Designing and testing a solution to fill ART knowledge gaps at primary healthcare level: WhatsApp-based microlearning

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Dedication

For my beloved parents, who enthusiastically encouraged me to do
my PhD, despite my returning to study at a (very) mature age.
While my lovely Mom didn't make it to see me finish,
she was my fiercest cheerleader.

Declaration

I, Briony Sue Chisholm, hereby declare that the work in this thesis is based on my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, or is being, submitted for another degree in this or any other university.

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1. Chisholm BS, Swart AM and Blockman M. South African healthcare workers' knowledge of dolutegravir's drug–drug interactions in the first year of its rollout: a cross-sectional online survey. *Journal of the International AIDS Society* 2022, 25:e25885. DOI: 10.1002/jia2.25885.
2. Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. *International Journal of Qualitative Methods* 2024, Volume 23: 1–15. DOI: 10.1177/16094069241284205.
3. Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. *Nurse Education in Practice* 2025 Mar. 6:104326. DOI: 10.1016/j.nepr.2025.104326. Online ahead of print.
4. Chisholm BS, Wallace ML, Blockman M and Orrell CJ. "WhatsApp is best!" Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised study. In press at *Nurse Education in Practice*.

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Abstract

South Africa has the world's largest antiretroviral treatment programme, with 7.7 million people on treatment in 2023. Treatment of HIV is informed by regularly updated national guidelines. Knowledge of the guidelines and ongoing training of healthcare workers (HCWs) are vital, to ensure optimal patient care. Human, financial and infrastructural challenges make ongoing training difficult. Innovative solutions are needed.

In the first study, South African HCWs' knowledge of dolutegravir's drug interactions – detailed in the guidelines – was established using an anonymous online survey. Descriptive and inferential analysis was done on the 1 950 surveys received from across the country. Significant gaps in knowledge were shown: 70% of participants were aware that dolutegravir has interactions; knowledge of which drugs interact and how to adjust dosing ranged between 5.1 and 79.7%. Access to guidelines and training were positively associated with knowledge, but only 69% of respondents had access to guidelines and 56% had received training. Training was desired by 90% of respondents, with computer-based online training (51%) and cell phone-based training (41%) being the preferred methods.

The second study, a pragmatic, mixed-methods, parallel-group cluster-randomised study aimed to close the knowledge gaps by designing, testing and evaluating the effect of WhatsApp group-based microlearning for HIV training on HCWs' knowledge. Nurses and community health workers (CHWs) at 50 predominantly rural clinics in the Eastern Cape were invited to join the training at in-person recruitment visits.

Uptake and participation were good: 232/293 nurses and 207/271 CHWs participated. Lessons were read within two weeks by 96% (nurses) and 88% (CHWs). Significant intervention effect on knowledge was seen, based on online knowledge questionnaires: nurses (0.5 units; p=0.0499) and CHWs (0.7 units; p=0.004). Data from focus groups noted that participants found the training acceptable and beneficial.

Patient folders (n=1 083) were reviewed retrospectively to compare changes in patient care between the arms. Adjusting for pre-care differences, the intervention increased correct patient care by 21% (95% CI 10%-32%; p<0.001) in the year after the training.

WhatsApp-based microlearning for HCWs is effective, highly acceptable, feasible and well-received, making it a valuable option for simple, accessible, scalable continuing education.

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Chapter overview

Abbreviations

AIDS	Autoimmune Deficiency Syndrome
App	Mobile applications
ART	Antiretroviral treatment
ARV	Antiretroviral
AZT	Zidovudine
BC	Briony Chisholm (author/researcher)
CASP	Critical Appraisal Skills Programme checklist
CE	Continuing education
CHW	Community health worker
CI	Confidence interval
COP	Community of practice
COREQ	Consolidated Criteria for Reporting Qualitative Research checklist
DDI	Drug-drug interaction
FDA	Federal Drug Agency
HAART	Highly active antiretroviral treatment
HCW	Healthcare worker
HIV	Human Immunodeficiency Virus
HREC	UCT Faculty of Health Sciences Research Ethics Committee
ICC	Intracluster correlation coefficient
INSTI	Integrase strand transfer inhibitor
LMIC	Low- or middle-income country
NCD	Non-communicable disease
NDOH	National Department of Health
NGO	Non-governmental organisation
NIMART	Nurse initiation and management of antiretroviral treatment
OR	Odds ratio
PEP	Post-exposure prophylaxis
PHC	Primary health clinic
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PrEP	Pre-exposure prophylaxis
RA	Research assistant
SD	Standard deviation
SM	Social media
SMS	Short message services
TB	Tuberculosis
TIDieR	Template for Intervention Description and Replication checklist
UCT	University of Cape Town
USA	United States of America
UTAUT	Unified Theory of Acceptance and Use of Technology
UTT	Universal Test and Treat
VTP	Vertical transmission prevention
WHO	World Health Organisation

Definitions

Cell phone	Mobile telephone
Community health workers	Members of the community who have not had formal professional training but have received some health promotion training[1]
Continuing education	The ongoing learning of healthcare workers to maintain and update their professional skills and practice, ensuring competence and effectiveness in the workplace[2-4]
eLearning	An educational intervention that is mediated electronically via the internet[5]
Hotline	National HIV & TB Healthcare Worker Hotline, a telephonic helpline for healthcare workers, based at the Division of Clinical Pharmacology at the University of Cape Town
Loadshedding	Regular, scheduled periods of the electricity being cut off each day for long periods. This was prevalent during the study period, due to an energy crisis in the country. In smaller towns and rural areas this often results in cel phone networks being off
mHealth	The use of mobile wireless technologies for health[6]
Microlearning	Relatively short, small learning units and short-term focused activities[7]
mLearning	Learning delivered on a handheld mobile device, allowing accessibility independent of time and space[8-10]
Mobile-social learning	The combination of accessible mobile technology for learning with social networking for experience sharing and knowledge transfer[11]
NIMART nurses	Nurses who have received training to manage people living with HIV from testing through initiation and monitoring of ART, opportunistic infection screening, prophylaxis and referrals[12]
Social media	The collective term for different interactive platforms, websites and applications intended for digital networking, that allow individuals and organisations to create and share user-generated content digitally[13]
WhatsApp	A free, end-to-end encrypted instant messaging service which allows users to send text, voice and video messages, and share documents[14]

List of publications

Publication citation	Associated thesis chapters	Pages
Chisholm BS, Swart AM and Blockman M. South African healthcare workers' knowledge of dolutegravir's drug-drug interactions in the first year of its rollout: a cross-sectional online survey. Journal of the International AIDS Society 2022; 25: e25885. DOI: 10.1002/jia2.25885	Chapter 2 Chapter 5 Chapter 6	31-37 85-94 95-120
Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. *International Journal of Qualitative Methods* 2024; 23: 16094069241284205. DOI: 10.1177/16094069241284205.	Chapter 2 Chapter 4 Chapter 7	31-37 70-83 122-146
Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. *Nurse Education in Practice* 2025 Mar. 6:104326. DOI: 10.1016/j.nepr.2025.104326. Online ahead of print.	Chapter 2 Chapter 4 Chapter 7 Chapter 8	31-37 70-83 82-101 147-178
Chisholm BS, Wallace ML, Blockman M and Orrell CJ. “WhatsApp is best!” Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised study. Submitted for publication to *Nurse Education in Practice* (in review).	Chapter 2 Chapter 4 Chapter 7 Chapter 8	31-37 70-83 82-101 147-178

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Part 1: Introduction

Part 1 provides a background overview.

Chapter 1 is an introduction to the setting in which the studies were conducted: South Africa's HIV history, including the antiretroviral treatment programme and guidelines; current staff, including task-shifting and the training landscape, and placing Briony Chisholm within that.

Chapter 2 provides a broad overview of the two studies that make up the full project, including research questions, aims and objectives, and study designs.

Chapter 3 is the review of the literature, to place the research within the current context and establish research gaps.

Chapter 4 provides a detailed overview of the theoretical and conceptual frameworks used to guide the design of the studies, and the reasoning behind their choices.

Chapter 1 Introduction

This chapter provides an introductory overview of HIV and the antiretroviral treatment programme in South Africa; the national guidelines; task-shifting to nurses; and the current HIV/ART training landscape for healthcare workers. Lastly, it places the researcher within the context of the study.

1.1 A brief history of HIV in South Africa

The human immunodeficiency virus (HIV) attacks the immune system, destroying the CD4 cells. If left untreated, it progresses to acquired immunodeficiency syndrome (AIDS). It is most commonly transmitted through sexual intercourse, but also perinatally and through exposure to infected blood.[15]

The first cases of AIDS were reported in the United States of America (USA) in 1981[16] and, soon afterwards, in South Africa in 1982[17]. The socio-political conditions in South Africa, including a large migrant worker population, crowded conditions, and a deliberately under-developed healthcare system for Black South Africans under Apartheid allowed HIV to spread.[18]

Despite calls from the South African medical fraternity to take action quickly, the government ignored the incoming epidemic for years, driven by the then-government's prejudicial underpinning – one claim being that it was affecting only the homosexual community, which was their 'own affair'[19].

By 1987, 2 324 people were living with HIV.
Over 80 people had died.[20]

It was only in 1992 that an official AIDS strategy began, with the formation of the Networking HIV and AIDS Community of Southern Africa.[21] Two years later, a National AIDS Plan had been established.[22] In the same year, South Africa became a democracy, and the incoming government doubled the budget for AIDS Awareness programmes, mass media awareness campaigns and condom distribution, promoting a compassionate approach.[17]

In 1993, HIV prevalence was 4.3%.
By the end of 1994, it had risen to 7.6%.[23]

In the USA, the Federal Drug Agency (FDA) approved the first antiretroviral medicine (ARV), zidovudine (AZT) for treatment in 1987 and by 1996 the effectiveness of highly active antiretroviral therapy (HAART) was presented at the 11th International AIDS Conference in Vancouver.[16] By 1997, HAART was the standard of care in the USA.[16]

Antiretroviral treatment (ART) is used to suppress HIV, improve immunity through CD4 cell response and prevent opportunistic infections/co-morbid conditions.[15] Since the early days of ART, ARVs with lower toxicity, improved robustness against the development of resistance and drugs that are easier to take have been developed. Now, people living with HIV (PLHIV) taking ART can expect a near-normal lifespan[15] and good health. As numbers of PLHIV increased exponentially in South Africa, ART remained unavailable.

In 1998, HIV prevalence among antenatal clinic attendees in South Africa was 22.8%.[24]

Between 1998 and 2008 Thabo Mbeki's AIDS denialism and various delay tactics in implementing ART stalled the response.[25] Despite there being good data for the use of AZT for prevention of vertical transmission (VTP; previously known as PMTCT, or prevention of mother-to-child transmission), the government refused to fund it.[18]

HIV seroprevalence in pregnant women rose to 24.8% in 2001.[18]
Without ART, the perinatal HIV transmission rate from mother to child is 15-45%.[26]

After the AIDS Conference held in Durban in 2000, AIDS activists, scientists and healthcare workers (HCWs) challenged the government[18], with the Treatment Action Campaign and others taking the Minister of Health to court for failure to uphold human rights – access to healthcare – in its response to HIV treatment and prevention, specifically VTP[27]. In 2001, the Constitutional Court ruled that nevirapine must be provided to all HIV-positive pregnant women for VTP.[18]

Between 2003 and 2019, the vertical transmission of HIV in the first two months of life dropped from 23% to 0.7%.[28]

In 2002, the South African National AIDS Council was established to advise government on HIV and to develop 5-year strategic plans, bringing together government, civil society and the private sector to respond collectively to HIV, tuberculosis (TB) and sexually transmitted infections.[29]

In 2004, AIDS-related deaths were projected to overtake all other causes in South Africa.[30]

1.2 An introduction to South Africa's ART programme

In April 2004, the rollout of ART in the public sector was started but implementation was slowed by complicated accreditation criteria and restricted treatment eligibility, and it took over two years from the development of the operational plan to meet the goal of having one service point in each of South Africa's 53 districts.[25, 31]

345 640 people died of AIDS in 2006.
By 2007, South Africa bore 17% of the global burden of HIV.[18]

With the change of leadership in 2008, things evolved quickly and the 2010 ARV guidelines expanded treatment to a greater population.[25]

Between 2015 and 2020, the number of PLHIV
receiving ART went from 52% to 72%.[32]

HIV is now considered to be a chronic, manageable health condition.[33] South Africa has the world's largest ART programme.[32]

In 2023, South Africa had 7.7 million PLHIV.
5.9 million people (77%) were receiving ART.[34]

1.3 South African ART Guidelines

Local and international experts wrote and reviewed the first National Department of Health (NDOH) ART guidelines – in line with World Health Organisation (WHO) recommendations – which were released in 2004.[31] The guidelines recommended starting ART in patients with CD4 counts < 200 cells/mm^3 or with severe HIV disease, irrespective of CD4 count.[35] It had complicated criteria, such as the demonstration of patient reliability (three or more consecutive visits to the clinic) and a multi-disciplinary team meeting to decide whether patients should be started, before they could be initiated on ART.[35]

In 2010, with the rapid expansion of the programme and move to nurse-initiated and managed ARV treatment (NIMART)[36], the clinical guidelines were revised. Inclusions for initiation were expanded to people coinfected with TB/HIV and all pregnant women.[37]

Guideline development is based on assimilation of the latest evidence and review of current international guidelines. This necessitates constant updates. Since 2010, updated South African guidelines (Figure 1) were released in:

- April 2013: major changes included eligibility CD4 count increased to < 350 cells/μL; introduction of fixed-dose combinations[38]
- December 2014: major changes included eligibility CD4 count increased to < 500 cells/μL; move from WHO Option B (ART during pregnancy and breastfeeding) to Option B+ (lifelong ART) for VTP[39, 40]
- October 2019: major changes included the introduction of dolutegravir-containing fixed dose combinations for all eligible adults, adolescents and children over the age of 10 years and weighing 35 kg or more, but excluding women wanting to conceive, or in the first 6 weeks of pregnancy[41]
- March 2020: a minor update to the October 2019 guideline, which included amending the CD4 count threshold for TPT eligibility in pregnancy from 100 to 350 cells/μL[41]
- June 2023: major changes included optimised treatment regimens and the use of dolutegravir in first, second and third-line regimens[42]

Figure 1. South African NDOH Guidelines: 2010, 2019 and 2023

When new evidence requires important changes to treatment guidelines between formal guideline updates, circulars are sent out to the districts by the NDOH, for example:

- September 2016: implementation of the 'Universal Test and Treat' (UTT) strategy[43]
- June 2021: recommendation of dolutegravir as part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential[44]

Each guideline review necessitates updates in training across the entire country. Dissemination of guidelines, circulars and training are complicated by distance and logistics. Additionally, dissemination does not guarantee or confirm knowledge and uptake of new guidelines and circular recommendations in busy clinics.

1.4 Task-shifting: NIMART and CHWs

The WHO released a strategy in 2006 to respond to the shortage of HCWs, and how it would affect the response to HIV.[45] At the time, sub-Saharan Africa had 24% of the global burden of HIV and only 3% of global HCWs.[45] The situation has only worsened since, with staff shortages in Africa predicted to reach 5.3 million by 2030.[46] In South Africa, alone, a shortage of 97 000 skilled HCWs was projected by 2025.[47]

In 2008, the WHO released its guidelines to guide the adoption of task-shifting – task redistribution from highly qualified to less highly qualified/lower cadre HCWs – to address the shortage and allow rapid access to HIV care, especially in rural areas.[48, 49] Task-shifting has been shown to be effective, with studies showing as-good-as, or better patient care[50-52] and increased access to HIV services[53].

1.4.1 Nurse initiation and management of ART (NIMART)

In response to the increasing numbers of PLHIV and the need for rapid scale-up of ART, South Africa started task-shifting to nurses in 2010.[54] NIMART nurses initiated ART, re-prescribed it in stable patients and referred patients to doctors, where needed.[55] Initial difficulties included hasty implementation resulting in insufficient

training and nurses' concern with juggling time to provide individualised care to this additional cohort of patients.[55, 56]

Despite some initial negativity[56], as time passed and confidence grew, NIMART was shown to be positively accepted by nurses[55, 56] and patients[55]. Most importantly, the programme significantly improved ART access[54, 57, 58] and showed equally good patient outcomes[55, 59]. Current ART services in South Africa are predominantly nurse-delivered.

Ten years into NIMART implementation, Crowley et al[54] reviewed the published literature and established the enablers and barriers (Table 1).

Table 1. NIMART Enablers and barriers

Enablers	Barriers
1. Training and mentorship	1. Non-standardised training, inadequate mentoring
2. HIV/TB guidelines	2. Human resources constraints
3. Service integration	3. Health system challenges
4. Monitoring and support	4. Lack of support and empowerment
	5. Legislation, policy and guideline challenges
	6. Patient-related factors

NIMART training has been an issue, with poor coordination and no standardised curriculums or regulatory recognition.[56, 57] Much of the training was conducted by non-governmental organisations (NGOs) and private organisations like the Foundation for Professional Development and short courses through a number of universities.[54]

Effective, continuous and in-service training is necessary to ensure good quality care.[55, 57, 60] NIMART has now been incorporated into broader HIV training and nurses manage PLHIV from testing through initiation and monitoring of ART, opportunistic infection screening, prophylaxis and referrals.[12]

When tasks shift from doctors to nurses, logically there needs to be task-shifting of some of the nurses' responsibilities to a lower cadre HCW. The shortages of said HCWs was an issue, with nurses and managers left with only lay staff, including community health workers (CHWs) for delegation of their own tasks.[56]

1.4.2 Community Health Workers

CHWs are members of the community who have not had formal professional training but have received some health promotion training.[1] Often referred to as the 'foot soldiers' of community health services[61], they bridge communities and health services/facilities[62, 63]. In South Africa, their scope of practice includes health promotion, primary prevention of disease, adherence counselling, basic screening and referral, and palliative care services.[64]

The history of CHW programmes in South Africa starts in the 1980s, when it was funded by international donors[65]. With most CHWs employed by NGOs, there was a lack of coordination, regulation, sustainability and integration into the national health system.[63, 66-68] While the NDOH began formalising the programme in 2003 – with various policy changes since[64, 65, 69] – implementation has been slow, and dogged by political, budgetary and governance issues[61, 62, 70, 71]. These are beyond the scope of this thesis.

Most importantly, CHWs are an essential addition to allow for task-shifting.[56] They have been shown to be key in strengthening the ART programme in South Africa[67, 72, 73], improving patient knowledge about HIV[74] increasing testing[75] increasing the number of people who know their HIV status[73] and improving access of, and return to, care[61, 74]. Additionally, they are valued by the communities they work in[76, 77], and are perceived as patient advocates and important sources of health information[76].

The CHW programme has many challenges, including facing issues in the community beyond their scope/skills, e.g., poverty and mental health issues[72], staff shortages[78], and – reported most often – a lack of training[62, 66-68, 70, 72, 76, 78, 79].There is an urgent and expanding need for standardised and continuous training.[68, 76, 80]

1.5 Current training landscape

Knowledge facilitates the use of, and compliance with, guidelines.[57, 60] The WHO advises that, to facilitate task-shifting, needs-driven and continuous training is required.[48] Ongoing training of HCWs, especially in a dynamic field like HIV, is vital to ensure that the health services offered are of a high quality.[81] In resource-constrained

settings, continuous in-service training to support HCW knowledge is often not provided sufficiently, or at all.[82]

Traditionally, training on the ART guidelines has been done in the form of 1- to 10-day training sessions at centralised points, face-to-face. This requires HCWs to spend time away from the clinic. Keeping in mind that a vast majority of clinics are nurse-run and, in smaller places, run by a single nurse, this leaves clinics unstaffed. In addition, costs and constraints regarding transport, accommodation, catering, etc. are challenges.[82]

Staff shortages mean much of the training is done in a 'train-the-trainer' format, with the staff member who attends training expected to pass on the knowledge to others at the facility. While the method has been shown to be successful in continuing professional development of nurses[83], anecdotal experience shows this is often not the case[82].

More recently, online sessions (both live and recorded) have been introduced: 1–2-hour sessions, and longer format online courses. Here, too, time is needed, as well as access to computers and internet, all three of which are often in short supply, especially in more rural facilities.

1.6 The South African landscape

South Africa covers 122 million km².[84] Over 80% of the country is rural.[85] Eighty four percent of the population access health care in the public sector[86] – equating to around 52 million people[84]. In 2020, 211 296 HCWs worked in the public sector[47] and there are over 3 500 Primary Health Care Clinics (PHCs) in the country[87], many in hard-to-reach places (Figure 2).

Figure 2. Some of the roads driven to reach the study clinics

1.7 Placing the researcher

After graduating as a pharmacist from Rhodes University in 1996, I completed my internship at a mine hospital in Gauteng and then joined the Medicines Information Centre (MIC), based in the Division of Clinical Pharmacology at the University of Cape Town (UCT), as an information pharmacist in 1998.

In 2008, the MIC established the National HIV & TB Healthcare Worker Hotline (referred to as 'the hotline; in this thesis) and I found my passion in HIV. The hotline is staffed by pharmacists who answer clinical HIV/TB queries, received telephonically or electronically, from HCWs across South Africa. With the pharmacists' many years of experience and direct access to the UCT library system, in-house references, and the expertise of specialist consultants, the hotline can answer from the simplest to the most complicated clinical queries. In 2023, the hotline answered 4 856 queries from over 200 health facilities.

In 2016, I travelled around South Africa, visiting (mostly rural) clinics to market the hotline to the HCWs who need it most – those with little access to clinical support. We visited seven provinces, drove 9 950 km, mainly on back roads, and visited 260 facilities. It opened my eyes to the need for support for our HCWs in rural areas.

Also in 2016, I started the hotline's Facebook page, which I manage and post on daily. Each week, I do a 'query of the week' – a case-based 'lesson', which has proven the most popular posting each week (Figure 3).

Figure 3. An example of a 'Query of the Week' on the hotline Facebook page

In 2018, I returned to study part-time, while continuing my hotline work, completing my Diploma in HIV and TB Management through UCT. I discovered a passion for research while doing the diploma, which included a semester on operational research, so I registered for a research-based MSc, beginning 2020. After completing the MSc study – and finding gaps in knowledge - I upgraded to a PhD adding on a second, larger study to test an intervention to close knowledge gaps.

Chapter summary

After many fraught years of political wrangling, during which thousands of lives were lost, South Africa now has the largest ART programme in the world. The programme is well-developed, with regularly updated national guidelines in line with global recommendations.

Human resource challenges have necessitated task-shifting, with NIMART nurses now leading the ART programme and CHWs providing a link between clinics and the community to connect them to care and provide basic health education and support.

Ongoing training is vital in a dynamic field like HIV with regular evidence-based guideline updates, but it is dogged by challenges in the South African setting (especially the rural areas), including distance, cost, transport, being away from the clinic, and infrastructure.

The next chapter will provide an overview of the study rationale, research questions and the two studies that make up this thesis.

Chapter 2 Study overview

This chapter provides an overview of the development of the research questions and the rationale for the study chosen to answer these questions. The primary aims and objectives are presented, with a short overview of the two studies, to contextualise the flow from the first to second study.

Chapter 2 contains excerpts from the following papers:

Chisholm BS, Swart AM and Blockman M. South African healthcare workers' knowledge of dolutegravir's drug-drug interactions in the first year of its rollout: a cross-sectional online survey. Journal of the International AIDS Society 2022; 25: e25885. DOI: 10.1002/jia2.25885.

Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. International Journal of Qualitative Methods 2024; 23: 16094069241284205. DOI: 10.1177/16094069241284205.

Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

Chisholm BS, Wallace ML, Blockman M and Orrell CJ. "WhatsApp is best!" Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

2.1 Study rationale

Empirical data from years of experience at the hotline indicated that there may be gaps in HCWs' knowledge of current guidelines, especially drug-drug interactions (DDIs), but there was no data to support this assumption. Study 1 was conducted to establish a more robust view of this, backed up by rigorous study methods.

Study 2 aimed to close the gaps in knowledge shown in Study 1, using the HCW-reported preferences reported in Study 1. Using pedagogical techniques from previous studies and personal experience from 'teaching' nurses, both through answering queries and doing the weekly Facebook queries, a training intervention which is accessible for HCWs in rural areas was designed and tested to close the knowledge gaps and ultimately improve HIV patient care.

2.2 Research questions

2.2.1 Study 1

- Are healthcare workers involved in the care of South African PLHIV aware of the clinically significant drug interactions of dolutegravir and how to adjust dosages accordingly? What factors are associated with this knowledge?
- Do healthcare workers involved in the care of South African PLHIV have access to, and received training on, the national ART guidelines?

2.2.2 Study 2

- Is WhatsApp-based training for primary care nurses and CHWs in remote areas of South Africa an effective, acceptable, and feasible method to improve knowledge?
- Can WhatsApp-based training for primary care nurses and CHWs in remote areas of South Africa alter prescribing behaviour?

2.3 Overview of research aims, objectives and design of the two studies

This section gives a broad overview of the aims and designs of the two studies, which will be elaborated on in later chapters.

2.3.1 Study 1

The aim of this study was to determine gaps in dolutegravir drug interaction knowledge of South African healthcare workers involved in HIV care; and to describe which variables are associated with those gaps in knowledge.

Specific objectives

1. To determine the proportion of South African HCWs who know about dolutegravir's drug interactions and how to alter regimens accordingly
2. To determine the proportion of South African HCWs who have received training on dolutegravir and from whom
3. To determine the proportion of South African HCWs who have access to the 2019 guidelines and describe that access
4. To determine any association between HCW knowledge of dolutegravir interactions and independent variables (province, age, profession, ART experience, training, access to guidelines)
5. To determine any association between HCW confidence in their knowledge of dolutegravir interactions and independent variables (province, age, profession, ART experience, training, access to guidelines)
6. To determine HCW preferences for training

Study design

A quantitative, cross-sectional, descriptive study using an anonymous online survey of HCWs working in the field of HIV in South Africa.

Participants and sampling

The survey was disseminated to all HCWs who had used the hotline; and to other HCWs working in HIV by relevant HIV-focused organizations, such as the Southern

African HIV Clinicians Society and TB HIV Care, via e-mail, short message services (SMS) and social media, i.e. convenience sampling.

Data collection

The anonymous survey was designed, tested and piloted, and included sections on demographics, guideline access and training, interaction knowledge, and counselling. The online survey was conducted in August and September 2020.

Data analysis

Descriptive and inferential analysis was done using proportions and the 95% confidence interval (CI) to determine relationships between independent and dependent variables.

2.3.2 Study 2

The primary aim of the study was to design, test and evaluate the effect of WhatsApp group-based HIV training on nurses' and CHWs' knowledge in a remote area of South Africa. The primary outcome was effectiveness – a change in knowledge compared to a control group who did not receive training.

The secondary aims were to assess uptake, acceptability, and feasibility of the intervention; and to explore and describe the changes in prescribing, comparing the intervention group to the control group.

Specific objectives

1. To determine knowledge changes through knowledge testing of nurses and CHWs: test score change from baseline to immediately after training of intervention clusters; test score change from baseline to three months after training of intervention compared to control clusters
2. To determine knowledge retention through knowledge testing of nurses and CHWs three months after the intervention: changes in test score of intervention cluster from immediately after training to three months after
3. To explore and describe the changes in prescribing/clinical care due to the training intervention: changes in incorrect prescribing of the learning points in the

training, comparing intervention clusters to control groups for 48 weeks before the intervention to 48 weeks after; through folder reviews

4. To describe the uptake of WhatsApp-based training for nurses and CHWs: proportion of those offered the training who participated
5. To describe the participation in the training: proportion of participants in 'live' group and content viewed at timepoints up to two weeks after the live session; and retention: proportion who dropped out during the training period
6. To describe the acceptability of WhatsApp-based training for nurses and CHWs: quantitative and qualitative analysis of closed- and open-ended questions in the online knowledge questionnaire, focus group discussions and WhatsApp group interactions
7. To describe the feasibility of WhatsApp-based training for nurses and CHWs: quantitative and qualitative analysis of closed- and open-ended questions in the online knowledge questionnaire, focus group discussions and analysis of the WhatsApp groups

Study design

A pragmatic, mixed-methods, parallel-group cluster-randomised study.

Participants and sampling

Nurses and CHWs at 50 clinics in the Eastern Cape were invited to participate in the training during in-person recruitment visits. Sampling for focus groups was purposive and convenience, with an invitation to participate sent with the post-intervention questionnaire. Patient folders were sampled purposively pre- and post-intervention for clinical points learned.

Data collection

Uptake, feasibility, acceptability, changes in/retention of knowledge, and changes in patient care were measured using four data collection methods:

1. Online questionnaires: to test knowledge and retention of knowledge, and acceptability and feasibility

2. WhatsApp interactions: to measure and describe uptake, participation, feasibility and acceptability
3. Focus groups: to get in-depth feedback from participants on the acceptability and feasibility of the training
4. Retrospective patient folder reviews: to measure changes in prescribing practice

Data analysis

Quantitative data were analysed descriptively and inferentially. Qualitative data were analysed using template analysis.

Chapter summary

This chapter provided the rationale, aims and objectives of the two studies, and gave a short summary of them: firstly, to quantify the knowledge gaps of HCWs working in the field of HIV and their access to, and training on, the national guidelines; and secondly to design an intervention that could contribute to closing those gaps.

The next chapter is the literature review, to provide a contextual background and rationalise the study, and to position it within the current research in the field.

Chapter 3 Literature review

This chapter provides an overview of the current knowledge of guideline availability, accessibility, awareness and use. It then gives an overview of the current evidence on continuing education, focusing in, firstly, on eLearning (online training), then mLearning (mobile/cell phone-based), and the use of social media for training. Most pertinent to the study, it gives an overview of the current data on using WhatsApp as a training platform and microlearning – training done in 'bite-sized' snippets – as a teaching/learning technique. Finally, it summarises the research gaps revealed both by, and in, the literature reviewed.

Search strategy

The literature search was conducted using UCT's online library resources. Specific search engines used included PubMed, SCOPUS, Google Scholar and EBSCO. Searching on EBSCO was limited to health-related databases – Academic Search Premier, Africa-Wide Information, CINAHL, eBook Collection (EBSCOhost), Health Source: Nursing/Academic Edition, Library, Information Science & Technology Abstracts, Newspaper Source, Teacher Reference Centre and MasterFILE Premier Reference eBook Subscription.

Due to the considerable differences between high-income and low- or middle-income countries (LMICs) at health systems and infrastructural levels, preference was given to studies conducted in LMICs, with references from high-income countries included only when considered relevant.

Searching was limited to literature from the past ten years and, in some instances, five, due to the rapid evolution in using technology for education and to ensure reflection of the current situation. Review of the literature continued through the three years of the project, to include papers published after the initial review done in the planning stage. The literature review was not systematic or comprehensive but was limited to the scope of the project.

For the broader, introductory topics, such as 'online learning', where the search returned thousands of results, the most relevant reviews were used. In the areas most pertinent to the work, like the section on WhatsApp-based training, snowballing was used to get as comprehensive an overview as possible.

All relevant papers were loaded onto NVivo and assessed using line-by-line coding. During the coding, any additional relevant papers were sourced. The process flow of the literature review can be seen in Figure 4 and the search terms and filters used are listed in Appendix A.

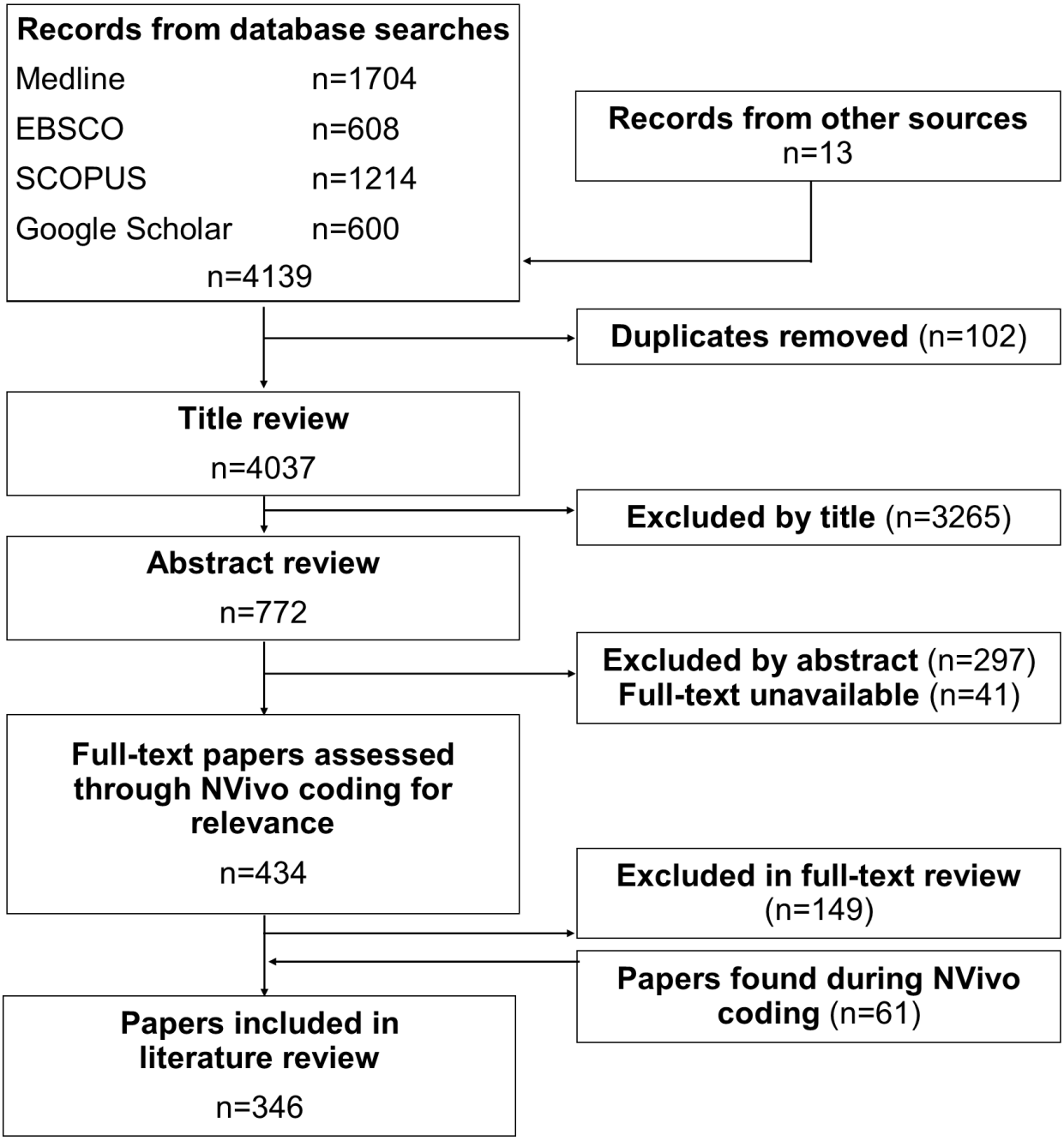

Figure 4. Flowchart of phases of literature review

Introduction

It is crucial to patient care for HCWs to know and understand the most current clinical guidelines[88-90] and to practice what is in them[60, 91, 92]. Clear guidelines, and knowledge thereof, improves professional practice[93-95], facilitates patient health across the range of HIV-associated services[95-102], and ensures the recognition of the need for urgent intervention[103].

Adherence to guidelines is associated with improved outcomes for patients[90] but this adherence is only possible if HCWs are aware of the existence of the guidelines and if they are available and easily accessible.[104] (Section 3.1)

The dynamic nature of HIV treatment and changing recommendations also requires ongoing dissemination of updates and training of HCWs in the field to ensure knowledge of, and adherence to, the guidelines.[81, 103, 105-109] (Section 3.2)

Ongoing training, especially in poorly resourced countries, is challenged by human resource, infrastructural and financial constraints. One way to overcome these barriers is to bring the training to the workplace.[4, 60, 90, 110, 111] Innovative, accessible and scalable solutions, using technology available in these settings, are needed. (Section 3.3)

Cell phone use is ubiquitous in South Africa, making mLearning – learning delivered on a handheld mobile device, allowing accessibility independent of time and space[8-10] – a viable option. Numerous studies have been conducted using various platforms and online teaching methods, allowing for a summary of key strategies to optimise mLearning interventions. (Section 3.4)

Many training formats require prolonged teaching/learning time, a precious resource in busy clinics. Microlearning involves ‘bite-sized’ learning in five- to 15-minute blocks. It has been used for continuing education across a wide range of medical specialities.[112-119] (Section 3.5)

There is a lack of data on the use of mLearning as a tool for continuing education, especially in LMICs. (Section 3.6)

3.1 Clinical guidelines: awareness, availability and HCW knowledge

The Oxford English Dictionary's definition of a guideline is:

"A rule, principle, or general statement which may be regarded as a guide to procedure, policy, interpretation, etc., or (especially) as giving authoritative guidance".[120]

In the clinical setting, the definition can be refined to being an essential, standardised, systematically developed tool to support evidence-based diagnosis, management and treatment of patients.[104, 121]

Guidelines provide a framework for effective clinical management[122, 123] and allow for uniformity of care across facilities[123, 124]. This is important in the South African setting, where there is a high degree of patient movement. Fox et al, in their large study of retention in HIV care analysis (n=55 836), found that 50% of patients transferred between clinics at some point in their care.[125]

To be effective, guidelines should be clear, simple and user-friendly.[60, 90, 126] HCWs in multiple studies have reported that complicated, overly detailed guidelines are hard to use.[90, 95, 97, 104, 127-130]

Guidelines across HIV treatment and services are updated frequently, as new evidence is found.[94, 97, 99, 103, 128] Updating evidence-based guidelines as evidence emerges is essential to ensure optimal patient care, but frequent changes can be confusing for HCWs.[82, 128, 131]

To demonstrate this frequency of updates, the 2023 edition of the South African National ART Clinical Guidelines[42] is the sixth edition of the guidelines since the first edition in 2010. Since its release in 2023, four updated versions have been published.

A pertinent example – reported on in several studies across sub-Saharan African countries – of how this dynamism can impact patient care is with the infant food choices for mothers living with HIV, a major concern in resource-limited settings where food scarcity is common.[88, 106-109, 128] At the start of treatment programmes, breastfeeding was discouraged due to the risk of vertical transmission. As new evidence has emerged and treatment access and viral suppression have increased, the guidelines have been

updated to first recommend exclusive breastfeeding for just six months, through various iterations, to exclusive breastfeeding for six months followed by ongoing breastfeeding for two years.[128] This has resulted in confusion amongst both HCWs and their patients about best practice and can result in suboptimal infant nutrition.[88, 91, 107, 109]

3.1.1 Awareness of guidelines

Primarily, awareness of guidelines and continuing communication around updates is vital[90, 109] but these are often lacking.[79] In Duque et al's study of South African HCWs' knowledge of the national seasonal influenza guidelines (n=1 164), they reported that only 74% of the HCWs were aware that the guidelines existed.[132] Similarly, in KwaZulu-Natal, Makhubo and Naidoo found that just 2% of HCWs (n=85) were aware of the provincial cervical cancer screening guidelines.[92]

In the field of HIV, similar gaps in awareness have been reported globally, across the range of HIV services and HCW cadres. In the USA, a survey of 225 pharmacists showed that 63% were unaware of the current pre-exposure prophylaxis (PrEP) guidelines.[133] In a qualitative Tanzanian study (n=26), HCWs reported being unaware of the WHO ART guidelines – which were adopted by the country.[134] This was perceived as a barrier to early ART initiation.[134] In South Africa, Raswese and Peu reported that only 45% of nurses (n=93) in a tertiary Gauteng hospital were aware of the hospital's HIV pre-exposure prophylaxis (PEP) guidelines.[135]

Awareness of guidelines is expected to increase over time, and the more common the treatment involved becomes, but this does not hold true. A multi-year study of PrEP knowledge amongst primary care HCWs (n=1 503) in the US showed that 8-10% had read the guidelines in 2011, 2012 and 2013, but in 2015 this had only increased to 22%.[101] While 2015 was early in terms of the PrEP landscape, less than a quarter of practicing primary care clinicians having PrEP knowledge, four years into the programme, particularly in a well-resourced country, is concerning.

Awareness alone may not equate to implementation.[96, 136-138] In an Indian study across HCW cadres (n=400), 90% said they were aware of the PEP guidelines to be followed after a needlestick injury, but only 37% knew the window in which PEP needs to be

started.[139] In Nigeria, 60% of HCWs (n=300) said they knew of PEP.[140] Of those, 81% were aware of the national guidelines, but just 60% knew the correct duration of PEP.[140]

In addition to HCW awareness, it is vital that these documents are available[94, 141-143] and accessible[89, 136].

3.1.2 Availability and accessibility of guidelines

While the terms 'available' and 'accessible' seem relatively interchangeable, in this context they are not. Available means "being present"[144] and accessible means "capable of being reached"[145].

Firstly, dissemination of guidelines from the central point where they are made is challenging, especially in resource-limited settings.[108, 128, 142] At facility level, Church et al, in their audit of HIV service delivery in 156 facilities in six sub-Saharan countries found that, overall, 75% had guidelines available.[146] South Africa scored highly in this audit, with 100% of facilities having guidelines available compared to only half of those in Uganda.[146]

In 52 KwaZulu-Natal clinics, Xaba, in their implementation study found that 98% had the most recent ART guidelines available.[147] Guideline availability was lower in Phetlhu et al's small study in the Western Cape, where 86% of nurses (n=44) in rural Western Cape facilities reported that HIV/TB policies were available to them.[136]

Availability may not equate to accessibility.[90] Guidelines may be stored or locked in management offices.[136, 142] There may only be one/limited guidelines for a whole facility[60, 90, 142], or only outdated versions[94, 142, 148, 149]. A Tanzanian study found that, while updated versions of the HIV guidelines were 'available', the updated version was in the in-charge's office and the outdated ones were at the workstation.[149] In a small South African study (n=19), only 28% of HCWs reported using the most recent drug resistant TB guidelines, the rest saying they were using previous, out-of-date versions.[94]

This is one of the challenges, especially in HIV and TB, where evidence is constantly generated, requiring regular guideline updates to ensure optimal patient care.

3.1.3 Guideline knowledge and adherence

The presence of guidelines may not translate to implementation thereof.[142] HCWs need to be knowledgeable about guideline contents and understand what has changed in updated versions, and why.[150] Knowledge of guideline recommendations has been shown to improve HCWs willingness to provide HIV services[91, 141, 151].

Studies of South African HCW knowledge of HIV-related guideline recommendations have contradictory results. While some report adequate knowledge of guideline recommendations including VTP[91, 103, 109, 152] and TB[98] guidelines, others report gaps in HCW knowledge of TB/HIV treatment guidelines[90, 98, 136], monitoring[153] and VTP[152].

Guideline knowledge – or a lack thereof – can affect patient care. In Adebimpe's study of Nigerian HCWs' knowledge of PEP (n=300), they found that just 2.7% had good knowledge, 57% moderate, and 40% poor knowledge.[140] This inadequate knowledge showed itself in practice, where only 66% of those who'd had a needlestick injury in the previous six months had used PEP, and only 86% said they'd encourage its use in occupationally-exposed colleagues and sexual assault victims.[140] These gaps in PEP knowledge were echoed in a South African study of nurses in Gauteng.[135]

Importantly, many studies reporting on HCW knowledge of guidelines do not mention whether the guidelines were available to the study participants.[92, 98, 101, 103, 140] This makes it hard to establish whether the lack of knowledge was due to not reading or becoming familiar with them, being unaware of their existence, or not having access to them.

Knowledge facilitates use of, and adherence to, guidelines[60, 108, 142, 154] but knowledge does not necessarily equate to adherence. Adherence to up-to-date guidelines is needed for good clinical outcomes.[90, 94, 98] It has, however, been shown to be low in many settings, across HIV guidelines.[90, 128, 155, 156]

Gunn et al found that 75% of the 12 American doctors they surveyed knew that pregnant women should be tested for HIV during the first and third trimester, yet only 50% offered testing to their pregnant patients.[137] In Brazil, Saraceni et al found that, while adherence to guideline-recommended CD4 and viral load testing was high,

adherence to routine TB monitoring and provision of prophylaxis was moderate to poor.[157]

In Uganda, Namuju et al found that only 19% of patients eligible for cryptococcal antigen screening according to the guidelines were screened.[158] In Nigeria, 53% of TB patients living with HIV were not started on ART, as recommended in the guidelines.[159] Only 39% of HCWs (n=242) adhered to ART initiation guidelines.[159]

In South Africa, multiple studies have shown the effect of non-adherence to guidelines on patient care. Ninety seven percent of the 114 of the nurses from 18 PHC facilities in the North West knew about the UTT strategy introduced in 2016, and yet only 63% had suggested it to their patients in the year prior to the study (2018).[141]

While a high proportion (97%) of the PHC nurses (n=103) surveyed in a study in Limpopo showed good knowledge of the HIV and Infant and Young Child Feeding guideline, only 32% were implementing them correctly.[109] The nurses and CHWs (n=38) in Motlhaoleng et al's small study in North West showed that 68% of them had adequate knowledge of the South African TB guidelines and 97% of patients received the correct TB treatment, but only 59% of those co-infected with HIV were on ART.[98]

Non-adherence to guidelines can have major repercussions not only on patient care, but HCWs' own health too. TB infection control practices are essential to protect the health of both HCWs and patients at facilities, yet three in ten Free State HCWs in Engelbrecht et al's study self-reported not implementing them.[160]

Finally, to highlight that knowledge of, and (perceived) adherence to, guidelines does not necessarily equate to improved patient care, Akamike et al's study of Nigerian HCWs (n=85) reported that, while 59% of respondents showed good TPT guideline knowledge, and 75% self-reported practicing the guidelines, only 18% of patients received TPT.[161] Lack of training was one of the challenges to guideline implementation, reported by HCWs in this study.[161] Ongoing training has been cited as important to facilitate guideline adherence.[60, 81]

3.1.4 Training on the guidelines

Once guidelines are available and accessible, HCWs need to receive ongoing training on them.[60, 90, 142] Formal training is associated with better knowledge[103, 161, 162] and improvements in confidence and competance[36, 162-164], and patient care[36, 165-167].

There is, however, a lack of training [81, 123, 136, 168], especially in resource-limited settings, as it requires a plethora of resources, including time, finances, transport and trainers[82, 169, 170]. This lack of training on guidelines leaves HCWs unable (or unwilling) to confidently implement them.[129, 143, 148] Gaps in training have been reported across the remit of HIV-associated guidelines across Africa.

In Ethiopia, just 30% HCWs (n=397) had received PrEP training three years after guidelines were introduced in 2019.[171] Further west, 39% of Nigerian PHC HCWs (n=113) in Okusanya et al's study reported not having any training on the VTP guidelines[108] and 40% had not had training on HIV/TB in Odume et al's study (n=333)[159].

In South Africa, the Tshwane Declaration of Support for Breastfeeding (2011) significantly changed the infant feeding recommendation from six months of exclusive formula feeding to exclusive breastfeeding for mothers living with HIV.[172] Four years later, Niewoudt and Manderson, in their small qualitative study of 11 nurses and CHWs from four community health centres found that, while some had received VTP training, none of them had had training on the Declaration.[150]

Two years later (2013), the Infant and Young Child Feeding Policy was revised, recommending that babies who tested positive for HIV should be breastfed for a year.[109] Sixty eight percent of PHC nurses (n=103) in Mpasha and Skall's study in Limpopo had not had training on this update in 2015.[109]

Calls for more training are found across studies on multiple HIV-related guidelines, including testing[95, 130, 173, 174], ART[127], safer conception for PLHIV[143, 175], PrEP[89, 154, 176-178], PEP[140], the educational activities of CHWs[179], integrated management of HIV and non-communicable diseases[148] and HIV and TB[90, 94, 180], opportunistic infections like cryptococcal meningitis[158, 181] and VTP[81, 108, 128].

