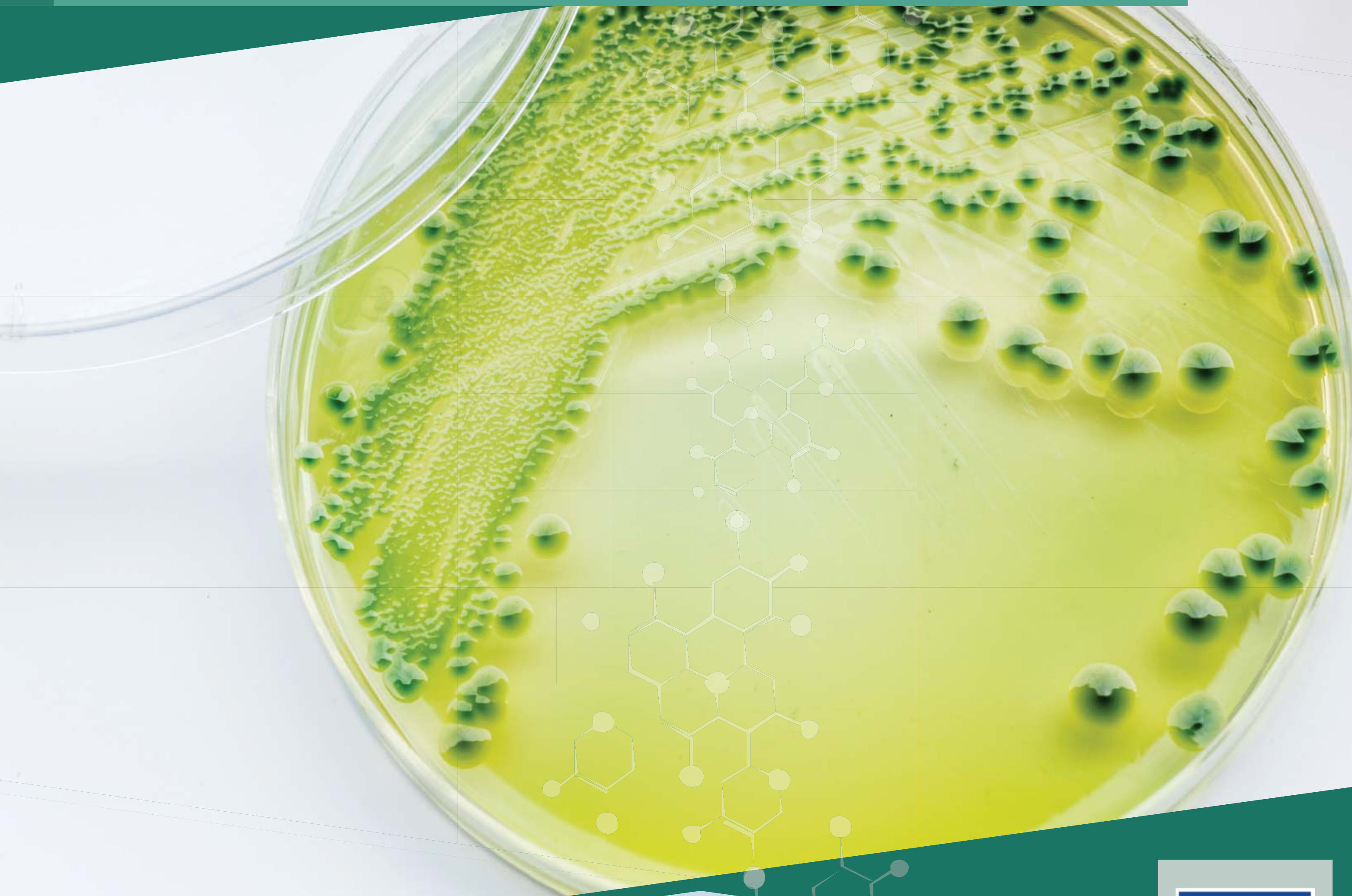
THE EPIDEMIOLOGY AND COST OF TREATING DIARRHOEA IN SOUTH AFRICA

Volume 3: The cost of treating diarrhoea in children under the age of 5 years in rural and peri-urban communities – A case study of Vhembe District of the Limpopo Province

N Potgieter, TG Barnard, LS Mudau and AN Traore



WATER RESEARCH COMMISSION

TT 762/18

THE EPIDEMIOLOGY AND COST OF TREATING DIARRHOEA IN SOUTH AFRICA

Volume 3

The cost of treating diarrhoea in children under the age of 5 years in rural and peri-urban communities – A case study of Vhembe District of the Limpopo Province

Report
to the Water Research Commission

by

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This report emanates from the Water Research Commission project, titled: *Epidemiological and economic implications of diarrhoea in water sources from rural and peri-urban communities in the Limpopo Province, South Africa* (K5/7150). The outputs of this research project are presented in three separate publications:

- **Volume I: Prevalence of diarrheagenic pathogens in water sources in the Vhembe District of the Limpopo Province (TT 760/18).**
- **Volume II: Prevalence and antibiotic profiles of diarrheagenic pathogens in children under the age of 5 years – A case of Vhembe District of the Limpopo Province. (TT 761/18)**
- **Volume III: The cost of treating diarrhoea in children under the age of 5 years in rural and peri-urban communities – A case study of Vhembe District of the Limpopo Province. (**This report**)**

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EXECUTIVE SUMMARY

BACKGROUND

Almost 1.3 million people die globally due to diarrhoea. The high number of diarrhoea cases among children increases cost and the need for hospital care. Treatment of diarrhoea in healthcare facilities differs among countries. Administering correct diarrhoea treatment is a challenge to most professionals in most developing countries. Despite the guidelines and regulations that are provided, most treatments prescribed by physicians and nurses are not the same. Most health practitioners use their own perceptions and observations to manage childhood diarrhoea, which lead to poor management and harmful practices (Carter et al., 2015).

The impact of diarrhoea diseases on poor and developing countries is greater wherein the treatment of diarrhoea disease comprises a major portion of their healthcare budget (Farthing, 2000). South Africa is regarded as one of the economic powerhouses of Africa and spends about 8.6% of its gross domestic products (GDP) on health service delivery. However, this does not have the health outcome that would be expected from such investment while some countries that spend less GDP on health have better health outcomes. In 2009–2010, estimated public and private spending on health service delivery exceeded about 8.6% of GDP, which is similar to the proportion spent on health in countries such as Brazil, Spain, Italy and England. This is mainly due to a lack of data on the cost of treating diarrhoeal diseases. Worldwide, the costs incurred for hospital care differ from one country to the other. It is however agreed that the information concerning the healthcare cost is valuable for decision-making and research regarding budgeting, hospital efficiency and cost-benefit analysis (WHO, 2003). Presently there are limited data available on the cost of treatment of diarrhoea in South Africa, especially for children under the age of 5 years who live in rural and peri-urban communities with little or non-existent water and sanitation infrastructure (Aikins et al., 2010).

AIM OF THE STUDY

To determine the cost of treating diarrhoea in children under the age of 5 years in the Vhembe District, Limpopo Province.

OBJECTIVES OF THE STUDY

- Determine the indirect and direct cost of diarrhoea treatment related to water, sanitation and hygiene (WASH).
- Determine the type of diagnosis, duration of stay and medicine prescribed.
- Assess the adherence to diarrhoea treatment.
- Determine the policy implication in relation to disease occurrence and treatment.

METHODS

The study was carried out in three hospitals of Vhembe District, Limpopo Province, over a period of 4 months during 2016. Two hospitals were situated in rural areas and one in an urban area; two were district hospitals and one a regional hospital. Only children under the age of 5 with acute diarrhoea were included in the study. Other criteria included a child who had diarrhoea for less than seven days, had at least three or more loose stools per day, and did not use any antibiotics when the stool sample was collected. To calculate the cost of diarrhoea, the professional service cost, as well as the medicine and facility cost such as intensive care unit (ICU) and high care unit costs were included. The Uniform Patient Fee Schedule was used to determine the cost for medicine and facility care. The cost considered outpatient and inpatient care. Ninety-one (91) stool samples were assessed for the prevalence of pathogenic diarrhoea-causing bacteria, viruses and parasites. WASH factors were also recorded and considered.

RESULTS AND DISCUSSION

There was a total of 106 patients who participated in the study. Eighty (80) were inpatients and 26 were outpatients. There were 58 (55%) patients who visited Tshilidzini Hospital, 38 (36%) who visited Donald Fraser Hospital, and 10 (9%) who visited Louis Trichardt Hospital. Of the children, 86% had loose stools; 13% had loose stools and cramps; and only 1% had loose stools, cramps and blood. The average hospital stay was two days.

The cost for outpatient care for all hospitals was R1027 at an average of R40 per patient. The total outpatient cost for Tshilidzini Hospital was R488 for 14 patients at an average cost of R35 per patient; the total cost for Donald Fraser was R88 for two patients with an average cost of R44 per patient; while the total treatment cost for Louis Trichardt was R451 for ten patients with an average cost of R44 per patient.

Inpatient cost was determined in two hospitals only. The total costs for inpatient care for 80 patients was R159 015. Donald Fraser had one patient who was admitted in ICU for two days and five patients who were admitted in high care for ten days, which increased the cost of treatment. The average cost for patients at Donald Fraser was R614 per day in a general ward. At Tshilidzini Hospital, the cost was R697. The total cost for hospital care including high care and ICU services in Donald Fraser was R98 088 for 84 days with an average of R1168 per patient, while the total cost for Tshilidzini Hospital was R59 899 for 86 days.

Unnecessary antibiotics were prescribed to treat patients across all hospitals. Medical doctors spent an average of 26 minutes per patient at a cost of R2021, followed by professional nurses who spent an average of 19 minutes per patient at a cost of R1483.

The presence of pathogenic organisms was associated with water sources used, sanitary conditions, and the use of pit latrines and flush toilets. Regression analysis indicated that storing water inside household containers has a 72% risk of infection to children under the age of 5. Not having water for more than two days showed a risk of infection for up to 45% to children under the age of 5. Handwashing was also a problem as more than 60% of caregivers reported that they forget to wash hands. Children who are not breastfed have a 145% chance of contracting an infection as compared with children who are breastfed.

LIMITATIONS OF THE STUDY

- The training and preparation time to use computer tablets to collect data from hospitals was problematic, which had an effect on the time available to collect stools from hospitals. It was realised that more workshops and more extensive training were required for fieldworkers. The device could not be used offline, which delayed the capturing of data especially when the network was not available.
- In hindsight, it was realised that the exclusion criteria used to select patients excluded many children with diarrhoea; therefore, this study could not determine the severity of infections in the study area.

CONCLUSIONS

The results indicated that diarrhoea is a challenge to rural and peri-urban communities in the Vhembe District as it escalates treatment costs in hospitals. The use of water sources, unavailability of water and storage conditions were linked to a risk of infection. The behaviour in terms of hygiene practices was also a concern.

Sustainable provision of safe water, adequate sanitation and good hygiene could reduce diarrhoea episodes. Continuous education to mothers and caregivers, training of healthcare workers and good management of diarrhoea infection could assist in reducing the costs. Water service authorities should scale up the provision of water and sanitation services to reduce diarrhoea in children under the age of 5 and ensure that these services are sustainable. An approach to provide hygiene education to the mothers and caregivers in these communities is crucial for public health gains.

RECOMMENDATIONS

- Continued assessment of clinical and environmental samples to assess the prevalence of diarrhoea-causing bacteria, viruses and parasites.
- Increased social behaviour education to rural household members, especially mothers and caregivers with young children, on WASH aspects.
- Educate health professionals on the use of antibiotics when treating diarrhoea.
- Strengthen the capacity of environmental health practitioners and health promoters on hygiene education.
- Scaling up WASH education is important to communities and the country as a whole.

CAPACITY BUILDING

Student name	Degree (University)	Title of study	Supervisors	Degree awarded
Lee Heine	DTech (University of Johannesburg)	Incidence and antimicrobial resistance of diarrhoeagenic bacteria in Vhembe region of South Africa	Prof. TG Barnard Prof. N Potgieter	In final stage
Tshikani Basil Minyuku	MTech (Tshwane University of Technology)	Cost implications of diarrhoea treatment related to water, sanitation and hygiene of children under 5 years in public health clinics of Vhembe District, Limpopo Province, South Africa	Dr LS Mudau Prof. MI Mokgobu	In final stage
Jean Pierre Kabue Ngandu	PhD (University of Venda)	Molecular characterization of norovirus strains circulating in rural communities of the Limpopo Province of South Africa	Prof. N Potgieter Dr E Meader Prof. PR Hunter	Graduated 2018
Ellen Ledwaba	MSc (University of Venda)	Prevalence of selected bacterial and viral entero-pathogens in children less than 5 years of age in Limpopo Province of South Africa	Prof. N Potgieter Prof. AN Traore	Graduated 2016
Simbarashe Karambwe	MSc (University of Venda)	Prevalence of diarrhoea-causing bacteria, viruses and parasites in water sources in the rural communities in the Vhembe District	Prof. N Potgieter Prof. AN Traore	Graduated 2017

LIST OF RESEARCH OUTPUTS

Published journal articles:

- Jean Pierre Kabue, Emma Meader, Paul R. Hunter and Natasha Potgieter. (2016). Human norovirus prevalence in Africa: A review of studies from 1990 to 2013. *Tropical Medicine and International Health* 21(1): 2–17.
- Jean Pierre Kabue, Emma Meader, Paul R. Hunter and Natasha Potgieter. (2016). Norovirus prevalence and estimated viral load in symptomatic and asymptomatic children from rural communities of Vhembe District, South Africa. *Journal of Clinical Virology* 84:12–18.
- Jean Pierre Kabue, Emma Meader, Paul R. Hunter and Natasha Potgieter. (2017). Genetic characterisation of norovirus strains in outpatient children from rural communities of Vhembe District, South Africa: 2014–2015. *Journal of Clinical Virology* 94:100–106.

Conference attendance:

- Jean Pierre Kabue, Emma Meader, Paul R. Hunter and Natasha Potgieter. (2016). Molecular characterization of norovirus strains circulating in rural communities of the Limpopo Province of South Africa. Oral presentation. 8th International Water and Health seminar. June 27–29. Cannes, France.
- Jean Pierre Kabue, Emma Meader, Paul R. Hunter and Natasha Potgieter. (2018). Genetic diversity of norovirus strains in outpatient children from rural communities of Vhembe District, South Africa, 2014-2015. Oral presentation. 20th International conference on Infectious Diseases. January 29–30. Sydney, Australia. *Presentation won best presentation award.*

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M Ratshivhadelo	Tshwane University of Technology	Data capturer
M Makhado	Management Sciences for Health	Data analysis
N Zitha	University of Venda	Sample collection
T Banda	University of Venda	Intern – Administrative Assistant
P Mukhuvha	University of Venda	Administrative assistant

CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACRONYMS AND ABBREVIATIONS

APW	–	Alkaline Peptone Water
BPW	–	Buffered Peptone Water
CCDA	–	Charcoal Cefoperazone Deoxycholate Agar
CDC	–	Centers for Disease Control and Prevention (United States of America)
CRF	–	Case Report Form
DALY	–	Disability-adjusted Life Year
EAEC	–	Enteroaggregative *E. coli*
EDC	–	Electronic Data Capture
EHP	–	Environmental Health Practitioner
EIEC	–	Enteroinvasive *E. coli*
EPEC	–	Enteropathogenic *E. coli*
ETEC	–	Enterotoxigenic *E. coli*
GDP	–	Gross Domestic Product
ICU	–	Intensive Care Unit
LiST	–	Lives Saved Tool
ORS	–	Oral Rehydration Solution
spp	–	Species
TCBS	–	Thiosulfate-citrate Bile Salts Sucrose Agar
UNICEF	–	United Nations Children Educational Fund
UPFS	–	Uniform Patient Fees Schedule
WASH	–	Water, Sanitation and Hygiene
WHO	–	World Health Organization
WRC	–	Water Research Commission

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CHAPTER 1 BACKGROUND

1.1 Introduction

South Africa is regarded as an economic powerhouse in Africa and spends about 8.6% of its gross domestic products (GDP) on health service delivery (Naledi et al., 2011). However, this does not have the health outcome that would be expected from such investment while some countries that spend less GDP on health, have better health outcomes. During 2009/2010, the estimated public and private spending on health service delivery exceeded the 8.6% of GDP, which is similar to the proportion spent on health in countries such as Brazil, Spain, Italy and England (Naledi et al., 2011).

In 2010, public sector healthcare facilities experienced frequent shortages of medicine and finished all the stock available: the budget was exhausted. In the 2016/2017 financial year, South Africa recorded more than 34 000 diarrhoea admissions in public hospitals (Department of Health, 2017). The number of hospitalisations has a large impact on the economy of the country. South Africa is actually underachieving in relation to its gross national income, primarily because of a weak developed primary healthcare system with challenges that include inadequate access, coverage and quality of water and sanitation services, limited management capacity, and limited human resources (Cullinan, 2006). Despite challenges faced by hospitals, conditions that are preventable through correct interventions are still found due to poor investment on primary healthcare programmes such as environmental health services.

A study conducted in Kwa-Zulu Natal by Pegram et al. (1998) that estimated the costs of diarrhoea and epidemic dysentery, indicated that approximately 43 000 South Africans die every year from diarrhoeal diseases; on average, one in every 14 South Africans requires formal diarrhoea treatment every year. Pegram et al. (1998) further reported that the annual public and private direct costs for healthcare incurred due to diarrhoea are estimated at R30 billion. In Ghana, treatment of outpatients suffering from diarrhoea costs 4.9 USD per person while treatment of inpatients costs up to 133 USD per person (Aikins et al., 2010). In a study done in Mumbai, the results indicated that the high costs incurred by households to treat diarrhoea surpass the costs that could be used to provide safe water in each household – one family was losing 3635 USD due to diarrhoea illness (Patel et al., 2013). Zambia reported the same results regarding escalated costs for diarrhoea treatment because of poor sanitation (Water and Sanitation Program, 2012). The Water and Sanitation Program (2012) also reported that poor water quality and unsafe water cost the government in Zambia 16.4 USD per person and affects the GDP (Water and Sanitation Program, 2012). Consequently, these studies had proven that the burden of diarrhoea in households contributes to poverty and decrease the productivity in communities.

To improve knowledge and treatment behaviour as recommended by Walker et al. (2015), continuous training of healthcare workers on the appropriate management of childhood diarrhoea needs to be strengthened. The *Essential Medicines List for South Africa* provides guidelines to administer diarrhoea treatment and treatment for other diseases in public health facilities. The purpose of the guidelines is to ensure proper treatment and avoid unnecessary prescription of antibiotics, which causes resistance (Department of Health, 2016). Despite the availability of the guidelines, unnecessary prescription of medicine is still prevalent in South Africa. A study done by Audie et al. (2016) in KwaZulu-Natal indicated that guidelines on using zinc is not followed, although it is known that zinc influences the speedy recovery and prevents reoccurrence of diarrhoea after being administered (WHO/UNICEF, 2013). The appropriate use of antibiotics could be extremely beneficial as it could decrease mortality due to dysentery to 99%. Therefore, following the guidelines and using correct medicine for treatment are beneficial to patients and indirectly reduce the cost of treatment and hospitalisation.

Worldwide, the costs incurred for hospital care differ among countries. It is however acknowledged that the information pertaining the healthcare cost is valuable for decision-making and studies regarding budgeting, hospital efficiency and cost-benefit analysis (WHO, 2003). There are different costing models to determine the cost of diarrhoea related to water, sanitation and hygiene (WASH). The Institute for International Programs (2016) introduced the Lives Saved Tool (LiST) model, which is a mathematical model to estimate the impact of scaling up health and nutrition interventions on newborn children and maternal health. The LiST model could be a good tool for determining the impact of intervention to deal with specific childhood diarrhoea, which will determine the estimated rate of survival and mortality. The model was also used by Chola et al. (2015) to determine the cost and impact of scaling up 13 interventions related to childhood diarrhoea for prevention and treatment. Bhutta et al. (2013) used the same model to measure the preventive and treatment interventions against childhood diarrhoea and pneumonia to assess the effect of mortality when therapeutics interventions were applied. The study outcome indicated that the use of zinc treatment could reduce mortality by 46% and hospitalisation by 23%.

The Centers for Disease Control and Prevention (CDC) (2007) in the United States developed an approach to calculate healthcare cost from available data to determine the epidemiological burden of disease due to disease outbreaks related to water quality. This method was developed to close the gap as the analysis of outbreaks could not estimate the actual incidence and the burden of outbreaks related to water illnesses. This method allows the different populations affected to be compared. To calculate the estimation of the person days ill or the duration of illness, the average duration of illness is multiplied by the number of cases. The rate of medical consultations – the rate in which people consult the medical practitioner for the same symptoms of diseases – is used to estimate the unreported cases. To determine emergency room visits, an estimation is done based on less than 75% visit, but where the visit is more than 75%, the situation is recorded as severe; thus assuming that a few cases were treated as outpatients. Hospitalisation and death were based on the 99% information reported in the hospital register.

The epidemiological burden estimate was determined by analysing epidemiological data such as etiologic agent (type of pathogen associated with more illnesses), water system type (owner of the system such as community), water system deficiency (untreated water, breakdown system, intermittent water supply etc.) and water source type (surface, borehole etc.) used by affected community. Approach for monetary burden is determined through cost of illness approach. This approach includes direct and indirect costs. The direct cost includes cost of medication, healthcare practitioner's visits, emergency room visits and duration of hospital stays. The indirect cost estimate is based on loss of productivity due to a fraction of the duration of illness. The monetary value of epidemiological burden of disease take cognisance of the data available to calculate the cost incurred to reduce the outbreak or eradicate it. The information related to water that is being used is also very important and could determine the economic impact of the burden of waterborne diseases.

