to establish zinc status and deficiency. A dietary assessment in conjunction with a clinical assessment of signs and symptoms as well as biochemical values such as serum zinc levels, can be used to reach a conclusion on zinc status (Willoughby & Bowen, 2014:581).

Only 0.1% of zinc in the human body is found in the blood and serum zinc is used quickly when the body's requirements increase. This means that levels can fluctuate by almost 20% in a day resulting in serum zinc being an inaccurate measure of zinc levels in the body. Serum zinc levels are easily influenced by normal physiological processes such as eating and overnight fasting as well as infection, stress and growth. Despite these shortfalls, serum zinc is still broadly used and considered to be the most useful tool to determine deficiency (Willoughby & Bowen, 2014:581; Roohani et al., 2013:146; Maret & Sandstead, 2006:3). Some researchers (Willoughby & Bowen, 2014:581; Maret & Sandstead, 2006:6) have hypothesized

that zinc deficiency can be present even when serum levels are considered normal. The normal range for serum zinc in children is 10.7-22.9 µmol/L (70-150 µg/dL) (Willoughby & Bowen, 2014:581; Maret & Sandstead, 2006:6).

Zinc is bound to albumin, which acts as a carrier in the blood and any changes to albumin levels will affect zinc levels. Conditions which cause hypoalbuminaemia, such as liver failure, renal failure and malnutrition also cause a decrease in serum zinc levels. Hemo-dilution in cases of fluid overload, pregnancy, the use oral contraceptives as well as steroid use will all show lowered zinc levels. In contrast diseases which cause hemolysis release higher concentrations of zinc from cells into the blood and will result in increased serum zinc levels (Roohani et al., 2013:153; Maret & Sandstead, 2006:6).

Other biochemical indicators that can be used to determine zinc status include alkaline phosphatase, an enzyme that is zinc dependent and found in all tissue in the body, with the highest concentration found in the liver, bile ducts and bones. It is presumed that children with zinc deficiency will have reduced levels of this enzyme (Willoughby & Bowen, 2014:581).

2.5.4. BIOAVAILABILITY AND DIETARY REFERENCE VALUES FOR ZINC

Zinc requirements are dependent on age. Children needing larger amounts due to rapid cellular growth, are therefore more vulnerable to deficiency (Hassan et al., 2012:2; Lazzerini & Ronfani, 2008:3; IZINCG, 2004:S96).

The most biologically available dietary forms of zinc are found in animal sources, such as meat, poultry, milk and shellfish. Other sources include nuts and beans, and zinc fortified cereals, although the zinc content of animal sources is more bioavailable (Kee et al., 2015:218; Gallagher, 2008:121).

The biggest factor impacting on the bioavailability of zinc, is the diet populations consume. High amounts of protein and single amino acids increase bioavailability of zinc, while diets high in zinc chelating compounds such as phytates and phosphates as well as cations (e.g. copper, magnesium, calcium, nickel, cadmium and iron) reduce absorption from the GIT (Overbeck et al., 2007:17). These factors need to be highlighted when analysing efficacy studies as variables which can possibly interfere with outcomes.

The recommended dietary allowance (RDA) of zinc for healthy infants aged birth to six months is 2 mg and for those aged 7-36 months it is 3 mg daily. For children from one to three years of age it is 3 mg and for children four to eight years of age the RDA is 5 mg. In malnourished children the risk of severe zinc deficiency is high. As such, the RDA for zinc is higher at 2-4 mg/kg per day, to compensate for the increased requirements. However, the exact amount of zinc needed in young infants to maintain a positive zinc balance in populations with a high prevalence of zinc deficiency is unknown (Lazzerini & Ronfani, 2013:5; Hassan et al., 2012:2; Gallagher, 2008:123; IZINCG, 2004:S96).

The formulation of zinc supplements has always been a challenge because it is difficult to maintain the bioavailability of a soluble form of zinc. It is necessary to maintain solubility and absorption of zinc ions to keep the beneficial properties of zinc. When analysing the formulation of zinc supplements it is essential to consider the bioavailability of the different types of zinc used in the supplement, other components added (i.e. micronutrients) and the manufacturing process. Zinc salts that have used organic anions like acetate, histidine and methionine have a higher bioavailability than those containing inorganic salts like zinc sulphate. Zinc oxide has the lowest bioavailability of all zinc supplements (Overbeck et al., 2007:16; Hulisz, 2004:596).

2.5.5. DEFICIENCY

Zinc is the second most abundant trace element in the body, only second to iron and it is spread throughout the body. The highest concentrations occur in the liver, pancreas, kidneys, bones, muscles, prostate and parts of the eye. However, it is also found in the skin, hair, nails and sperm. The total bodily content of zinc is around 2-3 grams (Gallagher, 2008:121; Maret & Sandstead, 2006:3) and the level of bodily zinc is determined by the balance of dietary intake, absorption, and losses (Maret & Sandstead, 2006:3).

Zinc is an essential trace element with only small amounts being stored in the body, as 50% of dietary zinc is being excreted via the GIT. It is therefore necessary for the body to acquire sufficient daily amounts of this trace element from external sources to maintain homeostasis and prevent deficiency. Zinc is associated with many zinc-reliant functions, most of which include enzymatic functions and daily intake is

needed to preserve these functions and prevent deficiency (Hassan et al., 2012:2; Lazzerini & Ronfani, 2008:2-3; Gallagher, 2008:122; Overbeck et al., 2008:15; IZINCG, 2004:S96).

There are many causes of zinc deficiency: however, in low to middle income countries the primary cause of deficiency is the high intake of cereals which have a high phytate content. This, in addition to the low intake of animal sources of protein, leads to zinc deficiency. High biologically available food sources of zinc including animal products are often expensive and difficult to obtain in low to middle income countries due to socioeconomic constraints. Alternately cereals and legumes high in phytates are readily available and cheap and form the staple diets of many in poorer populations. The limited intake and absorption of zinc can result in widespread deficiency, especially in vulnerable populations like children. Zinc deficiency is less likely to occur in high income countries, due to the availability of food and the majority of the cereal foods being processed and fortified with zinc (Hassan et al., 2012:2; Gallagher, 2008:120; Lazzerini & Ronfani, 2008:2). In children, especially those under the age of five years, meat intake is often low due to personal preference, with children in many cases preferring traditional complementary or weaning foods such as cereals and dairy products over meat products. Breastmilk generally provides sufficient amounts of zinc (2 mg per day) for infants younger than six months of age (unless the mother is zinc deficient). However, zinc requirements in infants over the age of six months increase and breastmilk alone will not provide enough zinc for these infants. In this age group complementary foods rich in zinc will need to be provided (Willoughby & Bowen, 2014:581). Without appropriate interventions, a child whose diet does not provide them with enough zinc will eventually develop zinc deficiency and the complications associated with it (Hassan et al., 2012:2). Other causes of zinc deficiency include acrodermatitis enteropathica, malabsorption syndrome, and hyperzincurea as seen in renal disease, liver failure, sickle cell disease, blood loss, diarrhoea, fever and excessive sweating in hot climates. Lastly, intentionally restrictive diets such as vegetarianism, veganism and others limiting animal sources of protein are also a cause of zinc deficiency (Roohani et al., 2013:154; Prasad, 2008:354).

The negative effects of insufficient zinc intake were first noted more than 50 years ago by Prasad et al (1963:537). As discussed in the background of zinc, studies

investigated 'nutritionally dwarfed' boys and their common characteristics included short stature, delayed sexual maturity and low levels of plasma zinc. By supplementing the boys with zinc, the early studies showed a significant improvement in stature and equally significant progression in gonadal development (Gallagher, 2008:121). Since these first studies, zinc deficiency has been widely identified, with approximately 17% of the world's population being affected. Those affected are primarily located in low to middle income countries (Wessells & Brown, 2012:1; Prasad, 2008:353).

Clinical manifestations of zinc deficiency range in severity from mild or marginal to moderate and severe. The severity depends on the duration of deficiency and the cause of the deficiency (Prasad, 2008:353). The clinical manifestations of deficiency are listed in Table 2.2 below. Some of the clinical signs associated with zinc deficiency include hypogeusia, anorexia, alopecia, cognitive dysfunction, skin lesions or dermatitis, delayed wound healing and suppressed immunity, impaired growth and stunting as well as neurobehavioural disorders (Hassan et al., 2012:2; Gallagher, 2008:123). Physical growth, specifically linear growth is particularly sensitive to zinc deficiency in childhood, with increased stunting rates observed in areas where zinc deficiency is prevalent. The most prevalent clinical sign associated with zinc deficiency is dermatitis, concentrated around the limbs and bodily openings or orifices (Willoughby & Bowen, 2014:581).

Table 2.2: Clinical manifestations of zinc deficiency (Prasad, 2008:353-354; Overbeck et al., 2007:16)

Mild Manifestations	Moderate Manifestations	Severe Manifestations
Lower serum testosterone	Hypogonadism (Specifically in adolescent males)	Bullous pustular dermatitis
Oligospermia	Skin roughness	Diarrhoea
Lower natural killer cell activity	Loss of appetite and mild growth retardation	Emotional and behavioural disorders
Lower interleukin-2 production	Mental fatigue	Severe growth retardation including, Weight loss Stunting (during infancy, childhood and adolescence)
Lower thymulin activity	Poor wound healing	Infections due to immune dysfunction
Hyperammonemia	Cell-mediated immune dysfunctions	Infertility
Decreased eye adaption in low light conditions	Sensory changes to taste and smell	Sensory disorders
Lower lean body mass		Ulcers
		Thymic atrophy
		Poor pregnancy outcome
		Teratology
		Alopecia

According to numerous reviews and clinical trials, the association between zinc deficiency, suppressed immunity and infectious diseases, specifically diarrhoea have been consistently observed in early childhood. Moderate zinc deficiency has been shown to increase the risk of developing diarrhoea by as much as 50%, as well as increasing duration of diarrhoea. The results were most significant in malnourished children (Lazzerini & Ronfani, 2013:10; Hassan et al., 2012:2; Gallagher, 2008:123; Lazzerini & Ronfani, 2008:2).

Zinc deficiency has also been associated with higher rates of other infectious

diseases, such as skin infections, respiratory infections and malaria (Lazzerini & Ronfani, 2013:10; Hassan et al., 2012:2; Gallagher, 2008:123; Lazzerini & Ronfani, 2008:2).

The International Zinc Nutrition Consultative group (2004:S96) has recommended a method to determine the risk of zinc deficiency in certain population groups, using indicators such as the prevalence of stunting and the adequacy of available zinc in the population's food supply. According to these indicators countries were classified as low, medium or high risk for zinc deficiency. The majority of countries in South Asia, sub-Saharan Africa and Central and South America were classified as high risk populations. South Africa was considered to be at medium risk for zinc deficiency. In these countries at risk of deficiency, all children should be considered at risk especially those between 6 and 59 months of age (Black et al., 2008:249; IZINCG, 2004:S96).

The National Food Consumption Survey (NFCS) conducted in 1999 in South Africa, assessed the nutritional status and dietary intake of children aged one to nine years. The NFCS found that the five most commonly consumed foods by children in South Africa were; maize, sugar, tea, whole milk and brown bread (Labadarios et al., 2008:253). From the assessment of dietary intake, the survey concluded that South African children consumed less than 45.3% (Labadarios et al., 2008:264) of the RDA's for zinc and were considered to be at risk for deficiency. Inadequate zinc intake was more common in younger children under five years of age. The survey also found that one in five children aged one to nine years were stunted. This information was then used to formulate decisions on a food fortification programme and other interventions promoting the intake of foods rich in zinc as well as supplementation policies (Labadarios et al., 2008:264; NICUS, 2003:1).

Legislation on food fortification was passed in October 2003, which made it mandatory for manufacturers to add zinc and other micronutrients to staple foods identified namely, maize and wheat bread flour (Labadarios et al., 2008:253).

2.5.6. SIDE EFFECTS AND TOXICITY

According to numerous safety and efficacy trials with over a 1000 respondents, zinc supplementation (dosages 5–45 mg per day) was found to be well tolerated, with no severe adverse reactions reported (Liberato et al., 2015:186; Vakili et al., 2009:375;

WHO, 2006:21). However, some trials have reported infrequent, minor adverse effects. If vomiting was present with diarrhoea on initiation of zinc supplementation, the vomiting was prolonged. This could be in part due to the unpleasant metallic taste or as a result of zinc causing gastric irritation (Liberato et al., 2015:186; Vakili et al., 2009:375; WHO, 2006:21; Eby & Halcomb, 2006:36; Prasad et al., 2000:249). Other non-severe adverse reactions which have been experienced with supplementation include; heartburn, stomach discomfort and nausea. Side effects that could occur but that are rarely experienced include fever, sore throat, mouth sores and malaise (Fatima et al., 2014:14). Clinical trials have shown no differences in side effect profiles of the different zinc salts that have been used in these trials (WHO, 2006:21).

In zinc supplementation in excess of 45 mg per day, patients are at increased risk for possible side effects and it is purported that high dosages of zinc will interfere with the absorption of other essential micronutrients such as iron, copper and magnesium (Fatima et al., 2014:14). It was suggested in one clinical trial that standard dosages of zinc, used for the treatment of diarrhoea, decreased copper levels in children with diarrhoea. However, there is no significant evidence to support this (WHO, 2006:21). Where high dosages (greater than 150 mg per day) oral zinc is used, it is known to increase the production of the transport protein metallothionein which chelates with dietary sources of copper in the GIT and excretes it (Kee et al., 2015:218). High dosages of oral zinc can have the opposite effect to standard dosages and can impair immune function as well as possibly hinder the action of certain medications. These medications include antibiotics such as quinolone and tetracycline, chelating agents like penicillamine, as well as some diuretics such as thiazides (Willoughby & Bowen, 2014:583; Spruill & Wade, 2008:619). It is therefore recommended as a safety measure, that zinc and antibiotics not be administered at the same time and zinc should be given at least two hours after the antibiotic dosage (Kee et al., 2015:218; Spruill & Wade, 2008:619).

2.5.7. ZINC IN THE TREATMENT OF DIARRHOEA

2.5.7.1. BACKGROUND

The proposed modal of effect of zinc treatment on the duration and severity of diarrhoea has been proposed since the 1980's, where trials showed improved fluid and electrolyte absorption by the intestinal mucosa, regeneration of intestinal epithelium, raised numbers of enterocyte brush-border enzymes and increased clearance of infections (Hassan et al., 2012:2). Zinc supplementation in the management of diarrhoea is believed to improve the body's immune response and recovery rate of the epithelium (WHO, 2006:4; Thapar & Sanderson, 2004:648). The specific action of zinc in preventing diarrhoea is still not clearly understood, but zinc appears to be beneficial at the membrane level of the cell. Zinc ions appear to reduce the penetration of the cell membrane and cellular damage, by limiting permeability of the membrane. Zinc ions change the capillary membrane of the epithelium, in doing so preventing transcapillary movement of proteins and pathogens (Hulisz, 2004:595).

