Integrating HIV care into primary health care services in the Free State: process and impact

by

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Declaration

I declare that the thesis hereby submitted for the qualification *Philosophiae Doctor* at the University of the Free State is my own independent work. Co-workers and co-authors have been acknowledged where appropriate. I have not previously submitted the same work for a qualification at another university or faculty.

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Dr Kerry Elizabeth Uebel

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Chapter 1

The nature, rationale, aims and strategies of the study

1. Background and statement of the problem

1.1 The scale and impact of the global AIDS epidemic – with emphasis on South Africa

Worldwide, in 2010, 34 million people were estimated to be living with Human Immunodeficiency Virus (HIV), 2,7 million acquired new HIV infections in that year and 1,8 million deaths occurred due to Acquired Immunodeficiency Syndrome (AIDS) [1]. The global prevalence rate in adults 15-49 years was estimated at 0,8%. Over the last decade the epidemic worldwide appears to be stabilising with the peak of the spread of the epidemic occurring in 1997 with an estimated 3,2 million new infections acquired in that year [2]. The largest burden of HIV infection in 2010 was in sub-Saharan Africa with 22,9 million people living with HIV, an estimated 1,9 million new infections and an adult prevalence of 4,8% [1]. By 2008 it was estimated that 14,1 million children in the region had lost one or both of their parents to the epidemic [3]. Although worldwide approximately equal numbers of men and women are infected, in sub Saharan Africa, where HIV is predominantly a heterosexual epidemic and women are more vulnerable to infection, 59% of those infected with HIV are women [1].

Southern Africa is the worst hit region in the world. In 2010, 34% of the world's population with HIV were living in Southern Africa [1]. The UNAIDS 2008 global report, indicated that the nine countries with the highest prevalence rates in the world were all in Southern Africa with adult (15-49 years) prevalence rates above 10%. Of these nine, Swaziland had the highest adult prevalence at 25,9%. Lesotho and Botswana had rates above 20%, South Africa, Namibia, Zambia and Zimbabwe had rates above 15% while Malawi and Mozambique had rates above 10% [4]. In southern Africa, women are also disproportionately affected, with young women aged 15-24 years being three times more likely to be infected with HIV than

men of the same age [3]. The epidemic in southern Africa also appears to be stabilising, albeit at very high prevalence rates, and in six countries (Botswana, Lesotho, Malawi, South Africa, Zambia and Zimbabwe) there is evidence of falling adult prevalence rates – in at least some sections of the population [1].

South Africa is the country with the largest number of people living with HIV in the world – estimated at 5,6 million in 2010 [1]. The 2008 South African anonymous household HIV survey showed that overall prevalence in people over two years of age had levelled out at 10,9%. Amongst adults aged 15-49 years, the prevalence was reported to be 16,9% [5]. There were marked variations in adult prevalence across the nine provinces of South Africa with KwaZulu-Natal (25,8%), Mpumalanga (23,1%), and the Free State (18,5%) the three worst affected provinces, while the Western Cape (5,3%) was the least affected province [5]. Figures from the annual antenatal HIV prevalence survey also suggest that HIV prevalence is levelling out in adult South African women with the prevalence of 30,2% in 2010 showing no significant change over the last 5 years [6]. The HIV prevalence in pregnant women in 2010 also demonstrates the marked variation across different provinces with KwaZulu-Natal (39,5%), Mpumalanga (35,1%) and Free State (30,6%) being the three worst affected provinces. The Western Cape (18,5%) and the Northern Cape (18,4%) had the lowest prevalence [6].

However, temporal trends in prevalence data are becoming more complex to interpret as more widespread access to antiretroviral treatment (ART) is beginning to significantly increase prevalence by decreasing HIV-related mortality. A more accurate way of monitoring the epidemic is by looking at incidence of new infections. Measuring actual incidence of new HIV infections is difficult and UNAIDS currently recommends estimating incidence from changes in prevalence in young adults from household surveys or in young women from antenatal surveillance studies [4]. HIV incidence in South Africa has been estimated in this manner amongst people aged 15-20 years and in the 2008 household survey appeared to be dropping significantly by at least 50% in 16, 17 and 18 year olds [5]. This is an encouraging trend suggesting that behavioural changes were beginning to make an impact. One of the important goals of the South African National Strategic Plan for the period 2007-11 was to decrease new infections by 50% and especially to focus on behavioural change in 15-24 year olds [7]. One of the important goals of the new National Strategic Plan on HIV, STIs and TB:

2012-2016 is to specifically decrease sexual transmission of HIV by 50% over the period 2012-2016 [8].

HIV infection has significantly impacted average life expectancy in the Southern African region. It has decreased sharply from over 60 years in the early 1990's to below 50 years and in Zimbabwe was even below 40 years [4]. Actual AIDS death rates are not generally available as AIDS is rarely recorded as the cause of death on death certificates in Southern Africa. However, death rates from AIDS in South Africa have been estimated by looking at changes in total annual death rates. The Health Systems Trust has released estimated crude death rates in South Africa. These rates almost tripled from 4,9 per 1000 of the general population in 1994 to a high of 15,5 per 1000 by 2005 [9] and these increases were attributed to AIDS. Statistics South Africa estimates that in the 12 months to July 2011 there were 591,366 deaths in South Africa of which 43,6% were thought to be due to AIDS and average life expectancy was 57,1 years [10].

These figures have improved since 2005 when AIDS accounted for an estimated 52% of total deaths and life expectancy was 51,9 years [10]. This improvement is most likely due to the number of people now accessing ART in South Africa [1]. Analysis of mortality trends in adults in an area of KwaZulu-Natal with high HIV prevalence showed a significant decrease in HIV related mortality in young men and women in the first three years (2004-2006) of the rollout of the public ART programme. This was achieved in an area where 71,5% of deaths in 25-49 year olds had been due to AIDS and where by the end of 2006 the health services had achieved an estimated ART coverage rate for that area of 84% of those people thought to be in need of ART [11]. There are similar encouraging figures from Botswana where there has been a decrease of 50% in annual AIDS deaths between 2002 and 2009 while ART coverage was over 90% [2]. These encouraging results reinforce the urgent need to tackle the global AIDS epidemic with international efforts to bolster prevention programmes and to support the rollout of ART programmes capable of saving millions of lives.

1.2 Approaches to tackling the AIDS epidemic – globally and in South Africa

In the early 2000s there were sustained international calls to start rolling out ART programmes with a view to addressing the looming social and economic crises in resource

poor countries such as those of sub-Saharan Africa. These calls were accompanied by pledges for more international funding, through funds such as the Global Fund to fight AIDS Tuberculosis and Malaria (Global Fund) and the President's Emergency Plan For AIDS Relief (PEPFAR), and by sustained efforts to decrease the costs of antiretroviral drugs [12]. In 2003, the World Health Organization announced an ambitious programme to enrol 3 million people in low and middle-income countries on to ART by 2005, the so-called "3 by 5" programme [13]. Although significant progress was made, it took until 2007, i.e. two years longer, to reach 3 million people on ARVs. Consequently the General Assembly of the United Nations then agreed to set a target of reaching universal ART coverage by 2010 – defined as 80% or more of people eligible for ART accessing such treatment [14].

Previously, the WHO had estimated that 10 million people would be in need of ART by 2010. By the end of 2010, an estimated 7,4 million people worldwide were receiving ART with 6,6 million of these in low- and middle-income countries and just over 5 million in sub-Saharan Africa [1]. The WHO decision in 2010 to increase the CD4 count cut-off point for eligibility for ART from 200 to 350 cells/μl meant that the estimated number of people in need of ART worldwide increased from 10 million to 15 million [15]. Thus, with this new target, by the end of 2010, it was estimated that ART coverage worldwide was only 47% of those in need of treatment [1].

The public-sector rollout of ART in South Africa began only in early 2004 after several years of political delays characterised by repeated government statements denying the link between HIV and AIDS and questioning the efficacy of ART [16]. Despite this delay and boosted by significant changes in political commitment to tackling the AIDS epidemic in South Africa in 2009, South Africa had almost 1,4 million people receiving ART by the end of 2010 [1] – the largest number of people on ART in any country in the world. However, this was still only 55% of the 2,7 million South Africans estimated to be in need of ART and well short of the UN target of 80% coverage [1]. A detailed analysis of estimated ART coverage across the provinces in 2008 showed markedly different provincial coverage rates of adults eligible for ART according to Department of Health criteria: Free State had the lowest coverage at 25,8%, then Mpumalanga at 31,2%, Limpopo at 32,2%, Eastern Cape at 32,4%, North West at 35,4%, KwaZulu-Natal at 39,4%, Gauteng at 43,5%, Northern Cape at 61,1% and Western Cape had the highest coverage at 71,1% [17]. Worldwide, and particularly in sub-Saharan

Africa, there is thus an urgent need to identify sustainable models of delivering HIV care that can provide universal access to treatment for people with HIV.

1.3 The debate on appropriate models of HIV care

There has been polarised debate for many years on the comparative merits of vertical (non-integrated, stand-alone, disease-specific programmes) *versus* horizontal models of delivering health care (care for various diseases delivered at one health care delivery point) [18, 19]. Victora et al. [20] however, have pointed out that there is a place and merit for both vertical and horizontal approaches for different health programmes in different contexts. The horizontal approach, on the one hand, is best suited to delivering care for endemic diseases as this approach is more likely to achieve good coverage with people able to access care for these diseases from any health care facility. However, a horizontal approach to delivery of care needs a strong, functional general health system. A vertical approach, on the other hand, is better suited for rapid rollout of health care in weak health systems for epidemic or rare diseases which need highly technological skills and specific donor funding. The disadvantages of delivering health interventions with vertical programmes are firstly, that they do not strengthen existing health systems, and secondly, that they cannot achieve universal coverage for endemic diseases [20].

Given the serious constraints and problems with health resources and infrastructure in many countries in sub-Saharan Africa – such as poor facilities and laboratory services, drug shortages and shortages of skilled health care workers – the initial response in many of these countries was to set up vertical HIV care programmes supported by donor funding with separate budgeting, staff and facilities in an effort to rapidly rollout ART treatment programmes [20, 21]. It was clear that this approach could only be an initial strategy, because such programmes did not have the capacity to achieve universal ART access in high HIV-burden countries and could also undermine other struggling general health programmes by draining away scarce staff and resources, particularly in the light of the significant donor funding allocated to HIV programmes [22]. New strategies were needed to transform and locate the delivery of HIV care within existing general health systems particularly given the context of severe shortages of health care workers in many countries with high prevalence of HIV.

International attention to the crisis in human resources for health is needed to increase training of health care workers, define new cadres of health care workers, involve communities in health care and redefine roles of conventional health care professionals [23]. Van Damme and Kegels [24] emphasised the need to develop models of HIV care delivery that were relevant to specific contexts. In countries with dire shortages of health care professionals, new models of care able to function with fewer doctors and nurses need to be implemented. Many types of task-shifting, and specifically those shifting or delegating tasks from doctors to nurses and from nurses to lay health workers, have been successfully implemented in countries in sub-Saharan Africa and have demonstrated good patient outcomes on ART [25-28]. The lessons learnt in these type of programmes have led to the publication of clear guidelines on task shifting to nurses and to lay health workers by the World Health Organization [29]. These guidelines include: establishing regulatory frameworks; ensuring on-going quality of care; ensuring sustainable financing; and the reorganising of clinical roles. However, as pointed out by Phillips et al. [30], task-shifting is not a panacea. Firstly, there is a need to retain, support and pay professional and lay health care workers properly, secondly, there is a need to also address deficiencies in public health systems, so that good quality sustainable HIV care can be offered to all at primary care level as well as for any other chronic disease [31].

Calls have been made to use international funding and support for HIV care with a view to strengthening general health systems in order that HIV care could be broadened from vertically run programmes and be integrated into general health systems – a strategy now called the diagonal approach [32, 33]. There are however, few guidelines on how to implement this strategy especially in such a way that it does not weaken already strained general health systems [22]. There are various reasons for this lack of guidelines. For one, integration itself is a very broad concept with varying definitions; and in addition, it has provoked polarising debate on its advantages and disadvantages [19]. Furthermore, although there have been calls over many years to integrate other health care programmes, such as reproductive health and mental health into primary care [34-36], there is still a lack of strong evidence that integration of specific health care programmes into primary health care services does indeed improve patient outcomes [37, 38].

1.4 Integration of health services: the concept and strategies to achieve integration

Integration has been defined very broadly as "a variety of managerial or operational changes to health systems to bring together inputs, delivery, management and organisation of particular service functions" [39]. Atun et al. [40] have described six critical areas of health system functioning in which health programmes have to operate: governance, financing, planning, monitoring and evaluation, service delivery and demand generation (from communities). Within any one functioning health programme, each of these areas could be run in an integrated fashion or not. For example, maternal health services may be financed from a general health budget, but have a separate monitoring and evaluation system. Service delivery is the public face of integrated care with which the community interacts, but integrated service delivery can be difficult to achieve if no attention is given to integration, or at least coordination, in the other areas of health system functioning. A framework has been suggested using these six areas to fully describe integration in specific health care programmes in order to effectively compare data on the effectiveness of these strategies [40]. This framework also emphasises the importance of describing the functional relationships between different programmes which may vary from *no integration* (no relationship between programmes) to *partial integration* (programmes may have linkage or even coordination relationships) to *full integration* (where programmes merge) [38].

These descriptions of integration have concentrated on the mechanisms of integration. In contrast, a recent technical brief from the World Health Organization presents a pragmatic definition of integration focusing first and foremost on people's experience of accessing care: "the organisation and management of health services so that people get the care they need, when they need it, in ways that are user friendly, achieve the desired results and provide value for money" or, put more succinctly, providing the "right care" in the "right place" [19]. This brief also suggests that despite polarising debates which argue for an "all or none" attitude to integration, it should be seen as a continuum. The emphasis should not be on providing all services in one place, but rather that services should be provided, in a way that is not disjointed for people accessing them [19]. In a systematic review of reports of integration of targeted health interventions across 55 sites, Atun et al. [41] reported that there was a wide spectrum of integration in these different settings and that few were either completely integrated or non-integrated across all the areas of health system functioning. Their

observations of a range of integration across different settings support the suggestion that integration needs to be seen as a continuum and that there are advantages of both integration and non-integration in different contexts [21, 40].