The cost-effective analysis is based on the conventional intervention of the improvement of water quality at the source (well, borehole, stand pipe etc.) and at household level (treatment of water using chlorination, filtration, solar disinfection and combined flocculation or disinfection) (Clasen & Haller, 2008). The methodology measures disability-adjusted life year (DALY) and estimated healthcare cost savings from implementing the intervention. Household chlorination is most cost-effective, while solar is less cost-effective, it is not effective. The improvement at the source is more beneficial than household chlorination as it increases the DALYs. This method indicated that even though it is expensive to make improvements at the source, improving water systems does improve DALYs. Therefore, governments who implement and incur high costs to improve access to water quality, could save on the intervention needed for diarrhoea disease.

1.2 Objectives of Study

- Determine the indirect and direct cost of diarrhoea treatment related to WASH.
- Collect information on the type of diagnosis, duration of stay and medicine prescribed.
- Make an assessment on the adherence to diarrhoea treatment.
- Determine the policy implication in relation to disease occurrence and treatment.

1.3 Ethical Approval

Ethical approval was obtained from the University of Venda’s Higher Degree Committee and from the Limpopo Department of Health. The Vhembe District manager and the chief executive officers from the respective hospitals gave permission to access local hospitals. Letters from the Limpopo Department of Health and the Vhembe District Department of Health were sent to each hospital where the study would be conducted. Information on the study was presented at a meeting at each hospital and all stakeholders involved attended the meeting and discussion. The hospital staff were given a chance to ask questions about the study. Permission was granted by each hospital and the research team members were introduced to the hospital staff. All the arrangements required were made prior to data collection.

CHAPTER 2 DESCRIPTION OF THE STUDY AREA AND BASELINE INFORMATION

2.1 Study Area

The study was conducted in rural and peri-urban/urban public health facilities in Vhembe District Municipality, Limpopo Province. Two district hospitals (Louis Trichardt Memorial Hospital and Donald Fraser Hospital) from rural and urban settings as well as one regional hospital (Tshilidzini Hospital) were included in the study to determine the cost of diarrhoea treatment of children under the age of 5 (Figure 1). Tshilidzini Hospital is the referral centre for all district hospitals in the Vhembe District Municipality. Tshilidzini Hospital has 538 beds; Louis Trichardt Hospital 55 beds, and Donald Fraser Hospital 65 BEDS.

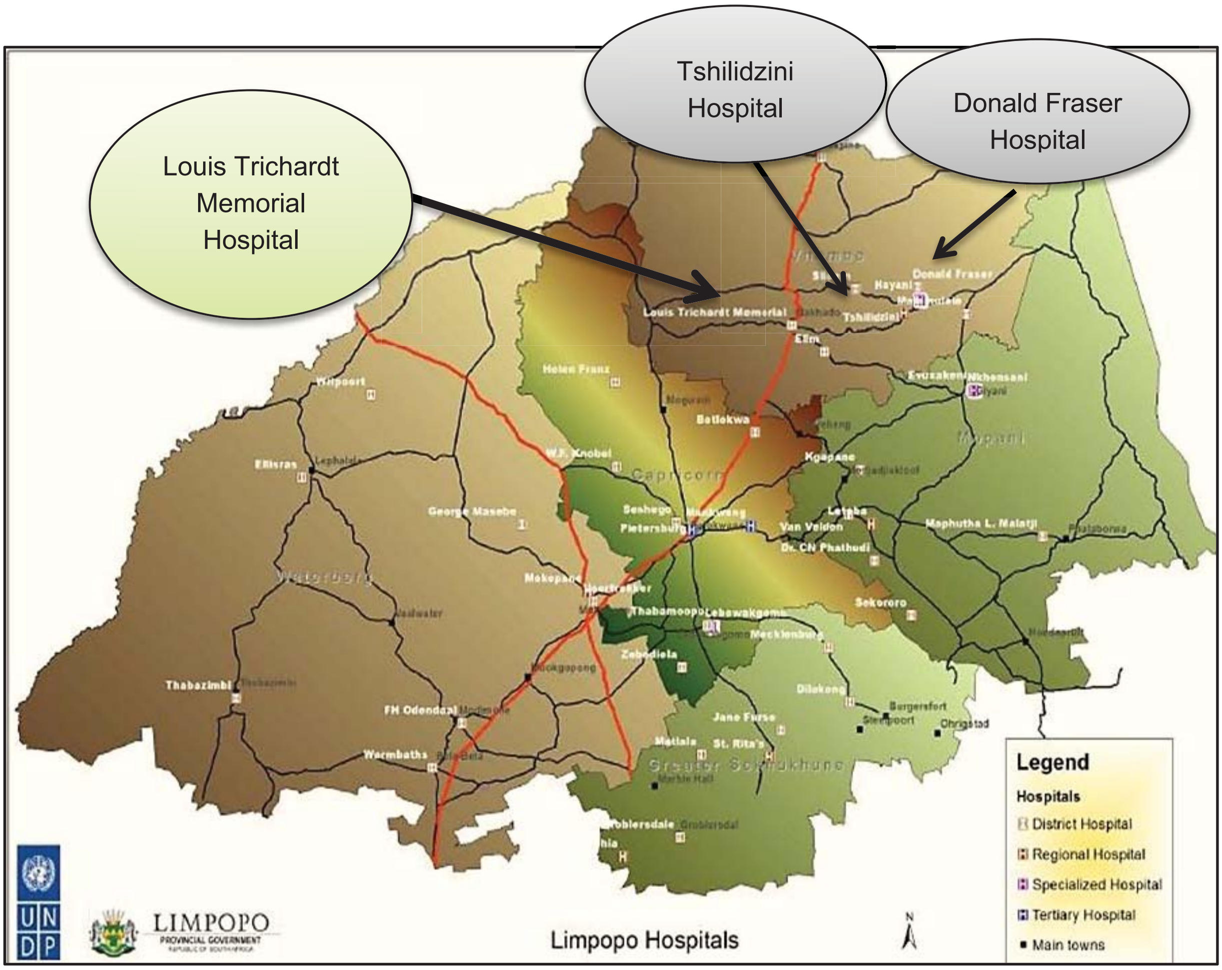


Figure 1: Limpopo hospital maps (Limpopo Department of Health, 2015b)

2.2 Data Collection

Each of the selected hospitals nominated at least one staff member to assist the project team with the research. The hospital staff advised the research assistants on suitable times to collect data from the mothers and caregivers. A meeting between the research team and the hospital staff member in each hospital was held before data collection. The purpose of the meeting was to establish the protocols and procedure that need to be followed during the study. The research assistants reported to the identified staff member every time they reported to the hospital. The staff member also introduced the research assistants to other healthcare workers, as well as to the mothers and caregivers in the specific wards where information was collected. The research assistants provided the information to the other health personnel and the mothers and caregivers.

The mother or caregiver of each child had to give consent prior to data collection, which included collecting relevant information from the child, taking stool samples and providing information on WASH in the patient's household. A leaflet with information about the study was read to each caregiver. If the mother or caregiver agreed to participate into the study, the research assistant provided copies of the study leaflet and the signed consent form to the mother or caregiver. Where the caregiver refused to participate in the study, no data collection was done. The research assistants used paper and pen to provide information to the participants and signing of the consent form prior to data collection.

A review of hospital records for all children under the age of 5 years with diarrhoea was recorded in 2016 (April to August) from all three hospitals. A prospective study was done from September 2016 to December 2016 for inpatients and outpatients under the age of 5 years with diarrhoea visiting the three hospitals. This study used a computer tablet with the Nukleus program (developed by PharmaLTX (Pty) Ltd team and managed by TCDOR company) to capture the primary and secondary data.

2.3 Data Capturing Using the Nukleus Program

2.3.1 Description of the Nukleus program

Using technology including tablet computers, cell phones with appropriate software and programming such as Android™ and Windows®, and other applications for data collection, is gaining popularity and is preferred rather than the traditional paper-and-pen method (Couper, 2005; Benson et al., 2006). The Nukleus program is an electronic data capture (EDC) computerised system, which is designed for collecting clinical data in electronic format for use mainly in human clinical trials. The EDC system provides a graphical user interface component for data entry, a validation component to check user data, and a reporting tool for analysing collected data.

2.3.2 Adapting the Nukleus program for the project

2.3.2.1 Repurposing the program

The use of technology such as the innovative Nukleus program to do the diarrhoea survey brings an opportunity to deal with survey effectively in the clinical field, which is still limited in South Africa. It is cost-effective, improves data quality and assists in meeting deadlines. The use of tablets for clinical data collection followed the criteria outlined by Eysenbanch (2016), which included survey design, survey delivery, survey completion and survey return.

Research assistants were recruited to collect data to determine the hospital costs for a maximum of 150 diarrhoea patients under the age of 5 years suffering from diarrhoea. All research assistants were trained prior to data capturing for a period of two weeks by the research team to be familiar with the questions and the use of the tablet. A dummy form was created so that the data capturers could practise and get used to data capturing using an online electronic case report form (e-CRF). English was the language used to design the questionnaire. The survey went through different quality checks that included assessment of each question with the data management team and research assistants responsible for data collection.

2.3.2.2 Content design

A detailed e-CRF was designed to capture the relevant data from children in the Vhembe District in Limpopo. The design of content for the computer tablet was done considering features such as length of survey, general format, as well as assessing the progress during survey, response format and visual presentation. This ensured that the research assistant interacted well and assisted the participant to respond effectively. The design of the questions was made to fit the screen to allow a set of questions to be answered. The questionnaire was made to last for 30 minutes to avoid the participants' boredom or withdrawal from the study. The questions were answered through touchscreen and typing where additional information were given.

2.3.2.3 Data capture

The research assistant ensured that the participant met all the inclusion and exclusion criteria as stated on the dashboard of the computer tablet. If the respondent met the criteria, the research assistant continued capturing the data. The inclusive and exclusive criteria were set in such a way that if the criteria were not met, the survey could not continue. The questions covered all the aspects included when paper-and-pen questionnaires were prepared. The survey was developed using different headings such as basic information, clinical information, treatment costs, medical costs and caregiver's information.

The child's information (captured under basic information) included weight, age, the name of the facility visited, the place of residence and the relationship to the caregiver. Clinical information included the diagnosis and symptoms, whether the patient was an inpatient or outpatient; number of days that the child had diarrhoea and days of admission, number of loose stools per day and who provided the treatment. The direct and indirect costs related to the patient's treatment were also recorded. Information obtained from the caregiver included the money lost due to hospital stay, the water and sanitation status at home as well as hygiene practices in the household and information concerning the feeding of the child.

The computer system used role-based security, which ensured access to authorised users only. The survey was done online, which allowed collected data to be uploaded automatically to the secure server, which only worked when the wireless connection was available. The limitation was that the system could not function when wireless connection was unavailable. When the system was offline, the research assistant used paper and pen to complete the survey and entered it manually when the connection was available for proper submission. In areas where 3G or 4G signal was not available, the process of data collection became very slow. All completed questionnaires were submitted electronically to the project quality team for quality assurance immediately after data capturing.

2.3.2.4 Data management and quality assurance

The system had a query management tool to allow queries to be raised throughout the process of conducting clinical trials and administration. The system allowed for automated communication and enabled the alerts to be sent and received. The user-friendly interface allowed easy monitoring and navigation of specific patient forms to enable queries to be raised automatically/manually.

The system was also designed to allow the data management team to track the progress of data collection from any location where the network was available. The system also allowed queries to be made and addressed using an icon that the data quality team and research assistants could identify and attend to the query. It allowed communication between team members.

Monitoring of data quality was done using a secure password. The research team only accessed the research questions through enhanced device security by logging in to the system where a password was used to limit access and use. The device also used GPS as a tracking device that automatically wiped information captured in case the tablet was lost or stolen. The data was encrypted and decrypted using an authorised encryption key.

2.3.2.5 Data analysis

The information was transferred by the research analyst to the database prepared in a Microsoft Excel™ spreadsheet for further analysis. Data was stored and protected with a password. A confidentiality disclosure form was signed by the research analyst assisting with data analysis to ensure there was no unauthorised access to the data.

2.3.3 Step-by-step instructions on the use of the Nukleus system

In computer systems security, role-based access control is an approach to restrict system access to authorised users only. For this study, the TCDOR company was provided with individual email addresses of all people who would be involved with the data collection process and who would use the system. Each of the individuals were given separate access to Nukleus; they had to log in with their email address and enter a self-created secure password (Figure 2). An e-CRF was created and built specifically for this project after approval of the CRF by the sponsor. Folders and forms containing each of the questions were created/built in Nukleus, which were categorised by the following headings: basic information; clinical information, outpatient treatment, inpatient treatment, caregiver and laboratory assessments (Figure 3). Nukleus was personalised for the University of Venda and this study specifically by adding the logo to the top left-hand corner of the EDC.

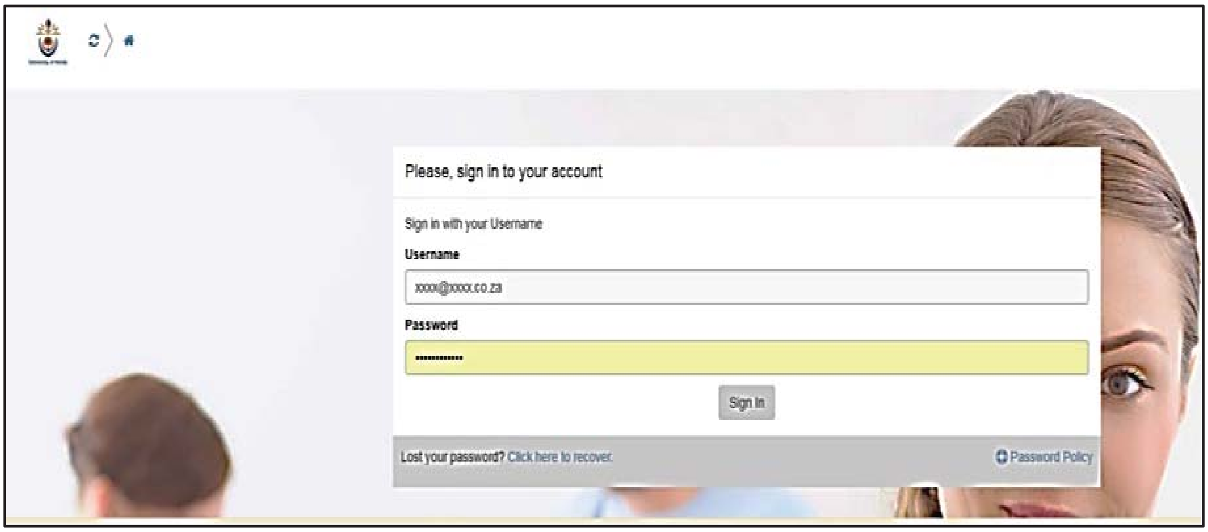


Figure 2: Log in landing page of Nukleus system

There were exclusion and inclusion criteria to ensure the correct participants were selected (Table 1). In cases where patients did not meet any of the listed criteria, the system did not allow the research assistant or fieldworker to proceed with the process. The fieldworker had to enter the reason why the participant did not meet the criteria. The system would then allow the research assistant to start screening the next participant. Where participants met all the requirements, it allowed the data collection process to proceed.

Table 1: Patient inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
The patient has lived in the Vhembe District for at least 7 days or more.	The patient did not take any antibiotics during the past week.
The patient had 3 or more watery stools per day.	The patient is not less than 3 months old.
	The patient is not older than 5 years.
	The diarrhoea has not been ongoing for more than 7 days.

Data was entered for each question by the data capturers at the hospital. Data was immediately and automatically saved onto a cloud-based server. Data capturers were provided with a paper-based CRF completion guide during EDC training. The completion guide is an exact paper replica of the online questionnaire and the e-CFR (Figure 3). Data managers could view the entered data from any location in real time. TCDOR, the sponsor and the data managers within the data collection team could manage data points from any location without having to visit the sites with the data capturers.

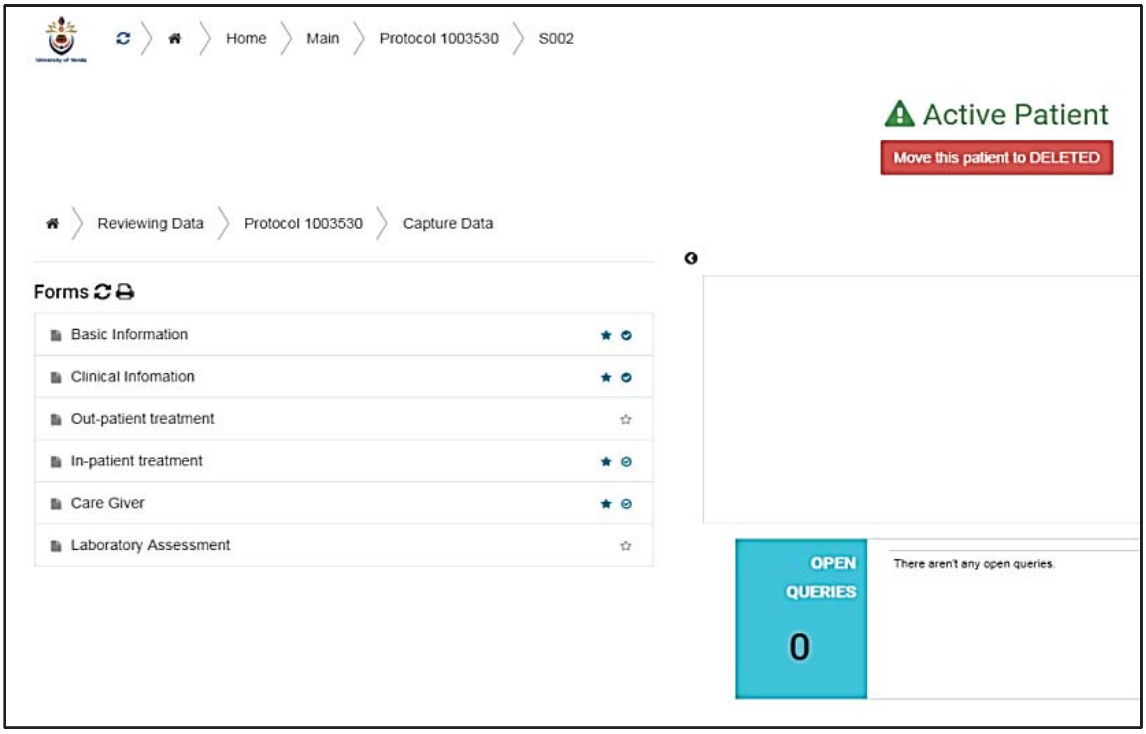


Figure 3: Folder categories of CRF

Data queries were raised throughout the data collection process; a query management tool was essential in dealing with this administration process. The query management tool allowed for automated communication and alerts to be sent and received. The user-friendly interface allowed monitors to navigate specific patient visits/forms where queries were raised automatically/manually (Figure 4). If the data manager or the monitor had any queries regarding any data points, they would raise the query on the system. The data capturer was able to see the number of data queries to address per patient entered (Figure 4).

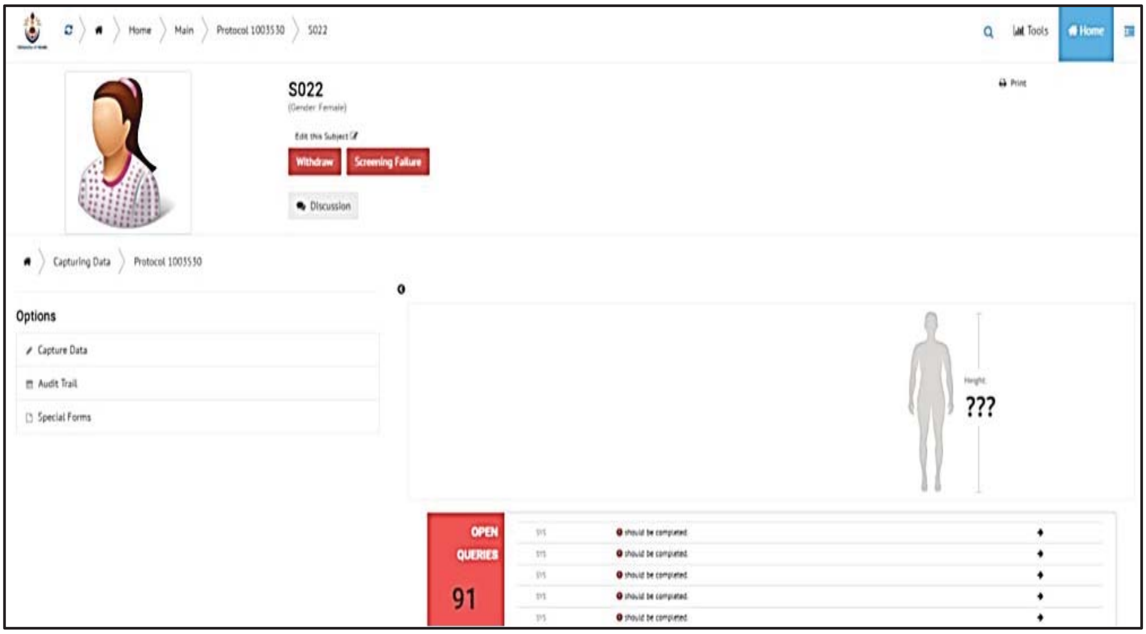


Figure 4: Visualisation of the open queries on patient dashboard

When the data manager indicated missing data, an exclamation mark would appear next to the item where a query needed to be addressed (as outlined in Figure 5 and Figure 6). The data was updated and corrected online by the data capturer. This ensured a clean and complete database for analysis. The dashboard also indicated the specific code in case of missing data (Figure 5).