A number of randomized controlled trials (WHO, 2006:21; Eby & Halcomb, 2006:36; Prasad et al., 2000:249) were conducted in the 1980's and 1990's which showed benefits of zinc supplementation in childhood diarrhoea. This lead to the WHO arranging an expert panel in New Delhi, India in 2001 to review the evidence. All the trials were randomized placebo-controlled trials, conducted in infants and children one month to five years of age, using a dosage of 5-45 mg per day of elemental zinc. The panel concluded, based on these trials that, children recovered significantly quicker when given zinc supplements with a 20% reduction in diarrhoeal episodes lasting longer than seven days. The hospital-based trials that measured stool output showed a reduction of stool output by 18-59% (irrespective of age and nutritional status). The results from these trials showed no significant difference in effectiveness between the different types of zinc namely; zinc sulphate, zinc acetate or gluconate and there was also no clinical benefit shown beyond 20 mg per day of elemental zinc. The panel concluded that 10-20 mg per day of elemental zinc is effective at reducing the severity and duration of childhood diarrhoea (WHO, 2006: 4-5; Thapar & Sanderson, 2004:648).

In updated meta-analyses on the efficacy of zinc supplementation, data have

correlated with earlier results. These meta-analyses showed reductions in the severity and duration of acute and persistent diarrhoea in children less than five years of age and indicated zinc may have a benefit in reducing childhood mortality (Lazzerini & Ronfani, 2013:5; Guarino et al., 2012:19). The majority of the evidence was obtained from low to middle income countries in South Asia, where zinc deficiency and malnutrition are common and evidence supports a larger effect in children that are malnourished (Lazzerini & Ronfani, 2013:5; WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419; Guarino et al., 2012:19).

Lazzerini and Ronfani (2013:5) reported in a Cochrane review, that due to the trials being conducted in Asia, the data may not be applicable in other areas of the globe. The results of the review showed that zinc supplementation may reduce the duration of acute diarrhoea by 10 hours and persistent diarrhoea by 16 hours in children over six months of age. While a reduction in duration of diarrhoea of 27 hours was reported in malnourished children (Lazzerini & Ronfani, 2013:5). The review concluded that there is limited data and of poor quality about the impact of zinc supplementation on hospitalization and mortality rates in children with diarrhoea and therefore they believe it to be impossible to deduce any value from the data. This is due in part to the fact that some of the trials could not separate the effect of zinc supplementation from the effect of other interventions such as ORS. This review concluded that current data support the use of zinc supplementation in regions where zinc deficiency and malnutrition is prevalent (Lazzerini & Ronfani, 2013:5).

The WHO and UNICEF along with other researchers have reported differing results and concluded that the use of zinc supplements during an episode of acute or persistent diarrhoea reduces the duration and severity of a diarrhoeal episode by 25%. This data suggests that zinc supplementation reduces childhood mortality rates by 23% and the incidence of recurrent childhood diarrhoea by 14-15% (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419; WHO & UNICEF 2009:17).

Data from the widespread introduction of zinc supplementation in treatment programmes for childhood diarrhoea in India, Mali and Pakistan have proposed that the use of zinc may be even more beneficial than clinical trials have shown. As zinc supplementation appears to reduce overall treatment failure by improving ORS acceptance and by lowering inappropriate drug use, especially that of antibiotics and

antidiarrhoeal medication. Zinc treatment also appeared to increase appetite (UNICEF & WHO, 2009:17).

2.5.7.2. CURRENT STANDARD TREATMENT GUIDELINES FOR ZINC

The current standard treatment guidelines for the use of zinc in childhood diarrhoea were first recommended by the WHO and UNICEF in 2004, after a joint statement was released to help reduce the burden and mortality rate in children due to diarrhoea. Those guidelines are as follows (WHO, 2006: 23):

- 10 mg elemental zinc should be given to children less than six months of age and 20 mg of elemental zinc to children over six months of age, for 10-14 days (UNICEF & WHO, 2009:17; WHO, 2006:23);
- soluble zinc salts should preferably be used e.g. zinc acetate, zinc sulphate or zinc gluconate;
- syrup or dispersible tablet formulations of zinc can be given, depending on availability and cost;
- ideally syrup formulations should have 10 mg per 5 ml or 20 mg per 5 ml concentration of elemental zinc;
- the zinc formulation used should ideally only consist of zinc, and iron should never be added but in some circumstances copper can be added at a concentration of 1 mg per dosage; and,
- formulations should be manufactured according to the good manufacturing practices for pharmaceuticals (WHO, 2006:23).

The WHO has also set out clear monitoring and surveillance indicators for the implementation of interventions for the management of diarrhoea, which include:

- Reporting on the percentage of health care staff that have received training on the WHO management guidelines for diarrhoea;
- reporting on availability of zinc supplements and the new ORS formulation;
- reporting on the percentage of HCFs with the IMCI treatment guide;
- reporting on the percentage of diarrhoeal episodes in children younger than five years of age prescribed zinc; and,
- reporting on the percentage of diarrhoeal cases that received zinc for 10-14 days (WHO, 2006:23).

Since these recommendations were first introduced by the WHO and UNICEF to decrease mortality rates among children with diarrhoea, 46 countries have revised their diarrhoea treatment guidelines to include the new ORS and zinc supplements. Unfortunately very few countries are actually effectively implementing the guidelines, which means that many children with diarrhoea are not being treated correctly (Liberato et al., 2015:186). In low to middle income countries treatment rates of implementation have been found to be low, with only 39% of children with diarrhoea receiving the appropriate management. There is currently limited data on zinc supplementation coverage levels in the management of diarrhoea for South Africa. Sadly, the lack of implementation of life-saving interventions usually occurs in areas with the greatest need, with low coverage, resulting in mortality rates continuing to be high (Young et al., 2012:6).

South Africa has nationally adopted the IMCI programme including the operational guidelines for the treatment of diarrhoeal diseases set out by the WHO and UNICEF. These operational guidelines were published in the Standard Treatment Guidelines and Essential Medicines list for South Africa, Hospital level Paediatrics. In these guidelines, zinc supplementation is promoted as part of the general treatment for diarrhoea in childhood, although the guidelines differ slightly from those of the WHO. They state that zinc should be given for 14 days at a dosage of 10 mg elemental zinc for children weighing less than 10 kg and 20 mg elemental zinc for children weighing more than 10 kg (National Essential Medicines List Committee, 2013:26; (UNICEF & WHO, 2009:17; WHO, 2006:23;National Essential Drugs List Committee, 2006:32).

Diarrhoea continues to be a burden in children younger than five years of age. In this vulnerable population diarrhoea can lead to dehydration, malnutrition and is a mortality risk. In order to prevent and manage this burden, the WHO and UNICEF have set out easy to follow and cost-effective guidelines using only scientifically proven treatment methods. These include nutritional interventions such as continued breastfeeding, and appropriate complementary feeding as well as using zinc supplementation during diarrhoeal episodes. Medical treatment should focus on ensuring adequate hydration in the form of ORS and antimicrobials when dysentery is present. These treatment guidelines are well established, simple to implement and need to be propagated in order to reduce the burden of diarrhoea.

CHAPTER 3: METHODOLOGY

3.1. INTRODUCTION

This chapter will focus on the methodology used to carry out the research described in this mini dissertation. It includes the study design, sampling, measurement techniques and procedures as well as the data analysis methods. Attention will also be given to the ethical considerations of this research.

3.2. STUDY DESIGN

This study is a retrospective, prescription audit of case folders for all infants and children, aged birth to five years, admitted to the GMPW at a tertiary hospital in the Eastern Cape from 1 January 2013 to 31 December 2013, with the diagnosis of diarrhoea.

3.3. STUDY POPULATION AND SAMPLING

According to data collected for the District Health Information System (DHIS) and the Child Problem Identification Programme (CPIP) at the tertiary hospital, 1 483 infants and children were admitted to the GMPW from 1 January 2011 to 31 December 2011. Of these children, 347 were of the age birth to five years of age and admitted with the primary diagnosis of diarrhoea (Harper et al., 2013b:1). For the 12 month period between 1 January 2013 and 31 December 2013, the admission rate increased since 2011, with 385 infants and children aged birth to five years being admitted to GMPW ward, due to diarrhoea (Harper et al., 2013b:4).

The population for this study included all infants and children aged birth to five years of age, admitted to the hospital with the primary diagnosis of diarrhoea. As the majority of diarrhoeal cases admitted to the hospital are admitted to the GMPW ward, a convenient sample was used, consisting of all the children admitted due to diarrhoea to this ward between 1 January 2013 and 31 December 2013 aged birth to five years. This period was selected to describe adherence to the zinc supplementation policy over a calendar year. Case folders were included for a 12 month period to allow for any seasonal variances in incidence of diarrhoea and rotation of medical staff.

3.3.1. INCLUSION CRITERIA

All case folders of children between birth and five years of age, admitted with

diarrhoea to the GMPW ward at the hospital, between 1 January 2013 and 31 December 2013 were considered for inclusion in the study. Admission data, medical notes and prescription charts for each case were assessed for this study period.

3.3.2. EXCLUSION CRITERIA

All case folders not found at the records office or at the mortuary were excluded from the study. Cases where a child had multiple readmissions for diarrhoea in the study period or those cases which were first admitted to other paediatric wards before being transferred to the GMPW were also excluded from the study.

3.4. MEASUREMENT

3.4.1. VARIABLES AND OPERATIONAL DEFINITIONS

For the purpose of this study, variables included the general demographic characteristics of the case, information on the diarrhoeal episode and details on zinc prescription. If available, any barriers to zinc supplementation from the case folder were noted and regarded as variables for this study.

The following information was collected from the case folders and captured in duplicate to Microsoft Excel (2010) for Windows 7 spreadsheets using the Information sheet as a guide (Addendum A). This information was used to develop a profile for the participating cases:

3.4.1.1.   GENERAL CHARACTERISTICS OF THE CASE
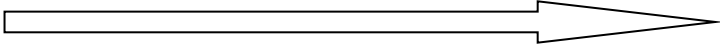
i)   Date of birth (day, month and year was noted and the age of the child on admission was calculated);

ii)   gender;

iii)   admission date (day and month were noted);

iv)   any co-morbidities present on admission, such as HIV, TB, malnutrition, LRTI, measles, renal failure, liver failure and meningitis;

v)   weight on admission and discharge (first and last weight recorded during hospitalisation);

vi)   discharge date (day and month were noted);

vii)   length of hospital admission to the GMPW (number of days);

viii)   prescriber level – this was obtained from the prescriber number as recorded on the prescription chart, all prescriber numbers begin with a letter, this letter indicates the classification or level of the prescriber, this changes when the level of the prescriber changes; intern doctors will have an 'I' at the beginning of the prescriber number, community service doctors will have an 'S', medical officers an 'M' and consultants a 'C'. It is prescribing law in South Africa that when a doctor fills out a prescription chart they sign as well as write their prescriber number; and,

ix)   dietitian assessment (any assessment conducted by a dietitian during the admission period as indicated in the medical notes was recorded).

3.4.1.2.   DIARRHOEAL EPISODE

i)   Duration of diarrhoea before admission (number of days of loose/watery stools preadmission according to the admission assessment as noted in the folder);

ii)   number of diarrhoeal stools on admission (number of loose/watery stools noted in admission assessment notes);

iii)   presence of blood in the stool at any time during admission or pre-admission (any occult blood in stools recorded pre-admission or during hospitalisation);

iv)   presence of pyrexia (any temperature readings greater than 37.8˚C on day of admission was recorded) this is classified as any oral or axillary temperature recording greater than 37.8˚C (Harper et al., 2013a:114);

v)   presence of vomiting (the presence of vomiting preadmission according to the admission assessment as noted in the file);

vi)   presence of dehydration (on admission as noted in the folder) as described in Table 3.1; and,

vii)   presence of shock (on admission as noted in the folder) as described in Table 3.1.

Table 3.1: Assessment criteria for dehydration/shock (Harper _et al._, 2013a:124)

Assess for shock first and then dehydration.	→	
C SHOCK One of the signs below:	B DEHYDRATION 2 of the signs below but not shock:	A NO VISIBLE DEHYDRATION No signs of dehydration.
Capillary filling time > 3 seconds.	Restless or irritable.	Well, alert.
Rapid/ thready pulse.	Eyes sunken.	Non sunken eyes.
Decreased level of consciousness.	Thirsty, drinks eagerly.	Drinks normally, not excessively thirsty.
Decreased blood pressure.	Decrease in skin turgor (skin pinch returns slowly).	Skin pinch goes back immediately.

3.4.1.3.   PRESCRIPTION OF ZINC

The following information was obtained from the prescription chart in the case folder:

i) Was zinc prescribed (any supplements noted on the prescription chart);

ii) was zinc available (records from pharmacy were used to ascertain availability and type of zinc available during the study period);

iii) type of zinc prescribed (as noted on the prescription chart), possible types of zinc include, zinc acetate, zinc sulphate, zinc gluconate, zinc picolinate, elemental zinc or trace elements;

iv) dosage of zinc prescribed (as indicated on the prescription chart);

v) dosage of elemental zinc prescribed (determined from the type and dosage of zinc prescribed), this was compared to the WHO Treatment guidelines and

Standard Treatment Guidelines and Essential Medicines list for South Africa (Addendum B);

vi) duration zinc was prescribed during hospitalisation (number of days during hospitalisation as noted on the prescription chart), this was compared to the WHO treatment guidelines and Standard Treatment Guidelines and Essential Medicines list for South Africa (Addendum B);

vii) first day of zinc prescription (day of hospital stay on which zinc was prescribed according to prescription chart);

viii) was zinc prescribed on discharge (as indicated on discharge summary and prescription chart); and,

ix) duration of zinc supplementation prescribed for home use (number of days zinc was prescribed on discharge according to discharge summary and prescription chart) was compared to the WHO guidelines and Standard Treatment Guidelines and Essential Medicines list for South Africa (Addendum B).

3.4.1.4.   BARRIERS TO THE ADMINISTRATION OF ZINC SUPPLEMENTS

Any barriers noted in the case folders that may have hindered the provision of zinc supplementation was recorded. These included lack of availability of zinc supplements or refusal of the case to take the supplement. The availability and forms of zinc supplements during the research period was obtained from pharmacy records and the case's prescription chart. A list of these barriers was compiled during the research process.