One of the reasons for the polarising debate that has taken place is that although integration theoretically should improve accessibility of care and therefore patient outcomes, there is not much evidence that integration does indeed improve health outcomes. A systematic review of studies of integration concluded that there was some evidence that service linkages may improve utilisation of services, but there is no strong evidence that full integration of services does improve health outcomes [37].

There have been isolated reports on the effectiveness of integration of other health care interventions such as sexual health, family planning and nutrition services. These showed mixed results, among others, that integration of family planning services into primary care leads to better uptake, while integration of sexual health services into primary care leads to poorer utilisation of services by men and sex workers [39, 42]. There has also been research describing models of integrating existing vertically run HIV programmes into general health systems. These have ranged from efforts to co-locate vertically run HIV programmes within existing primary care facilities [43], to models of down-referral of patients stable on ART from central ART facilities to decentralised or peripheral primary care clinics[44, 45], and to the provision of outreach support from ART clinics to primary care clinics starting to provide HIV care for their patients [46]. Other reports have described strategies to integrate HIV care into the care provided at any primary care consultation with attention to staff training in integrated management of HIV and other diseases especially tuberculosis, combined medical records, standardised protocols and regimens [47], combined waiting areas, and the inclusion of provider-initiated HIV testing into triage [48].

These reports have given useful descriptions of the strategies used, but none have been conducted as randomised controlled trials, or have been able to provide evidence of improved health outcomes or service utilisation. There have also been detailed descriptions of models of HIV care which were primary-care-driven from start-up, often with significant community support and in the context of task-shifting with either doctor initiation of ART care at primary care level [49] or nurse initiation of ART [25, 26]. These programmes have described significant progress towards universal access to ART with primary-care-driven models of HIV care. But

again, none of these studies have been conducted as controlled trials, and thus cannot provide good quality evidence of improved outcomes.

In order then, to describe guidelines for providing HIV care within general health systems in high-burden countries, there is an urgent need for evidence from randomised controlled studies of the outcomes of programmes to integrate HIV care into primary care services. These studies need to document, firstly, which health system functions are being integrated, secondly, what strategies are used [40], thirdly, the effect of these integration strategies on health outcomes, and fourthly, the views of patients on their preferences and experiences in accessing services [19, 37].

2. Characteristics of the public-sector ART programme in South Africa

2.1 The long road to a national public-sector ART rollout: milestones in national government AIDS policies from 1990 to 2010

South Africa has the largest number of HIV positive people in the world and yet government approaches have been characterised until recently by fragmentation, gaps between policy and implementation, scandals, denialism, confrontations, litigation and budgetary shortfalls [50]. Initially, in the late 1980s, the epidemic was predominantly due to HIV-1 sub-clade B and mostly affected white homosexual men. In the early 1990s sub-clade C became the predominant strain and was particularly affecting the black heterosexual community. The explosive growth of HIV in the 1990s in the heterosexual community in South Africa has been documented in the national anonymous survey of the prevalence of HIV and Syphilis in pregnant women booking at public facilities, which has been conducted annually since 1990 (see Table 1). The prevalence increased from 0,8% in 1990, to 24,5% in 2000. The epidemic continued to grow, and by 2005 had reached 29,5% at which level it reached a plateau and has stayed around 29-30% for the past six years [6].

The following section describes government responses to the AIDS epidemic between 1990 and 2010 in South Africa and is a summary of comprehensive notes by Heunis, Wouters and Kigozi [50]. These have also been summarised in Table 1, alongside the course of the growing epidemic, as illustrated by the national HIV prevalence figures for pregnant women for each year from 1990 [6].

Table 1 South African government responses to HIV/AIDS and changes in antenatal HIV prevalence in the years 1990-2010. Sources: Heunis CJ et al (2012) [50] and Department of Health (2011) [6]

Government AIDS policies or policies impacting AIDS policy	Characteristics of South African Government policy on AIDS	Antenatal HIV prevalence
1990-1993 National AIDS convention of South Africa	Health care provided along race and socio-economic class lines Years of apartheid established conditions in which HIV spread rapidly Government suggestions that HIV be a notifiable disease worsen the stigmatisation of HIV Multi-sectoral response to AIDS begun with National AIDS convention of South Africa	0.8% (1990) 1,4% (1991) 2,4% (1992) 4,3% (1993)
1994-1995 National AIDS Plan	Comprehensive plan aimed at social, economic and political drivers of AIDS Poor implementation of social action by national Department of Health	7,6% (1994) 10,4% (1995)
1996-1997 GEAR policy	Significant spending cuts impact implementation of AIDS Plan and functioning of health care facilities High profile scandals (Sarafina 2 and Virodene) Growing authoritarian approach by government	14,2% (1996) 17% (1997)
1998-1999 Government AIDS Action Plan	AIDS a priority in all Government departments Government refusal to provide AZT for PMTCT Treatment Action Campaign founded Confrontations between civil society and government	22,8% (1998) 22,4% (1999)
2000-2002 HIV/AIDS and STD Strategic Plan	No commitment to treatment in Strategic Plan President promotes views denying the link between HIV and AIDS and the efficacy of ART Civil litigation to force government to make treatment available Two provincial governments make treatment available	24,5% (2000) 24,8% (2001) 26,5% (2002)
2003-2006 Operational Plan for Comprehensive HIV/AIDS management and treatment	First government commitment to provide public sector ART Goals to provide universal access to ART by 2007 Massive increase in budget for treatment Very vertical implementation plan Goals of universal access to ART not achieved with estimated ART coverage of only 28% by 2007	27,9% (2003) 29,5% (2004) 30,2% (2005) 29,1% (2006)
2007-2010 HIV/AIDS and STI National Strategic Plan	Clear goals to reduce new infections and expand access to ART STRETCH Trial in the Free State as a pilot of nurse initiated ART Removal of President Mbeki and Health Minister 2008; Budget shortfalls in allocation for ARVs 2008 Massive budget increases for ARVs HCT programme to test 15 million people in 2010	29,4% (2007) 29,3% (2008) 29,4% (2009) 30,2% (2010)

The period 1990-1993 saw the last four years of apartheid government which for almost 50 years had sown the social and economic conditions for the spread of the epidemic in Southern Africa, and had fragmented health care provision along racial and economic lines. The new democratic government, elected in 1994, drafted the National AIDS plan [51] with good intentions to address the socio-economic drivers of the epidemic. However the plan was poorly implemented by the national and provincial Departments of Health with few efforts at interdepartmental collaboration. The new GEAR economic policy [52] introduced significant budget cuts in social services including the health services and spending on the AIDS plan in the years 1996-1997. This same period saw the beginnings of high-handed authoritarian approaches to AIDS policy from the national government as well as the first of many high profile scandals involving government ministers with the Sarafina 2 and Virodene scandals.

A new plan, the Government AIDS Action Plan, was launched in 1998, with the intention to make AIDS a priority in every government department. However, the period 1998-1999 also saw the first missed opportunity to introduce treatment for HIV with the government refusing to implement Zidovudine (AZT) for HIV positive pregnant mothers to prevent mother to child transmission. Partly in response to this, a civil advocacy group, the Treatment Action Campaign (TAC), was founded to begin advocating for HIV-positive people's right to access treatment. Confrontation between civil society and the government escalated in the period 2000-2002 as the new HIV/AIDS and STD Strategic Plan [53] did not make any provision for access to treatment for HIV. The then State President Mr Mbeki and the Minister of Health Dr Tshabalala-Msimang were, at the time, promoting dissident views that denied the link between HIV and AIDS, promoted theories that AIDS was caused by nutritional deficits, and warned of the supposed toxicities of ARVs. As a result, the Minister of Health refused to introduce either Nevirapine prophylaxis for pregnant mothers or ART treatment programmes, and instead promoted various fruits, vegetables and micronutrients as treatment for AIDS. This refusal to introduce life-saving treatments prompted international condemnation and litigation by civil society against the government in an attempt to force the government to introduce ART treatment programmes. During this period, two provincial governments introduced their own limited ART treatment programmes in defiance of the national government.

In late 2003, the South African Department of Health finally acknowledged the need for a public treatment programme and published their Operational Plan for Comprehensive HIV

and AIDS Care, Management and Treatment for South Africa (known as the Operational Plan) [54] in order to begin the public-sector ART rollout to counter the AIDS epidemic. The government maintained that this had been prompted by falling prices for antiretroviral medication in 2003, but civil advocacy for treatment had also become too strident to ignore. The Operational Plan set ambitious targets of having at least one ARV service point in every health district by the end of the first year of the programme and achieving 100% coverage of all people in need of ART after 5 years [54].

Although the Operational Plan's stated aim was to provide comprehensive HIV care in an integrated fashion, the management and delivery of the rollout were accomplished as a vertical programme with each ARV service point accredited by the national Department of Health and each having separate funding, staff, facilities and record keeping for the ART programme [16]. Moreover the rollout was interpreted and implemented in different manners in the different provinces. By 2007, an estimated 250 000 people were receiving ART in the public sector [55], however a further 567 000 people were thought to be in need of ART [56] while ART sites were gradually reaching points of saturation with little capacity to take on more patients [57].

In the next national response, the HIV and AIDS and STIs Strategic plan for South Africa 2007-2011 (known as the National Strategic Plan or NSP 2007), the national Department of Health acknowledged that there were still many people with AIDS in South Africa who were not able to access treatment. This new plan had therefore set two main targets relevant in this context: first, to reduce new infections by 50% by 2011; and second, to increase the number of new people accessing ART each year incrementally to 420,000 or 80% of those in need of treatment by 2011 [7]. It also acknowledged the need to provide "... universal access to a comprehensive package of treatment for HIV including ARVs and integration of HIV and tuberculosis care." [7].

The intention of integrating ART into the primary health care structure was underlined by the specific goal that 90% of care for HIV should be provided by primary care staff by 2011. There was little detail however, on how these services were to be integrated into primary care. The plan also specifically referred to task shifting, including nurses initiating and monitoring ART, and involving lay counsellors in tasks such as finger-pricking to obtain blood for HIV testing and support roles in the ARV programme. Here also, the NSP set

markedly ambitious goals – that 60% of patients were to be initiated on ARVs by nurses and 70% on ARVs monitored by nurses by 2011 – without outlining a clear strategy to train and authorise nurses in primary care facilities to take on these new clinical responsibilities. In South Africa then, in the years up to 2007, the public-sector ART rollout, despite intentions to provide an integrated service, was delivered as a predominantly vertical service and failed to meet the goals to achieve universal access to ART in the public health sector.

2.2 The Free State Province: magnitude of the epidemic and the public-sector ART rollout

The Free State Province, with an estimated population of 2,75 million in 2011 [10], had the third highest HIV prevalence of the nine provinces in South Africa in 2008, with 18,5% of 15-49 year olds found to be HIV-positive in an anonymous national household survey [5]. Although the first Operational Plan and the subsequent National Strategic Plan 2007 spoke of integrating HIV care within primary health care, the programme in the Free State, as in the rest of the country, was delivered as a predominantly vertical programme with designated facilities, staff, finances, patient records and monitoring and evaluation systems. The first phase of the public-sector ART programme in the Free State was rolled out between May and December 2004 in all five districts and treatment was delivered in 20 designated ART sites which were one of three types [16]:

1) Nurse-led ART assessment sites situated within selected existing primary care clinics, with ART nurses appointed to provide care for all HIV positive patients referred from clinics in that area and from primary care nurses within that clinic (there were 13 assessment sites across all five districts in the first phase)

2) Doctor-led ART treatment sites situated in district hospitals where patients could be referred from the ART assessment sites for initiation and three to six monthly monitoring of ART (there were one each in four of the five districts in the first phase)

3) Combined ART sites, situated in selected primary care clinics in remote areas far from hospitals, where doctors visited and supported ART appointed nurses and where the functions of assessment and treatment sites were combined (there were three in the fifth district in the first phase)

Patients diagnosed as HIV-positive by primary care nurses within ART assessment sites and in clinics with no assessment site, were referred to ART nurses at ART assessment sites for assessment and on-going HIV care. Those not yet eligible for ART (CD4>200 cells/μl and Stage 1,2 or 3) were seen six to twelve monthly for repeat assessments and care including CD4 counts, staging and screening for TB, and provision of cotrimoxazole prophylaxis. Those eligible for ART (CD4 $\leq$ 200 cells/μl or Stage 4) could receive drug readiness training and monthly ART supplies from the ART nurses at that site, but had to be referred to doctors at treatment sites (or the visiting doctor in the case of combined sites) for initiation of ART and for three to six-monthly reviews of ART prescriptions.

The second phase of the rollout was implemented between December 2005 and the end of 2006. New ART sites were established in all five health districts and at the end of 2006 there was at least one ART site in 14 of the 20 local municipal areas (sub-districts) in the province constituting a total of 20 assessment sites, 11 combined sites (31 sites in total in PHC clinics) and nine treatment sites.

The slow pace of the rollout in the Free State was criticised in these first few years [16], and there was evidence that some patients enrolling in the programme and who were eligible for ART were not getting onto ART, because of delays and bottlenecks in the system. Patients who did receive ART had showed commendable outcomes with an 86% reduction in mortality rates [58] and improvements in physical and emotional health [59, 60]. However, programmatic data up to the end of 2005, showed the 12 month mortality rate amongst patients eligible for ART was 53%, the majority of whom died before they could access ART [58]. By mid-2008 estimated coverage of those in need of ART was still only 25% [17]. Amongst staff – despite positive reports of enthusiasm because of the availability of treatment for their patients [61] – many nurses were stressed by the large numbers of patients being seen in inadequate facilities. High workloads for ART nurses [62] and high rates of occupational fatigue and burnout in nurses working in PHC facilities (including ART sites) were also reported [63]. Research also documented that the appointment of nurses to the ART programme and ART facilities (in higher level posts) was draining nurses from the general health services in the province [64]. The Free State public-sector ART rollout, like the national rollout, was a typically vertical programme struggling to achieve the goals of universal access. In fact, by 2008, it was the province with the lowest estimated ART coverage (25,8%) of all nine provinces in South Africa [17].

2.3 Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) study in the Free State – background and rationale

Given the high mortality rates of patients waiting for ART and a critical shortage of doctors in the Free State to initiate and manage patients on ART in the public-sector, the Free State Department of Health approached the Knowledge Translation Unit (KTU) of the University of Cape Town Lung Institute to assist the province to implement a task shifting intervention to train nurses to initiate and manage patients on ART. The KTU had already developed and piloted in the Free State, the PALSA PLUS guidelines [65-67], a set of primary care guidelines for nurses to manage HIV and respiratory diseases including TB. The Department of Health requested that nurse prescription of ART be included in the guideline and that training be conducted in all ART sites in the province.