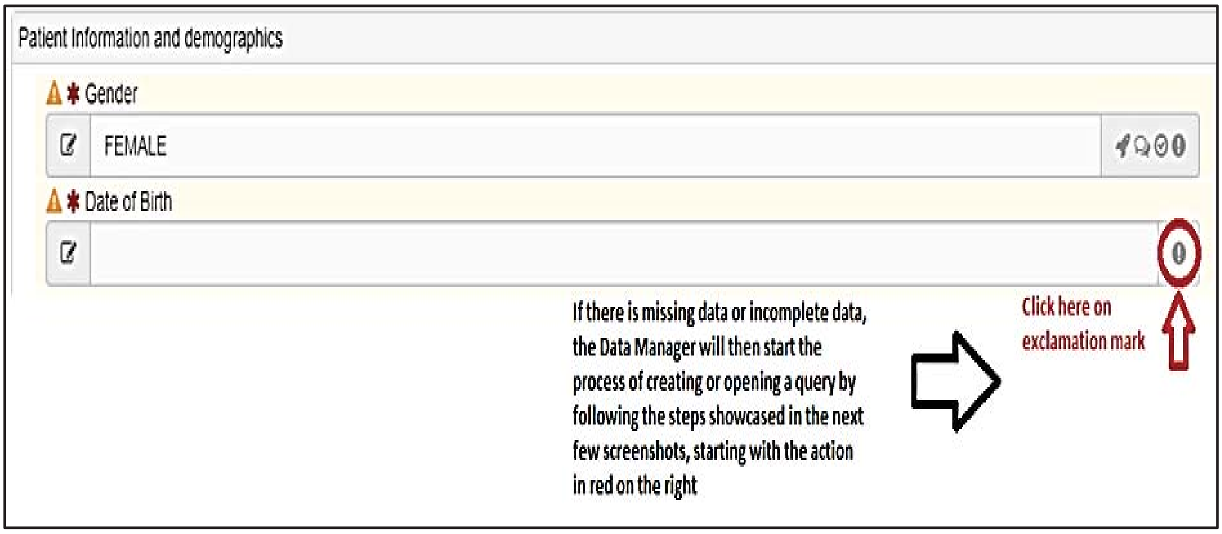


Figure 5: Dashboard visualisation of missing data query

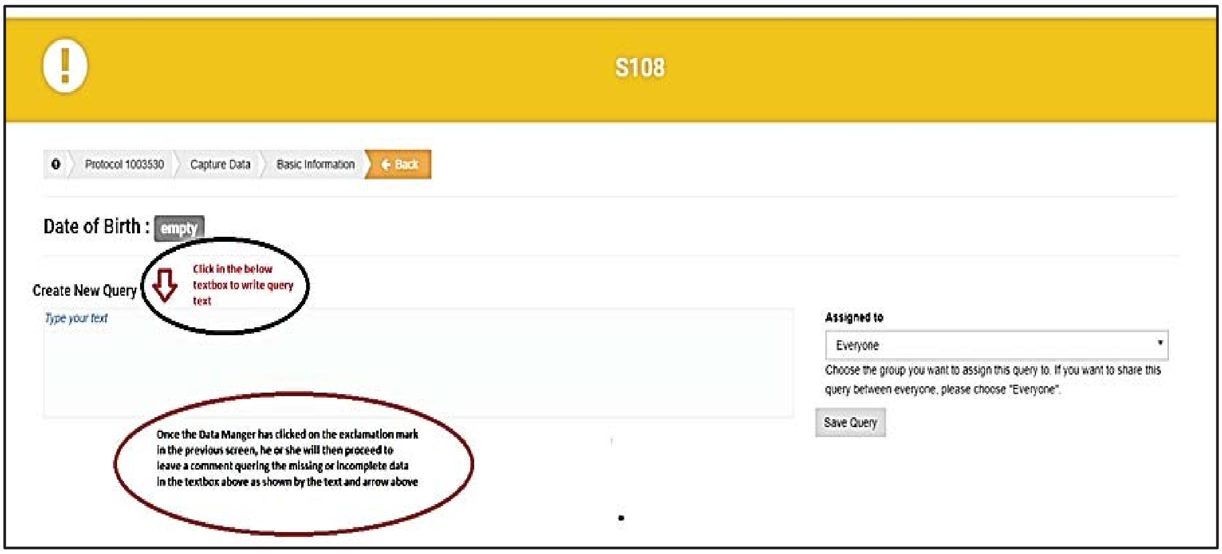


Figure 6: Example of missing data query

The queries were raised immediately after the research assistant completed entering the data so that follow-up could be done immediately. The data manager proceeded checking the data and indicated areas that needed attention by indicating the reason of the query so that the research assistant would know what had to be addressed (Figure 7).

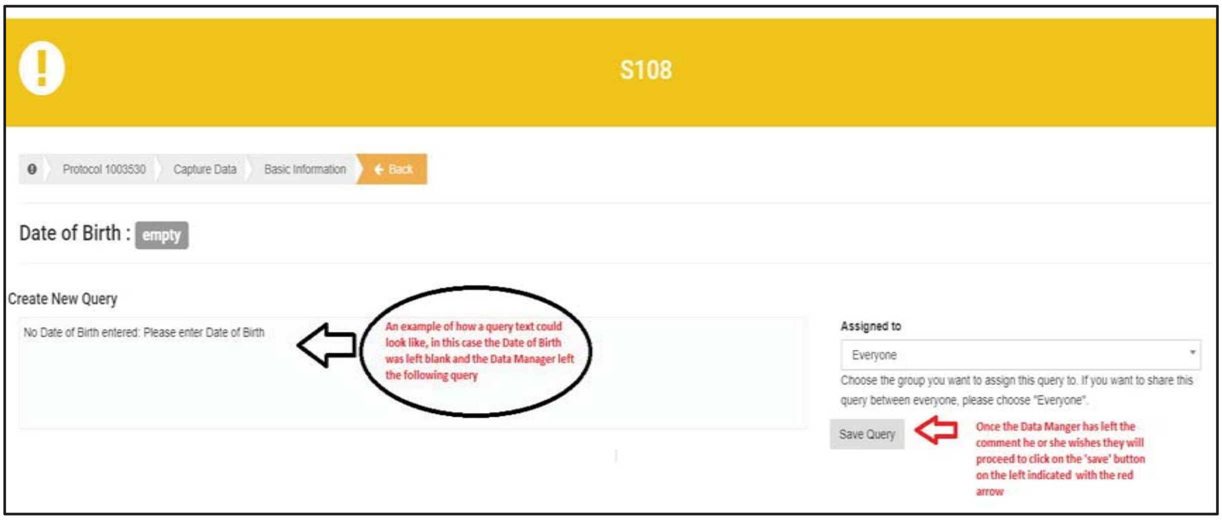


Figure 7: Example of how the data manager makes a query

Once the data manager completed a query, the information related to the query would appear on the dashboard of the research assistant responsible for entering the data (Figure 8).

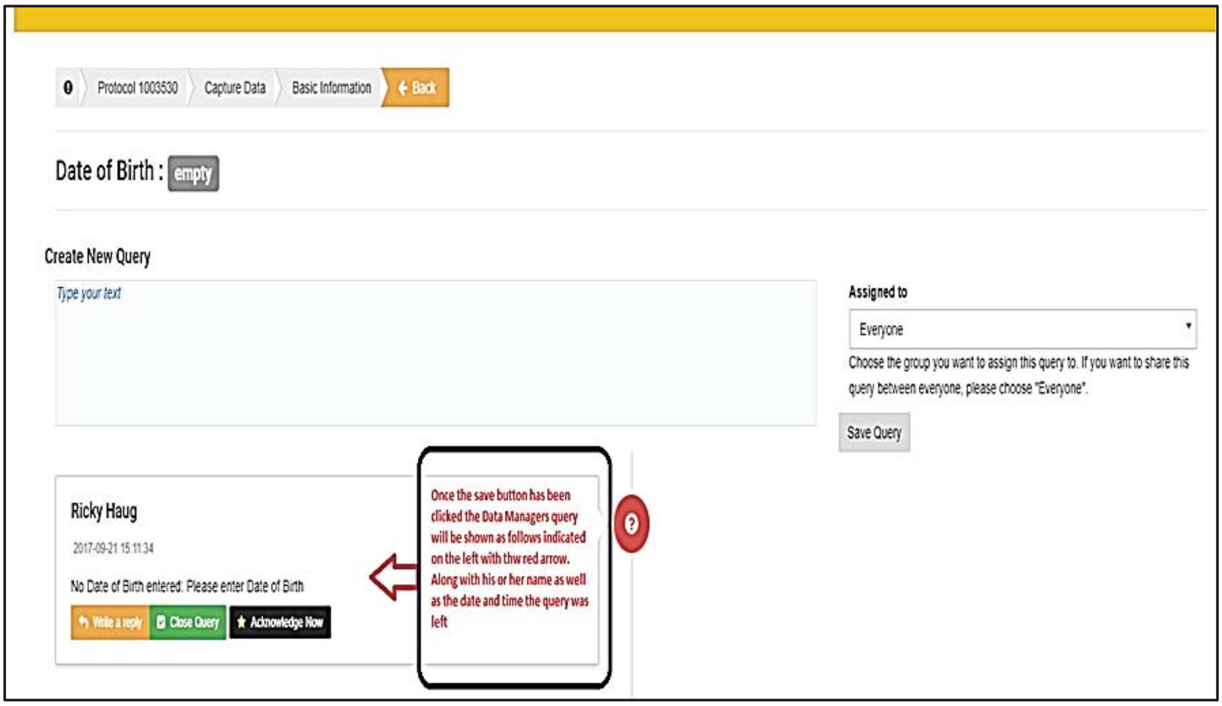


Figure 8: Visualisation of the query from the research assistant's dashboard

Once the research assistant realised there was a query, the query had to be addressed as soon as possible. Figure 9 indicates the query area that the research assistant had to click to attend to the query. In cases where the research assistant did not understand the query, a response had be sent to the data manager for clarification. Once everything was cleared, the research assistant proceeded by responding to the query (Figure 10).

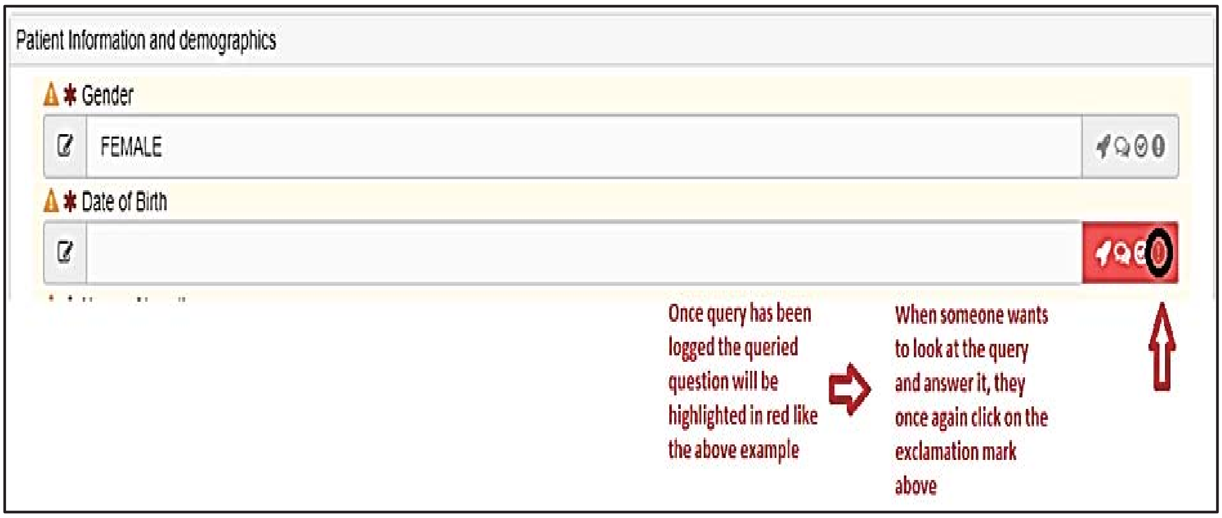


Figure 9: Example of area that supposed to be clicked when attending to a query

Once the research assistant or fieldworker answered the query, the information requiring the research assistant to acknowledge the answer or the response, popped out on the screen. The research assistant would then click *"Yes, I acknowledge it*" (Figure 10). The pop-up information would disappear because the query was confirmed and answered.

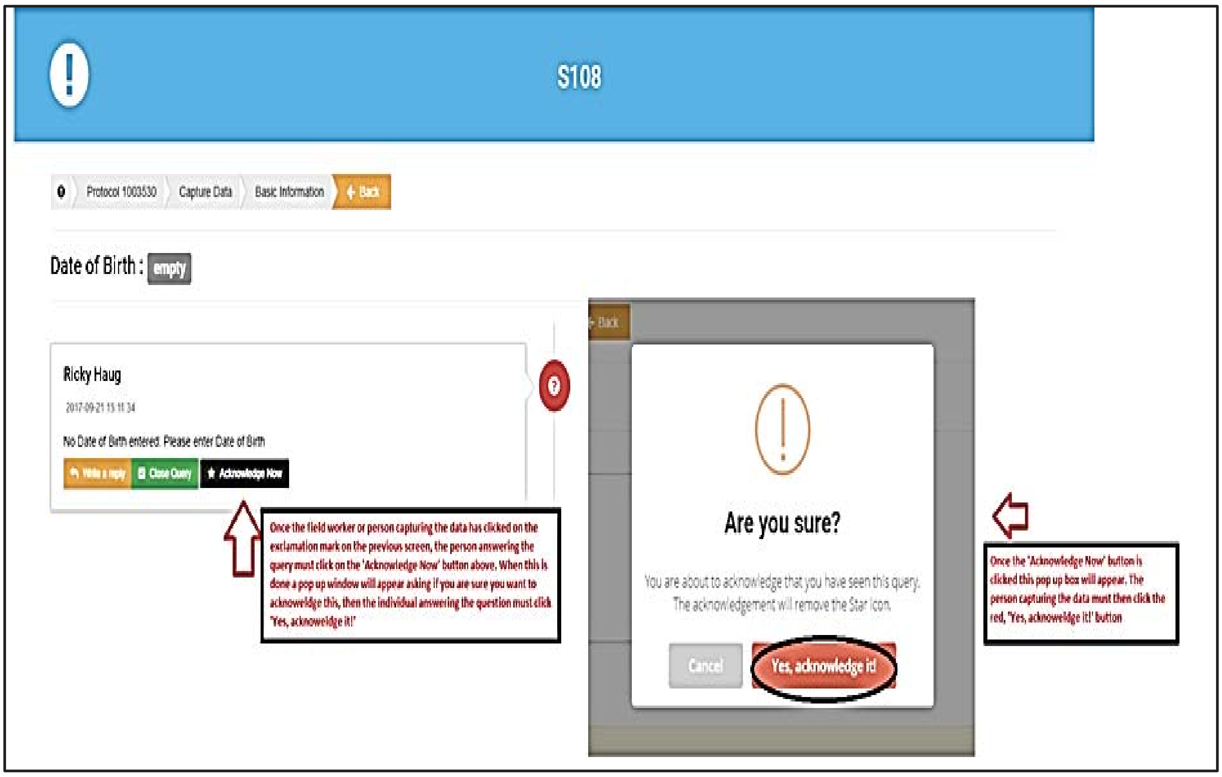


Figure 10: Visualisation of the dashboard when answering a query

Once the research assistant captured and acknowledged the data entry, the research assistant would save the information on the screen. The information would appear on the screen (Figure 11) indicating that the query has been answered.

Figure 11: Visualisation of acknowledgement of query

The data manager reviewed the query to determine if it was answered correctly. The screen showed the question and how it was answered (Figure 12). Once the manager was satisfied with the answer, the data manager closed the query and clicked the exclamation mark, which made it disappear and confirmed that the query was cleared (Figure 13).

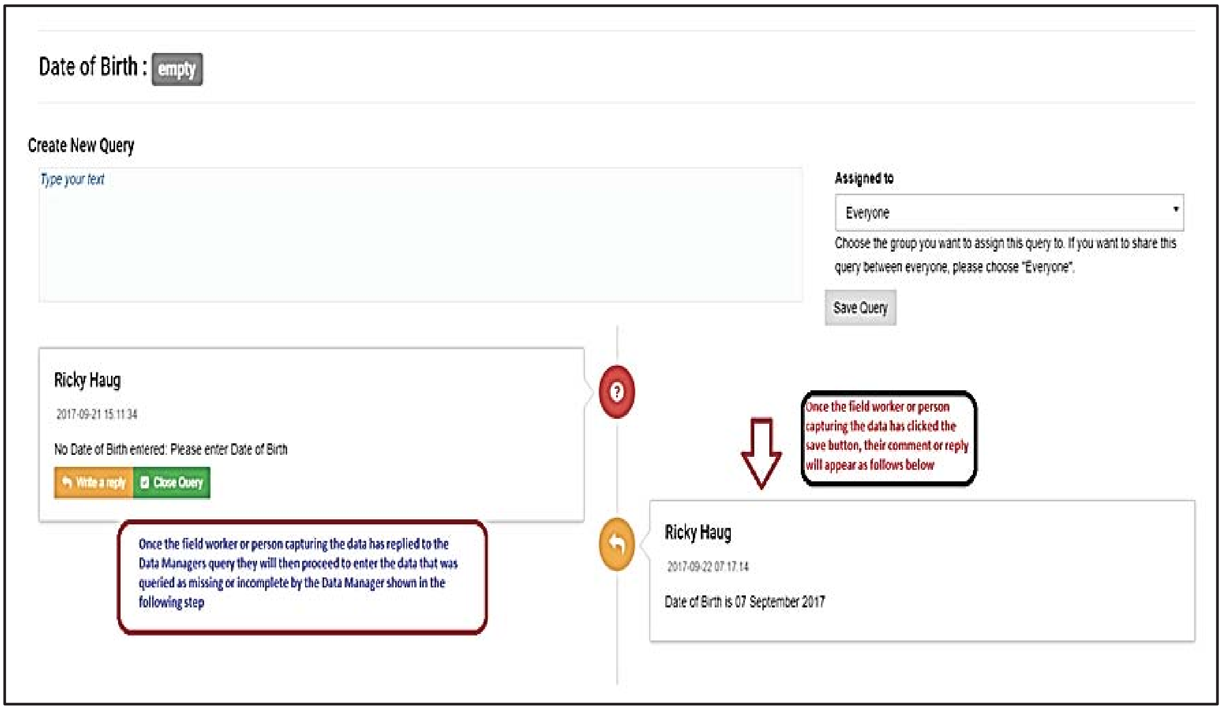


Figure 12: Example of the answered query appearing on manager's dashboard

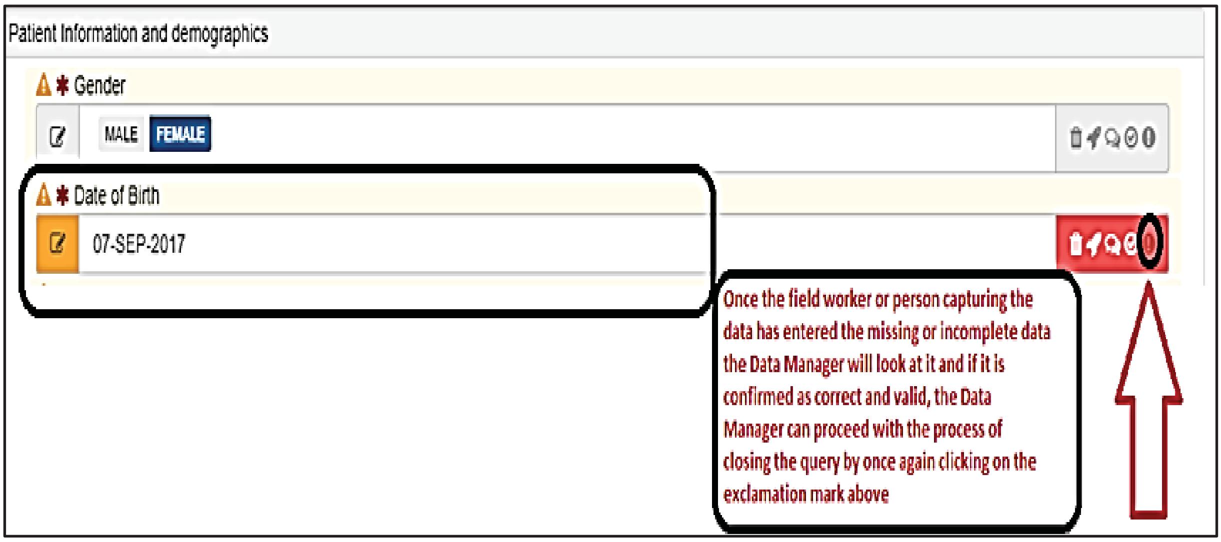


Figure 13: Example of how the data manager closes the query

The data manager had to click the *Save* button before closing the query. The pop-out message appeared and the data manager had to acknowledge the closing of the query (Figure 14). When the data manager clicked the *OK* icon on the "*Closing this query*" pop-out information, it confirmed that the query was cleared (Figure 14).