3.4.2. MEASUREMENT TECHNIQUES

When a paediatric diarrhoeal case presents to casualty or POPD at the hospital, the nursing staff and attending clinicians complete an admission assessment in the case folder. This includes the medical history, clinical assessment of shock, dehydration and anthropometric measurements to assess nutritional status. Once admitted, all information on the clinical assessment, problems and plans for treatment are described on a daily basis by the clinicians in the progress notes in the case folder. The medication prescribed is indicated on a pharmacy prescription chart in the case folder and includes information such as; the type, dosage and duration of drugs

used, as prescribed by a clinician. It is then ordered from the hospital pharmacy, using the clinician's specific prescriber number. Nursing staff are then required to administer the medication and sign on the prescription chart that they have administered the medication or indicate any reasons for not administering the medication.

Due to the nature of retrospective studies, the researcher had to rely on the variable information found in these case folders, therefore no specific measurement techniques were performed by the researcher. The following variable information was taken from the folders and considered true as far as possible.

3.4.2.1. NUTRITIONAL STATUS

Weight is measured in all cases seen at casualty or POPD by nursing staff and is recorded in the case folder. Weight is normally measured once daily in the GMPW, unless the child is in shock or dehydrated in which case the nursing staff will measure the weight every 4-8 hours or as ordered by the clinician. Accurate weight checks are the most accurate method of determining improvement in hydration status (Harper et al., 2013a:126). For the purpose of this study the weight measurements that were recorded, were the first and last weight measured during admission and on discharge. These weights were used to determine the nutritional status of each case.

In the GMPW at the hospital, a calibrated digital baby scale is used to take the weight measurement to the nearest 10 g for cases weighing less than 10 kg, and a calibrated digital adult scale is used for cases over 10 kg, measuring weight to the nearest 100 g. The scales are calibrated and checked when necessary to ensure accuracy of the weight measurement. When the measurement is performed on infants the case is undressed, which includes the removal of the nappy and is then placed on the scale. The scale is sanitized after each weight measurement. When the case is an older child, the child is weighed in minimal clothes, usually a hospital gown (Shaw & Lawson, 2008:5; Cape Town Metropole Paediatric Interest Group, 2007:5).

The weight of each case was compared to the WHO growth charts for weight-for-age for infants and children according to gender. Each case was assessed according to the weight-for-age z-scores for infants and children 0-60 months of age, to indicate

standard deviation from the median for weight as shown in Table 3.2. The WHO Anthro (Software v.3.2.2, January 2011) was used to calculate the z-scores and the researcher interpreted the results according to Table 3.2. Although weight is easily measured and a useful tool to assess trends in nutritional status and fluid balance, it does not however differentiate between lean muscle mass, oedema and body fat (Shaw & Lawson, 2008:5). Weight, is the measurement most often used to assess the nutritional status of an individual and in calculations to determine macronutrient and fluid requirements (Cape Town Metropole Paediatric Interest Group, 2007:5). This growth indicator as a singular measurement can only be used to determine whether a child is underweight or severely underweight, and cannot be used to classify a child as overweight, obese, wasted or stunted (WHO, 2008:5). Weight is therefore not recommended as an individual or stand-alone measurement to determine nutritional status. Length or height is required in addition to weight to determine the presence of acute and chronic malnutrition (Cape Town Metropole Paediatric Interest Group, 2007:5).

Recumbent length or standing height is a valuable measurement and important indicator of growth. This measurement is used to determine height/length-for-age and in conjunction with weight, weight-for height/length can be determined. This measurement is also useful in children to determine the creatinine height index to establish renal function. Height/length-for-age and weigh-for-height/length are recommended by the WHO to be important nutritional indicators for children younger than five years, specifically to determine the degree of stunting and wasting (Cape Town Metropole Paediatric Interest Group, 2007:5). The weight-for-height/length indicator is specifically used to diagnose severe acute malnutrition according to the WHO classifications in Table 3.2 (WHO & UNICEF, 2009:2).

Table 3.2: The WHO classifications of growth indicators (WHO, 2008:14)

Z-score	Growth Indicators		
	Length/height for-Age	**Weight-for-age**	**Weight-for-length/height**
Above 3		Infant/child who falls in this range may have a growth problem, but this is better assessed from weight-for-length/height.	Obese
Above 2			Overweight
Above 1			Possible risk of overweight
0 (median)			
Below -1			
Below -2	Stunted	Underweight	Wasted (Moderate acute malnutrition)
Below -3	Severely Stunted	Severely underweight	Severely wasted (Severe acute malnutrition)

Another anthropometric measurement recommended by the WHO and UNICEF to be used to assess nutritional status in children younger than five years is the mid-upper arm circumference (MUAC). It is a non-invasive, inexpensive and basic tool to assess nutritional status. It is useful in children that cannot be measured accurately (i.e. cerebral palsy or oedema) or where there is no access to scales and stadiometres (Cape Town Metropole Paediatric Interest Group, 2007:5). According to the WHO and UNICEF, MUAC is a good tool to indicate wasting and the cut off for the diagnosis of severe acute malnutrition in children 6-60 months, is any MUAC value less than 115 mm (WHO & UNICEF, 2009:2).

The measurement of length and MUAC are not measured as often as weight in casualty, POPD or in the GMPW and it is often difficult to obtain reliable, accurate measurements. For the purposes of this study, MUAC and length values were not

taken into account; however the number of measurements taken was indicated in the results of this study.

3.5. STUDY PROCEDURES AND DATA COLLECTION

Permission to perform this study was obtained from the hospital management and the hospital ethics committee (Addendum C) as well as the Ethics Committee of the Faculty of Health Sciences, University of the Free State (Ethics reference: ECUFS NR 173/2014).

Once permission was granted, a pilot study was conducted in the GMPW using the first five patient folders of the population group, to test the spreadsheet data collection process.

The researcher obtained the relevant data for this study directly from the case folders of the infants. The information collected was used to formulate the results and is accepted as correct by the researcher due to the nature of retrospective studies. There was no intervention or trial conducted with this study. None of the data collected was obtained from patient or nursing/staff interviews or by performing additional biochemical tests or anthropometric measurements.

The researcher initially identified the case folders through the GMPW admission register for the 12 month period. Folder numbers pertaining to admissions for cases with diarrhoea aged birth to five years were noted for possible inclusion in the study. According to hospital protocol the nursing staff record each new hospital admission in a ward register; this includes the patient's personal details and primary diagnosis. These details are then summarized on a list with the patient's name, folder number, age and primary diagnosis and then forwarded to hospital management for the compilation of hospital admission statistics. The researcher examined both the admission register and admission list, to ensure that every case with diarrhoea was recorded for possible inclusion. These details were then used to obtain the case folders from the medical records department. From each case folder the necessary data were extracted and recorded. Data were captured by the researcher in duplicate on Microsoft Excel (2010) for Windows 7 spreadsheets, using the information sheet (Addendum A) as a guide, and then verified electronically. The data were then analysed by the Department of Biostatistics, University of the Free State.

From data collection and analysis, the researcher extrapolated the results and conclusions of this research study.

The procedures of this study are shown in Figure 3.1.

Permission to perform the study was sought from the management of the Hospital, the Ethics Committee of the Hospital and the Ethics Committee, Faculty of Health Sciences, University of the Free State.

⇩

A pilot study was conducted in the GMPW of the Hospital during October 2014.

⇩

Data collection was performed during the period October 2014 to August 2015. The researcher obtained case folders from the Medical Records Department for all cases admitted to the GMPW for the diagnosis of diarrhoea during 1 January 2013 to 31 December 2013. The researcher then entered the data of each case in duplicate on Microsoft Excel (2010) spreadsheets.

⇩

The data entered were compared and verified electronically by the researcher and analysed by the Department of Biostatistics, University of the Free State

⇩

The data were interpreted in a mini-dissertation by the researcher and a report sent to the hospital.
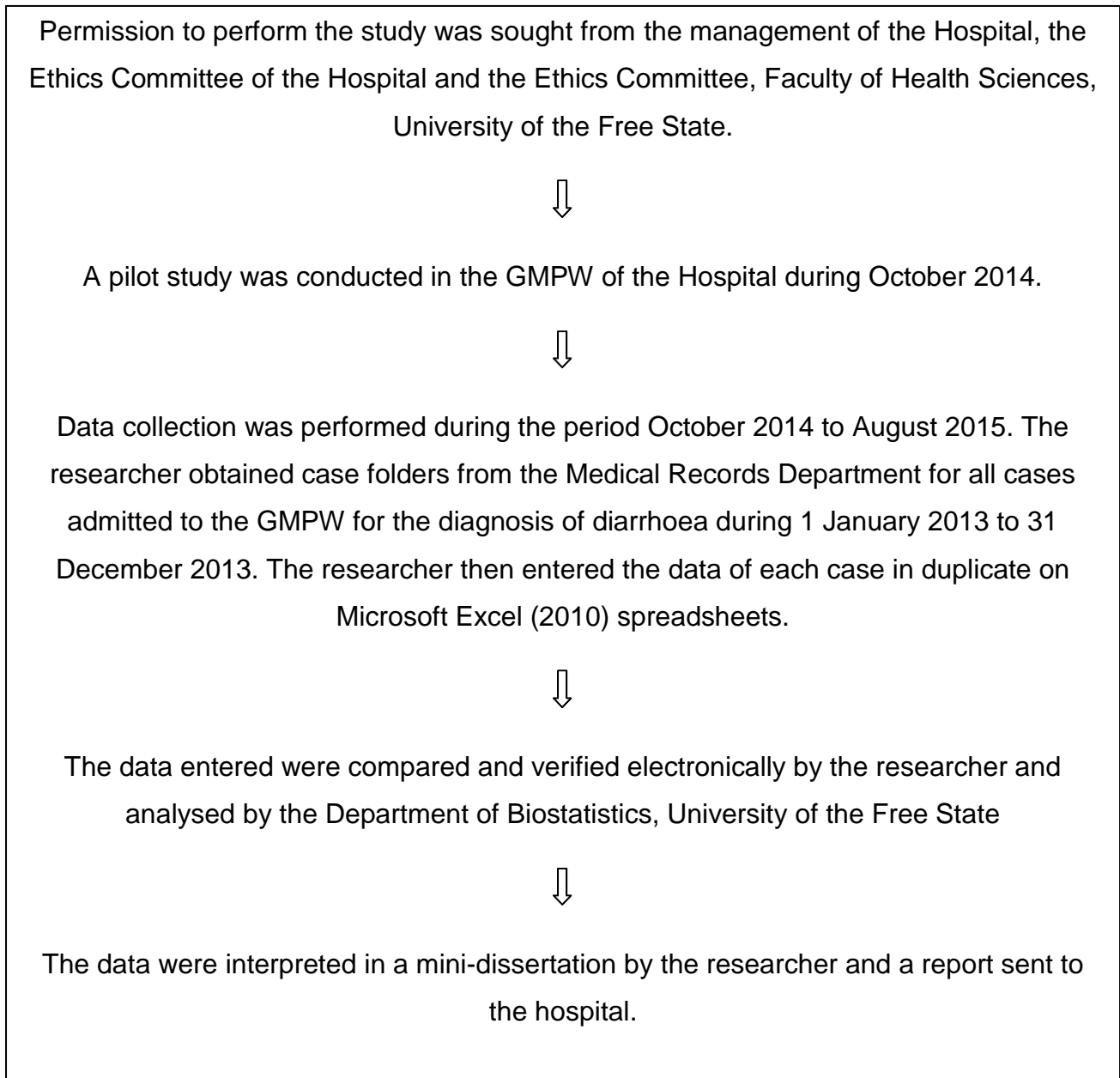
Figure 3.1: Flow diagram of research procedures

3.6. VALIDITY AND RELIABILITY

The validity of a measurement as described by Leedy and Ormrod (2005:31) is the extent to which the instrument measures what it is supposed to measure. Reliability refers to the consistency with which a measuring instrument yields a certain result when the entity being measured hasn't changed. It is a crucial part of any study to use reliable measuring instruments, to ensure that if the study was to be duplicated it would yield similar results (Leedy & Ormrod, 2005:31).

Due to the retrospective design of this study the validity of the data collected relied on the accurate record keeping of the attending medical staff. The possible inaccurate and subjective assessment of cases and record keeping by medical staff, as well as missing or incomplete records is the biggest limitation of a retrospective study design. For this reason the researcher accepted all the information in the case folder as correct, as it was impossible to ascertain any mistakes or omissions that were made by medical staff.

For the purposes of this study, validity was ensured by the researcher consulting other relevant studies to obtain valid and standard methods for data collection, assessment and interpretation. Once relevant methods and techniques were obtained the researcher tested the research process and information captured, during the pilot study. Where possible, the researcher used standard techniques to assess and interpret collected anthropometrical data from each case folder.

An information sheet (Addendum A), compiled by the researcher, was used to guide the capturing of data and reliability was ensured by capturing the data in duplicate in Microsoft Excel (2010) spreadsheets.

3.7. PRACTICAL IMPLEMENTATION OF THE STUDY

The results of this adherence audit would assist the management of the institution as well as policy makers to determine whether the treatment guidelines for the management of diarrhoea are being implemented effectively. It would also show any shortcomings or areas that may need to be targeted with awareness campaigns. The data would also act as a baseline for future studies.

3.8. STATISTICAL ANALYSIS

Statistical analysis was performed by the Department of Biostatistics, University of

the Free State using SAS/STAT software, Version 12.4 of the SAS system for Windows (© 2010 SAS Institute Inc.).

Descriptive statistics namely means and percentiles for continuous data, and frequencies and percentages for categorical data, were calculated. The change in weight from admission to discharge was calculated and described by means of 95% confidence interval for the median difference for paired data.

3.9. ETHICAL CONSIDERATIONS

The researcher has taken into account all ethical considerations for this research study. Permission was obtained from the management of the Hospital, the Ethics Committee of the Hospital and the Ethics Committee, Faculty of Health Sciences, University of the Free State to view medical folders of patients that were admitted to the GMPW during 2013, with the primary diagnosis of diarrhoea. Due to the retrospective nature of the study none of the cases were in the ward at the time of the study, as such it was impossible to obtain informed consent from the patients' parents. All patients' personal data as well as prescriber information was kept confidential and reporting focused on group trends of treatment procedures instead of individual patient data. The name of the hospital was removed as required by the hospital management and cannot be used for formal reporting and publishing.