There was widespread ambivalence at the time in other centres in the country, about the ability of nurses to successfully manage patients on ART and a lack of clear support or policies from the national Department of Health, despite goals in the National Strategic Plan that spoke of nurse initiation and management of ART. It was therefore decided to pilot the intervention and monitor its effects using a pragmatic, cluster randomised controlled trial. The pragmatic trial design was chosen to determine the effectiveness of task shifting in real world conditions and not just in specially selected "ideal" clinics [68]. Thus, all 31 ART sites established in primary care clinics in the province by the end of 2006 (20 assessment sites and 11 combined sites) were randomised to 16 intervention and 15 control clinics. Clinics were randomised within nine clusters consisting of clinics that referred patients to the same treatment site in order to ensure a balanced representation of clinics across different contexts in each arm of the study. ART nurses in ART assessment sites were known to be overloaded already with large numbers of patients accessing all their HIV care at the ART sites, and thus shifting ART initiation and re-prescription to these nurses was unlikely to improve access to care, unless other elements of HIV care were also shifted to primary care nurses. There were thus two main task shifting interventions: 1) equipping ART nurses to initiate and re-prescribe ART for uncomplicated adults; and 2) integrating elements of HIV care into primary care services. This type of intervention is known as a complex health intervention as it involved several different interdependent components [69]. The implementation of the STRETCH interventions involved training, authorisation and support of ART nurses, the

reorganisation of roles of doctors, primary care nurses and pharmacists and changes in the distribution of drugs.

Such complex interventions need, firstly, to be developed in consultation with staff expected to implement the intervention so as to ensure the intervention is acceptable, relevant and implementable and the process of reformulating the intervention may proceed over several phases of repeated consultations with staff [70]. When such complex interventions are implemented across many facilities – as in the STRETCH intervention – the intervention may also need to be flexible and tailored to the differing contexts of each facility [71, 72].

Secondly, in order to compare outcomes of such complex health interventions and for the results of such trials to be useful and applicable in other settings, it is important to describe in detail all the components of the intervention [73]. The Workgroup for Intervention Development and Evaluation Research (WIDER) recommends that such reports on interventions include the following: characteristics of trainers and recipients of training, the setting, the mode of delivery, the intensity and the duration of training, the content of the training and the fidelity of the training to protocols. The workgroup also recommends that training manuals and protocols should be made available, that there are detailed descriptions of active processes in control groups as well as in intervention groups, and that change processes thought to be important in implementation are specified in descriptions of the intervention [74]. All of these descriptions are important to enable an intervention to be successfully replicated elsewhere [75].

Thirdly, the process of implementing such complex interventions needs to be evaluated [76]. Formal process evaluations of randomised controlled trials of complex interventions are able to explore the implementation, acceptability, context and fidelity of an intervention and are particularly useful in multi-site trials to explore local variations in implementation. Evaluations need to be conducted at both intervention and control sites because during the trial it cannot be assumed that changes would only take place in the intervention clinics [76]. Process evaluations can include quantitative as well as qualitative data using a number of data collection methods, such as questionnaires, structured field notes of participants, focus groups discussions and in-depth interviews. The results of a thorough process evaluation can assist in the interpretation of outcomes in such trials [76].

3. Rationale for the research

Given international calls for vertical HIV care programmes to be integrated into primary care and the challenges in the Free State Province with a vertical programme delivering the lowest coverage of ART treatment of the nine provinces in South Africa, the STRETCH trial was a timely opportunity to conduct further research specifically on the integration of HIV care into primary care services as one of the interventions in this complex task shifting intervention. The author (KU) was appointed as the manager of the STRETCH trial based in the Free State with responsibilities to oversee implementation and data collection and liaise with the Department of Health and the research team, and was therefore in a position to conduct further research on integration during the trial.

In the context of calls for more research using randomised controlled trials to document evidence of the impact of integration on patient outcomes [37, 41], the important research questions relevant to integration during the STRETCH trial were:

1) Is there evidence that integration of HIV care into primary care services improves patient outcomes?

2) If so, what level of integration of HIV care is effective in improving outcomes?

3) What impact do strategies to integrate HIV care have on primary care services?

The concern expressed by the Free State Department of Health in 2006 about severe limitations on further expansion of the vertical ART rollout and the subsequent report in 2008 that percentage ART coverage in the Free State was the lowest of all the provinces [17] suggested that a retrospective review of the ART rollout in the Free State should elucidate some of the challenges of the first four years of programme leading up to the STRETCH trial. The integration of HIV care into primary care services was arguably the more complex of the two main interventions during the STRETCH trial. Thus, the integration component of the STRETCH intervention particularly, needed to be developed in consultation with clinic staff and different levels of management to ensure the intervention was relevant and implementable. Because the STRETCH trial was conducted as a randomised controlled trial with effects on patient survival as one of the primary outcomes, it was an appropriate setting in which to look for evidence of the independent effect of integration on patient survival. In order to correlate the effect of integration on patient survival, there was a need to develop a tool to monitor and quantify the degree of integration achieved at each clinic during the trial.

Qualitative data on the impact of integration on clinic functioning were collected by the author (KU) during many visits to clinics from 2007 to 2010. Two other qualitative studies linked to the STRETCH study also explored changes in clinic functions: a process evaluation of the STRETCH trial led by a STRETCH team member Daniella Georgeu [77], and a separate doctoral study in a selection of primary care and ART clinics investigating the impact of HIV care on the organisation of nursing care which was conducted by Andy Guise [78]. The findings of these three studies provided a rich source of qualitative data on the impact of the strategies to integrate HIV care into primary care on staff, patients and clinic function during the STRETCH trial.

This research captured and recorded in this study was therefore a sub-study, conducted by the author (KU), as part of the STRETCH trial focussing on three main aspects concerning integration during the trial:

1) the context of the study with a retrospective review of the achievements and challenges in the Free State in the years leading up to the trial, 2004-2007

2) the development of the integration components of the intervention and a tool to monitor integration, and the results of this monitoring

3) a quantitative analysis of the effect of integration on patient survival, and a qualitative assessment of the impact of integration on clinic function.

4. Aims and objectives

4.1 Hypothesis

The hypothesis of this study is that the integration of elements of HIV care into primary care services during the STRETCH trial will improve access to care and thus survival of HIV-positive patients with CD4 $\leq$350 cells/µl and not yet receiving ART at enrolment in the study.

4.2 Aims

The aims of this study are to develop and implement a practical approach to integrating elements of HIV care into primary care services in the Free State Province, to develop a tool to monitor the level of integration achieved, and then to analyse the effect of integration on survival of patients needing ART as well as its impact on primary care services.

4.3 Objectives

The four main objectives of this study are to:

1. Develop and implement a practical strategy to integrate HIV care into primary care services as part of the STRETCH trial.

2. Monitor over time the progress of integration of elements of HIV care into primary care services that was achieved during the STRETCH trial.

3. Assess the impact of integration of HIV care on survival of patients with CD4≤350 cells/μl and not yet on ART.

4. Monitor the impact of efforts to integrate HIV care on primary care services.

5. Structure of the thesis

This thesis is being presented as a series of research articles which have already been published in different scientific journals. These articles along with the introductory and concluding chapters of this thesis, give a full report of the methodologies, results and discussions of the findings of this study on integration as a whole. These six articles have already been published and are reproduced as Chapters 2-7. These articles are presented as follows in three groups.

5.1 Documenting the context of the study on integration

The context in which the study of integration was conducted is described in the first two articles. The first article, presented as **Chapter 2**, is a retrospective review of the achievements and challenges of the Free State public-sector ART programme in the first four years of the rollout leading up to the implementation of the STRETCH trial (2004-2007) with a particular emphasis on progress made towards achieving universal access to ART. The researcher (KU) was the initiator and first author of this article, and the research strategy used as well as a summary of the methodology are included below in **Section 6.1**. The second article, presented as **Chapter 3**, represents the main research report of the STRETCH trial with integration of HIV care into primary care services being one of the interventions. The first author was the principal investigator of the STRETCH trail, Dr Lara Fairall. The

researcher (KU) was a co-author of this article and was involved in the development and implementation of the main STRETCH trial, as well as the analysis of results and writing of the manuscript. The research strategy and a summary of methodology are also included below in **Section 6.1**.

5.2 Developing and monitoring the integration intervention

The next two articles describe the research conducted to achieve the first two objectives of this study on integration. These articles focus on the development of the integration intervention and of a tool to monitor integration, as well as an analysis of integration achieved during the trial. The first of these two articles, presented as **Chapter 4,** is a description of the development and the contents of the integration and task shifting interventions in the STRETCH trial. The second article, presented as **Chapter 5,** is a report of the development of a tool to monitor integration during the trial as well as an analysis of the progress of integration achieved during the STRETCH trial. The researcher (KU) was the initiator and first author of both of these articles, and the research strategy and summary of methodology are included below in **Section 6.2**.

5.3 Describing the impact of integration

The last two articles describe the research conducted to achieve the third and fourth objectives of the study on integration, namely: the impact of integration achieved during the STRETCH trial, firstly, on patient survival and, secondly, on primary care services. The first of these two articles, presented as **Chapter 6,** is a report of the correlation between clinic integration scores and survival of patients with CD4≤350 cells/μl and not yet on ART at enrolment. The second article, presented as **Chapter 7**, is the report of a synthesis of the findings of three qualitative studies on the impact of integration on primary care services. The researcher (KU) was the initiator and first author of both of these articles, and the research strategy and summary of methodology are included below in **Section 6.3.**

A summary of the main findings, conclusions and recommendations arising from the research have been compiled in Chapter 8. Several documents relevant to this research have been reproduced in the Appendices, including documents referred to in two of the articles as additional files or supplementary digital content.

6 Research design, strategy and methodology

This section describes the research design and strategy for each of the articles in the study and includes a summary of the methodologies used.

6.1 Documenting the context of the study on integration

6.1.1 A retrospective review of achievements and challenges of the Free State public ART programme for the years 2004-2007

In the light of conclusions in the literature that vertically implemented ART programmes are unlikely to achieve universal ART access and HIV care needs to be integrated into primary care services, a retrospective analysis of the Free State public ART rollout was conducted. This strategy was chosen because the ART rollout in the Free State was conducted in a highly vertical manner and evidence on outcomes of patients accessing HIV care suggested that many patients were dying before being started on ART [58]. Such a retrospective analysis of achievements and challenges in the first four years of the ART programme would provide a useful description of the context in which the STRETCH study and the present research on the integration of HIV care into primary care services were conducted.

A retrospective review was done of the achievements and challenges of the Free State public ART rollout from 2004-2007. Figures on monthly patient enrolments from mid-2004 till the end of 2007 were obtained from Meditech – the Free State electronic patient record system. Figures on budgetary financial allocations for each year were obtained from provincial staff and the National Treasury website. Figures on staff vacancies and the establishment of new sites were obtained from staff at head office of the Free State Department of Health. Estimates of the number of new AIDS patients in the Free State needing treatment each year were obtained from the Actuarial Society of Southern Africa's 2003 model of demographic indicators of the HIV epidemic. Figures on the number of patients enrolled and the number of new AIDS patients in the Free State needing treatment were used to estimate percentage coverage annually for the years 2004-2007 and then projections were made of the expected increases in patient enrolments for 2008 and 2009 if the same model of ART rollout was continued.

A full report of this study is reproduced as **Chapter 2**. This article has already been published:

Uebel K, Timmermans V, Ingle S, Van Rensburg D, Mollentze WF. Towards universal ARV access: achievements and challenges in Free State Province, South Africa. *South African Medical Journal* 2010;100(9):589-593.

6.1.2 The main STRETCH trial

As the STRETCH trial was investigating the impact of a complex intervention involving task shifting and integration of HIV care on survival of patients needing ART, the research design chosen was a pragmatic, cluster randomised controlled trial. It was conducted in all 31 existing ART assessment clinics in the Free State Province at the time of randomisation – the end of 2006. It was thus a pragmatic trial conducted over an entire province and not just in selected research clinics. Pragmatic trials of health system interventions are conducted in order to determine whether an intervention is effective in real conditions which may include shortages and high turnover of staff, shortages of medication and funding problems [68]. Clinics were randomised within clusters of clinics referring patients to the same treatment site to ensure a balance of clinics in each arm of the trial.

All 31 nurse-run assessment ART sites in the Free State Province at the end of 2006 were randomised, within clusters of clinics referring to the same ART treatment sites, and subsequently into **16 intervention sites** and **15 control sites**. The two main interventions consisted of:

1) Equipping nurses at intervention ART sites to initiate and manage uncomplicated adults on ART

2) Integrating elements of HIV care into the work of primary care nurses within the ART clinic and in clinics referring patients to the ART sites.

Two subgroups or cohorts of patients were enrolled with a view to monitor the outcomes of the STRETCH intervention. **Cohort 1** consisted of all patients at a clinic, who had a CD4 count result below 350 cells/μl during the period of the trial and were not yet on ART at the time of enrolment. These patients were either eligible for ART (CD4< 200 cells/μl) or were likely to become eligible for ART during the trial and were monitored for a minimum of 12 months and a maximum of 18 months to assess the impact of the intervention on patient survival. The primary outcome was time from enrolment to death. Deaths were recorded either on the Free State electronic patient record system or by linkage with the national death

register using patients' identity numbers. Secondary outcomes included time to ART, percentage of patients commencing ART, proportion diagnosed with tuberculosis, and number of doctor and nurse visits.

Cohort 2 consisted of patients already on ART for at least six months and still receiving care at the trial clinic at the time of enrolment. These patients were monitored to evaluate the effect of the intervention on the quality of care given to patients on ART. The primary outcome in this group was proportion of patients who had an undetectable viral load (<400 copies/mL) after twelve months of the intervention – a good indicator of continuing treatment effectiveness and good adherence. Viral load results were obtained either from the Free State electronic patient record system or by linkage and manual searches of blood results within the National Health and Laboratory Services (NHLS) database. Secondary outcomes in this group included proportion lost to follow-up, proportion diagnosed with tuberculosis and number of nurse and doctor visits.

A full report of the STRETCH study is reproduced as **Chapter 3**. This article has already been published:
Fairall L, Bachman M, Lombard C, Timmerman V, Uebel K, Zwarenstein M, et al. Task shifting of antiretroviral treatment from doctors to primary care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. *The Lancet* 2012;380(9845):889-98.