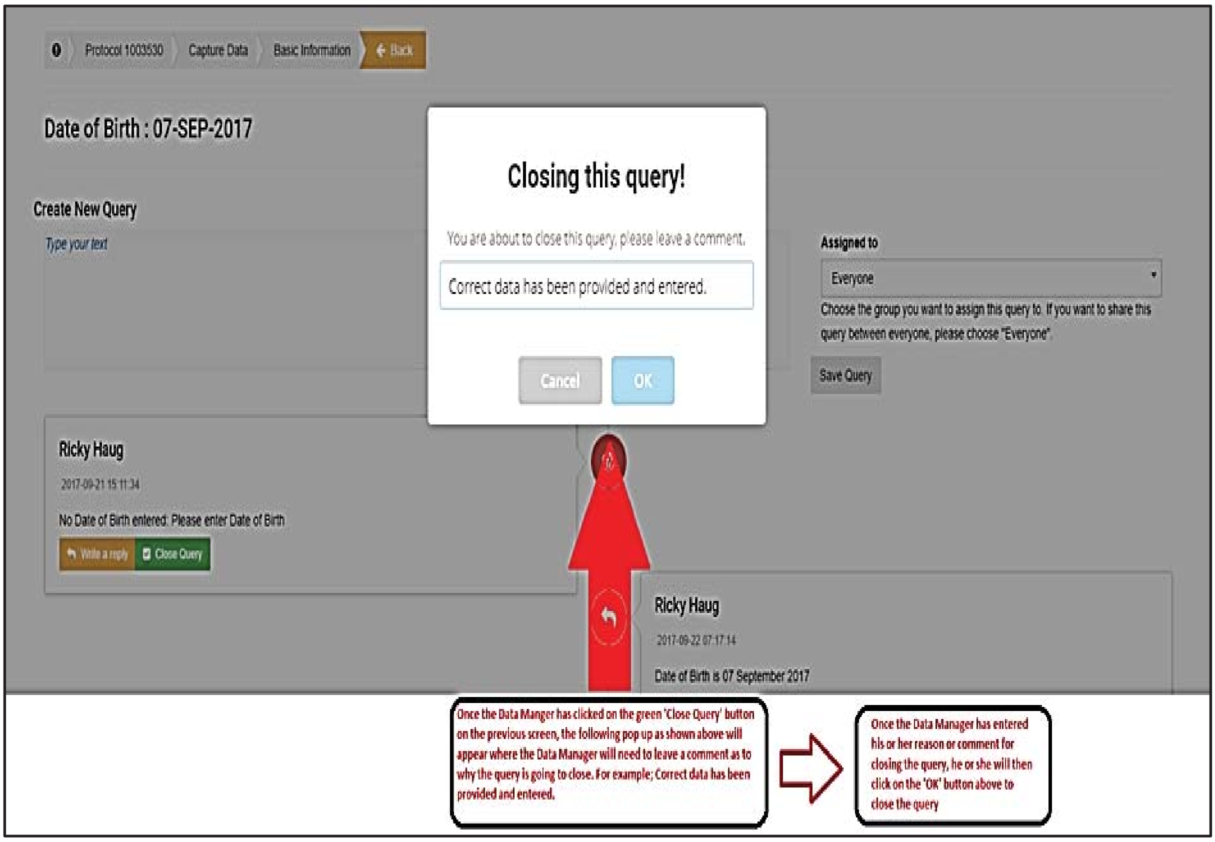


Figure 14: Example on how the query is closed

The screen then showed that the correct data was cleared and answered (Figure 15). The screen of the data manager returned to its original state once the query dashboard was closed (Figure 16).

Figure 15: Visualisation of screen when the query is cleared

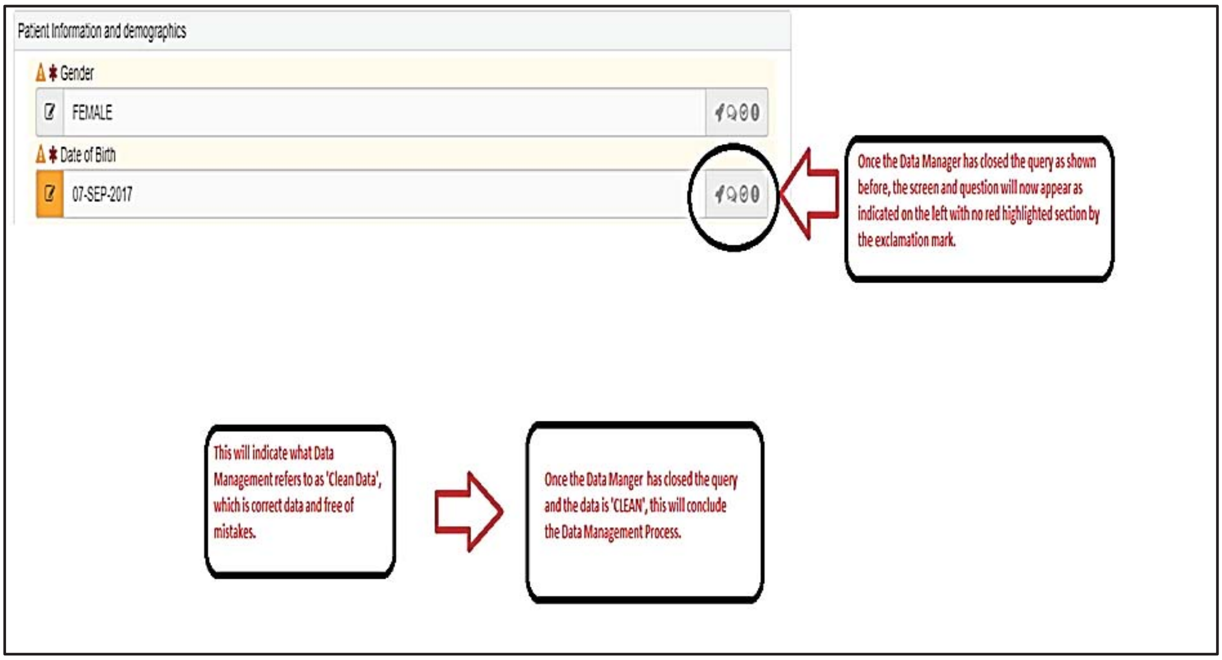


Figure 16: Example of original screen after answering the query

The system would then allow the data manager to confirm that the correct data was ready for further data management processes. The data was exported directly from Nukleus into an Excel™ spreadsheet database with each question in the CRF as a column in the Excel™-based database.

2.4 Basic Information of the Study Cohort

2.4.1 The study cohort

A total of 106 patients and their caregivers were enrolled from three hospitals where the study was conducted. Thirty-eight (38%) participating patients were from Donald Fraser, 10 (9%) from Louis Trichardt Memorial and 58 (55%) from Tshilidzini Hospital. In all these facilities, 45% of patients were treated in the paediatric medical ward, 33% were treated in the gastroenteritis ward and 22% did not specify the type of ward where the patient was treated.

There were fewer females with diarrhoea (44%) than males (56%). Most patients were inpatients (75%) and the remaining 25% were outpatients. Fifty-eight percent (58%) were referred from other health facilities while 42% went directly to hospital. The proportion of patients seeking medical attention for the first time in hospital were 93% and those patients seeking medical assistance elsewhere prior to hospital visit were 7%. The average age of the patients varied from 3 months to 60 months with the average weight ranging from 6 kg to 12 kg (Table 2).

Table 2: Weight summary grouped per age band

Age group	Average weight	Minimum weight	Maximum weight
3–6 months	6 kg	3 kg	9 kg
6–12 months	8 kg	3 kg	11 kg
12–24 months	9 kg	5 kg	13 kg
24–36 months	10 kg	8 kg	12 kg
36–48 months	12 kg	8 kg	14 kg
48–60 months	12 kg	10 kg	14 kg

2.4.2 Clinical information of the study cohort

The study indicated that 53% of the patients experienced diarrhoea with vomiting. High fever was recorded for 45% of the patients. Only 5% of patients had other diseases before the diarrhoea diagnosis. The diseases included asthma (one patient); flu (three patients) and malnutrition (one patient). Children with diarrhoea had an average of four and a maximum of nine loose stools per day. The sample with loose stools per hospital was calculated as a proportion of patients in that hospital (Table 3).

The proportion of patients with loose stools differed significantly ($p < 0.001$) between the Donald Fraser Hospital and the Louis Trichardt Memorial Hospital, as well as between Tshilidzini Hospital ($p = 0.013$). A statistically significant difference was found between Donald Fraser and Tshilidzini Hospital ($p = 0.028$). In addition, there was a statistically significant difference ($p = 0.0036$) between the patients who visited two hospitals with the symptoms of loose stools with cramps.

Table 3: Diarrhoea related symptoms at the current evaluation per hospital

Type of stool	Healthcare facility	Number of patients	P value between hospitals
Loose stools	Donald Fraser Hospital	38 (36%)	p < 0.001
	Louis Trichardt Memorial Hospital	4 (4%)	
	Tshilidzini Hospital	49 (46%)	
Loose stools = 91 (86%)			
Loose stools with cramps	Louis Trichardt Memorial Hospital	6 (6%)	p = 0.7055
	Tshilidzini Hospital	8 (8%)	
Loose stools with cramps = 14 (13.2%)			
Loose stools with cramps and blood	Tshilidzini Hospital	1 (0.9%)	N/A
Loose stools with cramps and blood = 1 (0.9%)			
Grand Total 106 (100%)			

2.4.3 Caregivers accompanied children in hospital

Nighty-four percent (94%) of children were accompanied by their mothers while the remaining (6%) were accompanied by grandmothers, guardians and other people. Thirteen (13; 12%) of the caregivers took their time off work to take children to the hospital.

Table 4 shows the number and proportion of caregivers who had to take time off work to bring their child to the facility for treatment. No statistically significant difference was found between the three hospitals in relation to the caregivers who took time off work (p = 0.1452). However, there was a significant difference (p = 0.05655) between the three hospital's caregivers who were not working or losing income.

Table 4: Number/proportion of caregivers who took time off from work to take patient to hospital

Did you take time off work?	Healthcare facility	Number of caregivers	P value per hospital
No	Donald Fraser	36 (34%)	p < 0.001
	Louis Trichardt Memorial	9 (9%)	
	Tshilidzini	47 (45%)	
Total = 92 (88%)			
Yes	Donald Fraser	1 (1%)	
	Louis Trichardt Memorial	1 (1%)	
	Tshilidzini	11 (11%)	
Total = 13 (12%)			
Grand Total = 105 (100%)			p = 0.1452

2.4.4 Household water supply and its impact on diarrhoea

Water, adequate sanitation and good hygiene must be provided to prevent diarrhoea to children under 5 years and the associated high cost of treatment. Households with children under 5 years with diarrhoea used a variety of water sources including communal taps, boreholes, canals, wells and rivers. The results indicated that households who accessed water from canals and/or rivers, and who used both borehole and tap water had the highest chance of contracting pathogenic bacteria and viruses (Figure 17). Communal tap water was safer than any other water source.

The results also support the findings from other researchers who tested the water and found that the water from communal taps was less contaminated than water from wells, rivers and boreholes (Brown et al., 2008 Mudau et al., 2016). A study done by Potgieter et al. (2006) indicated that there was a significant amount of water contamination of the borehole used by the communities in the Vhembe District Municipality. Traore et al. (2016) indicated microbial contamination in water from rivers that was used for water consumption.

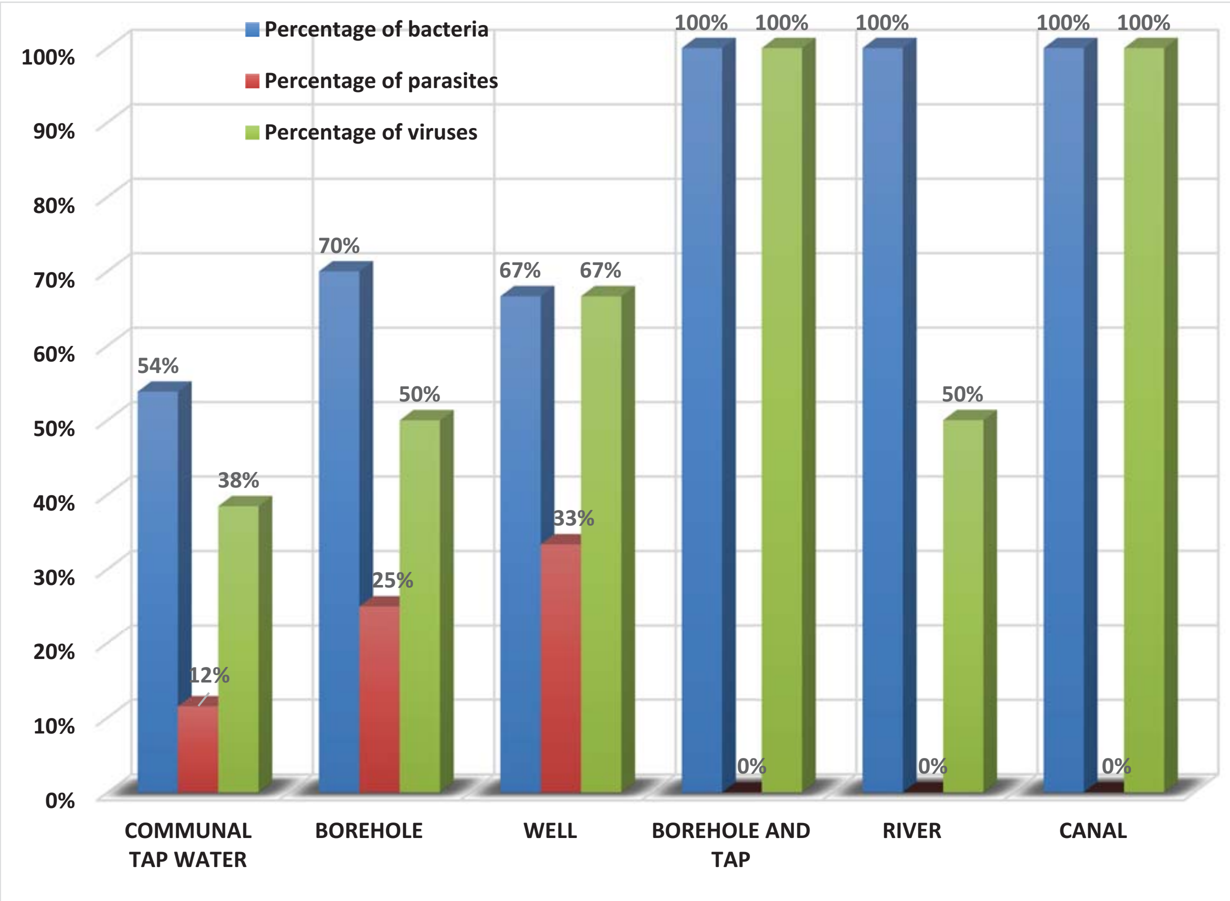


Figure 17: Bacteria, parasites and viruses in households using a specific primary water source

A multinomial logistic regression model was used to analyse the relationship between the primary water source of households and the presence of bacteria, parasites and viruses in the stool of babies who had diarrhoea as well as the facility they were treated (Table 5). The model used communal tap water as reference case for the dependent variable and Tshilidzini Hospital as reference case for the facility. The results indicated the relative risk (odds ratio) of having bacteria present in the baby's stool is 1.20 (an increase of 20%) and (increase of 90%) chance of having virus pathogens when using borehole instead of communal tap water. *ND* indicates instances that the data was not sufficient to fit that specific model. The worst scenario was detected in Donald Fraser (increase of 60%) as compared to other hospitals when assessing viruses, bacteria and parasites.

Table 5: Multinomial logistic regression model for primary water source

	Primary water source				
	Borehole	**Well**	**Borehole and tap**	**River**	**Canal**
Bacteria	1.202	1.257	ND	ND	ND
SE	**−0.607**	**−1.546**	**−0.213**	**−0.358**	**−0.277**
Parasites	2.8	ND	ND	ND	ND
SE	**−0.736**	**−1.02**	**0**	**0**	**0**
Viruses	1.897	ND	ND	1.605	ND
SE	**−0.567**	**−0.7**	**−0.213**	**−1.536**	**−0.277**
Donald Fraser Hospital	1.604	ND	ND	ND	ND
SE	**−0.602**	**−0.548**	**−0.213**	**−0.358**	**−0.277**
Louis Trichardt	ND	ND	ND	ND	ND
SE	**−0.78**	**0**	**0**	**0**	**0**
Constant	0.101^{***}	0.000^{***}	0.000^{***}	0.000^{***}	0.000^{***}
SE	**−0.599**	**−0.548**	**−0.213**	**−0.358**	**−0.277**
Akaike information criterion	193.744	193.744	193.744	193.744	193.744

ND – Not Detected SE – standard error $^{*}p^{**}p^{***}p < 0.01$

2.4.5 Water availability

The availability of the water sources in patients' households was reported for patients admitted in each hospital. The impact of unavailability of water versus the risk of contracting pathogenic organisms is shown in Table 6. A multinomial logistic regression model used Tshilidzini Hospital as the reference case for the dependent variable, and 1–2 days a week as reference case for the water availability. *ND* refers to where the data was not sufficient to fit that specific model. The results indicated that patients from Donald Fraser Hospital usually faced an intermittent water supply. The results indicated that the relative risk (odds ratio) of having bacteria present in the baby's stool is 1.45 (an increase of 45% of patients treated in Donald Fraser as compared to Tshilidzini Hospital). Sustainable access to safe water supply was a problem especially to patients in Donald Fraser where most people reside in rural areas.

Table 6: Multinomial logistic regression model of water availability between Donald Fraser and Louis Trichardt hospitals

	Donald Fraser Hospital	**Louis Trichardt Hospital**
Bacteria	1.453	ND
SE	**−0.466**	**−0.527**
Parasites	0.376^{*}	1.816
SE	**−0.763**	**−0.926**
Viruses	ND	ND
SE	**−0.467**	**−0.908**
Water available 4–5 days a week	0.387	0.612

	Donald Fraser Hospital	Louis Trichardt Hospital
SE	**−0.96**	**−1.172**
Water available everyday	ND	ND
SE	**−0.526**	**−0.962**
Water not available for more than a week	0.961	ND
SE	**−0.719**	**0**
Constant	0.943*	0.00000*
SE	**−0.512**	**−0.527**
Akaike information criterion	205.981	205.981

ND – Not Detected SE – standard error *p**p***p < 0.01

The study found that children staying in households with intermittent supply are at risk of getting diarrhoea. A study by Majuru et al. (2011) indicated that intermittent water supply increases the chance of diarrhoea in communities especially to vulnerable groups, which include children under the age of 5. Bivins et al. (2017) indicated that the pressure of climate change, pipe breakages and poor water management increase the chances of intermittent supply. The authors further indicated that where intermittent water supply is a challenge, most water sources are found to be contaminated by faeces: this causes millions of children to be affected by diarrhoea. Consequently, the burden of diarrhoea demands the use of healthcare resources to treat and manage such illnesses.

2.4.6 Risk of storing water inside household storage containers

Due to the intermittent water supply, many households store water inside household storage containers. Different types of container such as buckets, jerry cans or cans with small top screws, and drums were used to store water. The results in Table 7 show that the relative risk (odds ratio) of having bacteria present in a baby's stool is 1.72 (an increase of 72%) when water is stored in a bucket and small screw-cap jerry can versus the reference of water not stored. Loose stools were the reference for the type of stool variable.

ND refers to where the data was not sufficient to fit that specific model. From the storage containers used in the study group, 95% of households responded that their containers did have a lid, and 93% of water was stored inside the house. In this study, most children who tested positive for the prevalence of pathogenic bacteria and viruses were using water stored in containers in the households. These findings support the study done by various authors indicating high contamination of water stored in containers (Shwe, 2010; Vannavong et al., 2017). Mudau et al. (2017) indicted that there is higher risk of getting diarrhoea using water stored inside a container than using water directly from a tap. Hunter et al. (2010) indicated that using stored water inside a container attributes to health impact. Bartram and Cairncross (2010) suggested that point-of-use water treatment increases health gain.

Table 7: Multinomial logistic regression model for storage containers

	Storage containers								
	Bucket	**Bucket and small screw jerry can**	**Drum**	**Drum and small screw jerry can**	**Drums and buckets**	**JoJo water**	**Small screw-cap jerry can**	**Tank**	**Do not store water**
Bacteria	1.718	1.653	2.945	1.657	ND	ND	1.83	2.95	ND
SE	**−0.98**	**−1.611**	**−1.521**	**−1.62**	**−0.681**	**0**	**−0.971**	**−1.346**	**−0.461**
Parasites	0.549	6.183	1.453	2.127	ND	ND	0.738	0.494	0.00003
SE	**−1.318**	**−2.079**	**−1.737**	**−1.795**	**0**	**0**	**−1.289**	**−1.698**	**−910.85**
Viruses	1.111	9.137	2.032	1.103	0.994	0.00000^{***}	1.892	0.000^{***}	ND
SE	**−0.977**	**−1.837**	**−1.403**	**−1.571**	**−1.714**	**−0.00001**	**−0.964**	**0**	**−0.461**
Loose stools with cramps	0.298	0	0.495	0.894	0.000^{***}	ND	0.158^{*}	0.000^{***}	0.000^{***}
SE	**−1.03**		**−1.495**	**−1.561**	**0**	**−0.728**	**−1.055**	**0**	**0**
Loose stools with cramps and blood	ND	ND	ND	ND	ND	ND	ND	ND	ND
SE	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Constant	5.919^{**}	0.117	0.285	0.311	ND	ND	6.328^{**}	1.25	ND
SE	**−0.732**	**−1.746**	**−1.31**	**−1.299**	**−0.681**	**−0.728**	**−0.728**	**−0.986**	**−0.461**
Akaike information criterion	396.425	396.425	396.425	396.425	396.425	396.425	396.425	396.425	396.425

ND – Not Detected SE – standard error $^{*}p^{**}p^{***}p < 0.01$

2.4.7 Sanitation conditions in households of patients

The impact of sanitation and hygiene status in patient's households was assessed. The majority (93%) of caregivers have toilets at home. The majority of caregivers at Tshilidzini Hospital used pit latrines (43.3%) followed by caregivers from Donald Fraser Hospital (29.9%) (Table 8).