CHAPTER 4: ADHERENCE TO ZINC SUPPLEMENTATION GUIDELINES IN THE MANAGEMENT OF ACUTE DIARRHOEA IN HOSPITALIZED CHILDREN

This article reports the findings of the research study. The aim of this research was to determine adherence levels of health care professionals to zinc supplementation guidelines in the management of diarrhoea in children birth to five years of age at a tertiary hospital. In order to achieve this aim, four objectives for data collection were set. The findings from these objectives are described in this article namely; the general characteristics of cases admitted for diarrhoea, details on the diarrhoeal episode, information on zinc prescriptions and any barriers to prescribing and administering zinc supplementation noted by medical staff in the case folders.

This article is written according to the author guidelines of the South African Journal of Clinical Nutrition, included as Addendum D. As required by the journal, this article also includes two abstracts, one structured according to the required headings and the second in simpler language. A social media message, consisting of less than 140 characters is also included according to the journal requirements. The referencing system however is in accordance with requirements of the Department of Nutrition and Dietetics, University of the Free State.

4.1. STRUCTURED ABSTRACT

Objectives: To determine adherence to zinc supplementation guidelines in the management of diarrhoea in hospitalized children.

Design: A retrospective, prescription audit.

Setting: A general medical paediatric ward (GMPW) at a tertiary hospital in the Eastern Cape, South Africa.

Subjects: Case folders of children aged birth to 5 years admitted with the diagnosis of diarrhoea during 2013 were included in the study. Of those identified, 290 case folders of children were available from 385 admissions with diarrhoea.

Outcome measures: To determine how many cases of diarrhoea were prescribed zinc and adherence of these prescriptions to the current World Health Organization (WHO) and United Nations Children's Fund (UNICEF) recommendations of 10 mg elemental zinc for infants under six months and 20 mg for infants and children over six months for a period of 10-14 days.

Results: Of the case folders admitted due to diarrhoea, zinc was prescribed in 69.3% (n=192) of cases on admission. Adherence to guidelines regarding dosages was higher on discharge (43.5%) compared with admission (37.6%), while overall adherence to treatment duration guidelines was only 7.1% (n=14). Complete adherence to dosage and duration guidelines including admission and discharge was found in only 6 cases (3.1%).

Conclusions: Low adherence to zinc prescription guidelines used in the treatment of children with diarrhoea was found. This study recommends that training and awareness campaigns focusing on these guidelines be implemented among medical staff, along with the development of an institutional policy on the treatment of childhood diarrhoea including the zinc guidelines.

4.2. SIMPLIFIED ABSTRACT

The study assessed whether treatment guidelines for infants and children with diarrhoea are being followed at a tertiary hospital, specifically whether medical staff are prescribing the correct amount of zinc, for the appropriate length of time. Although 69% of children admitted with diarrhoea received zinc, only 3% received it according to guidelines. This study provides motivation for awareness campaigns and training of medical staff to encourage implementation of treatment guidelines for the management of diarrhoea.

4.3. SOCIAL MEDIA MESSAGE

Zinc is a cheap and effective treatment to help reduce diarrhoea in children, but implementation of this WHO and UNICEF guideline is low at a hospital in the Eastern Cape.

4.4. INTRODUCTION

The World Health Organization (WHO) defines diarrhoea as the presence of three or more watery or loose stools per day; however any abnormally high output of stools can be noted as diarrhoea. In high income countries, children that present with acute diarrhoea will generally develop mild or moderate fluid losses and co-morbidities. This is not the case in low to middle income countries with a combined burden of malnutrition and infectious diarrhoea and with limited access to medical interventions. In these cases fluid and electrolyte losses can be severe and, if not treated promptly, can lead to death (WHO & UNICEF, 2013:10; White Johansson &

Wardlaw, 2009:9; UNICEF & WHO, 2009:16; Thapar & Sanderson, 2004: 646).

Diarrhoea is easily preventable and treatable and much has been done over the years to reduce the number of deaths caused by diarrhoea. Despite this, diarrhoea is still one of the leading causes of death globally among children younger than five (WHO & UNICEF, 2013:10). This burden translates roughly to one in 10 child deaths or an estimated 600 000 thousand deaths in 2013 (Liu et al., 2015:432; Chola et al., 2015:1). These deaths are predominantly in low to middle income countries, with Africa and Asia accounting for almost 80% of these deaths (Wang et al., 2014:1; WHO & UNICEF, 2013:10; Bhutta et al., 2013:1417). Statistics South Africa has reported diarrhoea to be the largest cause of death in children younger than five years in South Africa, as it accounted for 14% of total deaths in 2014 (Statistics South Africa, 2015:35). An estimated 60 000 new cases of childhood diarrhoea develop every month in South Africa, according to the 2010 General Household Survey (Chola et al., 2015:1).

The most common infectious causes of acute diarrhoea in children are the rotavirus and pathogenic *Escherichia coli*. Rotavirus is responsible for approximately 70-80% (Fatima et al., 2014:12) of diarrhoeal episodes in low to middle income countries and 40% of all diarrhoeal disease admissions to hospital in higher income countries (Guarino et al., 2012:17; Steyn, 2009:31). In total, 88% of global diarrhoeal deaths can be attributed to contaminated water sources, poor sanitation facilities and inadequate hygiene, with over 99% of these deaths occurring in low to middle income countries (Chola et al., 2015:1; Pengpid & Peltzer, 2012:149). In South Africa, these infections generally present more frequently in the summer months, due to the increased growth of pathogens in food and water as a result of warm and humid weather conditions, however outbreaks can occur throughout the year (Steyn, 2009:32).

Goals for the management of diarrhoea were developed by WHO and the United Nations Children's fund (UNICEF) and revolve around lowering the total impact of the disease by reducing incidence, co-morbidities and mortality. In these guidelines, zinc supplementation is promoted as part of the universal treatment of childhood diarrhoea (WHO & UNICEF, 2013:15; Bhutta et al., 2013:1419). The dosage recommended is 10 mg of elemental zinc for children younger than 6 months and 20

mg for children older than 6 months of age per day, for 10-14 days. Zinc supplementation in the form of water-soluble compounds such as zinc sulphate, zinc acetate or gluconate are recommended (Guarino et al., 2012:19; WHO, 2010:2; Lazzerini & Ronfani, 2008:3; WHO, 2005:14). These guidelines were based on efficacy trials and a range of 10 mg to 20 mg elemental zinc daily was found to be safe in children (Hassan et al., 2012:2). These guidelines were first implemented in 2006 in South Africa and published in the Standard Treatment Guidelines and Essential Medicines list for South Africa, Hospital level Paediatrics (National Essential Medicines List Committee, 2013:26; National Essential Drugs List Committee, 2006:32).

Zinc is an essential mineral which functions primarily as an intracellular ion in association with over 300 enzymes and is vital for adequate functioning of the human immune system. The body is only able to store small amounts of zinc, absorbing approximately 33% of oral intake. Therefore, sufficient amounts are needed daily in order to maintain homeostasis and prevent deficiency (Basnet et al., 2015:163; Gallagher, 2008:122). Zinc levels in the body are determined by the balance of dietary intake, absorption, and losses. Bodily losses of zinc via the gastrointestinal tract are exacerbated by episodes of diarrhoea. Zinc requirements are dependent on age, with children needing the highest amounts due to rapid cellular growth. Children are therefore, most vulnerable to deficiency (Hassan et al., 2012:2; Lazzerini & Ronfani, 2008:3; IZINCG, 2004:S96). Without appropriate intervention, a child whose diet does not provide them with enough zinc will eventually develop zinc deficiency and the complications associated with it (Hassan et al., 2012:2).

The association between zinc deficiency, suppressed immunity and infectious diseases, specifically diarrhoea have been consistently observed in early childhood. Moderate zinc deficiency has been shown to increase the risk of developing diarrhoea by as much as 50%, as well as increasing duration of diarrhoea (Lazzerini & Ronfani, 2013:10; Hassan et al., 2012:2; Gallagher, 2008:123; Lazzerini & Ronfani, 2008:2). In countries at risk of deficiency, all children should be considered at risk, especially those between 6 and 59 months of age (Black et al., 2008:249; IZINCG, 2004:S96). Along with suppressed immunity other clinical signs associated with zinc deficiency include hypogeusia, anorexia, growth retardation and stunting,

alopecia, cognitive dysfunction, skin lesions and delayed wound healing (Hassan <u>et al</u>., 2012:2; Gallagher, 2008:123).

A number of randomized placebo-controlled trials as well as meta-analyses have reported on the efficacy of zinc supplementation and shown significant reductions in the severity and duration of acute and persistent diarrhoea in children younger than five years. The effect was reported to be higher in children suffering from severe malnutrition (WHO & UNICEF, 2013:15; Bhutta <u>et al</u>., 2013:1419; Guarino <u>et al</u>., 2012:19). However, there is varying data on the efficacy of zinc at reducing childhood mortality in diarrhoea (Lazzerini & Ronfani, 2013:5). The majority of evidence was obtained from low to middle income countries, where zinc deficiency and malnutrition are more prevalent (Lazzerini & Ronfani, 2013:5; Guarino <u>et al</u>., 2012:19). The proposed effect of zinc supplementation on the duration and severity of diarrhoeal episodes, include improved fluid and electrolyte absorption by the intestinal mucosa, regeneration of intestinal epithelium, raised numbers of enterocyte brush-border enzymes and increased clearance of infections (Hassan <u>et al</u>., 2012:2).

Zinc supplementation for the treatment of diarrhoea is a relatively easily implemented and inexpensive intervention (Mayo-Wilson <u>et al</u>., 2014:7). However, despite the availability of supporting data for the use of zinc in the management of childhood diarrhoea and reported awareness amongst medical staff in low to middle income countries, actual adherence and administration to zinc supplementation guidelines appear to be low (Omuemu <u>et al</u>., 2012:69).

Two prescriber awareness and adherence studies were conducted in Nigeria and India respectively and both demonstrated low adherence to standard treatment guidelines. Poor adherence was found not only in lower level prescribers but also in specialist paediatricians (Omuemu <u>et al</u>., 2012:69; Pathak <u>et al</u>., 2011:1). In Nigeria only one in three medical staff prescribed zinc for diarrhoea and although in the majority of cases the dosage was correct, fewer than half prescribed it for the correct period of time (Omuemu <u>et al</u>., 2012:71). In India the situation was worse. Pathak <u>et al</u>. (2011:1) reported that out of 843 prescriptions for diarrhoea, only six adhered to the recommended treatment guidelines for zinc. Currently there is no data concerning the awareness and adherence levels amongst medical staff in implementing zinc supplementation guidelines in South Africa.

The aim of the study was to determine adherence to the WHO treatment guidelines for zinc supplementation in the management of childhood diarrhoea, by health care professionals at a tertiary hospital in South Africa.

4.5. METHODS

The setting for this study was a tertiary hospital situated in the Eastern Cape province of South Africa. It is a 900 bed hospital which receives referrals from the Northern and Eastern parts of the Eastern Cape, where there are limited health care facilities. The areas serviced by the hospital are classified as urban and peri-urban; however the broader catchment area can vary vastly from urban to rural (Harper et al., 2013b:1). The hospital has a single general medical paediatric ward (GMPW) and the majority of diarrhoeal cases in children under 12 years are admitted to this ward for medical management. The GMPW has 28 beds and this restricted capacity as well as high demand has led to the ward having one of the highest patient turn-over rates in the hospital. Day to day patient care is generally managed by interns and a medical officer or registrar, and supervision is given by the paediatrician specialists.

According to data collected for the District Health Information System and the Child Problem Identification Programme, 1 483 infants and children were admitted to the GMPW from January 2011 to December 2011. Of those children, 347 were younger than five years of age and admitted with the primary diagnosis of diarrhoea (Harper et al., 2013b:1). According to hospital statistics for the 12 month period between 1 January 2013 and 30 December 2013, the admission rate increased from 2011, with 385 infants and children younger than 5 years being admitted to the GMPW ward, due to diarrhoea.

This retrospective, prescription audit included case folders of all infants and children from birth to 5 years, admitted between 1 January and 30 December 2013 to the GMPW with the diagnosis of diarrhoea. This period of time was selected to describe adherence to the zinc supplementation guidelines over a 12 month period in order to take any seasonal variances in incidence of diarrhoea and rotation of medical staff into account. The sample selection process is described in a flow diagram in Figure 4.1. All case folders that were not found at the records office or at the mortuary were excluded, as well as cases of multiple readmissions for diarrhoea in the study period

or those cases admitted to other wards.

Admission data, medical notes and prescription charts of each case folder were examined. Variables collected from each case, included: demographical data, anthropometrical data, nutritional status, information on the diarrhoeal episode and details on zinc prescription. If barriers to zinc supplementation were indicated in the case folder these were also noted.

From this data the recorded weight was used to determine the weight-for-age standard deviation (SD) using the WHO Anthro Software v.3.2.2. The SDs were then compared to the WHO classifications of growth indicators (WHO, 2008:14). For the purposes of this study, mid upper arm circumference (MUAC) and length was not taken into account; however the total number of measurements taken was indicated for the results of this study.

The amount of elemental zinc and duration of zinc supplementation was determined from the data obtained from the prescription and compared to the WHO and UNICEF guidelines (UNICEF & WHO, 2009:17; WHO, 2006:23).

Data were captured by the researcher in duplicate directly on Microsoft Excel (2010) for Windows 7 spreadsheets and compared and verified electronically. Statistical analysis was performed by the Department of Biostatistics, University of the Free State using SAS/STAT software, Version 12.4 of the SAS system for Windows (© 2010 SAS Institute Inc.). Descriptive statistics, medians and percentiles were calculated for continuous data, and frequencies and percentages for categorical data. The change in weight from admission to discharge was calculated and described by means of 95% confidence interval for the median difference for paired data.

Permission to conduct the study was obtained from the hospital management as well as the Ethics Committee of the Faculty of Health Sciences, University of the Free State (Ethics reference: ECUFS NR 173/2014).