Once-off training is not sufficient where guidelines are regularly updated. To facilitate adherence to guidelines, ongoing training is needed,[36, 60, 92, 98, 129, 134, 141, 156, 161, 182], something requested by HCWs themselves in studies in the African[164] and South African[55, 183, 184] settings, especially in isolated/rural settings[136, 185].

3.2 Continuing education

Continuing education (CE) – also referred to as continuing professional development, in-service training, or continuing medical education[186] – describes the ongoing learning of HCWs to maintain and update their professional skills and practice, ensuring competence and effectiveness in the workplace.[2-4] For health care systems to run well, CE is essential[2] and it is one of the NDOH's objectives to meet Goal 3 of the *2030 Human Resources for Health Strategy:* "to produce a competent and caring multi-disciplinary health workforce through an equity-oriented, socially accountable education and training system".[187]

In-service training boosts performance and closes gaps in implementation[98]. Murudi-Manganye et al, in their conceptual model to strengthen integrated management of HIV and non-communicable diseases by NIMART nurses in Limpopo, place in-service training as one of the essential components to ensure healthcare service sustainability.[148]

Crowley et al's review of the first ten years of NIMART in South Africa, found that inadequate training was mentioned as a barrier in most of the papers included in the review, concluding that there was a need for standardised, in-service, training.[36] This was echoed in a qualitative study on factors facilitating NIMART nurses' adherence to HIV/TB guidelines, where the need for ongoing training within facilities was highlighted.[60]

3.2.1 On-site continuing education

The most regularly cited barriers to traditional CE, especially in rural areas, are distance and time needed for attendance.[110, 169, 188] In resource-limited settings, often one or two HCWs from a clinic attend training at a centralised point and are expected to go back to their facilities and share what they learnt with their colleagues.[128, 170] This can be

thought of as an informal version of a train-the-trainer model, where individuals attend training and then cascade the training down to others.[189]

The 'trickle down' concept, however, is often not successful.[81, 82] This is understandable when placed in context: one nurse from a facility attends a 3-day course on the HIV guidelines and returns to a busy clinic which has been without a staff member – remembering some rural clinics have just one nurse – and is expected to relay all they've learnt to the rest of the clinic staff during clinic hours.

Rather than moving HCWs to training, the training should be brought to them, in the workplace, to reduce these barriers.[4, 60, 90, 110, 111] Hosey et al reported on their process to develop an online continuing professional development library for the 17 member countries of the East, Central, and Southern Africa College of Nursing (including South Africa).[170] This began with a survey of nursing and midwife leaders in all 17 countries to identify needs, including the preferred method of teaching: 62% chose clinical on-site learning.[170] Just 2.7% chose clinical off-site learning.[170] In Feldacker et al's survey of HCWs in sub-Saharan Africa who had completed an online HIV management course, 52% reported preferring online CE, 31% on-site and 17% away from work.[3]

It is clear that innovative CE solutions are needed that are non-traditional[190], flexible[188] and cost-effective[191]. Technology-based distance learning can meet these needs.[5, 93, 190, 192]

3.2.2 Moving continuing education online

Since the start of the internet in 1983[193], its capabilities and use have expanded exponentially. It is now used across all aspects of life, including education and training.

Figure 5, shows the results from a simple PubMed search using 'online learning' and 'health'. In 2000, 152 papers were published. In 2020, as the COVID pandemic resulted in virtually all medical – and other – education moving online, published papers increased exponentially.[194] In 2024, 3 455 papers were published.

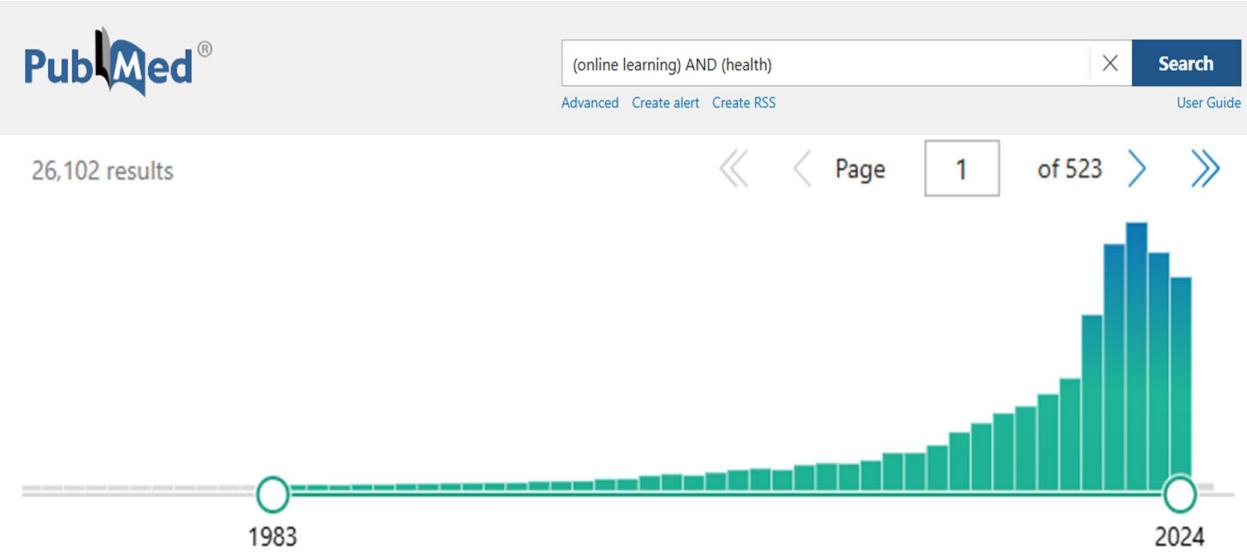

Figure 5. PubMed search of 'online learning' and 'health'

eLearning has many synonymous terms – web-based learning, online learning, internet-based learning – and multiple definitions. For the purposes of this thesis, Vaona et al's simple definition, in their Cochrane review of eLearning for health professionals, will be used: "an educational intervention that is mediated electronically via the internet".[5] It is broadly divided into three types:[10, 195, 196]

1. **Synchronous:** training done in real time, e.g. video conferences
2. **Asynchronous:** training done offline, i.e. not in real time, but in the participants' own time, when it suits them, e.g. online courses
3. **Blended:** a combination of face-to-face and online training

As technology has advanced, so has eLearning, encompassing a plethora of teaching methods, concepts, approaches and technological platforms.[197, 198] COVID-19 switched the delivery of medical education quickly and profoundly[199, 200], with virtual learning becoming essential to ensure that HCWs could continue with CE[201].

Large volumes of studies and, therefore, literature resulted.[194] This, in turn, has allowed a multitude of reviews on the papers produced, which will be used for this broad overview of online learning.[194, 198, 201-206] There is vast heterogeneity in specialities

taught, HCWs included, geographical regions, and the methods used in both training and the assessment of outcomes.[204, 206] Many studies are of low quality, making it impossible to draw robust conclusions.[194, 197, 198, 201-206]

A meta-analysis of digital problem-based learning using pooled effect sizes concluded that digital learning is as effective for knowledge improvement as face-to-face learning, and may be more effective at improving skills, while acknowledging the bias introduced by the heterogeneity of the studies.[197] Similarly, a systematic review of technology use for evidence-based medicine training found that technology-based training was more effective than face-to-face training.[206] Martinengo et al found that online training on chronic wound management was more effective than no training, and blended training was more effective than online training for improving knowledge.[198] Lastly, Brusamento et al's review and meta-analysis of CE in paediatrics concluded that digital education was more effective for improving knowledge and skills than no training and at least as effective as traditional training, also acknowledging the high risk of bias of the included studies.[207]

Rouleau et al reviewed reviews of eLearning for nurses' CE, finding 22 eligible reviews, and a lack of robust data regarding effectiveness.[208] Of the 20 reporting on knowledge,13 showed improvement and seven showed no effect.[208] Nurses' reactions to eLearning were mostly positive (8/11).[208]

This is an important finding. Effectiveness alone is not enough to favour any education platform. Participant acceptance is essential. In one review, participants found eLearning to be more engaging than asynchronous and traditional learning[202] but another review concluded that, while in some studies participants found the experience of online training positive, others found it inferior[203]. Commonly reported disadvantages were technological challenges, distractions (home/work)[201, 203, 208] and 'Zoom fatigue'[194, 201]. Both reviews reporting this were done on training interventions during the COVID-19 pandemic, when there was an overload of online meetings and lectures.

What is clear is the advantages of online learning where time and geography are major challenges.[10, 209] These include accessibility, improved facilitation, peer discussions and saved time[11, 201, 203, 210], resulting in participants being more satisfied[201, 206]. The

flexibility, accessibility and efficiency of eLearning[3, 201, 211-214] is particularly suited to dynamic fields such as HIV. Mobile applications (Apps) can facilitate this further.[201, 206]

3.3 mLearning

The vast majority of online education studies in the health sector were conducted in high income/developed countries[197, 199, 201, 204, 206] using platforms such as Zoom and Microsoft Teams to deliver both synchronous and asynchronous training[194, 202, 204]. Using platforms like Zoom for training ideally requires a computer or tablet, something which is not always readily available in lower-resourced countries like South Africa. In 2023, over 100% penetration of cell phones was documented in the country.[215]

mLearning – a sub-set of eLearning – is learning delivered on a handheld mobile device, allowing accessibility independent of time and space.[8-10] It may be an ideal option in areas where cell phone use is common but access to computers is limited[216], providing a way for HCWs in hard-to-reach places to access learning.[217]

3.3.1 Participant perceptions of mLearning

The perceived advantages of mLearning include accessibility, flexibility and time-saving[11, 210, 216, 218, 219] cost-effectiiveness[11, 220] usefulness and ease of use[219, 221, 222] and its ability to enable connectedness[11, 221, 223]. A number of reviews of mLearning studies have concluded that participants have a positive attitude toward learning on a mobile platform and report increased confidence[210, 217, 224] and improved patient care[10, 208, 218, 222, 225]. As with the eLearning reviews, more data were available from high-resource countries.

The setting makes a significant difference when assessing methods of training, especially those relying on technological infrastructure. Guillaume et al conducted an integrative review of CE using mobile-social learning in LMICs.[11] In 27 of the 31 eligible papers included, participants reported positive learning outcomes.[11]

Studies conducted on the African continent also show participant enthusiasm for the delivery of training via mobile devices. Kenyan HCWs receiving malaria treatment training via SMS perceived it as relevant and useful.[221] In the Democratic Republic of

Congo, an App teaching basic emergency obstetric and newborn care to HCWs was self-described as feasible and acceptable, with positive effects on knowledge, skills and confidence.[217] Woods et al tested a CE programme using lessons on maternal care for nurses via SMS in South Africa, concluding that the majority enjoyed it and felt it had improved their clinical knowledge.[226]

3.3.2 Knowledge and skills improvement with mLearning

While self-reported improvements in knowledge show acceptance and enthusiasm for the delivery of training via mobile devices[210, 218], more robust data are necessary to make any conclusion on the effectiveness of mLearning in LMICs.

A large systematic review and meta-analysis of mLearning in health professions concluded that mLearning is at least as effective as traditional learning, but only five of the 29 studies were conducted in LMICs.[10] Kim and Parks' systematic review and meta-analysis of mLearning for nurses found that only seven of the 11 eligible studies reported on the effect of the intervention on knowledge and skills – with all of them showing a significant effect.[224] Only two of these papers were from LMICs.

When looking at individual mLearning studies conducted in LMICs – Kenya[221, 227], Ethiopia[228], India[210, 229], Tehran[230], Vietnam[216], the Democratic Republic of Congo[217], Rwanda[231] and South Africa[209, 232, 233] – 11 showed improvements in knowledge and one found no change. Many of these studies were small, with the associated risk of bias.

While mLearning seems to be a viable option for CE in LMICs, it is not without its challenges.

3.3.3 Challenges of mLearning

Donkin et al's review reported that technology issues were the most commonly reported challenge of eLearning and mLearning, followed by time constraints, inadequate feedback and ability to contribute, and distracting work environments.[203]

The situation is no different in LMICs and is often more pronounced. Guillaume et al's review of studies in LMICs reported that infrastructural/technology issues were the

primary barrier to mobile-social learning.[11] This was echoed by HCWs participating in mLearning interventions to provide family planning training in Senegal[218] and maternal and child health training in Nigeria[222].

Many mLearning interventions involve the use of technologically advanced and/or data-expensive elements such as Apps[217, 228, 231, 234], podcasts[235], and Moodle management systems[233]. These can be costly, require stable internet connectivity and may require a high level of digital literacy.[200, 218, 223] In poorly resourced countries, data costs are at a premium, and consistent internet access is often a challenge. The key to finding an innovative solution is simplicity.

Mobile-social learning – combining accessible mobile technology for learning with social networking for experience sharing and knowledge transfer – supports the learning process and allows peer engagement and the creation of communities of learning.[11]

3.3.4 WhatsApp-based learning

Social media (SM) is defined in the World Medical Association's statement on professional and ethical use of SM, as "the collective term for different interactive platforms, websites and applications intended for digital networking, that allow individuals and organisations to create and share user-generated content digitally".[13]

SM platforms include Facebook, Instagram, TikTok and WhatsApp. These platforms are free, easily accessible and widely used: 64% of the global population were users of SM in 2024.[236] It is increasingly being used by medical professionals for communication, networking, sharing information and education/training.[11, 237]

In 2023, WhatsApp was the most popular SM platform in South Africa, with 94% of internet users using WhatsApp.[238] WhatsApp is a free, end-to-end encrypted instant messaging service which allows users to send text, voice and video messages, and share documents[14], both in real-time and asynchronously, allowing for online group 'conversation'. WhatsApp Business – a subsidiary of WhatsApp – allows the administrator to have more control.[239] Communities of up to 1 024 people can be made and the administrator controls who can or cannot send messages, and can delete messages from members in the group.[239]

WhatsApp provides a cheap, simple, effective way of communicating[240] which may offer benefits in the field of CE[241]. While the field is still relatively new, studies have shown participant enthusiasm and acceptability of the platform.[191, 242-245] On the African continent, WhatsApp has been used for a variety of purposes in healthcare, for patients, HCWs and researchers.

At the patient level, WhatsApp has been used as an appointment reminder in South Africa[246]; peer support for patients in Kenya[247, 248] and South Africa[249, 250] and to share public health messages in South Africa[249] and Malawi[251]. In the field of research, it has been used to recruit participants in South Africa[252] and Uganda[253], deliver surveys and collect data in Rwanda[254] and Nigeria[255, 256], and to conduct study interviews in South Africa[81].

At HCW level, WhatsApp has been used in several ways:

- To share administrative information in Malawi[257, 258] and Uganda[259]
- As a discussion forum 'add-on' to other, longer forms of training in Nigeria[260, 261], Zimbabwe[191] and Zambia[262]
- As a clinical case discussion forum in South Africa[245, 263] and Nigeria[264]
- To share clinical results between facilities in Kenya and Mozambique[265]
- For specialist referral in South Africa[266]
- As a means of mentorship in Tanzania[267]
- For supervision and professional development in Nigeria[268]
- For CE in South Africa[243, 263], Egypt[269] and Zimbabwe[191]

One of the earliest studies (2015) in the African healthcare setting was Pimmer et al's investigation of the use of WhatsApp in mLearning for rural CHWs (n=41) and their facilitators in Malawi.[257] They created two WhatsApp groups, each with CHWs and a moderator sharing information on HIV and other health topics over five months. It was found to be easy to use, overcoming geographical challenges and improving connection amongst isolated HCWs. Overall, WhatsApp was perceived as a good platform on which to learn.[257]

WhatsApp ticks the technical and logistical boxes, but acceptability and effectiveness are important for uptake of CE. WhatsApp-based interventions across a range of HCW cadres, medical specialities and uses have reported improved knowledge, but there is a paucity of robust studies on knowledge changes and other factors affecting usability.

A Malawian study using WhatsApp for HIV consultations between clinical officers (n=30) and a specialist reported that participants felt that they learnt from the case discussions and improved their skills.[270] An 'add-on' discussion forum on WhatsApp during a blended training course on HIV counselling for HCWs in Zimbabwe (n=293 from 233 facilities) found that the WhatsApp discussions were highly endorsed by the participants.[191] They reported that the discussions helped to identify gaps in their knowledge and provided learning opportunities, with moderators reporting increased knowledge and skills.[191]

Both studies were descriptive. One of the few randomised controlled studies in the field, was Elzeky and Shahine's study using WhatsApp to train Egyptian nurses (n=70) on blood pressure monitoring.[269] Twenty four teaching sessions, in the form of videos, text, audio clips or images, were delivered via WhatsApp in a group on which participants could also ask questions.[269] While not implicitly stated in the paper, it appeared to be asynchronous.[269] A statistically significant improvement in knowledge, but no improvement in performance, was shown.[269]

In the South African setting, Woods et al used WhatsApp as a clinical case discussion forum and learning tool after an advanced HIV management course for doctors practicing in rural Eastern Cape facilities.[245] Use was reported descriptively (n=92): half of the participants posted cases and responded to others' cases; 86% said that the forum had increased their clinical confidence; and almost all of them reported using the group's guidance at some point.[245]

WhatsApp groups for newly graduated nurses in Nigeria, with moderators sharing knowledge and stimulating group discussions, showed improved knowledge and, importantly, lower professional isolation, an important consideration, especially in rural settings with minimal support.[264]

Drawing from these, and other studies, several key strategies to optimise an mLearning intervention using a social network like WhatsApp were collated.

3.4 Key strategies for mLearning

Addotey-Delove et al completed a scoping review of mHealth in the developing world. HCW adoption was affected by factors including community participation, context and content, flexibility, cost and personnel workload.[271] mHealth is "the use of mobile wireless technologies for health".[6] While mHealth usually refers to clinical uses, such as collecting clinical data and real-time vital sign monitoring[272], the principles behind mHealth's use, especially in resource-limited settings, can be applied to mLearning. In this section, the key strategies – and how WhatsApp has been used within the strategies – will be described.

3.4.1 Simplicity

The simplicity of text messaging is key.[210, 219, 227] Krah and De Kruijf explored the evidence behind the use of mHealth to improve African community health.[273] They found that, while most study assessments were highly optimistic, evidence of sustainability and scalability was weak.[273] Importantly, simplicity and success were causally connected.[273] Complicated interventions using high tech devices or expensive applications requiring ongoing specialist oversight are unlikely to be sustainable in poorly-resourced areas.[218, 263, 265]

A randomised controlled trial of a South African mHealth intervention illustrates this need for simplicity. An App to improve engagement in HIV care was developed and tested in Gugulethu (less than 20 km from Cape Town's city centre).[274] Challenges encountered in the study included trouble with installation; more than a third of participants getting different phones, with only 16% of them reinstalling the App; and technical issues with both the App and study dashboard, resulting in them being unable to demonstrate feasibility.[274]

While the participants in this study were not HCWs, the technological concepts and challenges are the same. The study concluded that future research should be aimed at

using tools that are currently used, such as WhatsApp, which 94% of their participants reported was their favourite App.[274, 275]

WhatsApp removes the challenges of geography and time.[210, 219] Kearney et al, in their paper on the pedagogy of mLearning term it well: “mLearning creates malleable spatial-temporal contexts for learning’’.[276] This is especially advantageous in large countries with extensive rural areas, such as South Africa, which covers 1.2 million km^2, 38% of it rural.[84, 277] The platform is simple to use[257], and used widely in South Africa[238].

Simplicity is key, but context is important, too[278], especially in LMICs.

3.4.2 Context

A deep understanding of the context in which an intervention is implemented is required for success.[273, 278-281] Interventions must be considerate of the organisational culture; flexible to, and aligned with, the needs of HCWs; user-friendly, cost-effective and scalable within the local context.[11, 269, 271, 280-282]

Multiple mLearning models have been conceptualised, which include contextual factors as key elements.[279, 283] Zidoun et al used three of the most cited mLearning frameworks to define five factors for optimisation, all of which require in-depth examination and consideration of the context in which the intervention is given:[279]

1. **Pedagogy**: the teaching method and practice, which needs to fit within the learning and working environment
2. **Content**: what will be taught, to fit within the scope of practice, national guidelines, etc.
3. **Mobile technology**: which device and platform to use in the context, e.g., what is accessible, available, affordable in the setting
4. **Learning environment**: the context in which learning will occur, where, when, etc.
5. **Learner’s profile**: current knowledge, personal characteristics

The authors recommended that pedagogy be the starting point because it guides the contextual choices for the other four.[279] This is echoed by Kearney et al, in their development of an mLearning pedagogical framework.[276]

The lack of human and financial resources, vast distances and widespread use of cell phones and WhatsApp, were the primary contextual factors considered in this project. The importance of a defined pedagogy was, however, not minimised. To define the pedagogy, especially in a mixed-methods study with a considerable qualitative component, it is necessary to first define the philosophical underpinnings of the research. A full discussion of the theoretical frameworks and pedagogy is in Chapter 4.

3.4.3 Cost-effectiveness

By cutting out the need for travelling to centralised points, and the expenses of in-person training (venue hire, accommodation, etc.), distance learning saves costs.[11, 267] WhatsApp is free to download and requires relatively little bandwidth, making it functional at even 3G level.[270] Data for WhatsApp is affordable, with many South African cell phone providers offering low-cost WhatsApp-specific bundles.[284]

3.4.4 'Live learning' with a trainer present

Initial mLearning interventions used SMS, which was limiting both from a content point of view (maximum 160 characters) and that it allowed only one-way communication.[209, 221, 227, 285] Some nurses in a Senegalese pilot study using SMS to link to voice recordings for family planning training, suggested they would prefer more contact with the course coordinator.[218]

They are not alone in this preference. Real-time feedback from colleagues and mentors was reported by students as beneficial to clinical practice in 12 of the 16 studies included in Guillaume et al's review of mobile social learning for CE in LMICs.[11] Continued participant engagement requires an active trainer and timely feedback, according to Mosher et al, in their synthesis review of factors affecting engagement in synchronous online learning.[202]

Physicians using 'WhatsApp CME India' (n=571), which consists of seven WhatsApp groups to share "collective experiential knowledge", cited continuous moderation being appreciated by the majority (70%) and case discussions as the most useful part of the groups (77%).[286] Similarly, multiple African studies, reported that, while interaction with

trainers was perceived as beneficial, active participation with colleagues was equally important.[257, 268]

3.4.5 Interactive learning

Mobile-social learning – combining accessible mobile technology for learning with social networking for experience sharing and knowledge transfer – supports the learning process and allows peer engagement and the creation of communities of learning.[11]

The previously mentioned African Health Profession Regulatory Collaborative online CE library development project first collected data to identify the needs of nursing leaders in the 17 member countries.[170] When asked what the preferred teaching methods were, 60% of the participants chose group discussions.[170] Feldacker et al's survey of HCWs in sub-Saharan Africa (n=464 from 13 countries), after an online HIV management course, showed the same: group discussion was the most preferred learning method.[287]

Across HCW cadres, participants in studies using WhatsApp appreciated belonging to a supportive community and the decreased feeling of isolation/increased feelings of connectedness; the case discussions and sharing of insights across facilities; and the feedback from peers and supervisors.[191, 243, 244, 257, 264, 270, 288, 289]

Using WhatsApp as a discussion forum with an online primary health care course for young family doctors from the World Organisation of Family Doctors in 20 countries, participants appreciated the connection it promoted.[290] The study reported a 65% completion rate, a vast improvement on the reported baseline of 13%.[290]

In a quasi-experimental study of newly graduated Nigerian nurses (n=114) using WhatsApp to share knowledge, lower feelings of isolation and better knowledge in the intervention group were reported, the effect greater for those who actively participated.[264] Similarly, in Woods et al's descriptive Eastern Cape study, clinicians reported that they learnt from the shared case discussions, and those who were most interactive in the group were significantly more clinically confident (OR 8.44), although the study was small (n=92).[245]

While one realist synthesis review found conflicting results on the use of interactive 'chat' during online learning[202], many other reviews and studies have reported that interactive learning is preferred and has positive outcomes.[3, 4, 11, 93, 163, 244, 278, 291]

3.4.6 Saving time

Across the board, HCWs report that disruptions in work flow and time issues are challenges to CE[163, 169, 170, 188, 191, 219, 287], a concern especially in the South African setting, where there is a shortage of HCWs[46, 81]. Time is a precious resource.

Several studies have suggested that short bursts of learning content– like microlearning – can save time and could maximise engagement.[292]

3.5 Microlearning

The term 'microlearning' has various definitions. For the purposes of this study, Hug's definition, "microlearning deals with relatively short, small learning units and short-term focused activities"[7] will be used. The literature reveals differing opinions on a defined length of microlearning, ranging between five seconds and 15 minutes.[293-296]

Essentially, microlearning is learning delivered in bite-sized nuggets, often via a mobile device, allowing quick, easy and engaging access.[296-299] Buchem and Hamelmann, in their paper on a strategy to use microlearning for ongoing professional development, list five design principles that simply illustrate the definition:[297]

1. **Format**: small, easy to read, standard output type
2. **Focus**: clear, based on one topic or idea
3. **Autonomy**: self-contained, no need to look for further information
4. **Structure**: has essential elements, such as topic or URL
5. **Addressability**: a single resource or reference

Microlearning has been met with enthusiasm by CE participants across a range of medical specialities including pharmacy[112], paediatric critical care medicine[300], mental health[114, 115], haematology[116], pulmonology[117], geriatrics[118], and trauma care[119].

Theoretically, the underpinning of microlearning can be placed primarily on the Cognitive Load Theory.[298, 301, 302] Proposed by Sweller, it surmises that cognitive load

consists of intrinsic load (how complex the information is), extraneous load (how it is presented) and germane load (how hard processing it is).[303, 304] Microlearning can be used to lower the cognitive load.[302] As with any teaching technique, it has both advantages and disadvantages.

3.5.1 Advantages of microlearning

3.5.1.1 Improved knowledge, skills and confidence

Improved knowledge was reported in both studies that relied on participants' self-reporting[114] and measurement[113, 114, 116, 117, 119, 305]. None of these studies were randomised. They included descriptive[114], pretest-posttest[117, 119, 305], and quasi-experimental[113, 306] study designs. Improved clinical skills were reported both by self-reporting[114-116, 306] and measurement scales[118, 307].

Additionally, improved confidence was reported.[115, 305] Zarshenas et al showed a significant improvement in self-efficacy of nursing students (n=46) in the intervention group of their quasi-experimental pretest-posttest study using micolearning.[308]

3.5.1.2 Up-to-date training

Due to its flexibility and accessibility, electronically-delivered microlearning can provide training on new developments and/or updates.[117] This was appreciated by participants in a Kenyan study of HCWs (n=119) who participated in an SMS-based malaria training programme over six months.[221]

3.5.1.3 Time saving

As mentioned previously, time is precious. Microlearning interventions were praised for their brevity and focussed content by the HCWs in the Kenyan study above and several others:

- American nursing home staff (n=481) who received a weekly microlearning video on dementia care for a year[115]
- Informal carers in England (n=32) who received a 6-week pressure ulcer training intervention via App[309]

- Australian physicians (n=51) learning about eating disorders through a 10-week series of case vignettes[114]

3.5.1.4 Improved engagement, attention and retention

Microlearning increases engagement, something which is more easily measurable when using social media, as most platforms have in-built analytics.[295] Ingram Nissen et al designed a training intervention for primary care providers consisting of four 15-minute segments to improve genetic cancer risk assessment and management, which they disseminated in various forms – links, shorter sections, etc. – via Twitter, e-mail and search engines.[310] At its launch in 2014, 56 people enrolled, and by 2022, more than 15 000 had signed up.[310]

A cross-sectional study comparing bite-sized learning to synchronous, two hour-long Zoom lectures on anatomy and physiology for 455 first year allied health professions students in China reported better attention and motivation in the bite-sized learning than the online lectures.[311] They did, however, conclude that the combination of the two is ideal, to allow each technique to complement the other[311], but this study was specific to undergraduates, as opposed to CE.

Finally, both the conciseness and potential for repetition, and the integration of microlearning and social media which allows interactive, peer-to-peer learning, may improve knowledge retention.[119, 295, 310]

3.5.2 Disadvantages of microlearning

Sozmen, in her overview of the pros and cons of microlearning in health education, lists four main disadvantages:[302]

1. It does not teach analytical thinking or soft skills
2. Most of the responsibility lies on the teacher
3. Student interest/motivation determines its effects
4. There is a lack of data on whether it results in behaviour change

While her paper was from the perspective of primary to tertiary education[302], some of the points apply to CE.

Medicine and clinical skills can be complex, making microlearning (and social media) unsuitable for some subjects.[295, 296, 299] This was highlighted in Adams et al's online CE programme for asthma (n=523 doctors), an eight module microlearning curriculum delivered in multiple forms.[117] While the pretest-posttest study showed good engagement and improved knowledge, the authors warned that fragmenting a complex subject like asthma may result in gaps or misunderstanding of the treatment and rationale.[117]

This was also illustrated by the allied health students learning a complex subject, muscle physiology, in the Chinese study mentioned above.[311] Many of the students requested more explanation of the microlearning snippets in the post-intervention quiz.[311]

A significant risk when combining microlearning with social media is distraction.[295] It is easy to fall down a 'worm-hole' that is not related to the learning, while using social media. Additionally, depending on the frequency and type of interaction, 'message fatigue' can result in disengagement.[203, 221, 223]

Lastly, evaluation and outcome measurement of microlearning can be difficult.[295, 300]

3.5.3 Types of microlearning

Microlearning-based interventions have been tested using a variety of platforms and media, and technological complexity.[296] The most common are short videos[112, 115, 117, 306-308, 311] with links delivered via platforms including Facebook[312], LinkedIn[313], Twitter[314] and WhatsApp[119]. Other interventions have used Apps[118, 309, 315, 316], virtual training platforms[116, 317], QR codes[318] and, simply, SMS for both patients[319] and nurses[113]. Microlearning is regularly recommended as an add-on to other training content, rather than a standalone intervention.[118, 296, 302, 310, 320]

Most microlearning interventions are asynchronous[112, 309, 311, 314, 318], many based on just-in-time training[115, 118, 305-307], with some definitions saying that this is a key characteristic of microlearning[302]. Just-in-time training originated in the motor industry and has become common in the medical setting.[321] As its name implies, just-in-time

learning is learning available as and when the learner needs it, which implies asynchronicity.

The lack of interaction that results from asynchronous interventions has been reported in some studies as one of its disadvantages[311] and, as discussed in Section 3.4.5, interactive learning is desired by many. Research on using microlearning in a synchronous manner is lacking, as with many other aspects of CE.

3.6 Research gaps

Increasing the effectiveness and efficiency of CE using non-classroom-based approaches is clearly needed, especially as resources diminish and skilled HCW shortages become critical.[4] Numerous studies have concluded that innovative solutions are required for regular CE for HCWs[88, 103, 122], especially those in rural areas[136, 322, 323]. Below, the reported research gaps from the studies and reviews analysed through the literature review are divided into thematic sections.

3.6.1 Lack of rigorous studies

Several systematic and scoping reviews of the use of technology for medical education concluded that many of the studies included were of poor quality and had a risk of bias.[198, 205, 206] In Rowe et al's large systematic review (n=337) of studies of strategies to improve HCW performance in LMICs, they found most had evidence of low quality.[324] This was demonstrated above, with the use of self-reported outcome measurements in numerous of the microlearning studies.

3.6.1.1 Kirkpatrick's four levels of training evaluation

This lack of robust outcome reporting is a broadly reported gap in current research in the field, with a call for rigorously designed randomised controlled trials to evaluate the effectiveness of eLearning for HCWs.[325]

To ensure rigour, a comprehensive method of evaluation is necessary. Originally conceptualised by Kirkpatrick in 1959, the four levels of Kirkpatrick's training evaluation have become the most widely used strategy for training intervention evaluation.[299] The

model is simple, practical and covers all areas of training, allowing for rigorous conclusions to be drawn.

Kirkpatrick divides the evaluation into four levels:[326]

1. **Reaction**: how participants feel about the training, including format, timing, teacher
2. **Learning**: what knowledge participants have gained
3. **Behaviour**: how participants change how they do things at work, because of the training
4. **Results**: how training affects workplace results, e.g., quality of care, productivity, lower employee turnover

While the levels are explicitly defined, evaluation of the higher levels require more time and expense[326], which often results in a lack of their measurement.[194] Numerous reviews have highlighted this, which is illustrated in Table 2.

Table 2. Reporting of Kirkpatrick's training evaluation levels

Review	Number of studies included	Kirkpatrick's level, n (%)			
		Reaction	Learning	Behaviour	Results
Microlearning in health education *De Gagne et al*[299]	17	16 (94.1)	14 (82.4)	5 (29.4)	0 (0.0)
WhatsApp in continuing education *Coleman and O'Connor*[327]	23	13 (56.6)	8 (34.8)	1 (4.3)	0 (0.0)

3.6.1.2 Poor reporting of theoretical frameworks and intervention design

To maximise effectiveness and ensure the developmental integrity of any training intervention, the pedagogy used to design it is important. There are gaps in the reporting and/or use of theoretical frameworks and pedagogical methods used in studies of eLearning, mLearning and the use of social media.[10, 194, 203, 212, 295, 328]

Just five of the 23 studies included in Coleman and O'Connor's review of WhatsApp for CE reported on a learning theoretical framework, but the authors acknowledged that there was evidence of the use of a number of theories in many of the other papers, even though they were not explicitly reported[241], so this may be a problem of non-reporting over non-use.

Finally, there is a need for better reporting of the intervention itself, to allow for replicability, using a checklist like the Equator Network's template for intervention description and replication checklist and guide.[329]

3.6.1.3 Lack of qualitative data

Without participant acceptance of an intervention, there is no intervention. Gathering data on participant opinions is vital to inform researchers of their experiences, what works and does not work, their needs and challenges, etc. This allows for ongoing adaptions and development. There are, however, a lack of qualitative and mixed method studies to understand HCW experiences of CE and mLearning.[82, 330]

3.6.2 Studies in resource-limited settings

Research on eLearning[198, 199, 201, 202, 206, 212, 331], mobile digital CE for HCWs[10], mobile-social learning[11], blended learning[204] and mHealth[225] is largely conducted in high income countries. There is a lack of data on CE and mLearning in resource-limited countries.[3, 332]

This lack of data extends especially to rural settings[322] and Africa[242, 332]. Kaisara and Bwalya, in their 2022 systematic review of mLearning research in sub-Saharan Africa highlighted this[328], quoting Crompton and Burke's systematic review of mLearning in higher education (n=72), which found that just 3% of the eligible papers included in their review were from Africa[333].

This is an important consideration. To be effective, CE needs to be designed taking all of the contextual factors of the setting in which it is delivered into consideration, and to address the contextual issues of that setting.[93, 242, 291, 328] There is a need for robust research of this.[194]

3.6.3 Studies including CHWs

CHWs, who form a vital part of the health system, especially as tasks shift from doctors to nurses, have rarely been studied.[324] Rowe et al, in their systematic review of the effectiveness of strategies to improve HCW practices in LMICs (n=337) highlighted that there were few studies involving CHWs and the ones found were highly biased.[3, 324]

3.6.4 Microlearning and social media

The concept of microlearning seems viable for CE in a setting such a South Africa, but it is relatively new to the field. While it has been shown to improve knowledge and skills and be highly acceptable to learners, research on microlearning is still in the early stages.[296]

Much of the research that has been done on using microlearning and social media is of poor quality, with descriptive surveys to report outcomes.[295] Rigorous study of its effectiveness and best practices is needed.[296, 334, 335]

In addition, many of the studies of microlearning have used it as an add-on to other training[296] and there is a lack of data on whether it could be effective as a standalone intervention.

3.6.4.1 WhatsApp-focused interventions

The same applies to the data on the use of WhatsApp, which has been used, most commonly, as a discussion forum in addition to other training.[191, 260, 290, 292, 336, 337] There is a lack of rigorous research on WhatsApp's effective use for CE.[223, 241, 264]

Chapter summary

To optimise patient care, up-to-date clinical guidelines need to be available and accessible, and HCWs need to be aware of, trained on, and adherent to, them. The literature review has shown that all of these aspects are challenging, especially in settings like South Africa with large rural areas. As a result, knowledge of and use of guidelines is often poor.

Training in this context is also challenging, with infrastructural, financial and human resource barriers. The literature shows that on-site training is preferred and interventions using mLearning have shown promise. Key strategies were collated, including simplicity, context, interactive learning and microlearning to save time, and discussed.

There are, however, gaps in rigorous data, with solid theoretical underpinnings, on the use of mLearning, specifically with WhatsApp as a platform, especially from LMICs like South Africa.

The theoretical and conceptual frameworks will be discussed in the next chapter.

Chapter 4 Theoretical and conceptual frameworks

This chapter outlines the philosophical assumptions and theoretical and conceptual frameworks used in the design of the study, with the rationale behind their use.

Chapter 4 contains excerpts from the following papers:

Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. International Journal of Qualitative Methods 2024; 23: 16094069241284205. DOI: 10.1177/16094069241284205.

Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

Chisholm BS, Wallace ML, Blockman M and Orrell CJ. "WhatsApp is best!" Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

4.1 Introduction

To ensure research quality, explicit and transparent descriptions of the methods used are vital. This entails examination of the theoretical and philosophical assumptions underlying the research procedures[338-340], a critical step in study design which is often left out of research practice[338, 341].

Michael Crotty, in his book, *The Foundations of Social Research*, described a well-designed research study as having four elements: (1) theoretical framework (philosophical); (2) epistemology; (3) methodology; and (4) methods.[342] Figure 6 demonstrates graphically how theory drives research design, informed by Crotty[342], Grant and Giddings[343] and Braun and Clarke[344].

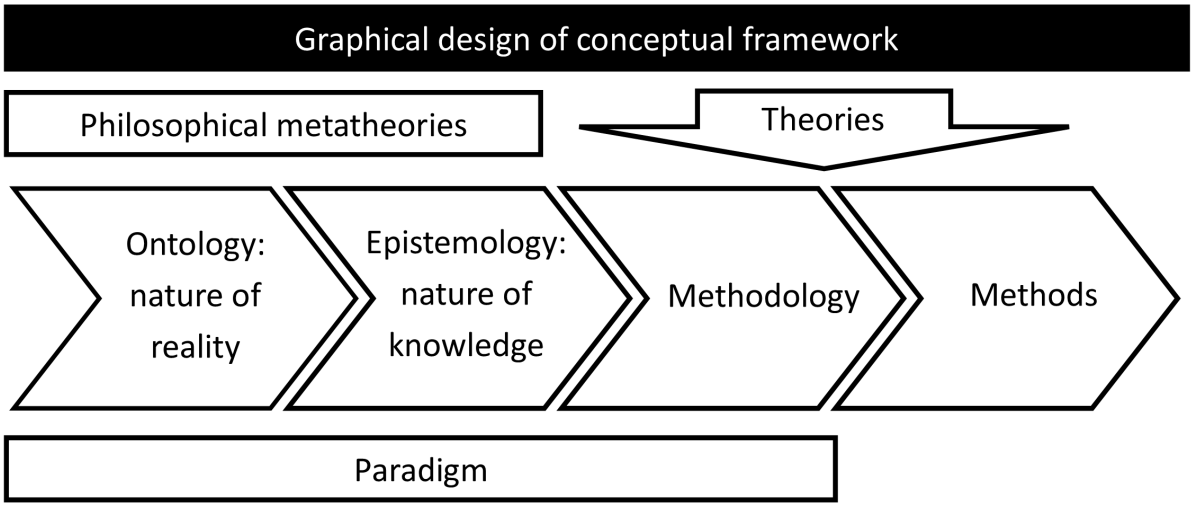

Figure 6. Graphical representation of the conceptual framework of qualitative studies

4.2 Metatheory: the philosophical paradigm

The need for a compatible philosophical paradigm and methods for the intended research purpose, especially when undertaking mixed methods research, is imperative.[340, 345] The philosophical paradigm encompasses the philosophical assumptions (metatheory) underpinning the study and provides "a framework to make order out of the chaos of social life".[343] While social studies put great emphasis on theoretical paradigms, qualitative interpretation in the context of nursing – which tends

to prioritise subjective, experiential knowledge – requires an iterative approach, not necessarily bound to one established theory.[346]

Metatheories refer to worldviews or assumptions regarding the nature of reality[347] and the explicit metatheoretical assumptions underpinning the research and analysis are needed to give coherent results.[348] Metatheories can be divided into epistemological and ontological assumptions, each of which has multiple philosophies, across the sciences and humanities. Getting consensual definitions of the philosophical and theoretical perspectives that define qualitative enquiry is impossible, purely by its nature. It is also beyond the scope of this project.

For the purposes of this project, two main texts were used to define an overarching philosophical underpinning of the study: Tom Fryers' *A short guide to ontology and epistemology: Why everyone should be a critical realist*[349] and Braun and Clarke's *Thematic analysis: a practical guide*[344].

4.3 Ontology: what is real?

Ontology refers to theories about the nature of reality and, in the broadest sense, can be divided into two camps: relativism and realism[344] or irrealism and realism[349].

Relativism subscribes to the notion of reality being a product of human action and interaction, i.e., there is no one truth, everything is subjective, situated, and anti-foundational.[344] Working within this theory requires a critical orientation and focuses on meaning-making rather than an ultimate meaning, making it better suited for sociological and psychological studies. Irrealism shares a similar philosophy and is exactly as it appears: it denies that there is a 'real' world.[349]

Realism proposes a reality which can be uncovered in an accurate and objective way i.e., there is one – discoverable – truth.[344, 349] Realism can be roughly divided into naïve realism, a mind-independent truth; and critical realism, which allows for a 'contextualised' version of the mind-independent truth.[344, 350]

4.4 Epistemology: what is knowledge?

Epistemologies are theories of knowledge: what is it and how can we access it? Broadly, epistemology can be divided into objective and subjective positions, with many positions between them.[349] Objectivist theories, like positivism, assume one reality, uninfluenced by context, which can be discovered/researched using rigorous scientific methods.[344, 349] Subjectivist theories acknowledge the fallibility of knowledge.[349]

As the name implies, contextualism emphasises that knowledge is situated within a context i.e., knowledge can't be separated from the person who knows/'created' it.[344] Constructionism/constructivism proposes that research produces, rather than reveals data.[344, 349]

Fryer uses the four definitions – realist/irrealist and subjective/objective – to give four possible positions (below) the second of which – critical realism – makes logical sense for what this research hoped to capture.[349]

Realist | objectivist	→	Positivist
Realist | subjectivist	→	**Critical realist**
Irrealist | objectivist	→	Very confused
Irrealist | subjectivist	→	Constructivist

Critical realism

Critical realism combines ontological realism – there is a single truth – and epistemological subjectivism – direct access to that truth is impossible, acknowledging that the world is real, but that the production of knowledge is fallible and theory-dependent.[349] Often blanketed under a number of philosophies referred to as 'limited realism'[351], critical realism grew out of criticism of positivism and posits that, while what we observe may be close to the truth, it is always subjective to human perception, allowing us to understand it within a specific context.[350]

First described by philosopher Roy Bhaskar (1944-2014), critical realism postulates that the real world is stratified, that there are real (mechanisms, events and experiences), actual (events and experiences) and empirical (experiences) domains.[352] There has

been some recent debate – again, beyond the scope of this thesis – on whether it is really necessary to keep referring to these complex concepts, when experiences, events and causal mechanisms are more intuitive.[353, 354] Sturgiss and Clarke, in their paper on using critical realism in primary care research, state that "a critical realist approach can help us to answer research questions about how and why interventions and programmes work within the complexities of primary care".[350]

Simply put, critical realism focuses primarily on 'the real' and is used to explain why interventions have a certain outcome, accounting for individual, interventional and contextual factors.[347] For the purposes of this study, the critical realist stance that there is a reality, but our understanding of that reality is influenced and limited by context, human practices and social forces[344, 351] will be adopted.

4.5 Theory of language

Stuart Hall stated "language is the privileged medium in which we 'make sense' of things"[355], and how language is interpreted is important in a study like this, using focus groups to gather data. Hall's theories of representation[355] translate well to language[344]. He distinguishes representation in three ways: reflective, intentional, and constructionist; the first of which underlies the study. Reflective language acts like a mirror, reflecting the true nature of things, i.e., a mind-independent truth[344], fitting in with the realist philosophy underpinning the study.

4.6 Pedagogy: theories of learning

Pedagogy is "the art, occupation, or practice of teaching; the theory or principles of education; or a method of teaching based on such a theory".[356] A clear pedagogical framework has been cited by many as vital to ensure smooth implementation, especially for adult learners using technological interventions, which may necessitate a shift in learning theory and 'teacher beliefs'.[278, 280, 327, 357-359] Integration of technology, pedagogy, content and collaboration is needed to design an optimal mLearning intervention.[281]

O' Connor et al's 2022 systematic review of theories used to inform eLearning for nurses found 29 learning theories were used in the 33 eligible studies included.[360] Citing

that the review was focused solely on pedagogy and not design and delivery, the authors conducted a second review in 2023, to identify theories that supported design and delivery.[360] In that review, they found 20 theories that included frameworks to inform design and delivery in 34 studies.[360] Similarly, Bajpai et al's review of digital education for HCWs found 42 different theories used in the 81 studies that reported on the theory used.[357]

It is clear that the field of pedagogy is vast and varied. A full discussion of the theories of learning is beyond the scope of this thesis, but a short summary of the 'founding' theories, to act as an introduction, follows. The theories and concepts used within the context of this project are discussed in more detail.

The basics of learning theories and their concepts can succinctly be summarised in relation to medical education as:[361, 362]

1. **Behaviourism:** repetition, feedback, and reinforcement leading to behaviour change (teacher-led)
2. **Cognitivism:** using insight, perception, information processing and memory to learn (teacher-facilitated)
3. **Constructivism:** developing knowledge by building on and adapting previous understanding (teacher-facilitated)
4. **Humanism:** learning to fulfil a person's desire to reach their full potential (student-led)
5. **Social/sociocultural learning:** learning through interaction with teachers and peers/colleagues (student- and teacher-led)

Education has changed and technology has advanced, so new theories have been defined, and older theories have been redefined/refined. As explained by Badyal and Singh, many of them essentially complement each other, and often multiple theories are used in any educational intervention.[361]

In terms of mLearning pedagogy, numerous frameworks using different theories have been developed, which will be discussed below. The overarching foundational theory, however, that applies to mLearning using social media platforms like WhatsApp is sociocultural.

4.6.1 Sociocultural/Social learning theory

In 1978, Vygotsky defined a pedagogy which postulated that learning occurred best if done collaboratively, with both learners and teachers actively involved, terming it social constructivism.[363] This theory is well-suited to mLearning using social networks.[363]

Contrary to behaviourism, social learning theory posits that rehearsal/repetition is not necessary for learning, but rather that watching/interacting with others allows learning to occur (which borrows from cognitivism).[362] The socio-cultural perspective suggests that learning tools affect learning, and vice versa.[276] Essentially, the relationship between the environment and the people (community) creates the learning.[361]

A community of practice model is one form of sociocultural learning that has been used across several mLearning studies.[243, 292]

Community of practice

Coined initially by Lave and Wenger, a community of practice (COP) is a group of people who collaborate and engage, to learn from each other.[364] Naidoo and Mtshali conducted a qualitative study to understand the learning strategies needed to support nurses from KwaZulu-Natal working in the HIV sector, finding that a COP provided continuous education, high engagement levels and a supportive network to solve shared issues.[288]

While that study was done on in-person communities of practice[288], Abiodun et al investigated the use of a WhatsApp-based community of practice for newly graduated nurses in urban and rural facilities in the Western Cape in a pre- and post-evaluation study[243]. It had high rates of engagement (n=76; 95% wrote messages, 92% read them); a significant increase in participants' sense of belonging; and most found it useful and easy to use.[243]

The Baylor International Paediatric AIDS Initiative Network – which supports a network of NGOs in LMICs – used a COP framework to design a CE programme for HCWs in Botswana, Lesotho, Malawi and Tanzania.[292] They used WhatsApp to encourage interaction and knowledge sharing between participants in an online CE programme which included asynchronous and synchronous online learning.[292] They concluded that

having interaction beyond synchronous learning optimised it; accessibility and learning could be improved by using technology; and short bursts of learning content – like microlearning – could maximise engagement.[292]

While metatheory permeates through the research, aptly described by Braun and Clark[344] as "like the air we breathe", research design should also draw upon previous minor theories or frameworks[365].