6.2 Developing and monitoring the integration intervention

6.2.1 Objective 1: To develop and implement a practical strategy to integrate HIV care into primary care services as part of the STRETCH trial

As the STRETCH trial was a complex health intervention and a pragmatic trial conducted under real conditions, both components of the intervention; the task shifting and particularly the integration of HIV care into primary care services needed to be developed with staff from the Department of Health so that they were relevant, practical and implementable. The research strategy used to develop the interventions was a method called participatory action research [79] involving staff from clinics and local, mid-level and senior management.

A detailed description is given of the method used to develop the intervention and the resulting components of the intervention, in the STRETCH trial. Members of the research

team consulted over many months with senior management and middle managers from the Free State Department of Health and finally with staff from the 31 ART clinics in the trial. This was an iterative process described as participatory action research to develop both the task shifting and integration of HIV care into primary care services so that they were relevant and implementable.

A full report of this study is reproduced as **Chapter 4**. This article has already been published:

Uebel K, Fairall L, Van Rensburg D, Mollentze WF, Bachmann MO, Lewin S, Zwarenstein M, Colvin CJ, Georgeu D, Mayers P, Faris G, Lombard C, Bateman E. Task shifting and integration of HIV care into primary care in South Africa: the development and content of the streamlining tasks and roles to expand treatment and care of HIV (STRETCH) intervention. *Implementation Science* 2011;6:86.

6.2.2 Objective 2: To monitor over time the progress of integration of elements of HIV care into primary care services that was achieved during the STRETCH trial

The research strategy used was a prospective, longitudinal review conducted at all trial clinics (intervention and control) at intervals during the trial. An integration survey tool was developed and validated, then administered during semi-structured interviews with clinic managers or ART nurses. This review of integration formed part of the process evaluation of the STRETCH trial focusing on the integration of the elements of HIV care into primary care services.

In order to monitor the progress of integration of HIV care into primary care services during the STRETCH trial, a semi-quantitative questionnaire was developed after consultation with staff at the 31 trial clinics and piloted at the 16 intervention clinics. The questionnaire was then used to conduct structured interviews with clinic managers or senior ART nurses at both intervention and control clinics during the trial. Internal consistency was checked with calculation of Cronbach's alpha coefficients. Soon after the first round of interviews a second observer repeated the assessment at five clinics to check for inter-observer reliability. Four assessments were conducted at regular intervals during the trial. The questions were designed to assess patients' ability to access integrated HIV care. There were questions on both pre-ART care for patients not yet eligible for ART and ART care for those eligible for ART.

Integration of care was assessed at two levels: patients ability to access HIV care from their local primary care clinic that had previously been referring patients for HIV care to ART sites (mainstreaming HIV care); and their ability to access HIV care from any nurse within ART sites (internal integration). Scores for each question were combined into a **total integration score** and four component integration scores namely **pre-ART** and **ART integration scores** and **mainstreaming HIV** and **internal integration scores**. Results of these assessments at each clinic were then scored for the five integration scores. Mean integration scores at intervention and control clinics at all four assessments were then compared using one way analysis of variance ANOVA to ascertain if the intervention had resulted in significant differences between intervention and control clinics at any of the assessments, while ANOVA repeated measures were used to ascertain if the intervention had resulted in significant progress in integration during the trial.

A full report of this study is reproduced as **Chapter 5**. This article has already been published:

Uebel K, Joubert G, Wouters E, Mollentze WF, Van Rensburg D. Integrating HIV care into primary care services: quantifying progress of an intervention in South Africa. *PLoS ONE* 2013;8(1):e54266. doi:10.1371/journal.pone.0054266.

6.3 Determining the impact of integration

6.3.1 Objective 3: To assess the impact of integration of HIV care on survival of patients with CD4≤350 cells/µl and not yet on ART

The research strategy used was a prospective cohort study looking at the survival of patients in Cohort 1 of the STRETCH study over 12-18 months and using Cox proportional hazards analysis to determine whether there was any correlation between patient survival and clinic integration scores derived from administration of the integration tool.

In order to test the hypothesis of this study that integration of HIV care into primary care would improve survival of patients not yet on ART, survival of patients in Cohort 1 was analysed for the effect of integration scores obtained for each clinic at the first assessment early in the trial. Cox proportional hazards analysis was conducted on all patients in Cohort 1 (CD4<350 cells/µl and not on ART at enrolment) to determine the effect on patient survival of the five different integration scores conducted early in the trial – total integration score,

pre-ART and ART integration scores, and mainstreaming HIV and internal integration scores. These analyses were adjusted for possible confounders known to affect patient survival or ascertainment of survival: strata, arm of study and patient characteristics (sex, age, enrolment CD4, whether the patient received ART during the trial, and whether the ID number was ascertained) and then in addition, two clinic characteristics (rural vs. urban clinic and patient: staff ratio) known to have an impact on patient survival in clinics in the Free State and which may have been impacted by the integration achieved during the trial.

A full report of this study is reproduced as **Chapter 6**. This article has already been published:

Uebel K, Joubert G, Lombard C, Fairall L, Bachmann MO, Mollentze WF, Wouters E. Integration of HIV care into primary care in South Africa: Effect on survival of patients needing antiretroviral treatment. *Journal of Acquired Immunodeficiency Syndrome* 2013; doi:10.1097/QAI.ObO13e318229baab.

6.3.2 Objective 4: To monitor the impact on primary care services of efforts to integrate HIV care

The research strategy chosen was a synthesis of the findings of three linked qualitative studies conducted in both STRETCH clinics and primary care clinics in the Free State during the time of the STRETCH trial. These three studies used a variety of methods, including participant observation, ethnographic observations, interviews and focus group discussions.
A meta-ethnographic approach was used to synthesise the findings of these three studies on the integration of HIV care into primary care services. The **first study** comprised participant observations of the trial coordinator (KU) based on notes taken during approximately 170 clinic visits done over the four years of the STRETCH trial. The **second study** was a qualitative process evaluation conducted during the STRETCH trial by a research nurse with the support of senior qualitative researchers using focus group discussions with clinic staff and with patients at intervention and control sites, as well as at referring primary care clinics. In-depth interviews were also conducted with doctors and pharmacists from the trial clinics, and local area managers and senior managers from the provincial Department of Health. The **third study** was an ethnographic study of the effect of incorporating HIV care into the work of primary care clinics on the organisation of nursing work. It was conducted in several primary care and ART assessment clinics in the Free State (including some STRETCH study

clinics) by a PhD student working in consultation with the STRETCH research team. He conducted 59 interviews with nurses, other staff and patients at ten clinics and sustained observations were conducted at four clinics. An iterative process was used to identify common themes from each study, major categories and sub categories of findings were described and higher order interpretations of all these findings were then synthesised.

A full report of this study is reproduced as **Chapter 7**. This article has already been published:

Uebel K, Guise A, Georgeu D, Colvin CJ, Lewin S. Integrating HIV care into nurse-led primary health care services in South Africa: a synthesis of three linked qualitative studies. *BMC Health Services Research* 2013; 13:171 .

7. Ethical considerations

Written permission to conduct the STRETCH trial in public health facilities was given by the Head of the Free State Department of Health. The trial protocol was approved by the ethics committees of the Faculties of Health Sciences at the University of Cape Town and the University of the Free State. Intervention clinic managers, in consultation with the clinic staff, provided written informed consent to take part in the trial. As the STRETCH trial was an educational and managerial intervention aimed at entire clinics and their staff, all patients in the intervention clinics would thus be exposed to the same intervention. Informed consent was not requested from individual patients. Nevertheless, written information about the trial in three local languages was made available at all intervention clinics for patients to read. Ethical principles for use of medical records for research without patients' consent were followed: the research had a clear public benefit; approval was obtained for the study from the lead doctors and nurses managing the programme; use of the data for research did not influence the care of individual patients; the data were already being used by the research team for programme evaluation on behalf of the provincial health department; and data confidentiality was strictly enforced. Only selected data managers had access to personal identifiers. Anonymised data were provided only to the principal investigators, the lead statistician and the health economist. This consent procedure was approved by both ethics committees. The STRETCH trial is registered at isrctn.org (ISRCTN46836853).

Permission to conduct this research as a sub-study of the STRETCH study in the Free State was given by the Head of Department of Health in the Free State. The protocol was approved by the Ethics Committee of the Faculty of Health Sciences of the University of the Free State. Written consent to conduct semi-structured interviews for the integration questionnaire survey was obtained from all clinic managers. Written consent to conduct observations and record in-depth interviews and focus group discussions as part of the qualitative research was obtained from participants.

8. The author's role and contributions to this work

The author conducted this study as a sub-study within the STRETCH trial. In addition, the author was appointed by the STRETCH research team as the full-time trial coordinator in the Free State in January 2007 and worked in this position until December 2010. The principal investigator of the STRETCH trial was Dr Lara Fairall of the Knowledge Translation Unit of the University of Cape Town Lung Institute based in Cape Town. The author was involved, together with the other STRETCH team members, in developing and facilitating the implementation of the STRETCH interventions, the training of nurses at intervention sites, the analysis and checking of quantitative data, the planning of interviews and focus groups for qualitative data collection and the compiling of reports on the trial. The author was responsible in the Free State for communication between senior managers of the Free State Department of Health and the STRETCH trial research team; for providing on-going clinical support of nurses trainers and doctors at ART and primary care clinics; for coordinating the establishment and support of clinic based and local area management teams; for the recording of detailed qualitative observations; and for coordinating the work of a team of data capturers responsible for quantitative and economic data during the trial.

For this research on integration during the STRETCH trial, the author – with the assistance of Dr Sue Ingle and Ms Venessa Timmerman – was responsible for collection and analysis of retrospective data from 2004-2007 on the rollout of the Free State public ART programme. The author was also responsible for the further development and implementation particularly of the integration intervention as well as the development, validation, testing of reliability and administration of a questionnaire to monitor integration during the trial. In this, the author was assisted by Sr Tsotsa Polinyane and Prof Gina Joubert. Testing of consistency of the questionnaire and statistical analysis of the results were conducted by the author, Prof Gina

Joubert and Prof Edwin Wouters. Cox proportional hazards analysis of individual patient survival of patients in cohort 1 and the effect of integration scores was conducted by Dr Carl Lombard, the STRETCH trial statistician, with advice and direction from the author, Prof Max Bachmann and Dr Lara Fairall from the STRETCH trial investigation team. Qualitative data on the impact at clinic level of efforts to integrate HIV care into primary care were collected as part of three qualitative studies which were conducted and findings synthesised by the author, Ms Daniella Georgeu and Dr Andy Guise, with advice and direction from Dr Chris Colvin and Dr Simon Lewin also from the STRETCH trial investigation team. Prof Willie Mollentze and Prof Dingie van Rensburg supervised the doctoral thesis and, in this capacity, gave academic advice and guidance to the author during the research.

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Chapter 2

Towards universal ARV access: achievements and challenges in Free State Province, South Africa

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Towards universal ARV access: Achievements and challenges in Free State Province, South Africa

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Objective. To study the progress and challenges with regard to universal antiretroviral (ARV) access in Free State Province, South Africa.

Methods. Data from the first 4 years of the public sector ARV roll-out and selected health system indicators were used. Data were collected from the public sector ARV database in Free State Province for new patients on ARVs, average waiting times and median CD4 counts at the start of treatment. Information on staff training, vacancy rates and funding allocations for the ARV roll-out was obtained from official government reports. Projections were made of expected new ARV enrolments for 2008 and 2009 and compared with goals set by the National Strategic Plan (NSP) to achieve universal access to ARVs by 2011.

Results. New ARV enrolments increased annually to 25% of the estimated need by the end of 2007. Average waiting times to enrolment decreased from 5.82 months to 3.24 months. Median CD4 counts at enrolment increased from 89 to 124 cells/μl. There is a staff vacancy rate of 38% in the ARV programme and an inadequate increase in budget allocations.

Conclusion. The current vertical model of ARV therapy delivery is unlikely to raise the number of new enrolments sufficiently to achieve the goals of universal access by 2011 as envisaged by the NSP. The Free State is implementing a project (STRETCH trial) to broaden the ARV roll-out in an attempt to increase access to ARVs.

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South Africa, with an estimated 5.7 million people living with HIV, has the largest burden of HIV disease globally.[1] By 2009, an estimated 2.9 million South Africans had died of AIDS, with an annual AIDS mortality of 374 000.[2] The Free State (FS), one of 9 provinces in South Africa, with an estimated population of 2 792 000,[2] has an AIDS prevalence rate of 18.5% among 15 - 49-year-olds, compared with the national figure of 16.9%.[3]

To combat the social disaster in high-burden countries, calls were made in 2003 to start the formidable task of getting antiretrovirals (ARVs) to people who needed them.[4] By the end of 2008, the World Health Organization (WHO) estimated that over 4 million people had accessed ARVs in developing countries. In South Africa, specifically, 700 500 people were reported to be accessing ARVs.[5] UNAIDS has published estimates of the total need for ARVs in different regions, defined as the number of people accessing ARVs plus those who qualify for ARVs, i.e. either with stage 4 disease (AIDS) or a CD4 count <200 cells/μl. Using this definition, an estimated 42% of people in developing countries who need ARVs are accessing them.[5]

In 2003, the South African National Department of Health (DOH) launched the national ARV roll-out with its Comprehensive Plan for the Care, Management and Treatment of HIV and AIDS (Operational Plan). Its aim was to achieve universal ARV access (an estimated 1.4 million people in need of ARVs at that stage) within 5 years.[6] Although the OP's stated aim was to provide comprehensive HIV care in an integrated fashion, the roll-out was delivered as a vertical programme with dedicated funding, staffing and administration, and closely controlled national accreditation of ARV sites.[6]

International debate continues on the merits of horizontal versus vertical programmes for delivering HIV care in developing countries. The advantage of vertical (stand-alone) programmes is their ability to deliver rapid roll-out of the type of complex health intervention needed to tackle HIV.[7] However, it is thought that such vertical programmes will not be able to achieve universal access and that they need to be broadened using the new so-called diagonal approach.[8] By 2006 it was clear that universal access to ARVs in South Africa would take more than 5 years to achieve. Less than 30% of those in need were accessing ARVs.[5] In 2007, the DOH published its National Strategic Plan (NSP) with detailed annual goals, aiming to achieve access to ARVs for 80% of the people who would need them by 2011,[9] and defining the need for ARVs as the number of new AIDS patients, estimated at about 520 000 annually, from 2007 to 2011.[3] In contrast with the WHO definition of need for ARVs, the former was an annual figure against which one can measure the number of new patients accessing ARVs each year, but it does not include estimates of people with a CD4 count below 200 cells/μl and therefore probably underestimates need.