4.6.   RESULTS

Of the 385 cases admitted to the GMPW for treatment of diarrhoea between 1 January and 31 December 2013, 95 were found to be ineligible. The final sample size was 290, which included 16 case folders with missing prescription charts. These

case folders were included as some data could still be collected from case notes. The sample selection is reported in Figure 4.1.
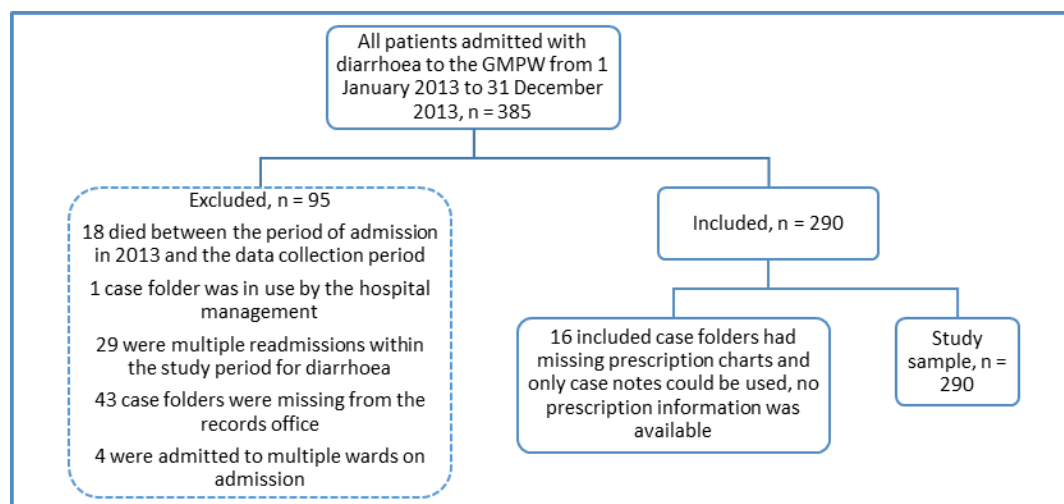
GMPW: General medical paediatric ward
Figure 4.1: Flow diagram of sample selection

In Table 4.1 the monthly distribution of cases admitted due to diarrhoea is reported. The frequency distribution of children admitted due to diarrhoea, was comparable between the different months of the year, with June having the highest number of admissions and September the lowest.

Table 4.1: Distribution of diarrhoeal cases per month admitted to the GMPW in 2013

Month	Frequency (n)	Percentage (%)
January	23	7.93
February	31	10.69
March	24	8.28
April	34	11.72
May	34	11.72
June	37	12.76
July	24	8.28
August	15	5.17
September	12	4.14
October	17	5.86
November	24	8.28
December	15	5.17

Table 4.2 describes the demographic background of the sample, as well as the 10 most frequent comorbidities that presented along with the cases of diarrhoea.

Table 4.2: Demographics, comorbidities and information on diarrhoeal episodes

	Frequency (n)	Percentage (%)	Minimum	Maximum	Median
Gender					
Female	128/290	44.1	-	-	-
Male	162/290	55.9	-	-	-
Age (months)	-	-	0.1	60.0	8.0
Birth to <6 months	100/290	34.5	-	-	-
6 months to <2 years	152/290	52.4	-	-	-
2 years to 5 years	38/290	13.1	-	-	-
Length of hospital stay (days)	-	-	1.0	31.0	4.0
Co-morbidities listed on admission					
Lower respiratory tract infections	94/290	32.4	-	-	-
Malnutrition	69/290	23.8	-	-	-
Human immunodeficiency virus exposed	62/290	21.4	-	-	-
Herbal ingestion/intoxication	61/290	21.0	-	-	-
Dermatitis	32/290	11.0	-	-	-
Tuberculosis	29/290	10.0	-	-	-
Dysentery	28/290	9.7	-	-	-
Metabolic acidosis	27/290	9.3	-	-	-
Oral candida	25/290	8.6	-	-	-
Seizures	24/290	8.3	-	-	-
Information on diarrhoeal episode on admission					
Duration of diarrhoea pre-admission (Days)	281/290	96.9	0.5	43.0	3.0
Number of loose stools per day	132/290	45.5	1	14	3.5
Presence of blood in stool	33/288	11.5	-	-	-
Presence of pyrexia	92/289	31.9	-	-	-
Presence of vomiting	237/289	82.0	-	-	-
Presence of dehydration	219/289	75.8	-	-	-
Presence of shock	54/289	18.7	-	-	-

The majority of cases included were male (55.9%), with a median age of 8 months. Most (52.4%) of the cases were between 6 months and 2 years of age, the median length of stay in the GMPW being 4 days.

In this study the two most frequently recorded co-morbidities on admission by medical staff were lower respiratory tract infections (32.4%) and malnutrition (23.8%). 21.4% of cases were classified as HIV-exposed due to the HIV status of the mother, with only 23 cases (7.9%) having a confirmed diagnosis of HIV infection. The median duration of diarrhoea prior to admission was three days, with 95% of children being admitted with acute diarrhoea, 5% with persistent diarrhoea and 28 (9.7%) cases admitted with dysentery.

A total of 74 (25.9%) cases were assessed and treated by a dietitian during admission. Of the 69 cases that were initially diagnosed as malnourished by medical staff on admission, 48 (74%) cases were assessed by a dietitian.

Of the cases 82% experienced vomiting and 75.8% experienced dehydration due to diarrhoea, with 18.7% presenting with severe hypovolaemic shock.

Table 4.3 summarizes available anthropometric data recorded in the case folders that were used to evaluate nutritional status.

Table 4.3: Anthropometry and nutritional status

	Frequency (n)	Percentage (%)	Minimum	Maximum	Median
Weight					
Weight on admission (kg)	289/290	99.7	1.5	19.6	7.9
Weight on discharge (kg)	285/290	98.3	2.0	20.9	8.0
Difference in weight (kg)	284/290	97.9	-3.3	3.2	0.2
Admission weight-for-age (SD)	-	-	-7.7	2.6	-0.9
Discharge weight-for-age (SD)	-	-	-6.5	3.3	-0.8
WHO weight-for-age classification on admission					
Normal weight (above -2 SD for weight-for-age)	204/289	70.6	-	-	-
Underweight (below-2 SD to -3SD for weight-for-age)	45/289	15.6	-	-	-
Severely underweight (below -3 SD for weight-for-age)	40/289	13.8	-	-	-
Length taken during admission	28/283	9.9	-	-	-
MUAC taken during admission	7/290	2.4	-	-	-

SD: Standard deviation, WHO: World health organization, MUAC: Mid upper arm circumference

In 99.7% of cases weight was recorded at admission, in 9.9% of cases height or length was recorded and 2.4% of cases had MUAC recorded in the case folder. The median difference in weight on admission and discharge was a 0.17kg gain in weight. The median admission weight-for-age standard deviation (SD) was -0.93 while the median discharge weight-for-age SD was -0.75. The admission weight-for-age SD was used to classify the nutritional status of each case according to the WHO classifications. The majority (70.6%) were classified in the group considered to be normal weight (including infants thought to be at risk of overweight with a higher SD), 15.6% were classified as underweight and 13.9% as severely underweight.

Table 4.4 provides an overview of zinc prescription practices during admission and discharge and how these prescriptions adhere to the WHO and UNICEF guidelines

for the management of diarrhoea in infants and children birth to five years.

Table 4.4: Zinc prescription and adherence with WHO and UNICEF guidelines

	Frequency (n)	Percentage (%)	Minimum	Maximum	Median
Zinc prescribed on admission	192/277	69.3			
Dosage of elemental zinc prescribed (mg)			1.0	125.0	10.0
Adherence to WHO guidelines for dosage (10-20mg)	74/187	39.6			
Duration of zinc prescribed on admission (days)			1.0	30.0	3.0
Zinc prescribed on discharge	92/274	33.6			
Dosage of elemental zinc prescribed (mg)			1.0	51.0	11.5
Adherence to WHO guidelines for dosage (10-20mg)	40/92	43.5			
Duration of zinc prescribed on discharge (days)			3.0	92.0	14.0
Total duration of zinc prescribed on admission and discharge (days)			1.0	107.0	5.0
Adherence to WHO guidelines for duration of treatment (10-14 days)	14/196	7.1	1.0	107.0	5.0
Complete adherence to dosage and duration of treatment guidelines	6/196	3.1			

WHO: World health organization

In this sample, 192 (69.3%) of the cases were prescribed zinc during admission and 92 (33.6%) of cases were prescribed zinc on discharge to be taken at home. In 39.6% of cases guidelines for dosage were adhered too during admission and 24% on discharge. Zinc was prescribed for a median of 5 days during admission and discharge, while the majority (82.1%) of prescriptions were initiated on day one of admission.

Total adherence to prescription guidelines for dosage and duration of treatment was found in 6 cases (3.1%), where zinc was prescribed. In only one case folder a barrier to zinc prescription was recorded by pharmacy staff; namely that zinc was out of stock. However, neither the clinicians nor nursing staff noted this barrier in the prescription charts.

4.7.   DISCUSSION

This is the first prescription audit on adherence levels to WHO and UNICEF zinc supplementation guidelines to be conducted in children birth to five years in South Africa and as such there is no local data to compare to the results of this study.

However, there have been prescription audits conducted in other low to middle income countries and the data were compared with these findings.

The highest number of diarrhoeal cases were admitted to the tertiary hospital over the autumn/winter months of April-June 2013, with the highest frequency of admitted cases occurring in June 2013. The results of this study do not support the expected norms in South Africa, which indicate that the summer months should experience the highest number of infectious diarrhoeal cases (Steyn, 2009:32).

The majority of cases admitted with diarrhoea in this study were male (55.9%), with 52.4% being 6-24 months of age. The median age of the children in this study was 8 months. These characteristics are comparible to what was reported by Weru (2013:19) at a provincial hospital in Kenya and Panchal et al. (2013:336) at a tertiary hospital in India, where 60% and 54% of participants were male and the median age was less than 12 months of age respectively. The high proportion of children admitted between 6-24 months of age, may possibly be attributed to inappropriate and unhygienic weaning practices. This is also a vulnerable time as the babies own antibodies and immunity have yet to develop and the maternal antibodies start to decrease in a child's body (Panchal et al., 2013:336).

The median length of stay in the GMPW was 4 days which is comparable to the 3 days reported by Weru (2013:28).

In 21% of cases admitted for diarrhoea in this study, the care giver admitted to using varying 'traditional or herbal medicines' as indicated in the assessment notes before and during the episode of diarrhoea. Unfortunately these 'traditional or herbal medicines' are unregulated by the South African government and as such can contain toxic or harmful substances.

This current study could not report accurately on the rate of malnutrition in the cases admitted with diarrhoea, as only 9.9% and 2.4% of cases had length/height and MUAC measurements taken respectively. Length/height and MUAC measurements are essential in diagnosing and defining severe acute malnutrition as per the WHO classifications (WHO, 2008:14). Despite the lack of appropriate measurements, 23.8% of admissions were classified as 'malnourished' by health care professionals on admission. This shows a lack of awareness amongst health care professionals on

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the definition and assessment methods of malnutrition. This is a concern as the link between malnutrition and darrhoea is well established (WHO, 2008:14) and the risk of treatment mismanagement is increased without the appropriate assessment.

The results of this study indicated that 69.3% of cases were prescribed zinc during admission for diarrhoea, which is less than the treatment coverage goals of 80% set by the WHO and UNICEF (2013:9). It is however, comparable with two studies which showed 68% coverage at an Indian Academic hospital (Priyadarshini et al., 2013:204) and 77% at a Kenyan hospital (Ford, 2014:204). This is, however, higher than the results from one Nigerian study that reported only 6.2% of cases having received zinc supplementation (Meremikwu et al., 2015:315).

A separate Nigerian survey that reported on the awareness and prescription patterns of health care professionals, indicated that only 35.1% of health care professionals said they would prescribe zinc when treating childhood diarrhoea. Of those health care professionals, 48.7% were able to prescribe zinc for the correct duration and 84.6% for the appropriate dosage (Omuemu et al., 2012:70).

There is currently limited global and South African data on the precise adherence levels to dosage and duration of zinc supplementation according to WHO and UNICEF guidelines, with the majority of prescription audits on the treatment of diarrhoea focusing on overall coverage of zinc supplementation and not accuracy of dosage and duration of treatment. This makes it difficult to compare results, however a single prescription audit of children aged 2-59 months admitted with diarrhoea in Kenya found that 92% of cases were administered zinc and of those, 84% of the dosing and 69.4% of the treatment duration were correct according to the guidelines (Weru, 2013:33). Weru (2013:33), credited these adherence levels to the extensive awareness among health care professionals of the necessity and benefits of treating childhood diarrhoea with zinc supplementation. This is in contrast to the results of this current study where the appropriate dosage was only prescribed in 39.6% of cases on admission and 43.5% on discharge, while only 7.1% of cases received zinc supplementation for the appopriate duration of time.

Although no specific coverage data are available in South Africa, the zinc coverage results obtained from this study were found to be higher than the projected coverage (2014) for South Africa which was reported to be 10% according to Chola et al.

(2015:4). There are varying levels of coverage for zinc supplementation between the different studies that were compared. This could be due to differences in regional awareness of childhood diarrhoea treatment guidelines among medical staff or a lack of access to the treatment.

4.8. LIMITATIONS

This is a retrospective, single-centre study and therefore results are relevant for cases diagnosed with diarrhoea admitted to a GMPW at a tertiary hospital in the Eastern Cape, South Africa and extrapolation of data to other populations should be made with caution.

As this study collected data from case folders, some data were missing or incomplete, either because it was misplaced or not recorded. Due to the retrospective nature of the study, it was not possible to verify the data, especially with respect to whether zinc supplements were dispensed as prescribed and whether anthropometrical measurements and clinical assessments were performed correctly. The primary objective of the study was however not to assess accuracy of reporting in case files and as such the accuracy of measurements such as weight, height or length, MUAC or accuracy of dehydration assessment are unknown.

Weight specifically can fluctuate significantly with hydration status changes and as such as a singular measurement is not an accurate indicator of nutritional status especially in cases of dehydration, however it is the most frequently available anthropometric measurement.

4.9. CONCLUSION AND RECOMMENDATIONS

The results indicated poor use of anthropometric screening measurements such as height/ length and MUAC. Although weight was taken in most cases during hospitalisation, this measurement as a singular measurement does not indicate wasting or severe acute malnutrition and has to be used in conjunction with height/length and MUAC to diagnose severe malnutrition.

Of concern was the number of cases classified with malnutrition on admission yet not assessed or managed by a dietitian. More focus has to be placed on this vulnerable group and improving screening and access to appropriate nutritional management.

This study has shown low adherence levels to treatment guidelines for zinc supplementation in children with diarrhoea at a tertiary hospital in the Eastern Cape, South Africa. The results reinforce the need to perform training among health care professionals to increase awareness and improve implementation of these guidelines. Continued monitoring and surveillance is also needed to ensure sustainability of any progress made in implementation. It is also recommended that the hospital develop an institutional policy that incorporates zinc supplementation guidelines.

4.10. DECLARATION

The authors have no conflict of interest to declare.

4.11. ACKNOWLEDGEMENTS

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CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1. INTRODUCTION

A literature review was conducted to explore the topic of childhood diarrhoea; it made reference to the definitions, prevalence, causes and management, both nutritional and medical. The management focused on the use of zinc supplementation as a proven treatment intervention in childhood diarrhoea, the background of zinc supplementation, mechanisms of action, the literature supporting the use in diarrhoea, any negative effects from the use of zinc and the treatment guidelines as developed by the WHO and UNICEF were explored. This included a summation of recommended outcomes and an overview of current implementation of zinc supplementation, monitoring and surveillance research (Chapter 2). According to the research problem there is limited data concerning the awareness and adherence levels amongst medical staff in implementing zinc supplementation in the management of childhood diarrhoea in South Africa (Chapter 1).