4.7 Minor theories and frameworks

The first, and most relevant framework for this project, which crosses the divide between pedagogical and design theories, is the mLearning model.

4.7.1 mLearning

mLearning has multiple frameworks developed by various researchers and educators, each defining different – often intersecting – factors that lead to the success of the interventions.[276, 279, 281, 283]

Thomas Cochrane, a leading investigator of mLearning interventions, used his experiences from 35 projects to define six critical success factors (Table 3).[280] Similarly, Kearney et al used a design-test-analyse-refine cycle iteratively, with inter-and intra-researcher validation, testing on two projects and expert critique, to define a succinct framework for mLearning pedagogy (Table 3).[276]

Table 3. Key factors in Cochrane and Kearney et al's mLearning frameworks

Cochrane[280]	**Kearney et al[276]**
1. Pedagogical integration of technology 2. Lecturer modelling of the tool's pedagogical use 3. Collaboration: supportive community learning 4. Appropriate choice of mobile devices/technology 5. Technological and pedagogical support 6. Sustained interaction between teacher and learner	1. Authenticity: using realistic tasks or problems to teach 2. Collaboration: connection with people and resources 3. Personalisation: giving the learner agency

The projects discussed in both Cochrane and Kearney et al's papers were all based in high income countries[276, 280], an important consideration when designing an intervention that depends on technology. As previously discussed, context is key.

Okai-Ugbaje conducted a robust project to develop a framework that would suit the pedagogical and socioeconomic needs of LMICs.[281] They conducted a systematic review of the mLearning studies conducted in LMICs between 2008 and 2015, critically reviewed the existing frameworks, piloted the conceptual framework and then tested it in two empirical studies.[281] They concluded that student-centred learning was achievable in LMICs and cost-effectiveness and reliability were essential (Figure 7).

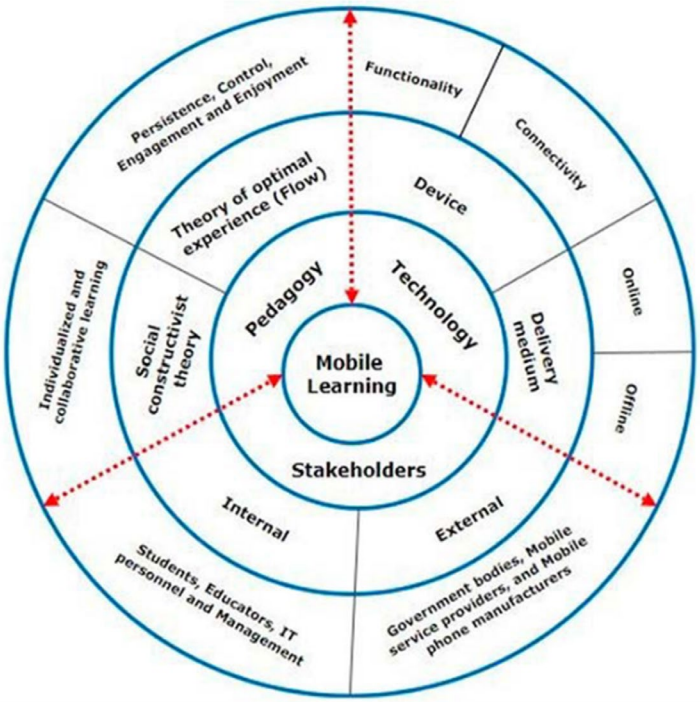

Figure 7. Okai-Ugbaje's conceptual framework for mLearning in LMICs[281]

Here, too, the high prevalence of WhatsApp use – which is free to download – in South Africa, fits within Okai-Ugbaje's recommendations for low cost, reliable interventions in LMICs.

4.7.2 Platform design

Reviews have shown a gap in the use and/or reporting of the theoretical underpinnings of the design used in digital education studies.[357, 366] Due to the intervention using WhatsApp, which requires no technological design, no design theories were used for the platform design.

There was careful consideration to ensure that the pre-existing functionality and flexibility of WhatsApp fitted within the learning theories and outcome measurements, and vice versa.[360]

4.7.3 Study design

Two theories were used to guide the design of the study – the all-encompassing Unified Theory of Acceptance and Use of Technology (UTAUT)[367] and the more pragmatic framework used by Asiimwe et al[368], which was based on Jeng's Usability Assessment of Academic Digital Libraries[369]. Figure 8 shows the three theories and how they intersect.

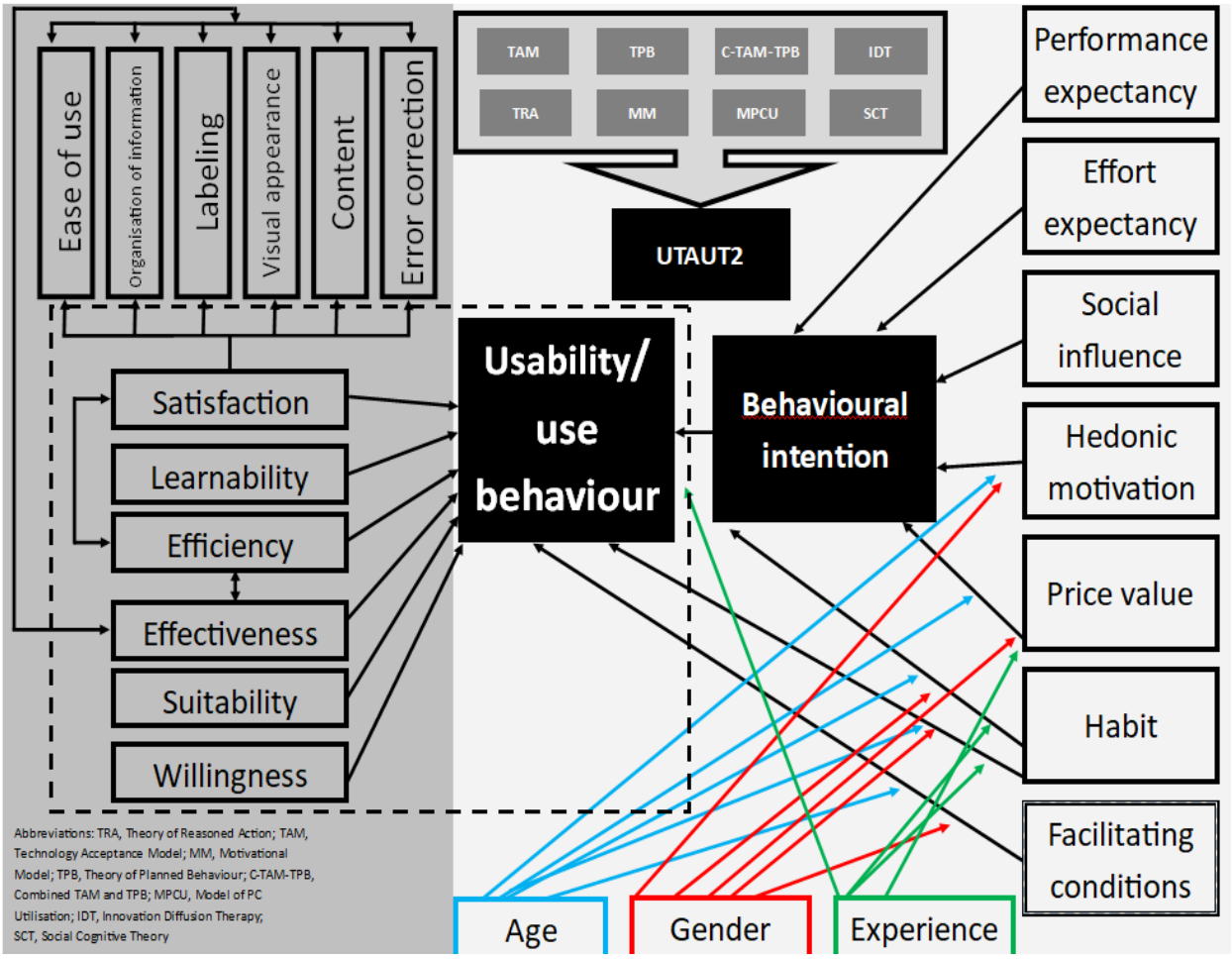

Figure 8. Theoretical framework showing Jeng's model of digital library usability evaluation on the left in dark grey, Asiimwe et al's adaption thereof in the dashed lines; and Marikyan & Papagiannidis's Unified Theory of Acceptance and Use of Technology including learnability, willingness, suitability, satisfaction, efficiency, effectiveness, on the right

4.7.3.1 Unified Theory of Acceptance and Use of Technology

With exponential growth in technology since the 1980s, research into what drives the acceptance of technology has advanced. By 1999, extensive research had collectively suggested that user acceptance could be predicted by the characteristics of the individual, technology and organisation[370] and models/theories – from different disciplines – were numerous[367].

At the beginning of the 21st century, Venkatesh et al reviewed the literature to develop a unified theory to explain user acceptance across forms of technology.[367, 371] The result was the UTAUT which combined eight theories and proposes that technology adoption is explained by performance and effort expectancy, social influence and facilitating conditions (Table 4), moderated by age, gender, experience and voluntariness[371].

Table 4. Theories combined in the Unified Theory of Acceptance and Use of Technology

Discipline	Theory	Main assumption(s)	Performance expectancy	Effort expectancy	Social influence	Facilitating conditions
Socio-psychological	Theory of Reasoned Action	Behavioural intentions are a function of beliefs and attitudes [372]			X	
	Theory of Planned Behaviour	Intentions are determined by personal attitude, subjective norms and perceived behavioural control [373, 374]			X	X
	Social Cognitive Theory	Learning occurs within a social context; new behaviours learnt by observing others and consequences thereof [375, 376]	X			
Information systems management	Technology Acceptance Model	Behaviour predicted by perceived ease of use, usefulness and behavioural intention [377, 378]	X	X	X	
	Technology Acceptance Model 2	Social influence processes and cognitive instrumental processes influence user acceptance [379]	X		X	X
	Innovation Diffusion Theory	Adoption of innovation is influenced by system characteristics and properties [380]	X	X	X	X
	Model of PC Utilisation	Technology acceptance is influenced by job fit, complexity, consequences, social factors and facilitating conditions [381]	X	X	X	X
Behavioural psychology	Motivation Model	Adoption and use behaviour is influenced by rewards (extrinsic motives) and/or enjoyment, satisfaction and fun (intrinsic motives) [382]	X			

As technology and its uses expanded, so did UTAUT. In 2012, UTAUT 2 was published, which removed voluntariness and added hedonic motive, perceived value/cost, and habit.[383]

UTAUT has been used widely, across sectors including technological tools for nurses[384-386] however, many studies cited it but didn't use the model[387], as is the case here. The modelling itself was not utilised but its driving factors were used to inform the survey questions and focus group semi-structured interview guide.

4.7.3.2 Usability of academic digital libraries: effectiveness, efficiency, satisfaction, and learnability

Jeng reviewed 21 methods and instruments used to assess digital library usage – determining what attributes were considered to affect it – and developed an evaluation model based on the International Organisation of Standardisation (ISO) 9241-11 definition of usability: "the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency, and satisfaction in a specified context of use".[369]

While the model was aimed at digital libraries, the factors affecting usability that it suggested were adapted by Asiimwe et al[368] to inform the framework to assess the feasibility, accessibility and use of point-of-care malaria tests in Uganda. This adaption – and further adaptions thereof – have been used widely to guide the qualitative testing of usability across a range of point-of-care interventions in LMICs including South Africa[388], Zambia[389] and Thailand[390].

While these studies were used to test the usability of point-of-care interventions, it was thought that the simplicity of the WhatsApp-based intervention fitted within the simple parameters of the model, and it was used to inform the qualitative focus group and survey questions. Asiimwe et al's[368] definitions were adapted to fit within the context of this study to answer the research questions, across the mixed methods. The adapted study definitions are found in Chapter 7, the methodology used for Study 2.

4.7.4 Message design

The design of the messages themselves, however, is also an important factor to consider, one which has not undergone much research. Wang and Shen, in their overview of message design for mLearning, suggest four principles to be used:[391]

1. Design for the lowest common denominator, or the simplest device
2. Design short, condensed materials for smart phones
3. Design for eLearning, adapt for mLearning
4. Be creative when designing for mLearning

While the first two principles are useful and applicable to this project, taking into consideration the poorly resourced context in which it was run, the latter two do not. This is a perfect example of the developed world-centricity of many studies in the field, as discussed in the section on research gaps (Section 3.6).

Chapter summary

This chapter explains the rationale behind the philosophical underpinnings of the research. The study was conducted under the metatheory of critical realism, which combines ontological realism with epistemological subjectivism – simply put, it postulates that there is a single truth but that that truth is fallible and influenced by context and language. The sociocultural or social learning theory was used as the underlying pedagogy – the idea that the relationship between the participants and the environment creates the learning.

In addition, minor theories were drawn from for both the pedagogy and design of the intervention to ensure robust outcome measurement. Part 2 details the full methodology (Chapter 5) and results (Chapter 6) of Study 1.

Part 2: Establishing HCW knowledge of guidelines

Part 2 describes Study 1, to establish HCW's knowledge of important points in the national ART guidelines, dolutegravir's interactions – what they are and how to adjust dosing, and current guideline and training access.

Chapter 5 details the methodology of the study.

Chapter 6 reports on the results of the study.

Chapter 5 Research methods: HCW survey

This chapter describes the methods used for Study 1 (2020-2021), a cross-sectional descriptive study using an online survey of South African HCWs working in the field of HIV, to establish their knowledge of the interactions of dolutegravir (clearly stated in the national guidelines), what affects that knowledge, and the current state of guideline access, training, and desired training.

It presents the study designs, settings, populations and sampling, recruitment, interventions, study instruments, data collection and analysis, and ethical considerations of the studies.

Chapter 5 contains excerpts from the following paper:

Chisholm BS, Swart AM and Blockman M. South African healthcare workers' knowledge of dolutegravir's drug-drug interactions in the first year of its rollout: a cross-sectional online survey. Journal of the International AIDS Society 2022; 25: e25885. DOI: 10.1002/jia2.25885.

5.1 Study design

A cross-sectional, descriptive study using an anonymous online survey of HCWs in the field of HIV in South Africa. An online survey was chosen over other potential designs, like focus groups, for three main reasons: (1) the study was conducted during the COVID-19 pandemic; (2) the reach of an online survey is large and country-wide data was sought; and (3) it minimises the risk of social desirability bias[392].

5.2 Study setting

The study was conducted from the National HIV and TB Healthcare Worker Hotline, which is based at the Medicines Information Centre, in the Division of Clinical Pharmacology at UCT. This toll-free hotline has been running since 2008. Specially trained pharmacists answer around 500 HIV- and TB-related clinical queries a month, from HCWs across South Africa, mainly telephonically but also via e-mail and WhatsApp.

5.3 Study population, sampling and recruitment

The study population included HCWs in the field of HIV in South Africa. Participants were recruited through e-mail, SMS, and social media announcements to users of the hotline (~3 700 emails) and by relevant HIV-focused organisations (convenience sampling).

Using the exact confidence interval method of Clopper-Pearson[393], a sample size of 200 responses would result in a 95% confidence interval of 0.43 to 0.57 around a proportion of 0.5, which was considered acceptable precision.

The survey was conducted in English and was designed to exclude participants who did not provide consent, and who were not HCWs in the field of HIV in South Africa. Inclusion and exclusion criteria are listed in Table 5.

Table 5. Inclusion and exclusion criteria for online survey of HCWs' knowledge of dolutegravir's interactions

Inclusion criteria	Exclusion criteria
• Healthcare workers (i.e. doctor, nurse, pharmacist, community healthcare worker or other healthcare worker) • Access to the internet • The survey was in English, so required participants to be able to read English • Informed consent	• Not meeting the eligibility criteria • No informed consent

5.4 Survey design

No similar published surveys were found, so it was designed on REDCap, with input from experts and laypeople to ensure reliability and validity. A literature search was conducted, and the survey methodology was adapted from numerous previous studies. Broad survey principles recommended in a number of these publications[392, 394-396] and guidance from The SAGE Handbook of Survey Methodology[397] were followed with Edward Tufte's summary of achieving survey design excellence as a blueprint:

"*Ask the simplest, clearest questions in the shortest time using the fewest words on the fewest pages and, most importantly, ask only what you need to know*".[398]

The survey was expected to take 10 minutes to complete. It used branching logic and consisted of five sections (Appendix B):

1. **Demographic data**: survey access type, province, profession, age, HIV experience, area (rural/urban), sector (public/private), type of facility (seven questions)
2. **Access to guidelines and training**: if training had been received, and from whom, access to guidelines and type; a 5-point Likert scale to measure confidence in knowledge of interactions (five questions)
3. **Interaction knowledge**: general awareness of interactions, knowledge of specific interactions, knowledge of specific dosage recommendations for each interacting drug (14 questions)

4. **Healthcare worker-reported counselling on interactions**: who is counselled, barriers, preferred tools for aiding counselling; and a 5-point Likert scale to measure HCW confidence in counselling ability (six questions)
5. **Effect of COVID-19 pandemic**: assessed by two multiple-choice questions and one open-ended question (four questions)

5.4.1 Validity and reliability

The survey was reviewed by both experienced HIV clinicians and researchers within the Division of Clinical Pharmacology (clinical input) and the AIDS and Society Research Unit at the Centre for Social Science Research (social input) at UCT, to evaluate content validity and ensure questions were appropriate, relevant and phrased to minimise bias. The recommended adjustments from these experts were made.

To ensure reliability and validity, three tests were run before the pilot:

1. **Face validity**: four laypeople (two on desktop, two on mobile) and the seven HIV hotline pharmacists checked the survey for readability, layout and clarity, and suggested edits were made.
2. **Content validity**: five HIV experts, three social scientists and a layperson completed a Content Validity Index (CVI), which had an average of 0.9. Questions are considered valid if CVI > 0.78.[399]
3. **Test-retest for reliability**: five HIV hotline pharmacists completed the survey twice, two weeks apart and the Pearson's coefficient was calculated to be 0.99. Reliability is considered to be good if correlation coefficient > 0.7.[400]

5.4.2 Pilot study

Once human research ethics approval was obtained, the survey was piloted by nine HCWs in the field. Results from the pilot study were excluded from the final survey sample. Pilot study participants were asked to comment on comprehension and ease of completion. Minor adaptions were made following the pilot, and amendments were sent for ethical approval by the ethics committee.

5.5 Survey dissemination

During the research design period, contact with suitable organisations was made via known colleagues, Facebook pages and websites. Once correct contact details were obtained, an e-mail requesting assistance was sent (Appendix C). The full list of organisations who agreed to assist in survey distribution, and the platforms of communication for each can be seen in Table 6.

Table 6. Organisations involved in dissemination and methods of dissemination

	Method of dissemination			
	e-mail	SMS	Website	Facebook
Dissemination by organisation				
Hotline contacts	✓	✓	✓	✓
Southern African HIV Clinicians Society	✓	✓	✓	✓
Foundation for Professional Development	✓	✓	✓	✓
Aurum Institute	✓			✓
South African Medical Association	✓			✓
South African National AIDS Council			✓	✓
Rural Doctor's Association of South Africa	✓			✓
Health Systems Trust	✓			
South African Society of Clinical Pharmacy	✓	✓	✓	✓
Western Cape Department of Health	✓			
Right to Care	✓			
Pharmaceutical Society of South Africa				✓
Netcare	✓			
Desmond Tutu HIV Foundation	✓			✓
UCT PG Dip TB/HIV Management class	(VULA)		✓	
Keth'Impilo	✓			
TB HIV Care		✓		
CHIVA South Africa				✓
MediClinic	✓			
Dissemination by investigator				
SA Pharmacy Today				✓
Pharmacy SA				✓
SA Medical Doctors Comm Serve				✓
South African Medical Officer Posts				✓
Medical Women's Association, SA				✓
NIMART – Wonderful Nurses				✓
SA Doctors Unite				✓

Abbreviations: Comm Serve: Community Service; PG Dip: Postgraduate Diploma; SA: South Africa

Most organisations disseminated the information at no cost, once or twice during the study period, and all HCWs were encouraged to share it with their colleagues. During the four-week study period (24 August to 21 September 2020), the URL was sent to the hotline's contacts three times (weeks 1, 2 and 4). To maximise reach, a paid marketing strategy was established with the Southern African HIV Clinicians Society, our target group; and a 'trade deal' was made with the Foundation for Professional Development – their free, online COVID-19 seminars for HCWs were shared on the hotline's Facebook pages and in the MIC news, in return for them sharing the survey URL on their platforms.

The Southern African HIV Clinicians Society sent a mailer twice (week 1 and week 3), posted on their Facebook page twice (week 1 and week 3), had a banner on their website and sent two SMSs (weeks 1 and 3). The Foundation for Professional Development did the same but also posted it on Twitter and Instagram. A more detailed overview, with numbers of contacts reported by each organisation and followers of pages, such as Facebook, is included as Appendix D.

Due to the online nature of the study and the use of numerous organisations, an exact number of recipients across all methods could not be calculated.

5.6 Data cleaning

While the nature of this survey i.e. it has no anthropometric variables, such as height and weight; and the use of an electronic, online survey, with no manual data manipulation minimises errors made, it by no means precludes it from data errors. All efforts were made to minimise the risk of errors during the design of the survey, such as giving minimum and maximum allowable values for age.

A data cleaning protocol was designed and manually carried out in a stepwise manner:

1. Raw data was downloaded from REDCap into an Excel spreadsheet.
2. Surveys with no or too few demographic details for analysis were removed by using concatenation of province, profession, age, experience, area, sector and facility.

3. Surveys not meeting inclusion criteria (outside SA; not involved in HIV care) were removed manually from answers to ‘other’.
4. Where ‘other’ had been chosen for ‘survey access’ and ‘profession’, data were cleaned to relevant categories. Where uncertain, supervisor input was sought, and surveys from professions that did not fit into the inclusion criteria were removed.
5. Age and HIV experience were analysed for errors, by each variable:
    a. Variable was sorted from smallest to largest and manually assessed
    b. A scattergram was created to visualise outliers
    c. Where logical, outliers were corrected to the mean; if no logic found, the survey was removed

5.7 Data analysis

Simple descriptive statistics were calculated on Excel and statistical analyses were performed using STATA software (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). Descriptive statistics were used to describe demographic data, access to guidelines and training, and interaction awareness and knowledge.

Analysis was performed on completed and incomplete surveys, using the number of responses to each question as the denominator. As an example, when calculating the number of HCWs who knew the specific dosage/dosing changes, the denominator used was the number of people who saw the question (by branching logic, those who were not aware of an interaction with the drug did not see the question on dosing changes), so these proportions describe only the knowledge of those who knew of an interaction. Blank responses were excluded in the inferential analyses of differences in knowledge by variable.

In the inferential analysis, proportions were used to describe positive responses to each question and the 95% confidence interval (95% CI) was calculated to find statistical differences. All tests were two-sided, and $p \leq 0.05$ was considered statistically significant.

To determine if any relationships existed between independent and dependent variables, proportions tests were used at a significance level of 0.05. The number of variables to compare was large so, instead of performing individual proportions tests within variables to significantly compare proportions, the 95% CI was chosen to perform the tests.

To explain this approach briefly, a hypothesis was tested: H_0: μ=0. The 95% CI about this variable was tested and if 0 was not included within this interval the null hypothesis was rejected it was concluded that μ≠0, given a 5% level of significance.

With the same logic, variables were compared binomially and determined if they were significantly different from one another: H_0: $\mu_x = \mu_y$. Here, too, the 95% CI for each variable respectively was calculated. If these intervals overlapped, the null hypothesis was not rejected, and it was concluded that no significant difference exists between the two variables. If the intervals did not overlap, it was concluded that they were significantly different, given a 5% level of significance.

Using this approach, it was possible to calculate the 95% CI for the large number of variables and to compare the intervals, allowing the determination of the existence of significant differences between variables, without completing a proportions test for each relationship of interest.

As the outcome variables were categorical, the equation used to calculate these 95% CI was:

$$\mathbf{95\%}\ \boldsymbol{CI}\mathbf{:}\ \boldsymbol{p} \pm \mathbf{1.96} * \sqrt{\frac{\boldsymbol{p}(\mathbf{1}-\boldsymbol{p})}{\boldsymbol{n}}}$$

p: proportion of responses; n: sample size

5.8 Ethical considerations

The study was undertaken in accordance with the principles of the Declaration of Helsinki adopted by the 18th World Medical Assembly, Helsinki 1964 and revisions up to and including Fortaleza, 2013[401] as well as the South African Good Clinical Practice Guidelines[402]. Before any research occurred, ethics approval was obtained from UCT's Human Research Ethics Committee (HREC 357/2020) (Appendix E).

The study posed minimal-to-no risk to participants as all data was collected anonymously, online, using no personal identifiers.

5.8.1 Incentive

It has been shown that the offering of an incentive increases survey response, with Edwards et al concluding that the odds of response were increased by half using a non-monetary incentive, such as a gift card.[394] A systemic review of methodologies improving survey responses from physicians found that even a small incentive increased participation by 18-20%.[403]

To maximise response, without risking inducement, a modest two-pronged voluntary opt-in incentive was offered: a package of the hotline's publications (interaction booklet, guideline posters etc.) to be posted and entry into a draw for a hamper worth R1 000.

Those who chose to receive a package of the hotline's toolkits (posters and booklets) and wished to be entered into the draw at the end of the survey were asked for their personal details. These were collected and saved in a separate instrument on REDCap, unlinked to their survey data, to protect anonymity.

5.8.2 Informed consent

Online informed consent was obtained before participants started the survey. The survey link opened on a thorough information section, which included the ethics approval and the ethics committee's contact details. Participants were required to tick a box to confirm their consent to participate at the end of the information section (Appendix F).

Chapter summary

Chapter 5 described the methodology of Study 1, a cross-sectional descriptive study using an online survey of South African HCWs working in the field of HIV, to establish their knowledge of the interactions of dolutegravir, which were clearly described in the national guidelines, and their access to, and training on, the guidelines.

An online survey was designed and tested for reliability and validity, ethics approval obtained, and a pilot study was run. Dissemination through electronic sharing (SMS, e-mail and social media platforms) of the survey link was planned via callers to the hotline and through multiple HIV-associated stakeholders and organisations. The data analysis plan included both descriptive and inferential methods.

Chapter 6 will describe the results, discussion and conclusion of Study 1, which led to the design of Study 2.

Chapter 6 Results: South African healthcare workers' knowledge of dolutegravir's drug-drug interactions

This chapter provides a short introduction to Study 1 – an online survey to establish South African healthcare workers' knowledge of dolutegravir's drug-drug interactions – and then details the results: what their knowledge is, what affects their knowledge; and the current (2020) state of guideline access, training, and desired training.

Chapter 6 contains excerpts from the following paper:

Chisholm BS, Swart AM and Blockman M. South African healthcare workers' knowledge of dolutegravir's drug-drug interactions in the first year of its rollout: a cross-sectional online survey. Journal of the International AIDS Society 2022; 25: e25885. DOI: 10.1002/jia2.25885.

6.1 Introduction

The South African national HIV guidelines were updated in December 2019 to recommend dolutegravir-based ART as first-line treatment[404], in line with WHO recommendations[405]. Dolutegravir, an integrase strand transfer inhibitor (INSTI), has been shown to be safe, effective and well tolerated[406] with a shorter median time to viral suppression compared to other ARV regimens[406, 407] and a high barrier to the development of drug resistance[408].

Most professional staff receive interaction training as part of their tertiary education but this would not have included training on dolutegravir, a new drug in the South African context, at the time of the study. When updated guidelines are released, training of all HCWs is conducted by the NDOH, various NGOs and private trainers at a national and provincial level both online and face-to-face, often using the 'train the trainer' method. CHWs and counsellors are included in this training in some districts.

While one of the touted advantages of dolutegravir is its lower potential for DDIs[409], pharmacokinetic studies have shown interactions with some commonly used drugs. These include cation-containing medicines like calcium, iron and magnesium[410, 411], metformin[412], rifampicin[413, 414] and some anti-epileptic drugs[415-417]. Dolutegravir's lack of an interaction with oral contraceptives[418, 419] is a major advantage.

The DDIs require adjusted dosing and/or dosing schedules – clearly stated in the South African national ART guidelines[404] – to prevent adverse effects and loss of efficacy of dolutegravir. Failure to adjust correctly could result in the development of HIV-1 resistance, treatment failure, and HIV transmission.

Several ARV prescription audits have been conducted in the African setting showing a prevalence of clinically relevant DDIs in 18.7 to 84% of patients[420-422]. These studies, however, included non-INSTI regimens, which may be more vulnerable to DDIs. While information on DDIs, the steps required to prevent them and the prevalence of prescribing errors due to DDIs is available, there is a paucity of information on the knowledge of HCWs regarding interactions, especially in the context of ARVs, in the nursing profession, and in the South African setting.

International studies of HCW knowledge of non-ARV DDIs have shown low levels of knowledge.[423-425] One small study of physicians in a United Kingdom-based hospital showed that only 36% of clinically relevant interactions with ART were identified.[426] An American survey showed that 30% of resident and attending physicians and 90% of infectious disease/HIV specialists correctly answered case-based ART DDI questions.[427]

The primary aim of this study was to determine dolutegravir interaction knowledge of South African healthcare workers involved in HIV care and to describe which variables were associated with gaps in knowledge. The methodology of the study is found in Chapter 5, and the results follow.

NOTE ON REPORTING OF RESULTS:

The online survey was designed using branching logic, as illustrated in Figure 9. Analysis was done using the number of responses to each question as the denominator. As an example, when calculating the number of HCWs who knew the specific dosage/dosing changes, the denominator used was the number of people who saw the question (by branching logic, those who were not aware of an interaction with the drug did not see the question on dosing changes), so these proportions describe only the knowledge of those who knew of an interaction. Blank responses were excluded in the inferential analyses of differences in knowledge by variable.

The tables of descriptive statistics separate out responses by those who completed the full survey and those who dropped out during the survey. The tables of inferentially analysed results used all responses received on each question, regardless of whether the respondent completed the survey or not. Number of respondents for each section is reported in the tables and was used as the denominator when calculating frequencies.

Only significantly different results are reported in this section. Groups were significantly different at the 95% confidence level ($p \leq 0.05$), so reporting of significantly different results refers to this level.

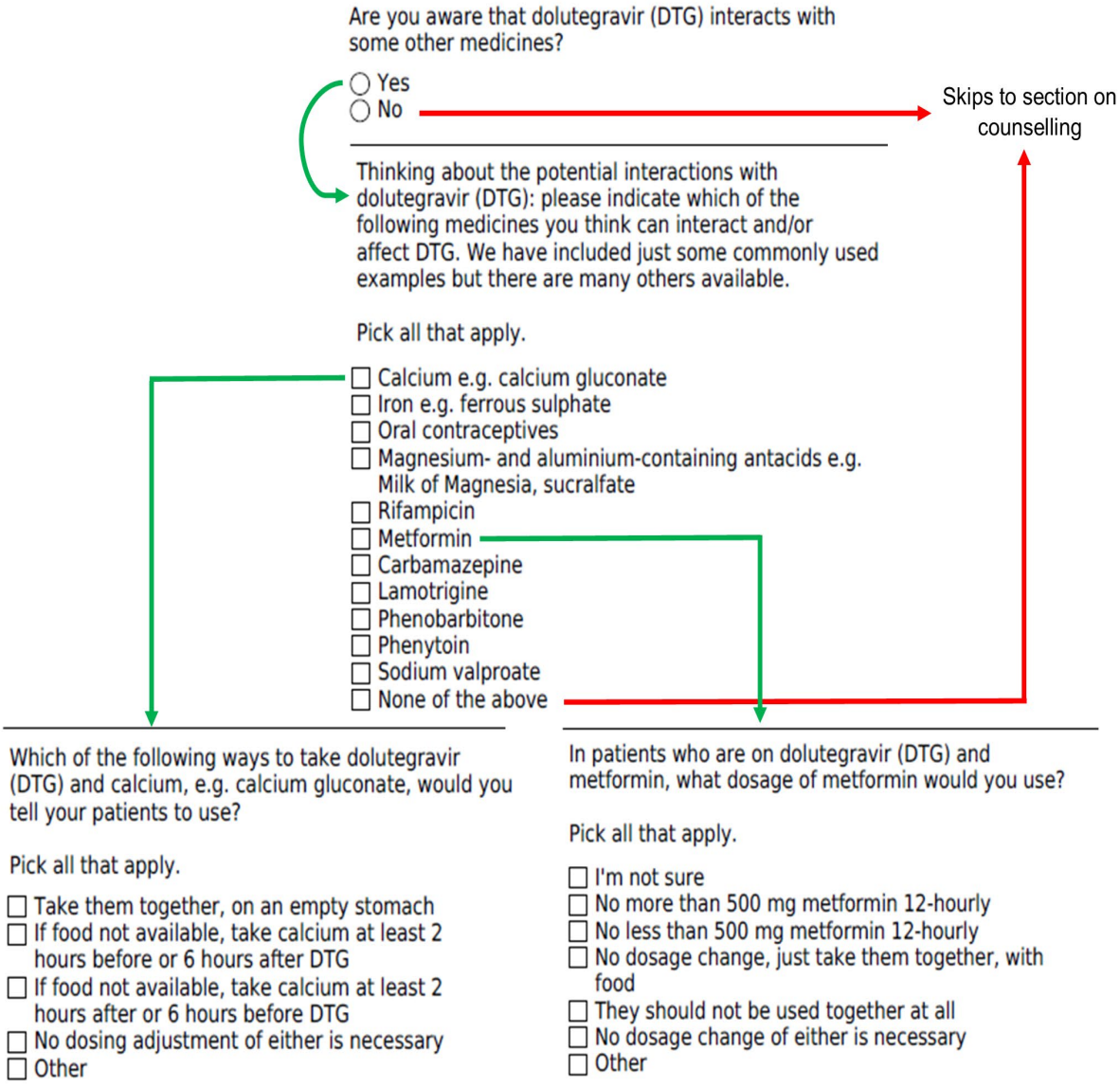

Figure 9. Illustrative example of the HCW survey's branching logic

6.2 Response, participation, access and dropout rate

Due to the nature of the dissemination of the survey URL via multiple platforms, it was not possible to calculate a response rate. 2 549 submitted surveys were downloaded from REDCap. Of the surveys submitted, 599 were not suitable for analysis. Surveys with no demographic data or too few demographic responses to allow analysis (472), those not meeting the inclusion criteria (21), and those with non-ART-related professions (106) were excluded, leaving 1 350 completed surveys and 6 00 incomplete surveys. For the response, participation, access and demographics, descriptive statistics are divided into complete and incomplete surveys.

Survey notification and access

Most respondents heard about the survey via e-mail (54.7%), followed by SMS (33.9%) and some respondents received notification via multiple channels. Access to the survey was predominantly via cell phone (71.1%) (Table 7).

Table 7. Survey notification source and access

	Complete n=1350	**Incomplete n=600**	**Total n=1950**
Source of notification, n (%)[1]			
Word of mouth/from a colleague	56 (4.1)	25 (4.2)	81 (4.2)
e-mail	785 (58.1)	281 (46.8)	1066 (54.7)
SMS	427 (31.6)	234 (39.0)	661 (33.9)
Social media	154 (11.4)	73 (12.2)	227 (11.6)
Other	10 (0.7)	12 (2.0)	22 (1.1)
Device on which survey was accessed, n (%)			
Cell phone	934 (69.2)	453 (75.5)	1387 (71.1)
Tablet	30 (2.2)	13 (2.2)	43 (2.2)
Desktop computer	189 (14.0)	67 (11.2)	256 (13.1)
Laptop computer	197 (14.6)	56 (9.3)	253 (13.0)
Blank	0 (0.0)	11 (1.8)	11 (0.6)

[1]Multiple answers were allowed. [2]Blank responses represent those that did not answer the question.

6.2.1 Dropout rate

To describe the point of dropout in the incomplete surveys, results were concatenated on Excel, into the sections of the survey. Points of dropout are illustrated in Figure 10. Most respondents who didn't complete the survey dropped out within the section on specific dosing/dosage changes required due to the interactions (189/286, 66.1%).

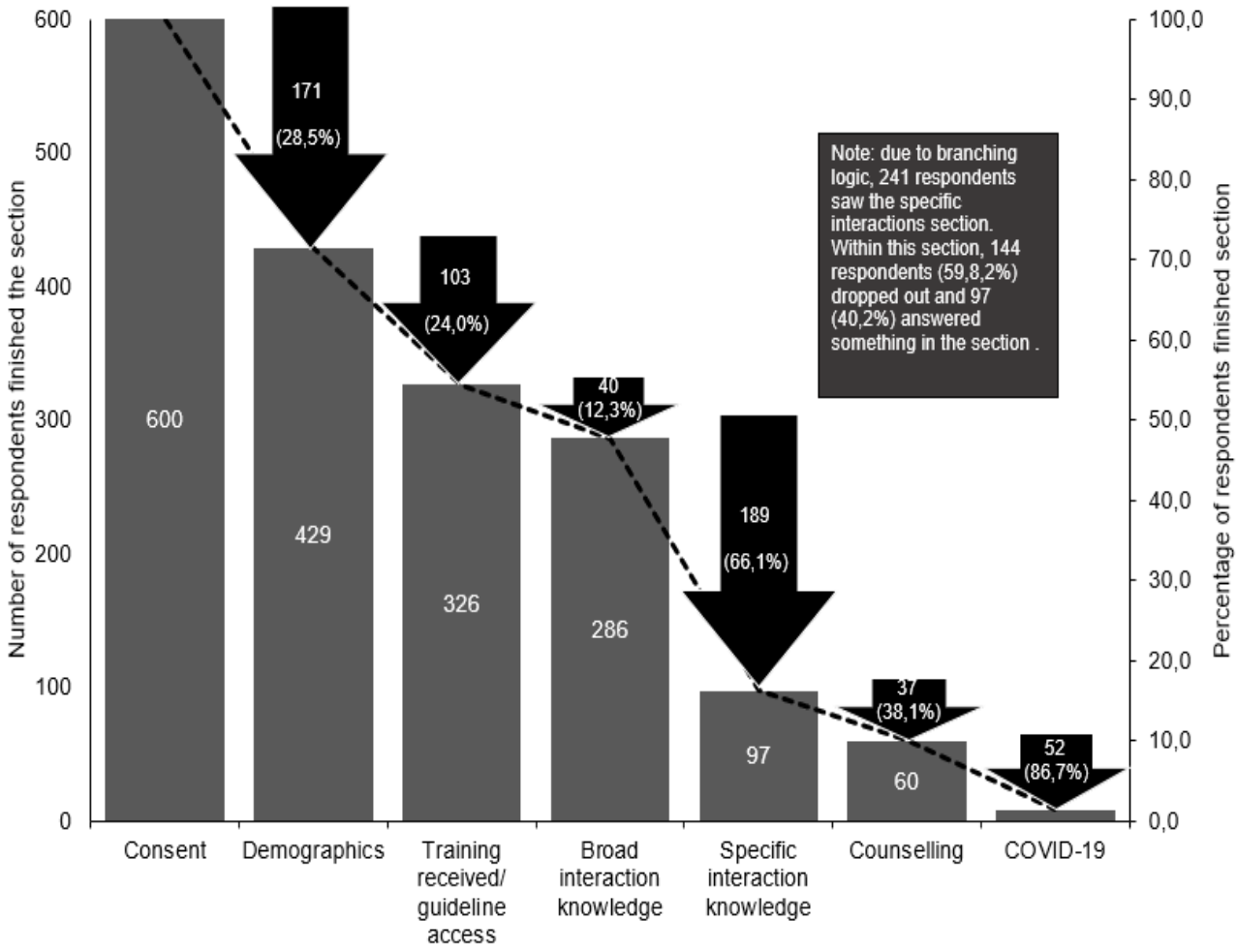

Figure 10. Point of dropout in incomplete surveys

6.3 Demographics

Most respondents were nurses (918, 47.1%), then doctors (699, 35.8%) and pharmacists (173, 8.9%), with a mean age of 42 years (standard deviation (SD) 12) and the mean number of years of HIV experience of 10 years (SD 7). Respondents were evenly spread across urban (1 138, 58.4%) and rural (800, 41.0%) areas and the majority were from the public sector (1 512, 77.5%) (Table 8).

Table 8. Survey respondent demographics

	Complete, n=1350	Incomplete, n=600	Total, n=1950
Profession, n (%)			
Community health worker	23 (1.7)	12 (2.0)	35 (1.8)
Counsellor	28 (2.1)	19 (3.2)	47 (2.4)
Doctor	521 (38.6)	178 (29.7)	699 (35.8)
Nurse	588 (43.6)	330 (55.0)	918 (47.1)
Pharmacist	138 (10.2)	35 (5.8)	173 (8.9)
Other healthcare worker	52 (3.9)	21 (3.5)	73 (3.7)
Missing	0 (0.0)	5 (0.8)	5 (0.3)
Age, years, mean (SD)	41 (11)	45 (12)	42 (12)
Missing	0 (0.0)	11 (1.8)	11 (0.6)
HIV experience, years, mean (SD)	10 (7)	11 (7)	10 (7)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Area			
Rural	557 (41.3)	243 (40.5)	800 (41.0)
Urban	793 (58.7)	345 (57.5)	1138 (58.4)
Missing	0 (0.0)	12 (2.0)	12 (0.6)
Sector			
Public	1058 (78.4)	454 (75.7)	1512 (77.5)
Private	292 (21.6)	135 (22.5)	427 (21.9)
Missing	0 (0.0)	11 (1.8)	11 (0.6)
Facility			
Mobile clinic	15 (1.1)	9 (1.5)	24 (1.2)
Satellite clinic	7 (0.5)	8 (1.3)	15 (0.8)
Primary health clinic	461 (34.1)	198 (33.0)	659 (33.8)
Community health centre	181 (13.4)	95 (15.8)	276 (14.2)
District hospital	211 (15.6)	66 (11.0)	277 (14.2)
Regional/tertiary/specialised hospital	190 (14.1)	79 (13.2)	269 (13.8)
Private practice	109 (8.1)	59 (9.8)	168 (8.6)
Private hospital	58 (4.3)	7 (1.2)	65 (3.3)
Other	118 (8.7)	71 (11.8)	189 (9.7)
Missing	0 (0)	8 (1.3)	8 (0.4)

Abbreviation: SD, standard deviation.

Provincially, most responses were received from Gauteng (459, 23.5%), the Western Cape (446, 22.9%) and KwaZulu-Natal (299, 15.3%) (Figure 11).

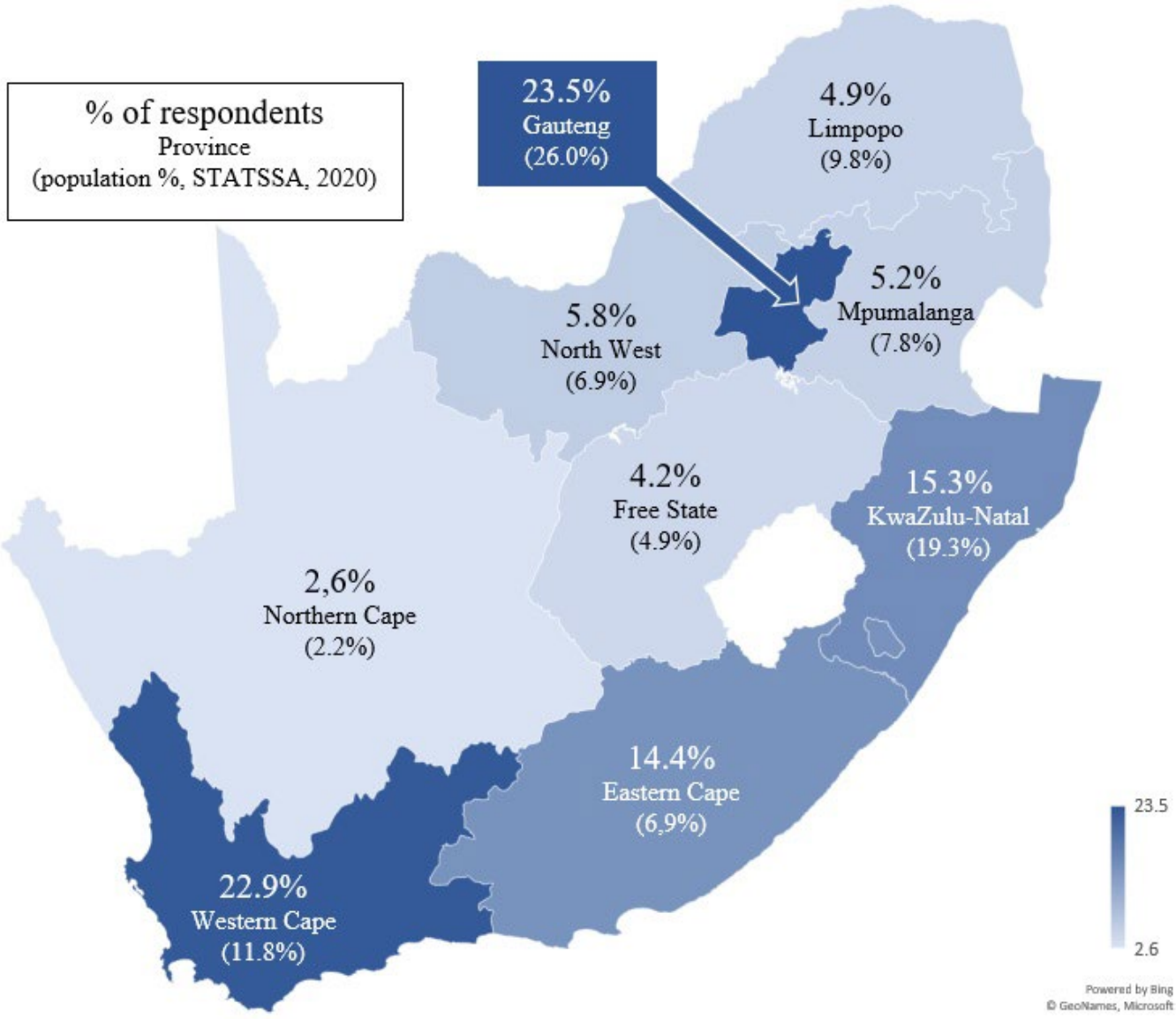

Figure 11. Spread of participants in HCW survey, provincially

6.4 Awareness of dolutegravir interactions

Including all surveys analysed (1 950), 1 365 (70%) of all HCWs answered 'yes' to the question 'Are you aware that dolutegravir interacts with other medications?'; 271 (13.9%) responded 'no'; and 314 (16.1%) had dropped out of the survey by this point. When excluding those who had dropped out by/in this section, 1 365 (83.4%) were aware that dolutegravir has DDIs (Table 9).

Of those who were aware that dolutegravir has interactions, between 53.5 and 61.5% were aware of the interaction with cations; 86.9% with rifampicin, and 78.2% with metformin. With the antiepileptics, proportions of respondents aware of the interactions with carbamazepine, phenobarbitone and phenytoin were 58.7%, 44.4% and 50.1%, respectively. Looking at drugs that do not interact with dolutegravir, 17.6% thought there was an interaction with oral contraceptives (Table 9).