Bacteria, parasites and viruses found in the stools of children where households use either a pit latrine or a flush toilet are shown in Figure 18. The type of sanitary system available at home did not suggest the absence of pathogenic bacteria, viruses and parasites in stools.

Table 8: Types of toilet facilities available in households per facility

Sanitation type	Health facility	No. and proportion (%) of patients
Pit latrine	Donald Fraser Hospital	29 (29.9%)
	Louis Trichardt Memorial Hospital	4 (4.12%)
	Tshilidzini Hospital	42 (43.3%)
Flush toilet	Donald Fraser Hospital	6 (6.19%)
	Louis Trichardt Memorial Hospital	3 (3%)
	Tshilidzini Hospital	11 (11.34%)
Ventilated improved pit	Louis Trichardt Memorial Hospital	2 (2.06%)
Grand total		**97 (100%)**

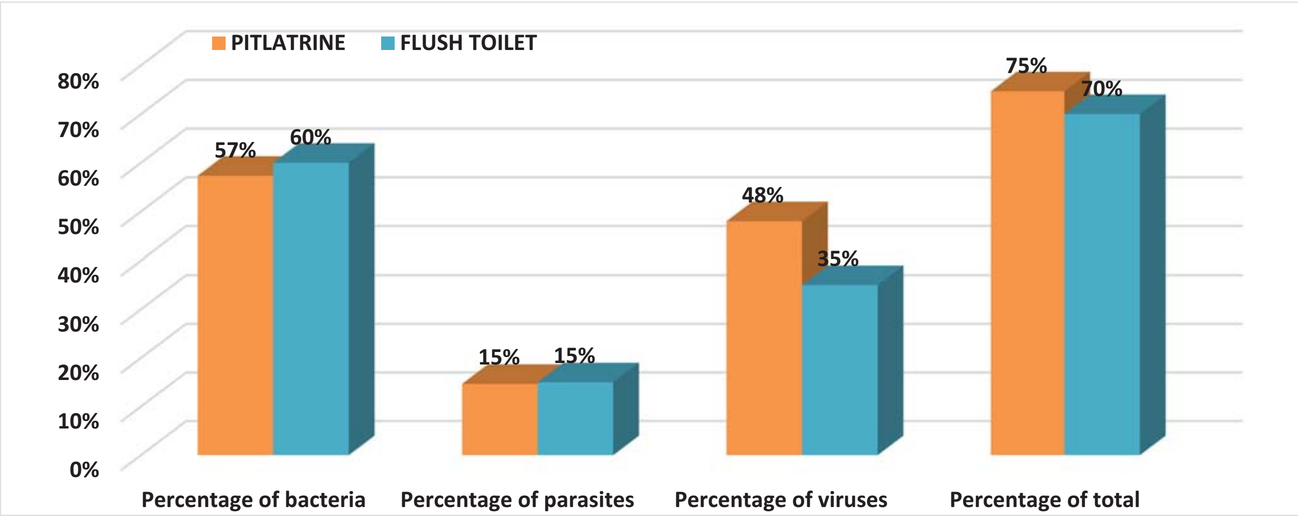


Figure 18: Bacteria, parasites and viruses in stools of children in households using pit latrine/flush toilet

The study assessed sanitation and hygiene status in patients' households. Caregivers were asked to provide information concerning the cleanliness of their household and sanitary facilities. The caregivers who claimed to use clean toilets were 94%. A total of 48% reported that they have observed flies in their toilets (Figure 19). It was noted that where pit latrines are used most, caregivers were able to detect the availability of flies. It is well-known that the presence of flies contributes to transmission of diseases as indicated by Conant and Fadem (2008) and Phoku et al. (2014).

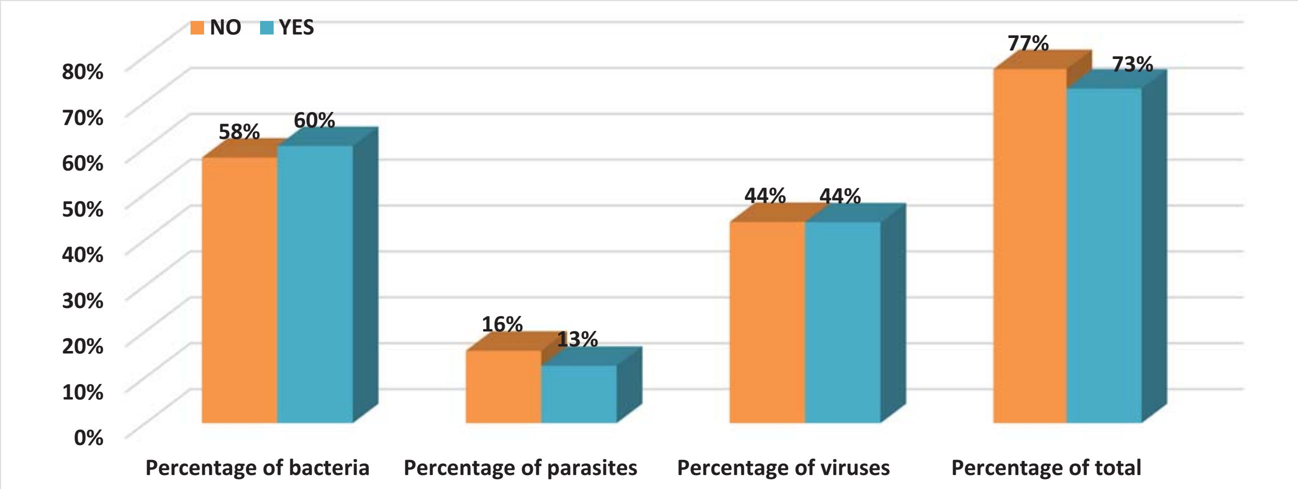


Figure 19: Bacteria, parasites and viruses in stools of children in households who observed flies in their toilets

2.4.8 Hygiene practices in households of patients

2.4.8.1 Handwashing with soap

The number of caregivers reported to wash their hands with soap was 60%. In most cases, handwashing was reported to be done before eating, when hands were soiled, after touching waste, when preparing food and when changing nappies. Mothers/caregivers who did not wash their hands blamed it on forgetfulness and the scarcity of water being a challenge. Townsend et al. (2017) indicated that the annual cost of not washing hands in India costs the government billions in USD. A statistically significant difference was found between patients who do not wash their hands before handling the baby between three hospitals at a global level ($p < 0.001$) (Table 9).

Table 9: Caregivers who wash their hands before handling their baby (per hospital)

	Name of facility	**Number and proportion (%) of patients**
Do not wash hands	Donald Fraser Hospital	5 (4.72%)
	Louis Trichardt Memorial Hospital	6 (5.66%)
	Tshilidzini Hospital	41 (38.68%)
Wash hands	Donald Fraser Hospital	32 (30.19%)
	Louis Trichardt Memorial Hospital	4 (3.77%)
	Tshilidzini Hospital	17 (16.04%)
Grand total		106 (100.00%)

There was a significant difference between Donald Fraser and Louis Trichardt ($p = 0.013$), as well as between Donald Fraser and Tshilidzini Hospital ($p < 0.001$). A statistically significant difference ($p < 0.001$) was found between patients who wash their hands before handling the child between the three hospitals. Significance difference was seen between Donald Fraser and Louis Trichardt hospitals ($p = 0.028$), and between Donald Fraser and Tshilidzini hospitals ($p < 0.001$).

No statistically significant difference was found between the percentage of bacteria ($p = 0.633$), parasites ($p = 0.248$) and viruses ($p = 614$) of caregivers who do wash their hands versus caregivers who do not wash their hands (Figure 20). The reason the caregivers do not wash hands frequently indicated that 25% do not have handwashing facilities, majority of them forget (63%), 10% felt it was not important, and 2% did not have a reason.

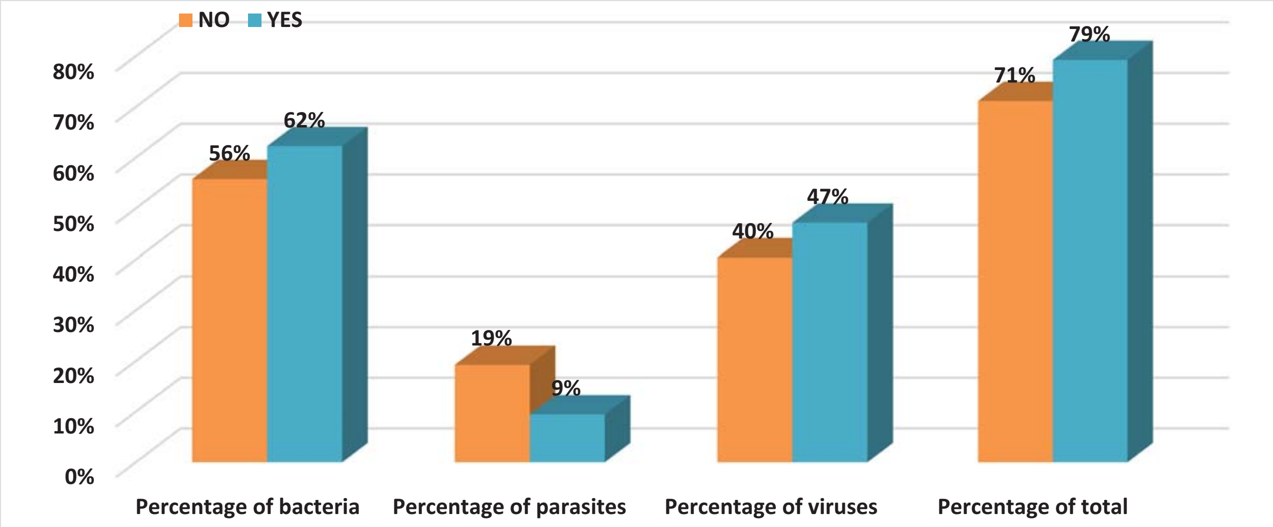


Figure 20: Bacteria, parasites and viruses in stools of children of caregivers who wash their hands before handling the child

2.4.8.2 Handwashing during food preparation

The results in Table 10 indicate that the relative risk (odds ratio) of having bacteria present in a baby's stool is 2.442 (an increase of 142%) when using formula milk with boiled water compared to breast milk. Loose stools were the reference for the type of stool variable. High percentages of bacteria were observed across all methods used for food preparations (Figure 21).

Table 10: Multinomial logistic regression model for method of food for children

	Food given to children	
	Formula milk using boiling water	**Other**
Bacteria	2.442	1.161
SE	−0.702	−0.465
Parasites	0.528	2.156
SE	−1.22	−0.694
Viruses	1.04	1.06
SE	−0.663	−0.467
Loose stools with cramps	1.766	2.622
SE	−0.984	−0.714
Loose stools with cramps and blood	ND	0.017
SE	ND	−6.636
Constant	0.202^{***}	0.914
SE	−0.611	−0.374
Akaike information criterion	221.415	221.415

ND – Not Detected SE – standard error $^{*}p^{**}p^{***}p < 0.01$

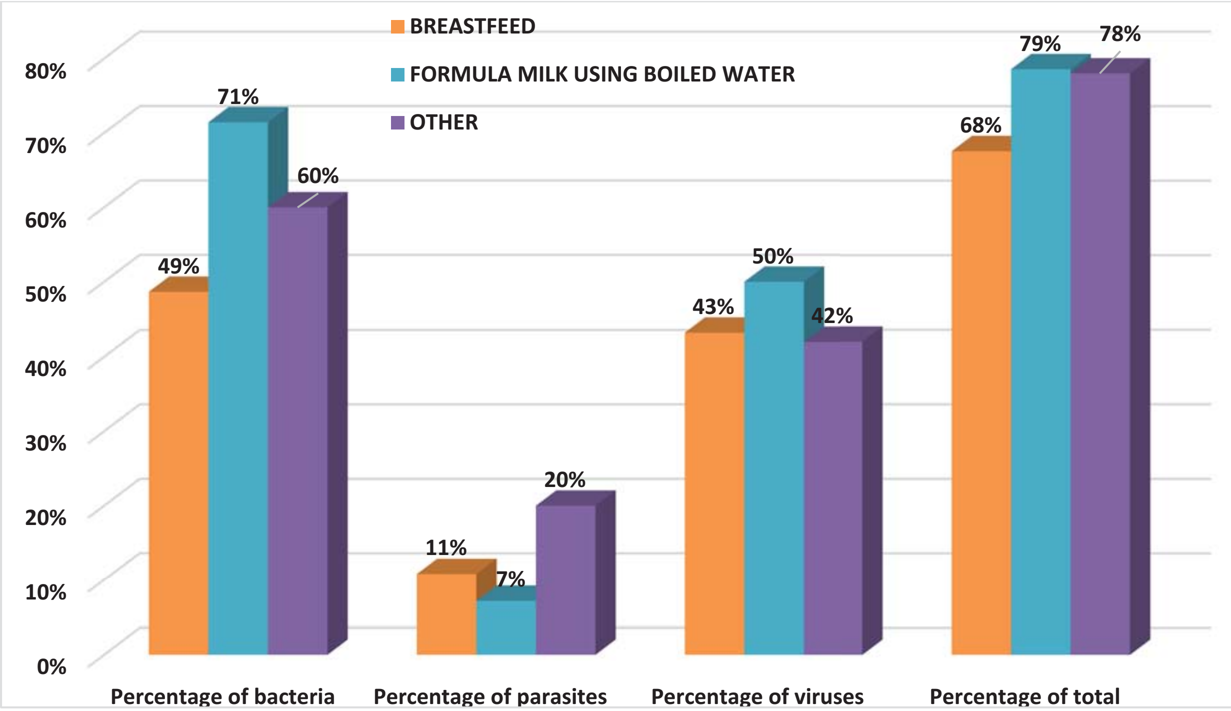


Figure 21: Bacteria, parasites and viruses in stools of children given the method of food preparation by their caregiver

CHAPTER 3 ESTIMATING THE COST OF TREATING DIARRHOEA

3.1 Introduction

Diarrhoeal disease has a great impact on poor and developing countries as the treatment of diarrhoeal diseases comprises a major portion of their healthcare budget. Treatment of diarrhoea in healthcare facilities differs among countries. Administering correct diarrhoea treatment is a challenge to most professionals in most developing countries. Despite the guidelines and regulations that are provided, most treatments prescribed by physicians and nurses are not the same. Health practitioners generally use their own perceptions and observations to manage childhood diarrhoea, which in many cases leads to poor management and harmful practices (Carter et al., 2015).

Most countries use the guideline suggested by the World Health Organization (WHO, 2005). However, many healthcare professionals do not follow these guidelines. Oral rehydration solution (ORS) is recommended for acute diarrhoea. A study by Bhutta et al. (2013) indicated that using ORS in children under 5 years reduces diarrhoea mortality by 69% and treatment failure by almost 2%. Mothers and caregivers are also taught to use ORS to control diarrhoea. The most common challenge is that most professionals and caregivers believe that ORS alone cannot cure diarrhoea (Zwisler et al., 2013).

A study done in Ghana indicated that most caregivers do not administer ORS (El-Khouri et al., 2016) as they claim that their children cannot take it; hence, many may resort to the use of antibiotics, which is not necessary for acute diarrhoea to be treated. In India, a study in Maharashtra Hospital on the use of drugs and cost of treatment of diarrhoea in secondary level government hospitals reported that most general medical practitioners prescribed antibiotics in cases where only ORS is required (Shillcutt et al., 2017). In this section, the cost of treating diarrhoea in children under the age of 5 years in the Vhembe District, Limpopo Province, is determined.

3.2 Methods

3.2.1 Prevalence of diarrhoea pathogens in stool samples

A faecal swab with Cary Blair transport media was obtained from each child, stored inside a cooler box with ice, and transported to the laboratory at the University of Venda. A total of 91 stool samples were collected to establish the presence of pathogens related to water and sanitation as the anticipated risk for diarrhoea prevalence. Stool samples were analysed according to the procedures described in Appendix 1.

3.2.2 Diarrhoea costing model

The diarrhoea costing model adopted from the epidemiological burden of disease model developed by the CDC (2007) was used to assess the treatment cost of diarrhoea. The study selected essential areas with high ability to escalate the healthcare budget. The variables identified were professional service required by patients, emergency unit including intensive care unit (ICU) and high care services as well as prescribed medical treatment. The study calculated direct and indirect cost of diarrhoea. Diarrhoea costing was also done to assess socio-economic measures.

3.2.3 Statistical analysis

Microsoft Excel™ was used for data capturing, management and descriptive statistics. R Studio version 0.99.489 was used for analysis. Significance level was tested at the 95% where a p value of 0.05 was considered statistically significant. Test of significance includes the pairwise comparisons. Where the dependent variable was nominal with more than two levels, a multinomial logistic regression analysis was conducted. Multinomial regression is an extension of logistic regression, which analyses dichotomous (binary) dependents. Multinomial regression was used to describe data and to explain the relationship between one dependent nominal variable and one or more continuous-level (interval or ratio scale) independent. Regression was used to estimate the risk of infection related to WASH. Correlation of diarrhoea information and risk analyses was done.

3.3 Pathogenic Microorganisms in Stool Samples

Ninety-one (n = 91) stool samples were collected to analyse bacteria, parasites and viruses. The presence of each organism detected in diarrhoea stools are shown in Table 11. Enteroaggregative *Escherichia coli* (EAEC) (50%), Enteropathogenic *E. coli* (EPEC) (37%), norovirus (32%), entero–toxigenic *E. coli* (ETEC) (24%), *Shigella*/enteroinvasive *E. coli* (EIEC) (19%), adenovirus (14%) and *Campylobacter* (13%) were the most detected pathogenic organisms in diarrhoea stools.

Table 11: Pathogenic microorganisms detected in diarrhoea stools

Microorganism	Type of microorganism	Number of stools with pathogen	Percentage
Campylobacter	Bacteria	12	13%
C. difficile toxin A/B	Bacteria	3	3%
Plesiomonas shigelloides	Bacteria	2	2%
Salmonella	Bacteria	3	3%
Vibrio	Bacteria	0	0
V. cholerae	Bacteria	0	0
Yersinia enterocolitica	Bacteria	0	0
EAEC	Bacteria	45	50%
EPEC	Bacteria	34	37%
ETEC	Bacteria	22	24%
STEC	Bacteria	2	2%
E. coli O157	Bacteria	0	0
Shigella/EIEC	Bacteria	17	18.7%
Cryptosporidium	Parasite	10	11%
Cyclospora cayetanensis	Parasite	0	0
Entamoeba histolytica	Parasite	0	0
Giardia lamblia	Parasite	7	7.7%
Adenovirus F 40/41	Virus	13	14.3%
Astrovirus	Virus	1	1.1%
Norovirus GI/GII	Virus	29	31.9%
Rotavirus A	Virus	9	9.9%
Sapovirus	Virus	2	2.2%

3.4 Estimating the Cost of Diarrhoea Treatment

3.4.1 Caregiver's indirect costs

Caregivers were asked if they have taken time off from work to bring the child to hospital to determine the productivity time and income lost due to accompanying child to hospital. Seeking medical care for children affected by diarrhoea could take valuable time that could have been used for other activities. Most caregivers were involved in informal business and casual work. Out of 13 caregivers (12%) who took time off work to bring their child to the facility, 11 (85%) lost the money they should have earned on that day because they had to bring their child to the facility. The average amount lost by these caregivers for a day was R134 and the total income lost by all caregivers in a day was R1478.00.

Loss of income by caregivers could affect households where caregivers are breadwinners. It is of interest to find out that the study done by MacIntyre and De Villiers (2010) in one of the tertiary hospitals indicated the loss of income by caregivers. The study further reported on the indirect cost such as transport fees paid to bring the child to hospital as well as other expenses incurred when seeking healthcare treatment somewhere (MacIntyre & De Villiers, 2010). Carvajal-Vélez et al. (2016) indicated that good management of diarrhoea illnesses at home could reduce the need of medical care and save the costs required to seek medical care.

3.4.2 Medicine prescribed for outpatient's treatment

A total of 26 patients were treated for diarrhoea as outpatients. Table 12 indicates the type of treatment provided, symptoms presented by the patients and the facility that prescribed the medicine. The treatment types are further broken down by diarrhoea condition (

Table 13) and facility (Table 14).