An investigation into the current zinc implementation practices was undertaken at a tertiary hospital in the Eastern Cape, South Africa. The study assessed individual childhood cases of diarrhoea at the hospital to determine retrospectively the management practices at the hospital (Chapter 3). The aim of the study was to determine adherence to WHO treatment guidelines for zinc supplementation by health care professionals in the management of diarrhoea at a tertiary hospital (Chapter 1). Conclusions of this research according to the objectives are discussed in this chapter.

5.2. CONCLUSION

In order to achieve the aim of this research, four objectives were investigated, namely: to determine the general characteristics of cases admitted for diarrhoea; to collect information on diarrhoeal episodes; to collect information on zinc prescriptions; and, identify barriers to prescribing and administering zinc supplementation. From the data obtained from these objectives the aim of the study was achieved. On the basis of the literature reviewed, the problem statement and aim of the study, the following conclusions were formulated.

The literature review indicated a close link among diarrhoea, pneumonia and malnutrition. The results of this study supported this link by showing that the majority

of cases admitted with diarrhoea also presented with pneumonia. However, the results could not be extrapolated to malnutrition due to the infrequent use of malnutrition screening measurements to diagnose and define malnutrition in the hospital.

Anthropometric measurements necessary for the screening of malnutrition, specifically height/length and MUAC were rarely measured in the GMPW, according to the results of this study. Although weight was taken in most of the cases during hospitalization, this measurement as a singular measurement, does not indicate stunting or wasting and has to be used along with height/length and MUAC to diagnose severe acute malnutrition. Weight can also significantly fluctuate with hydration status changes and as such is not an accurate indicator of nutritional status in cases of dehydration.

Another concern highlighted from the study was the number of children classified by clinicians as 'malnourished', yet not referred to, assessed or managed by a dietitian or nutritionist. More focus should be placed on screening for this vulnerable group and improving access to appropriate nutritional and medical management according to the WHO guidelines.

This study has indicated low adherence levels to the treatment guidelines for zinc supplementation both for dosage and duration of treatment in children with diarrhoea at a tertiary hospital in the Eastern Cape, South Africa. Although comparable with other low to middle income countries, it is still a concern if South Africa is to meet the WHO and UNICEF outcomes targets of 80% for coverage of treatment for childhood diarrhoea and ultimately reduce childhood mortality rates.

Barriers to zinc supplementation were not routinely indicated in the folders or prescription charts. It was also evident from the results that health care professionals are not aware of the appropriate dosage and duration of zinc supplementation to be used in cases admitted with diarrhoea. The only barrier to zinc supplementation was noted in the prescription chart by the pharmacy department of the hospital; it was a single case of zinc being prescribed and not administered due to a lack of stock. However for the majority of this study zinc availability and accessibility was not a problem.

5.3. RESEARCH SIGNIFICANCE

No other prescription audits of zinc supplementation in the treatment of childhood diarrhoea have been conducted in South Africa, thus this is the first, and will provide a baseline for further research. It will provide a baseline to evaluate further intervention outcome targets and any progress made to achieve childhood diarrhoea management goals as set by WHO and UNICEF.

5.4. LIMITATIONS OF THE STUDY

This is a retrospective, single-centre study and therefore results are relevant for cases diagnosed with diarrhoea admitted to a GMPW at a Tertiary hospital in the Eastern Cape, South Africa. Extrapolation of data to other populations should be made with caution, as this study focuses on a narrow population.

As this study included retrospective data from case folders, some data were missing or incomplete, either because it was misplaced or not recorded. Due to the retrospective nature of the study, it was not possible to verify the data, especially with respect to whether zinc supplements were dispensed as prescribed and whether anthropometrical measurements and clinical assessments were performed correctly. The primary objective of the study was however not to assess accuracy of reporting in case files and as such the accuracy of measurements such as weight, height or length, MUAC as well as accuracy of the clinical assessment are unknown.

5.5. RECOMMENDATIONS

This section focuses on recommendations obtained from this study in connection with recent developments, resource limitations and existing infrastructure.

In practice more health care professionals working with paediatric patients, need to be made aware of the use of zinc supplementation in the treatment of diarrhoea, the benefits and importance of its use in reducing the burden of diarrhoea. Along with the importance of zinc supplementation, health care professionals need to be instructed on the correct treatment guidelines to implement the correct dosage of zinc supplementation and for the appropriate duration.

Specifically nursing and medical staff need more training in their curriculum at academic institutions on the importance of nutrition and interventions such as zinc supplementation and the role it plays in patient outcomes. Training should include all

IMCI guidelines including growth monitoring, which incorporates screening, diagnosing and treating severe acute malnutrition, vitamin A supplementation as well as zinc supplementation.

Anthropometric measurements, specifically malnutrition indicators should be standard practice in all institutions treating infants and children younger than five years of age; this includes emergency or casualty departments, out-patient departments as well as hospital wards. Institutional protocols, with sufficient equipment should be in place to ensure that each child has weight, recumbent length or standing height and MUAC measured when clinically assessed, to identify those children with stunting and wasting according to the WHO classifications. It is imperative to identify the extent of the problem, so that all children can receive the appropriate treatment and to improve outcomes of concomitant diseases associated with malnutrition.

Another recommendation of this research is that institutions develop up to date institutional policies for the management of diarrhoea that incorporate the WHO and UNICEF treatment recommendations for the use of zinc. These guidelines are simple to follow and have been developed for ease of use to encourage implementation. The institutional policies should be widely available and easy to access when needed. This will remove any confusion on dosage and duration of treatment. The ultimate goal of all these interventions is to reduce childhood mortality rates specifically in children younger than five years of age.

Finally, more research needs to be conducted in South Africa on the implementation of zinc supplementation guidelines in community health care centres as well as hospitals. The current research is inadequate to reflect adherence levels for the province of the Eastern Cape and South Africa as a whole and thus more research is needed to determine if South Africa is meeting the outcome targets set by the WHO and UNICEF.

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ADDENDUM A: INFORMATION SHEET

Data Information Sheet

Respondent number:

Hospital Folder no.:_____

Availability: _____	Missing (0)	Available (1)	Currently in use by other departments (2)	Readmission (3)
	Deacesed (4)	Admitted to multiple wards (5)		

Section A: General Patient Information

1. Date of Birth: _____

2. Gender:	Missing (0)	Female (1)	Male (2)

3. Date of admission:_____	Missing (0)

4. Date of discharge:_____	Missing (0)

5. Length of hospital stay (days): _____

6. Co-Morbidities:	Missing (0)	None (1)
HIV (2)	LRTI (3)	TB (4)
Meningitis (5)	Renal Impairment/Failure (6)	Liver Impairment/Failure (7)
Malnutrition (8)	Measles (9)	Other (10)

If other specify:_____

7. Weight on admission:_____	Missing (0)

8.1. Weight-for-age Z-score:_____

8.2. Z-score Interpretation:_____

>= +3 SD(1)	<+3 SD and >= +2 SD (2)	< +2 SD and >=+1 SD (3)	< +1SD and >= 0SD (4)
<0 SD and >=-1 SD(5)	<-1SD and >=-2SD (6)	<-2SD and >=-3 (7)	<-3 SD (8)

9. Weight on discharge:_____	Missing (0)

10.1. Weight-for-age z-score:_____

10.2. Z-score classification:_____

>= +3 SD(1)	<+3 SD and >= +2 SD (2)	< +2 SD and >=+1 SD (3)	< +1SD and >= 0SD (4)
<0 SD and >=-1 SD(5)	<-1SD and >=-2SD (6)	<-2SD and >=-3 (7)	<-3 SD (8)

11. Nutritional Status:_____	Missing (0)	Normal (1)	Underweight (2)	Severely Underweight (3)

12.1. Prescriber Level: _____	Missing (0)	1st Year Intern (1)	Com Serve (2)
	Medical Officer (3)	Consultant (4)	

12.2. Prescriber Code/Name as indicated on the prescription chart:_____

13. Was the prescriber code present: _____	Missing (0)	Yes (1)	No (2)

14. Was the patient assessed by a Dietitian?	Missing (0)	Yes (1)	No (2)

ADDENDUM A: INFORMATION SHEET CONTINUED

Section B: Information on diarrhoeal episode

1. Duration of diarrhoea pre-admission (in days): _____

Missing (0)	

2. Number of loose/watery stools noted on admission:_____

Missing (0)	

3. Presence of blood in the stools:

Missing (0)	Yes (1)	No (2)

4. Presence of Pyrexia (>37.8˚C):

Missing (0)	Yes (1)	No (2)

5. Presence of vomiting on admission:

Missing (0)	Yes (1)	No (2)

6. Presence of dehydration on admission:

Missing (0)	Yes (1)	No (2)

7. Presence of shock on admission:

Missing (0)	Yes (1)	No (2)

Section C: Information on prescription details

1.1. Lower range of Zinc dose requirements 1mg/kg: _____

Missing (0)	

1.2. Upper limit Max dose recommendations 20 (mg)

2. Was zinc prescribed on admission? _____

Missing (0)	Yes (1)	No (2)

If yes continue with the following questions:

3.1. Type of zinc prescribed:_____

Missing (0)	Trace elements (1)	Zinc acetate (2)	Zinc sulphate (3)	Zinc picolinate (4)	Elemental Zinc (5)
Zinc chloride (6)	Other (7)				

If other specify:_____

3.2. Type of zinc prescribed:_____

Missing (0)	Trace elements (1)	Zinc acetate (2)	Zinc sulphate (3)	Zinc picolinate (4)	Elemental Zinc (5)
Zinc chloride (6)	Other (7)				

If other specify:_____

4.1. Dose of zinc prescribed:_____

Missing (0)	

4.2. Dose of zinc prescribed:_____

Missing (0)	

5. Dose of total elemental zinc prescribed (mg): _____

Missing (0)	

6. Was prescribed dose within dosage range for wt (kg) and Max dose

Missing (0)	Yes (1)	No (2)

7. Duration of time zinc was prescribed for (Days):_____

Missing (0)	

8. On which day of admission was zinc initiated:_____

Missing (0)	

9. Was zinc given on discharge:

Missing (0)	Yes (1)	No (2)

10. If yes duration of time zinc was prescribed for (Days):_____

Missing (0)	

11.1. Dose of zinc prescribed:_____

Missing (0)	

11.2. Dose of zinc prescribed:_____

Missing (0)	

12. Dose of total elemental zinc prescribed (mg): _____

Missing (0)	

13. Was prescribed dose within dosage range for wt (kg) and Max dose

Missing (0)	

14.1. Type of zinc prescribed:_____

Missing (0)	Trace elements (1)	Zinc acetate (2)	Zinc sulphate (3)	Zinc picolinate (4)	Elemental Zinc (5)
Zinc chloride (6)	Other (7)				

14.2. Type of zinc prescribed:_____

Missing (0)	Trace elements (1)	Zinc acetate (2)	Zinc sulphate (3)	Zinc picolinate (4)	Elemental Zinc (5)
Zinc chloride (6)	Other (7)				

15. Barriers to zinc supplementation:_____

ADDENDUM A: INFORMATION SHEET CONTINUED

Section D: Extra Information

1. Did the patient ingest Herbal/tradiotional Medicines:____

Missing (0)	Yes (1)	No (2)

2. Any previous admissions to hospital for AGE:_____

Missing (0)	Yes (1)	No (2)

3. Was Length/Height measured during admission:____

Missing (0)	Yes (1)	No (2)

4. Length/Height (CM):_____

Missing (0)

5. Length/Height-for age on admission Z-score:_____

6. Length/Height Z-score classification:__

Missing (0)	Normal >=-2SD and <= +2SD (1)	Stunted <-2SD and >-3 SD(2)	Severely Stunted <=-3SD (3)

7. Weight-for-height on admission Z-score:_____

8. Weight -for-height interpretation:_____

Missing (0)	Normal (1)	Wasted (2)	Severely Wasted (3)
Overweight (4)	Obese (5)		

9. Was MUAC measured:_____

Missing (0)	Yes (1)	No (2)

10. MUAC measured (CM):_____

Missing (0)

11. MUAC z-score:_____

12. Interpretation of MUAC

Missing (0)	Normal MUAC > 13.5 CM (1)	MAM MUAC <12.5CM (2)	SAM <11.5CM (3)	AT RISK 12.5-13.5CM (4)

13. Feeding methods:_____

Missing (0)	Breastfeeding (1)	Formula feeding (2)	Soft Diet (3)	Full Diet (4)

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA

2.2.4 DIARRHOEA, ACUTE
A09.0

DESCRIPTION
Diarrhoea is a serious common childhood illness evidenced by the passing of frequent profuse loose watery stools. Vomiting may or may not be present.

Diarrhoeal disease is often caused by viral infection but may be due to bacterial infection, dietary or other causes.

Dehydration and metabolic disturbances are common if treatment is not instituted early and may result in severe disease, irreversible organ damage and death in children.

Malnutrition is a serious co-morbidity and/or result of diarrhoeal disease and must be managed correctly employing ongoing feeding. Feeding, minerals, micronutrients and vitamins are continued except during ileus or shock. See section 2.4: Malnutrition.

In severe malnutrition or in the young infant (< 2 months of age) bacterial co-infection is common.

DIAGNOSTIC CRITERIA
Clinical

> The assessment of shock and dehydration in children is not always simple. A good initial assessment and frequent re-assessments (4-hourly if dehydration is present. In the presence of shock continuous reassessment with appropriate adjustment of care are vital in the care of these children.

Shock is shown by one or more of the following:
Compensated shock:
» delayed capillary refilling time (> 3 seconds);
» rapid, weak pulse rate;
» cool peripheries.
Late (Preterminal):
» decreased level of consciousness,
» decreased blood pressure,
» decreased pulse volume.

Dehydration is treated after shock is dealt with:

Severe dehydration	Some dehydration
Sunken eyes	Sunken eyes
Very slow skin pinch (≥ 2 sec)	Slow skin pinch (< 2 sec)
Drinking poorly	Drinks eagerly
	Irritable/restless

Other indicators of dehydration may be sought but do not add substantially to assessment, e.g.: depressed fontanelle, absent tears, decreased passage of urine.

Also assess for signs of metabolic, nutritional and other co-morbidities:
» severe malnutrition,
» decreased level of consciousness,
» abnormal tone or floppiness,
» abdominal distension,
» decreased bowel sounds,
» increased respiratory rate and chest indrawing,
» persistent or bile stained vomiting,
» urine for leucocytes or nitrites.