Table 9. Awareness that dolutegravir has interactions and of specific drugs

	Participants who answered section, n (%)	**All participants, n (%)**
Awareness that dolutegravir has interactions	**n=1636†**	**n=1950**
Yes	1365 (83.4)	1365 (70.0)
No	271 (16.6)	271 (13.9)
Missing	0 (0)	314 (16.1)
Awareness of specific dolutegravir interactions	**n=1333‡**	**n=1636 §**
Calcium	820 (61.5)	820 (50.1)
Iron	714 (53.6)	714 (43.6)
Magnesium/aluminium	713 (53.5)	713 (43.6)
Rifampicin	1158 (86.9)	1158 (70.8)
Metformin	1042 (78.2)	1042 (63.7)
Carbamazepine	783 (58.7)	783 (47.9)
Phenobarbitone	592 (44.4)	592 (36.2)
Phenytoin	668 (50.1)	668 (40.8)
Non-interacting medicines		
Oral contraceptives	234 (17.6)	234 (14.3)
Lamotrigine	181 (13.6)	181 (11.1)
Sodium valproate	349 (26.2)	349 (21.3)

†This denominator excludes those who had dropped out by/in this section (314). ‡The survey was designed using branching logic. Those who answered that they were not aware that dolutegravir has interactions did not see this question and those who dropped out (missing) were excluded. §This denominator includes those who were unaware of interactions but excludes those who had dropped out by/in this section.

6.4.1 Variables influencing awareness of dolutegravir's interactions

Nurses (82.5%, 95% CI 80-85) were less likely than doctors (90.7%, 95% CI 88-93) to be aware that dolutegravir has any interactions (Figure 12).

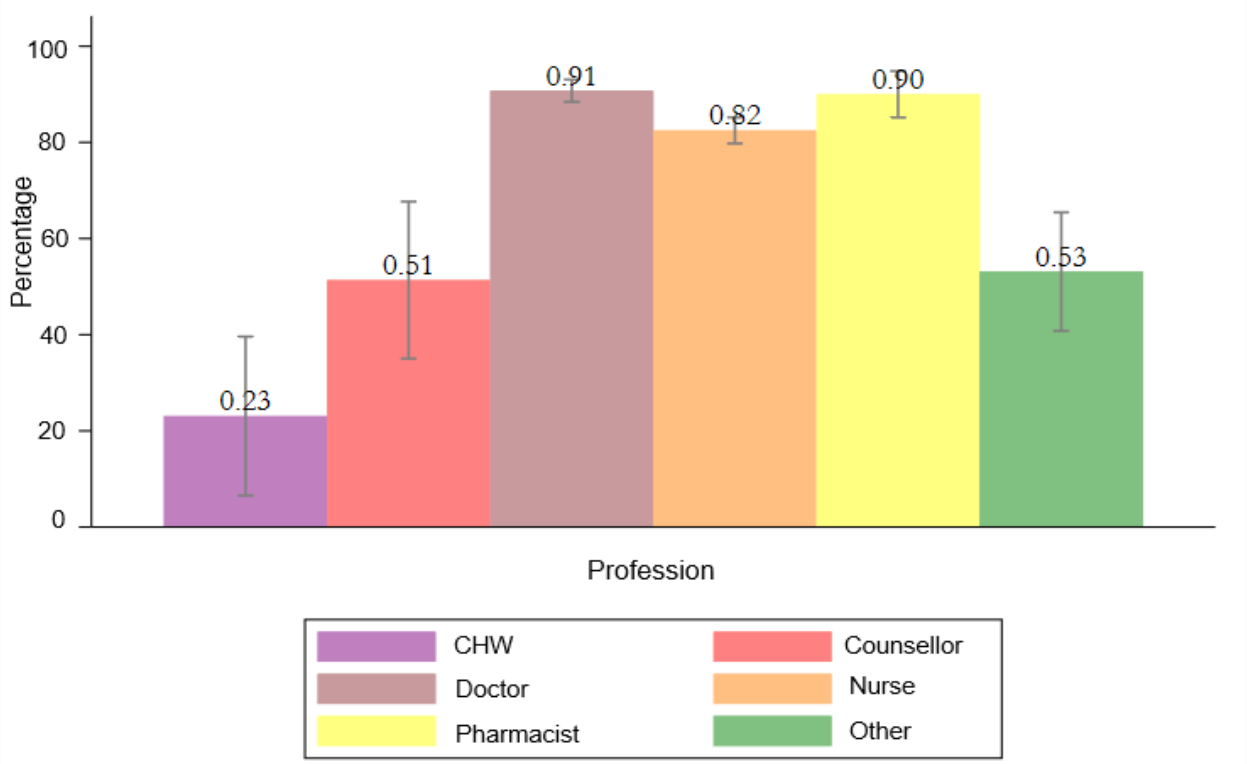

Figure 12. Awareness of dolutegravir's interactions, by profession

HCWs with guideline access were more likely to be aware that dolutegravir has interactions that those without access (90.5%, 95% CI 88.7-92.1 vs. 61.6%, 95% CI 56.6-66.4). Similarly, training was positively associated with interaction awareness (96.6%, 95% CI 95.3-97.6 vs. 61.9%, 95% CI 57.9-65.7) (Table 10).

Table 10. Awareness that dolutegravir has interactions by training and guideline access

	Received training, n=1636[1]
Training	
Training received	96.6 (95.3-97.6)
Training not received	61.9 (57.9-65.7)
Guideline access	
Access to guidelines	90.5 (88.7-92.1)
No access to guidelines	61.6 (56.6-66.4)

[1]Blank responses i.e. those that did not answer the question were excluded.

6.4.2 Variables influencing awareness of which drugs interact with dolutegravir

The full table of awareness of which drugs interact with dolutegravir, by profession, guideline access and training is found in Appendix G and selected drugs of interest are listed in Table 11.

Table 11. Awareness of dolutegravir's interaction with iron, carbamazepine, metformin and rifampicin, by profession, training and guideline access

n=1333[1]	Iron	Carbamazepine	Metformin	Rifampicin
Profession				
CHW	16.7 (0.4-64.1)	16.7 (0.4-64.1)	33.3 (4.3-77.7)	50.0 (11.8-88.2)
Counsellor	15.8 (3.4-39.6)	10.5 (1.3-33.1)	31.6 (12.6-56.6)	47.4 (24.5-71.1)
Doctor	59.0 (54.7-63.2)	60.7 (56.4-64.9)	80.6 (77.0-83.9)	91.6 (89.0-93.8)
Nurse	48.7 (44.6-52.7)	58.4 (54.4-62.4)	78.5 (75.0-81.7)	84.9 (81.8-87.7)
Pharmacist	61.2 (52.4-69.5)	62.7 (53.9-70.9)	78.4 (70.4-85.0)	88.1 (81.3-93.0)
Training				
No training	37.9 (33.0-43.1)	46.1 (40.9-51.3)	61.0 (55.8-66.0)	80.2 (75.8-84.2)
Training received	59.5 (56.4-62.7)	63.6 (60.5-66.6)	84.8 (82.3-87.0)	89.4 (87.3-91.3)
Guideline				
No Access	34.5 (28.4-40.9)	43.4 (37.0-50.0)	62.1 (55.6-68.4)	76.6 (70.7-81.9)
Has Access	57.7 (54.7-60.6)	62.0 (59.1-64.9)	81.6 (79.2-83.9)	89.1 (87.1-90.9)

[1]Blank responses were excluded.

Significant differences in awareness of which drugs interact with dolutegravir, by profession, were found. CHWs had low awareness of the interactions with cations (iron 16.7%, 95% CI 0.4-64.1) and doctors (iron, 59.0%, 95% CI 54.7-63.2) were more likely than nurses (iron, 48.7%, 95% CI 44.6-52.7) to be aware of these interactions. The statistically higher awareness of doctors over nurses extended across all interacting drugs, except metformin and carbamazepine, which were both non-statistically lower in nurses (Table 11, Appendix G).

Across the board, guideline access and training significantly increased awareness of dolutegravir's specific drug interactions (Figure 13).

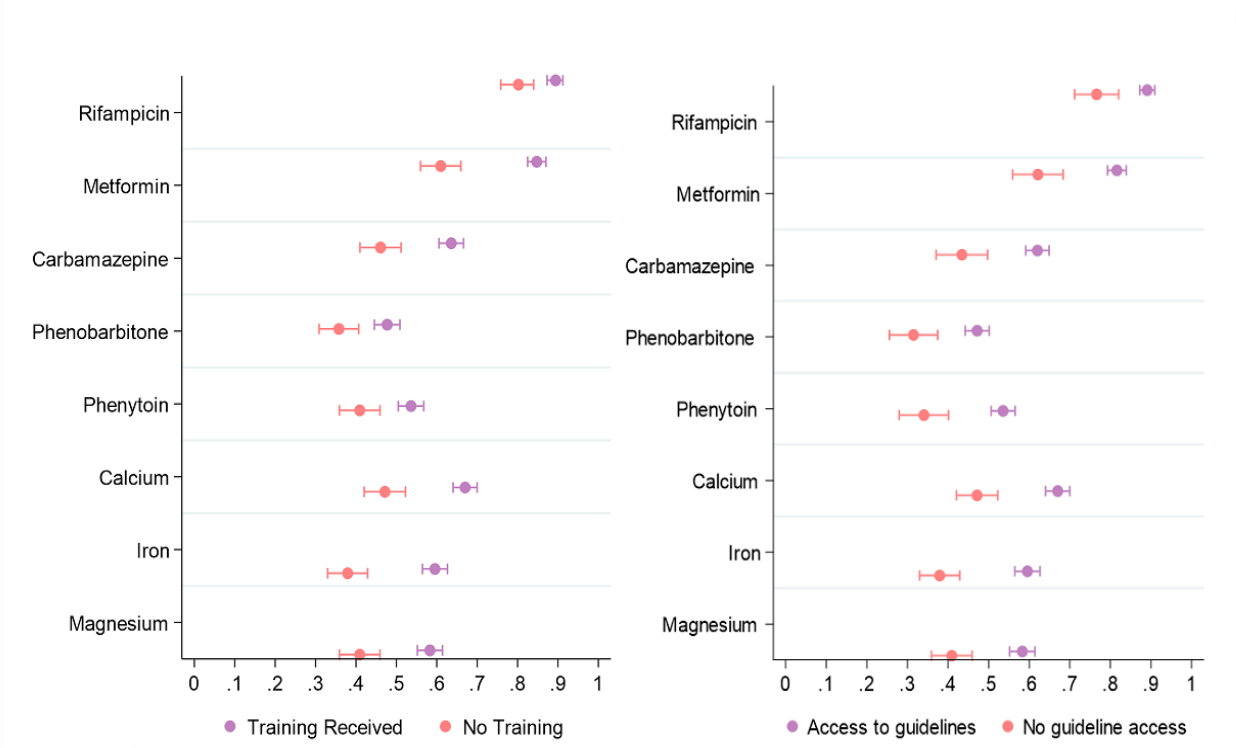

Figure 13. Awareness of specific interactions by training and guideline access (proportion; whiskers denote 95% CI)

6.5 Knowledge of specific dosing changes

By branching logic, only participants who were aware of the interaction with a specific drug were shown the question on how to adjust dosing.

Knowledge of how to adjust dosing was poor, except with rifampicin and metformin (Figure 14). When asked to pick the correct dosage regimen to counteract the interaction between cation-containing medicines and dolutegravir (with food or two hours after/six hours before dolutegravir), 5.1% (calcium) and 5.7% (iron) picked both correct options, and 33.7% (calcium) and 37.0% (iron) picked one of the two correct options (Figure 14).

With the antiepileptics, 10.1% chose both correct options for carbamazepine and 54.8% chose one of the two correct options. The contraindication to using phenobarbitone and phenytoin in patients on dolutegravir was known by 45.8% and 45.6% of HCWs, respectively (Figure 14).

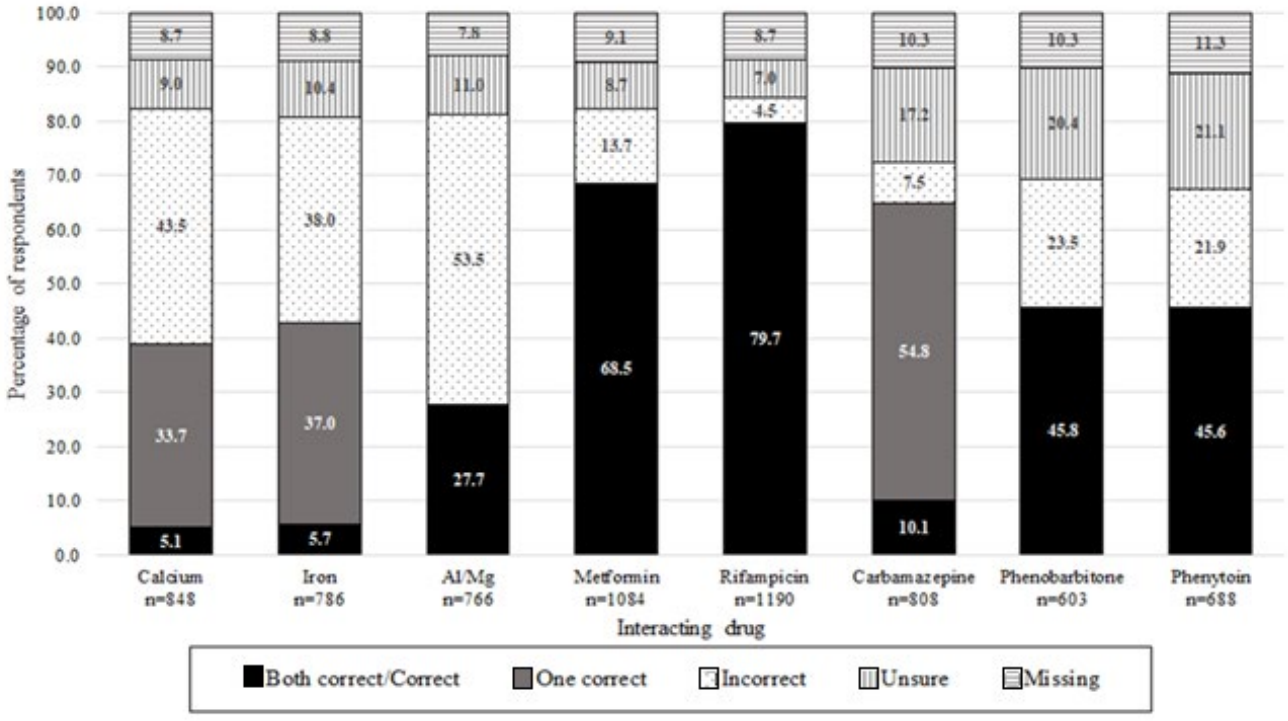

Figure 14. Proportions of HCWs knowing specific dosing adjustments

6.5.1 Variables influencing specific dosing knowledge

The full table of knowledge of the dosage adjustments required due to dolutegravir's interactions, by profession, guideline access and training is found in Appendix H and selected drugs are listed in Table 12.

There were no significant differences in knowledge of dolutegravir's interactions with cation-containing medicines, carbamazepine and metformin by demographic variables or guideline access (Table 12).

HCWs were, however, more likely to be aware of the dosing adjustments needed with rifampicin if they had guideline access (91.4%, 95% CI 89.4-93.2 vs. 66.5%, 95% CI 59.0-73.4) and if they had received training (92.5%, 95% CI 90.5-94.3 vs. 72.7%, 95% CI 67.1-77.8) (Table 12).

In addition, training – but not guideline access – was significantly associated with increased knowledge of the dosage adjustments needed when giving metformin with dolutegravir (80.4%, 95% CI 77.4-83.2 vs. 58.2%, 95% CI 51.4-64.8) (Table 12).

Table 12. Knowledge of dose adjustments needed due to dolutegravir's interactions with iron, carbamazepine, metformin and rifampicin, by profession, training and guideline access

n=1333[1]	Iron	Carbamazepine	Metformin	Rifampicin
Profession				
CHW	0.0 (0.0-84.2)	*	66.7 (9.4-99.2)	50.0 (1.3-98.7)
Counsellor	20.0 (0.5-71.6)	0.0 (0.0-84.2)	37.5 (8.5-75.5)	55.6 (21.2-86.3)
Doctor	9.1 (6.2-12.8)	11.7 (8.3-15.8)	80.7 (76.6-84.3)	88.7 (85.5-91.4)
Nurse	3.8 (1.9-6.6)	8.5 (5.7-12.1)	68.2 (63.6-72.6)	86.1 (82.6-89.1)
Pharmacist	5.0 (1.3-12.3)	22.5 (13.9-33.2)	87.0 (78.8-92.9)	91.5 (84.8-95.8)
Training				
No training	4.0 (1.5-8.5)	12.0 (9.5-15.0)	80.4 (77.4-83.2)	92.5 (90.5-94.3)
Training received	6.9 (5.0-9.3)	8.8 (4.9-14.3)	58.2 (51.4-64.8)	72.7 (67.1-77.8)
Guideline				
No Access	2.2 (0.3-7.7)	11.9 (9.4-14.7)	79.5 (76.6-82.1)	91.4 (89.4-93.2)
Has Access	6.9 (5.0-9.1)	7.8 (3.5-14.9)	52.7 (44.3-61.0)	66.5 (59.0-73.4)

[1]Blank responses were excluded. *No responses.

6.6 Access to guidelines

Three-quarters of respondents reported having access to guidelines of some kind. Of those who had access to guidelines, 62.3% had online access to the ART guidelines and 56.3% hard copy, while access to the VTP guidelines was lower, at 42.1% online and 36.6% hard copy, and 14.5% of respondents had access to guidelines on an App. It should be noted that multiple answers to this question was allowed, so some respondents may have access to more than one type of guideline (Figure 15).

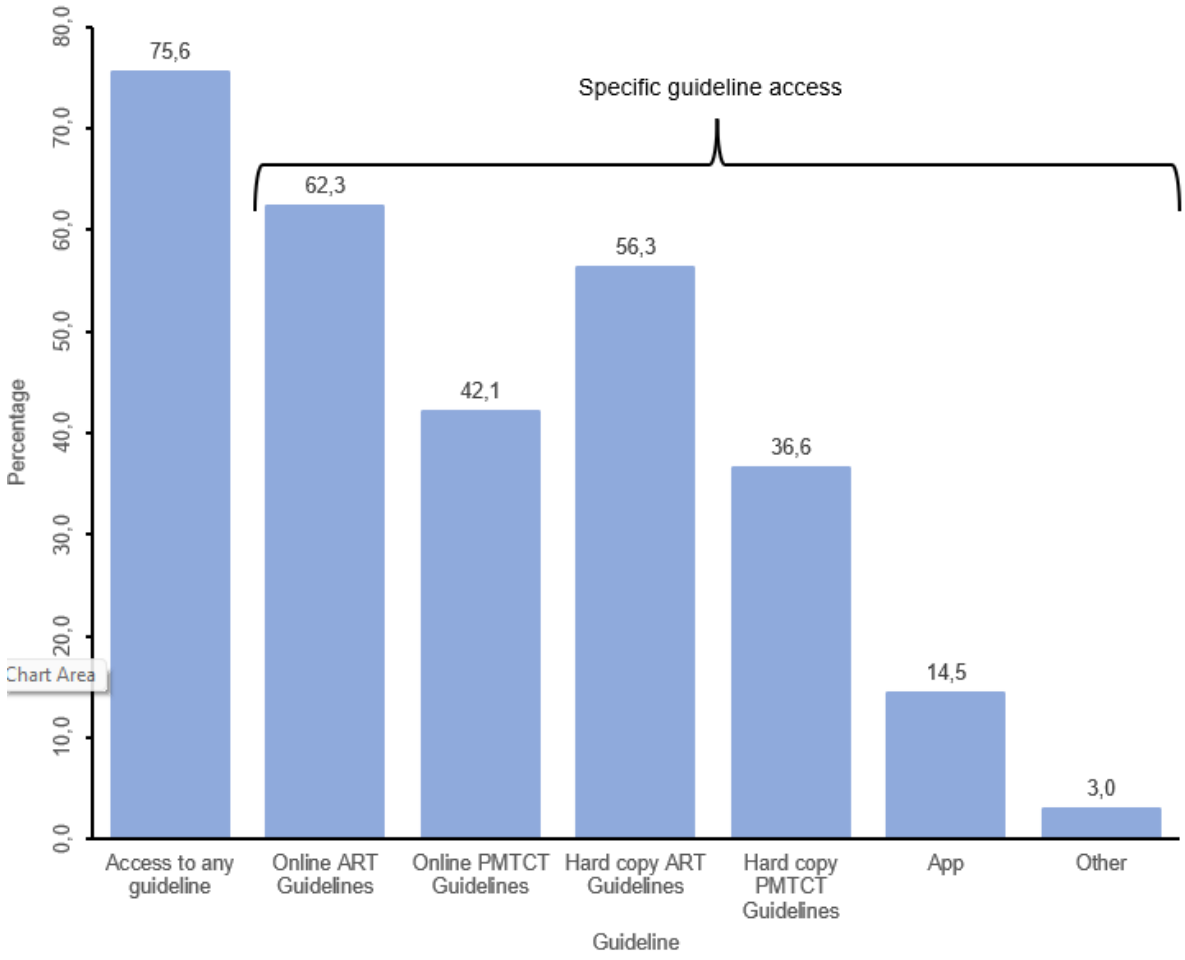

Figure 15. Guideline access and source

6.6.1 Variables influencing guideline access

On inferential analysis by sector breakdown, HCWs in the public sector were less likely than their private sector colleagues to have online ART guideline access (58.5%, 95% CI 55.6-61.5 vs. 79.2%, 95% CI 73.6-84.1), but more likely to have hard copy access to both ART guidelines (61.2%, 95% CI 58.2-64.1 vs. 34.3%, 95% CI 28.4-40.6) and VTP guidelines (41.0%, 95% CI 38.1-44.0 vs. 16.7%, 95% CI 12.3-22.0) (Table 13).

Table 13. Guideline access by facility, area and sector

n=1340[1]	Online ART guideline	Online VTP guideline	Hard copy ART	Hard copy VTP
Sector, %				
Public	58.5 (55.6-61.5)	41.6 (38.7-44.6)	61.2 (58.2-64.1)	41.0 (38.1-44.0)
Private	79.2 (73.6-84.1)	44.1 (37.8-50.5)	34.3 (28.4-40.6)	16.7 (12.3-22.0)
Area, %				
Rural	60.4 (56.2-64.5)	41.9 (37.8-46.2)	57.7 (53.5-61.8)	43.7 (39.6-48.0)
Urban	63.7 (60.2-67.1)	42.2 (38.7-45.8)	55.2 (51.7-58.8)	31.5 (28.2-34.8)
Training, %				
Received	60.4 (57.2-63.5)	43.1 (39.9-46.3)	61.6 (58.4-64.7)	42.6 (39.4-45.8)
Not received	67.4 (62.4-72.0)	39.7 (34.8-44.8)	42.8 (37.8-48.0)	21.4 (17.4-25.9)

[1]Blank responses i.e. those that did not answer the question were excluded.

Having received training was significantly associated with increased access to hard copy, but not online, guidelines (Table 13).

6.7 Training

Just over half (56.6%) of the respondents reported that they had received training on dolutegravir, of which 93.8% reported that training on dolutegravir's interactions was included in that training (Table 14).

Most of the respondents had received their training from the NDOH (55.1%) followed by NGOs (24.1%) (Table 14).

Table 14. Training received and desired, source of training and confidence in knowledge

	Participants, n (%)
DTG training received, n=1950	
Yes	1103 (56.6)
No	676 (34.7)
Not answered	171 (8.8)
Training included DTG interaction, n=1101[1]	
Yes	1033 (93,8)
No	24 (2.2)
Unsure	44 (4.0)
Training source (multiple allowed), n=1099[1]	
Department of Health	606 (55.1)
Training from a colleague	193 (17.6)
Online training	81 (7.4)
Non-governmental organisation	265 (24.1)
Training on DTG desired (unaware of interactions), n=261[2]	
Yes	240 (92.0)
No	6 (2.3)
Unsure	15 (5.7)
More training desired (aware of interactions), n=1120[3]	
Yes	1009 (82.7)
No	149 (12.2)
Unsure	62 (5.1)
Preferred training method, n=1254[4]	
Face-to-face training	306 (24.4)
Online training (computer)	642 (51.2)
Online training (cell phone)	513 (40.9)
Hard copy tools	598 (47.7)

Abbreviations: DTG, dolutegravir. The survey was designed with branching logic. [1]Those who checked 'yes' on 'received DTG training' moved on to this question. [2]Those who indicated they were unaware that DTG has interactions saw the question. [3]Those who indicated that they were aware that DTG has interactions saw the question. [4]Those who desired more training saw this question.

6.7.1 Desire for training

Most HCWs (1 249/1 381, 90.4%) expressed a desire for training on dolutegravir and its interactions – both those who were previously aware of dolutegravir's (82.7%) and those who were not (92.0%). The preferred methods of training were computer-based online training (51.2%), hard copy tools (47.7%) and cell phone-based online training (40.9%) (Table 14).

On inferential analysis, there were no significant differences in desire for training by profession, area, sector and facility. It was, however, different by province, guideline access and training (Table 15). While there were no significant differences in desire for training in those unaware of any interactions, by province, in HCWs who were aware, those in Limpopo (98.3%, 95% CI 90.9-100.0) were more likely than those in Gauteng, Kwazulu-Natal and the Western Cape (81.6%, 95% CI 76.5-86.1; 83.8%, 95% CI 78.0-88.7; 75.1%, 95% CI 69.8-79.9), to desire further training (Table 15).

The desire for additional training in those who were unaware that dolutegravir has interactions did not differ significantly in those with access to guidelines or those who had previously been trained. Training was desired by significantly more of the HCWs who were aware of the interactions but had no access to guidelines (94.6%, 95% CI 90.7-97.2 vs. 80.1%, 95% CI 77.5-82.5), or had had no training (94.4%, 95% CI 91.4-96.6 vs. 78.2%, 95% CI 75.3-80.9) (Table 15).

Table 15. Variables affecting desire for (further) training: province, guideline access and training

	Desire training (previously unaware of interactions) n=261[1], % (95% CI)	**Desire more training (previously aware of interactions) n=1220[2], % (95% CI)**
Province		
Eastern Cape	100.0 (91.6-100.0)	85.1 (78.8-90.1)
Free State	92.3 (64.0-99.8)	89.4 (76.9-96.5)
Gauteng	91.2 (81.8-96.7)	81.6 (76.5-86.1)
KwaZulu-Natal	87.5 (73.2-95.8)	83.8 (78.0-88.7)
Limpopo	100.0 (63.1-100.0)	98.3 (90.9-100.0)
Mpumalanga	90.9 (58.7-99.8)	81.9 (71.1-90.0)
North West	91.7 (61.5-99.8)	88.0 (78.4-94.4)
Northern Cape	100.0 (59.0-100.0)	93.9 (79.8-99.3)
Western Cape	88.3 (77.4-95.2)	75.1 (69.8-79.9)

Profession		
CHW	90.0 (68.3-98.8)	100.0 (47.8-100.0)
Counsellor	87.5 (61.7-98.5)	100.0 (79.4-100.0)
Doctor	87.3 (75.5-94.7)	77.9 (74.0-81.5)
Nurse	95.3 (90.0-98.3)	87.0 (83.9-89.7)
Pharmacist	100.0 (78.2-100.0)	78.1 (70.0-85.0)
Guideline access, %		
No guideline access	89.9 (83.9-94.26)	94.6 (90.7-97.2)
Guideline access	94.6 (88.7-98.0)	80.1 (77.5-82.5)
Training, %		
No training	91.6 (87.2-94.9)	94.4 (91.4-96.6)
Training received	94.1 (80.3-99.3)	78.2 (75.3-80.9)

[1]Blank responses i.e. those that did not answer the question were excluded.

6.7.2 Preferred training methods

The preferred methods of training differed between profession, area and sector. Doctors were less likely to prefer face-to-face training (15.6%, 95% CI 12.4-19.2) compared with nurses and CHWs (24.4%, 95% CI 21.1-28.0; 62.5%, 95% CI 40.6-81.2). CHWs were more likely than nurses, doctors and pharmacists to prefer face-to-face training, and nurses were more likely than doctors and pharmacists to prefer cell phone-based training (45.5%, 95% CI 41.5-49.5 vs. 34.6%, 95% CI 30.3-39.2; 29.8%, 95% CI 22.0-38.7) and less likely to want computer-based training (Table 16).

HCWs in rural were more likely than those in urban areas, to desire face-to-face (27.2%, 95% CI 23.5-31.1 vs. 20.2%, 95% CI 17.4-23.2) and cell phone-based training (44.0%, 95% CI 39.8-48.2 vs. 35.0%, 95% CI 31.6-38.5) and less likely to desire computer-based training (43.8%, 95% CI 39.6-48.0 vs. 51.9%, 95% CI 48.3-55.5) (Table 16).

At sector level, HCWs in the private sector were less likely than those in public to prefer face-to-face (17.6%, 95% CI 13.5-22.5 vs. 24.7%, 95% CI 22.1-27.4) and cell phone-based training (31.5%, 95% CI 26.3-37.2 vs. 40.8%, 95% CI 37.8-43.9) (Table 16).

Table 16. Preferred training method by profession, area and sector

n=1324[1]	Face-to-face, % (95% CI)	Online (computer), % (95% CI)	Online (cell phone), % (95% CI)	Hard copy (posters), % (95% CI)
Profession				
Community health worker	62.5 (40.6-81.2)	41.7 (22.1-63.4)	12.5 (2.7-32.4)	29.2 (12.6-51.1)
Counsellor	50.0 (31.9-68.1)	31.3 (16.1-50.0)	40.6 (23.7-59.4)	37.5 (21.1-56.3)
Doctor	15.6 (12.4-19.2)	62.8 (58.2-67.2)	34.6 (30.3-39.2)	42.9 (38.3-47.5)
Nurse	24.4 (21.1-28.0)	36.7 (32.9-40.6)	45.5 (41.5-49.5)	48.2 (44.2-52.2)
Pharmacist	24.2 (17.0-32.7)	60.5 (51.3-69.1)	29.8 (22.0-38.7)	49.2 (40.1-58.3)
Other healthcare worker	36.4 (23.8-50.4)	49.1 (35.4-62.9)	27.3 (16.1-41.0)	32.7 (20.7-46.7)
Area				
Rural	27.2 (23.5-31.1)	43.8 (39.6-48.0)	44.0 (39.8-48.2)	45.4 (41.2-49.7)
Urban	20.2 (17.4-23.2)	51.9 (48.3-55.5)	35.0 (31.6-38.5)	45.0 (41.4-48.6)
Sector				
Public	24.7 (22.1-27.4)	44.9 (41.8-43.9)	40.8 (37.8-43.9)	47.1 (44.0-50.2)
Private	17.6 (13.5-22.5)	61.0 (55.2-66.6)	31.5 (26.3-37.2)	38.3 (32.7-44.1)

[1]Blank responses i.e. those that did not answer the question were excluded.

6.7.3 Variables influencing training

Nurses were more likely to have received training than their doctor and pharmacist colleagues (69.3%, 95% CI 66.0-72.4 vs. 59.6%, 95% CI 55.7-63.4 and 54.3%, 95% CI 46.3-62.2); and CHWs (27.6%, 95% CI 12.7-47.2) were less likely than doctors or nurses, to have received training (Table 17).

HCWs in the public sector were more likely to have received training than those in the private sector (67.5%, 95% CI 64.9-69.9 vs. 42.4%, 95% CI 37.4-47.5) (Table 17).

Table 17. Training by profession and sector

	Received training, n=1779[1]
Profession	
CHW	27.6 (12.7-47.2)
Counsellor	51.2 (35.5-66.7)
Doctor	59.6 (55.7-63.4)
Nurse	69.3 (66.0-72.4)
Pharmacist	54.3 (46.3-62.2)
Sector	
Public	67.5 (64.9-69.9)
Private	42.4 (37.4-47.5)

[1]Blank responses i.e. those that did not answer the question were excluded.

6.8 Confidence in knowledge

Just under one-fifth of respondents (17.7%) did not answer the Likert-scaled confidence in dolutegravir interaction knowledge question. Most respondents who answered were either confident in their knowledge (34.0%) or neutral (30.4%) (Table 18).

Table 18. HCW confidence in dolutegravir knowledge

	Participants, n (%)
Confidence in DTG interaction knowledge, n=1064[1]	
Not confident (0-19)	202 (12.6)
Somewhat not confident (20-39)	116 (7.2)
Neutral (40-59)	487 (30.4)
Somewhat confident (60-79)	253 (15.8)
Confident (80-100)	546 (34.0)

Abbreviations: DTG, dolutegravir. The survey was designed with branching logic.

Inferentially, training was significantly associated with an increase in HCWs' confidence in their knowledge (72.2%, 95% CI 71-74 vs. 41.4%, 95% CI 39-44); as was access to guidelines (66.9%, 95% CI 65-68 vs. 42.2%, 95% CI 39-45) (Figure 16).

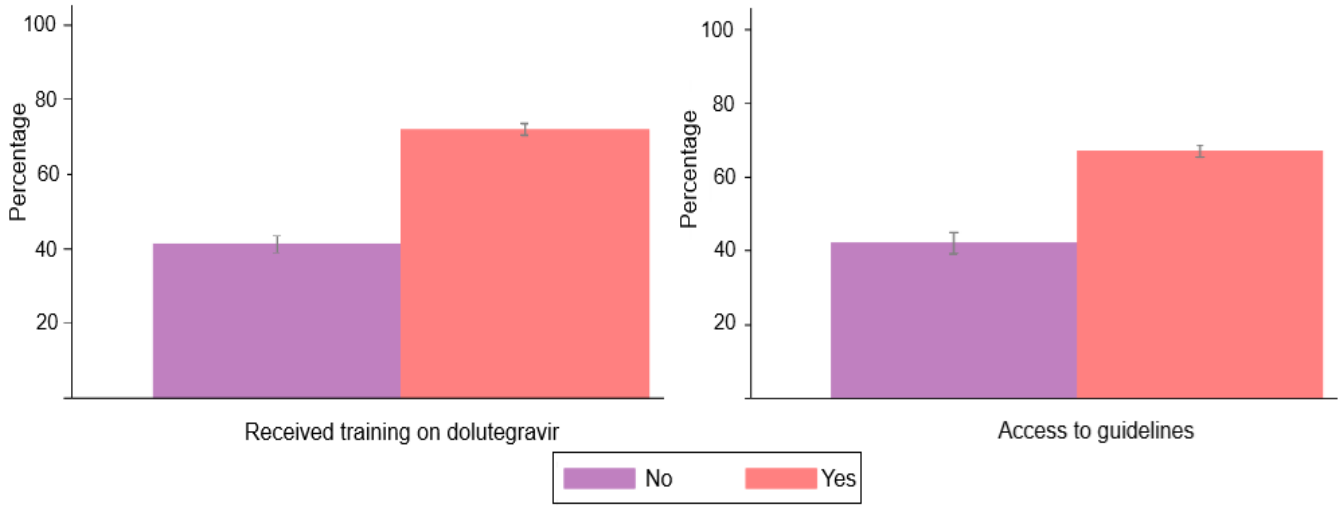

Figure 16. Variables affecting confidence in knowledge: training and guideline access

6.9 Discussion

The study revealed that just over two-thirds (70.0%) of South African HCWs working in the field of HIV were broadly aware that dolutegravir has drug interactions. In this population, awareness of specific drug interactions ranged between 44.4-86.9%, higher than reported in a previous UK-based study of ARV DDI knowledge (not including dolutegravir), which showed 36% of HCWs identified the DDIs included.[426]

Awareness of which drugs interact and knowledge of how to adjust dosing, was poor, except with rifampicin and metformin. While it is reassuring that a good proportion of the respondents were aware of the interaction with rifampicin (86.9%) and knew of the need to double the dose of dolutegravir (79.7%), this proportion did not include all respondents, as the branching nature of the survey excluded those unaware of interactions at all, meaning that the proportions found give the impression of higher knowledge levels. As an example, when including only the respondents who saw the interaction section, the proportion who were aware of the rifampicin interaction was

1 158/1 636 (70.8%) and the proportion who knew of the dosing adjustments needed was 949/1 636 (58.0%). This is especially concerning in a country with a TB incidence of 427/100 000 in PLHIV in 2023.[428]

Awareness of the interaction with magnesium/aluminium-containing antacids was lowest at 53.5%. If all respondents on the general dolutegravir awareness question were included, this would drop to 43.6%. The significant gap in the knowledge of interactions with cation-containing medicines is a major concern, especially in pregnant women, who routinely take calcium and/or iron and antacids. Serious repercussions on maternal health and the risk of vertical transmission may result.

Almost one-fifth of respondents incorrectly thought that dolutegravir interacts with oral contraceptives (17.6%). This gap in knowledge may affect women's reproductive health and choices. The *Unwanted Fertility in South Africa* report showed that just 46% of observed births, between 2011-2016, were wanted at the time of conception[429], highlighting the need for appropriate access and information about safe contraceptive choices.

Profession, access to guidelines and training were the most significant factors affecting both awareness and knowledge. Most concerning, nurses were less likely than doctors to be aware that dolutegravir has interactions, and which drugs interact. Due to the huge burden of HIV and TB in South Africa, and staff constraints, task-shifting to NIMART was implemented in 2010.[54] In many facilities, doctors visit infrequently, placing nurses at the frontline of HIV care. It is imperative that nurses are fully versed in dolutegravir's interactions and the necessary dosing adjustments.

The number of community health workers and counsellors was small, and their knowledge of interactions was poor. This was expected, as they are not trained in interactions, but they may be a good cohort to include in basic interaction training – such as with cations, for pregnant women – as they have regular contact with the community, in their homes.

Access to guidelines was associated with better awareness that dolutegravir has interactions, which drugs interact, and how to adjust dosing of rifampicin. Kredo et al, in their qualitative study of South African health managers, found that guideline access –

mostly due to budgetary constraints – was one of the perceived barriers to the implementation thereof.[430] It is logical to expect a lack of knowledge, with 75% of HCWs in the field having access to guidelines in this study. This is a concerning drop in guideline access from previous studies conducted in KwaZulu-Natal which reported 98% ART guideline access (52 clinics)[147]; rural Western Cape with 86% (44 clinics)[136]; and North-West, 84% (18 clinics)[141].

Similarly, as expected, training improved knowledge, and HCWs' confidence in their knowledge. A study of primary care nurses, also by Kredo et al, found that inconsistent and non-inclusive training on the guidelines was a major barrier to their use.[431] With only just over half of our respondents (56.6%) having received training, this is a key point for intervention.

With most participants wanting training, all that is missing is its availability.

6.10 Strengths and limitations

The primary strength of this study was the good uptake and broad access to HCWs across South Africa, allowing the results to be generalisable. Using an online, anonymous survey may have limited social desirability bias. The study had several limitations.

Firstly, the survey was sent out between the first and second waves of the COVID-19 pandemic in South Africa, so training and guideline access may have been negatively influenced by 'rolling' countrywide lockdowns, strained healthcare resources and physical distancing. While this is a limitation, the COVID-19 pandemic also showed opportunities. The need for online-/mobile phone-based training and guideline access was highlighted. In a country such as South Africa, with many health facilities in rural, hard-to-reach places, this will be doubly beneficial. Training preferences of HCWs were gathered in the survey.

Secondly, the study had the potential for selection and non-response bias. Dissemination to users of the hotline and HIV-centred organisations meant that we were targeting the 'interactive' group i.e., HCWs who actively seek information. Similarly, the survey was targeted at HCWs working in the field of HIV, which may have resulted in

over-reporting. In a country with an HIV incidence of 4.55/1 000 in 2023[34], ARVs may routinely be prescribed and dispensed by HCWs not specifically working in the HIV sphere.

Lastly, the survey was taken at the respondents' leisure, in the setting of their choosing. They may have answered the questions using the guidelines, or other sources, as reference. While this may have skewed the results slightly, this was deemed to be a negligible limitation as it is not expected of HCWs to possess this knowledge – although this would be ideal – but to know where to find it in the guidelines.

6.11 Conclusions

The study revealed critical gaps in the awareness and knowledge of dolutegravir interactions and how to adjust dosing amongst South African HCWs in the field of HIV. Failure to recognise these interactions and adjust dosing of dolutegravir could result in increased morbidity and mortality due to adverse effects, increased HIV resistance and failure, and increased vertical transmission. This, in turn, may have major implications for public health and prevent the attainment of the United Nation's 90-90-90 targets.

The study highlighted the need to train more HCWs, especially nurses, who are at the forefront of HIV care in South Africa. The development of novel, inexpensive, and accessible training methods, for all professions, especially in countries with large rural populations and facilities, is vital.

Chapter summary

This chapter reported the results, discussion and conclusions of the online survey of South African HCWs working in the field of HIV. Important gaps in knowledge of dolutegravir's interactions were found. These may have repercussions on public health. Training was significantly associated with better awareness of dolutegravir's interactions, and how to adjust dosing due to them; and the vast majority of participants wanted to be trained.

The results from Study 1 provided the primary rationale and a participant-centric guide to the design of Study 2.

The methodology of Study 2 is reported in Chapter 7, and results from Study 2 will be presented in Chapter 8.

Part 3: WhatsApp-based training

Part 3 describes Study 2, to design and test the usability of WhatsApp-based HIV microlearning for HCWs.

Chapter 7 details the methodology of the study.

Chapter 8 reports on the effectiveness, uptake and participation, feasibility and acceptability results of the study.

Chapter 7 Research methods: WhatsApp-based training

This chapter describes the methods used for Study 2 (2021-2024), a pragmatic, mixed-methods, parallel-group cluster-randomised study to design and test a WhatsApp-based training intervention. It presents the study design, setting, populations and sampling, recruitment, intervention, study instruments, data collection and analysis, and ethical considerations of the study.

Chapter 7 contains excerpts from the following papers:

Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. International Journal of Qualitative Methods 2024; 23: 16094069241284205. DOI: 10.1177/16094069241284205.

Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

Chisholm BS, Wallace ML, Blockman M and Orrell CJ. "WhatsApp is best!" Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

7.1 Rationale for study and intervention design

Study 1 revealed gaps in HCWs' knowledge of dolutegravir's drug interactions, which are clearly stated in the guidelines. It also showed a lack of training, and a desire for training, with preference for cell phone-based interventions. These findings were used as the basis for the design of the training intervention and delivery thereof.

7.2 Introductory note: choice of methodology

The methodology is "a body of methods, rules, and postulates employed by a discipline: a particular procedure or set of procedures".[432] The methodology informs the research question(s), methods, collection of data and analysis[433], underpinned by ontology and epistemology[434].

The most used – or 'foundational' – qualitative methodologies include grounded theory, phenomenology and ethnography.[339, 433] More recently, 'generic' methodologies have been described, allowing for mixed-methods methodologies designed to fit within the philosophical underpinnings and research question of a study.[339, 435]

Generic methodology

Research questions within the nursing sector are situated in complicated contexts, with multiple variables, making the use of the established methodologies constrictive and illogical.[436] An established methodology with an explicit philosophical foundation may not fit a specific study, necessitating a 'generic one'. Caelli et al defined generic qualitative study as studies that either blend methodological approaches or claim to have no methodological framework at all.[435]

Research using a generic methodology can draw from different methodologies and methods to create a framework that is congruent with the research question that needs answering, within the context in which the research is happening.[339] Generic methodologies can be sub-categorised into (1) qualitative description, producing a 'low-inference' description, or 'data-near' findings; and (2) interpretive description, producing an interpretive account through informed questioning and reflexivity.[339, 436, 437]

Critical realism fits within a generic methodology.[438] It has been used, and is recommended, as a philosophical framework across many fields of health, including nursing[439], midwifery[440], mental health research[441] and education[442]. Realist frameworks accommodate mixed-methods studies, but a reflexive approach is needed to both the qualitative and quantitative parts.[341, 443, 444]

In the study, we used a generic methodology informed by critical realism, with descriptive, inferential and thematic analysis.[351, 445]

7.3 Study design

A pragmatic, mixed-methods, parallel-group cluster-randomised study (Figure 17).

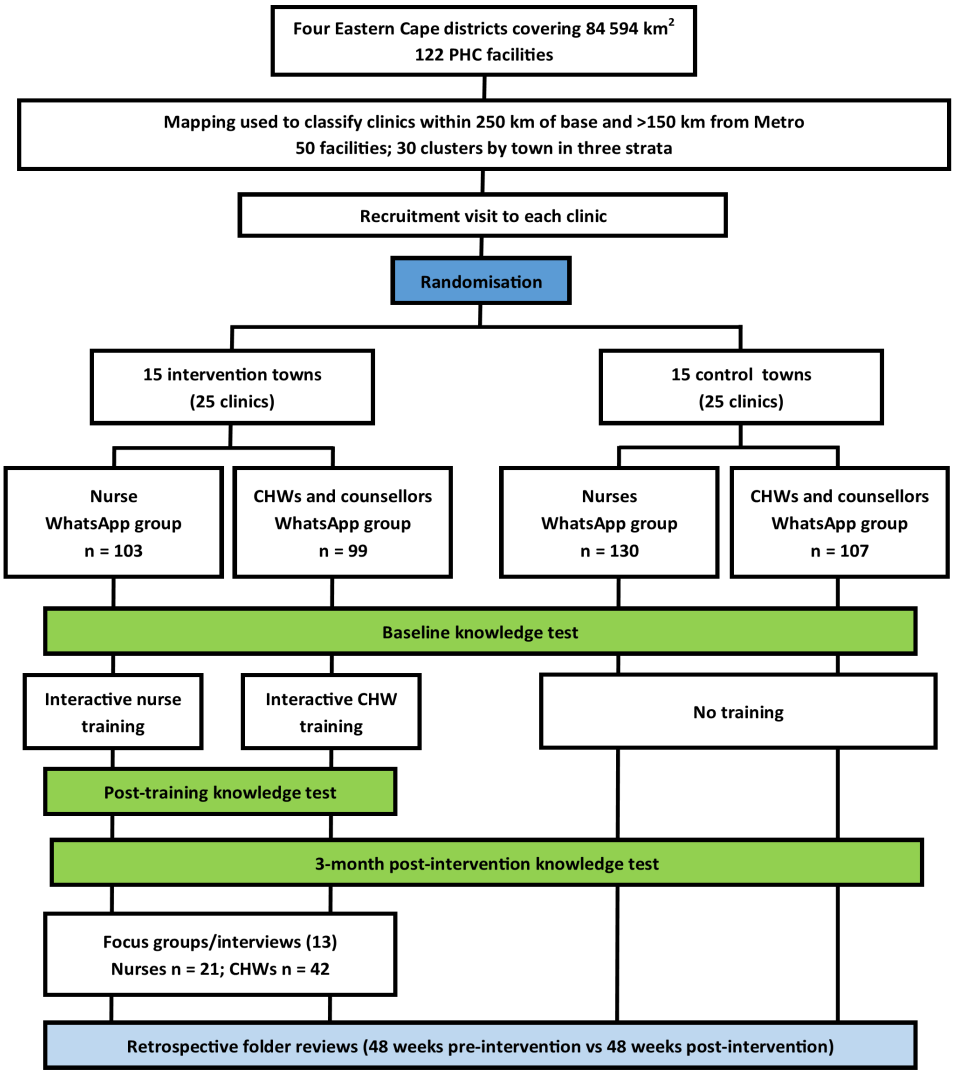

Figure 17. Study flowchart

Quantitative analysis was used to determine the effectiveness of WhatsApp-based training on increasing knowledge and altering prescribing behaviour. Both quantitative and qualitative analysis was used to describe uptake, acceptability and feasibility of the intervention as a training tool.

Qualitative research aims to understand the contextual experiences of people or groups.[446] While social science-based qualitative study often aims to establish or refine

theories, applied qualitative research aims to generate insights that can be used practically and provides understanding of interventions and programmes within healthcare.[346, 447] Qualitative approaches highlight the human side of healthcare, bringing experiences and perceptions of HCWs to the fore.[448]

Qualitative data was sought to add substance to the quantitative descriptive data gathered from the surveys, especially to meet the objectives:

- To describe the acceptability of WhatsApp-based training for nurses and CHWs in primary care facilities.
- To describe the feasibility of WhatsApp-based training for nurses and CHWs in primary care facilities.