Table 12: Types of treatment provided for treating diarrhoea out of hospital

Types of treatment provided for treating diarrhoea out of hospital	Number and proportions (%) of patients
ORS and antibiotics	8 (31%)
ORS and pain medicine	10 (38%)
ORS only	8 (31%)
Total	**26 (100%)**

Table 13: Treatment provided for treating diarrhoea out of hospital (by diarrhoea condition)

Types of treatment provided for treating diarrhoea out of hospital	Number and proportion (%) of patients	
	Loose stools	Loose stools with cramps
Rehydration and antibiotics	3 (3%)	5 (36%)
Rehydration and pain medicine	7 (8%)	3 (21%)
Rehydration only	7 (8%)	1 (7%)
Total	**17**	**9**

Table 14: Types of diarrhoea treatment provided for outpatients as per hospital facility

Types of treatment provided for treating diarrhoea out of hospital	Number and proportion (%) of patients		
	Donald Fraser Hospital	Louis Trichardt Memorial Hospital	Tshilidzini Hospital
ORS and antibiotics		7 (70%)	1 (2%)
ORS and pain medicine	2 (100%)		8 (14%)
ORS only		3 (30%)	5 (9%)
Total	**2**	**10**	**14**

A two-sample test for equality of proportions was used to calculate the difference regarding the types of treatment provided between patients with different diarrhoea symptoms. The proportion of each type of treatment per diarrhoea condition was calculated as a proportion of patients who had that condition. There was a statistically significant difference in the proportion of patients on ORS and antibiotics between those with loose stools and those with loose stools and cramps ($p< 0.001$). There was no significant difference in the proportion of patients who received rehydration and pain medicine and between those with loose stools and those with loose stools and cramps ($p = 0.254$). There was no significant difference in the proportion of patients who received rehydration only between those with loose stools and those with loose stools and cramps ($p = 1$).

The significance difference on the types of treatment provided between the three hospitals were tested using the three-sample test for equality of proportions without continuity correction. The proportion of each type of treatment per hospital was calculated as a proportion of patients in that facility as indicated in Table 14. There was a statistically significant difference in the proportion of patients who received ORS and antibiotics treatment between the different facilities ($p < 0.001$). The proportion of patients who received ORS and antibiotics differed significantly ($p < 0.001$) between Donald Fraser Hospital and Louis Trichardt Hospital as well as between Louis Trichardt Hospital and Tshilidzini hospitals ($p < 0.001$).

There was no statistically significant difference between Donald Fraser and Tshilidzini hospitals ($p = 1$). For ORS and pain medicine, no statistically significant differences were found between all hospitals ($p = 0.212$). For ORS only, a statistically significant difference was found between all hospitals ($p = 0.005$). There was a statistically significant difference between Donald Fraser and Louis Trichardt hospitals ($p = 0.018$), but not between any of the other facilities ($p = 0.319$).

Table 14 indicates the medicines prescribed for each treatment provided to outpatients. There was a whole range of different antibiotics prescribed, which was unnecessary when benchmarking according to the *Standard Treatment Guidelines and Essential Medicines List for South Africa – Hospital Level Paediatrics* (Department of Health, 2014a; 2014b) and the *Standard Treatment Guideline and Essential Medicine List for South Africa*. Table 15 and Table 16 show diarrhoea caused by different organisms.

Table 15: Standard Treatment Guidelines and Essential Medicines List for South Africa (Department of Health, 2014a; 2014b)

Diarrhoea condition	Organism	Antibiotics	Other
Acute diarrhoea	All		Zinc (elemental) Potassium chloride

Diarrhoea condition	Organism	Antibiotics	Other
Acute diarrhoea	Dysentery	Ceftriaxone Ciprofloxacin	
	Entamoeba histolytica	Metronidazole	
	Typhoid	Ceftriaxone	
	Severe malnutrition or very young infants (28 days old)	Ampicillin Gentamicin	
	V. cholerae	Ciprofloxacin	Zinc (elemental)
Persistent diarrhoea (diarrhoea for longer than two weeks)	*Campylobacter*	Erythromycin	
	G. lamblia	Metronidazole	
	Y. enterocolitica	Ceftriaxone Cefotaxime	
	Isospora belli		Co-trimoxazole
	Cyclospora cayetanensis		Co-trimoxazole
	Microsporidia		Albendazole
Dysentery (persistent diarrhoea with blood in stool)	*Shigella*	Ciprofloxacin Cefotaxime Ceftriaxone	
	Entamoeba histolytica	Metronidazole	

Table 16: The treatment guidelines for diarrhoea treatment in South Africa (Department of Health, 2014a; 2014b)

Condition	Description	Treatment
Diarrhoea, acute in children	A sudden onset of increased frequency of stools that are looser than normal, with or without vomiting. Commonly caused by a virus but may be caused by bacteria or parasites. The cause of acute diarrhoea cannot be diagnosed without laboratory investigation. It may be an epidemic if many patients are infected at the same time.	Ceftriaxone, intramuscular, 80 mg/kg/dose immediately as a single dose.
		Sodium chloride 0.9%, intravenously, 20 mL/kg.
		ORS, oral, 80 mL/kg over 4 hours, e.g. 5 ml/kg every 15 minutes.
		Zinc (elemental), oral for 14 days.
Diarrhoea, persistent in children	Diarrhoea for 7–14 days.	Vitamin A (retinol), oral.
		Infants 6–11 months old, 100 000 1 capsule.
		Children 12 months to 5 years, 200 000 2 capsules.
		Zinc (elemental), oral for 14 days.

The medicines prescribed for treating diarrhoea out of hospital are shown in Table 17. Data on medicines prescribed for diarrhoea out of hospital was not provided for five patients. Table 17 indicates the pathogenic microorganisms causing the diarrhoea as well as the medicine prescribed. The study indicated that antibiotics were prescribed where pathogenic organisms were not detected. For patients linked to Donald Fraser Hospital, medicines such as oral rehydration sachets, paracetamol and Ilvitrim were prescribed. This was not in line with treatment guidelines for treatment of acute diarrhoea. For patients linked to Louis Trichardt Hospital, several patients were not treated as per guidelines (for instance, patients receiving co-trimoxazole/Ilvitrim and Amyn/amoxicillin). For patients linked to Tshilidzini facility also, most patients were not treated as per standard guidelines (for instance, patients receiving co-trimoxazole/Ilvitrim and Amyn/amoxicillin).

Table 17: Medicines prescribed for treating diarrhoea for outpatients and organisms causing diarrhoea

Medicines prescribed	Number of patients	Organism isolated from stool
ORS	1	EAEC EPEC Norovirus GI/GII
ORS, gentamicin	1	EPEC ETEC
ORS, zinc, co-trimoxazole, vitamin B complex	1	EAEC EPEC Norovirus GI/GII
ORS and Amyn	1	No organism specified
ORS and zinc	1	No organism specified
ORS (2), paracetamol and Ilvitrim	4	Organisms specified for one patient only: *Campylobacter* EAEC EPEC ETEC *Shigella*/EIEC Norovirus GI/GII
ORS, Amyn, Ilvitrim and paracetamol	1	No organism specified
ORS, Ilvitrim, paracetamol and vitamin B syrup	1	No organism specified
ORS, paracetamol, zinc and multivitamin syrup	2	Organisms specified for one patient only: EAEC EPEC *Giardia lamblia*
ORS, zinc and Amyn	3	Organisms specified for one patient only: EAEC Norovirus GI/GII
ORS, paracetamol and Ilvitrim	1	No organism specified
ORS (2), zinc and paracetamol	2	No organisms specified
ORS, zinc and paracetamol	1	No organism specified
ORS, Flagyl suspension and paracetamol	1	No organism specified
Total	**21**	

Table 18: Medicines prescribed for treating diarrhoea out of hospital (by facility and diarrhoea condition)

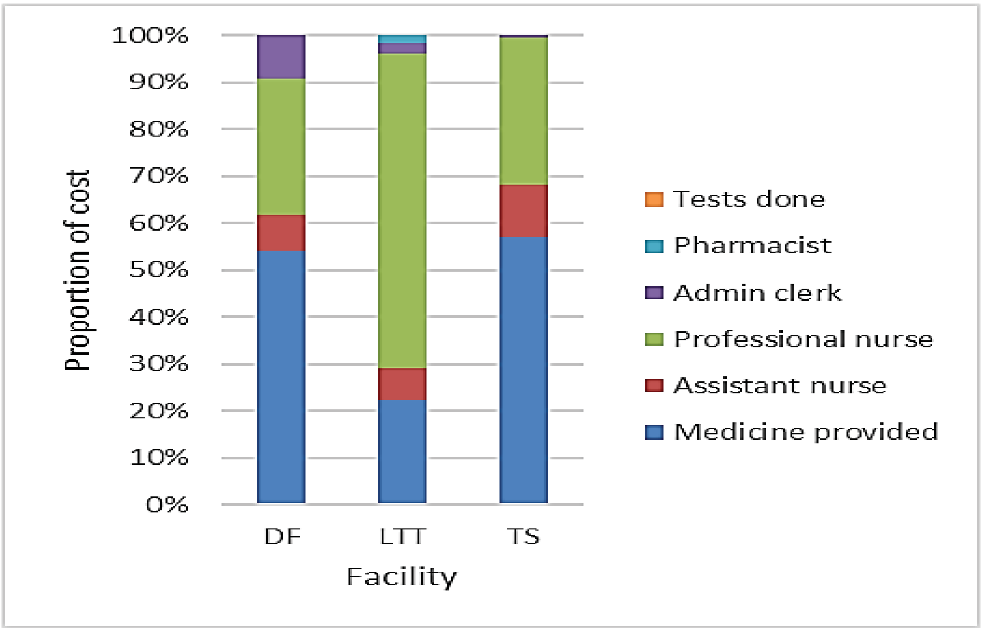
Medicines prescribed	Donald Fraser Hospital	Louis Trichardt Memorial Hospital		Tshilidzini Hospital	
	Loose stools	Loose stools	Loose stools with cramps	Loose stools	Loose stools with cramps
ORS			1		
ORS, gentamicin			1		
ORS, zinc, co-trimoxazole, vitamin B complex			1		
ORS, Amyn					1
ORS, zinc				1	
ORS, paracetamol, Ilvitrim	2			2	
ORS, Amyn, Ilvitrim, paracetamol					1
ORS, Ilvitrim, paracetamol, vitamin B syrup				1	
ORS, paracetamol, zinc, multivitamin syrup		1		1	
ORS, zinc, Amyn			1	2	
Rehydration, paracetamol, Ilvitrim				1	
ORS, zinc, paracetamol				3	
ORS, Flagyl suspension, paracetamol					1
Total	**2**	**1**	**4**	**11**	**3**

From Table 18 it is clear that all hospitals prescribe antibiotics where not necessary, which is a waste of resources. One patient was indicated to have received treatment for a disease other than diarrhoea out of hospital. This patient was indicated to have had flu. This patient received ORS only for diarrhoea.

Loose stools at Donald Fraser facility were treated with ORS, paracetamol and Ilvitrim. In Louis Trichardt Hospital, loose stools were treated with ORS, paracetamol, Zinc and multivitamin syrup. In Tshilidzini Hospital, loose stools were treated with a variety of medicine, including ORS, paracetamol, Ilvitrim and Zinc. Loose stools with cramps were treated with a variety of medicine, including ORS and zinc, at Louis Trichardt Memorial hospital, while this was treated with other medicine including ORS, paracetamol and/or Amyn at Tshilidzini Hospital.

3.4.3 Direct cost for outpatient treatment

Figure 22 indicates the distribution of costs by facility between different cost elements. The highest amount was spent on medicine provided in the Donald Fraser and Tshilidzini facilities, followed by the amount of time spent on professional nurse services. The highest amount in Louis Trichardt was spent on professional nurses, followed by medicine provided. The total costs for treatment of outpatients with diarrhoea by facility are shown in Table 19.



DF – Donald Fraser, LTT – Louis Trichardt Memorial, TS –Tshilidzini

Figure 22: Proportion of cost for outpatient care

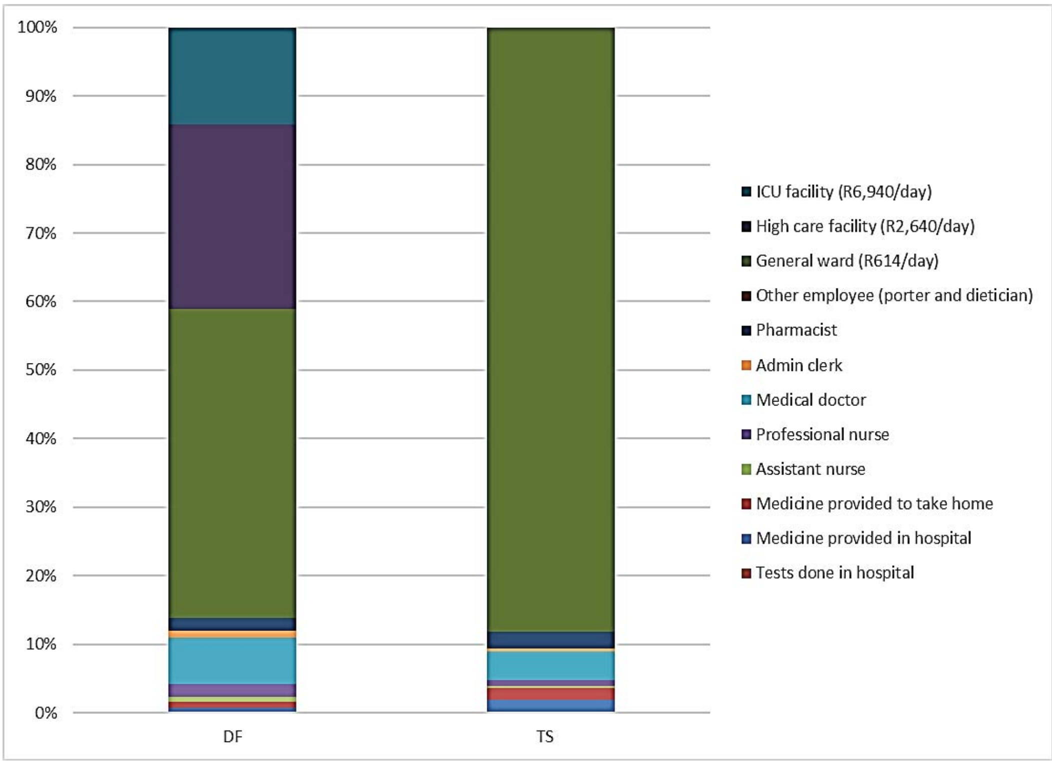
Table 19: Total costs associated with outpatient treatment of diarrhoea

Cost parameters	Cost (ZAR)
Tests done	N/A
Medicine provided	R426
Assistant nurse	R92
Professional nurse	R481
Admin clerk	R20
Assistant pharmacist	R7
Total	R1027

Table 20 and Figure 23 compare the direct cost incurred out of hospital. Table 20 illustrates the average cost of treating outpatients with diarrhoea calculated by dividing the total cost by the number of total outpatients (R1027/26 = R40). The average cost of treating a patient as an outpatient with diarrhoea (for a patient at Donald Fraser facility) was calculated by dividing the total cost by the number of patients treated as outpatients at Donald Fraser Hospital (R88/2 = R44). The average cost of treating a patient for diarrhoea as an outpatient (for a patient at Louis Trichardt facility) was calculated by dividing the total cost by the number of outpatients at Louis Trichardt Memorial facility (R451/10 = R44).

Table 20: Total costs associated for treating outpatients with diarrhoea (by facility)

Cost parameters	Cost (ZAR)		
	Donald Fraser Hospital	**Louis Trichardt Memorial Hospital**	**Tshilidzini Hospital**
Tests done	0	0	0
Medicine provided	R47	R101	R278
Assistant nurse	R7	R31	R55
Professional nurse	R25	R303	R153
Admin clerk	R0	R0	R0
Assistant pharmacist	R8	R10	R3
Total	**R88**	**R451**	**R488**



DF – Donald Fraser, TS – Tshilidzini

Figure 23: Distribution of costs associated with treating patients with diarrhoea who are treated in hospital (by facility, per cost element)

The average cost of treating outpatients for diarrhoea (for patients at Tshilidzini facility) was calculated by dividing the total cost by the number of outpatients treated at Tshilidzini facility (R488/14 = R35) as outlined in Table 21. One outpatient was indicated to have received treatment for a disease other than diarrhoea. This patient was indicated to have had flu. The total cost for treating the flu was indicated to be R20 (this is the cost of medicine provided – Allergex syrup, cough mixture and paracetamol).

Table 21: Comparison of direct cost for outpatients between facilities

Cost parameter	Cost (ZAR)			
	Donald Frazer Hospital	Louis Trichardt Hospital	Tshilidzini Hospital	Total
Number of patients	2	10	14	26
Min	R40	R23	R24	R23
Max	R48	R97	R48	R97
Mean/average	R44	R45	R35	R40
Median	R44	R33	R36	R36
Standard deviation	R6	R26	R7	R17
Total cost (sum)	**R88**	**R451**	**R488**	**R1 027**

3.4.4 Treatment provided for inpatient care

Eighty (80) patients were admitted to three hospitals. The average length of stay for patients in both Tshilidzini and Donald Fraser facility was two days. The treatment provided for most patients was ORS and antibiotics (49%). The types of treatment provided for treating diarrhoea in hospitals are shown in Table 22.

Table 22: Types of treatment provided for inpatients

Types of treatment provided for treating diarrhoea in hospital	Number and proportion (%) of patients
Other	2 (3%)
ORS and antibiotics	39 (49%)
ORS and pain medicine	26 (33%)
ORS only	13 (16%)
Total	**80 (100%)**

For patients treated with other treatments, there were no significant differences in the proportion of patients with different diarrhoea conditions ($p = 0.845$). Apparently also with patients treated with rehydration and antibiotics, there were no significant differences in the proportion of patients with different diarrhoea conditions ($p = 0.343$) as shown in Table 23. For patients treated with ORS and pain medicine, there were no significant differences in the proportion of patients with different diarrhoea conditions ($p=0.219$). For patients treated with ORS only, there were no significant differences in the proportion of patients with different diarrhoea conditions ($p = 0.295$).

Table 23: Types of treatment provided for treating diarrhoea in hospital (by diarrhoeal condition)

Types of treatment provided for treating diarrhoea in hospital	Number and proportion (%) of patients		
	Loose stools	Loose stools with cramps	Loose stools with cramps and blood
Other	2 (2.20%)		
ORS and antibiotics	34 (37.36%)	4 (28.57%)	1 (100.00%)
ORS and pain medicine	25 (27.47%)	1 (7.14%)	
ORS only	13 (14.29%)		
Total	**74**	**5**	**1**

For patients treated with other medicine, there were no significant differences in the proportion of patients between different facilities ($p = 0.301$). However, in patients treated with ORS and antibiotics, there was a significant difference in the proportion of patients treated at the Tshilidzini facility compared to the Donald Fraser facility ($p < 0.001$). While for patients treated with ORS and pain medicine, there was a significant difference in the proportion of patients treated at Donald Fraser compared to Tshilidzini facility ($p < 0.001$). While patients treated with ORS only, there was a significant difference in the proportion of patients treated at Donald Fraser compared to Tshilidzini facility ($p < 0.001$).

The medicines prescribed for treatment of diarrhoea in hospital are shown in Table 24. Table 24 also indicates the organisms causing diarrhoea. The medicines prescribed for treating diarrhoea in hospital, by diarrhoea condition and facility, indicated that there was more antibiotic treatment even for stools that did not contain any pathogenic microorganisms. The standard treatment guideline for South Africa was not followed.