In the FS, the ARV roll-out began in mid-2004 as a vertical programme with plans to establish ARV sites in each of its 20 local areas.[10] Two types of ARV sites were established. Treatment sites were led by doctors, where patients were referred for initiation and monitoring of ARVs. These were linked to nurse-led assessment sites

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in primary health care (PHC) facilities, where patients would be screened and prepared for ARVs and be able to collect medication. This model was adapted particularly for small-town sites with the accreditation of combined sites, i.e. a nurse-led assessment site with doctors visiting regularly. Reviews of the FS roll-out noted that the vertically run ARV programme drained staff from other PHC facilities and that problems were experienced with integration of ARV care into PHC services.[11]

Our study has lessons for achieving universal access to ARVs in high-burden countries. Our objective was to attempt to answer two questions: (*i*) what is the progress towards universal ARV access in the FS in the first 4 years of the roll-out; and (*ii*) how do the challenges in the FS inform the debate on the merits of vertical versus horizontal delivery systems in achieving universal ARV access in high-burden countries?

Methods

Study design and data collection

A retrospective, observational study was conducted using data from a variety of sources. Information on the number of ARV sites established in the FS from May 2004 until June 2008, expenditure, and staff vacancy rates for the ARV programme was obtained from the province's Directorate: Comprehensive HIV and AIDS Management. Information on conditional grant allocations was obtained from the National Treasury website.[12] Data on patients initiated on ARVs were obtained from the FS ARV database. Routine clinical data from all public sector ARV sites in the FS (with the exception of 3 small-town sites not yet online) were entered on an electronic record system (Meditech) by clinic-based data capturers. The data were incorporated in a data warehouse and used for monitoring and evaluation. This routinely collected dataset was supplemented by linkage to the National Health Laboratory Service (NHLS) database. Information on the estimated annual number of new AIDS patients in the FS was retrieved from the Actuarial Society of Southern Africa's 2003 model of demographic indicators for the HIV epidemic.[13]

Permission to conduct this study was granted by the Head of the FS Department of Health. The Ethics Committee of the Faculty of Health Sciences, University of the Free State, approved the protocol.

Staff training

The FS Department of Health runs a regular 2-week ARV training course for medical, nursing and ancillary staff. Information on staff training was obtained from the province's Directorate: Human Resource Management, and from district managers. It has also implemented on-site training in integrated management of respiratory illnesses, tuberculosis (TB), HIV (including ARVs) and sexually transmitted infections (STIs) in adults, using the PALSA PLUS guidelines.[14]

Statistical analysis

The monthly new ARV enrolments from 2004 to 2007 were plotted and an extrapolation of a linear trend line was fitted to the data to project expected increases for 2008 and 2009 using statistical packages available in Microsoft Excel. Median waiting times for ARV initiation were calculated using Kaplan-Meier estimates. Waiting time was defined as time between first CD4 count <200 cells/μl and initiation of ARVs. Patients who died before the start of treatment or who were not observed to start ARVs were censored in these analyses. Median CD4 counts at commencement of ARVs were calculated over 3-month periods. The significance of a trend over time in enrolment CD4 counts was checked using an extension of the Wilcoxon rank sum test. Survival analyses and tests for trend were done using Stata version 10.1.

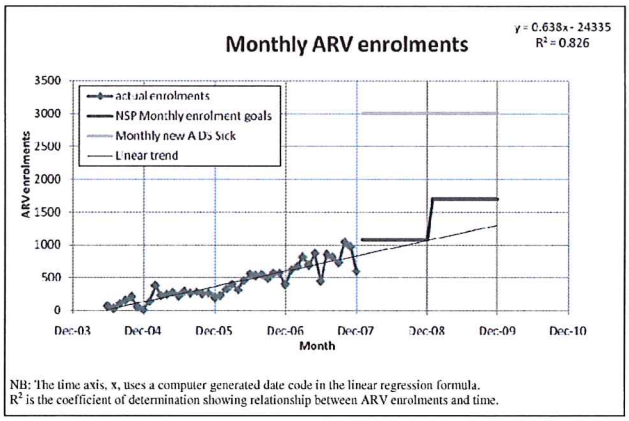
Results

The **number of all types of sites** increased steadily from 20 sites in 6 local areas by the end of 2004, to 56 sites by August 2008, with at least 1 site in each of the 20 local areas. There were 11 treatment sites, 27 assessment sites and 18 combined sites.

The **number of new patients** (adults and children) commencing ARVs each month increased steadily, peaking at 1 045 in October 2007 (Fig. 1). Comparing the annual number of patients starting ARVs with the estimated number of new AIDS patients for 2004 - 2007,[13] the percentage coverage increased from 2% in 2004 to 25% in 2007 (Table I). Patients were distributed unevenly across the 56 sites, with 7 urban sites each having initiated treatment on more than 1 000 patients.

Should the expansion of the ARV roll-out continue as in the period 2004 - 2007, monthly new ARV enrolments for 2008 and 2009 could be expected to have increased as in the trend line in Fig. 1. According to this projection, about 11 500 patients would have started ARVs in 2008 and about 14 300 in 2009, representing about 31% and 39% of estimated new AIDS patients, respectively.[13] These percentages would fall short of the goal of the NSP[9] to increase enrolment of new patients on ARVs to 35% of need in 2008 and 55% in 2009 (Table II). If, however, NSP goals were achieved in the FS, the cumulative number of patients on treatment at ARV sites would more than double to reach approximately 44 267 (Table II).

The **median waiting times** from eligibility (CD4 count <200 cells/μl) to starting ARVs decreased from 5.82 months in 2004 to 3.24 months in 2007 (Table III). The analysis of waiting times was



NB: The time axis, x, uses a computer generated date code in the linear regression formula.
R^2 is the coefficient of determination showing relationship between ARV enrolments and time.

Fig. 1. Monthly new enrolments (2004) plotted against need and goals as envisaged in the National Strategic Plan 2008 and 2009.

Table I. Annual enrolments on ARVs compared with estimated new AIDS patients in the Free State 2004 - 2007

Year	New AIDS patients	Total enrolled on ARVs (% of need)
2004	29 104	642 (2.2)
2005	32 124	3 091 (9.6)
2006	34 431	5 420 (15.7)
2007	36 012	9 157 (25.4)
Total	131 671	18 310

Table II. Goals for new enrolments on ARVs for the Free State as envisaged in the National Strategic Plan (NSP)

Year	New AIDS patients	Monthly new enrolments to meet need	Goals for new enrolments according to NSP (%)	Monthly new enrolments to meet NSP goals	Estimated cumulative numbers on ARVs*
2008	36 861	3 070	12 901 (35)	1 075	28 360
2009	37 059	3 090	20 382 (55)	1 700	44 267
2010	36 737	3 070	25 716 (70)	2 140	63 912
2011	36 042	3 000	28 834 (80)	2 400	85 225

*Cumulative numbers on ARVs assume a 15% dropout of new patients and a 5% dropout of previous patients owing to deaths and defaulting on ARVs.

Table III. Waiting time from eligibility to treatment for each calendar year and health district (*N*=22 496)*

District	Year of enrolment							
	2004		2005		2006		2007	
	N	MWT	*N*	MWT	*N*	MWT	*N*	MWT
Fezile Dabi	363	6.84	734	3.04	883	3.44	769	3.04
Xhariep	422	11.27	331	6.21	591	3.80	539	2.78
Motheo	1 624	6.02	1 599	7.90	1 126	5.02	2 428	3.83
Lejweleputswa	914	4.83	1 146	3.50	1 416	3.07	1 331	2.84
Thabo Mofutsanyane	676	4.86	1 544	6.55	2 210	6.28	1 850	2.74
Total	3 999	5.82	5 354	5.75	6 226	4.36	6 917	3.24

**N* represents patients who commenced ARVs and had a pre-ARV CD4 count available. The number of patients with missing CD4 results in the database increased in 2006 and 2007, probably owing to increased workload at the sites. MWT = median waiting time (months).

repeated using cumulative incidence functions to account for the competing risk of patients dying before accessing treatment. This made no difference to the trend of median waiting times decreasing over time. Pre-ARV CD4 cell counts were available in the dataset for 75% of the 17 847 patients who started ARVs by December 2007. Many CD4 results were not entered onto the database, particularly in 2006 and 2007, as workload increased and not all missing results could be matched from the NHLS database.

The **median baseline CD4 cell counts at commencement of ARVs** rose from 89 cells/μl (interquartile range (IQR) 49 - 156) in the second quarter of 2004 to 124 cells/μl (IQR 55 - 84) in the last quarter of 2007 (Fig. 2). There is strong evidence of a positive trend over time (z=7.71 Prob >|z|=0).

Human resources and training. By June 2008, 534 posts had been created in the ARV programme, although 207 (38.8%) were vacant. Of the professional posts, 39% nurses', 50% doctors' and 59% pharmacists' posts were vacant.

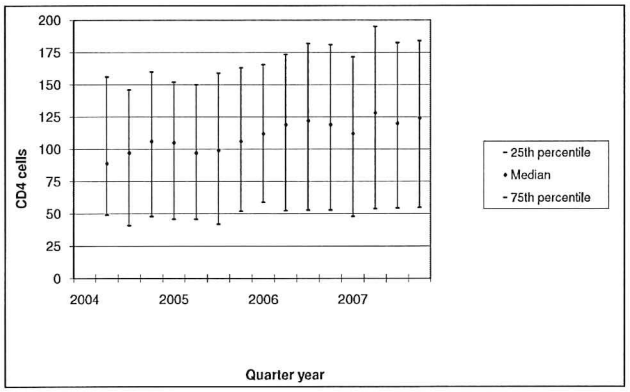


Fig. 2. Plot of median CD4 cell counts at initiation of ARVs and their IQRs at each quarter,* N=*5 918. (*Based on 5 918 patients with a CD4 result in the period 6 weeks before - 4 weeks after commencement of ARVs.)*

Training of staff in the management of HIV including ARVs was not restricted to staff from the ARV programme. From May 2004 until August 2008, 2 540 members of staff, including 251 doctors and 1 130 professional nurses, had completed the 2-week ARV training course. At least 1 professional nurse from every PHC clinic in the province had been trained. By August 2008, staff in 139 of the approximately 240 PHC clinics had been trained in managing patients using the PALSA PLUS guidelines.

Funding for the ARV roll-out is provided by the DOH, with an annual allocation to the provinces of a conditional grant for comprehensive HIV and AIDS management. Amounts allocated to the FS have improved annually, with more than 40% increases over the first 2 years, a 24% increase in 2007/2008 for the 2008/2009 financial year, and a 20% increase from 2008/2009 to 2009/2010. Of the R153 646 000 allocated in the 2007/2008 conditional grant to the FS, 35% was spent on drugs and laboratory tests, and 39% on staff remuneration for full-time and lay workers in the ARV sites. The rest was spent on training, prevention programmes, infrastructure, step-down care and programme management.

Discussion

The public sector ARV programme in the FS achieved steadily rising numbers of monthly new enrolments on ARVs and decreasing waiting times for those eligible for ARVs. CD4 counts were higher at commencement of ARVs, and ARV services were provided in all its 20 local areas. These findings suggest that the programme is making inroads into the shortfall, and people are accessing ARVs more readily. Published figures show good outcomes of patients receiving ARVs in the public sector in the FS, with a 7% mortality rate and an 82% viral load suppression rate at 1 year.[15]

A strength of this study is the availability and completeness of data for patients before and during ARV initiation, supplemented by linkages with the NHLS database. A weakness as a retrospective study is that, because of an increasing data entry backlog, no accurate figures are available on patient retention in the ARV programme. Furthermore, these findings do not include data for patients on ARVs outside the public sector in the FS.

However, assuming that most people who need ARVs in the FS will only have access to public facilities, the percentage that accessed ARVs is small and the FS has a long way to go towards universal ARV coverage. From 2004 to 2007, only 18 310 people were initiated on ARVs in the public sector (Table I), whereas an estimated 131 671 developed AIDS in those 4 years.[13] Even in 2007, ARV initiations reached only 25% of the estimated need. Presumably, many of those who did not start ARVs have died. In the FS public sector, the mortality rate of people with CD4 counts <350 cells/μl is 53% at 1 year, most of whom (87%) did not start ARVs.[15]

Projections of patients starting ARVs in 2008 and 2009, based on the performance of the programme in the first 4 years, suggest that by 2009 only 39% of the newly ill patients with AIDS would access ARVs in the public sector. This figure is below the NSP's goal of 55% of patients who need ARVs being able to access them by 2009.[9] If the FS manages to achieve NSP goals, the cumulative number of people on ARVs would increase by about 150%. The 7 large urban sites handling chronic ARV care for more than 1 000 patients by the end of 2007 would increase patient load to more than 2 500. Subsequently, this increasing load of chronic care would soon see clinics exceed their capacity, a problem noted by other ARV sites in South Africa.[16]

Considering the shortage of human and financial resources, even modest projected increases for 2008 and 2009 may not be achievable, especially if the ARV roll-out is continued as a vertical programme. Of the 534 new posts created in the ARV programme, 38.8% were vacant by June 2008. This may be related to findings of a high level of burnout and compassion fatigue among ARV and PHC nurses in the FS.[17]

Funding of comprehensive HIV care in the FS increased by only 24% in the 2008/2009 budget, and by 20% in the 2009/2010 budget, whereas expected costs for drugs and laboratory tests (costs directly related to the number of people on ARVs and already taking up 35% of the budget) would have increased by 150% if there were over 44 000 people on ARVs by the end of 2009. Although the public sector ARV programme in the FS is increasing the access to ARVs for people who need them, human and financial resources appear insufficient to achieve universal coverage, particularly if the vertical approach is continued.