Definitions

Acceptability: "worthy of being accepted; regarded favourably"[449]

Feasibility: "capable of being done or carried out"[450]

Study definitions were adapted from Asiimwe et al's[368] definitions to fit within the context of this study, and to answer the research questions across both quantitative and qualitative methods (Table 19).

Table 19. Study definitions based on Asiimwe et al's model[368]

Usability factor	Definitions in study context	Affects and informs
Learnability	Ability to understand the lesson and absorb the knowledge	Acceptability, uptake
Willingness	Willingness of HCWs to take part in the training	Acceptability, uptake, feasibility
Satisfaction	Feeling that the training is convenient and/or enjoyable	
Efficiency	Ability to attend and/or read the messages of the training	
Retention	Retention of knowledge at three months post-intervention	Effectiveness and knowledge retention
Effectiveness	The change in HCW knowledge and in patient care	

7.4 Study setting

The study was conducted in four predominantly rural districts in the Eastern Cape province of South Africa (Figure 18). Adult HIV prevalence in the province was 18.8% in 2022.[451] The Eastern Cape is a resource-poor area with 58% of the population living in rural areas.[277]

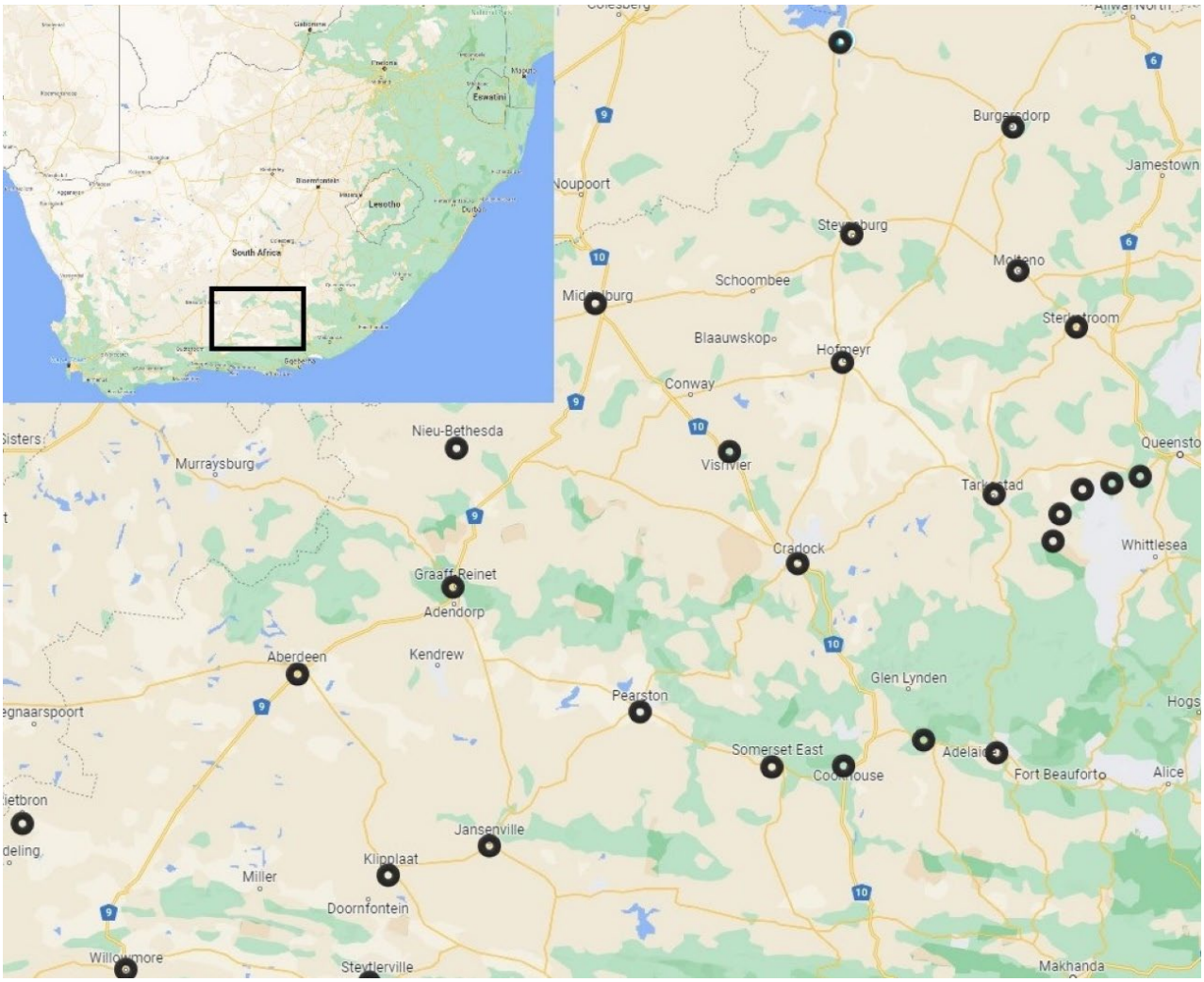

Figure 18. Map of study district and towns, in South Africa

Cluster randomisation[452] by town was used to minimise inter-HCW contamination. Stratification across clusters was done by number of HCWs and patients attending facilities, to obtain two equally sized groups and minimise variance between groups.[453] Clusters were randomly allocated within each stratum by the study statistician. Due to the nature of the intervention, blinding was not possible.

7.5 Study population, sampling and recruitment

7.5.1 Healthcare workers for training

Clinics in this area are predominantly staffed by nurses, CHWs and counsellors, with weekly, fortnightly or monthly visits from a shared doctor. Few have an on-site pharmacist. Doctors and pharmacists were excluded from the study to minimise contamination across clinics.

Sample size calculations, powered to 90% to detect a 2-point difference in mean HCW knowledge, accounting for the cluster design of the study with an intracluster correlation coefficient (ICC) of 0.01, required a sample size of 24 clusters (12 in each arm, with an average of three HCWs in each cluster) to give 5% significance. Fifty primary care clinics in 30 towns (clusters) were included, to ensure power.

Sampling for the training intervention was purposive, with all CHWs, counsellors and nurses in the facilities invited to participate during recruitment visits to the clinics and through flyers (Appendix I) left for those not there on the day, with the option to join the study via WhatsApp.

7.5.2 Healthcare workers for focus groups

Sampling for the focus groups, post-intervention, was purposive, to get rich data relevant to the training.[454] All HCWs who completed the training were asked if they were willing to participate in a focus group during the online post-intervention questionnaire, and then convenience sampling was used to pick the clinics that were included, considering distance, number of agreeable participants and time.

While methodologies like grounded theory require sampling to ‘saturation’ or ‘data adequacy’[455], there has been much debate about the concept within qualitative study[454], especially when using thematic analysis, which relies largely on reflexivity: each researcher may capture different nuances from the data collection and analysis.[456] More recent sample size discussions have recommended that sample size should be guided by the study characteristics e.g., theoretical approach, nature and scope of the study being conducted, aims, data quality and researcher skills/experience.[454] For the

purposes of this study, Dey's definition of 'theoretical sufficiency' – data collection stops when the researcher has reached a sufficient understanding – was used.[457]

7.5.3 Folders for review

Sampling of the patient folders was purposive, to include folders of patients with conditions that had the measurable outcomes from the learning points in the training (Table 20):

Adults (>18 years old) living with HIV and:

- initiating ART
- pregnant
- on rifampicin
- on metformin
- on antiepileptic drugs

Table 20. Main learning points with measurable outcomes

NURSES	Learning points	Measurable (folder review)
Introduction 2023/01/23	• Introduction and objectives of the training • Meaning of 'drug-drug interaction' • Overview of which drugs interact with dolutegravir	
Lesson 1 2023/01/25	• Use of dolutegravir in ALL women, including during pregnancy • GeneXpert for pregnant women at first antenatal visit • No interaction between dolutegravir and oral contraceptive	✓ ✓
Lesson 2 2023/01/27	• TPT for all clients on ART, regardless of CD4, except during pregnancy • TPT is only given in pregnancy if the CD4 is under 350 • Exclude TB before starting TPT	✓ ✓
Lesson 3 2023/01/30	• Rifampicin-dolutegravir interaction: double dolutegravir until two weeks after stopping rifampicin	✓
Lesson 4 2023/02/01	• Antiepileptic-dolutegravir interactions: avoid carbamazepine, phenytoin and phenobarbitone, if possible. If unavoidable, double dolutegravir dose. Sodium valproate, lamotrigine and levetiracetam do not interact with dolutegravir • Metformin-dolutegravir interaction: no more than 500 mg bd metformin, in patients on dolutegravir	✓ ✓

Lesson 5 2023/02/06	• Calcium/iron-dolutegravir interactions: calcium and/or iron need to be taken with food if on dolutegravir. If no food, they must be taken a minimum of 2 hours after or 6 hours before dolutegravir • Aluminium/magnesium (antacids)-dolutegravir interactions: must be taken a minimum of 2 hours after or 6 hours before dolutegravir	
Lesson 6 2023/02/08	• Summary of the learning points	
Community health workers		
Introduction 2023/01/23	• Introduction and objectives of the training • Meaning of 'drug-drug interaction' • Overview of which drugs interact with dolutegravir	
Lesson 1 2023/01/24	• Booking pregnancy in PLHIV as soon as possible – refer to clinic, counsel on ART to protect baby • Dolutegravir safety in pregnancy • TPT for all clients on ART – refer to clinic, if they are not/haven't been on TPT	✓ ✓
Lesson 2 2023/01/26	• Rifampicin-dolutegravir interaction: double dolutegravir until two weeks after stopping rifampicin – refer to clinic, if not taking an extra dose of dolutegravir	✓
Lesson 3 2023/01/31	• Calcium/iron/antacid-dolutegravir interactions: refer to clinic to discuss with nurse, if taking any cation-containing medicines	
Lesson 4 2023/02/02	• Summary of the learning points	

Previous prescription reviews have shown rates of incorrect prescriptions due to drug-drug interaction rates of 18.7-43.0%, adjusted mean 20.0%.[420, 422, 426, 458-460] Crude population calculations were used, to establish population sizes for measurable outcomes.[461-464]

Using an expected 10% effect size for sampling calculations, at 80% power, 5% significance, with an ICC of 0.03, between 30 and 40 patient folders per cluster (if 24-26 clusters), was needed.

7.5.4 Inclusion and exclusion criteria

Participants in the training intervention and focus group sessions, by nature of their working status, were ≥18 years old and not considered to be part of any vulnerable population within the context of this study. Inclusion criteria are listed in Table 21.

Table 21. Inclusion criteria for training intervention, focus groups and folder reviews

Training intervention	Focus groups	Folder reviews
• CHWs, counsellors and nurses • Training was conducted in English, so required English comprehension • Access to a phone with WhatsApp • Informed consent	• Participation in all WhatsApp group sessions of the training • Focus groups/interviews were conducted in English, required English comprehension • Informed consent	• Adult patients on ART

7.6 Training intervention

The TIDieR (Template for Intervention Description and Replication) checklist was used to guide the description of the intervention (Appendix J).[329]

Design of the lessons – six for nurses, four for CHWs – was led by principles outlined in Corbeil, Khan & Corbeil's *Microlearning in the digital age: the design and delivery of learning in snippets*[465]; Crompton's *Handbook of mobile learning*[466]; Bates' *Teaching in a digital age*[467]; and BC's 15+ years' experience with interacting with nurses on the hotline; and 5+ years' experience doing a weekly case study on the hotline's Facebook page[468], which she manages. Learning points were based on the National HIV guidelines[404] (Table 20) and the lessons were reviewed by a professor of pharmacology and tested in a pilot study. In line with their scope of work, for CHWs, lessons included who to refer to the nurse.

WhatsApp groups

WhatsApp groups were made for each of the control and intervention groups, divided by profession: CHWs and counsellors together in one group; nurses in the other. Initially, all four groups received cell phone data to facilitate access to online questionnaires and WhatsApp groups. Information messages with links to the baseline online questionnaire were sent and the online questionnaires remained open for at least three weeks.

Groups were then told whether they were in the intervention group (receive training immediately) or control group (receive training at the end of the study).

Each lesson consisted of cases and questions, sent in divided messages to encourage interaction, followed by the correct answer in both text and voice note (Figure 19).

Figure 19. Example of WhatsApp lesson: interaction between dolutegravir and carbamazepine

Case-based learning has been shown to be effective[4], is preferred by learners[170, 270, 315], and encourages engagement[268].

The training was conducted 'live' in WhatsApp groups: 10–15-minute lessons within the routine lunch break between 13:00 and 14:00. An introductory session was given, followed by the lessons, twice a week for three weeks for nurses, or twice a week for two weeks for CHWs. The full lesson plans are included as Appendix K and L.

Fifteen minutes before the beginning of each session, a 'housekeeping' page (Figure 20) was sent to the WhatsApp groups. The eight points on conduct within the group were guided by the draft social media ethical guidelines of the Health Professions Council of South Africa[469]; barriers reported in previous studies[240, 245] and review by an ethics expert.

Figure 20. Housekeeping rules for training intervention on WhatsApp

7.7 Pilot study

Once ethics approval was obtained, a pilot study was conducted with six nurses and six CHWs from a district in the Eastern Cape (not the clinics included in the study). Participants completed the pre-test questionnaire, received the training lessons, and completed the post-intervention questionnaire. Each pilot study participant was phoned, and their input was sought on all aspects of the intervention through semi-structured interview questions (Appendix M). Adjustments were made and amendments submitted to the ethics approval board.

7.8 Data collection and cleaning

Data was collected using multiple methods, to evaluate all four levels of the Gold Standard Kirkpatrick's levels of training evaluation[470] (Section 3.6.1.1), describe all aspects of usability, and to allow for triangulation of the data (Table 22).

Table 22. Tools and methods to measure outcomes, according to study definitions

Usability factor	Affects and informs	Sign-up lists	Surveys	WhatsApp analysis	Focus groups	Folder reviews
Learnability	Acceptability, uptake		X			X
Willingness	Acceptability, uptake, feasibility	X	X	X	X	
Satisfaction			X		X	
Efficiency			X	X	X	
Retention	Effectiveness and knowledge retention	X	X	X	X	
Effectiveness			X		X	X

7.8.1 Sign-up lists: uptake

Uptake data was collected using the sign-up list from the recruitment visits to the clinic. These were transferred into password-protected Excel spreadsheets. HCWs who joined via WhatsApp were added to the lists. The number of HCWs working at each clinic was requested during the visit.

7.8.2 Questionnaires: changes in knowledge and usability

The questionnaires were designed, completed and stored on LimeSurvey (Community Edition; Version 5.6.10+230313). The first section was basic demographic information including town, profession, age, gender and years of experience.

The second section tested knowledge – ten multiple choice questions for nurses (Appendix N); seven for CHWs (Appendix O). The final section asked about mentorship and, in the post-intervention questionnaire, questions on the usability of the intervention (Table 23).

Table 23. Questionnaire questions to measure usability of the intervention. Options: yes/no

Factors	Questionnaire questions
Learnability	Did you find the WhatsApp-based training easy to understand? Did you find the WhatsApp-based training easy to use? Do you think that this training will change how you do your day-to-day duties, treating clients on ARVs?
Willingness	Did you find the WhatsApp-based training easy to use? Did you enjoy the WhatsApp-based training? Would you prefer non-interactive WhatsApp-based training, i.e. info being sent as a message, with no interaction in the group? Would you participate in this kind of learning if it were a weekly session throughout the year?
Suitability	Did you find the WhatsApp-based training useful? Would you prefer face-to-face training rather than WhatsApp-based training? Do you think that this training will change how you do your day-to-day duties, treating clients on ARVs?
Satisfaction	Did you find the WhatsApp-based training useful? Did you find the WhatsApp-based training easy to use? Did you enjoy the WhatsApp-based training? Would you prefer non-interactive WhatsApp-based training, i.e. info being sent as a message, with no interaction in the group? What were the challenges you experienced with the WhatsApp-based training?
Efficiency	Did you find the WhatsApp-based training convenient? Were you able to access all 'live' sessions of the WhatsApp-based training at 13:00?
Effectiveness	Do you think that this training will change how you do your day-to-day duties, treating clients on ARVs?

At the end of both the post-intervention and 3-month post-intervention questionnaires, an open-ended question, '*If you have any suggestions, comments, or complaints about the course, please put them here. Your input is very valuable and will be used to improve the training'*, was asked, with a free text answer option.

Validity and reliability

The questionnaire was reviewed by both laypeople and experienced HIV researchers and clinicians within the Division of Clinical Pharmacology at UCT, to evaluate content validity and ensure questions were appropriate, relevant and phrased to minimise bias.

To ensure reliability and validity, three tests were run before the pilot study:

1. **Face validity**: two laypeople and two pharmacists checked the survey for face validity, i.e. readability, layout and clarity, and required edits were made.
2. **Content validity**: six doctors (three HIV experts, three Clinical Pharmacology registrars) and a pharmacist completed a Content Validity Index (CVI), which had an average of 0.8. Questions are considered valid if CVI > 0.78.[399]
3. **Test-retest for reliability**: seven HIV hotline pharmacists and five nurses completed the survey twice, two weeks apart, resulting in a Pearson's coefficient of 0.8. Reliability is considered to be good if the correlation coefficient > 0.7.[400]

The recommended adjustments were made.

A URL link to the online questionnaires was sent in the WhatsApp groups, with regular reminders to complete them. Multiple choice answers were set to change order at random, to minimise the risk of sharing of answers and/or memorisation.

Baseline knowledge was measured before participants were informed whether they were in the control or intervention group. The questionnaire was repeated by the intervention groups immediately after the training, and by both groups three months after the training. The control group did not do the immediate post-intervention questionnaire to prevent 'survey fatigue'.[192]

Pre-intervention questionnaires were open between 9 and 23 January 2023; post-intervention between 2 February (CHWs) or 9 February (nurses) and 30 March 2023; and 3-month post-intervention questionnaire between 8 and 26 May 2023.

Data collected was exported from LimeSurvey onto Excel and cleaned: those without data on knowledge and usability and duplicates were removed (first completion – by date stamp – of questionnaire were kept); and the data were anonymised for analysis.

7.8.3 WhatsApp group interaction: participation

Engagement of participants in sessions was measured using WhatsApp functionalities: WhatsApp Business allows the admin to see to whom messages have been delivered, and who has seen them.

Due to potential disruptions of loadshedding – South Africa has an energy crisis which resulted in regular, scheduled periods of the electricity being cut off each day for long periods during the time of training intervention – this did not necessarily have to be during the live session. Each participant's having 'seen' the messages in each lesson was defined as them having received the lesson. This was measured during the lesson, one hour after, 24 hours after, at the end of the week, and two weeks after the training.

All participant interaction was collected. Each day's messages were exported from WhatsApp and saved in a password-protected folder.

7.8.4 Focus groups: acceptability and feasibility

Traditionally, in health service and medical education research, focus groups were used to guide the development of research questionnaires, but there has been a move toward their use to get their 'voice' on the design, application and evaluation of curricula.[471-473]

Barbour describes focus groups as "coming into their own" when the aim is to generate research data relating to new developments or procedures that requires contributions from everyone to answer 'why?' (and 'why not?'), and to get different perspectives from the same group.[474] The nature of the training intervention – essentially, a group activity

– makes focus groups the ideal way to gain insight into the views and experiences of the healthcare workers of the WhatsApp-based training of the study.

Focus groups were conducted in English and Afrikaans, using a semi-structured interview guide (Appendix P), in a convenient, quiet, private location at the clinic or in the town. Separate sessions were held for nurses and CHWs. Participants in each focus group were from the same cluster (town). Only participants, the researcher, and the research assistant (RA) – who took notes only – were in the focus groups.

All sessions, except one, were recorded on two devices (dictaphone and mobile phone), with permission from the participants. One nurse in one group refused permission to record, so notes were taken by the RA.

Recordings were uploaded onto a password-protected cloud drive. Word 365 MSO (Version 2308) was used to transcribe the recordings. Recordings were listened to, and the word-for-word machine transcriptions were edited, with non-verbal cues added. A month later, the recordings and transcriptions were listened to again and edited, in combination with the notes taken by the RA during the focus groups. The transcriptions were uploaded to NVivo (Version 14, released 2023) and a third listen/read was done.

7.8.5 Folder reviews: change in patient care

Folder reviews were retrospective, and data was pulled for the period of 48 weeks before recruitment started (1 November 2021 to 30 September 2022) and 48 weeks from when the training sessions started (23 January 2023 to 22 December 2023). The period between the clinic visits for recruitment and the start of the training (1 October 2022 to 22 January 2023), prior to the intervention were excluded, to minimise confounding.

Folder reviews were conducted at all 50 clinics. The researcher was not blinded, as she conducted the training and the folder reviews. A list of the relevant folders was sent via WhatsApp to the managing nurse to organise the visit, 2-4 weeks before the visit. A reminder was sent 1-3 days before the visits. On arrival at the clinics, the list was given to the data capturer, who pulled the relevant folders. Folder review visits took place between January and June 2024.

Data was entered into an Excel spreadsheet and included patient data (age, gender, pregnancy); clinical data (HIV diagnosis date, ART initiation date; co-morbidities); record of GXP; drug data (dolutegravir start date, NRTI backbone, other co-prescribed drugs and relevant drug data) and prescriber (doctor/nurse).

Data was cleaned using Excel 365 (Microsoft Version 2409), to ensure all data points fitted within the inclusion criteria and to find any missing data and stored on a password-protected drive.

7.9 Data analysis

Data was analysed using Microsoft Excel 365 (Version 2410), Stata Statistical Software: Release 15.1 (College Station, TX: StataCorp LLC) and NVivo (Version 14, released 2023) at cluster, HCW and patient level, descriptively and using linear mixed-effects regression analysis, adjusted for cluster effects, with the primary analysis being of HCW knowledge score means.

7.9.1 Knowledge changes

Descriptive analyses were performed to calculate proportions of individual HCWs who answered each learning point correctly on the questionnaires, and of total scores, at each follow-up time point.

To analyse differences in changes in HCW total knowledge, an expanded multilevel linear mixed-effects regression model of knowledge score on intervention, time, time-and-intervention interaction, and stratification was done with cluster as the first random effect and participant as the second random effect nested within cluster. This model was also adjusted for age, gender and years of experience. Mean differences were estimated with their respective 95% confidence intervals.

7.9.2 Uptake, participation and interaction

Uptake, participation, and interaction were described using proportions. For uptake, the proportion who participated was calculated using the formula:

$$Uptake = \frac{HCWs\ who\ signed\ the\ list\ during\ clinic\ visits\ or\ sent\ a\ WhatsApp\ to\ join}{Number\ of\ HCWs\ working\ at\ the\ clinic}$$

For participation, proportions of participants immediately after the session (those who were present during the 'live' session); one hour and 24 hours after the session; and at two weeks after the session, were calculated. Record was kept of participants dropping out – leaving the WhatsApp group – during the training period.

$$\mathrm{P}articipation = \frac{Number\ of\ participants\ who\ have\ 'seen'\ messages\ at\ timepoint\ x}{Number\ of\ participants\ in\ session}$$

To quantify interaction, transcripts from each WhatsApp session were uploaded onto NVivo and coded to text (greetings, answers to questions on case and thank yous) or emoji groups, while doing the qualitative analysis through template analysis. Proportions of interaction within the training sessions were calculated using matrix queries of counts in NVivo.

7.9.3 Usability: acceptability and feasibility

Usability data from the questionnaires were analysed using qualitative analysis of the free-text questions, focus group discussions and WhatsApp group interactions in NVivo and quantitatively using Excel 365 to calculate proportions.

7.9.3.1 Qualitative analysis

Data from the free-text questions in the questionnaires, focus groups and WhatsApp interactions were analysed thematically, using template analysis[475] with predominantly descriptive coding within Brooks et al's thinking that there is no real defining line between descriptive and interpretive approaches[476].

Template analysis is a 'generic' thematic analysis approach that allows the researcher to choose the methodology and philosophy that best suit the needs of the study.[475] King and Brooks' method of template analysis is described as a midpoint between coding reliability approaches (e.g., grounded theory) and the reflexive approach, sharing the methods of theme creation of coding reliability but using the qualitative philosophy of the reflexive approach.[477]

The method has been used widely, across a diverse range of research areas[475], including psychology research[476], sports science[478], primary care guideline

implementation[479], and postgraduate medical education[480], and is suitable within the critical realist framework.

King and Brooks[475] situate template analysis within (limited) realist paradigms, where causal explanations are sought, by recommending three points to consider:

1. Template analysis can make use of *a priori* themes, drawing on existing theory or previous evaluation: in this case, data from the online questionnaires
2. Reflexivity is vital to develop themes that are not just due to researcher subjectivity
3. The reflexivity – and realist paradigm – does not rely on technical checks such as inter-rater reliability but rather relies on researchers constantly reflecting on possible threats to interpretation quality and how to minimise them

Template analysis has a six-step process (Figure 21) but is flexible in that it is an iterative process, and emphasises the need to repeatedly go back to the data – quality checks – to support and organise constructed themes.[481] It uses hierarchical coding with the creation of a flexible template that is added to, redefined, and deleted from, throughout the process.[476]

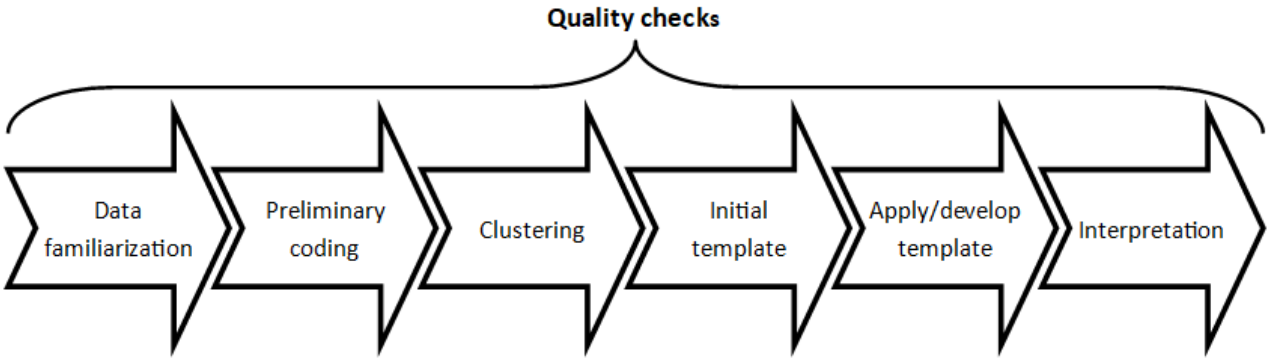

Figure 21. The six steps of template analysis

The use of *a priori* themes can be particularly useful in mixed-methods studies like this one, where data from the quantitative portion – in this case, the post-intervention questionnaire – can be used to inform those themes.[481] Template analysis allows researchers to take assumptions from existing data without them restricting the analytic process.[480] The flexibility of the method fits within the pragmatic design and research

questions of the study. NVivo was used throughout the analysis process, to ensure a comprehensive audit trail.

7.9.3.2 Quantitative analysis

Text and emoji interaction within the training sessions – that was not direct answering of case-based learning point questions – was extracted for descriptive quantitative analysis using NVivo (Version 14, released 2023).

All emoticons were counted in NVivo and used to create a descriptive word cloud on www.worditout.com, illustrating sentiment. Studies, both in non-clinical and clinical settings have shown that emojis are increasingly used to improve communication, add emotion, modulate intensity, contextualise and upgrade/downgrade text, and signal closing or opening of interactions.[482, 483]

7.9.4 Change in patient care

Descriptive analyses were performed to calculate proportions of patient folders where the treatment was correct for each measurable learning point for the 48-week periods before and after the intervention. The folders from the period before the trial and the period after were mainly not from the same patients, as many of the learning points were for acute conditions, e.g. TB. Also, some folders could have two measurable outcomes, e.g., a pregnant woman with TB.

A summary measure for outcome variables for each cluster was calculated. All ten learning points for nurses in each cluster were combined to obtain a 'knowledge' summary measure (proportion correct). The measurable treatment outcomes (Table 20) from the folder reviews in each cluster were combined for the patient care summary measure, using the following formula:

$$Proportion\ of correct\ care\ = \frac{Number\ of\ folders\ with\ correct\ treatment}{Number\ of\ folders}$$

As the summary measure for each cluster at the two time points represented a repeated measures design, a mixed effects linear regression model for the proportion correct patient care on intervention, time and their interaction was run with cluster as the

random effect. The test for a significant interaction was used to test the hypothesis of an intervention effect. The final intervention effect was based on the difference in differences, to account for the significant pre-care difference between the arms. For this, the change (post-pre) within each arm was compared between the arms and the mean difference was estimated and reported with 95% confidence intervals.

7.10 Ensuring qualitative rigour

Qualitative analysis exists at the intersection of the researcher, data and, importantly, contextual interpretation[344] and, as such, it has very different quality evaluation requirements to quantitative analysis. There is ongoing debate on the quality of qualitative research and how it can be defined in an arena with such an enormous array of methods, each of which is informed by the paradigm of the specific study[338, 339, 481, 484, 485], which is beyond the scope of this thesis. By virtue of the diversity of paradigms in qualitative research, a single set of quality criteria is impossible and they need to be reflexive.[485]

This said, numerous checklists for ensuring qualitative rigour have been drawn up over the past 50 years, intersecting each other in some cases, and contradicting in others[485] and while the development of a specific list of criteria for ensuring good quality qualitative research is controversial, they are invariably helpful, especially to researchers new to the field.

Critical realist research, such as this, needs to be aware of the interpretation of quality and establish a plan to address it, instead of relying on standardised checks.[444] King and Brooks back Symon and Cassell's recommendation that researchers should identify and explicitly justify criteria relevant to the study being done.[481]

This is echoed by Yadav[485], who recommends that novice researchers use a combination of the available checklists guided by the particular study paradigm. He conducted a review of the criteria for good qualitative research, briefly describing strategies used to meet quality criteria by researchers including Lincoln and Guba, and Merriam and Tisdell.[485]

Relevant points from Yadav's[485] synthesis of strategies and from two checklists – the 10-question qualitative research Critical Appraisal Skills Programme (CASP) checklist, designed and developed by experts based on *JAMA*'s user guides[486]; and the Consolidated Criteria for Reporting Qualitative Research (COREQ), a 32-item checklist for interviews and focus groups[487] – were used to develop a framework to ensure the rigour of this study, taking into account its theoretical underpinning, design and aims. The strategies were grouped by Yadav's[485] three suggested strategy groups: credibility, transferability, dependability and confirmability by (Table 24).

Table 24. Strategies to enrich trustworthiness in the context of the study[485]

	Strategy	**Key points in the context of this study**
Credibility	Triangulation*	Qualitative data (focus groups, open-ended questionnaire questions, WhatsApp discussion) with quantitative data (closed-ended questionnaire answers)
	Collecting data to saturation	Data collection until reach 'theoretical sufficiency' – when the researcher has reached a sufficient understanding
	Reflexivity	Use of a 'reflexivity diary' throughout process
	Peer review	Discussion with PhD supervisors to limit bias
	Prolonged engagement	In-person recruitment visits to facilities, WhatsApp interaction throughout training, in-person focus groups, multiple engagements with data before analysis
Transferability	Maximum variation	Focus groups sampled to include speakers from both dominant languages in the region (isiXhosa and Afrikaans); highly rural, small town and larger town
	Typical sampling	By virtue of including only nurses and CHWs on a subject pertaining to their work
	Thick description	Direct quotes will be used throughout the reporting
Dependability and confirmability	Audit trail	Procedures, decisions and reflections detailed throughout
	Peer debriefing	External audit by pharmacist colleague at HIV Hotline uninvolved in the study
	Triangulation*	Methodological and data triangulation
	Reflexivity	Transparency of research domain, question, methodology, data collection, data analysis, and in the writing and presentation of findings

*Triangulation: analysing a research question from more than one perspective.[488]

Reflexivity

Researcher bias is a common concern in qualitative results. During the research processes, the researcher's perspectives are fundamentally involved[489], so context is critical. Reflexivity is described by Braun and Clarke[344] as key to good quality analysis, and involves constant critical reflection on how personal philosophies, biases, ideological and political leanings, training and experience, knowledge of, and relation to, the research topic and participants informs the research. While their analysis method was not used, reflexivity was used as a tool throughout the trial to ensure rigour. The reflexivity diary is included as Appendix Q.

7.11 Ethical considerations

The study was undertaken in accordance with the Declaration of Helsinki adopted by the 18th World Medical Assembly, Helsinki 1964 and revisions up to and including Fortaleza, 2013[401] as well as the South African Good Clinical Practice Guidelines [402] and Ethics in Health Research Guidelines[490]. Ethical approval was obtained for the project through UCT's Research Ethics Committee (HREC 491/2022, Appendix R) and the Eastern Cape Health Research Committee (EC_202209_003, Appendix S).

HCWs were invited to participate and either signed up during recruitment visits or via WhatsApp. They received mobile phone data to cover the cost of accessing the online questionnaires and the WhatsApp training.

Patient-level consent for folder reviews was not feasible. This is a common challenge with cluster randomised studies, which resulted in the development of the Ottawa Statement in 2012.[491] In accordance with recommendations 6 and 7 of the Ottawa Statement, consent was obtained at provincial level. There was no risk to patients, as no personal identifiers were included in the reporting.

Focus group participants signed a written informed consent form (Appendix T) and received refreshments and a small reimbursement for time and travel.

All data collected was stored in password-protected files to which only the researcher had access. Anonymised data was given to the statistician for analysis and used for reporting.

Chapter summary

Chapter 7 described the design and methodology of Study 2, a pragmatic, mixed-methods, parallel-group cluster-randomised study to design and test a WhatsApp-based training intervention. Participants were nurses and community health workers from 50 clinics in the Eastern Cape. Recruitment was conducted through in-person visits to the clinics.

Outcomes were measured using sign-up lists and WhatsApp group participation, online questionnaires, focus groups, and retrospective patient folder reviews.

Quantitative analysis – both descriptive and inferential – of pre- and post-intervention questionnaires was used to determine the effectiveness of WhatsApp-based training on increasing knowledge; and of folder reviews, to measure changes in prescribing behaviour. Both quantitative and qualitative analysis of the questionnaires, focus groups, WhatsApp group interactions were used to describe uptake, acceptability and feasibility of the intervention as a training tool. Qualitative analysis was conducted using template analysis.

Chapters 8 will describe the results of Study 2.

Chapter 8 Results: WhatsApp-based training

Chapter 8 reports on the results from the WhatsApp-based training study.

Firstly, uptake and participation in the WhatsApp-based training, and its effectiveness, i.e. changes in HCW knowledge and patient care as a result of the training (Objectives 1-4 and 7) is reported.

Secondly, the acceptability and feasibility results from the study are reported, triangulating quantitative data from the online questionnaires and analysis of the WhatsApp group interactions; with qualitative data from the focus groups, free text sections of the questionnaires, and WhatsApp group interactions (Objectives 5 and 6).

Chapter 8 contains excerpts from the following papers:

Chisholm BS, Blockman M and Orrell CJ. A mixed-methods, cluster-randomised study protocol to design and test WhatsApp group-based HIV microlearning for rural South African healthcare workers. International Journal of Qualitative Methods 2024; 23: 16094069241284205. DOI: 10.1177/16094069241284205.

Chisholm BS, Mapahla L, Lombard C, Blockman M and Orrell CJ. Effectiveness and uptake of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

Chisholm BS, Wallace ML, Blockman M and Orrell CJ. "WhatsApp is best!" Acceptability and feasibility of WhatsApp-based HIV microlearning for healthcare workers in remote South African clinics: a pragmatic, mixed-methods, cluster-randomised trial. Nurse Education in Practice [submitted, under review].

8.1 Introduction

ART treatment is guided by national guidelines which are constantly updated as new evidence emerges and recommendations change. Ongoing HCW training is vital to ensure knowledge of current guidelines, changes in updated versions, and an understanding of why recommendations have changed.[150] Without this, patient care can be compromised.[90, 148]

In-service training is challenging in South Africa, which covers 1.2 million km^2, much of it rural. Traditionally, training has either been face-to-face at centralised points or long-form online training. Barriers to this include infrastructure and a lack of financial and human resources.[82, 110] There is a need for innovative solutions.

Online formats of training have been found to be acceptable to HCWs in sub-Saharan Africa, if limited resources are taken into consideration.[287] Mobile learning (mLearning) – providing education on mobile devices[492] – has rapidly gained traction over the past two decades.[493, 494] Several meta-analyses and reviews on the use of mLearning in nursing education have been conducted with an overall conclusion that it is beneficial[495], well accepted[237] and improves skills and knowledge[224, 496]. South Africa has over 100% mobile phone penetration.[215]

In their study of a workplace-based intervention to improve South African HCW knowledge of breastfeeding, Horwood et al showed positive effects on knowledge and nurses' perceptions of ongoing practice.[82] They suggested that WhatsApp might be a good platform for learning but concluded that further research was necessary, especially qualitative evaluation to understand HCWs' experiences.[82]

WhatsApp offers a free and accessible platform for training, even in the most remote clinics, and was used by 94% of South Africans in 2023.[238] It has been shown to be effective and acceptable to HCWs across several medical fields and training methods in LMICs.[269, 497, 498] Woods et al described the use of WhatsApp as an HIV discussion forum for clinicians working in the Eastern Cape, and showed that engagement in the group improved self-reported confidence and practical application of knowledge,

concluding that WhatsApp is an easy-to-use and implement continuing medical education platform.[245]

Time is a limited resource in many clinics with large workloads.[36] Microlearning – 'bite-sized' pieces of information transferred via technology, e.g. mobile phones[499] – is a feasible, accessible and flexible teaching strategy for nurses and positive effects on knowledge across health professions have been shown.[299]

There are gaps in the research field, though. Azad et al, in their narrative synthesis of continued nursing education in LMICs concluded that, while it is essential and effective in improving knowledge, there is a "profound lack of rigorously designed studies to evaluate the effectiveness of continuing nursing education interventions in LMICs".[189]

At the microlearning level, there are few rigorous studies of effectiveness, especially exploring more complex outcomes, e.g. changes in patient care.[299, 334] Coleman and O'Connor's scoping review on WhatsApp-based interventions notes that all except one intervention had only been evaluated up to Level 1 or 2 of Kirkpatrick's levels of training evaluation, the gold standard.[241] Kirkpatrick's levels are: (1) reaction; (2) learning; (3) impact/behaviour change; and (4) results/performance change.[500]

The aim of this study was to design and test the usability of WhatsApp group-based HIV microlearning for rural South African healthcare workers, measuring its uptake, acceptability, feasibility and effectiveness, i.e. all four levels of Kirkpatrick's assessment. The methodology of the study is found in Chapter 7.

8.2 Uptake

232/293 (79%) of nurses and 207/271 (76%) of CHWs agreed to participate in the study. After cluster-level randomisation by the study statistician, 101 nurses were in the intervention WhatsApp group, 131 in the control group. For the CHW groups, 99 were in the intervention group and 108 in control.

Mean uptake of the three online questionnaires was 62% and the demographics of those who completed the baseline questionnaire are listed in Table 25. Participants were predominantly female, reflecting professional norms. At baseline, the mean age of intervention group nurses was 40 years (SD 10), control nurses, 39 (SD 11) and of

intervention CHWs, 39 years (SD 10), control, 41 (SD 8). Mean experience working as a HCW was 9 years (SD 10) in both nurse groups; and 10 years (SD 6) in the CHW intervention group, 12 (SD 7) in control. The predominant home language was isiXhosa. Tests for demographic variables confirmed that randomisation was successful (p >0.05), and the groups were not different (Table 25).

Table 25. Characteristics of HCWs at baseline knowledge questionnaire

	Nurses			**CHWs**		
Characteristic	Intervention	Control	p	Intervention	Control	p
Healthcare workers, n (%)	84 (43)	110 (57)		70 (46)	83 (54)	
Gender, n (%)						
Female	67 (80)	96 (87)	0.232†	62 (89)	76 (92)	0.555†
Male	17 (20)	14 (13)		8 (11)	7 (8)	
Age (yrs), mean (SD)	40 (10)	39 (11)	0.622#	39 (10)	41 (8)	0.425#
Experience (yrs), mean (SD)	9 (10)	9 (10)	0.780#	10 (6)	12 (7)	0.312#
Home language, n (%)						
isiXhosa	47 (56)	58 (53)		47 (67)	47 (57)	
Afrikaans	25 (30)	43 (39)	0.588*	19 (27)	32 (38)	0.365*
English	9 (11)	7 (6)		2 (3)	4 (5)	
Other	3 (3)	2 (2)		2 (3)	0 (0)	
Highest level of education, n (%)						
Primary school	0 (0)	0 (0)		0 (0)	3 (3)	
High school	4 (5)	10 (9)	0.304*	55 (79)	66 (80)	0.483*
Tertiary	80 (95)	100 (91)		15 (21)	14 (17)	
Profession, n (%)						
Nurse	84 (100)	110 (100)		0 (0)	0 (0)	
CHW	0 (0)	0 (0)		39 (56)	59 (71)	
Counsellor	0 (0)	0 (0)		31 (44)	24 (29)	

Abbreviations: CHW, Community health worker; SD, standard deviation. †Chi-squared test of association; #Mann-Whitney test of association; *Fisher's exact test.

8.3 Participation

One nurse and three CHWs left the WhatsApp groups during the training period. In the intervention group, nurses' attendance of the 'live' sessions ranged from 27/101 (27%) to 51/101 (51%); and CHWs from 27/97 (28%) to 53/99 (54%). By 24 hours after the live sessions, between 85/101 (85%) and 94/101 (94%) of nurses, and between 69/97 (72%) and 78 (79%) of CHWs had read them. Two weeks after the lessons, a mean of 97/101 (96%) of nurses and 86/98 (88%) of CHWs had read them (Figure 22).

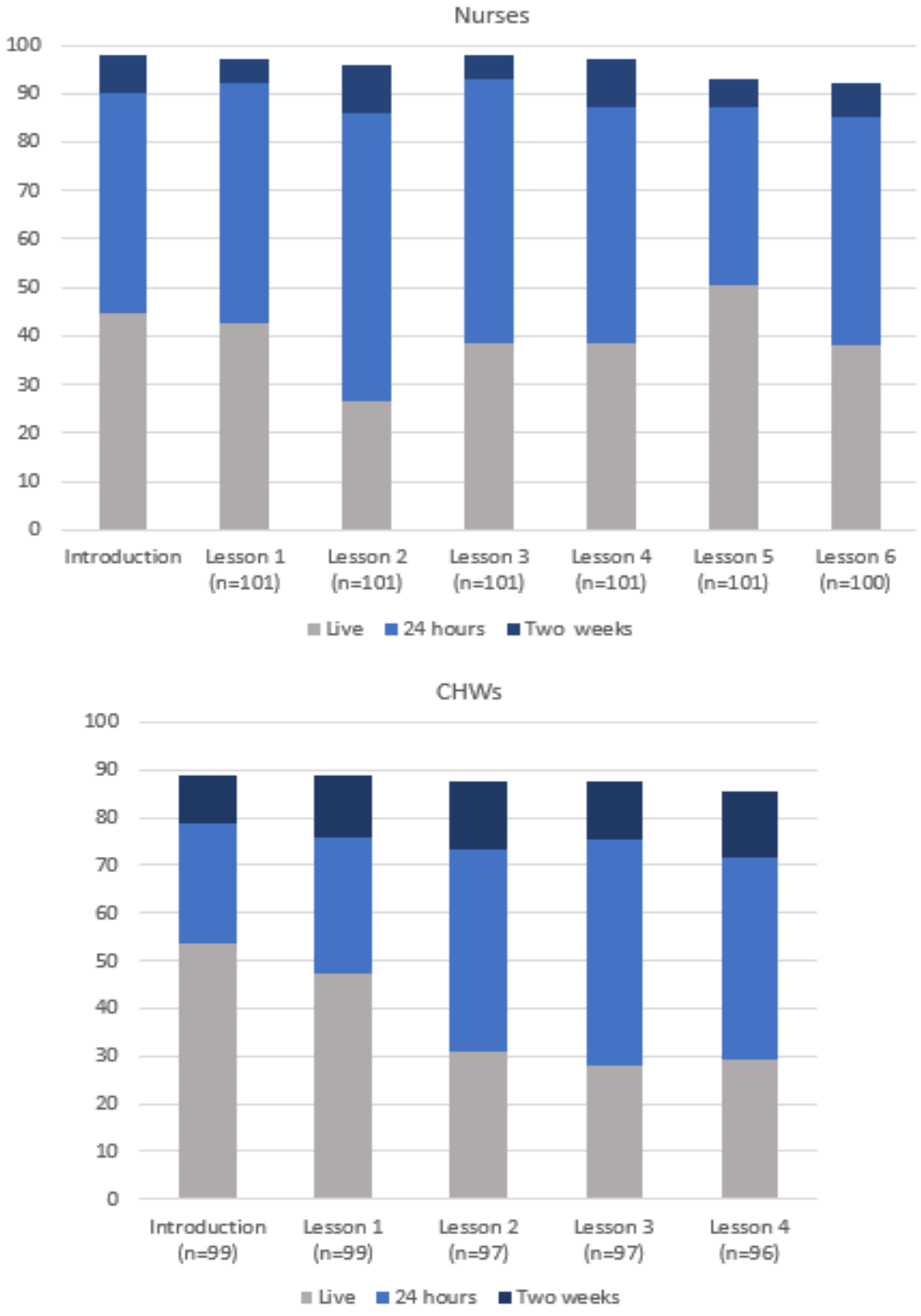

Figure 22. Proportion of participants that were in the live sessions and had read lessons by 24 hours and two weeks after

Using NVivo coding and counts, 1 295 participant interactions occurred (718 text, 72 emoji) during the seven nurse WhatsApp sessions; and 475 (213 text, 49 emoji) in the five CHW group sessions. The spread of the interactions is presented figuratively in Figure 23.

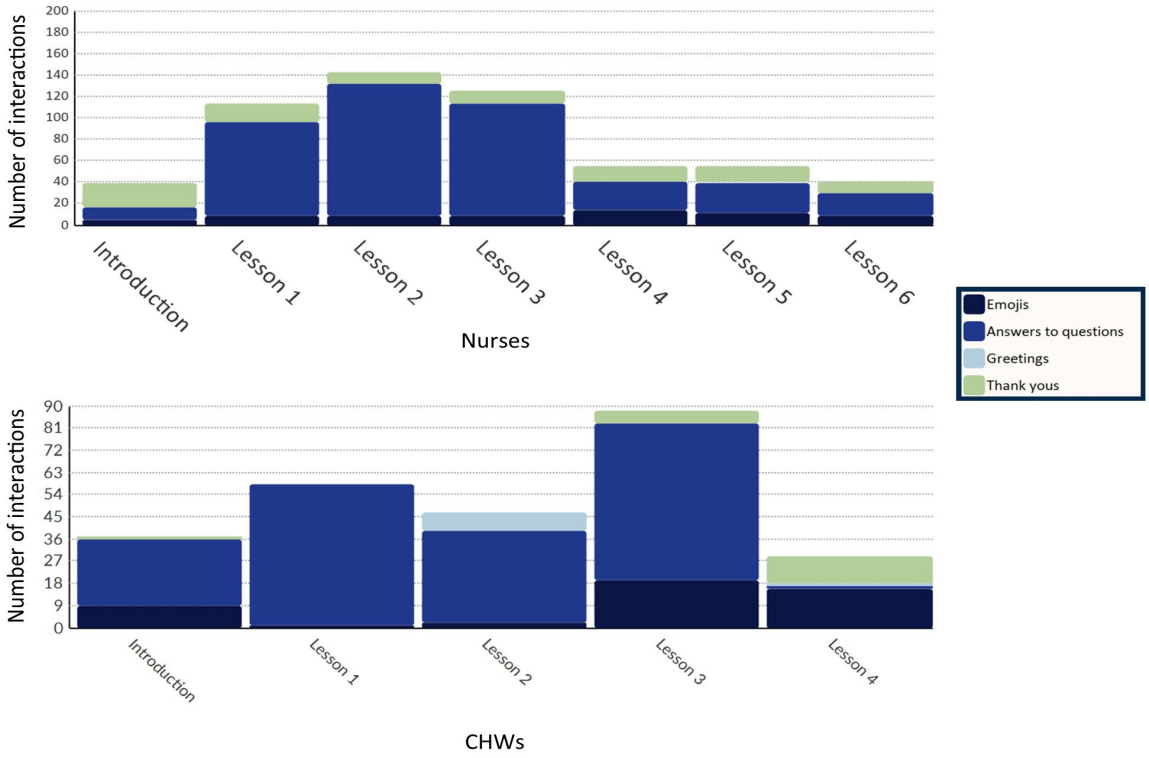

Figure 23. WhatsApp group interactions: greetings, emojis, gratitude and answers

8.4 Effectiveness: knowledge change

Over 70% of all nurses and 60% of all CHWs completed the three online questionnaires at baseline, immediately after the training (intervention group only) and three months after the training (Table 26).