Investigations
» After resuscitation, in children with severe dehydration, shock or other signs of metabolic, nutritional or other co-morbidities:
  > sodium, potassium, urea, creatinine, blood acid-base assessment.
» Stool culture, especially if at a sentinel site for infectious GIT disease, or suspected dysentery, typhoid, cholera.
» Urine test strip on fresh/clean urine specimen for leucocytes, nitrites and blood. Ascertain HIV status with consent in every child.

GENERAL AND SUPPORTIVE MEASURES
» Adequate initial assessment and frequent re-assessment, including weight, is vital.
» Re-assess the patient continuously while shock persists.
» If dehydration is present, re-assess the patient 4-hourly and immediately correct shock or deterioration.
» Monitor and maintain:
  > hydration and circulation,
  > blood pressure,
  > acid-base status.
  > normal blood glucose,
  > blood electrolytes,
» Monitor urine output, should be at least 1 mL/kg/hour. This may be difficult in small children with diarrhoea, especially in female infants.
» Monitor body mass regularly. Weigh daily, 6-hourly if unsure of hydration status and child is very ill or small. This can be used to indicate response of hydration.
» Continue oral feeds during period of diarrhoea:
  > if the child is breastfed, continue breastfeeds and encourage the child to feed longer at each feed;
  > if the child is exclusively breastfed, give oral rehydration solution (ORS) in addition to each feed;
  > if the child is not exclusively breastfed, give ORS and other appropriate feeds, e.g. breast milk substitutes or food based fluids;
  > if the child is severely dehydrated or shocked, withhold feeding until stable, usually a few hours only.

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA CONTINUED

MEDICINE TREATMENT

> There is no place for antidiarrhoeal medications, i.e. kaolin and pectin, atropine and diphenoxylate, loperamide, or antiemetics in the routine management of acute diarrhoea.

OUTLINE OF PRACTICAL FLUID THERAPY OF DEHYDRATING WATERY DIARRHOEA

With severe malnutrition the assessment of dehydration is more difficult. Avoid intravenous infusions, if possible.
Treatment of dehydration requires more care/more frequent assessments.

1. First treat shock, if present (If no shock, proceed to section 2 below)

> If an IV infusion cannot be set up within 5 minutes use an intra-osseous infusion. See section 1.1.8: Intra-Osseous Infusion in Emergencies. During treatment of shock administer oxygen.

- Sodium chloride 0.9%, IV, 20 mL/kg given as a bolus rapidly.
  - After each bolus reassess for persistence of shock, or evidence of circulatory overload.
  - Repeat the fluid bolus up to 3 times if shock still persists, provided that evidence of circulatory overload is not present.
  - If after the second bolus, i.e. total of 40 mL/kg has been given, the response is inadequate, a third bolus can be started. Move the patient to ICU for CVP monitoring and inotropic support.

Treatment of shock in severe malnutrition
Shock treatment should be more cautious in patients with severe malnutrition due to poor cardiac reserve and high prevalence of gram negative septicaemia.
- Sodium chloride 0.9%, IV, 10 mL/kg administered over 10 minutes.
  - Up to 4 boluses may be given. However, deterioration may be due to fluid overload and shock may be due to septicaemia, not always hypovolaemia.
  - After 4 boluses (40 mL/kg) further treatment should be in a high care unit.
  - Re-assess frequently during treatment of shock. Patients response should guide further fluid therapy.

If pulse and respiratory rate increases, increasing liver span and gallop rhythm are found suspect fluid overload/ cardiac dysfunction and manage appropriately. See section 1.1.7: Shock.

When shock has been treated proceed to the management of dehydration.

2. Severe dehydration or some dehydration
2a) If the child has not failed oral rehydration and was not in shock:
- Oral rehydration solution (ORS), oral, 80 mL/kg over 4 hours using frequent small sips (i.e. 5 mL/kg every 15 minutes for 4 hours).
  - Give more if the child wants more.
  - Show the caregiver how to give ORS with a cup and spoon.
  - If child vomits wait 10 minutes and then continue more slowly.
  - Encourage caregiver to continue feeding the child, especially breastfeeding.

Review after 4 hours:
- general condition,
- capillary filling time,
- level of consciousness,
- skin turgor,
- sunken eyes.
- respiratory rate,
- abdomen (liver span),
- if passing urine,
- number/quality of stools, and

Appropriate response at 4 hourly re-assessment:

Shock	• Treat for shock as under 1 above.
No improvement or more dehydrated	• Increase drip rate by 25%.
Improving (e.g. increase in weight) but still dehydrated	• Continue current drip rate.
No visible dehydration	• Decrease drip rate by 50%. • If remains well hydrated after a further 4 hours stop IV rehydration fluids and move to ORS. • For prevention of dehydration see under 3 below.

2b) If child fails the above oral treatment, was in shock or has already failed at primary health care level then:
IV fluid*
- ½ Darrows/dextrose 5%, IV, 10 mL/kg/hour administered for 4 hours, then re-assess.
*(This rate is in line with current safety evidence but the need for regular reassessment 4-hourly remains).
PLUS
Oral rehydration solution
- Oral rehydration solution (ORS), oral, 80 mL/kg over 4 hours using frequent small sips (i.e. 5 mL/kg every 15 minutes for 4 hours).
PLUS
Oral feeds at normal feed volumes and times.

CHAPTER 2	ALIMENTARY TRACT

Review after 4 hours:

» general condition,
» capillary filling time,
» level of consciousness,
» skin turgor,
» sunken eyes.

» respiratory rate,
» abdomen (liver span),
» if passing urine,
» number/quality of stools, and

Appropriate response at 4-hourly re-assessment:

Shock	• Treat for shock as under 1 above.
No improvement or more dehydrated	• Increase drip rate by 25%.
Improving (e.g. increase in weight) but still dehydrated	• Continue current drip rate.
No visible dehydration	• Decrease drip rate by 50%. • If remains well hydrated after a further 4 hours stop IV rehydration fluids and move to ORS. • For prevention of dehydration see under 3 below.

Give oral feeds if:
» the level of consciousness is normal,
» the child is not in severe distress,
» not shocked and,
» has no surgical abdomen.

3. No visible signs of dehydration on presentation or a child stable with no dehydration after treatment of dehydration.
Show the caregiver how to give ORS with a cup and spoon using frequent small sips.
Encourage caregiver to give 10 mL/kg after each diarrhoeal stool until diarrhoea stops.
Instruct the caregiver on how to make and use ORS/SSS at home.
Home made sugar and salt solution may be used if oral rehydration formula is not available.

HOMEMADE SUGAR AND SALT SOLUTION (SSS)
½ level medicine measure of table salt
plus
8 level medicine measures of sugar
dissolved in 1 litre of boiled (if possible) then cooled water
(1 level medicine measure = approximately 1 level 5 mL teaspoon)

Encourage the caregiver to continue feeding the child, especially breastfeeding.

CHAPTER 2	ALIMENTARY TRACT

Instruct the caregiver to give the child extra feeds after the diarrhoea has stopped to make up for the period of inadequate intake.

Child should return to hospital immediately if:
» no improvement,
» condition deteriorates,
» poor drinking or feeding,
» slow skin pinch.

» blood in stool,
» fever develops,
» sunken eyes,

Educate caregivers about hygiene, oral rehydration solution and danger signs of diarrhoea.

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA CONTINUED

Figure 2 Summary flow chart for correction of dehydration in diarrhoeal disease

Diarrhoeal Diseases Fluid Flow Chart Overview – "In Hospital" Care
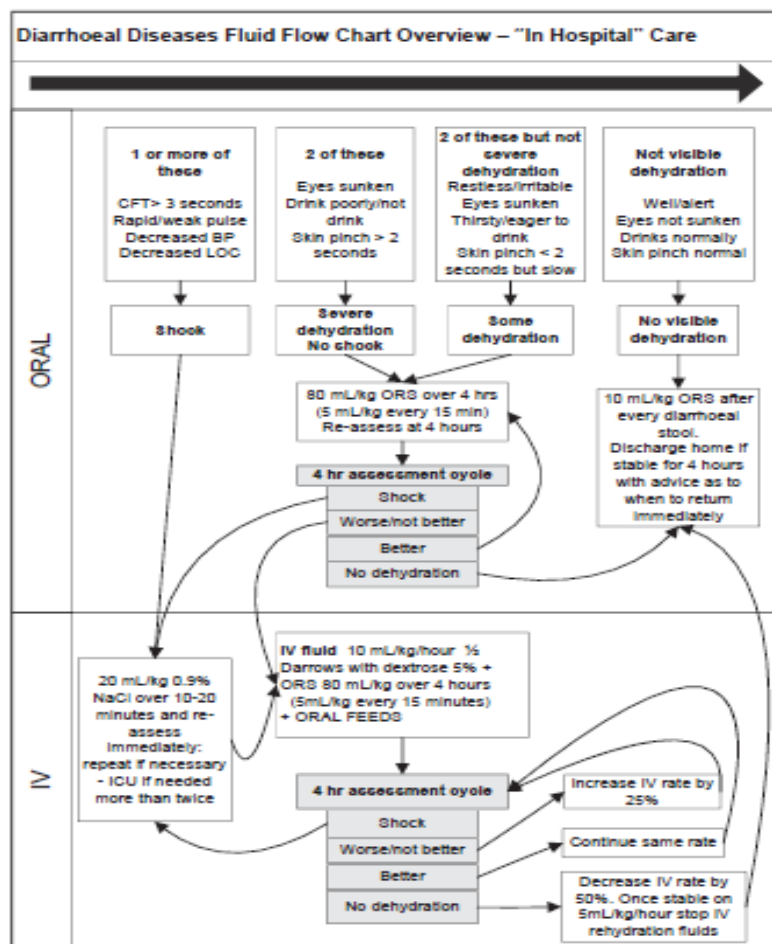
Metabolic disturbances

Acidosis

Metabolic acidosis does not require correction unless extremely severe, i.e. pH < 7.1, or i f the b ody is unable to c orrect the d eficit, e.g. s alicylate poisoning or renal failure.
Correction should only be considered with expert supervision.
Correcting the renal circulation and shock will lead to self-correction in almost all cases.
If correction is necessary: volume of sodium bicarbonate 4.2% required is:

- Sodium bicarbonate 4.2% in mL = 0.3 x base deficit x weight in kg.
  Review response to assess the need for further correction.

Hypokalaemia

Note: Potassium levels are affected by the degree of acidosis.

If potassium is < 3.5 mmol/L but > 2.5 mmol/L:

- Potassium chloride, oral, 25–50 mg/kg/dose 8 hourly.

If potassium is < 2.5 mmol/L:

- ½ Darrows/dextrose 5%, 200 mL **plus** potassium chloride 15%, 2 mL, into the vacoliter:
  - o 1 mL potassium chloride 15% = 2 mmol in the above dilution, gives combined K^+ of 37 meq/L – do not exceed this amount.
  - o Mix well before administration.
  - o Run at normal rehydration rate (as above).

Oral potassium may also be given during this period:

- Potassium chloride, oral, 25–50 mg/kg/dose 8 hourly.

Monitor serum potassium 8–12 hourly. Once above 3.0 meq/L, stop IV potassium and continue with oral.

Hypernatraemia (> 150 mmol/L)

Oral rehydration is preferable to IV rehydration.

If oral rehydration fails, rehydrate using IV over 48 hours but continue giving oral rehydration.

IV Fluid rate

Rate:

- o If 2–10 kg: 6 mL/kg/hour
- o If > 10–20 kg: 5 mL/kg/hour
- o If > 20–40 kg: 4 mL/kg/hour

Serum sodium ≤ 160 mmol/L

- ½ Darrows/dextrose 5%, IV.

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA CONTINUED

Serum sodium > 160 mmoL
Sodium chloride 0.9%/dextrose 5% plus potassium chloride (see below) is used to correct clinical dehydration for the first 48 hours. After changing to maintenance rates use oral rehydration, or if IV fluids are required change to ½ Darrows/dextrose 5%.
- Sodium chloride 0.9%/dextrose 5% **plus** potassium chloride (to 20 mmol/L), IV.

Repeat serum sodium every 8–12 hours to monitor progress.
Failure to decrease sodium levels usually means the rehydration rate is too slow.
Fall of sodium levels more than 1 mmol/L/hour on average means the rehydration rate should be reduced.

Frequent clinical reassessment is the key to the safe management of this situation. Serum sodium levels may be done more frequently where this is possible. Adjust the drip rate according to response.

If convulsions are considered likely, (decreased level of consciousness, hyper-irritable child), in the setting of high serum sodium, consider the use of prophylactic anticonvulsants:
- Phenobarbitone, IV, 20 mg/kg as a single dose.

OR
If IV phenobarbitone not available:
- Phenobarbitone, oral, 20–30 mg/kg as a single dose.

Hyponatraemia
The correction of hyponatraemia is usually only necessary where the serum sodium is significantly decreased (i.e. < 120 mmol/L), or if the patient is symptomatic.

Use sodium chloride 0.9% and add potassium chloride and dextrose as indicated below.
Give at the rate in dicated for dehydration and ex pect correction to hav e occurred after the following estimated volume:
Volume of sodium chloride 0.9% (mL) = (130–Na⁺) x body weight in kg x 4.

- Administer sodium chloride 0.9%, 200 mL **plus** potassium chloride 15%, 2 mL **plus** dextrose 50%, 20 mL into the vacoliter.
  - Mix well before administration.

After the calculated volume has been given, resume with:
- ½ Darrows/dextrose 5%, IV, at the required rate.
  - Recheck the serum electrolytes.

Antibiotic therapy
Note:
» Antibiotics are not routinely used for diarrhoeal disease.
» During diarrhoea, absorption of antibiotics may be impaired due to intestinal hurry. Give antibiotics orally if administered for intra-luminal effect.
» Other antibiotics for systemic action are best administered parenterally.
» Consider urinary tract infectio n, or septicaemia in children with severe malnutrition, the immunocompromised and infants < 2 months old.

Dysentery
Treat initially as shigella dysentery:
- Ceftriaxone, IV, 50 mg/kg as a single daily dose for 5 days.
OR
- Ciprofloxacin, oral, 15 mg/kg/dose 12 hourly for 3 days.

┌───┐
CAUTION: USE OF CEFTRIAXONE
After 28 days of age IV ceftriaxone and IV calcium containing fluids may be given but only sequentially with the giving set flushed well between the two products.

Note: Do not use ceftriaxone in neonates.
└───┘

For entamoeba histolytica (if demonstrated on stool microscopy, or strongly suspected - this is now a relatively uncommon condition in children in South Africa).
- Metronidazole, oral, 15 mg/kg/dose 8 hourly for 7 days.
  - Severe disease: treat for 10 days.