Several models of broadening an initial vertical approach to achieve universal ARV access include: (*i*) down-referral, where ARV sites refer stable patients to obtain their continuing ARV supply at PHC clinics.[18] This approach was mostly used as an afterthought to solve the problem of a saturated vertical service, but others see it as a gateway to integrate the provision of ARVs into PHC services; (*ii*) task shifting, a strategy supported by WHO,[19] the essence of which is to equip and utilise lower cadres of health care workers to deliver comprehensive HIV care as a strategy to overcome shortages of highly skilled health care workers; and (*iii*) integration of HIV and ARV care into PHC services, a strategy implemented by 3 rural subdistricts in South Africa that have almost reached universal access.[20]

The FS DOH decided to broaden the programme by using a combination of task shifting (equipping nurses to initiate and repeat ARV prescriptions for uncomplicated patients) and integration of comprehensive HIV care into PHC services. The intervention commenced in early 2008 and is being implemented and evaluated as a pragmatic randomised controlled trial (STRETCH trial) in 31 of the current ARV sites, and is due to be completed in June 2010.[21] The South African National DOH recently announced its accelerated AIDS plan with the aim of increasing access to antiretroviral therapy (ART).[22] Task shifting and integration of ART into primary care services are central components of this plan. The experience of the STRETCH trial should provide important lessons in how to implement such a diagonal approach to expanding ART care and particularly how to equip and support nurses in primary care services to provide ART care.[23]

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Chapter 3

Task shifting of antiretroviral treatment from doctors to primary care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial

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Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial

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Summary

Background Robust evidence of the effectiveness of task shifting of antiretroviral therapy (ART) from doctors to other health workers is scarce. We aimed to assess the effects on mortality, viral suppression, and other health outcomes and quality indicators of the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) programme, which provides educational outreach training of nurses to initiate and represcribe ART, and to decentralise care.

Methods We undertook a pragmatic, parallel, cluster-randomised trial in South Africa between Jan 28, 2008, and June 30, 2010. We randomly assigned 31 primary-care ART clinics to implement the STRETCH programme (intervention group) or to continue with standard care (control group). The ratio of randomisation depended on how many clinics were in each of nine strata. Two cohorts were enrolled: eligible patients in cohort 1 were adults (aged ≥16 years) with CD4 counts of 350 cells per μL or less who were not receiving ART; those in cohort 2 were adults who had already received ART for at least 6 months and were being treated at enrolment. The primary outcome in cohort 1 was time to death (superiority analysis). The primary outcome in cohort 2 was the proportion with undetectable viral loads (<400 copies per mL) 12 months after enrolment (equivalence analysis, prespecified difference <6%). Patients and clinicians could not be masked to group assignment. The interim analysis was blind, but data analysts were not masked after the database was locked for final analysis. Analyses were done by intention to treat. This trial is registered, number ISRCTN46836853.

Findings 5390 patients in cohort 1 and 3029 in cohort 2 were in the intervention group, and 3862 in cohort 1 and 3202 in cohort 2 were in the control group. Median follow-up was 16·3 months (IQR 12·2–18·0) in cohort 1 and 18·0 months (18·0–18·0) in cohort 2. In cohort 1, 997 (20%) of 4943 patients analysed in the intervention group and 747 (19%) of 3862 in the control group with known vital status at the end of the trial had died. Time to death did not differ (hazard ratio [HR] 0·94, 95% CI 0·76–1·15). In a preplanned subgroup analysis of patients with baseline CD4 counts of 201–350 cells per μL, mortality was slightly lower in the intervention group than in the control group (0·73, 0·54–1.00; p=0·052), but it did not differ between groups in patients with baseline CD4 of 200 cells per μL or less (0·94, 0·76–1·15; p=0·577). In cohort 2, viral load suppression 12 months after enrolment was equivalent in intervention (2156 [71%] of 3029 patients) and control groups (2230 [70%] of 3202; risk difference 1·1%, 95% CI −2·4 to 4·6).

Interpretation Expansion of primary-care nurses' roles to include ART initiation and represcription can be done safely, and improve health outcomes and quality of care, but might not reduce time to ART or mortality.

Funding UK Medical Research Council, Development Cooperation Ireland, and Canadian International Development Agency.

Introduction

Since 2006, efforts to increase access to antiretroviral therapy (ART) in Africa have emphasised task shifting—ie, delegation of clinical tasks from doctors to other health-care workers.[1] However, robust evidence of its effectiveness is scarce. A 2010 systematic review of task shifting in care of patients with HIV infection[2] showed that it is effective and can provide high-quality care, but of 25 original studies reviewed, only 11 made comparisons with alternatives, and only two of those were randomised trials. Neither trial assessed the effect of task shifting on mortality in people awaiting ART, which in both was initiated by doctors.[3,4]

In South Africa, a major obstacle to ART expansion has been the shortage of doctors available to initiate treatment, because of an absolute shortfall and also because doctors spend much of their time represcribing ART. Delayed ART initiation has resulted in high mortality rates in patients who are eligible for ART but waiting for treatment.[5,6] Thus, evidence from randomised trials is needed on whether other health workers can effectively and safely identify patients eligible for ART,

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start treatment, and then follow up and represcribe. In South Africa, nurses provide most primary care for the general population.

Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) is a complex health systems intervention with educational and organisational components. It trains nurses to assume responsibility for ART initiation and represcribing. It combines an educational outreach training model (Practical Approach to Lung Health in South Africa; PALSA and PALSA PLUS)[7–9]—previously shown to effectively improve care for respiratory disorders, tuberculosis, and HIV before ART is used—with additional organisational components. STRETCH is intended to rationalise ART and other services for people with HIV infection, to treat patients already stabilised on ART at clinics close to their homes, to increase the number of clinics in which ART can be initiated, and to raise the number of clinics and nurses providing high-quality pretreatment care. The purpose of our study was to assess the effects of STRETCH on mortality, viral suppression, and other health outcomes and quality indicators, compared with the present system in which only doctors can prescribe ART.

Methods

Study design and participants

We undertook a pragmatic, parallel, cluster-randomised trial in the Free State province of South Africa.[10] The province's public-sector ART programme started in 2004, in designated nurse-led primary-care clinics and doctor-led hospital outpatient departments. Patients are assessed and prepared for ART by nurses and referred to doctors for initiation and represcriptions. High mortality of patients awaiting treatment initiation by doctors[5] caused the provincial health department to introduce STRETCH and to commission us to assess its effect on outcomes for patients.

We enrolled patients from all 31 clinics participating in the ART programme between Jan 28, 2008, and June 30, 2009, and completed follow-up on June 30, 2010. We enrolled two cohorts to allow us to simultaneously assess the effect of the intervention when patients became eligible for ART initiation, and for individuals on long-term ART. Patients in cohort 1 were adults (aged ≥16 years) with CD4 counts of 350 cells per μL or less who had not yet started ART. They were either eligible for ART (CD4 ≤200 cells per μL) or likely to become eligible during the trial (CD4 201–350 cells per μL). They were followed up for at least 12 months. Patients in cohort 2 were adults who had already received ART for at least 6 months and were being treated at the time of enrolment. In clinics with more than 100 patients eligible for cohort 2, a random sample was taken electronically (sample size proportional to total number of eligible patients); in other clinics, all eligible patients were included. We excluded patients from both cohorts if they did not return to their clinic after enrolment, because they needed to visit a clinic more than once to initiate ART after obtaining CD4 results in cohort 1 or to be potentially exposed to the intervention in cohort 2.

The trial protocol was approved by the research ethics committees of the faculties of health sciences at the University of Cape Town (Cape Town, South Africa) and the University of the Free State (Bloemfontein, South Africa). Clinic managers provided written informed consent to take part in the trial. Informed consent was not requested from patients because the intervention was educational and managerial, and was aimed at entire clinics and their staff, not at individual patients, so all patients in the same clinic would be exposed to the same intervention irrespective of whether they consented to participate.[10,11] Patients in intervention clinics were given written information about the trial and the intervention. We adhered to ethical principles for use of medical records for research without patients' consent:[10,12] the research had clear public benefit; we obtained approval for the study from lead doctors and nurses managing the programme; use of data for research did not affect individuals' care; data were already being used by the research team for programme assessment on behalf of the provincial health department; and data confidentiality was strictly enforced. Only specific data managers had access to personal identifiers. Anonymised data were provided only to the principal investigators (LF, MOB), the lead statistician, and a health economist. With hundreds of patients in each clinic, individuals could not be identified from clinic names.

Randomisation and masking

Clinics and their patients were randomly assigned to either of two parallel groups. Randomisation was done within nine strata—one for each referral hospital in the province—to avoid confounding of outcomes by variation in care provided by doctors in each hospital. One stratum contained four clinics and another two clinics; the even numbers meant that randomisation could be done in a 1:1 ratio. The other seven strata contained odd numbers of clinics and were randomly allocated to have either one more or one less intervention clinic than control clinics with simple random sampling in nQuery Advisor. Six strata each had three clinics. Three of those were randomised with a ratio of two intervention clinics to one control clinic. The remaining three were randomised with a ratio of one intervention clinic to two control clinics. The last stratum had seven clinics, and was randomised with a ratio of four intervention clinics to three control clinics. Within each stratum, clinics were randomly assigned to intervention or control according to sequences of random numbers in a random number table (even numbers for control and odd numbers for intervention), with separate sequences for each stratum. In total, we had 16 intervention clinics and 15 control clinics. The trial statistician (CL) undertook

the randomisation before the trial started. Masking of patients and clinicians was not possible because implementation of the intervention was obvious. The interim analysis was blind, but data analysts were not masked after the database was locked for final analysis.

Procedures

The model of care in the control clinics was the standard of HIV and ART care in provincial health services of the Free State before the trial, and was continued during the trial (appendix). It was consistent with public sector health services in most parts of South Africa. Patients diagnosed with HIV infection were referred to designated nurse-led clinics to establish whether they were eligible for ART. According to treatment protocols at the time, adults were eligible for ART when their CD4 count was less than 200 cells per μL, they had had stage IV HIV infection (AIDS),[13] or were pregnant with a CD4 count of less than 350 cells per μL.[14] Patients not yet eligible for ART received routine care, such as regular CD4 testing, until they became eligible. Patients eligible for ART were referred to ART treatment sites in hospital outpatient departments for initiation of treatment and review of ART prescriptions every 3–6 months, both done by a doctor. To comply with national regulations that require ART to be dispensed by or under the supervision of pharmacists, who were not always located in clinics (appendix), drugs were dispensed at treatment sites in patient-named packages, then delivered to clinics where nurses issued them to patients every month in-between doctor visits. In some remote areas, visiting doctors provided ART initiation and on-site represcription in nurse-led clinics. Nurses in both control and intervention clinics continued to receive educational outreach training in the use of PALSA PLUS, which includes management of HIV infection and AIDS but not ART prescribing. Control clinics continued to receive routine managerial support and monitoring.

Intervention clinics implemented STRETCH (appendix).[15] Care of patients with HIV infection differed from control clinics in several ways. Prescribing nurses received at least four educational outreach training sessions about ART prescribing and side-effects with a special edition of the PALSA PLUS guidelines, which included algorithms to start and to monitor patients on ART, and to identify those needing referral to a doctor.[15] Patients had to meet certain criteria for nurse initiation and represcription of ART (appendix). Patients who did not meet these criteria were referred to doctors who, unlike nurses, were authorised to initiate tailored regimens, to change prescriptions, and to prescribe second-line drugs.

Nurse middle managers, who had already been trained as outreach trainers for PALSA PLUS, participated in an additional 2·5 day training course about STRETCH and delivered STRETCH educational outreach training to all nursing staff at every intervention clinic. After training, 103 nurses in intervention clinics were registered with the Free State's Pharmaceutical Services Department and authorised to initiate first-line ART drugs and repeat ART prescriptions during the trial. 24 doctors who supported these nurses were familiarised with the guidelines by the STRETCH trial co-ordinator (a doctor experienced in care of patients with HIV infection; KU).

The intervention was implemented in three phases to give nurses time to gain confidence with ART. First, training was delivered and the STRETCH trial co-ordinator visited every intervention clinic to establish a STRETCH team who were responsible for support of phased decentralisation of care. Second, nurses assumed responsibility for represcribing ART for patients already receiving treatment. The care for all stable patients given ART was consolidated in their clinic, so they did not need to travel to another treatment site for represcriptions. Third, nurses began to initiate ART in eligible patients. The rate of implementation was set by clinic staff, allowing well functioning clinics to progress rapidly,

See Online for appendix

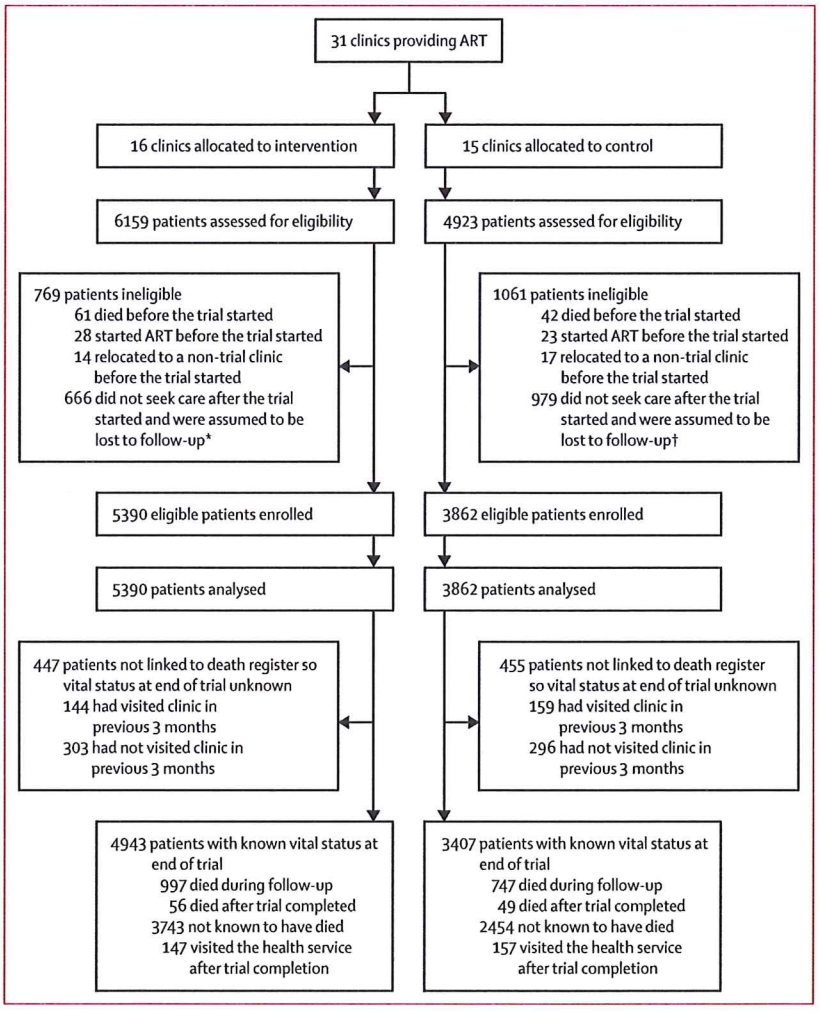

Figure 1: **Trial profile for cohort 1**
ART=antiretroviral therapy. *105 of these patients died after the trial started. †119 of these patients died after the trial started.