Table 26. Numbers of HCWs who completed the questionnaires

	Baseline	Post-intervention	3-month post-intervention
Nurses, n (%)			
Intervention, n=101	84 (83.2)	74 (73.3)	72 (71.3)
Control, n=131	110 (84.0)	-	103 (78.6)
CHWs, n (%)			
Intervention, n=99	70 (70.7)	62(62.6)	61 (61.6)
Control, n=108	83 (76.9)	-	64 (59.3)

8.4.1 Individual-level analysis

Descriptively, the mean individual knowledge score proportions across each question differed widely (Table 27). Between 29% and 83% of nurses in both the intervention and control groups answered the dolutegravir interactions questions correctly at baseline, with the worst scores for the cation interaction and the best for rifampicin (Table 27).

Proportions of nurses in both groups who knew to use dolutegravir in all women, that a GXP should be done at the first antenatal visit, and that TPT should be given to all patients on ART was above 75% (Table 27).

Post-intervention knowledge of both the nurse and CHW intervention group improved on all learning items (Table 27).

Table 27. Proportions of participants getting questions correct, by learning point

	Baseline		Post-intervention		3 mo-post-intervention	
	Int	Con	Int	Con*	Int	Con
Nurse knowledge						
Dolutegravir in WOCP	0.93	0.82	0.96	-	0.99	0.88
Interactions: dolutegravir/oral contraceptive	0.51	0.63	0.76	-	0.69	0.66
GeneXpert at first antenatal visit	0.80	0.85	0.89	-	0.86	0.89
TPT for all non-pregnant clients starting on ART	0.93	0.79	0.93	-	0.92	0.85
Interactions: dolutegravir and calcium	0.58	0.64	0.81	-	0.78	0.69
Interactions: dolutegravir and cations	0.36	0.29	0.41	-	0.35	0.45
Interactions: dolutegravir and rifampicin	0.83	0.73	0.92	-	0.92	0.76
Interactions: dolutegravir and metformin	0.60	0.59	0.81	-	0.78	0.65
Interactions: dolutegravir and antiepileptics	0.46	0.42	0.66	-	0.58	0.50
TPT for pregnant women with CD4 < 350 cells/L	0.75	0.73	0.78	-	0.74	0.78
CHW knowledge						
Dolutegravir in WOCP	0.79	0.86	0.94	-	0.92	0.91
Refer: dolutegravir and calcium	0.81	0.82	0.95	-	0.97	0.86
Interactions: iron and calcium	0.24	0.18	0.53	-	0.31	0.16
Refer: dolutegravir and cations	0.63	0.61	0.85	-	0.87	0.69
Interactions: dolutegravir and rifampicin	0.21	0.22	0.43	-	0.28	0.11
Refer: dolutegravir and metformin	0.89	0.86	0.95	-	0.98	0.94
Refer: dolutegravir and antiepileptics	0.86	0.90	0.97	-	0.97	0.92

Abbreviations: ART, antiretroviral treatment; Con, control; Int, intervention (grey); mo, month; TPT, tuberculosis preventative therapy; WOCP, women of childbearing potential, *The questionnaire was not repeated in the control group, to avoid survey fatigue.

At three months after the training, the nurses' knowledge had decreased slightly from immediately post-intervention for all learning points, except the use of dolutegravir in all women, which increased from 96% to 99% of nurses, and the interaction with rifampicin, which remained the same at 92% (Table 27). Scores for all points remained above baseline scores, except TPT in all patients on ART (baseline, 93%; 3-month, 92%) and the CD4 cut-off for TPT in pregnant women (baseline 75%, 3-month, 74%) (Table 26).

This trend was echoed in the CHW intervention group, with knowledge scores improving across all learning points immediately after training. At 3 months post-training, three learning points' knowledge scores had improved further (calcium interaction, 95% to 97%; cation interaction, 85% to 87%; metformin interaction, 95% to 98%); one remained the same, and three scores had decreased, but remained above baseline (Table 27).

Comparing the intervention to control groups at three months after training in nurses showed three knowledge means were worse in the intervention group than the control group (GXP at first antenatal visit, 86% and 89%; cation interaction, 35% and 45%; CD4 cut-off for TPT, 74% and 78%) (Table 26). In the CHW groups, knowledge at three months was better in the intervention group across all learning points (Table 27).

When combining scores to obtain a mean proportion of correct answers across all questions, the baseline mean individual knowledge scores were similar in both control and intervention groups: nurses, control 65%, intervention 68%; and CHWs, control 64% and intervention 63% (Table 28).

Table 28. Mean individual correct knowledge proportion at the three timepoints

Timepoint	Nurses				CHWs			
	n	Intervention	n	Control	n	Intervention	n	Control
At baseline	84	0.68	110	0.65	70	0.63	83	0.64
Post-intervention	74	0.79	-	-	62	0.80	-	-
3-months post-intervention	72	0.76	103	0.71	61	0.76	64	0.65

*The questionnaire was not repeated in the control group, to avoid survey fatigue.

Immediately post-intervention, the proportion with correct knowledge intervention groups' mean knowledge improved (nurse, 68% to 79%; CHW, 63% to 80%) and, while dropping slightly, knowledge at three months was still higher than baseline. Knowledge

scores at three months were higher in the intervention group (nurse and CHW 76%) than control groups (nurse 71%; CHW 65%) (Table 28). Cluster-level analysis confirmed this.

8.4.2 Cluster-level analysis

For the inferential analysis, summary scores were calculated at cluster level. There was no difference between arms at baseline of both cohorts (nurse, p=0.270; CHW, p=0.933). Knowledge of nurses and CHWs in both control and intervention groups improved immediately after the training, dropping by three months, but remaining above the baseline knowledge, though not significantly (Figure 24). When comparing control to intervention groups at 3-months post-intervention, the intervention groups in both showed better knowledge, but this was only significant in the CHWs (Figure 24).

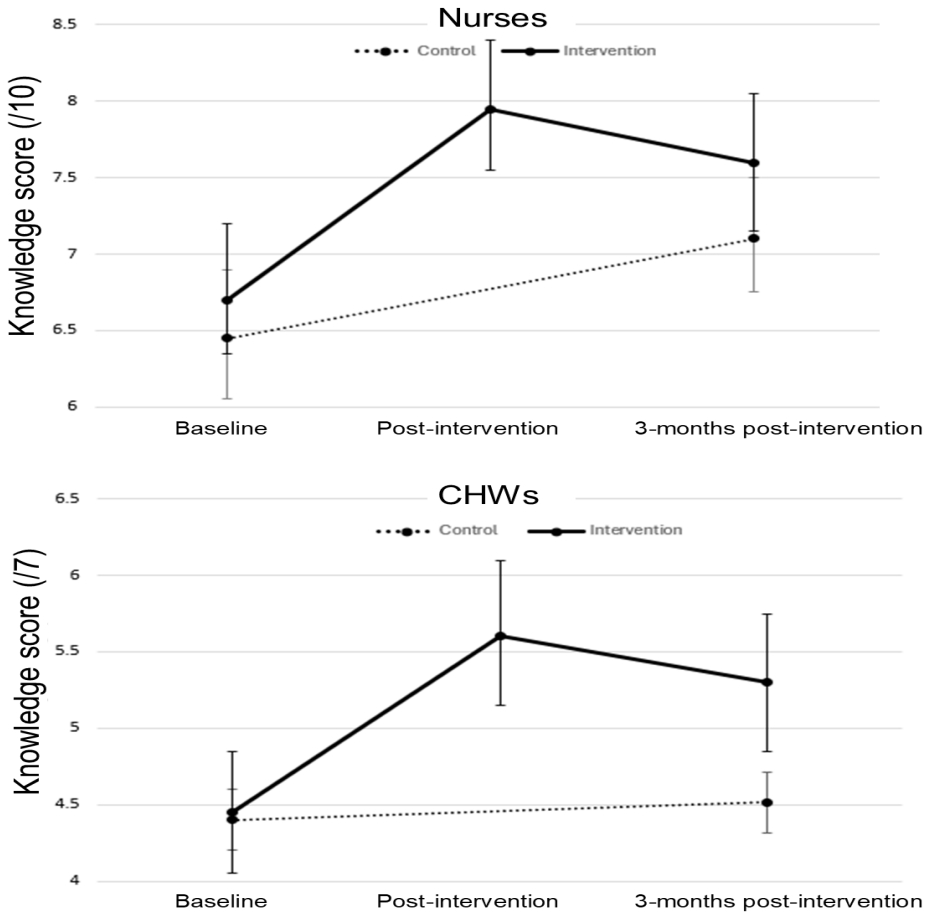

Figure 24. Summary mean scores at baseline, immediately after the training and three months after

Expanded linear mixed effects modelling was done, to adjust for age, gender, years of experience, stratification, clustering and repeated measures. This showed that, at three months post-intervention, there was a significant intervention effect, with mean proportions of correct score increasing for both nurses (0.5 points; 95% CI 0.1-1.0; p=0.049) and CHWs (0.7 points; 95% CI 0.2-1.36; p=0.004) (Table 29).

Table 29. Estimated intervention effects for the knowledge score at three months, based on a linear mixed effects model

Participant group	Intervention mean (SD)	Control mean (SD)	Mean difference	95% CI	p-value	ICC
Nurses	7.6 (1.4)	7.1 (1.9)	0.5	0.1-1.0	0.049†	0.001
CHWs	5.3 (0.9)	4.6 (1.2)	0.7	0.2-1.3	0.004†	0.115

Abbreviations: CI, confidence interval; ICC, intracluster correlation coefficient; SD, standard deviation. †Wald test.

Mean baseline knowledge score was positively associated with the final score in both groups. In the nurse group, age was negatively associated with total knowledge score, and years of experience was positively associated, but this was not mimicked in the CHW group (Lowess graph, 290Appendix U).

8.5 Effectiveness: change in patient care

To measure effect on patient care, 1 158 folders were reviewed at the clinics. During data cleaning, 16 data points were removed because the patient was < 18 years old at the relevant data point; and 33 were removed because the relevant data point was not within the trial period.

The original study plan was to access missing laboratory data through LabTrak, the National Health Laboratory Services results database. In June 2024, they were the victim of a cyber-attack, causing the system to be shut down[501] and no access was possible. We excluded 26 data points due to this. 1 083 data points from the folders were analysed.

There were almost double the data points for the ‘after’ 48 weeks. This is most likely due to the ‘before’ 48 weeks being during the COVID-19 pandemic, during which clinic visits were kept to a minimum, with many patients only attending the clinic 3-monthly.

Demographics, concomitant diseases and latest CD4 and viral load results are listed in Table 30. Two thirds were female, with a mean age of 37 years old (SD 12.0). Of those that had the data in the folders, the median CD4 count was 313 cells/mm^3 (IQR 150-508) and 53.6% had a VL <50 copies/mL (279/521).

Table 30. Demographics and medical values of participants from folder reviews

	Intervention		Control		Total	
Participants, n (%)	587	(54.2)	496	(45.8)	1083	(100.0)
Gender, n (%)						
Female	374	(63.7)	348	(70.2)	722	(66.7)
Male	213	(36.3)	148	(29.8)	361	(33.3)
Age, mean (SD)	36	(11.3)	38	(12.8)	37	(12.0)
Home language, n (%)						
isiXhosa	451	(76.8)	352	(71.0)	803	(74.1)
Afrikaans	121	(20.6)	137	(27.6)	258	(23.8)
English	4	(0.7)	1	(0.2)	5	(0.5)
Other	11	(1.9)	6	(1.2)	17	(1.6)
Concomitant diseases, n (%)*						
Hypertension	89	(15.2)	122	(24.6)	211	(19.5)
Diabetes	33	(5.6)	75	(15.1)	108	(10.0)
Epilepsy	20	(3.4)	19	(3.8)	39	(3.6)
Tuberculosis	137	(23.3)	101	(20.4)	238	(22.0)
Laboratory results						
Latest CD4 count (cells/mm^3)#						
Median, CD4 (IQR)	310	(156-509)	322	(147-508)	313	(150-508)
Unknown	117	(19.9)	132	(26.6)	249	(23.0)
Latest viral load# (copies/mL)						
<50	145	(24.7)	134	(27.0)	279	(25.8)
≥50	132	(22.5)	110	(22.2)	242	(22.3)
Unknown	310	(52.8)	252	(50.8)	562	(52.0)

*Folders were specifically drawn in line with inclusion criteria, so this is not reflective of the general population.
#Denominator used excluded unknowns.

8.5.1 Individual-level analysis

Descriptive data of the proportions of correct patient care between the pre- and post-intervention periods at the individual level are reported in Table 31. In the control group, no significant changes were seen.

In the intervention group, proportions of correct care improved in all measurements except all pregnant women getting a GXP at first antenatal booking (Table 31), but the

improvements were only significant for the use of dolutegravir in all women (WOCP, p=0.002) and double dosing of dolutegravir in patients on rifampicin (RIF, p<0.001) (Table 31).

Table 31. Proportions of correct care for each learning point before and after intervention at individual level

	Control					Intervention				
	Before		After			Before		After		
	n	Correct n (%)	n	Correct n (%)	p‡	n	Correct n (%)	n	Correct n (%)	p‡
TPT[1]	131	75 (57.25)	272	176 (64.71)	0.148	175	133 (76.00)	343	271 (79.01)	0.434
WOCP[2]	96	89 (92.71)	216	206 (95.37)	0.339	117	106 (90.60)	233	228 (97.85)	0.002
GXP[3]	30	17 (56.67)	62	23 (37.1)	0.076	46	19 (41.30)	79	28 (35.44)	0.514
RIF[4]	34	25 (73.53)	68	53 (77.94)	0.620	35	20 (57.14)	102	94 (92.16)	<0.001
MET[5]	30	19 (63.33)	47	27 (57.45)	0.608	12	4 (33.33)*	23	16 (69.57)	0.071*
AED[6]	6	1 (16.67)	11	1 (9.09)	1.000	6	1 (16.67)	13	7 (53.85)	0.177

‡Chi-squared test of association; *Fisher's Exact two-sided because failed assumption of chi-squared (> 5 points)
1. All clients initiating ART should receive TB Preventive Therapy (TPT); 2. TLD is the preferred regimen in all adults, including women of childbearing potential (WOCP); 3. At the first antenatal visit, all women living with HIV must have a GeneXpert test done, regardless of TB symptoms (GXP); 4. In patients on dolutegravir-containing ART and rifampicin, increase dolutegravir dose to 50 mg 12-hourly (RIF); 5. In patients on dolutegravir-containing ART and metformin, a maximum dose of 500 mg metformin 12-hourly should be used (MET); 6. In patients on dolutegravir-containing ART, carbamazepine, phenobarbital or phenytoin coadministration should be avoided, if possible. Double dolutegravir dose to 50 mg 12-hourly if an alternative anticonvulsant cannot be used (AED)

At the individual level, mixed logistic regression analyses of each measurable learning point were conducted, to obtain the odds ratios (OR) of correct care comparing intervention and control groups (Table 32). The regression was adjusted for time and included cluster as a random effect.

Increased correct treatment for TB preventative treatment (OR 1.70; 95% CI 0.88-3.29; p=0.111); use of dolutegravir in all women (OR 1.14; 95% CI 0.33-3.93; p=0840); dosing of dolutegravir in patients on rifampicin (0R 1.39; 95% CI 0.65-2.98; p=0.399) and on antiepileptic drugs (OR 7.36; 95% CI 0.61-89.36; p=0.117) was associated with the intervention arm, but not significantly so (Table 32).

For dosing of metformin in patients on dolutegravir, there was no better care in the intervention group (OR 0.90; 0.36-2.25; p=0.821); and for GeneXpert testing at first antenatal visit, there was a non-significant association with worse care (OR 0.39; 95% CI 0.10-1.56; 0.185) (Table 32).

Table 32. Odds of correct care for each measurable learning point with cluster as random effect, adjusted for time, using a mixed logistic regression model

	Intervention n (%)	Control n (%)	Odds ratio	95% CI	p-value	ICC
TPT[1]	271/343 (79.0)	133/175 (76.0)	1.70	0.88-3.29	0.111	0.540
WOCP[2]	228/233 (97.9)	106/117 (90.6)	1.14	0.33-3.93	0.840	1.382
RIF[4]	94/102 (92.2)	20/35 (57.1)	1.39	0.65-2.98	0.399	0.167
GXP[3]	28/79 (35.4)	19/46 (41.3)	0.39	0.10-1.56	0.185	1.946
MET[5]	16/23 (69.6)	4/12 (33.3)	0.90	0.36-2.25	0.821	0.160
AED[6]	7/13 (53.9)	1/6 (16.7)	7.36	0.61-89.36	0.117	0.696

Abbreviations: CI, confidence interval; ICC, intracluster correlation coefficient. 1. All clients initiating ART should receive TB Preventive Therapy (TPT); 2. TLD is the preferred regimen in all adults, including women of childbearing potential (WOCP); 3. At the first antenatal visit, all women living with HIV must have a GeneXpert test done, regardless of TB symptoms (GXP); 4. In patients on dolutegravir-containing ART and rifampicin, increase dolutegravir dose to 50 mg 12-hourly (RIF); 5. In patients on dolutegravir-containing ART and metformin, a maximum dose of 500 mg metformin 12-hourly should be used (MET); 6. In patients on dolutegravir-containing ART, carbamazepine, phenobarbital or phenytoin coadministration should be avoided, if possible. Double dolutegravir dose to 50 mg 12-hourly if an alternative anticonvulsant cannot be used (AED)

8.5.2 Cluster-level analysis

Analysis at cluster level, using mixed effects linear regressions showed a significant intervention effect: a higher proportion of correct patient care in the intervention group in the post-intervention period, compared to the control group, p<0.001 (Table 33).

Table 33. Estimated intervention effects on correct patient care

Correct care before and after the intervention					
	Intervention, n=15		Control, n=15		p-value
	Mean proportion	SD	Mean proportion	SD	
Pre-intervention	0.62	0.20	0.75	0.18	
Post-intervention	0.82	0.11	0.75	0.11	
Difference	**0.20**	**0.23**	**0.00**	**0.21**	**<0.001***

Abbreviations: SD, standard deviation. *Two-sample t-test

Conditional on arm, the mixed effects linear regressions also showed a positive change in the intervention arm of 20% (95% CI 13%-28%), compared to a drop of 1% (95% CI -8.0%-8.0%) in the control arm (Table 34).

Table 34. Estimated main intervention effects on correct patient care, using mixed effects linear regression model for the proportion correct care with cluster as the random effect

	Main effects					
	Time		Main effect test	Intervention		Main effect test
	Mean difference	95% CI	p-value	Mean difference	95% CI	p-value
Intervention	0.20	0.13-0.28	<0.001†			
Control	-0.01	-0.08-0.08	0.975†			
Pre-intervention				-0.14	-0.24-0.03	0.014†
Post-intervention				0.07	-0.04-0.18	0.208†
Difference-in-differences analysis, accounting for unbalanced pre-intervention means				**0.21**	0.10 to 0.32	**<0.001†**

Abbreviations: CI, confidence interval. †Wald test.

To account for the unbalanced pre-intervention means (intervention 62%; control 75%), a difference-in-differences analysis was conducted, which showed a statistically significant improvement in correct patient care of 21% (95% CI 10%- 32%; p<0.001) in the intervention arm (Table 34).

8.6 Acceptability and feasibility

Sixty-one nurses and 56 CHWs agreed to participate in the focus groups/interviews; and 74 nurses and 62 CHWs completed the feasibility and acceptability sections of the post-intervention questionnaires (Table 35). Participants were predominantly female, with their home language being isiXhosa. All nurses and a quarter of the CHWs had received a training college or university qualification.

Table 35. Demographic characteristics of focus group and questionnaire participants

	Focus groups				Post-intervention questionnaires			
	Nurses		CHWs		Nurses		CHWs	
Gender, n (%)								
Female	17	(81.0)	32	(88.9)	61	(82.4)	54	(87.1)
Male	4	(19.0)	4	(11.1)	13	(17.6)	8	(12.9)
Age, mean (SD)	45	(9)	40	(10)	40	(11)	39	(9)
Years of experience, mean (SD)	15	(9)	11	(7)	9	(10)	11	(7)
Home language, n (%)								
isiXhosa	9	(42.9)	24	(66.7)	41	(55.4)	39	(62.9)
Afrikaans	10	(47.6)	11	(30.6)	23	(31.1)	18	(29.0)
English	2	(9.5)	0	(0.0)	8	(10.8)	2	(3.2)
Other	0	(0.0)	1	(2.8)	2	(2.7)	3	(4.8)
Highest qualification, n (%)								
Primary school	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.6)
High school	0	(0.0)	27	(75.0)	0	(0.0)	47	(75.8)
University/training college	21	(100.0)	9	(25.0)	74	(100.0)	14	(22.6)

Abbreviations: CHWs. community health workers; SD, standard deviation.

8.6.1 Results from questionnaires

Responses to the questions on the usability of the WhatsApp-based training were overwhelmingly positive in both nurses and CHWs, with almost all of them saying they found the training useful, convenient, easy to use and understand, and enjoyable (Table 36). Ninety-seven percent of nurses and 98% of CHWs said they would attend such training if it were held on an ongoing basis, once a week. The majority felt the training had changed how they perform their day-to-day duties.

Table 36. Proportions of participants answering 'Yes' to usability questions in the post-intervention questionnaire

Question[Usability factor]	**Nurses n=71**[*]		**CHWs n=62**	
	Yes: n (%)		Yes: n (%)	
Did you find the WA training useful?[Su.Sa]	70	(98.6)	59	(95.2)
Did you find the WA training easy to understand?[L]	70	(98.6)	62	(100.0)
Did you find the WA training convenient?[W.Su.Sa.Effi]	66	(93.0)	60	(96.8)
Did you find the WA training easy to use?[L.W.Sa]	70	(98.6)	61	(98.4)
Did you find the WA training enjoyable?[W.Sa]	69	(97.2)	62	(100.0)
Would you prefer non-interactive WhatsApp-based training. i.e. info being sent as message. with no interaction in the group?[W.Sa]	22	(31.0)	30	(48.4)
Would you prefer face-to-face training rather than WhatsApp-based training?[Su]	17	(23.9)	19	(30.6)
Would you participate in this kind of learning if it were a weekly session throughout the year?[W]	69	(97.2)	61	(98.4)
Do you think that this training will change how you do your day-to-day duties. treating clients on ARVs?[L.Su]	69	(97.2)	59	(95.2)
What were the challenges you experienced with the WhatsApp-based training?[W.Sa]				
I didn't experience any challenges	22	(31.0)	22	(35.5)
Time: it was at a difficult time for me to attend	16	(22.5)	9	(14.5)
Time: the sessions took too long	0	(0.0)	0	(0.0)
Access: we have no cell phone network at our clinic	17	(23.9)	9	(14.5)
Access: we had no cell phone network during the session(s)	20	(28.2)	15	(24.2)
Data: I ran out of data	6	(8.5)	18	(29.0)
Language: I found the way the sessions were presented was hard to understand	0	(0.0)	0	(0.0)
Language: it would be easier if the sessions were in my home language	1	(1.4)	2	(3.2)
I felt shy to interact	0	(0.0)	2	(3.2)
How many of the 'live' sessions did you miss?[Su, Effi]				
1	6	(8.1)	6	(9.7)
2-3	13	(17.6)	9	(14.5)
4-5	8	(10.8)	3	(4.8)
All 6	0	(0.0)	2	(3.2)
Please tell us why you missed these session(s)?[Su, Effi]				
I was not at work for those sessions	0	(0.0)	2	(3.2)
I did not have data to attend	1	(1.4)	4	(6.5)
There was no cell phone reception	17	(23.0)	11	(17.7)
I was busy with a client	14	(18.9)	1	(6.5)
I forgot about the session(s)	1	(1.4)	1	(1.6)
Other	1	(1.4)	1	(1.6)

[*]Three nurses did not answer the usability section; Abbreviations: CHWs. community health workers. Usability factor abbreviations (superscripts): L. learnability; W, willingness; Su, suitability; Sa, satisfaction; Effi, Efficiency.

The results from the feasibility and acceptability sections of the post-intervention questionnaires (Table 36) will be triangulated and discussed together with the qualitative analysis, below.

8.6.2 Qualitative results with triangulation

After convenience sampling, 12 focus groups and one interview were conducted (nurse, n=21; CHW, n=36). The demographics of the focus group participants are listed in Table 35. The focus groups and interview took place in February and March 2023 and lasted an average of 35 minutes (range: 20-45). The average size of focus groups was 5 (range: 2-9).

Data from the free-text questions from the questionnaires, focus groups and WhatsApp interactions were analysed thematically, using template analysis with predominantly descriptive coding through the six steps[475]:

Steps 1-4. Familiarisation, a priori theme definition, preliminary coding, clustering and creating the initial template

All focus groups were run by BC, so she was immersed in the data from conducting the focus groups, through the three steps of transcription, and uploading the data onto NVivo. Once familiar with the data, points of interest were highlighted and *a priori* themes were defined[481] from the adapted usability model (Table 37).

Table 37. A priori themes

A priori theme	Definitions in study context
Learnability	Ability to understand the lesson and absorb the knowledge
Willingness	Willingness of HCWs to take part in the training
Satisfaction	Feeling that the training is convenient and/or enjoyable
Efficiency	Ability to attend and/or read the messages of the training
Effectiveness	The change in HCW knowledge and in patient care

Preliminary coding was done on a small data sample.[481] The participant groups were relatively homogeneous within the context of the trial, i.e. nurses and CHWs working in similar facilities with similar feeder populations, receiving the same HIV training. Two

each of the nurse and CHW transcripts were used for preliminary coding, one each from a predominantly isiXhosa-speaking, and a predominantly Afrikaans-speaking group.

Line-by-line coding[502] was used. During the preliminary coding, one theme – recognition and appreciation – and 76 codes under the themes were added. Themes were then clustered hierarchically into groups sharing meaning.[481]

Using NVivo allowed for some 'automatic' clustering during line-by-line coding, after which codes and themes were manually clustered within NVivo. The preliminary coding was worked through twice, concurrently referencing the data. Similar codes were combined into groups; some were moved under more suitable themes; and theme descriptions were updated. The research questions were the same for both nurses and CHWs and experience from the focus groups showed responses were similar, so one coding template was developed.

It was felt that the subset of data covered most issues and experiences, so the initial template was developed, consisting of six main themes and 18 codes (Table 38).

Table 38. Themes, sub-themes and descriptions on initial template

Themes and codes	Description
Effectiveness	The change in HCW knowledge and in patient care
1.1 Improved knowledge	
1.2 Improved patient care	
1.3 Improves service delivery	
Efficiency	Ability to attend and/or read messages of the training
2.1 Challenges to attendance	
2.2 Length of training	
2.3 Time of training	
2.4 WhatsApp works	
Learnability	Ability to understand lesson and absorb knowledge
3.1 Easy to use	
3.2 Interesting and informative	
3.3 Jargon was a challenge	
3.4 Live group advantageous	
3.5 Summary a necessity	
Satisfaction	Feeling that the training is convenient and/or enjoyable
4.1 Easy to participate	
4.2 Enjoyable	
4.3 Live, not shy, 'just a number'	
4.4 Message fatigue	

Willingness	Willingness of HCWs to take part in the training
5.1 Happy to take part weekly	
5.2 Sharing of messages	
Recognition and appreciation	A need for acknowledgement, to 'be seen'

Step 5-6. Developing and applying the template

The initial template was then applied to the remaining data sets, three transcripts at a time, modifying it iteratively after every three, until all relevant data was coded within the template.[481]

The final template was created by working through each theme and code with the data. Codes were compared, rearranged, combined, deleted and renamed, where needed, resulting in four themes, 12 codes, and 15 child codes (Table 39).

Table 39. Themes, sub-themes and descriptions on final template

Themes, codes and child codes	Description
WhatsApp group is the best	
1.1 Effectiveness	
1.1.1 Areas requiring training	
1.1.2 Improved knowledge	A change in HCW knowledge and patient care
1.1.3 Improved patient care	
1.1.4 Improves service delivery	
1.2 Efficiency	
1.2.1 Could read afterwards	The ability to attend and/or read the training messages of the training
1.2.2 Length of training	
1.2.3 Time of training	
1.3 Learnability	
1.3.1 Easy to use	The ability to understand the lesson and absorb the knowledge
1.3.2 Interesting and informative	
1.3.3 Like case-based learning	
1.3.4 Live group advantageous	
1.4 Satisfaction	
1.4.1 Easy to participate	The feeling that the training is convenient and/or enjoyable
1.4.2 Enjoyable	
1.4.3 ‘Just a number'	
Willingness	
2.1 Empowerment (staff/clients)	
2.2 Happy to take part weekly	The willingness of HCWs to take part in the training
2.3. Sharing of messages	
2.4 Worked as a group	
2.5 Summary a necessity	

Recognition and appreciation	
Challenges	
3.1 Infrastructure and technology	A need for acknowledgement, to 'be seen'
3.2 Message fatigue	
3.3 Language barrier	

One additional theme was added when going through the WhatsApp interactions – called, simply, WhatsApp – and codes were developed during line-by-line coding of all transcripts (Table 40).

Table 40. Codes and child codes for theme, WhatsApp

Codes and child codes		
Emoji interactions on WhatsApp		
1.1 Adore	1.9. Multi-layer heart	1.17. Surfer's hand
1.2 Ear	1.10. Peaking	1.18. Thank you
1.3 Face with heart eyes	1.11. Pink flower	1.19. Thumbs up
1.4 Face with three hearts	1.12. Rock on	1.20. Top notch
1.5 Giggle	1.13. Shaking hands	1.21. Tulip
1.6 Hands clapping	1.14. Smiley face	1.22. Two hearts
1.7 Heart	1.15. Stickers	1.23. Wave
1.8 High five	1.16. Sunflower	
Text interactions on WhatsApp		
2.1 Answers to questions	2.2 Greetings	2.3 'Thank you'

The final template was then applied to the full set of data to develop the data interpretation and was used to write up the findings.[481]

Results from template analysis

Overall sentiment was positive. Salient points, and those useful for further development and use of the method, are reported under three main themes:

1. "WhatsApp group is the best"
    - 1.1 Effective, efficient and interesting
    - 1.2 Easy and enjoyable
    - 1.3 Live learning in groups, with access afterwards, is good
    - 1.4 More, please
2. Challenges
    - 2.1 Infrastructure and technology
    - 2.2 Language barrier and jargon
    - 2.3 Message fatigue
3. Recognition, appreciation, and empowerment

8.6.2.1 "WhatsApp group is the best"

Participants expressed satisfaction with the use of WhatsApp for training, finding it interesting, enjoyable and easy to use. The short time spent, and the 'live' component, with a trainer present to ask questions, were appreciated.

> *"I think the WhatsApp method works."* (CHW, focus group)

> *"Short, sweet and simplified, the voice notes very beneficial."* (Nurse, WhatsApp)

This positive sentiment was echoed by analysis of emojis used during the training sessions (Figure 25, Appendix V).

Figure 25. Emoji word cloud created using counts of participant emojis during WhatsApp training sessions

Effective, efficient and interesting

Participants reported that the training was interesting and informative, improving their knowledge, which they felt would improve patient care and service delivery.

> *"The training was very interesting, and I've gained the most important information."* (Nurse, questionnaire)
>
> *"It is a good way to empower us with knowledge so we can provide patients with quality nursing care."* (Nurse, questionnaire)
>
> *"… with that confidence, I think, it can also improve our service delivery*." (Nurse, focus group)

This was reiterated by the questionnaire, where almost all participants said they found the training useful, and 69/71 (97.2%) of nurses and 59/62 (95.2%) of CHWs thought the training would change how they did their day-to-day duties (Table 36).

In the questionnaires, most participants found the length and time of training acceptable, with 66/71 (93.0%) and 60/62 (96.8%) of CHWs saying it was convenient. Somewhat incongruously, 16/71 (22.5%) of nurses and 9/62 (14.5%) of CHWs said it was a difficult time to attend (Table 36).

This was explored in the focus groups, where most participants found the length and time of training convenient. Some, however, said they'd prefer the training to be later, as they are sometimes busy through lunchtime, with patients or family responsibilities such as picking children up from school. A few participants also expressed that they'd like longer sessions.

> *"It was fine, the time was good for me also. It was actually very convenient because it was during lunchtime, and we could follow the communication very nicely. And what I liked also was it was a short period of time, So, it's short, focused time."* (Nurse, focus group)
>
> *"It was too short because you start realising that actually I'm learning a lot and I'm getting more interested and now the time's over."* (CHW, focus group)

"It was perfect because I felt like the timing, like it was 10 minutes per session, right? So, you weren't bombarding us with a lot of information a day. So now you have to hold a lot of stuff at the same time, so you're just giving us space to take in what we can per session." (CHW, focus group)

Easy and enjoyable

Participants found the training sessions enjoyable, useful and easy to use, due to its simplicity and their familiarity with WhatsApp from everyday use. This was also seen in the questionnaires with the vast majority finding the training easy to understand and use (Table 36).

"I think WhatsApp-based training is convenient and easy to use for everyone." (Nurse, questionnaire)

"Everything was clear and understandable." (CHW, WhatsApp)

"I actually enjoyed this system. To the point but very effective also. Time spent also okay. Would do it again and again. Very productive and an eye opener with information gathered from all sessions." (Nurse, questionnaire)

Solidifying this view, 69/71 (97.2%) of nurses and all the CHWs in the questionnaire said they found the training enjoyable (Table 36).

Live learning in groups, with access afterwards, is good

When asked if they would prefer non-interactive WhatsApp-based training, i.e. information being sent as message, a third of nurses and half of the CHWs (Table 36) said they would. In the focus groups, many participants said they enjoyed the fact that the training was done live, in a group, allowing for interaction between both colleagues and the trainer. The online 'anonymous' nature of the training allowed participants to answer freely, with many participants reporting this as an advantage.

"For me, it is also fine because you learn from your colleagues. Sometimes maybe you didn't know, and then the other one said no, you must do this and this. So, it was very learnful." (Nurse, focus group)

> *"Honest from that I can say it's more comfortable because at times you are shy to say something in front of someone … then with that platform anyone can say anything that she wishes to say. There was no one will laugh at you there or making fun of you. Because actually (s)he doesn't know who you are."* (CHW, focus group)

The availability of the trainer, both during live sessions and responding to questions about the learning points on the group, was highlighted as beneficial.

> *"For me, it was good, and it was informing because whenever there was wrong information, you could correct it and could give the correct version of it.*" (CHW, focus group)

> *"You see, that was the group, it was more interesting because at least you were expecting an answer and the voice notes. But when we are doing [pre-recorded, computer-based online training], it's only you."* (Nurse, focus group)

Availability of the sessions after the live session, and a summary of the lesson, was seen as vital, especially in this setting, where work commitments and technology and/or infrastructure may challenge access at specific times. Many participants mentioned that the voice note summary, especially, was useful.

> *"Even if there's a network issue for a whole week … in a week's time, those lessons are still there."* (Nurse, focus group)

> *"The shortness of it was actually exciting inasmuch as if we couldn't log on in time but the fact that it was short you knew that if you definitely have 5 minutes time you can go back and then be able to listen to your voice notes. And the availability of those voice notes is a recording that I can always keep. That was the biggest advantage."* (Nurse, focus group)

More, please

Although a quarter of nurses and third of CHWs said they'd prefer face-to-face training, 69/71 (97.2%) of nurses and 61/62 (98.4%) of CHWs said they would participate in this kind of training if it were held weekly throughout the year (Table 36). Similarly, when

asked the same in the focus groups, participants replied, almost unanimously, that they would.

> *"At least once a week is going to be good."* (Nurse, focus group)
>
> *"It's marvellous, wish to have more."* (CHW, questionnaire)

8.6.2.2 Challenges

Several challenges were highlighted by participants across questionnaires and focus groups, most often relating to network issues and data (Table 36). The quantitative and qualitative data on challenges were very similar.

Infrastructure and technology

All the clinics included are in relatively rural areas where access to cellular network reception can be intermittent. South Africa is in an energy crisis, with rolling blackouts, colloquially referred to as loadshedding: electricity cuts for set amounts of time, commonly resulting in loss of network.

Loadshedding and network issues were the biggest challenge. In this respect, it was reported that WhatsApp-based training was good, because participants could see the messages when electricity and/or network returned. Data was supplied to all participants, but a few reported that data was also a problem.

> *"Especially with us that are going out on the farms, we don't always have signal."* (Nurse, focus group)
>
> *"I could not log in on time. Network just came back now but I read the session."* (Nurse, WhatsApp)
>
> *"The only thing with the data. Yoh, you know, because you still … you want to participate but when you look, the data is finished."* (CHW, focus group)

This was echoed by the quantitative results in Table 36, where a third of participants reported missing live sessions, and a quarter reported that this was due to network issues.

Language barrier and jargon

A challenge discussed at length in one CHW focus group, was that it was not done in participants' mother tongue, making comprehension difficult, especially when medical jargon was used.

> *"Now sometimes because … it's not our mother tongue … Sometimes you said … OK is it the right answer or the right question or what … [and I was unsure].*" (CHW, focus group)

> *"The jargon that was used there. It was totally new to me. The medications were like, what is this? … So, I have to go around and ask what is this medication? But what is this one? So now I know like, this one's for TB and that is for that, I'm good."* (CHW, focus group)

The language barrier was only reported in the CHW group focus groups, although one nurse in the questionnaires listed it as a challenge (Table 36).

Message fatigue

Too many messages on the groups proved to be a challenge for many participants.

> *"I think, for me, the only challenging part is that … answers used to flood in so much. I'm trying to read this one and then there comes another."* (CHW, focus group).

While almost all messages that were posted were related to the training, many participants answered the questions from the live sessions, later, when they could access them.

> *"The whole day until you go to sleep it's coming …* [group laughter and agreement] *… Even on weekends! Because that person was not online at the time the class was."* (CHW, focus group)

8.6.2.3 Recognition, appreciation and empowerment

Several participants – especially CHWs – referred to feeling like there is a lack of empowerment, recognition and appreciation in their everyday work.

"Because most of the time we are doing works that we are not supposed to do, you see? … As very much as I'm not getting anything for what I'm doing or I'm being appreciated of anything that I'm doing but at least for me, it's something great because I've helped someone." (CHW, focus group)

"They don't recognise us as that ... they don't see what we are doing." (CHW, focus group)

Some participants said that the training played a part in motivating and empowering them. It was felt that this empowerment could be cascaded down to the patients, too.

"It is motivational and interesting to me." (Nurse, questionnaire)

"Everything was clear, and we gained a lot of information. Because some of us didn't know anything so by those voice notes and the messages that came, it was useful. You actually empowered us, truly." (CHW, focus group)

"… we can share now with the clients that information. Even to empower them and to help them to make the right decisions." (CHW, focus group)

8.7 Discussion

The study showed positive effects of the intervention at all four levels of Kirkpatrick's Levels of Training Evaluation.[500] Uptake of the training intervention was good, with close to 80% of invited staff participating. Knowledge of ART and drug interactions improved significantly after the WhatsApp intervention in both nurses and CHWs. This translated into improved patient care in the intervention arm as evidenced by changes in prescribing practice noted through folder reviews, taking clustering into account.

The short, sharp lessons were well accepted and enjoyed, with few barriers reported. The overall positive sentiment echoes that found in studies where WhatsApp was used for COVID-19 training in nurses in Pakistan[497]; and discussion forums on paediatric and adolescent HIV/AIDS care for nurses and counsellors in Zimbabwe[191] and management of complicated HIV/TB coinfected patients for doctors in rural Eastern Cape hospitals[245].

While participation levels in the live WhatsApp groups were relatively low (40% for nurses; 38% for CHWs), predominantly due to network and electricity issues, by two

weeks later, almost all participants (96% of nurses; 88% of CHWs) had read the lessons. Just four participants left the WhatsApp groups during the training. This highlights the accessibility of WhatsApp as a training platform, allowing both live sessions and 'catch up' after live sessions.

The participation rates, of 40-96%, were higher than those reported in other South African studies on mLearning. Chamane et al had a nurse participation rate of 64% in their study of an App to teach HCWs about point-of-care HIV testing[232]; and Woods et al reported a 50% participation rate in their WhatsApp-based clinical discussion forum for Eastern Cape clinicians[245]. The training period was short, so sustainability of high participation rates would require further research.

There was low baseline knowledge of dolutegravir's interactions, echoing the data from Study 1, the survey of South African HCWs. The low rates of knowledge – both before and after the intervention – of the cation interactions is particularly concerning because many women take calcium, iron, and/or aluminium/magnesium-containing antacids during their pregnancies, often bought over the counter. The dosage adjustment recommendations are confusing: in the absence of food, should be taken a minimum of 2 hours after or 6 hours before dolutegravir[42]. This highlights the need for simplifying dosing and training methods to overcome complexities.

While knowledge improvement has been shown in previous mLearning studies e.g. using WhatsApp for blood pressure (BP) monitoring training[269], Telegram for disaster preparedness training[503], and a Moodle App for HIV testing training[232]; studies in WhatsApp-based medical education, reporting on Kirkpatrick's Level 4 outcomes, i.e. results/performance change[500] are lacking[241]. In this study, after WhatsApp-based training, both knowledge and patient care improved significantly in the intervention arm, providing data at Kirkpatrick's level 3 and 4.

The accessibility, ease of use, enjoyment and usefulness of learning in a group with access to trainers reported by our participants was corroborated by the participants in both Bertman et al's Zimbabwean study[191] and Willemse et al's[504] study exploring South African nursing students' experiences of a mobile learning enactment via WhatsApp.

Tudor Car et al, in their systematic review of digital education on clinical practice guidelines, concluded that increased engagement and interaction may also improve educational gains[212], so participant's enjoyment of live, interactive sessions is an important point to note for not only acceptability, but also effectiveness, of training interventions.

The infrastructural/technology challenges found in this study echo those from a Ugandan study of medical and nursing student groups, who had a negative attitude toward e-learning – broadly – the main barriers cited as lack of electricity (56%), poor internet connectivity (84%) and internet costs (93%)[505]. Similarly, Willemse et al stressed the importance of being aware of data and internet costs and challenges.[504] Both of these studies, however, were looking at data-intensive platforms: the Ugandan study used platforms like Zoom and the South African one required students to upload videos.

The use of low data-use text and voice note messaging only, and the long-term availability of messages, even if there are electricity cuts or network interruptions, was hoped to minimise these challenges in the study. Many participants confirmed this to be the case.

While So et al's[506] definition of message fatigue, "an aversive motivational state of being exhausted and bored by overexposure to similar, redundant messages over an extended period of time", was not within the context of training, the concept exists in this platform, as demonstrated by this study. Message fatigue is an important consideration in further iterations of WhatsApp-based training, as it has been shown to increase (techno)stress, and result in discontinuation.[507]

Training and ongoing support/mentorship is critical to empowering CHWs[508] and nurses[36, 509]. Continuing professional development and recognition have been shown to lower nurses' intention to leave[510, 511]. Interventions that contribute to the retention of nurses are vital, especially in sub-Saharan Africa, where human health resource shortages are a concern. Nurses' intention to leave their jobs was found to be 51% in Ayalew et al's meta-analysis[510], so participants' feelings of recognition and empowerment from the training should be highlighted.

8.8 Strengths and limitations

Strengths of the study include its robustness covering all four Kirkpatrick's levels and the use of multiple methods of data collection to enable triangulation, allowing a more accurate overview of the training method's usability. The cost-effectiveness and universal nature of WhatsApp as a platform for training and this study being conducted in a poorly resourced province of South Africa points to generalisability in the rest of the country and other LMIC countries. Scale-up and implementation studies are needed to confirm this.

The study had several limitations. Firstly, it was pragmatic, so some participants answered only one questionnaire, despite multiple reminders each time. Non-responders may have skewed results and influenced validity due to sampling bias. Baseline knowledge scores were high (means of 7/10 and 5/7), leaving less room for improvement. The same questions were asked in the pre- and post-intervention questionnaires, which may also have resulted in improved knowledge in the control group by familiarity.

The pre-intervention period fell during the COVID-19 pandemic. The massive diversion of attention to COVID-19 and less frequent patient visits may have skewed the results. Additionally, the intervention was short, so may under-represent the effect that sustained training may have.

Focus groups were conducted in English and Afrikaans and many participants' home language – especially in the CHW groups – was isiXhosa. Bias may have been introduced at several points including population sampling: only participants who attended all sessions were invited to participate in the focus groups, so the more 'enthusiastic' participants may have agreed, possibly resulting in a more positive sentiment than reality.

There may also have been movement of staff between clinics, introducing a potential point of bias. Finally, the trial lead completed the folder reviews and was not blinded, which may have introduced further bias.

8.9 Conclusion

WhatsApp-based microlearning for HCWs on ART guidelines improves knowledge and correct patient care and is highly acceptable and well-received. This makes it a valuable option for simple, accessible, scalable continuing medical education for HCWs. To our knowledge, this is the first study to add qualitative insight into HCWs' perceptions of interactive training using WhatsApp and showing measurements across all four levels of Kirkpatrick's levels of training evaluation. Further research to compare this training method and others, the effect of ongoing, regular training on patient care, large-scale implementation, sustainability and cost-effectiveness is recommended.

Chapter summary

Chapter 8 details the effectiveness, uptake and participation in the WhatsApp-based HIV training intervention for HCWs, showing good levels of uptake and participation and improvement in knowledge and patient care.

Additionally, results showed that it was acceptable to HCWs, and feasible. Sentiment was, overall, positive, and HCWs expressed a desire for further training of this kind.

Chapter 9 reports the consolidated discussion of key findings from the studies, personal reflections and key recommendations for policy and practice, and further research.

Part 4: Conclusions

Part 4 concludes the project with the consolidated discussion, conclusion, implications for current policy and future research and personal reflections.

Chapter 9 Consolidated discussion, conclusions and personal reflections

The final chapter provides a consolidated discussion which integrates both studies, relating them back to their objectives and highlighting the implications of the study, the conclusions drawn, how the results can contribute to the healthcare service and what further research is recommended. Lastly, I reflect on my personal experiences, what I learnt through my PhD journey, and what's next.

9.1 Consolidated discussion of key findings

Lack of knowledge and poor adherence to the recommendations in clinical guidelines can compromise patient care.[98, 109, 141] Continuing in-service training is vital to improve knowledge[162] and adherence to guidelines[60]. Ongoing training is challenging in settings like South Africa. Barriers include infrastructure, distance and human and financial resource shortages.[110]

Summaries of the key findings of the studies are listed in Table 41 and Table 42.

In the first part of the study, South African HCWs' awareness of the drug interactions of dolutegravir and how to adjust dosages – recommendations from the NDOH ART guidelines – was established using an anonymous online survey. Only 70% of participants stated they knew that dolutegravir has any interactions. Knowledge of which drugs interact and how to adjust dosing was even lower.