Table 24: Medicines prescribed for treating diarrhoea in hospital, indicating organisms causing diarrhoea

Medicine prescribed	No. of patients	Organism detected in stool samples	Diarrhoea symptoms
Erythromycin	1	ETEC *Shigella*/EIEC	Loose stools
ORS rehydration	7	*Plesiomonas shigelloides* EAEC (4) ETEC (2) EPEC (3) STEC (1) *Shigella*/EIEC (3) Adenovirus F 40/41 (4) Norovirus GI/GII Rotavirus A (3) Salmonella (1) Giardia lamblia (1)	Loose stools
ORS, amoxycillin, ampicillin, paracetamol	1	Norovirus GI/GII	Loose stools
ORS, amoxycillin, paracetamol, intravenous rehydration, erythromycin	1	No organisms	Loose stools

Medicine prescribed	No. of patients	Organism detected in stool samples	Diarrhoea symptoms
ORS, ampicillin, amoxycillin	3	*Campylobacter* (1) EAEC (1) ETEC (1) *Cryptosporidium* (1) Norovirus GI/GII (1) Sapovirus (1)	Loose stools
ORS, ampicillin, paracetamol	2	No organism specified for one patient EAEC (1)	Loose stools
ORS, ferrous lactate, ampicillin	2	EPEC (1) ETEC (1) *Shigella*/EIEC (1) *Cryptosporidium* (2) *Giardia lamblia* (1)	Loose stools
Intravenous rehydration, ferrous lactate, paracetamol, gentamicin	1	None of the organisms	Loose stools
ORS, gentamicin	1	EAEC *Cryptosporidium*	Loose stools
ORS, gentamicin, amoxicillin, paracetamol	1	EAEC EPEC *Shigella*/EIEC Adenovirus F 40/41 Norovirus GI/GII Rotavirus A	Loose stools
ORS, gentamicin, ampicillin	8	*Cl. difficile* toxin A/B (1) EAEC (4) EPEC (6) ETEC (1) *Cryptosporidium* (1) Norovirus GI/GII (5) Rotavirus (1) Sapovirus (1)	Loose stools (7) Loose stools with cramps (1)
ORS, gentamicin, ampicillin, amoxycillin	2	EAEC (2) EPEC ETEC (2) *Shigella*/EIEC (2) Norovirus GI/GII (1)	Loose stools
ORS, gentamicin, ampicillin, ferrous lactate, paracetamol	1	*Cl. difficile* toxin A/B EPEC Norovirus GI/GII	Loose stools with cramps and blood
ORS, gentamicin, ampicillin, metronidazole	1	Rotavirus A	Loose stools
ORS, gentamicin, ampicillin, paracetamol	2	*Campylobacter* (1) EAEC (2) ETEC (1) *Cryptosporidium* (1)	Loose stools

Medicine prescribed	No. of patients	Organism detected in stool samples	Diarrhoea symptoms
ORS, gentamicin, ferrous lactate	1	EAEC EPEC Astrovirus	Loose stools
ORS, gentamicin, multivitamin syrup	1	EAEC EPEC	Loose stools with cramps
ORS, gentamicin, zinc	1	EAEC ETEC *Cryptosporidium*	Loose stools
ORS, metronidazole, ampicillin, paracetamol	1	*Campylobacter* Adenovirus F 40/41	Loose stools
ORS, metronidazole, gentamicin, erythromycin	1	EAEC EPEC	Loose stools
ORS, paracetamol	1	EAEC *Cryptosporidium*	Loose stools with cramps
ORS, paracetamol, erythromycin	1	*Campylobacter* EAEC EPEC Rotavirus A	Loose stools
ORS, paracetamol, gentamicin	3	Adenovirus F 40/41 (1) Norovirus GI/GII (1) EAEC (1) EPEC (1)	Loose stools (2) Loose stools with cramps (1)
ORS, paracetamol, metronidazole, gentamicin	1	ETEC Norovirus GI/GII	Loose stools with cramps
ORS, paracetamol, multivitamin	1	*Shigella*/EIEC	Loose stools
ORS, paracetamol, zinc	1	Norovirus GI/GII	Loose stools
ORS, paracetamol, zinc, metronidazole	1	*Salmonella* EAEC	Loose stools
ORS, paracetamol, zinc, multivitamin syrup	1	EAEC Adenovirus F 40/41	Loose stools
ORS, ampicillin	3	No organism specified for one patient EPEC (1) *Giardia lamblia* (1)	Loose stools
ORS, ampicillin, metronidazole	5	EAEC (2) *Giardia lamblia* (1) Adenovirus F 40/41 (1) Norovirus GI/GII (1) Rotavirus A (1)	Loose stools
ORS, zinc	4	No organisms specified for one patient Norovirus GI/GII (2) *Campylobacter* (1) EAEC (1) EPEC (2) ETEC (2)	Loose stools

Medicine prescribed	No. of patients	Organism detected in stool samples	Diarrhoea symptoms
ORS, zinc, ampicillin	9	No organism specified for one patient *Campylobacter* (1) *Plesiomonas shigelloides* (1) EAEC (3) EPEC (1) ETEC (2) STEC (1) *Shigella*/EIEC (2) *Cryptosporidium* (1) Adenovirus F 40/41 (3) Norovirus GI/GII (1)	Loose stools
ORS, zinc, metronidazole	7	No organism specified for one patient *Campylobacter* (2) EPEC (3) EAEC (3) ETEC (1) Norovirus GI/GII (2) Rotavirus A (1)	Loose stools
ORS	1	Norovirus GI/GII	Loose stools
ORS, metronidazole	1	None of the organisms	Loose stools
Total	**79**		

Data on medicines prescribed was not provided for one patient. Patients with loose stools at Donald Fraser facility were treated mostly with ORS/intravenous rehydration, zinc and ampicillin, ORS and ORS/rehydration, zinc and metronidazole. Patients with loose stools at Tshilidzini facility were treated mostly with ORS/intravenous, gentamicin, amoxycillin and paracetamol. Patients with loose stools with cramps at Tshilidzini facility were treated with five different treatment regimens. One patient at Tshilidzini facility was treated for loose stools with cramps and blood using intravenous rehydration, gentamicin, ampicillin, ferrous lactate and paracetamol. Most of the time, healthcare workers did not prescribe medicine following the prescribed policy guidelines as indicated in Figure 24, Figure 25 and Figure 26.

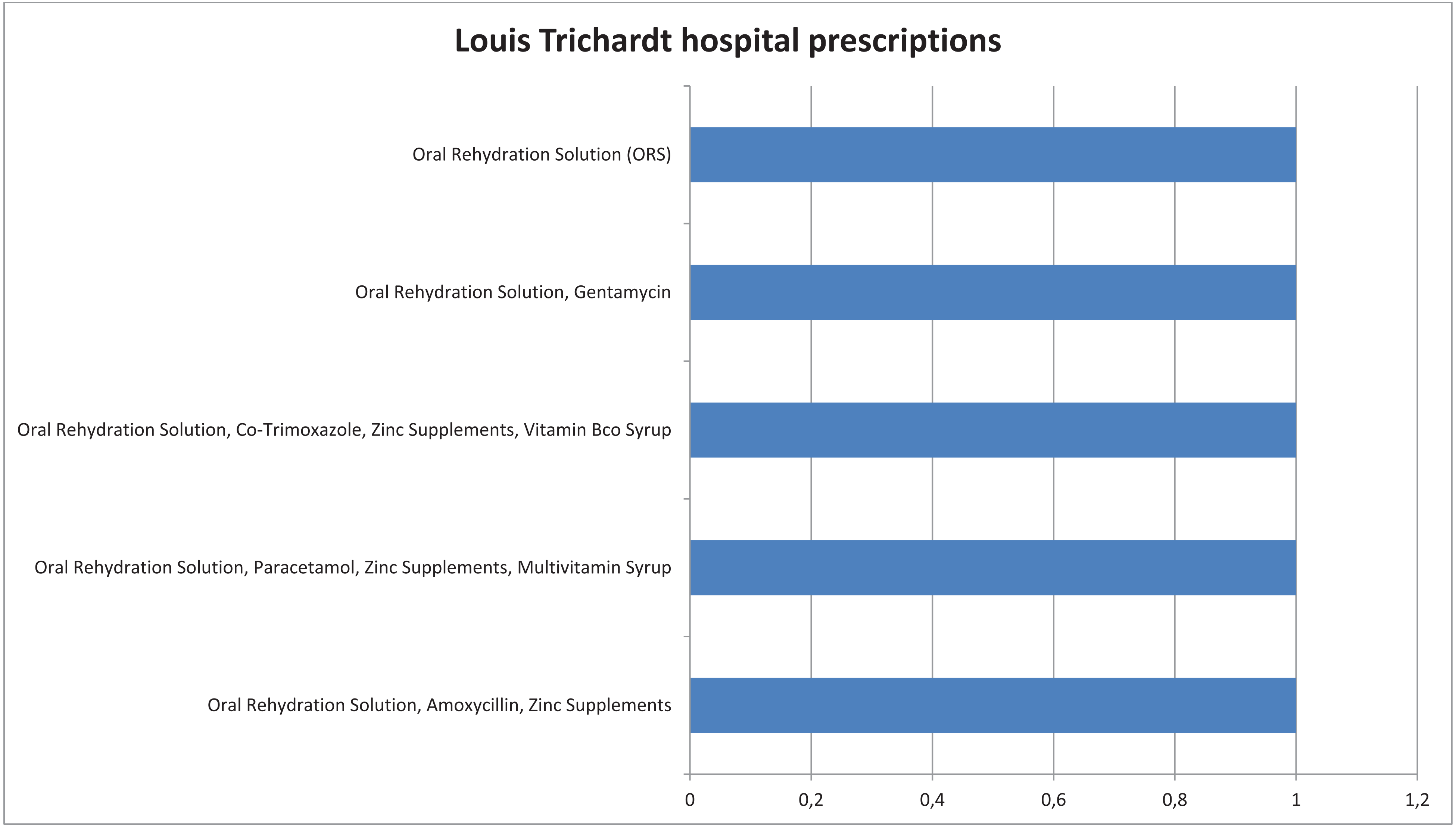


Figure 24: General medicine prescription pattern – Louis Trichardt Hospital

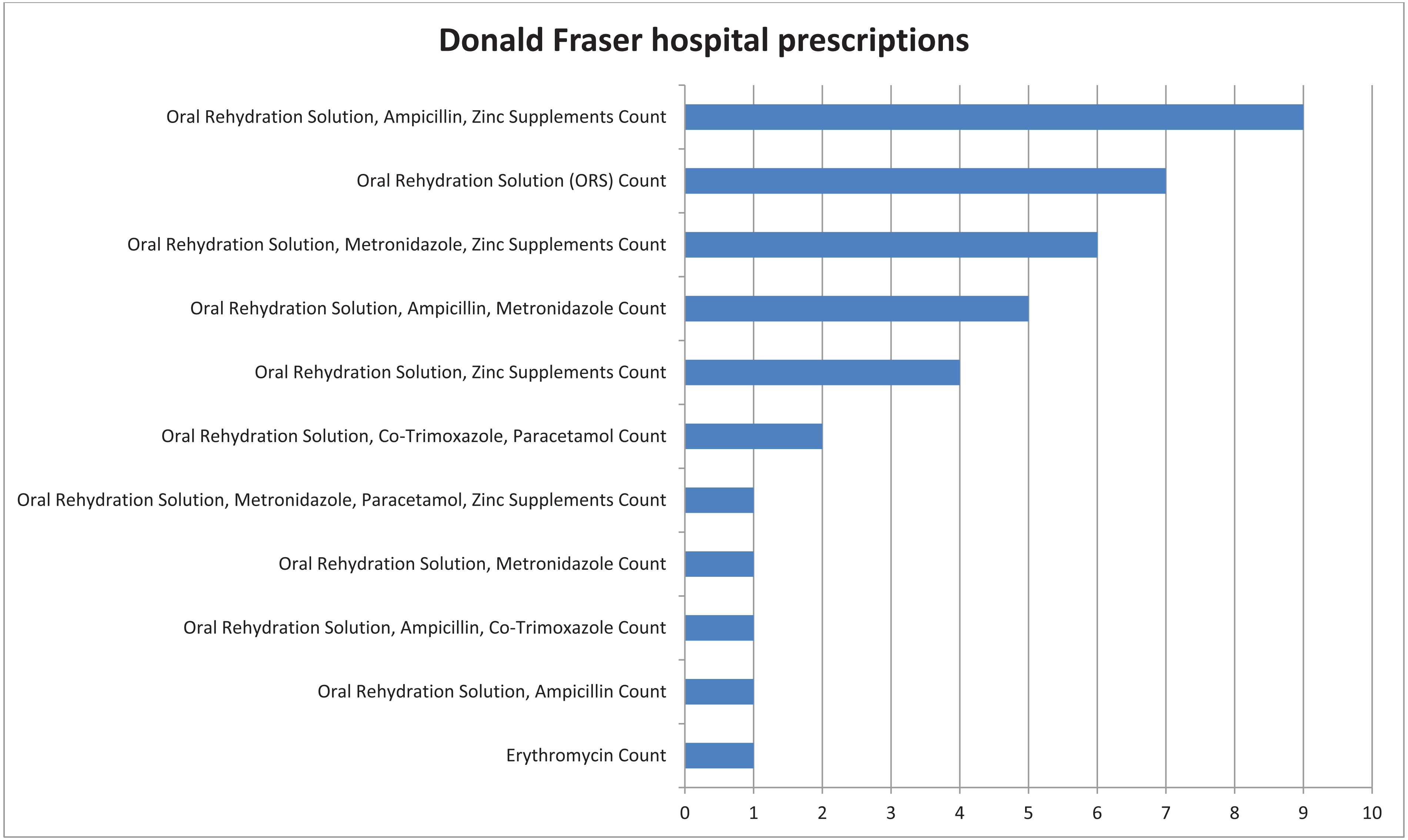


Figure 25: General medicine prescription pattern – Donald Fraser Hospital

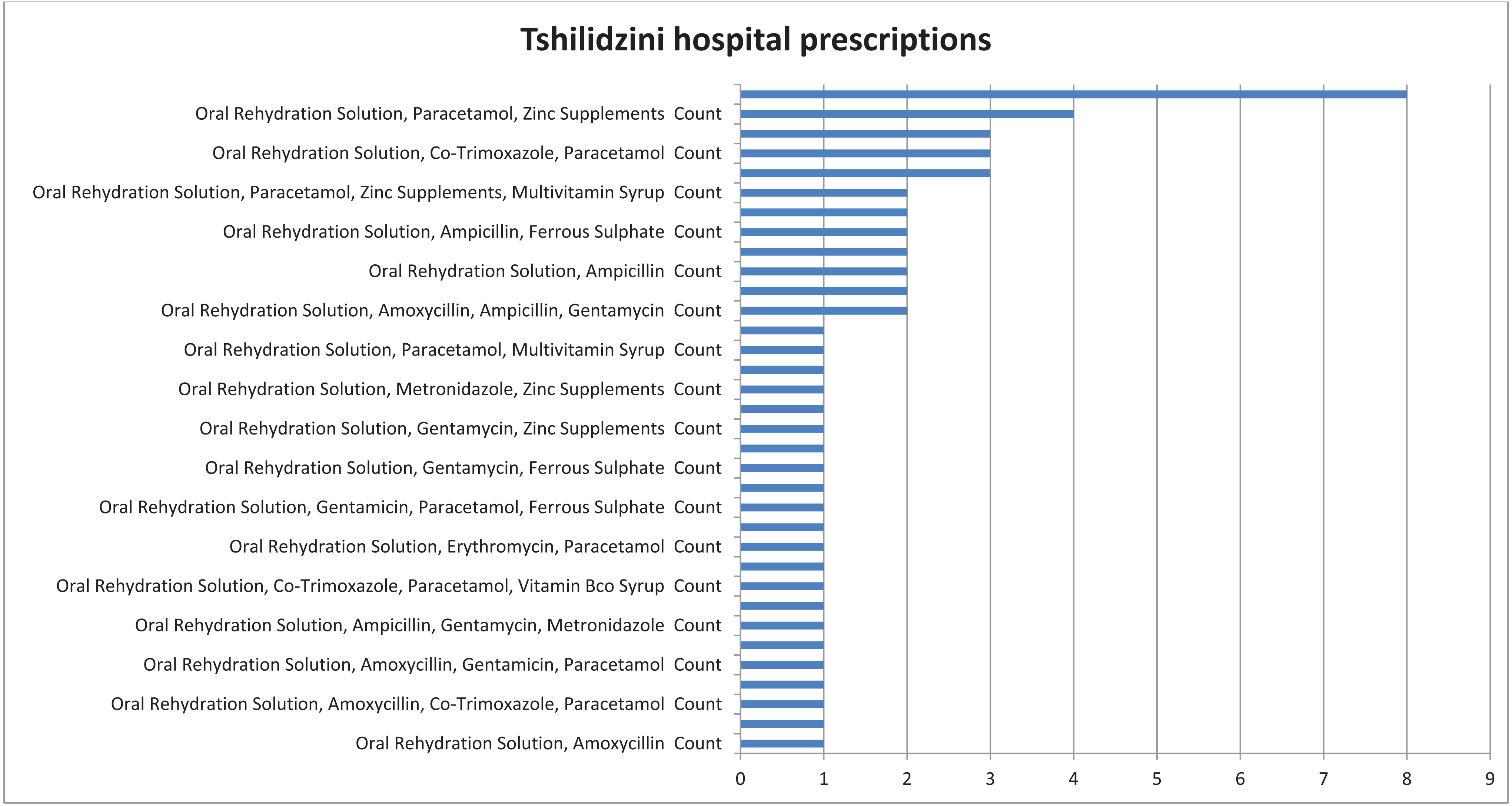


Figure 26: General medicine prescription pattern – Tshilidzini Hospital

3.4.5 Diarrhoea costs for inpatients

3.4.5.1 Average time spent (minutes)

The total and average time (in minutes) spent with each discipline are shown in Table 25. The average time was based on patients who were serviced by the respective discipline or profession in hospital. Medical doctors spent the most time with one patient admitted to hospital, professional nurses and assistant nurses came second and admin clerk came third.

Table 25: Total and average time (in minutes) spent with each discipline in hospital

Discipline	*Average time per patient who visited that discipline
Assistant nurse	15 minutes
Professional nurse	19 minutes
Medical doctor	26 minutes
Admin clerk	16 minutes
Pharmacist	12 minutes
Other employees (porter)	2 minutes
Other employees (dietician)	8 minutes

*The average time was based on the patients who visited that discipline in hospital.

3.4.5.2 Average cost of general ward stay

The average cost of a general ward stay is R614. The same cost included patients admitted in paediatric medical ward.

3.4.5.3 Estimated cost for a day in a high care facility

Five patients spent an average of two days in high care wards (ten days in total). The cost for a day in a high care facility was not specified. An estimated cost per day in a high care facility was obtained from the approved Uniform Patient Fees Schedule of (UPFS) 2016 Fee for Externally Funded Patients, effective 1 April 2016 (Code 0620, Level 2 facility):

$$\text{R1320 for 12 hours} = \text{R2640 per day}$$

3.4.5.4 Estimated cost for a day in ICU

One patient spent two days in ICU. The cost for a day in an ICU facility was not specified. An estimated cost per day in an ICU facility was obtained from the approved UPFS 2016 Fee Schedule for Externally Funded Patients, effective 1 April 2016 (Code 0630, Level 2 facility):

$$\text{R3470 for 12 hours} = \text{R6940 per day}$$

3.4.5.5 Estimated total cost of treating diarrhoea

The total costs associated with treatment of patients with diarrhoea in hospital is shown in Table 26. The total cost per facility was calculated by summing all the costs listed in Table 27 (up to ICU facility) per facility.

Table 26: Total costs associated with treating inpatients with diarrhoea

Cost parameter	Cost (ZAR)
Tests done in hospital	0
Medicine provided in hospital	R1 825
Medicine provided to take home	R1 833
Assistant nurse	R928
Professional nurse	R2 363
Medical doctor	R9 199
Admin clerk	R1 108
Pharmacist	R3 403
Other employee (porter and dietician)	R37
General ward (158 days @ R614/day)	R97 012
High care facility (10 days @ R2640/day)	R26 400
ICU facility (2 days @ R6940/day)	R13 880
Total cost	**R157 988**

Table 27: Total costs associated with treating inpatients with diarrhoea (by facility)

Cost parameter	Cost per hospital (ZAR)	
	Donald Fraser Hospital	Tshilidzini Hospital
Tests done in hospital	R0	R0
Medicine provided in hospital	R674	R1 151
Medicine provided to take home	R819	R1 014
Assistant nurse	R787	R141
Professional nurse	R1 857	R507
Medical doctor	R6 664	R2 535
Admin clerk	R872	R236
Pharmacist	R1 927	R1 477
Other employee (porter and dietician)	R0	R35
General ward (R614/day)	R44 208	R52 804
High care facility (R 640/day)	R26 400	R0
ICU facility (R6940/day)	R13 880	R0
Total cost	**R98 088**	**R59 899**

Summary:

- The average cost per patient treated in hospital for diarrhoea was R1975 (R157 988 divided by 80 patients treated in hospital).
- The average cost per patient treated for diarrhoea was R2725 in Donald Fraser facility (R98 088 divided by 36 patients treated at Donald Fraser facility), and R1361 per patient treated at Tshilidzini facility (R59 899 divided by 44 patients).
- The mean direct costs incurred in Donald Fraser facility was significantly higher than those incurred in Tshilidzini facility ($p = 0.003$) when using the T-test. As the normality assumption for the T-test was not met, a nonparametric test was also used (Wilcoxon rank sum test). When using a Wilcoxon rank sum test, the p value obtained was < 0.001 (true location shift is not equal to 0, meaning that the medians differ).
- The average cost per patient per inpatient day was calculated by dividing the total cost by the total number of days spent in hospital (R157 988 divided by 170 = R929).
- The average cost per patient per inpatient day was calculated at R1168 for the Donald Fraser facility (R98 088 divided by 84 days), and R697 for the Tshilidzini Hospital (R59 899 divided by 86 days).