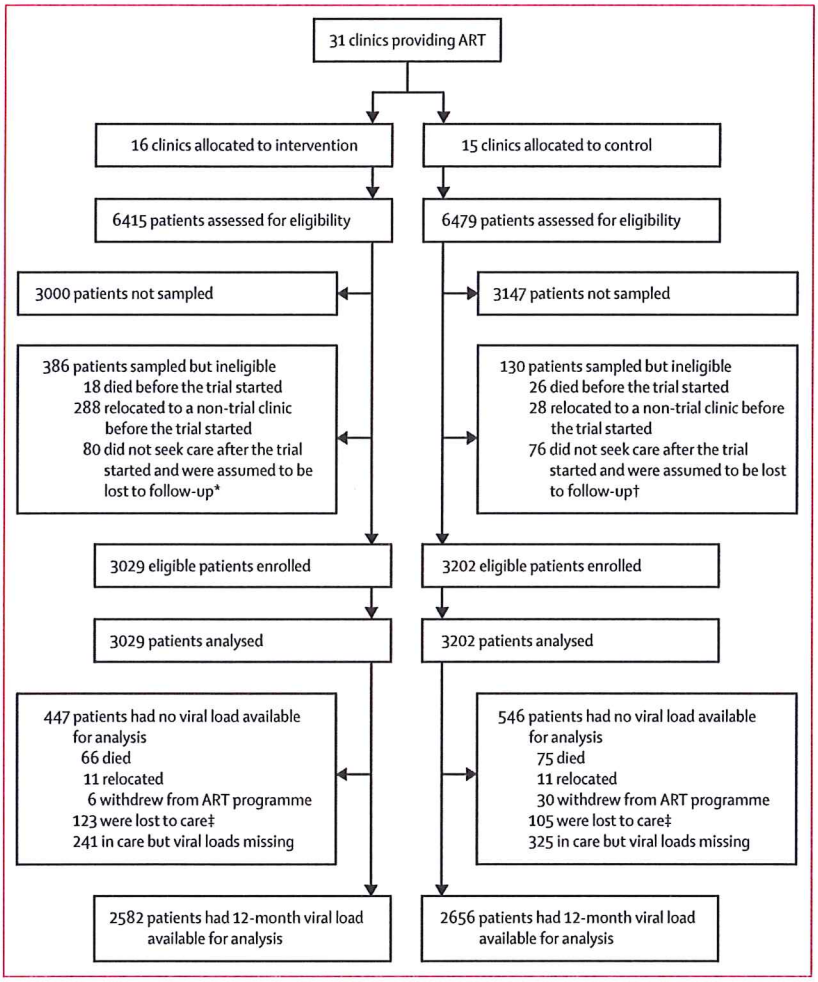

Figure 2: **Trial profile for cohort 2**
ART=antiretroviral therapy. *22 of these patients died after the trial started. †22 of these patients died after the trial started. ‡After 12 months of follow-up, patients had been recorded as withdrawn or relocated, or they had had no clinic visit or laboratory test in the previous 6 months, and we had no documentation of death.

while others took longer times. Implementation was phased between January, and December, 2008.

All 16 intervention clinics successfully implemented phases one and two; two clinics could not implement phase three because of difficulties with staffing and drug distribution, but remained in the trial. In each randomisation stratum, the first date on which patients in intervention and control clinics were enrolled in the trial was the date that the last intervention clinic started implementation of phase three to ensure that patients in both groups were enrolled at similar times. In the two strata with the intervention clinics unable to proceed to phase three, enrolment of patients in intervention and control clinics started on Dec 1, 2008.

Data for individual patients were obtained from routine electronic medical records that had been implemented as part of the treatment programme in 27 clinics. At every clinical visit, information was written on paper forms by clinicians and entered into the province's computer system by clerks in the clinic. At the four clinics without electronic records, research fieldworkers entered specific variables from paper forms in patients' folders into an electronic database.

We identified deaths from programme data and by linkage with the national mortality register with national identity numbers. The national mortality register is based on death certification and records 90% of all deaths,[16] including those that occur at home or in hospital that are not noted by the ART programme. We linked individuals' medical record data with the provincial health department's laboratory, hospital admission, and tuberculosis databases.

Data were downloaded to a central database every week. We implemented routine checks of data quality to minimise missing and unreliable data, prioritising variables used to assess eligibility and primary outcome measures. For example, patients with missing national identity numbers, or numbers that did not match their recorded date of birth or did not conform to the standard identity number algorithm used in South Africa were identified every 2–4 weeks. Eight research fieldworkers travelled to the trial clinics and searched for missing information in patients' paper records. A dedicated database manager co-ordinated data collection, management, and linkage, and reported weekly on enrolment, follow-up, and data quality.

The primary outcome for cohort 1 was time from enrolment to death. Each patient's follow-up was censored 12–18 months after enrolment, depending on whether patients were enrolled towards the end or beginning of the process, to ensure comparable follow-up across clinics that started implementation early or late. Secondary outcomes were measures of health status (changes in weight and CD4 cell counts, viral loads, hospital admissions, and inpatient days) and indicators of quality of care (ART initiation, time from enrolment to start of ART, detection of tuberculosis, co-trimoxazole provision, programme retention 1 year after enrolment, baseline CD4 cell count in patients who started ART, and clinic consultations with nurses and doctors).

For cohort 2, the primary outcome was the proportion with undetectable viral loads (<400 copies per mL) 1 year after enrolment. Secondary outcomes were measures of health status (time to death censored 12–18 months after enrolment, changes in weight and CD4 cell counts, hospital admissions, and inpatient days) and indicators of quality of care (programme retention, diagnosis of tuberculosis, co-trimoxazole provision, switching of ART regimens, and clinic consultations with nurses and doctors).

Statistical analysis

For cohort 1, sample size was calculated for a superiority trial, because we hoped that STRETCH would increase access to ART and thus reduce mortality in the intervention group. We analysed previous programme data

for patients with initial CD4 counts of 350 cells per μL or less in the trial clinics between 2004, and 2007, and noted that 29% of patients followed up for at least 1 year died within that year, with an intra-clinic correlation coefficient (ICC) of 0·01. A sample size of 6000 (3000 per group) would provide 90% power to detect a 6% difference in 1-year mortality (24% *vs* baseline frequency of 30%) at the 5% significance level (two-sided), assuming ICC was 0·01. On the basis of a 10% dropout rate in our previous trial,[7] the sample size was increased to 7400. This increased sample size was a conservative adjustment with the denominator (1–[rate of loss to follow-up])^2—ie, 6400/(0·9^2)—which accounts for the dropout in the intervention group and the proportion receiving the standard of care.[17] We planned for, and completed, an interim analysis 1 year after recruitment started. Neither of the prespecified stopping rules (difference between groups in either primary outcome with $p<0·001$)[10] for either cohort were met, and the trial monitoring committee recommended that the trial continue. However, the analysis of pooled data showed that the 1-year mortality rate was lower than had been previously assumed; therefore, more patients were enrolled into cohort 1 than was originally planned.

For cohort 2, sample size was calculated for an equivalence trial, because we hoped to show that nurse-led ART would be as effective in maintenance of viral suppression as is doctor-led treatment. In previous programme data, 82% of patients who had received ART for 12 months had undetectable viral loads, with an ICC of 0·005. A sample size of 4000 (2000 per group) would provide 90% power to show equivalence between groups with a 6% equivalence limit, with 5% significance and an ICC of 0·005. To allow for 10% dropout, the sample size was increased to 4900 (ie, 4000/[0·9^2]). This 6% equivalence limit was smaller than was the 9% equivalence limit for viral suppression used in the Jinja trial.[3] The interim analysis of pooled data showed that the proportion of patients with a measured viral load measured after 1 year was lower than had been previously assumed; therefore more patients were enrolled into cohort 2 than was originally planned.

Effects of the intervention were estimated by comparisons of patients in the intervention and control groups with multiple regression models and Huber-White robust adjustment of errors for intra-cluster correlation of outcomes; they were stratified by randomisation strata with Stata (version 11.1). All clinics and patients were analysed in the treatment group to which they were randomly assigned (intention-to-treat). Time from enrolment to death was analysed with Cox proportional hazards models. Time from enrolment to ART initiation was analysed by competing risks regression,[6] with death as a competing risk. For these time-to-event analyses, follow-up was censored on June 30, 2010, or 18 months after enrolment, whichever was earlier, thus providing 12–18 months of follow-up.

	Intervention group	Control group
Cohort 1		
Number of patients	5390	3862
Women	3604 (67%)	2681 (69%)
Age (years)	36 (30–43)	35 (29–42)
National identity number recorded	4767 (88%)	3184 (82%)
CD4 (cells per μL)	141 (70–201)	137 (70–197)
0–49	934 (17%)	678 (18%)
50–99	949 (18%)	720 (19%)
100–199	2141 (40%)	1547 (40%)
200–350	1366 (25%)	917 (24%)
WHO stage recorded*	3057 (57%)	1719 (45%)
Stage I	1582/3057 (52%)	551/1719 (32%)
Stage II	637/3057 (21%)	470/1719 (27%)
Stage III	725/3057 (24%)	653/1719 (38%)
Stage IV	113/3057 (4%)	45/1719 (3%)
Weight recorded	4400 (82%)	2875 (74%)
Weight (kg)	59 (14)	58 (14)
Present tuberculosis	301 (6%)	200 (5%)
Admitted in the year before enrolment	392 (7%)	313 (8%)
Cohort 2		
Number of patients	3029	3202
Women	2113 (70%)	2332 (73%)
Age (years)	38 (32–44)	38 (32–45)
National identity number recorded	2859 (94%)	2958 (92%)
Duration on ART (months)	13·9 (6·8–21·7)	13·7 (7·3–22·3)
ART regimen		
First line (stavudine, lamivudine, efavirenz)	1846 (61%)	2056 (64%)
First line (stavudine, lamivudine, nevirapine)	1012 (33%)	1011 (32%)
Second line (zidovudine, didanosine, lopinavir)	37 (1%)	28 (1%)
Other	109 (4%)	100 (3%)
Not known	25 (1%)	7 (<1%)
Viral load <400 copies per mL	2378 (79%)	2507 (78%)
Weight recorded	2886 (95%)	3128 (98%)
Weight (kg)	61 (13)	62 (13)
Present tuberculosis	241 (8%)	186 (6%)
Admitted in the year before enrolment	282 (9%)	299 (9%)

Data are n (%), median (IQR), n/N (%), or mean (SD). ART=antiretroviral theraoy. *Staged just before initiation of ART, usually after enrolment.

Table 1: **Baseline characteristics by cohort**

For the preplanned subgroup analysis of patients in cohort 1, we included an allocation-subgroup interaction term in the Cox model to separately estimate the effect of the intervention on survival in patients with CD4 counts higher and lower than 200 cells per μL at enrolment. We used binomial regression to estimate differences in proportions of patients with suppressed viral loads, and other secondary outcomes in cohort 2. We calculated risk ratios for secondary binary outcomes for cohort 1. We used linear regression to compare changes in CD4 count and weight in both cohorts, by comparing values at the end of follow-up while adjusting for the corresponding baseline values (ANCOVA).[18] Poisson regression was

used to estimate incidence rate ratios for count outcomes such as clinic visits, accounting for individuals' duration of follow-up. Secondary analyses further adjusted for potentially confounding baseline characteristics such as presence of a national identification number (potentially affecting ascertainment of death), baseline CD4 cell count, age, and sex.

This trial is registered, number ISRCTN46836853.

Role of the funding source

The sponsors of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study, and LF and MOB share final responsibility for the decision to submit for publication.

Results

Figures 1 and 2 show the trial profiles for each cohort. All 31 clinics completed the trial. Median follow-up was 16·3 months (IQR 12·2–18·0) in cohort 1 and 18·0 months (18·0–18·0) in cohort 2. In cohort 1 (figure 1), the median number of patients enrolled per clinic was 210 in the intervention group (IQR 154–323) and 260 (143–345) in the control group. More patients were enrolled in the intervention group than in the control group because it had one more clinic and, by chance, two intervention clinics had high numbers of eligible patients (1377 and 959 compared with a maximum of 596 in control clinics). Median duration of follow-up in this cohort was 16·4 months (IQR 12·4–18·0) in the intervention group and 16·3 months (11·5–18·0) in the control group. In cohort 2 (figure 2), the median number of patients enrolled per clinic was 176 (97–251) in the intervention group and 134 (96–349) in the control group. Median duration of follow-up in cohort 2 was 18·0 months (18·0–18·0) in both groups. Control group clinics tended to be smaller and were more likely to have on-site doctor support: 8/15 (53%) of control clinics and 5/16 (31%) of intervention clinics had a full or part time doctor available for on-site ART initiation. Table 1 shows patients' baseline characteristics.

In cohort 1, 997 (20%) of 4943 patients with known vital status at the end of the trial analysed in the intervention group and 747 (19%) of 3862 analysed in the control group died (ICC 0·008; figure 1). Time to death did not differ between groups (table 2, figure 3). Adjustment for baseline characteristics did not change this result (table 2, appendix). The preplanned subgroup analysis[10] showed that intervention-group patients with CD4 counts of 201–350 cells per μL at enrolment had a 27% lower risk of death than did those in the control group, but this difference was not significant; we recorded no difference between groups in patients with CD4 counts of 200 cells per μL or less at enrolment (table 2, figure 3). In patients with CD4 counts of 201–350 cells per μL, adjustment for characteristics strengthened the association between the intervention and mortality (table 2).

With pooling of patients in intervention and control groups in cohort 1, ART was associated with a 47% lower risk of death than no treatment (hazard ratio [HR] 0·53, 95% CI 0·42–0·68). The strength of this association did not differ between intervention and control groups (data not shown). Detection of tuberculosis, programme retention, and CD4 cell count at the end of follow-up were higher in the intervention group than in the control group (table 3). In the intervention group, 965 (26%) of 3712 ART initiations were by a nurse; in the control group, none were.