This is a serious concern when the drugs that interact include commonly used drugs like calcium, iron and magnesium, which are often taken during pregnancy; and rifampicin, which is first-line treatment for drug-sensitive TB. As an example, taking survey branching into consideration, Study 1 showed that 39% of HCWs knew how to adjust dosing in patients on dolutegravir and calcium. Calcium is often bought elsewhere (away from the clinic) by pregnant women. It is vital for HCWs to know of the interaction, ask about use, and recommend dosage schedules to avoid lowered dolutegravir levels, to prevent an increase in the risk of VTP.

The sample size in Study 2 was small in comparison to Study 1 and baseline knowledge of the calcium interaction was higher, with 61% of nurses knowing the required dosage adjustment. After the training, knowledge in the intervention group increased to 81%. While it had lowered slightly to 78% at three months, it was an improvement on the 39% seen in Study 1.

Just over half of the HCWs had received training on dolutegravir and 76% had access to ART guidelines. Training and guideline access were both associated with better knowledge, so those numbers are concerning. HCWs – both previously trained and not – wanted training, with a preference for online- or cell phone-based training. Training increases knowledge and improves care throughout the HIV treatment cascade.[36]

In Part 2, a WhatsApp-based training intervention for primary care nurses and CHWs in remote areas of South Africa was designed. It was tested for effectiveness, acceptability and feasibility using mixed methods. Previous research has been done using WhatsApp as an add-on to other training[290] and as a clinical discussion platform[245], but no studies were found using it with microlearning as a synchronous training platform.

Findings from the study showed it improved both knowledge and patient care and that the training was highly acceptable and feasible. The slight drop in knowledge at three months is a known problem within medical education of all types, which could be overcome by repetition.[512] With almost all participants saying they would participate if the training sessions were held weekly throughout the year, this is feasible.

An unexpected – and quantitatively unmeasured – result was feelings of empowerment and recognition amongst participants who had received the WhatsApp-based training. Training and ongoing support/mentorship is critical to empowering HCWs.[36, 508] The value of the finding that participants felt empowered by the training should not be underestimated in a setting where HCW retention is poor.[510] Continuing professional development and recognition have been shown to lower nurses' intention to leave.[510, 511]

Table 41. Key findings from Study 1

Study 1: Establishing HCW knowledge of dolutegravir's drug-drug interactions in the guidelines	
Objective	**Findings**
To determine the proportion of South African healthcare workers who know about dolutegravir interactions and how to alter regimens accordingly	• 70% of HCWs knew dolutegravir has DDIs • Of those, 54-62% knew of cation interaction; 87% rifampicin interaction; 78% metformin interaction; 44-59% interaction with antiepileptics • Of those who knew of the interactions, proportions who knew how to adjust dosing were: 5-28% cations; 80% rifampicin; 69% metformin; 10-46% antiepileptics
To determine the proportion of South African healthcare workers who have received training on dolutegravir and from whom	• 57% of HCWs had received training on dolutegravir • 94% reported training had included dolutegravir's DDIs • Most HCWs had received training from the NDOH (55%)
To determine the proportion of South African healthcare workers who have access to the 2019 guidelines and describe that access	• 76% of HCWs had access to ART guidelines • Online access to ART guidelines was most common (62%), with 56% having hard copy access • VTP guideline access was lower: 42% online, 37% hard copy • 15% of HCWs accessed guidelines via an App
To determine any association between healthcare worker knowledge of dolutegravir interactions and independent variables	• Nurses were less likely than doctors to know of dolutegravir's DDIs • There was a lack of knowledge of dolutegravir's interactions amongst CHWs • Guideline access and training were associated with better awareness of dolutegravir's DDIs; which drugs interact; and for rifampicin, knowledge of dosage adjustments required • Training, but not guideline access, was associated with better knowledge of how to adjust metformin dosing with dolutegravir
To determine any association between healthcare worker confidence in their knowledge of dolutegravir interactions and independent variables	• 34% of HCWs were confident in their dolutegravir interaction knowledge; 16% somewhat confident; 30% neutral and 20% somewhat or not confident • Training and guideline access were associated with better confidence in knowledge
To determine healthcare worker preferences for training	• 83% of those who'd received previous training desired more training on dolutegravir's interactions; and 92% who had not previously been trained, desired it • Doctors, nurses and pharmacists preferred training online (computer or cell phone-based) to face-to-face training; CHWs preferred face-to-face training to online

Table 42. Key findings from Study 2

Study 2: WhatsApp-based training	
Objective	**Findings**
To determine knowledge changes through knowledge testing of nurses and CHWs	• Descriptive and inferential analysis showed improved knowledge in both nurse and CHW groups after training • Intervention group knowledge was higher than control group at three months, but only significantly in CHWs • Adjusting for age, gender, years of experience, stratification, clustering and repeated measures showed a significant intervention effect
To determine knowledge retention through knowledge testing of nurses and CHWs three months after the intervention	• Knowledge decreased slightly at three months for most learning points, but remained above baseline knowledge in nurses • In CHWs, knowledge in three learning points improved at three months; one remained the same; two decreased slightly but were still above baseline
To explore and describe the changes in prescribing/clinical care due to the training intervention	• A significantly higher proportion of correct patient care was seen in the intervention group in the post-intervention period, compared to the control group • A difference-in-differences analysis, to account for unbalanced baseline means, showed a statistically significant improvement in correct patient care of 21% in the intervention arm
To describe the uptake of WhatsApp-based training for nurses and CHWs	• 79% and 76% of CHWs agreed to participate in the training • Mean uptake over the three knowledge questionnaires was 62%
To describe the participation in the training	• During the training, one nurse and three CHWs left the WhatsApp training groups • Live attendance ranged between 27-51% for nurses and 28-54% for CHWs • Two weeks after the training sessions, 96% of nurses, 88% of CHW had read the lessons • There was lively interaction in the groups: 1 295 interactions over the training period in the nurse group; 475 in the CHW group
To describe the acceptability of WhatsApp-based training for nurses and CHWs	• Over 90% of HCWs found the training useful, easy to use and understand, convenient and enjoyable • Qualitative data showed a high degree of acceptance and positive sentiment • A sense of recognition, appreciation and empowerment was described by participants
To describe the feasibility of WhatsApp-based training for nurses and CHWs	• 97% of nurses and 98% of CHWs said they would participate if it were weekly, throughout the year • Most common challenges reported were network issues and lack of data, both in the quantitative and qualitative analyses

9.2 Implications for policy and practice with recommendations

There is an urgent need for dissemination of up-to-date ART guidelines to all HCW's involved in the ART programme. Without access to guidelines, knowledge of, and adherence to the recommendations, is impossible. Additionally, ongoing training on the guideline recommendations and updates, as they happen, is essential. CHWs, an invaluable addition to the health service, must be included in ongoing training programmes, to optimise the sharing of tasks.

The findings reported from the two studies in this research thesis provide useful evidence for the current state of guideline knowledge. In addition, it offers a potential training solution, using WhatsApp to close the gaps in HCW knowledge.

This simple training platform and design has the potential for scale-up in a country like South Africa, that faces many infrastructural and resource challenges. WhatsApp is freely available, widely utilised and easy to use.

Key points and recommendations for the development and implementation of WhatsApp-based training for HCWs include:

- **Stakeholder engagement:** to enable implementation of this training at a national level, engagement with stakeholders in the NDOH and NGOs involved in training in South Africa would be ideal. Collaborating with the HCWS themselves may increase uptake and ensure sustainability.
- **Asynchronous/synchronous training:** the interactive, ‘live’ nature of the training – with a trainer ‘present’ to ask questions and/or moderate – was repeatedly referred to as a positive. Although this is time-intensive for trainers/moderators, the costs involved are expected to be a fraction of those for face-to-face training. If financial constraints force it, however, an asynchronous, or just-in-time version of the training may work.
- **Data compensation:** participants in the study were given a small amount of data. In the current socio-economic climate, this is believed to be essential to ensure participation, but this hypothesis needs to be tested (see Section 9.4).

- **Language and jargon:** particularly an issue in the CHW group, there is a need for training in the home language of participants. Additionally, special attention needs to be paid to not using medical jargon in both training and guidelines.

9.3 Study strengths and limitations

This research has several strengths, the first being the robust design of both studies. The use of mixed methods to test the WhatsApp-based training allowed both quantitative analysis and in-depth understanding of HCWs' needs. Measurement of the training across all four levels of Kirkpatrick's levels of training assessment, with multiple data collection methods allowing triangulation of results, provided an accurate view of the usability of the training.

The results of the survey are thought to be generalisable across the country, due to its good uptake, with participants across South Africa. Quantifying HCWs' baseline knowledge of recommendations in the national guidelines was a vital starting point to establish whether additional training was needed and to gain insight into what the HCWs themselves wanted in terms of training.

The cost-effectiveness and universal nature of WhatsApp as a platform for training, and this study being conducted in a poorly resourced province of South Africa also point to generalisability in the rest of the country and other LMIC countries.

The research had several limitations. While the online nature of the surveys in Study 1 and the questionnaires in Study 2 may have limited social desirability bias, there was the potential for both non-response and selection bias. This was also a risk in the focus groups. Additionally, all research was conducted by BC, who was not blinded to control/intervention groups.

In both the survey and knowledge questionnaires, participants completed them online and in their own time, introducing the possibility that they may have shared answers and/or sought the answers in references available to them. While this may have skewed results positively, it is considered a minor limitation because HCWs are not expected to know everything, but need to know where to find the information, if required.

Both the Study 1 survey and the pre-intervention retrospective folder review periods fell during the COVID-19 pandemic, so guideline dissemination, training, and patients attending clinics were limited.

Lastly, the WhatsApp training was tested on a small population relative to the South African HCW workforce, over a short period, so cost-effectiveness, scalability and sustainability cannot be assumed and require further investigation.

9.4 Recommendations for future research

The research in this thesis provides answers to several questions and a simple solution to provide training across South Africa. While the training could be rolled out, as is, there are areas that would benefit from further study, which could be done during scale-up and implementation.

9.4.1 Cost-effectiveness

There is a lack of cost-effectiveness studies for CE[190], microlearning[115] and mLearning[10]. Logically, costs associated with face-to-face training – travel, accommodation, time away from clinic – should be greater than those associated with an mLearning programme, but this needs to be confirmed with a cost-effectiveness analysis. Additionally, whether not providing data – a small amount was provided in the study – affects uptake, participation and long-term sustainability needs to be assessed.

9.4.2 Exploring opting and dropping out

Reasons for non-participation or leaving the group sessions could be useful for further optimisation of the method.

9.4.3 Microlearning as a standalone training platform

Most studies use microlearning as an add-on to other training. Yeoh[320] recommends that it not be used as a standalone method, but rather to complement other forms of training. While this is the ideal situation, the South African setting limits options. Further research to compare standalone microlearning to a combination of face-to-face/online learning with microlearning would be useful, if logistically possible.

9.4.4 Scale-up and sustainability

The study was small, and the feasibility of large-scale implementation needs to be investigated. Gimbel et al, in their review of HIV-related mHealth interventions in LMICs, highlighted that, while many pilot studies have been done, there is a paucity of research on these interventions at scale.[242]

9.4.5 Participant engagement

To increase sustained participation, participant involvement is key. While the participants' preferences for training from Study 1 guided the design of the training in Study 2, HCWs were not involved in the design of the training or learning points taught.

Involving participants in decisions regarding both guidelines and training may increase uptake and participation, but this requires investigation.

9.4.6 Recruitment

Lastly, recruitment for the study was done in-person, with BC visiting each clinic to introduce the study. On a large scale, this is impractical, so further research needs to be conducted to ascertain whether uptake will be as good using different levels of participant recruitment: in-person, phone/e-mail to individuals, facilities, district, provincial and/or national.

9.5 Next steps: roll out the training and scale up

Through this research, WhatsApp-based training has been shown to be effective, acceptable and feasible. The intervention harnesses simple, cheap, easily accessible technology to increase HCW training. It has the potential to impact the health system across all levels: a cost-effective training intervention impacts health budgeting from national to local levels; training has been shown to improve staff motivation and retention; and knowledgeable staff improves patient care. Improved patient care builds healthy communities.

The next step is to determine whether it is sustainable at large scale, across South Africa. A scale-up and implementation trial is being planned, led by BC, in her role as an information/research pharmacist at the hotline.

The Dynamic Sustainability Framework[513] will be used for the research during scale-up. It sees change and customisation throughout a project as vital to sustainability and recommends ongoing stakeholder and participant engagement.

Stakeholder engagement is planned at the onset. The NDOH, other organisations involved in training and the pharmaceutical industry will be consulted to obtain both buy-in and potential funding for the training and ongoing research. Relevant grants, such as the National Institutes of Health Mobile Health in LMICs Grant (PAR 25-233) and the National Institute for Health and Care Research Global Health Research Grants, will be applied for.

Scaling up will be done as quickly as possible – there is a need for training, now, especially as US funding is pulled from many of the South African NGOs involved in training. Recruitment, initially, will be through users of the hotline. Scale-up and optimisation will run concomitantly, with the main objectives being:

- Create lessons responsive to the requests of HCWs, stakeholders and gaps recognised through hotline queries
- Measure effects on uptake/participation of several variables, e.g., in-person vs. district-level recruitment; provision of data vs. no provision
- Measure effect on patient care: monitoring of relevant indicators
- Establish barriers/facilitators to optimisation through qualitative data collection
- Describe the effects of the intervention on HCW motivation/job satisfaction
- Describe sustainability of the training intervention: monitoring and evaluation
- Adapt/improve the intervention responding to data
- Measure cost effectiveness of the intervention

The trial will obtain ‘real world’ input: quantitative data to define changes in patient care and staff satisfaction; qualitative data to provide depth and context. All cadres of HCW will be included, including CHWs, with training tailored to scope of practice.

9.6 Conclusion

The research in this thesis revealed gaps in the knowledge of South African HCWs in the field of HIV and provided evidence to support the use of WhatsApp-based microlearning training to close the gaps.

There is a need to train more HCWs, especially nurses and CHWs, who are at the forefront of HIV care in South Africa. WhatsApp-based microlearning for HCWs on ART guidelines improved knowledge and correct patient care and is highly acceptable and well-received, making it a valuable option for simple, accessible, scalable continuing medical education for HCWs.

Figure 26. Contemplating the plan, February 2022; the final clinic visit, June 2024
Hofmeyr Clinic

9.7 Personal reflections

Completing Study 2 was incredibly challenging – we drove thousands of kilometres, often on dust roads, dealt with temperatures that ranged between highs of 40°C and lows under 0°C, had to pick our way around service strikes, change burst tyres, follow taxis to avoid potholes and deal with the (plentiful) logistics that come with visiting small towns blindly.

Despite the challenges, I would do it again in a heartbeat. It was incredibly inspiring. Interacting with the HCWs at all 50 clinics over the three years was a privilege and allowed me to gain valuable insights into the working conditions and experiences of HCWs in rural and small town South African clinics and has driven me to find a way to scale-up this training.

The most prominent outtake I got, was the acute need for recognition – of any kind, including having an interactive training group – of the amazing work that these HCWs are doing, often under difficult conditions. On our initial trips, we were met with some reticence but once we explained what we were there to do, we were welcomed enthusiastically at almost every clinic we visited, the HCWs were keen to participate, and we were greeted like old friends by the second and third visits.

One of the biggest anecdotal points learnt was that the smallest intervention can motivate people. Over and over, HCWs said that us visiting the clinic, giving the training, coming back when I said we would, meant a huge amount to people who often see nobody ‘official’. While personal visits to clinics is unsustainable, a simple intervention – with interaction – such as the WhatsApp training, may have a far greater effect than any that is measurable – motivation, recognition and empowerment all lead to staff retention, something that is desperately needed, especially in rural South Africa.

Once this thesis is handed in, I will return to full-time work at the National HIV & TB Healthcare Worker Hotline, where I will be engaging with stakeholders and the healthcare workers themselves, to implement scale-up of the WhatsApp-based training (Section 9.5) and conducting some of the research detailed in Section 9.4. I am excited for this next step.

"*Everything was clear and we gained a lot of information. Because some of us didn't know anything so by those voice notes and the messages that came, it was useful. You actually empowered us, truly.*" CHW

Figure 27. Mzamomhle Clinic, Bedford. November 2022

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Appendices

Appendix A: Search terms and filters used in the literature review

Topic	Database	Terms used	Filters
HCW knowledge of practice/HIV guidelines	Medline	((practice guidelines) AND (knowledge)) AND (HIV)	English, 20 years
		((guidelines) AND (knowledge)) AND (HIV)	English, 10 years
	EBSCO	guidelines AND knowledge AND HIV	English, 10 years, keywords in title
	SCOPUS	guidelines AND knowledge AND HIV	English, 10 years
	Google Scholar	guidelines AND knowledge AND HIV	10 years
Current in-service training	Medline	((((("Continuing Education") OR ("Continuing professional development")) OR (("inservice training") OR ("in-service training"))) AND (((((("healthcare professional") OR ("healthcare worker")) OR (nurse)) OR (doctor) OR ("community health worker") AND (hiv)	English, 20 years
	EBSCO	(continuing education or professional development or lifelong learning) AND (HIV) AND (healthcare workers or nurses or medical workers or healthcare professios)	English, 10 years, Africa
	SCOPUS	(“continuing education” or “professional development” or “lifelong learning”) AND (HIV) AND (“healthcare workers” or nurses or “medical workers” or “healthcare professionals”)	English, 10 years
	Google Scholar	“continuing education” AND HIV	10 years
Online learning: broad search (review/systematic review)	Medline	(("online learning") OR ("web-based learning")) AND (health)	English, 10 years, review/systematic review
	EBSCO	("online learning" OR "web-based learning") AND health; Major headings: health personnel, professional knowledge, primary health care	English, 10 years, peer-reviewed
	SCOPUS	("online learning" OR "web-based learning") AND health	English, 10 years, Subject area: medicine, health professions, nursing, review
	Google Scholar	"online learning" OR "web-based learning" AND health AND review	10 years
mLearning	Medline	mLearning AND health	English, 10 years
	EBSCO	mLearning AND health	English, 10 years, peer-reviewed
	SCOPUS	mLearning AND health	English, 10 years
	Google Scholar	mLearning AND health	10 years 7810 First 100 by relevance

Topic	Database	Terms used	Filters
WhatsApp-based continuing education	Medline	((whatsapp) NOT (student)) AND (hiv)	English
		((((("continuing education") OR ("continuing professional development")) OR (("in-service training") OR ("inservice training"))) AND (whatsapp))	
	EBSCO	(whatsapp) AND (hiv)	English, 10 years, LMIC
		whatsapp AND “continuing education”	
		whatsapp "continuing professional development"	
		whatsapp "in-service training"	
		whatsapp "inservice training"	
		whatsapp AND ("in-service training" OR "inservice training")	
	SCOPUS	whatsapp AND "continuing education"	English, 10 years
		whatsapp AND "continuing professional development"	
		whatsapp AND "continuing medical education"	
	Google Scholar	whatsapp "continuing medical education" HIV Africa	5 years
Pedagogy	Medline	((mlearning) OR (m-learning)) AND (pedagogy)	English, 10 years
	EBSCO	mlearning pedagogy	English, 10 years
		m-learning pedagogy	
	SCOPUS	mlearning AND pedagogy	English, 10 years
		m-learning AND pedagogy	
	Google Scholar	mlearning AND pedagogy AND in-service AND health	10 years 6770 First 100 by relevance
Microlearning	Medline	(microlearning) AND (health)	English, 10 years
	EBSCO	microlearning health	None
	SCOPUS	microlearning AND health	English, 10 years
	Google Scholar	microlearning AND health	10 years 7900 First 100 by relevance

Appendix B: Online survey for HCWs on knowledge of dolutegravir's interactions

Confidential

DEMOGRAPHICS
(Section 1 of 6)
This section includes questions on demographics e.g. which province you work in, your profession. There are nine questions in this section.

How did you hear about the survey?	☐ Word of mouth/from a colleague ☐ E-mail ☐ SMS ☐ Social media (Facebook, Twitter) ☐ Other
Please specify how you accessed the survey.	_____
Please specify through which organisation you accessed the survey.	_____
In which province do you work?	◯ Eastern Cape ◯ Free State ◯ Gauteng ◯ KwaZulu-Natal ◯ Limpopo ◯ Mpumalanga ◯ North West ◯ Northern Cape ◯ Western Cape ◯ Outside of South Africa
What is your profession?	◯ Community health worker ◯ Counsellor ◯ Doctor ◯ Person not involved in HIV care ◯ Nurse ◯ Pharmacist ◯ Other health care worker/allied profession
Please specify your profession.	_____
What is your age?	_____
For how many years having you been working with HIV patients?	_____
In which area do you primarily work?	◯ Rural ◯ Urban
In which sector do you primarily work?	◯ Public ◯ Private

At which type of facility do you primarily work?	◯ Mobile Clinic ◯ Satellite Clinic ◯ Primary Health Clinic ◯ Community Health Clinic/Centre ◯ District Hospital ◯ Regional Hospital ◯ Tertiary Hospital ◯ Specialised Hospital ◯ Private Practice ◯ Private Hospital ◯ Other
Please specify which type of facility.	_____
On what device have you accessed the survey?	◯ Cellphone ◯ Tablet ◯ Desktop computer (PC) ◯ Laptop computer

GUIDELINES AND TRAINING
(Section 2 of 6)
The following questions will be about sections of the new (2019) ART/PMTCT guidelines. There are seven questions in this section.

Have you received training on the use of dolutegravir (DTG)?	◯ Yes ◯ No
Who gave you training on the use of dolutegravir (DTG)? Pick all that apply.	☐ Department of Health ☐ Training from a colleague who was trained ☐ I'm not sure ☐ Online training ☐ Non-governmental organisation (NGO) ☐ Other
Please specify which online training.	_____
Please specify which NGO.	_____
Please specify who you received training from.	_____
Did the training include a section on the potential interactions of dolutegravir (DTG) i.e. how other medicines affect it?	◯ Yes ◯ No ◯ I'm not sure
Please rate the following statement on the scale: I feel confident with my knowledge of the interactions of some medicines with dolutegravir (DTG).	Strongly disagree — Neutral — Strongly agree *(Place a mark on the scale above)*
Do you have easy access to the 2019 guidelines (e.g. on your desk, wall or phone)?	◯ Yes ◯ No
Which of the following 2019 guidelines do you have daily access to? Pick all that apply.	☐ Online ART Guidelines ☐ Online PMTCT Guidelines ☐ Hard copy ART Guidelines ☐ Hard copy PMTCT Guidelines ☐ HIV Hotline posters online ☐ HIV Hotline posters printed ☐ App ☐ Other
Please specify which App.	_____
Please specify which other guidelines you have access to.	_____
If there are any other concerns or issues you'd like to bring up regarding access to guidelines, we'd welcome your thoughts.	_____

INTERACTIONS
(Section 3 of 6)
This section is on some of the potential interactions of dolutegravir (DTG) i.e. how other medicines affect it.

Are you aware that dolutegravir (DTG) interacts with some other medicines?	○ Yes ○ No
Thinking about the potential interactions with dolutegravir (DTG): please indicate which of the following medicines you think can interact and/or affect DTG. We have included just some commonly used examples but there are many others available. Pick all that apply.	☐ Calcium e.g. calcium gluconate ☐ Iron e.g. ferrous sulphate ☐ Oral contraceptives ☐ Magnesium- and aluminium-containing antacids e.g. Milk of Magnesia, sucralfate ☐ Rifampicin ☐ Metformin ☐ Carbamazepine ☐ Lamotrigine ☐ Phenobarbitone ☐ Phenytoin ☐ Sodium valproate ☐ None of the above
Thinking about the patients you've seen on dolutegravir-based regimens. Which of the following combinations have you come across in patients under your care? Pick all that apply.	☐ Dolutegravir-based regimen and calcium ☐ Dolutegravir-based regimen and iron ☐ Dolutegravir-based regimen and oral contraceptives ☐ Dolutegravir-based regimen and antacid ☐ Dolutegravir-based regimen and rifampicin ☐ Dolutegravir-based regimen and metformin ☐ Dolutegravir-based regimen and carbamazepine ☐ Dolutegravir-based regimen and lamotrigine ☐ Dolutegravir-based regimen and phenobarbitone ☐ Dolutegravir-based regimen and phenytoin ☐ Dolutegravir-based regimen and sodium valproate ☐ I have not seen any patients on these combinations ☐ I'm not sure

INTERACTIONS AND REGIMENS
(Section 4 of 6)
This section is on how regimens should be changed, if at all, due to the interactions of dolutegravir (DTG).

Which of the following ways to take dolutegravir (DTG) and calcium, e.g. calcium gluconate, would you tell your patients to use? Pick all that apply.	☐ I'm not sure ☐ Take them together, with food ☐ Take them together, on an empty stomach ☐ If food not available, take calcium at least 2 hours before or 6 hours after DTG ☐ If food not available, take calcium at least 2 hours after or 6 hours before DTG ☐ No dosing adjustment of either is necessary ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and calcium.	_____
How would you counsel your patient who is taking dolutegravir (DTG) and iron, e.g. ferrous sulphate? Pick all that apply.	☐ I'm not sure ☐ No dosing adjustment of either is necessary ☐ If food not available, take iron at least 2 hours before or 6 hours after DTG ☐ If food not available, take iron at least 2 hours after or 6 hours before DTG ☐ Take them together, with food ☐ Take them together, on an empty stomach ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and iron.	_____
How would you counsel the patient who is taking dolutegravir (DTG) and a magnesium- and/or aluminium-containing antacid, e.g. Milk of Magnesia, sucralfate? Pick all that apply.	☐ I'm not sure ☐ No dosing adjustment of either is necessary ☐ Take antacids at least 2 hours before or 6 hours after DTG ☐ Take antacids at least 2 hours after or 6 hours before DTG ☐ Take them together, with food ☐ Take them together, on an empty stomach ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and magnesium- and/or aluminium-containing antacids.	_____
In patients who are on dolutegravir (DTG) and metformin, what dosage of metformin would you use? Pick all that apply.	☐ I'm not sure ☐ No more than 500 mg metformin 12-hourly ☐ No less than 500 mg metformin 12-hourly ☐ No dosage change, just take them together, with food ☐ They should not be used together at all ☐ No dosage change of either is necessary ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and metformin.	_____

In patients who are on dolutegravir (DTG) and rifampicin, how would you adjust dosing of the two medicines? Pick all that apply.	☐ I'm not sure ☐ No dose adjustment of either is necessary ☐ Double the dose to DTG 50 mg 12-hourly ☐ Double the dose of rifampicin, by weight ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and rifampicin.	_____
In patients who are on dolutegravir (DTG) and carbamazepine, how would you adjust dosing of the two medicines? Pick all that apply.	☐ I'm not sure ☐ No dose adjustment of either is necessary ☐ Double the dose of DTG to 50 mg 12-hourly ☐ Double the current dose of carbamazepine ☐ They should not be used together, unless there is no other option ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and carbamazepine.	_____
In patients who are on dolutegravir (DTG) and phenobarbitone, how would you adjust dosing of the two medicines? Pick all that apply.	☐ I'm not sure ☐ No dose adjustment of either is necessary ☐ Double the dose of DTG to 50 mg 12-hourly ☐ Double the current dose of phenobarbitone ☐ They should not be used together ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and phenobarbitone.	_____
In patients who are on dolutegravir (DTG) and phenytoin, how would you adjust dosing of the two medicines? Pick all that apply.	☐ I'm not sure ☐ No dose adjustment of either is necessary ☐ Double the dose of DTG to 50 mg 12-hourly ☐ Double the current dose of phenytoin ☐ They should not be used together ☐ Other
Please specify how you would tell the patient to take their dolutegravir (DTG) and phenytoin.	_____
Would you like training on dolutegravir (DTG) and its interactions?	○ Yes ○ No ○ Unsure
Would you like further training on dolutegravir (DTG) and its interactions?	○ Yes ○ No ○ Unsure
Which method of training would you prefer? Pick all that apply.	☐ Face-to-face training ☐ Online training (computer) ☐ Online training (cell phone) ☐ Hardcopy toolkits e.g. posters, booklets ☐ Other

Please specify what other training you'd like.	_____
If there are any other concerns or issues you'd like to bring up regarding interactions and/or training, we'd welcome your thoughts.	_____

COUNSELLING
(Section 5 of 6)
In this section, we ask five questions on counselling patients.

Which patients, if any, do you counsel about the potential interactions with dolutegravir (DTG)?

Pick all that apply.

- ☐ None
- ☐ Patients who are being initiated on DTG
- ☐ Pregnant women on DTG
- ☐ At every visit for patients taking DTG
- ☐ Other
- ☐ I don't see patients

Please specify which other patients you counsel.

_____

Please rate the following statement on the scale:

I feel confident with counselling my patients on how to take their dolutegravir (DTG) when they are taking medicines that may interact with DTG.

Strongly disagree — Neutral — Strongly agree

(Place a mark on the scale above)

What makes it hard, for you as a busy health care worker, to counsel your patients on how to take their dolutegravir (DTG) with interacting medications?

Pick all that apply.

- ☐ No challenges
- ☐ Lack of time
- ☐ I am not sure of the interactions I should be counselling them on
- ☐ I received no training on how to counsel patients on interactions
- ☐ I don't have access to the guidelines
- ☐ Patients are not interested
- ☐ I'm not sure
- ☐ Other

Please specify what makes it hard for you to counsel patients on the interactions of dolutegravir (DTG).

_____

Do you feel like any of the following may make it easier/simpler to tell your patients on dolutegravir (DTG) about these interactions?

Pick all that apply.

- ☐ Posters for the wall detailing the interaction
- ☐ A desk-top guide on the interactions
- ☐ A patient-friendly leaflet for the patient to take home
- ☐ Stickers for pill containers
- ☐ Guidance on an App specific to interactions of DTG
- ☐ None of these
- ☐ Other

Please specify what other things would make it easier for you to counsel patients on interactions with dolutegravir (DTG).

_____

If there are any other concerns or issues you'd like to bring up regarding counselling patients on dolutegravir (DTG) interactions, we'd welcome your thoughts.

_____

COVID-19 PANDEMIC
(Section 6 of 6)
In this short, final section, we will ask three questions on what impact the global COVID-19 pandemic has had on your routine day's work.

Do you think the COVID-19 pandemic has impacted the care of your patients on ARVs?	◯ Yes ◯ No ◯ I'm not sure
What has been your biggest concern(s) about your being able to care for your patients during the COVID-19 pandemic? Pick all that apply.	☐ Pressure on staff to switch patients to dolutegravir-based regimens ☐ Pressure on patients to go onto dolutegravir-based regimens ☐ Patients not collecting their ARVs ☐ Limited time to counsel on risks and benefits of dolutegravir ☐ Limited time to counsel patients on interactions ☐ Worse adherence ☐ Missing adverse effects to ARVs ☐ None ☐ I don't know ☐ Other
Please specify what other concern(s) you have about your being able to care for your patients during the COVID-19 pandemic.	_____
If there are any other concerns or issues you'd like to bring up regarding the COVID-19 pandemic, we'd welcome your thoughts.	_____

Thank you for participating in this survey.

We hope to use the data collected to provide you with support in the workplace.

PLEASE CLICK ON SUBMIT TO FINISH THE SURVEY.

Timestamp_end	_____

Appendix C: Introductory e-mail for assistance with survey dissemination

Dear [insert name],

[As you know.] We have been running the toll-free National HIV & TB Health Care Worker (HCW) Hotline since 2008. based at the Medicines Information Centre (MIC) in the Division of Clinical Pharmacology at the University of Cape Town. We answer about 500 clinical queries a month from HCWs across South Africa and have a range of toolkits free for HCWs, e.g. guideline posters and an interaction booklet on interactions between ARVs and medicines on the Essential Medicines List.

We are planning a study using a short online survey to describe HCWs knowledge and training of the latest guidelines recommending dolutegravir-based regimens. I, Briony Chisholm, am the investigator (I have been an information pharmacist at the MIC since 1998 and am using this project for my MSc (Med)), under the supervision of Professor Marc Blockman. Annoesjka Swart, manager of the MIC, is a co-investigator.

This study has received ethics approval by the UCT Faculty of Health Sciences Research Ethics Committee (HREC 357/2020) and is currently being reviewed for updated approval after minor changes were made, post reliability and validity testing and piloting. The study will only be conducted once full approval is obtained.

We would be very grateful if you would agree to share the survey URL, with a short message which we would send to you, on the first day the survey goes live (we're hoping the third week of August), a reminder a week later. and another the day before it closes (it will run for two weeks). We will send all the messaging to you.

If you agree to be involved, please let me know on what medium you'll share it (Facebook. SMS and/or e-mail) and the numbers of healthcare workers on your mailing lists so we can keep a record of how many people were sent the URL to compare with how many responses we get. Please feel free to contact me on 084 555 0202 or briony.chisholm@uct.ac.za. if you have any questions.

Yours sincerely,
Briony Chisholm.

Appendix D: Dissemination of survey URL, organisations. dates and platforms

Note: Every effort was made to keep track of where and how the URL was disseminated but due to the nature and vastness of social media platforms, some sharing may have been missed	Platform						
	Posting dates	**FB follows**	**Web-site**	**e-mail**	**SMS**	**Twitter follows**	**IG follows**
POSTING BY ORGANISATIONS							
Users of the hotline	2020/08/24	5530	x	3757	4791		
	2020/09/04	5550		3757	4791		
	2020/09/14	5554	x	3757	4791		
CHIVA	2020/08/27	640				7868	
	2020/09/14	640					
Department of Health. Western Cape	2020/08/25			x			
	2020/09/07			x			
Desmond Tutu Foundation	2020/08/25	6285					
	2020/09/14	6310					
Foundation for Professional Development	2020/08/31	18660		32418	13478	9415	1500
	2020/09/16	13909			x	9408	
Pharmaceutical Society of South Africa	2020/08/25	778					
	2020/09/14	791					
Postgraduate Diploma HIV/TB class (UCT)	2020/08/31		VULA				
	2020/09/14		VULA				
Rural Doctors Association of South Africa	2020/08/25	631			x		
	2020/09/14	636					
South African National AIDS Council	2020/08/27	2989				7870	
	2020/09/14	3053					
Southern African HIV Clinicians Society	2020/08/25	12298	x	9294	4724		
	2020/09/14	12321	x	9137	4722		
Andy Gray (Health Systems Trust)	2020/08/25			750			
Aurum Institute	2020/09/15	16595		x		1472	
Health Systems Trust	2020/08/28			2000			
Keth'Impilo	2020/08/26			26			
MediClinic	2020/09/02			109			
Netcare	2020/09/14			200			
Right to Care	2020/08/25			2091			
South African Medical Association	2020/09/14	8100					
South African Society of Clinical Pharmacists	2020/08/25		x	420			
TB HIV Care	2020/08/27	10829					
DIRECT POSTING ONTO FACEBOOK							
Medical Women's Association of South Africa https://www.facebook.com/medicalwomenassociationofsouthafrica	2020/08/25	1680					
	2020/09/04	1680					
	2020/09/14	1680					
NIMART - Wonderful Nurses providing ART https://www.facebook.com/groups/1554832731404534	2020/08/25	6800					
	2020/09/04	6800					
	2020/09/14	6900					
PharmacySA https://www.facebook.com/groups/pharmacysa	2020/08/25	9936					
	2020/09/04	9936					
	2020/09/14	9936					
SA Doctors United	2020/08/25	7300					

https://www.facebook.com/groups /92643598408	2020/09/04 2020/09/16	7300 7300
SA Pharmacy Today https://www.facebook.com/groups /pharmacy2daysa/	2020/08/25 2020/09/04 2020/09/14	8200 8200 8300
South African Medical Officer Posts https://www.facebook.com/groups /291143507761905/	2020/08/25 2020/09/04 2020/09/14	7300 7300 7400
South African Medical Doctors Community Service https://www.facebook.com/groups /107541075948267	2020/08/25 2020/09/04 2020/09/14	8100 8100 8200

Appendix E: HREC approval for HCW survey of dolutegravir knowledge

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

02 July 2020

HREC REF:357/2020

Prof N Blockman
Division of Clinical Pharmacology
Room K45.53 OMB
Email: marc.blockman@uct.ac.za
Student: briony.chisholm@uct.ac.za

Dear Prof Blockman

PROJECT TITLE: DOLUTEGRAVIR INTERACTIONS: A CROSS-SECTIONAL SURVEY OF THE KNOWLEDGE, ATTITUDES AND PRACTICES OF SOUTH AFRICAN HEALTHCARE WORKERS IN THE FIELD OF HIV AND FACTORS AFFECTING THAT KNOWLEDGE-MSC CANDIDATE-MS BRIONY CHISHOLM

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020.

Approval is granted for one year until the 30 July 2021.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Ms Briony Chisholm will also be involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval, where necessary, before the research may occur.

Please quote the HREC reference number in all your correspondence.

HREC 357/2020sa

Appendix F: Consent information at start of online survey

Confidential

A cross-sectional survey of the knowledge, attitudes and practices of South African health care workers in the field of HIV and factors affecting that knowledge.

Timestamp_start

_____

We invite you to take part in a research study being run by the National HIV & TB Health Care Worker Hotline at the University of Cape Town (UCT). This study has ethical approval from the UCT Faculty of Health Sciences Research Ethics Committee (HREC Reference: 357/2020).

We know you are extremely busy and appreciate your taking the time to help us with this short survey, which should take no longer than 15 minutes to complete.

STUDY PURPOSE
The overall aim of the study is to establish and understand the knowledge, attitudes and practices on parts of the new dolutegravir-based ART guidelines and to establish whether you have received enough support and training about them. The study is open to all health care workers in the field of HIV in South Africa.

PARTICIPATION
Participation is entirely anonymous and voluntary and there will be no negative consequences of any kind, whether you choose to participate or not. We have invited you to participate as we believe you can provide useful information that is relevant to the study.

INCENTIVE
Should you wish to receive a pack of our printed tools and be entered into a draw for a hamper worth R1 000, you can leave your details for postage at the end of the survey. This is entirely voluntary and, to protect your anonymity, these details will be stored separately from your responses to the survey.

DATA SECURITY
You do not need to fill in any identifying information to complete the survey. All information provided will be stored securely and in accordance with South Africa's Protection of Personal Information Act.

WHAT WILL THE RESULTS OF THE STUDY BE USED FOR?
The anonymous findings will be used to design interventions to assist health care workers and improve the transfer of important ART-related information to the patient. They will be reported to relevant parties and, if deemed useful, training recommendations will be made at a national level. The results will also be submitted for publication in a relevant medical journal (all data anonymous).

WHO CAN I CONTACT, IF I HAVE CONCERNS?
If you have questions about the ethics of the study and your rights as a participant, you can contact Ms. Lamees Emjedi at the Human Research Ethics Committee, Faculty of Health Sciences, telephone (office): 021 406 6338. If you have concerns or questions regarding the survey, you can contact the investigator, Ms. Briony Chisholm, at briony.chisholm@uct.ac.za.

Please ensure that you have read the information about the study.

Do you consent to participate?

◯ Yes
◯ No

The survey consists of mostly multiple choice questions and should take no longer than 15 minutes to complete. You may stop at any point and, if you wish to return to the survey to complete it, you can.

PLEASE CLICK ON 'NEXT PAGE' TO START THE SURVEY.

Appendix G: Awareness of specific drugs that interact with dolutegravir, by variable

n=1333[1]	Calcium	Iron	Mg/Al	Carbamazpine	Phenytoin	Metformin	Rifampicin
Profession, n[†]							
CHW, n=6	16.7 (0.4-64.1)	16.7 (0.4-64.1)	16.7 (0.4-64.1)	16.7 (0.4-64.1)	16.7 (0.4-64.1)	33.3 (4.3-77.7)	50.0 (11.8-88.2)
Counsellor, n=19	26.3 (9.2-51.2)	15.8 (3.4-39.6)	36.8 (16.3-61.6)	10.5 (1.3-33.1)	21.1 (6.1-45.6)	31.6 (12.6-56.6)	47.4 (24.5-71.1)
Doctor, n=537	67.4 (63.3-71.4)	59.0 (54.7-63.2)	64.1 (59.8-68.1)	60.7 (56.4-64.9)	54.9 (50.6-59.2)	80.6 (77.0-83.9)	91.6 (89.0-93.8)
Nurse, n=604	56.6 (52.6-60.6)	48.7 (44.6-52.7)	42.2 (38.2-46.3)	58.4 (54.4-62.4)	46.0 (42.0-50.1)	78.5 (75.0-81.7)	84.9 (81.8-87.7)
Pharmacist, n=134	67.2 (58.5-75.0)	61.2 (52.4-69.5)	68.7 (60.1-76.4)	62.7 (53.9-70.9)	60.4 (51.6-68.8)	78.4 (70.4-85.0)	88.1 (81.3-93.0)
Training	n=774[†]	n=717[†]	n=706[†]	n=725[†]	n=610[†]	n=985[†]	n=1086[†]
No training	47.2 (42.0-52.4)	37.9 (33.0-43.1)	40.9 (35.9-46.1)	46.1 (40.9-51.3)	40.9 (35.9-46.1)	61.0 (55.8-66.0)	80.2 (75.8-84.2)
Training received	67.0 (63.9-70.0)	59.5 (56.4-62.7)	58.3 (55.1-61.4)	63.6 (60.5-66.6)	53.6 (50.4-56.8)	84.8 (82.3-87.0)	89.4 (87.3-91.3)
Guideline							
No Access	42.6 (36.2-49.2)	34.5 (28.4-40.9)	37.4 (31.2-44.0)	43.4 (37.0-50.0)	34.0 (28.0-40.5)	62.1 (55.6-68.4)	76.6 (70.7-81.9)
Has Access	65.6 (62.7-68.4)	57.7 (54.7-60.6)	56.9 (53.9-59.9)	62.0 (59.1-64.9)	53.6 (50.6-56.5)	81.6 (79.2-83.9)	89.1 (87.1-90.9)

[1]Blank responses were excluded. †The survey was designed using branching logic. Only those who answered that they were aware of that dolutegravir has interactions saw the follow-up questions

Appendix H: Knowledge of the dosage adjustments required due to dolutegravir's interactions, by profession, guideline access and training

n=1333[1]	Calcium	Iron	Mg/Al	Carbamazpine	Phenytoin	Metformin	Rifampicin
Profession							
CHW	0.0 (0.0-97.5)	0.0 (0.0-84.2)	0.0 (0.0-97.5)	0.0	0.0	66.7 (9.4-99.2)	50.0 (1.3-98.7)
Counsellor	0.0 (0.0-52.2)	20.0 (0.5-71.6)	0.0 (0.0-45.9)	0.0 (0.0-84.2)	50.0 (7-93)	37.5 (8.5-75.5)	55.6 (21.2-86.3)
Doctor	6.1 (3.8-9.2)	9.1 (6.2-12.8)	30.5 (25.7-35.6)	11.7 (8.3-15.8)	63.6 (58-69)	80.7 (76.6-84.3)	88.7 (85.5-91.4)
Nurse	4.7 (2.7-7.7)	3.8 (1.9-6.6)	31.5 (25.7-37.8)	8.5 (5.7-12.1)	37.8 (32-44)	68.2 (63.6-72.6)	86.1 (82.6-89.1)
Pharmacist	7.8 (3.2-15.4)	5.0 (1.3-12.3)	26.9 (18.2-37.1)	22.5 (13.9-33.2)	53.8 (42-65)	87.0 (78.8-92.9)	91.5 (84.8-95.8)
Training	n=774†	n=717†	n=706†	n=725†	n=610†	n=985†	n=1086†
No training	1.8 (0.4-5.2)	4.0 (1.5-8.5)	26.1 (19.4-33.7)	12.0 (9.5-15.0)	52.2 (48.0-57.0)	80.4 (77.4-83.2)	92.5 (90.5-94.3)
Training received	6.6 (4.7-8.8)	6.9 (5.0-9.3)	31.1 (27.3-35.2)	8.8 (4.9-14.3)	48.9 (40.0-58.0)	58.2 (51.4-64.8)	72.7 (67.1-77.8)
Guideline							
No Access	2.0 (0.3-7.2)	2.2 (0.3-7.7)	22.3 (14.4-32.1)	11.9 (9.4-14.7)	54.2 (50.0-59.0)	79.5 (76.6-82.1)	91.4 (89.4-93.2)
Has Access	6.1 (4.4-8.1)	6.9 (5.0—9.1)	31.2 (27.6-35.1)	7.8 (3.5-14.9)	32.5 (22.0-44.0)	52.7 (44.3-61.0)	66.5 (59.0-73.4)

[1]Blank responses were excluded. †The survey was designed using branching logic. Only those who answered that they were aware of that dolutegravir has interactions saw the follow-up questions

Appendix I: Participant information flyer left at clinics during recruitment visits

EXCITING NEWS FOR NURSES & CHWS!

Your clinic has been chosen to be part of a new training project

You are invited to take part in a research study run by Briony Chisholm, a PhD student and pharmacist at the National HIV & TB Hotline, UCT. The study is funded by an educational grant. We aim to test WhatsApp-based training on some sections of the ART guidelines. Participation is voluntary and if you join the study, you may withdraw at any point.

All participants who complete the sessions and surveys will receive a Certificate of Attendance.

WHAT IS THE STUDY ABOUT?

Microlearning – bite-sized chunks of information – on WhatsApp, wherever you are. We are hoping to prove that this is a good training method to improve access for HCWs, especially in remote areas, and to improve awareness and use of the HIV Hotline for mentorship and clinical help.

WHAT WILL PARTICIPANTS NEED TO DO?

One group will be required to join an online introductory session and then six sessions over three weeks (nurses) or four sessions over two weeks (CHWs) starting on Monday, 9 January 2023.

During these sessions, you will need to be on the WhatsApp group for 10-15 minutes. Sessions will be scheduled between 13:00 and 13:15 on Mondays and Wednesdays (nurses) or Tuesdays and Thursdays (CHWs). The other group will be offered online training at the end of the study.

Both groups will be asked to fill in three short online surveys during the study period. After the training, participants will be invited to join focus groups or interviews, to discuss what you liked and didn't like. This will give us more information on whether you found the training useful and what could improve it. Participation in these will also be entirely voluntary.

Participants will receive data vouchers to cover data costs

Questions? Call/WhatsApp/send a 'please call me' to Briony on 063 336 7893

WHO CAN PARTICIPATE?

Community health workers, counsellors and all cadre of nurses. The study will be conducted on WhatsApp in English, so participants need to have a cell phone with WhatsApp. Data will be provided.

WHERE WILL THE COLLECTED INFO GO?

All electronic data will be stored on UCT's secure servers in password-protected files. Results may be submitted for publication and shared in reports to relevant training organisations. No personal details will be shared.

PRIVACY AND CONFIDENTIALITY

The information gathered here will be collated anonymously and used to try to improve your working experience and support. This study has been reviewed and approved by the UCT Faculty of Health Sciences Research Ethics Committee (HREC 491/2022) and permission to conduct it has been obtained from the Eastern Cape Department of Health.

QUESTIONS

If you have questions about the study, you can contact the study coordinator, Briony Chisholm on 063 336 7896, via WhatsApp, or send her a 'please call me' and she'll call you back.

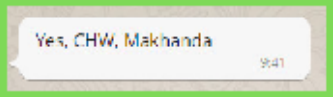
If you have questions about your rights as a participant, you can contact Lamees Emjedi at the Human Research Ethics Committee, Faculty of Health Sciences on 021 406 6338.

NATIONAL HIV & TB HEALTH CARE WORKER HOTLINE
0800 212 506

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

HOW TO PARTICIPATE

If you consent to participate in this training project, please send a WhatsApp saying: 'YES, cadre, town' to 063 336 7896 e.g.