3.4.6 Total and average direct treatment cost of diarrhoea

The total cost for treating diarrhoea was calculated by adding the total cost for patients treated out of hospital to the total cost for patients treated in hospital (R1027 + R157 988 = R159 015).

$$\mathbf{Total\ cost} = \mathbf{cost_{out\ of\ hospital}} + \mathbf{cost_{in\ hospital}} = \mathbf{R1,027} + \mathbf{R157,988} = \mathbf{R159,015} \quad (1)$$

The average cost per patient for treating diarrhoea in the study was calculated by dividing the total cost (R159 015) by the total number of patients in the study (106) = R1 500.

$$\mathbf{Average\ cost\ per\ patient} = \mathbf{cost_{total}/n} = \mathbf{R159,015/106} = \mathbf{R1,500} \quad (2)$$

The total cost for treatment of diarrhoea at Donald Fraser facility was calculated by adding the total cost for patients treated out of hospital to the total cost for patients treated in hospital at Donald Fraser facility (R88 + R98 088 = R98 176).

$$\mathbf{Total\ cost_{DF}} = \mathbf{cost_{out\ of\ hospital\_DF}} + \mathbf{cost_{in\ hospital\_DF}} = \mathbf{R88} + \mathbf{R98,088} = \mathbf{R98,176} \quad (3)$$

The average cost per patient for treating diarrhoea at the Donald Fraser facility in the study was calculated by dividing the total cost for Donald Fraser facility (R98 176) by the total number of patients linked to the Donald Fraser facility in the study (38) = R2 584.

$$\mathbf{Average\ cost\ per\ patient_{DF}} = \mathbf{cost_{total_{DF}}/n_{DF}} = \mathbf{R98,176/38} = \mathbf{R2,584} \quad (4)$$

The total cost for treatment of diarrhoea at Louis Trichardt facility was calculated by adding the total cost for patients treated out of hospital to the total cost for patients treated in hospital at Louis Trichardt facility (R451 + R0 = R451).

$$\mathbf{Total\ cost_{LTT}} = \mathbf{cost_{out\ of\ hospital\_LTT}} + \mathbf{cost_{in\ hospital\_LTT}} = \mathbf{R451} + \mathbf{R0} = \mathbf{R451} \quad (5)$$

The average cost per patient for treating diarrhoea at the Louis Trichardt facility in the study was calculated by dividing the total cost for Louis Trichardt facility (R451) by the total number of patients linked to the Louis Trichardt facility in the study (10) = R45.

$$\mathbf{Average\ cost\ per\ patient_{LTT}} = \mathbf{cost_{total_{LTT}}/n_{LTT}} = \mathbf{R451/10} = \mathbf{R45} \quad (6)$$

The total cost for treatment of diarrhoea at Tshilidzini facility was calculated by adding the total cost for patients treated out of hospital to the total cost for patients treated in hospital at Tshilidzini facility (R488 + R59 899 = R60 387).

$$\mathbf{Total\ cost_{TS} = cost_{out\ of\ hospital\_TS} + cost_{in\ hospital\_TS} = R488 + R59,899 = R60\ 387} \qquad (7)$$

The average cost per patient for treating diarrhoea at the Tshilidzini facility in the study was calculated by dividing the total cost for Tshilidzini facility (R60 387) by the total number of patients linked to the Tshilidzini facility in the study (58) = R1041.

$$\mathbf{Average\ cost\ per\ patient_{TS} = cost_{total_{TS}}/n_{TS} = R60\ 387/58 = R1\ 041} \ (8)$$

CHAPTER 4 CONCLUSIONS AND RECOMMENDATIONS

4.1 Conclusions

The aim of the study was to determine the cost of diarrhoea treatment in children under the age of 5 years from rural and peri-urban communities in the Vhembe District in the Limpopo Province. Statistics South Africa (2014) reported that in 2011 diarrhoea was one of the leading causes of death in children under the age of 5 years. The diarrhoea burden increases the Department of Health's budget due to the healthcare required for patients. Unsafe WASH contributes greatly to diarrhoea exposure and increasing medical costs.

The Constitution of South Africa affirms the right to water and sanitation services to every citizen of South Africa. It is the duty of every municipality to ensure such rights are realised (South Africa, 1996). The South African Water Service Act (1997) requires every municipality to ensure that citizens' rights to water and sanitation are adhered to. Poor water service and an intermittent water supply affect health, and increase the occurrence of diarrhoea and other communicable diseases.

Government spends millions every year to provide water and sanitation infrastructures. However, most South Africans are still living without sustainable water services. It has been noted that most patients use a variety of water sources for consumption. Communal tap water was identified as a safer water source than other water sources used. However, in most areas where water is not always available, secondary sources such as wells, rivers and boreholes were identified as high risk due to the number of children affected. Some of these sources are documented as unimproved by the WHO/UNICEF (2013).

The Blue Drop incentive base regulation (Department of Water Affairs, 2009) assesses the management of risks in communal water sources in various water service authorities or municipalities. These initiatives play a role in improving safety of drinking water in South Africa. Environmental health practitioners (EHPs) in various municipalities are mandated through the National Health Act (Department of Health, 2015b) to provide municipal health services, which include water monitoring. The Act further requires an investigation to take place in case of pollution and non-compliance with norms and standard (Department of Health, 2015b). It is the duty of EHPs to educate communities using unsafe water sources and poor sanitary facilities. Furthermore, EHPs must conduct health surveillance, which includes assessing diarrhoea prevalence in healthcare settings used by the communities (Department of Health, 2015b).

Clasen (2010) recommended the treatment of water at the point of use to reduce diarrhoea episodes. Chola et al. (2015) recommended the provision of safe water and proper sanitation to reduce diarrhoea of children under 5 years. Emphasis on the provision of adequate sanitation and hygiene is important because such interventions reduce between 38–48% of diarrhoea in children under the age of 5 years (Wang et al., 2017). Implementation of appropriate policies, as well as monitoring and evaluation, could save enormous amount of money required for treatment. Therefore, provision of WASH with sustainable education could save lives of children under the age of 5 if given appropriate attention. The United Nations 2030 Sustainability Development Goal 6 requires countries to provide safe water that is affordable and available every time as well as adequate sanitation. Most sub-Saharan countries are still experiencing challenges with providing safe water in their communities. There is a need to fast-track the sustainable provision of safe water supply and provision of adequate sanitation and hygiene in communities by the municipality for long-term benefits. This will reduce diarrhoea infection among children under the age of 5 years.

Health surveillance further includes the assessment of sanitary facilities and hygiene situation in particular settings. The Water Service Act (South Africa, 1997) and Municipal Structures Act (South Africa, 1998) require water service authorities to provide sanitation services to the community. However, South Africa is still behind in providing toilets to its citizens. Most communities in the Vhembe District are still using unimproved sanitation infrastructures that include ordinary pit toilets, which are sometimes shared by more than one household. Ventilated improved pit latrines are recommended to improve public health because of their ability to prevent flies and reduce smell (Conant & Fadem, 2008). However, ventilated improved pit latrines are usually allocated to the indigent. The study further indicated that handwashing facilities were not available. The Draft National Sanitation Policy of South Africa (Department of Water and Sanitation, 2016) emphasizes hygiene education and health promotion to ensure prevention of diseases caused by poor hygiene and prevention of flies that could transmit communicable diseases. The monitoring of handwashing and hygiene is also part of the responsibilities of EHPs. Seemingly, involvement of EHPs and other health workers in hygiene education and promotion is not sustainable (Mudau et al., 2016).

The cost of medicine and services given by the hospital staff was among the highest cost observed in both outpatients and inpatients affected by diarrhoea who visited the public health hospitals to seek medical care. The high cost of medicine was due to poor management and treatment of diarrhoea symptoms in children suffering from diarrhoea. All hospitals reported the unnecessary use of antibiotics. A study in Ghana that assessed medicine-prescribing practices used in the treatment of diarrhoea, indicated that most healthcare workers unnecessarily prescribed antibiotics. This study further showed that such practices was also influenced by the caregivers as they reported that most children were not taking ORS because it was considered not palatable to young children (Asante et al., 2017). This practice was also observed from this study, as the prescription of only ORS was not given when antibiotics were not needed. The majority of children showed the symptoms of loose stools and according to the guidelines, only ORS and zinc was supposed to be prescribed. However, the majority of children were given antibiotics. The practice of uncontrolled use of antibiotics was also discouraged by the WHO (2017) and the Minister of Health in South Africa (Department of Health, 2015a). Other developing countries indicated that continuous training of healthcare workers could reduce the use of antibiotics (Walker et al., 2015).

Healthcare workers should use the presence of diarrhoea illness in a child as an opportunity to educate mothers and caregivers. The healthcare workers are instructed to use the integrated management of childhood illness guide (Department of Health, 2014a) and *Standard Treatment Guideline and Essential Medicine List of South Africa – Hospital Level Paediatrics* (Department of Health, 2014b). These guidelines provide specific procedures on how acute diarrhoea should be managed and how medicine should be prescribed. According to Wittenberg (2012), education should reduce caregivers' expectation to obtain drugs once they have taken a child to the hospital and not to pressure health workers not to make proper prescription as stipulated in the guidelines.

This study highlighted the inconsistencies to policies and guidelines implementation, which led to diarrhoea infection. Most hospital also did not have a dehydration station, which prolonged hospital stay.

4.2 Recommendations

Based on these findings, the following is recommended:

- Sustainable caregiver education to change hygiene practices such as handwashing is important.
- Caregivers should be educated on the management of diarrhoea at household level to take appropriate measures for treatment when it is required.
- Health workers should be trained to provide education to the caregivers who take their children to healthcare facility due to diarrhoea infection.
- EHPs should provide and strengthen hygiene education and appropriate point-of-use treatment communities to prevent diarrhoea due to poor environmental health practices.

- Healthcare workers need to be trained to follow the standard treatment guidelines to prevent unnecessary prescription of drugs in order to prevent high cost of diarrhoea treatment.
- The Department of Health and the Department of Water and Sanitation should come up with an integrated approach that will assist the public hospital to reduce cost of hospital admission and treatment due to diarrhoea.

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APPENDIX 1 – STOOL SAMPLE ANALYSIS

Stool sample analysis using the BioFire® FilmArray® Gastrointestinal (GI) Panel

All stool samples were analysed using the BioFire® FilmArray® GI Panel, which is a qualitative multiplexed nucleic acid-based in vitro diagnostic test, intended for use with FilmArray® systems. The FilmArray® GI Panel can simultaneously detect and identify nucleic acids from multiple bacteria, viruses and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. A total of 22 organisms that included the following were analysed in each diarrhoea sample:

- Parasites: *Cryptosporidium, Cyclospora cayetanensis, Entamoeba histolytica, Giardia lamblia*.
- Bacteria: *Campylobacter, C. difficule* toxin A/B, *Plesiomonas shigelloides*, *Salmonella, Vibrio, V. cholera, Yersinia enterocolitica*, EAEC, EPEC, ETEC, Shiga toxin-producing *E. coli* (STEC), *E. coli* O157, *Shigella*-EIEC.
- Viruses: adenovirus F40/41, astrovirus, norovirus GI/GII, rotavirus A, sapovirus.

The principle of the test is shown in Figure 27.

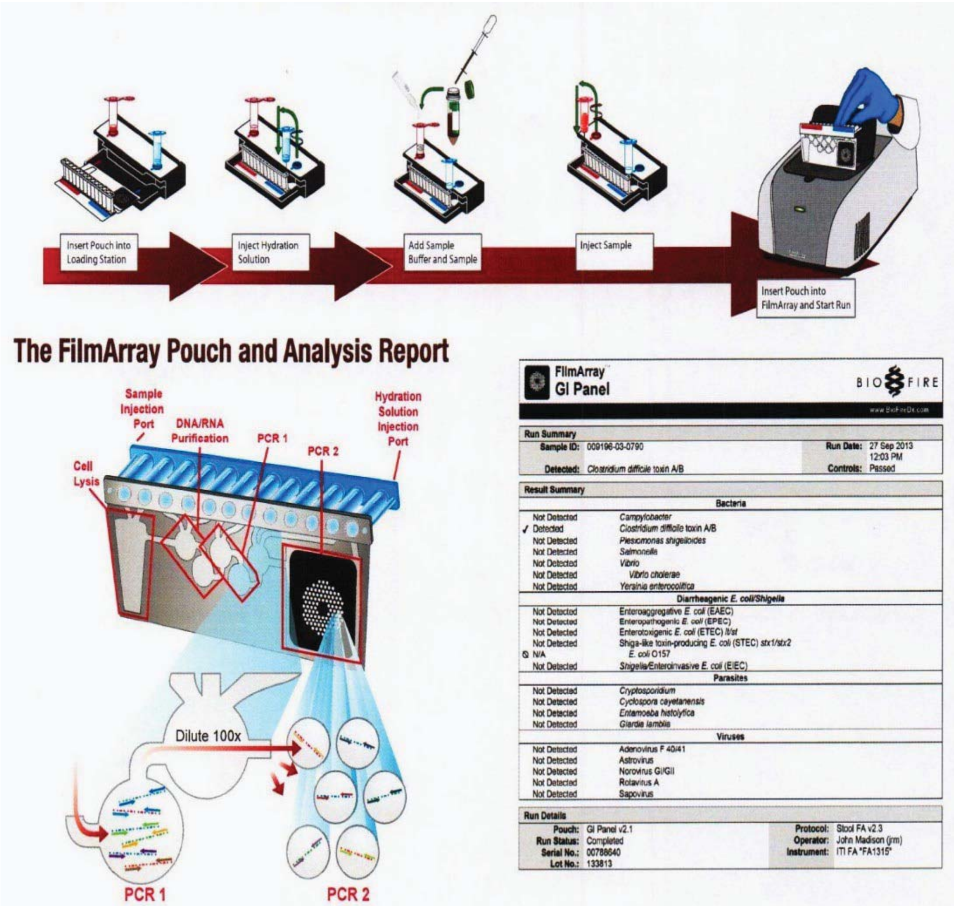

Figure 27: The BioFire® FilmArray® procedure

Isolation of bacterial pathogens

The frozen and fresh stool samples were analysed as outlined in Figure 28. The frozen samples were subjected to an additional initial enrichment step to increase the revival and recovery of bacteria from the samples. This isolation protocol was chosen to isolate aerobic and micro-aerophilic bacteria associated or responsible for diarrhoea, as outlined in the following sections.

Fresh and frozen stool samples were enriched in either alkaline peptone water (APW; Oxoid; Cat no. CM1028) or buffered peptone water (BPW; Oxoid; Cat no. CM0509) to enhance the likelihood of isolating *Vibrio* species (APW) or *Salmonella* and *Shigella* species (BPW) from stool samples. The APW and BPW were inoculated with a loopful of the sample and incubated for 24 hours at 35°C. Following incubation, an inoculation loopful of the sub-cultured sample was plated onto the different agar media (Figure 28). For frozen samples, an inoculation loopful of stool sample was also enriched in brain heart infusion broth (BHI; OXOID; Cat no. CM1135) at 35°C for 24 hours. Following incubation, the enriched sample was treated as a fresh stool sample and analysed as such.

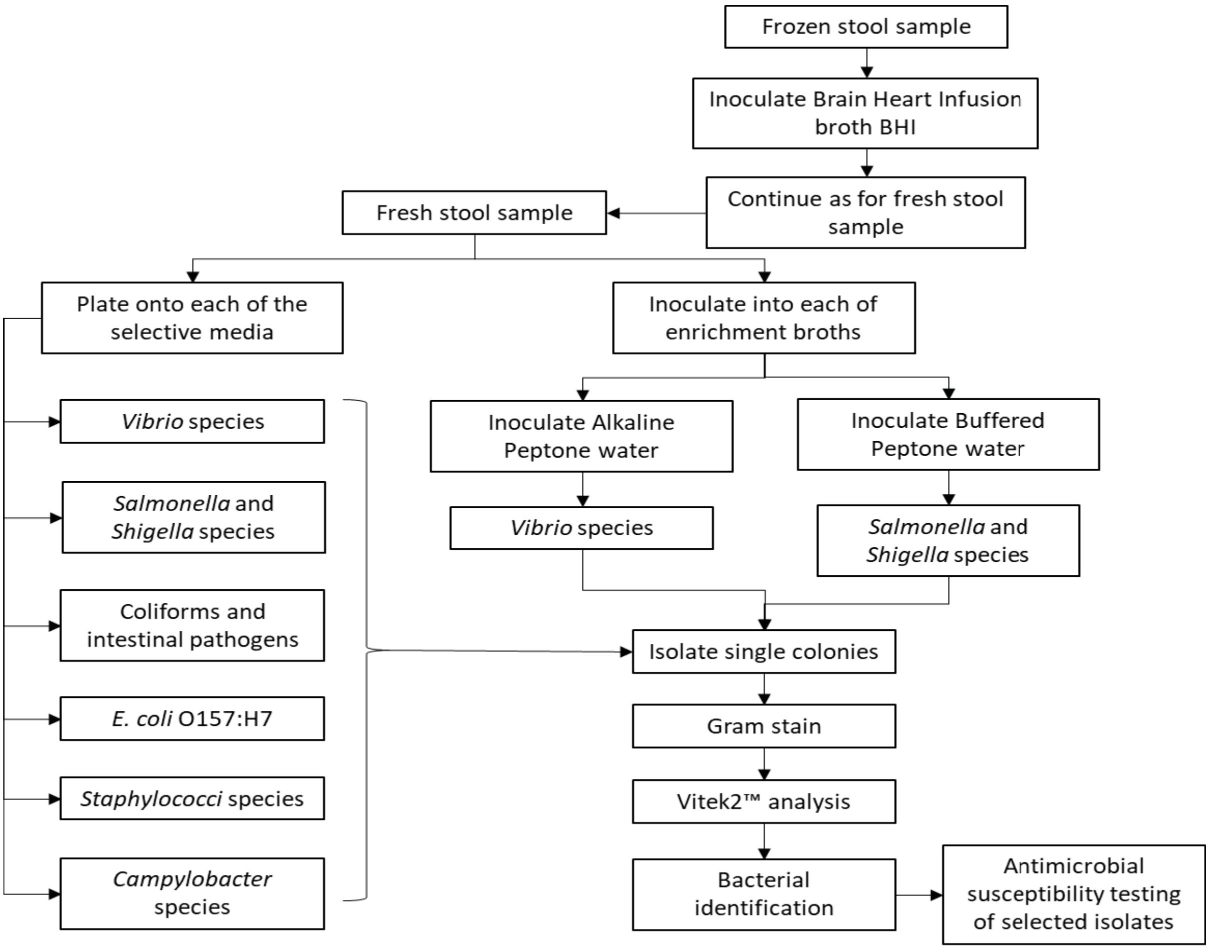

Figure 28: Illustration of the protocol followed to isolate, identify and characterise bacteria from the collected stool samples (fresh and frozen)

Vibrio species

Samples were analysed for the presence of *Vibrio* species using Oxoid thiosulfate-citrate bile salts sucrose agar (TCBS; Cat no. CM0333). An inoculation loopful of either the stool sample or sample sub-culture in APW was plated onto TCBS plates and incubated aerobically at 35°C for 24–48 hours. Presumptive colonies (from either 24- or 48-hour incubation) were sub-cultured onto TCBS plates (to confirm single colonies) or Müeller–Hinton agar (Oxoid; Cat no. CM0337) for VITEK 2™ analysis.

Salmonella and Shigella species

Samples were analysed for the presence of *Salmonella* and *Shigella* species by plating an inoculation loopful of faecal sample or sample sub-cultured in BPW onto deoxycholate citrate agar (Oxid, Cat no. CM0227) plates. Plates were incubated at 35°C for 48 hours with presumptive colonies sub-cultured for single colonies on deoxycholate citrate agar (to confirm single colonies) or on Müeller–Hinton agar (Oxoid; Cat no. CM0337) for VITEK 2™ identification.

Coliforms and intestinal pathogens

Samples were analysed for the presence of coliforms and other intestinal bacteria (*E. coli, Enterococcus* species, *Aeromonas aerogenes, Staphylococcus* species and *P. aeruginosa*) using MacConkey agar (Oxoid; Cat no. CM0007). An inoculation loopful of faecal sample was plated onto the media and incubated for 48 hours at 35°C with presumptive colonies sub-cultured for single colonies on MacConkey agar (to confirm single colonies) or on Müeller–Hinton agar (Oxoid; Cat no. CM0337) for VITEK 2™ identification.

Escherichia coli O157:H7

Samples were tested for the presence of *E. coli* O157:H7 using sorbitol MacConkey agar (Oxoid; Cat no. CM0813). An inoculation loopful of faecal sample was plated onto the media and incubated for 48 hours at 35°C with presumptive colonies sub-cultured for single colonies on sorbitol MacConkey agar or on Müeller–Hinton agar (Oxoid; Cat no. CM0337) for VITEK 2™ identification.

Staphylococci species

Samples were tested for the presence of pathogenic *Staphylococci* strains using mannitol salt agar (Oxoid; Cat no. CM0085). An inoculation loopful of faecal sample was plated onto the media and incubated for 48 hours at 35°C with presumptive colonies sub-cultured for single colonies on mannitol salt agar or on Müeller–Hinton agar (Oxoid; Cat no. CM0337) for VITEK 2™ identification.

Campylobacter species

An inoculation loopful of the sample was plated onto two *Campylobacter* blood-free selective media plates (Oxoid; Cat no. CM0739) supplemented with charcoal cefoperazone deoxycholate agar (CCDA) selective supplement (Oxoid; Cat no. SR0155) and incubated at 42°C in aerobic and micro-aerophilic (candled jar) atmospheres. Plates were incubated for 48 hours with growth monitored and presumptive colonies sub-cultured after 24 and 48 hours of incubation. Single colonies were isolated on 10% sheep blood agar plates obtained from the National Health Laboratory Service (Cat no. DMPA0115) and incubated in micro-aerophilic atmosphere for 24 hours. Single colonies from these plates were used for bacterial identification and antimicrobial sensitivity testing with the VITEK 2™ system.

Isolate identification

A representation of all presumptive bacterial pathogens and other intestinal bacteria was selected for testing using the VITEK 2™ system. Bacterial isolates were grown on Müeller–Hinton agar plates as described above. Each colony was Gram-stained for classification as either Gram-negative or Gram-positive to select the appropriate identification and susceptibility testing card.

A single colony was collected from the plate and suspended in sterile saline solution (bioMérieux South Africa; Cat no. V1204) in sterile 5 ml plastic tubes (bioMérieux South Africa; Cat no. 69285) and compared to the VITEK 2™ DensiCHEK™ Plus standards (bioMérieux South Africa; Cat no. 21255) to obtain a test solution with a turbidity that compares to a 0.5 McFarland standard. Isolates were identified using the Gram-negative (bioMérieux South Africa; Cat no. 21341) and Gram-positive (bioMérieux South Africa; Cat no. 21342) specific testing cards.

Statistical analysis

All data was imported to an Excel™ spreadsheet and analysed with Strata 14 statistical package.

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