Cholera
Treat according to current sensitivities of the organism during epidemic.
See section 2.2.1: Cholera.

Typhoid
- Ceftriaxone, IV, 50 mg/kg once daily for 10–14 days.

┌───┐
CAUTION: USE OF CEFTRIAXONE
After 28 days of age IV ceftriaxone and IV calcium containing fluids may be given but only sequentially with the giving set flushed well between the two products.

Note: Do not use ceftriaxone in neonates.
└───┘

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA CONTINUED

Severe malnutrition
See section 2.4.1: Malnutrition, severe acute.
- Ampicillin, IV, 50 mg/kg/dose 6 hourly for 5 days.
PLUS
- Gentamicin, IV, 6 mg/kg as a single daily dose for 5 days.
  o Confirm normal renal function before second dose.

Very young infants , 28 days old
- Ampicillin, IV, 25–50 mg/kg/dose 6 hourly for 5 days.
PLUS
- Gentamicin, IV, 6 mg/kg as a single daily dose for 5 days.
  o Confirm normal renal function before second dose.

Mineral and micronutrient supplementation
All children with diarrhoea.
- Zinc (elemental), oral,
  o If < 10 kg: 10 mg/day.
  o If > 10 kg: 20 mg/day.

- Potassium chloride, oral, 8 hourly.
  o If < 6 months: 125 mg.
  o If > 6 months: 250 mg.
    Unless: hyperkalaemic or anuric.

REFERRAL
- » Inability to correct/treat shock/dehydration.
- » Metabolic complications.
- » Unresolving diarrhoea.

2.2.5 DIARRHOEA, PERSISTENT
K52.9

DESCRIPTION
Persistent diarrhoea: diarrhoea for longer than two weeks.

Persistent diarrhoea results in significant morbidity and mortality associated with poor nutrition.

Persistent diarrhoea is most frequently due to:
- » temporary loss of disaccharidase activity in the intestinal microvillous brush border, e.g. lactase loss; or
- » luminal infection/infestation, which may be non-specific bacterial overgrowth.
Rare causes include food allergies, cystic fibrosis and coeliac disease.

DIAGNOSTIC CRITERIA
Clinical
- » Persistent diarrhoea without weight loss or dehy dration — consi der Toddler's diarrhoea.
- » Persistent diarrhoea with weight loss and dehydration — consider small bowel mucosal injury, e.g. lactose intolerance or small bowel bacterial overgrowth.
- » Persistent diarrhoea with weight loss but no dehydration — consider a malabsorption syndrome, e.g. coeliac disease, allergic enteropathy, cystic fibrosis, etc.
- » Consider the possibility of HIV infection.

Investigations
Where weight gain falters, dehydration recurs, the child is ill or the diarrhoea continues:
- » full blood count,   » urine and stool microscopy,
- » serum proteins,   » culture and sensitivity tests (MCS),
- » stool-reducing substances > 0.5% reducing sugar is abnormal if on a lactose-containing diet.

GENERAL AND SUPPORTIVE MEASURES
Treatment strategy includes a stepwise approach with modification of the diet, which are not mutually exclusive and are applied according to local resources.
- » Monitor hydration, stools, nutritional status, weight gain, growth and other nutritional parameters such as serum proteins.
- » Nutritional support:
  > Aim to p rovide at least 110 kcal/kg/day orally within three day s to protect nutritional state.
  > Where the stepwise approach is not possible:
    Under 4 months:
    Encourage exclusive breastfeeding if lactose intolerance is not severe. If not exclusive breastfeeding, use breast milk substitutes that are low in lactose, e.g. yoghurt or amasi or specialised formulae or lactose-free milk formula.
    Children aged 4 months and older:
    Feeding should be restarted as soon as the child can eat, with small meals 6 times a day.
  > Nasogastric feeding may be required in children who eat poorly. If the response is good, give additional fruit and well-cooked vegetables to children who are responding well. After 7 day s of tr eatment with an effect ive diet, r esume an appropriate diet for age, including milk, which provides at least 110 calories/kg/day. Follow up re gularly to e nsure recovery from diarrhoea, continued weight gain and adherence to feeding advice.

ADDENDUM B: STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR DIARRHOEA CONTINUED

MEDICINE TREATMENT

CAUTION
Antidiarrhoeal and anti-emetic agents are **NOT** recommended.

Antibiotic therapy
Antibiotics are only indicated when specific infections are suspected or where they are used in the Step-Wise Drug Based Empiric Protocol for Management of Diarrhoea.

All persistent diarrhoea with blood in stool should be treated as dysentery. See section 2.2.6: Dysentery.

For campylobacter:
* Erythromycin, oral, 10 mg/kg/dose 6 hourly for 7 days.

For *G. lamblia*:
* Metronidazole, oral, 7.5 mg/kg/dose 8 hourly for 5–7 days.

For *Y. enterocolitica*:
* Ceftriaxone, IV, 50 mg/kg/dose once daily.
OR
* Cefotaxime, IV, 50 mg/kg/dose 6 hourly.

CAUTION: USE OF CEFTRIAXONE

After 28 days of age IV ceftriaxone and IV calcium containing fluids may be given but only sequentially with the giving set flushed well between the two products.

Note: Do not use ceftriaxone in neonates.

For *Cryptosporidium*:
No effective treatment available in the presence of HIV related immunosuppression.

For *Isospora belli*:
* Co-trimoxazole, oral, 5 mg/kg/dose of trimethoprim component 6 hourly for 10 days then 12 hourly for 3 weeks.

For *Cyclospora cayetanensis*:
* Co-trimoxazole, oral, 5 mg/kg/dose of trimethoprim component 6 hourly for 5 days.

For *Microsporidia*:
* Albendazole, oral. (Specialist supervision)

STEP-WISE EMPIRIC PROTOCOL FOR MANAGEMENT OF DIARRHOEA

Commence management at the most appropriate step according to previous management – many infants with persistent diarrhoea will already have failed the "day 1-2" stage and will commence management on "day 3-5".

Day 0
    Rehydration: Recommence breast or full-strength formula feeds within 12–24 hours.
    Additional oral rehydration solution (ORS) to maintain hydration.

Day 1–2
    Continue full-strength feeds with additional ORS as required.

Day 3–5
    Change to lactose-free feeds if not breastfed.
    Continue additional fluids as required.
    If diarrhoea resolves, discharge, but continue with lactose-free feeds for 2 weeks.

Day 6–8
* Gentamicin, **ORAL**, 8 mg/kg/dose 4 hourly for 3 days only. Specialist initiated.
* Consider change to lactose-free feeds if not breastfed.

Day 9–11
    Semi-elemental formula, sucrose- and lactose-free, protein hydrolysate, medium chain triglyceride.
    Continue additional fluids as required.
    If diarrhoea resolves, discharge if possible on semi-elemental feeds for at least 2 weeks. If this is not possible a trial of lactose free feeds before discharge is sometimes successful and, if so, the child can be discharged on the lactose free feeds.

If giardia is not excluded:
* Metronidazole, oral, 7.5 mg/kg/dose 8 hourly for 5 days.

In HIV infected children: *Isospora belli* and *Cyclospora*:
* Co-trimoxazole, oral, 5mg/kg/dose of trimethoprim 12 hourly for 10 days.

Day 14+
    Consider total parenteral nutrition until diarrhoea has stopped. Thereafter gradually reintroduce semi-elemental feeds.

After success as indicated by weight gain, return of appetite and decrease of diarrhoea, less elemental diets can be judiciously and slowly re-introduced.

Mineral and micronutrient deficiencies
- Zinc (elemental), oral,
  - If < 10 kg: 10 mg/day.
  - If > 10 kg: 20 mg/day.

Provide nutritional support.

REFERRAL
» Inability to maintain hydration.
» Seriously compromised nutrition.
» Lack of local resources to support the stepwise protocol at any step.
» All cases not responding by day 12–13 of the stepwise protocol.
» Recurrent diarrhoea.

2.2.6 DYSENTERY
A03.9

DESCRIPTION
Passage of blood and mucus in the stools.
Shigella infection is the most common serious cause in children in South Africa.

Complications include:
» dehydration,
» shock,
» acidosis,
» renal failure, and
» convulsions,
» toxic megacolon,
» rectal prolapse,
» haemolytic uraemic syndrome.

DIAGNOSTIC CRITERIA
Clinical
» Sudden onset.
» Abdominal cramps, peritonism, urgency, fever and diarrhoea with blood and mucus in the stools.
» Meningismus and convulsions may occur.
» Exclude intussusception. Evidence of intussusception includes:
  > pain or abdominal tenderness,
  > bile-stained vomitus,
  > red currant jelly-like mucus in stool,
  > appearance of the intussusceptum through the anus.

Investigations
» Stool culture to confirm diagnosis of Shigellosis.
» Polymorphs and blood on stool microscopy.
» Immediate microscopy of warm stool to diagnose amoebic dysentery.

GENERAL AND SUPPORTIVE MEASURES
» Monitor fluid and electrolyte balance.
» Ensure adequate nutrition and hydration.

MEDICINE TREATMENT
Fluid and electrolyte replacement
See section 2.2.4: Diarrhoea, acute.

Antibiotic therapy
Treat as Shigella during an epidemic of Shigellosis, or if the child is febrile, "toxic"-looking, has seizures or if Shigella is cultured from the stool and the child is still ill.

- Ciprofloxacin, oral, 15 mg/kg/dose 12 hourly for 3 days.

Where oral medication cannot be used:
- Cefotaxime, IV, 75 mg/kg/dose 8 hourly for 5 days.
OR
- Ceftriaxone, IV, 50 mg/kg as a single daily dose for 5 days.

CAUTION: USE OF CEFTRIAXONE

After 28 days of age IV ceftriaxone and IV calcium containing fluids may be given but only sequentially with the giving set flushed well between the two products.

Note: Do not use ceftriaxone in neonates.

For entamoeba histolytica (only if demonstrated on stool microscopy, or strongly suspected):
- Metronidazole, oral, 15 mg/kg/dose 8 hourly for 7 days.

REFERRAL
» Dysentery with complications, e.g. persistent shock, haemolytic uraemic syndrome and toxic megacolon.

2.2.7 GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)
K21

DESCRIPTION
Gastro-oesophageal reflux is rep etitive regurgitation/reflux of gastri c contents into the oesophagus.

ADDENDUM C: HOSPITAL REQUEST FOR APPROVAL TO CONDUCT RESEARCH STUDY

Hospital Management

Director: Clinical Governance

Dear Sir

REQUEST FOR PERMISSION TO CONDUCT A RETROSPECTIVE, DESCRIPTIVE PRESCRIPTION AUDIT OF CASE FOLDERS OF ALL INFANTS AND CHILDREN (BIRTH TO 5 YEARS) ADMITTED WITH DIARRHOEA TO THE GENERAL MEDICAL PAEDIATRIC WARD, FROM 1 JANUARY to 31 DECEMBER 2013.

I am enrolled for a Master's degree in Dietetics at the University of the Free State. As part of this course I am required to perform a research study. I would like to conduct a research study at this tertiary hospital. The aim of the research study is to determine adherence levels to the treatment guidelines for diarrhoea in infants and children, specifically regarding the prescription of zinc supplementation. I will gather information for the study from the case folders of infants and children admitted to the general medical paediatric ward between January 2013 and December 2013. From statistics obtained from the Department of Information Technology, it was determined that 385 infants and children under 5 years of age were admitted to the hospital during this period and would be included in the study. The study is purely a retrospective, descriptive study, with no interventions or contact with patients necessary. All information will be obtained from case folders, specifically the prescription charts and medical notes. General patient information, prescription information and medical information will be collected from the folder.

The results obtained from this study will be used to assess and improve the treatment management of paediatric patients admitted with acute diarrhoea.

If permission is granted to complete the study at the hospital, I will apply for ethical

approval from the Ethics Committee of the Faculty of Health Sciences, University of the Free Sate.

There are no risks involved for the participants or the hospital and study participants will not be contacted or exposed to any harm or discomfort. This study is purely a case folder audit. All personal information will be kept confidential, no patient or prescriber names will be used and the name of the hospital will not be disclosed in research publications, once permission is obtained.

Should you require more information please contact myself, Lyndal Audie during office hours at (043) 709 2427 or after hours at 0720864503.

Yours Sincerely

Lyndal Audie

ADDENDUM D: AUTHOR INSTRUCTIONS FOR THE SOUTH AFRICAN JOURNAL OF CLINICAL NUTRITION

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Ethnic classification
Work that is based on or contains reference to ethnic classification must indicate the rationale for this.

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Short items are more likely to appeal to our readers and therefore to be accepted for publication. Manuscript should not exceed 4000 words in total all contents inclusive.

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Short reports or scientific letters, which include case reports, side effects of nutrient supplements/drugs and brief or negative research findings should be 1000 words or less, with 1 table or illustration and no more than 6 references.

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process.

Review articles are rarely accepted unless invited.

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- Please submit your manuscript electronically at www.sajcn.co.za
- Research articles should have a structured abstract not exceeding 250 words (50 for short reports) comprising: Objectives, Design, Setting, Subjects, Outcome measures, Results and Conclusions.
- A second abstract should be written in simple and clear spoken language highlighting the reason(s) that the research work was undertaken, the key findings and the key recommendations **WITHOUT**, overtly or covertly implying or containing any claims of whatsoever nature, but rather explaining how the work will help scientists (and/or lay persons) better understand and address the topic of investigation. The abstract should not exceed an absolute maximum of 75 words. In addition, please also include a < 140 character, "strong" message that can be used for social media.
- Refer to articles in recent issues for guidance on the presentation of headings and subheadings.
- Abbreviations should be spelt out when first used in the text and thereafter used consistently.
- Scientific measurements should be expressed in SI units except: blood pressure should be given in mmHg and haemoglobin values in g/dl.

If in doubt, refer to www.icmje.org/index.html

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1. Figures consist of all material that cannot be set in type, such as photographs and line drawings.
2. Tables and legends for illustrations should appear on separate sheets and should be clearly identified.
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References should be inserted in the text as superior numbers and should be listed at the end of the article in numerical and not in alphabetical order.
Authors are responsible for verification of references from the original sources.

References should be set out in the Vancouver style and approved abbreviations of journal titles used; consult the List of Journals in Index Medicus for these details.

Names and initials of all authors should be given unless there are more than six, in which case the first three names should be given followed by et al. First and last page numbers should be given.

Journal references should appear thus:
1. Price NC . Importance of asking about glaucoma. BMJ 1983; 286: 349-350.

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1. Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975: 96-101.
2. Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974: 457-472.

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