Questions/no data? Send a 'please call me' to Briony on 063 336 7896 and she'll call you back

Appendix J: TIDieR checklist for WhatsApp-based training intervention

The TIDieR (Template for Intervention Description and Replication) Checklist:

	Item	Where located Page number
	BRIEF NAME	
1.	Provide the name or a phrase that describes the intervention.	34-36
	WHY	
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	131-133
	WHAT	
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	254-255
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	257-279
	WHO PROVIDED	
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	28-29
	HOW	
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	131-133
	WHERE	
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	127-128
	WHEN and HOW MUCH	
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	129-130
	TAILORING	
9.	If the intervention was planned to be personalised, titrated, or adapted, then describe what, why, when, and how.	N/A
	MODIFICATIONS	
10.	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A
	HOW WELL	
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	137
12.	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	149-152

Appendix K: Lesson plan for nurses

Intro: Basic interaction explanation	Welcome to the microlearning project and thank you for being a part of it. We hope that you will find it useful and interesting. A quick introduction: I am Briony Chisholm, and I have been one of the pharmacists answering queries at the National HIV & TB HCW Hotline at UCT since it started in 2008. I'm now doing my PhD with this project which, I hope, will improve support and access to training, especially to those in more remote areas. Some admin: At the end of the six sessions, you will be asked to complete a survey. In three months, you will be asked to do another survey, after which you will be directed to a second form which you can fill out to receive your **OBJECTIVES** 1. Understand the basics of how drugs interact with each other 2. Understand the interactions between dolutegravir and: a. Rifampicin (TB) b. Calcium, iron, antacids c. Carbamazepine/phenytoin/phenobarbitone (epilepsy) d. Metformin (diabetes/sugar) 3. Learn how to adjust dosing when you have patients on the combinations 4. Learn about the use of dolutegravir in women of childbearing potential (WOCP) 5. Learn about giving TPT to clients starting ART 6. Learn about the HIV Hotline and its availability for clinical support **certificate of attendance.** These details will not be linked to your survey answers, to protect your anonymity. The objectives and what you'll be learning: **So, what does 'drug-drug interactions' mean?** When two or more drugs are used together, they can affect the way each other work. Enzymes (mainly in the liver) can be induced (made to work more) or inhibited (stopped from working) by drugs. This may change how other drugs are metabolised (broken down) causing an increase or decrease in levels of the drug(s) and/or causing side effects.

	Dolutegravir (DTG) has fewer interactions than many other ARVs, but it does have important interactions with some commonly used drugs, that require us as HCWs to adjust dosing. **Q1.** Any ideas of which drugs can interact with DTG? *Commonly used drugs that interact with DTG include rifampicin, calcium, iron, metformin, magnesium/aluminium (antacids) and some antiepileptic drugs.* Drug interactions can result in suboptimal drug levels (too low) which can cause: • an elevated viral load • drug resistance, due to replicating virus in the presence of suboptimal drug levels For pregnant mothers, this could increase the risk of mother-to-child transmission. Over the next six sessions, we'll learn about dolutegravir's interactions, using dolutegravir in women of childbearing potential and TPT. Sessions will be 15 minutes max: we know how busy you are! See you on Monday at 13:00. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** When two or more drugs are used together, they can affect the way each other work. Enzymes (mainly in the liver) can be induced (made to work more) or inhibited (stopped from working) by other drugs. This may change how other drugs are metabolised (broken down) causing an increase or decrease in levels of the drug(s) and/or causing side effects. DTG has fewer interactions than many other ARVs, but it does have

	important interactions with some commonly used drugs, that require us as HCWs to adjust dosing. Drug interactions can result in suboptimal drug levels (too low) which can cause: • an elevated viral load • drug resistance, due to replicating virus in the presence of suboptimal drug levels For pregnant mothers, this could increase the risk of mother-to-child transmission. Commonly used drugs that interact with DTG include rifampicin, calcium, iron, metformin, magnesium/aluminium (antacids) and some antiepileptic drugs.
Lesson 1: DTG in WOCP	Welcome back! Let's start. Today we're going to look at the use of dolutegravir in women. We'll start with a case: Maria, 26, has come into the clinic to book her first pregnancy and has tested positive for HIV. She is 5 weeks pregnant and has received counselling and says she is ready to start ARVs. **Q1.** Which ARVs should we recommend for her? *Maria should be offered TLD.* **Q2: (Expect questions on using DTG in WOCP/pregnancy. In case nobody asks, will have extra person in group to post):** The guidelines say DTG is contraindicated in women wanting to fall pregnant and in pregnancy < 6 weeks. They say women of childbearing potential (WOCP) should be counselled regarding the risk of neural tube defects (NTDs) and be allowed to make an informed choice. *That is true. Initial data showed there may be a risk of neural tube defects with DTG. As more data came out, it has been shown that the benefits of DTG outweigh the risks. In June 2021 the NdoH sent out a circular (2021/06/29/EDP/01) stating:* *"DTG is therefore recommended as part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential."*

	In other words, evidence has shown that there is no increased risk for NTDs on DTG-containing regimens and the new guidelines – which will be out soon- recommend TLD for all adults and adolescents, including pregnant women and those who wish to fall pregnant. **Q3:** Why do we prefer TLD as a first choice? *Dolutegravir causes rapid viral suppression, which protects the baby. It also has a high barrier to resistance.* **Q4:** Maria is clinically well and shows no symptoms of TB on screening. Should we do a GXP for her? *Yes. A TB GeneXpert should be done for all HIV-positive women at first visit to the antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women.* **Q4.** After Maria has had her baby, can she use the OC? *Yes, she can use the OC. There is no interaction between DTG and the oral contraceptive.* See you on Wednesday at 13:00. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** Looking at the use of dolutegravir in women of childbearing potential and pregnant women: While initial data showed there may be a risk of neural tube defects with DTG, as more data came out, it has been shown that the benefits of DTG outweigh the risks.

	TLD is preferred as the first choice in pregnant women and women of child-bearing potential because dolutegravir causes rapid viral suppression, which protects both the baby and the mom. It also has a high barrier to resistance. While we're talking about reproductive health, a note that dolutegravir does NOT interact with the oral contraceptive. Women on DTG-based regimens can use oral contraceptives, if that is their choice of contraception. A last note: do remember that the TB symptom screen has lower sensitivity in pregnant women, so a TB GeneXpert should be done for all HIV-positive women at their first visit to the antenatal clinic.
Lesson 2: TPT	Hi everyone! Let's get started on our second lesson. **Case:** Sara, 25, has been diagnosed with HIV today. She has been counselled and is starting TLD. She was treated for TB in 2010 and has been well since. **Q1:** Should TB preventive therapy (TPT) be considered for Sara? *Yes. All clients starting ART, or already on ART, and who have not yet received TPT, should be considered for TPT.* **Q2:** Do we need to wait for Sara's CD4 count, before deciding whether she needs TPT? *No, TPT is given to all clients who haven't had it before, regardless of CD4 count.* **Q3:** If Sara was pregnant, do we need to check her CD4 count before starting TPT? *Yes. TPT is only given in pregnancy if the CD4 is under 350. For pregnant women with a CD4 above 350, TPT is deferred until 6 weeks after the baby is born.* 

	Q4: What do we need to check before starting Sara on TPT? *We need to exclude TB (screen for symptoms) and exclude any contraindications to TPT: active liver disease, alcohol abuse, or known hypersensitivity to isoniazid. If she's pregnant, we need to do a Gene Xpert test.* Have a lovely weekend. See you on Monday at 13:00. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** All clients starting ART, or already on ART, and who have not yet received TPT, should be considered for TPT, regardless of CD4 count, unless the client is a pregnant woman. TPT is only given in pregnancy if the CD4 is under 350. For pregnant women with a CD4 above 350, TPT is deferred until 6 weeks after the baby is born. Before giving TPT to any client, we need to exclude TB (screen for symptoms) and exclude any contraindications to TPT, which include active liver disease, alcohol abuse, or known hypersensitivity to isoniazid.
Lesson 3: DTG/ rifampicin	Welcome back! I hope you all had a good weekend. Let's get right to it. **Case:** Thando, 65, has been on TLD for six months and has tolerated it well, taking it at night. He has come to the clinic complaining of night sweats and coughing over the past three weeks. GeneXpert comes back positive for TB, rifampicin sensitive. Thando will be started on TB treatment (RHZE) today. **Q1.** Do we need to adjust Thando's TB medicine dosing due to his being on DTG? *No, the DTG does not interfere with RHZE.* **Q2.** Do we need to adjust Thando's ARV dosing due to his being on RHZE? *Yes, rifampicin can lower the levels of DTG, so we need to adjust the DTG*

dose. This happens because rifampicin is an enzyme inducer. This means that rifampicin makes the enzymes work more which, in turn, causes increased metabolism (breakdown) of DTG and lower levels of it.

Q3. How do we adjust Thando's DTG dosing?
We need to double the dose of DTG to make sure his levels remain high enough to work against the HIV. This means he needs to get DTG 50 mg twice daily (every 12 hours). Thando will take 50 mg DTG in the morning and then continue taking his TLD at night (12 hours later). He will continue with this double dosing until two weeks after stopping his rifampicin.

Q4. Any questions on the DTG/rifampicin interaction?

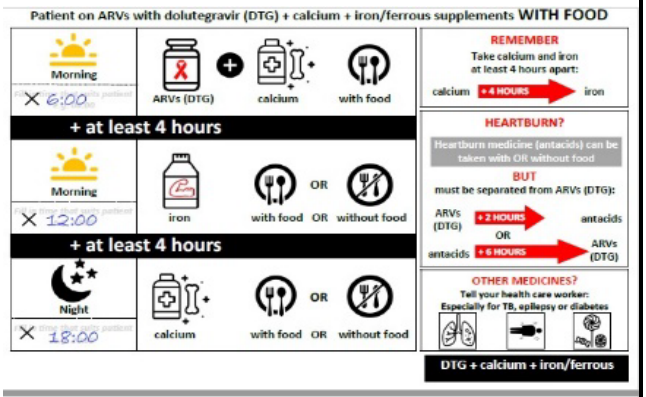
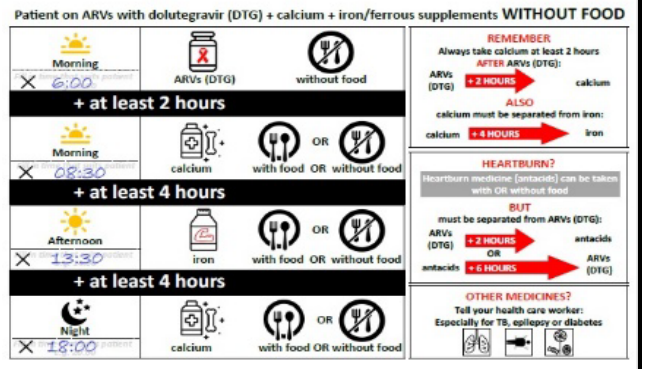
See you on Wednesday at 13:00.

If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs.

Voice note recap: Looking at the dolutegravir-rifampicin interaction: rifampicin can lower the levels of DTG, so we need to adjust the DTG dose. This happens because rifampicin is an enzyme inducer. This means that rifampicin makes the enzymes work more which, in turn, causes increased metabolism (breakdown) of DTG and lower levels of it. To counteract this interaction, we need to double the dose of DTG to make sure its levels remain high enough to work against HIV. This means clients on rifampicin need to get DTG 50 mg twice daily (every 12 hours). As an example, the client will take 50 mg DTG in the morning and then continue taking his TLD at night (12 hours later). This double dosing will be continued until two weeks after stopping rifampicin.

Lesson 4: DTG/anti-epileptic drugs and metformin	Hi everyone! Let's start. **Case:** Elizabeth is 32-years old and has just been diagnosed with epilepsy after a head injury. She is RVD-positive and virologically suppressed on TLD. The clinic she attends often struggles with medicine stock and currently only has stock of carbamazepine. **Q.** What would the best option to treat Elizabeth's epilepsy be? *Ideally, a plan needs to be made to get lamotrigine, levetiracetam or topiramate, as they do not interact with DTG. Carbamazepine is best avoided. This is because they induce enzymes involved in the breakdown of DTG.* **Q.** If we have to use carbamazepine, here, how do we adjust the dosing of carbamazepine and/or DTG? *Elizabeth's DTG dose will need to be doubled to 50 mg twice daily because carbamazepine lowers DTG levels.* **Q.** Why are we not using sodium valproate? *While sodium valproate does not interact with DTG, it is contraindicated in women of childbearing potential because it can cause birth defects. Sodium valproate would be a good choice only in men and in women who are no longer of childbearing potential.* **Q.** Any questions on the DTG/anti-epileptics interaction? **Moving on to our second case:** Thandi, 36, has been diabetic for years and is well controlled on 850 mg metformin twice daily. She has now been diagnosed with HIV and will be starting TLD. **Q.** Are there any concerns with Thandi taking metformin with her TLD? *Yes, DTG increases metformin levels due to it inhibiting a transporter that helps eliminate metformin. This could result in increased side effects.* **Q.** How would we adjust her dosing of TLD or metformin or both? *Her TLD dosing will remain the same: one tablet daily. Her metformin will*

	need to be dropped to 500 mg twice daily and her diabetic control monitored. No more than 500 mg metformin twice daily (12-hourly) should be taken by people on DTG-containing regimens. Any questions on the DTG/metformin interaction? See you next week for our last two sessions. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** When looking at anti-epileptic drugs for patients on DTG-based regimens, we need to consider drug-drug interactions. **C**arbamazepine is best avoided. This is because they induce enzymes involved in the breakdown of DTG, causing lower levels of DTG. Ideally, a plan needs to be made to get sodium valproate, lamotrigine, levetiracetam or topiramate, as they do not interact with DTG. If carbamazepine is the only option, the DTG dose will need to be doubled to 50 mg twice daily because carbamazepine lowers DTG levels. An important note on sodium valproate: it is contraindicated in women of childbearing potential because it can cause birth defects. Sodium valproate would be a good choice only in men and in women who are no longer of childbearing potential. Thinking of our diabetic patients on metformin and DTG: DTG increases metformin levels due to it inhibiting a transporter that helps eliminate metformin. This could result in increased side effects. No more than 500 mg metformin twice daily (12-hourly) should be taken by people on DTG-containing regimens.

Lesson 5: DTG/ cations	Welcome back! Let's get right to it. Today, we've got two cases. **Case:** Priscilla is a 30-year-old woman who is 20 weeks pregnant. She is on TLD once daily, which she takes in the morning, and takes calcium (1 g twice daily) because she's pregnant. Today, her Hb is low, so we want to give her iron (ferrous fumarate 200 mg daily). **Q1.** How should we tell Priscilla to take her medicines? *Priscilla needs to take her TLD with food and her calcium in the morning, iron at lunchtime and second dose of calcium at night. Calcium and iron also affect each other's absorption, so they need to be separated by at least four hours.*   What if she has no food? *If she has no food, she should take her TLD first thing, then her calcium at least two hours later. She can then take her iron at lunchtime (at least four hours after her calcium) and her other calcium in the evening. You can use our patient booklet to help Priscilla remember (jpeg):* *To fill out the form, chat to Priscilla about how her day runs, and fill in times that suit her (see Xs and blue writing) and give her the sheet to take home.* *If you would like more copies of the DTG patient handout booklet, please send me a message after this session and I will organise to get you some.*

Q2. Why do we need to do this?

*Calcium and iron supplements decrease DTG concentrations if taken together **on an empty stomach**.*

Q3. Any questions on the DTG/calcium/iron interaction?

Okay, let's move onto the second case.

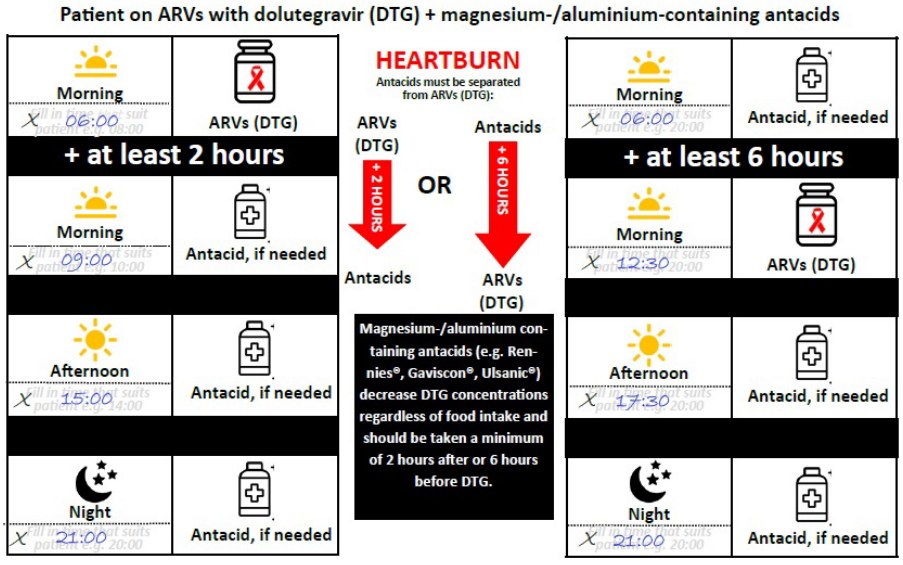
Case: John, who is 54-years old, comes to the clinic for his routine visit. He is doing well on TLD once daily but has been struggling with heartburn, so he's been taking an antacid (sucralfate) three times a day.

Q1. What do we need to be aware of here?

Magnesium/aluminium/sucralfate containing antacids (e.g. Rennies®, Gaviscon®, Ulsanic®) decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG.

Q2. How should we advise John to take his medicine?

He should take his TLD in the morning and take his antacid at least two hours after OR take his antacid first thing in the morning and wait at least six hours before taking his TLD. Here you can see how we'd plan his dosing after asking what his usual day looks like:



Q3. Any questions on the DTG/antacids interaction?

See you on Wednesday at 13:00 for our last session: a summary of what we've learnt.

If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs.

Voice note recap: Calcium and iron supplements decrease DTG concentrations if taken together on an empty stomach. If clients are taking both TLD and calcium **OR** iron, they must be taken together, with food. If the client has no food, they should take their TLD first thing, then calcium **OR** iron at least two hours later. If they are taking both calcium **AND** iron, we must remember to counsel them that iron and calcium can't be taken together. They must be separated by at least four hours. An example, if the client has no food, would be: TLD, first thing, let's say at 6:00AM, wait at least two hours, and take calcium at 8:30AM; then have at least four hours between the calcium and iron, so take the iron at 1:00PM and the second dose of calcium can be taken in the evening.

Magnesium/aluminium/sucralfate containing antacids (e.g. Rennies®, Gaviscon®, Ulsanic®) decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG.

Lesson 6: Summary	Hi everyone! Let's get started on our last session. **In summary:** Dolutegravir-based regimens are the preferred first line ART regimen for all adults and adolescents living with HIV, **including pregnant women and women of child-bearing potential.** All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), **should be considered for TPT**. Prior to initiating TPT, active TB should be ruled out by screening for TB symptoms. In pregnant women with a CD4 above 350, TPT is deferred until 6 weeks after delivery. When two or more drugs are used together, they can affect the way each other work. Enzymes (mainly in the liver) can be induced (made to work more) or inhibited (stopped from working) by drugs. This may change how other drugs are metabolised (broken down) causing an increase or decrease in levels of the drug(s) and/or causing side effects. DTG has fewer interactions than many other ARVs but it does have interactions with some commonly used drugs, that require us as HCWs to adjust dosing. This is the summary table from the NDOH Guidelines (Page 9):

Interacting Drug	Effect of Co-Administration	Recommendation
Rifampicin	↓ Dolutegravir	Double DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose
Polyvalent cations (Mg^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) e.g. antacids, sucralfate, multivitamin and nutritional supplements	↓ Dolutegravir	Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food. Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. However, calcium and iron supplements must be taken at least 4 hours apart. Magnesium/aluminium containing antacids decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG
Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin	↓ Dolutegravir	Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Remember that valproate is contra-indicated during pregnancy. Double DTG dose to 50 mg 12-hourly for carbamazepine if an alternative anticonvulsant cannot be used
Metformin/DTG	↑ Metformin	DTG increases metformin levels. Maximum metformin dose 500 mg 12-hourly

Any questions?

With that, the sessions are done! We hope that you found it useful and interesting, and we will be very grateful if you could fill in the survey at [url]. Please be completely honest so we know how to improve it! At the end of the survey, you'll be asked if you're willing to be part of a focus group with me, to discuss what you liked and didn't like about the training. This is completely voluntary, but we'd love for you to say yes, so we can see if it was useful and take suggestions for improvements: your opinion is valuable!

	You will receive another survey in three months' time, after which you'll be directed to a second form which you can fill out to receive your certificate of completion. These details will not be linked to your survey answers, to protect your anonymity. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **In summary (voice):** **Voice note recap:** Dolutegravir-based regimens are the preferred first line ART regimen for all adults and adolescents living with HIV, **including pregnant women and women of child-bearing potential.** All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), **should be considered for TPT**. Prior to initiating TPT, active TB should be ruled out by screening for TB symptoms. In pregnant women with a CD4 above 350, TPT is deferred until 6 weeks after delivery. When two or more drugs are used together, they can affect the way each other work. Enzymes (mainly in the liver) can be induced (made to work more) or inhibited (stopped from working) by interacting drugs. This may change how other drugs are metabolised (broken down) causing an increase or decrease in levels of the drug(s) and/or causing side effects. DTG has fewer interactions than many other ARVs but it does have interactions with some commonly used drugs, that require us as HCWs to adjust dosing, see the summary table from the NDOH Guidelines, above, for interacting drugs, and how to adjust dosing.

Appendix L: Lesson plan for CHWs

Intro: Basic interaction explanation	Welcome to the microlearning project and thank you for being a part of it. We hope that you will find it useful and interesting. A quick introduction to me: I am Briony Chisholm and have been one of the pharmacists answering queries at the National HIV & TB HCW Hotline at UCT since it started in 2008. I'm now doing my PhD with this project which, I hope, will improve support and access to training, especially to those working in more remote areas. Learning goals: **OBJECTIVES** 1. Understand that drugs can interact with each other 2. Know which drugs interact with dolutegravir: a. Rifampicin for TB b. Calcium, iron, antacids c. Some drugs for epilepsy and diabetes/sugar 3. Learn about the use of dolutegravir in women of childbearing potential (WOCP) 4. Learn about TPT in clients starting ART 5. Know which patients to refer back to clinic for review 6. Learn about the HIV Hotline and its availability for clinical support Some admin: At the end of the four sessions, you will be asked to complete a short survey. You'll be asked again in three months and, after that survey, you'll be directed to a second form which you can fill out to receive your **certificate of attendance.** These details will not be linked to your survey answers, to protect your anonymity. Today we'll just be talking about what drug-drug interactions mean. When two or more drugs are used together, they can affect the way each other work. This can cause an increase or decrease in levels of the drug(s) meaning that they may not work or there may be more side effects.

	Dolutegravir (e.g. TLD), the new ARV, has fewer interactions than many other ARVs but it does have interactions with some commonly used drugs, that we all need to be aware of. As Community Health Workers, you interact with clients all day, often in their homes, so you are a very important part of making sure clients on ARVs take their medicines properly and safely. **Q1.** Any ideas of which drugs can interact with DTG? *Commonly used drugs that interact with DTG include rifampicin for TB, calcium and iron, which is often taken during pregnancy, metformin for diabetes, antacids and some drugs for epilepsy.* Over the next three sessions, we'll learn about dolutegravir's interactions, using dolutegravir in women and TPT. Sessions will be 10 minutes max: we know how busy you are! See you on Monday at 13:00. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** When two or more drugs are used together, they can affect the way each other work. This can cause an increase or decrease in levels of the drug(s) meaning that they may not work or there may be more side effects. This is called drug-drug interactions. Commonly used drugs that interact with DTG include rifampicin for TB, calcium and iron, which is often taken during pregnancy, metformin for diabetes, antacids and some drugs for epilepsy.

Lesson 1: DTG in women and TPT	Welcome back! Let's get to it. We're going to discuss one case and one learning point today. **Case:** You check in on Maria, 36, who is pregnant with her third child but has not yet booked her pregnancy. She knows she has HIV but hasn't been back to the clinic to start ARVs because she's worried they'll harm her baby. **Q1.** What should we recommend for Maria? *We should recommend that Maria go to the clinic to start ARVs because if she doesn't take ARVs to suppress her HIV, it may pass on to her baby.* **Q2: (Expect questions on using DTG in WOCP/pregnancy. In case nobody asks, will have extra person in group to post):** They say that DTG can harm the baby, so how can we recommend that? *Thank you for bringing that up. At the beginning, it was thought that DTG (in TLD) may be a risk to the baby. As more information has come out, it has been shown that this is not such a concern and that the benefits outweigh the risk. In June 2021, the NDOH sent out a circular that says:* *"DTG is therefore recommended as part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential."* We need to encourage Maria to go to the clinic as soon as possible, to start ARVs to protect both her and her baby. **Q3:** Any questions? **Learning point:** All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), should be considered for TPT. **Q1:** How can you, as CHWs, help with this? *When checking in on clients, ask them if they've received TPT. If they haven't, or they're not sure, refer them to the clinic, to discuss this with the nurse.*

	That's all for this week, see you on Thursday at 13:00. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** TLD is preferred as the first choice in pregnant women and women of child-bearing potential because dolutegravir causes rapid viral suppression, which protects both the baby and the mom. It also has a high barrier to resistance. We need to encourage all pregnant women to book their pregnancies early and go on ART if they need it, as soon as possible, to keep themselves and their babies healthy. All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), should be considered for TPT.
Lesson 2: DTG/ rifampicin	Hi everyone! Welcome back. Let's get started. **Case:** Thando, 65, has been on TLD since October 2021 and has tolerated it well, taking it in the morning. He now has TB and was started on RHZE. He lives alone and you visit him daily at home, to make sure he is remembering to take his ARVs and TB medication. **Q1.** Thinking of interactions, what do we need to be aware of? *The rifampicin in the TB medicine can lower the levels of dolutegravir (ARV). While he's on TB treatment he needs an extra dose of dolutegravir.* **Q2.** How do we check? *We need to ask Thando if he's taking ARVs twice daily. If he is not, we need to ask him to go to the clinic and speak to the nurse.* **Q3.** Any questions on the DTG/rifampicin interaction?

	See you on Tuesday at 13:00. Enjoy your weekend. If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs. **Voice note recap:** When thinking about our patients on DTG and TB treatment, we need to remember that the rifampicin in the TB medicine can lower the levels of dolutegravir. While he's on TB treatment he needs an extra dose of dolutegravir. We need to ask our clients on both DTG and rifampicin if they are taking ARVs twice daily. If they are not, we need to ask them to go to the clinic and speak to the nurse.
Lesson 3: DTG interaction	Hi everyone! Today we're going to talk about which clients we need to look out for, when thinking about the ARV, dolutegravir's, interactions with other medicines. **Case:** Priscilla is a 30-year-old woman who is 20 weeks pregnant. She is on TLD once daily and takes calcium and iron because she's pregnant. She sometimes takes antacids because she gets heartburn. She buys her own calcium, iron and antacids from Shoprite in town. **Q1.** What do we need to be aware of? *Calcium, iron and antacids can lower the levels of the ARV, dolutegravir, if taken together. There are ways to take them that will lower this risk, so it's important to ask clients if they're taking any of these. Priscilla needs to speak to the nurse at the clinic, as soon as possible, about how best to take her medicines.*

Q2. Can Priscilla take her calcium and iron together?
No. Calcium and iron also affect each other's absorption. They need to be taken at least four hours apart.

Q3. Any questions on the DTG/calcium/iron interaction?

Q4. Clients with which other conditions do we need to look out for when thinking about dolutegravir's interactions?
Clients with epilepsy and/or diabetes.

Q5. Why do we need to be aware of these clients specifically?
Dolutegravir interacts with some medicines used to treat diabetes and epilepsy. The interactions mean that clients' epilepsy and diabetes medicine may need to be changed or how they take it may need to be changed.

Q6. What should we do for these clients?
We need to advise these clients to speak to the nurse or doctor at the clinic about whether they are still on the right medicine, at the right dose, for their epilepsy and/or diabetes, now that they're taking the ARV, dolutegravir.

Q7. Any questions?

See you on Thursday at 13:00 for the last session.

If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs.

Voice note recap: To recap what we learnt today, calcium, iron and antacids can lower the levels of the ARV, dolutegravir, if taken together. There are ways to take them that will lower this risk, so it's important to ask clients if they're taking any of these. If they are, they need to be referred to

	the nurse at the clinic, as soon as possible, to ask about how best to take their medicines. Dolutegravir interacts with some medicines used to treat diabetes and epilepsy. The interactions mean that clients' epilepsy and diabetes medicine may need to be changed or how they take it may need to be changed. We need to advise these clients to speak to the nurse or doctor at the clinic about whether they are still on the right medicine, at the right dose, for their epilepsy and/or diabetes, now that they're taking the ARV, dolutegravir.
Lesson 4: Summary	Hi everyone! Today, in our last lesson, we're going to just summarise what we've learnt: Dolutegravir-based regimens are the preferred first line ART regimen for all adults and adolescents living with HIV, **including pregnant women and women of child-bearing potential.** All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), **should be considered for TPT**. Prior to initiating TPT, active TB should be ruled out by screening for TB symptoms. If clients have not received it, they should be referred to the clinic. With our clients who are on dolutegravir, e.g. TLD, we need to look out for: • Clients on tuberculosis (TB) treatment • Diabetic clients (high blood sugar) • Clients with epilepsy • Clients on calcium, iron, heartburn medicines • We need to especially check in with pregnant clients who might be taking calcium, iron or heartburn meds that they're buying themselves All of these clients should be advised to check in with the nurse at the clinic to make sure they're taking them correctly. **Voice note recap:** To summarise all we've learnt: dolutegravir-based regimens are the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-

	bearing potential. All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), should be considered for TPT. If clients have not received it, they should be referred to the clinic. With our clients who are on dolutegravir, e.g. TLD, we need to look out for clients on tuberculosis (TB) treatment; diabetic clients (high blood sugar); clients with epilepsy; clients on calcium, iron, heartburn medicines and we need to especially check in with pregnant clients who might be taking calcium, iron or heartburn meds that they're buying themselves. All of these clients should be advised to check in with the nurse at the clinic to make sure they're taking them correctly. With that, the sessions are done! We hope that you found it useful and interesting, and we will be very grateful if you could fill in the survey at [url]. Please be completely honest so we know how to improve it! Remember, results won't be linked to your name in any reporting – you will remain anonymous. At the end of the survey, you'll be asked if you're willing to be part of a focus group with me, to discuss what you liked and didn't like about the training. This is completely voluntary but we'd love for you to say yes, so we can see if it was useful and take suggestions for improvements: your opinion is valuable! In three months' time, you'll be sent another survey, after which you'll be directed to a second form which you can fill out to receive your **certificate of attendance**. Again, these details will not be linked to your survey answers in reporting, to protect your anonymity.  If you need help with your HIV- and/or TB-infected clients, feel free to contact the **National HIV & TB HCW Hotline**. Toll-free calls to **0800212506** or WhatsApp/send a 'please call me' to **0718401572**. They are there to give **free** clinical support to HCWs.

Appendix M: Pilot study participant semi-structured interview questions

1. Did you manage to join?
2. If not, what was difficult?
3. Were sessions at a reasonable time?
4. Were sessions too long/short?
5. Were sessions easy to understand and follow?
6. Were any of the learning points too complicated?
7. Was there enough time between messages/questions?
8. Were the learning points easy to understand?
9. Were the surveys easy to do?
10. Any other comments or suggestions?

Appendix N: Nurses' knowledge questions (pre- and post-intervention)

HIV Guidelines

In this section, we'll ask ten questions on dolutegravir (DTG). Please answer the questions honestly, with what you know. There is no pass/fail mark.

1. Can women of childbearing potential (WOCP) and pregnant women use dolutegravir-based ART regimens, such as TLD?

Choose one of the following answers

Yes

I'm not sure

No

2. A woman on dolutegravir (DTG) asks to take the oral contraceptive (OC) for contraception. What would you say?

Choose one of the following answers

No, there is an interaction between DTG and the OC: another form of contraception, e.g. the Depot injection, must be used

Yes, they can be used together, but only a high-dose OC

Yes, the OC can be used with DTG

I'm not sure

3. Should all women at their first antenatal visit be tested for TB with a Gene Xpert test (GXP)?

Choose one of the following answers

No

Yes

I'm not sure

---

4. Should all non-pregnant clients starting on ART – who have not received TB preventive therapy (TPT) before – get TPT?

Choose one of the following answers

No

I'm not sure

Yes, after excluding TB and contraindications to TPT

---

5. Which of the following ways to take dolutegravir (DTG) and calcium (e.g. calcium gluconate) would you tell your clients to use?

Choose one of the following answers

I'm not sure

Take them together, with food

Take them together, on an empty stomach

No dosing adjustment of either necessary

---

6. How would you counsel the client who is taking dolutegravir (DTG) and a magnesium- and/or aluminium-containing antacid e.g. Milk of Magnesia, sucralfate?

Choose one of the following answers

Take antacids at least 2 hours before or 6 hours after DTG

Take antacids at least 2 hours after or 6 hours before DTG

Take them together, with food

I'm not sure

---

7. For clients who are on dolutegravir (DTG) and rifampicin, how would you adjust dosing of the two medicines?

Choose one of the following answers

I'm not sure

No dose adjustment of either is necessary

Double the DTG dose to 50 mg 12-hourly, i.e. TLD + DTG 50 mg 12 hours later

Double the dose of rifampicin, by weight, i.e. RHZE + rifampicin 12 hours later

---

8. In clients who are on dolutegravir (DTG) and metformin, what dosage of metformin would you use?

Choose one of the following answers

No less than 500 mg metformin 12-hourly

They should not be used together

No more than 500 mg metformin 12-hourly

I'm not sure

---

9. In clients who are on dolutegravir (DTG) and carbamazepine, how would you adjust dosing of the two medicines?

Choose one of the following answers

No dose adjustment of either is necessary

They should not be used together, unless there is no other option. If no other option, double the dose of DTG to 50 mg 12-hourly

I'm not sure

They should not be used together, unless there is no other option. If no other option, double the current dose of carbamazepine

---

10. Should pregnant women with a CD4 count under 350 cells/µL get TB preventive treatment (TPT)?

Choose one of the following answers

Yes

I'm not sure

No

Appendix O: CHWs knowledge questions (pre- and post-intervention)

HIV Guidelines

In this section, we'll ask seven true/false questions. Please answer the questions honestly, with what you know. **There is no pass/fail mark.**

Dolutegravir (DTG) is the newest ARV that most clients are being started on/switched to.

The most commonly used fixed-dose combination is called **TLD**.

1. Women of childbearing potential and pregnant women can use dolutegravir-based ART regimens, such as TLD.

Choose one of the following answers

I'm not sure

False

True

2. It's important for clients who are on dolutegravir-containing ARVs and also taking calcium or iron, to have their medicines reviewed by the nurse/doctor.

Choose one of the following answers

False

I'm not sure

True

3. Clients taking both iron (ferrous) and calcium can take them at the same time.

Choose one of the following answers

False

I'm not sure

True

---

4. Antacids (medicines used to treat heartburn) may interact with dolutegravir, so it's important to ask clients if they're taking them. Those who are, should be referred to the nurse/doctor, to discuss how to take them together.

Choose one of the following answers

False

I'm not sure

True

---

5. A person taking ARVs that include dolutegravir, e.g. TLD and RHZE (Rifafour or Rifinah) for TB can continue on their normal dose of TLD, once a day.

Choose one of the following answers

I'm not sure

True

False

---

6. It's important for clients with diabetes (blood sugar), who are on dolutegravir-containing ARVs, to have their diabetic medicines reviewed by the nurse/doctor.

Choose one of the following answers

I'm not sure

False

True

---

7. It's important for clients with epilepsy, who are on dolutegravir-containing ARVs, to have their epileptic medicines reviewed by the nurse/doctor.

Choose one of the following answers

True

False

I'm not sure

Appendix P: Semi-structured focus group questions

Training: First, let's each share our first name and our home language. I am Briony, and my home language is English. Okay, we're going to talk a bit about the WhatsApp lessons we did together.

1. How did you feel about what you learned and what was taught in the lessons?
2. Do you think that the training has changed how you do your day-to-day duties, treating clients on ARVs?
3. We did the sessions at 13:00. How did you feel about the time and length of the training sessions?
   Prompts: did it feel too long? Too short? Do you have ideas for how long it should be in future?
4. How did you feel about the training being 'live' or in real time?
5. What did you think of the WhatsApp group?
   Prompts: Was it comfortable interacting there? Was it useful to have everyone's input during the lessons? Why or why not?
6. Did you share the messages and/or voice notes with colleagues not in the training?
7. Did you experience any challenges during the training sessions?
   If so: Can you tell me a bit about these challenges?
8. Would you be interested in this kind of training if it happened every week throughout the year?
9. If the training was happening weekly, what would make it easier for you to join it?
10. Do you have any suggestions/comments/complaints about the training that we haven't talked about?
11. Thinking about training on HIV, what training have you had before we did the lessons?
    Prompts: What kinds of training did you get, how often did you get training, did you

feel like you got enough training, what kinds of training do you wish you had more of etc.

HIV Hotline and mentorship: We are now going to talk a bit about the HIV Hotline and your feelings about mentorship. When I say “mentorship” I mean the clinical support you get when you discuss case management or the correct use of guidelines with senior colleagues

1. How do you feel about the mentorship and support you get at the moment?
   Prompt: is there enough support for you? Are there a few people you can talk to about these things or only one person? Is it easy or difficult to talk with that person when you need to?
2. How do you feel about the HIV Hotline as a form of mentorship and support?
   Prompt: where did you hear about it, what do you know about it at the moment etc.
3. Has anyone here used the HIV Hotline? If yes:
    a. What was your experience of using the HIV Hotline?
       Prompts: describe what happened one time that they used it; the same each time or different
4. Do you have any suggestions/comments/complaints about the HIV Hotline?

Is there anything you’d like to say that we didn’t ask?

Appendix Q: Reflexivity diary

Baseline

At the start of the study, reflecting on the assumptions and values that shape me, I acknowledged my and the participants' significantly differing circumstances and contexts.

I am white; middle-aged; female; and physically disabled (quadriplegic). I come from a position of privilege, having grown up financially stable and remaining so. English is my first language; I speak Afrikaans fluently; but do not speak isiXhosa. I have postgraduate qualifications and am currently doing my PhD.

I was accompanied only by the research assistant, who has no clinical experience. She was present in all of the focus groups, but did not participate, other than to record and take notes. She is a white, middle-aged woman from a privileged background; fluent in English and Afrikaans, with some basic isiXhosa.

I am a healthcare worker (pharmacist), but I have worked only in academia. I do have some 'inside knowledge'/perspective due to having worked on the National HIV and TB Healthcare Worker's Hotline for the last 18 years, so having (telephonic) contact with nurses within this sector. I would call it 'Ivory Tower' experience of the public health system.

I would be considered an outsider researcher.

My pre-conceived ideas: HIV training of healthcare workers is not happening, and is difficult; resources, including human resources, at the study clinics are limited.

After the recruitment visits and focus groups

My personal circumstances (see Baseline) stand in stark contrast to most of the study participants who, mostly, come from previously disadvantaged groups. They are, in the majority, Black or Coloured people who speak isiXhosa and Afrikaans, from low-income backgrounds, and remain poorly resourced, financially.

Most participants have some tertiary qualification (nurses) or, at most, secondary school qualifications (CHWs). There was a degree of power dynamics, as I was perceived by many as coming from/being in a ‘higher’ and/or governmental position (which I clarified wherever possible as not true). This also came with some degree of suspicion.

My pre-conceived ideas – that HIV training of healthcare workers is not happening, and is difficult; resources, including human resources, at the study clinics are limited – all seemed relatively accurate, but to an even greater degree than I expected. Human resources, mentorship/support and HIV training were all huge challenges in the setting.

During qualitative analysis

I am a relatively new researcher, with this project being my first that includes both field work and a qualitative component. This means that I come from an essentially positivist, quantitative, background but have done extensive reading to familiarise myself with the vast array of qualitative analyses and methodologies.

While I am drawn to analyse this data from a purely qualitative point of view, I realised that the nature of the project, and what I hope to report on, requires slightly less in-depth analysis, so chose predominantly descriptive template analysis with some *a priori* themes.

Throughout the template analysis, I tried to keep putting my assumptions and values to the test. Being a PhD student without resources to employ a second coder, I went through the processes of the transcription and analysis of the qualitative data over six months, leaving it for significant periods between the six steps to ensure that I could look at it with ‘fresh eyes’.

Appendix R: HREC approval for WhatsApp-based training intervention study

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

09 September 2022

HREC REF: 491/2022

Prof C Orrell
Desmond Tutu Health Foundation
IDM - FHS
Email: Catherine.orrell@hiv.research.org.za
Student: briony.chisholm@uct.ac.za

Dear Prof Orrell

PROJECT TITLE: TESTING WHATSAPP-BASED MICROLEARNING FOR SOUTH AFRICAN PRIMARY CARE HEALTHCARE WORKERS, TO FILL KNOWLEDGE GAPS AND TO EXTEND THE REACH OF THE NATIONAL HIV AND TB HEALTHCARE WORKER HOTLINE
(PhD CANDIDATE - MS BRIONY CHISHOLM)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 September 2023.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Ms Briony Chisholm will also be involved in this study.

Please quote the HREC REF 491/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

HREC/ref 491.2022

Appendix S: Eastern Cape Department of Health approval for WhatsApp-based training intervention study

Province of the
EASTERN CAPE
HEALTH

Enquiries: Yvonne Sitole Tel no: 079 0740859

Email: ecdohresearch22@gmail.com

Date: 19 September 2022

Testing WhatsApp-based microlearning for South African primary care healthcare workers, to fill knowledge gaps and to extend the reach of the National HIV and TB Healthcare Worker Hotline. (EC_202209_003)

Dear Ms. Briony Chisholm

The department would like to inform you that your application for the above mentioned research topic has been approved based on the following conditions:

1. During your study, you will follow the submitted protocol with ethical approval and can only deviate from it after having a written approval from the Ethics Research Committee.

2. You are advised to ensure, observe and respect the rights and culture of your research participants and maintain confidentiality of their identities and shall remove or not collect any information which can be used to link the participants.

3. The Department of Health expects you to provide a progress update on your study every 3 months (from date you received this letter) in writing.

4. At the end of your study, you will be expected to send a full written report with your findings and implementable recommendations to the Eastern Cape Health Research Committee secretariat. You may also be invited to the department to come and present your research findings with your implementable recommendations.

5. Your results on the Eastern Cape will not be presented anywhere unless you have shared them with the Department of Health as indicated above.

Your compliance in this regard will be highly appreciated.

SECRETARIAT: EASTERN CAPE HEALTH RESEARCH COMMITTE

TOGETHER, MOVING THE HEALTH SYSTEM FORWARD

Appendix T: Focus group consent form

Informed consent

You are invited to take part in this interview/focus group as part of a research study being run by Briony Chisholm, a PhD student and pharmacist at the National HIV & TB Hotline, University of Cape Town (UCT). The study is funded by an educational grant from Aspen. Participation is voluntary and if you join the session, you may withdraw at any point.

What is the focus group about? In this discussion, we will talk about your experiences with the WhatsApp-based training that you completed in February. At the same time, we'll discuss your thoughts and experiences with using the HIV Hotline as a form of mentorship and clinical help.

What will participants have do? You will be asked a few questions and we'd like you to answer them honestly. If you prefer not to answer any of them, you are free to say so, and we'll move on. You are also free to withdraw at any point. The session should not take more than an hour.

Who can participate? CHWs, counsellors and all cadre of nurses who completed the training. The session will be conducted in English. Each participant will receive a small stipend to reimburse time, inconvenience, and travel costs; and we will provide a snack for in-person groups.

Where will the information collected go? Sessions will be recorded on two devices and then transcribed word-for word. The recordings and transcripts will be stored on UCT's secure servers in password-protected files. Results may be submitted for publication and shared in reports to relevant training organisations. All shared information will be anonymised.

Privacy and confidentiality The information gathered here will be collated anonymously and used to try to improve your working experience and support. Because we are in a group, please do not disclose any sensitive/personal information. Please also respect your colleague's privacy and do not discuss what we've spoken about in the group with others.

This study has been reviewed and approved by the UCT Faculty of Health Sciences Research ethics committee (HREC 491/2022) and permission to conduct it obtained from the Eastern Cape DOH (EC_202209_003).

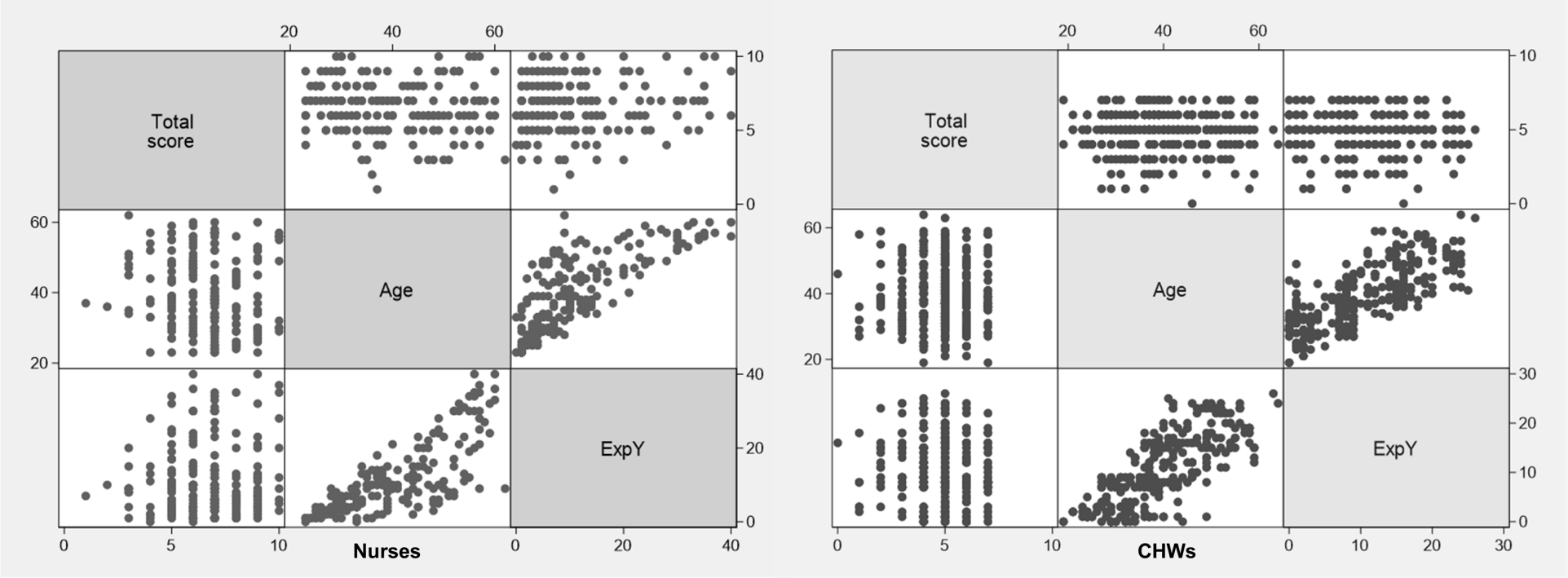
If you have questions about the study and your rights as a participant, you can contact Lamees Emjedi at the Human Research Ethics Committee, Faculty of Health Sciences on 021 406 6338 or the study coordinator, Briony Chisholm on 084 555 0202.

I, _____, consent to being part of this research.

Signature: _____ **Date:** _____

Researcher: _____ **Date:** _____

Appendix U: Lowess graph showing associations of knowledge, age and years of experience



Appendix V: Participant emoji counts during WhatsApp training sessions

Emoji interactions on WhatsApp	Count
Adore	1
Ear	1
Face with heart eyes	1
Face with three hearts	1
Giggle	1
Hands clapping	12
Heart	11
High five	11
Multi-layer heart	1
Peaking	1
Pink flower	2
Rock on	1
Shaking hands	2
Smily face	1
Stickers	5
Sunflower	1
Surfer's hand	2
Thank you	33
Thumbs up	21
Top notch	1
Tulip	3
Two hearts	1
Wave	7
Text interactions on WhatsApp	**Count**
Answers to questions	587
Greetings	11
Thank you	120