In cohort 2, viral suppression a year after enrolment did not differ between intervention and control patients, and the prespecified equivalence limit of 6% was met (table 4). Adjustment for patients' baseline characteristics did not change this result (appendix). Gains in CD4 cell count and weight (data not shown), and probability of switching ART drugs (table 4), were higher in the intervention group than in the control group. 47 (77%) of 61 patients in the intervention group who switched regimens had documentation of detectable viraemia beforehand, compared with 20 (74%) of 27 patients in the

	Intervention group			Control group			Hazard ratio (95% CI)	p value	Adjusted hazard ratio (95% CI)†	Adjusted p value
	Number of deaths	Person-years at risk	Hazard of death per 100 person-years at risk (95% CI)*	Number of deaths	Person-years at risk	Hazard of death per 100 person-years at risk (95% CI)*				
Primary analysis (n=9252)	997	74256	1·34 (1·26–1·43)	747	51861	1·44 (1·34–1·55)	0·94 (0·76–1·15)	0·532	0·92 (0·76–1·12)	0·401
Subgroup analysis: baseline CD4 count 201–350 cells per μL (n=2283)	102	20710	0·06 (0·03–0·10)	90	13224	0·68 (0·55–0·84)	0·73 (0·54–1·00)‡	0·052	0·70 (0·52–0·95)§¶	0·020
Subgroup analysis: baseline CD4 count ≤200 cells per μL (n=6969)	895	53546	1·67 (1·56–1·78)	657	38637	1·70 (1·57–1·83)	1·00 (0·80–1·24)	0·999	0·94 (0·77–1·16)	0·577

*Binomial exact confidence intervals. †Adjusted for patients' age, sex, CD4 cell count at enrolment, and record of an identity number. ‡Interaction between group and CD4 cell count stratum p=0·050. §Adjusted for patients' age, sex, and record of an identity number. ¶Interaction term between group and CD4 cell count stratum p=0·049.

Table 2: **Effect of the intervention on time from enrolment to death in cohort 1**

control group, suggesting that the increased numbers of switches in the intervention group were appropriate. Time to death did not differ between groups (figure 3).

Patients in the intervention group visited nurses more often than did those in the control group in both cohorts, and doctors in cohort 1 (appendix). Adverse events of interest were deaths and admissions to hospital (figures 1, 2, appendix).

Discussion

We have shown that task shifting of the primary responsibility for ART from doctors to primary-care nurses in a large-scale public sector programme did not improve survival of patients not yet taking ART with CD4 counts of 350 cells per μL or less, but did in patients with CD4 counts of 201–350 cells per μL, although the difference was not significant. It did achieve its second primary goal of equivalent viral load suppression in patients already taking ART at enrolment. The 95% CI for the comparison of viral load suppression were more precise in our study than in the Jinja trial of ART task shifting,[3] because our sample size was larger. Additionally, the STRETCH intervention improved several other health outcomes and quality indicators. No outcomes were worse in intervention groups than in control ones.

Our encouraging evidence supports task shifting of ART from doctors to nurses and other health workers, which seems essential for ART expansion in South Africa and elsewhere in Africa. Since our trial ended in 2010, South African national policy has changed to promote nurse initiation and management of ART.[19] However, if such a strategy is implemented without sufficient clinical and management support, it could be less effective than the STRETCH programme was in our trial.

Our trial was done to a high standard, with enrolment exceeding our planned sample sizes, and with data for primary outcomes available for 94% of participants. With two cohorts of patients, we could simultaneously assess effects on both short-term and long-term care. Linkage of electronic clinical, laboratory, hospital, and mortality data made the examination of a wide range of health outcomes and indicators of care quality possible for large and generalisable samples of patients. However, our study was limited by the restriction of follow-up to 18 months. Furthermore, we were missing data for weight and CD4 cell count in both cohorts, and for viral load after 12 months of ART in cohort 1.

Outside of the trial, the Free State Health Department attempted to improve access to doctors so as to accelerate ART provision from July, 2008. Doctors who were part of the ART programme were instructed to visit specific clinics to review problem cases, to complete repre-scriptions, and to initiate patients on ART. This change in programme might have unintentionally favoured the control group if these doctors thereby provided more intensive and expert care than would otherwise have been available. Intervention clinics were less likely to

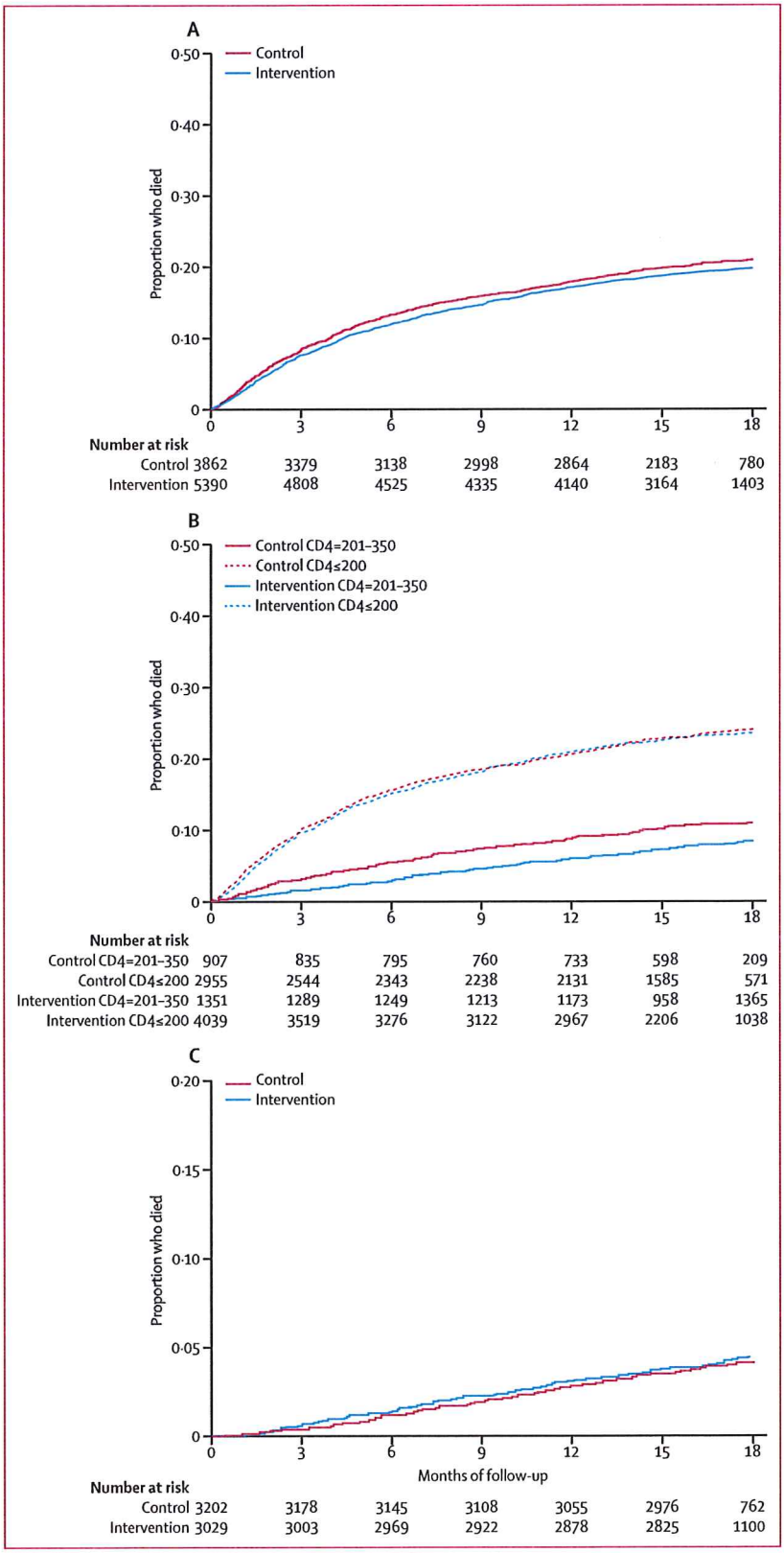

Figure 3: Kaplan-Meier curves of time to death
(A) Cohort 1. (B) CD4 subgroups of cohort 1. (C) Cohort 2.

	Intervention group	Control group	Effect estimate*		p value	Intra-cluster correlation coefficient	Regression model*
			Type	Estimate (95% CI)			
Started on ART	3712/5390 (69%)	2418/3862 (63%)	Risk ratio	1·24 (0·88 to 1·73)	0·218	0·065	Binomial
Time to ART†‡	..	..	Subdistribution hazard ratio	1·14 (0·92 to 1·43)	0·232	0·065	Competing risk
New tuberculosis diagnosis	1057/5390 (20%)	510/3862 (13%)	Risk ratio	1·46 (1·18 to 1·81)	0·001	0·051	Binomial
Received co-trimoxazole prophylaxis	3899/5390 (72%)	2767/3862 (72%)	Risk ratio	1·03 (0·93 to 1·13)	0·608	0·149	Binomial
Programme retention§	3373/5390 (63%)	2254/3862 (58%)	Risk ratio	1·10 (1·04 to 1·16)	<0·001	0·019	Binomial
Baseline CD4 cell count of patients starting ART	132 (82); n=3470	131 (82); n=2083	Difference in means	0·102 (–13·1 to 13·4)	0·988	0·030	Linear
Suppressed viral load in patients who started ART¶	1706/2375 (72%)	1062/1449 (73%)	Risk ratio	0·97 (0·90 to 1·03)	0·324	0·040	Binomial
Proportion with a missing viral load in patients who started ART	1274/3712 (34%)	945/2219 (43%)	Risk ratio	0·86 (0·71 to 1·04)	0·120	0·014	Binomial
Weight at follow-up (kg)	62·6 (14·0); n=2712	62·4 (13·7); n=1503	Difference in means	0·10 (–1·35 to 1·56)	0·884	0·019	Linear
CD4 count at follow-up (cells per μL)	161·3 (175·2); n=2345	141·7 (161·6); n=1544	Difference in means	22·3 (3·6 to 40·9)	0·021	0·026	Linear

Data are n/N (%) or mean (SD), unless otherwise stated. ART=antiretroviral therapy. *Regression models adjusted for randomisation strata and intra-cluster correlation of outcomes. †Follow-up censored, so no mean time to ART listed. ‡Adjusted for the competing risk of death. §Patients were judged to be retained by the programme when after 12 months they were alive, were not known to have withdrawn or relocated, and had documentation of a clinic visit or laboratory test in the previous 6 months (if started ART or last known CD4 count was less than 200 cells per μL) or in the past 9 months (if they had not started ART and last known CD4 count was more than 200 cells per μL). ¶Patients with at least 6 months of ART and viral load results available.

Table 3: **Secondary outcomes in cohort 1**

	Intervention group	Control group	Effect estimate*		p value	Intra-cluster correlation coefficient	Regression model*
			Type	Estimate (95% CI)			
Primary outcome							
Suppressed viral load†	2156/3029 (71%)	2230/3202 (70%)	Risk difference	1·1% (–2·3 to 4·6)	0·534	0·010	Binomial
Secondary outcomes							
Time to death‡	..	..	Hazard ratio	1·05 (0·84 to 1·31)	0·684	0·005	Cox
Programme retention§	2733/3029 (90%)	2926/3202 (91%)	Risk difference	–0·3% (–2·1 to 1·54)	0·758	0·013	Binomial
New tuberculosis diagnosis	119/3029 (4%)	113/3202 (4%)	Risk difference	0·21% (–0·40 to 0·84)	0·487	0·019	Binomial
Received co-trimoxazole prophylaxis	2143/3029 (71%)	2578/3202 (81%)	Risk difference	9·8% (–33·7 to 14·2)	0·424	0·477	Binomial
Change in ART drugs during trial	161/3029 (5%)	57/3202 (2%)	Risk difference	1·25% (0·65 to 1·86)	<0·001	0·044	Binomial
Weight at follow-up (kg)	63·0 (13·5); n=2136	63·2 (14·1); n=2271	Difference in means	0·62 (0·01 to 1·23)	0·045	0·010	Linear
CD4 count at follow-up (cells per μL)	438·8 (219·5); n=1733	418·4 (201·8); n=1691	Difference in means	24·2 (7·2 to 41·3)	0·007	0·007	Linear

Data are n/N (%) or mean (SD), unless otherwise stated. *Regression models adjusted for randomisation strata and intra-cluster correlation of outcomes. †All patients enrolled in the trial were included in the denominator; of these 2308/3029 (76%) of patients in intervention group and 2499/3202 (78%) in control group had been receiving ART for more than 2 years when viral load was measured; 1084/3029 (36%) patients in intervention group and 1125/3202 (35%) in control group had been receiving ART for more than 3 years. ‡Follow-up censored, so no mean time to time to death listed. §Patients were judged to be retained by the programme when after 12 months they were alive, not known to have withdrawn or relocated, and had documentation of a clinic visit or laboratory test in the previous 6 months.

Table 4: **Primary and secondary outcomes in cohort 2**

have doctor-provided ART initiation on site at the start of the trial and by the middle of the study, this disparity had increased with on-site doctors at 11 (73%) of 15 control clinics and seven (44%) of 16 intervention clinics. Therefore, a clinic's ability to expedite ART initiation in patients whom nurses thought needed to

be assessed by a doctor might have been reduced in intervention groups.

This pragmatic trial realistically shows practical problems with large-scale implementation of ART in Africa. Several reasons could explain why the intervention did not accelerate ART initiation or reduce mortality in cohort 1, and why only a quarter of patients who started ART had treatment initiated by nurses. First, our qualitative research showed that many STRETCH nurses were initially hesitant to initiate ART when they had the option of referrals to doctors. Second, allocation of increased numbers of doctors to control clinics during the trial probably placed intervention clinics at a comparative disadvantage. Third, difficulties with funding and delivery of ART to clinics reduced STRETCH nurses' ability to initiate ART promptly. For example, initiation of ART was suspended for 3 months from November, 2008, to February, 2009, because the provincial health department temporarily exhausted its ART budget,[20] as in other countries when donor funding has decreased.[21] Fourth, during the trial several clinics that were not in the study started to provide ART. This change could have reduced the workload of trial clinics, thus decreasing the extent to which STRETCH could accelerate ART initiation compared with control clinics. The favourable results for cohort 1 patients with CD4 counts of 201–350 cells per μL at enrolment, and for cohort 2 patients, suggest that nurses in intervention clinics could competently build on what they had done before—ie, preparation of patients for ART initiation and monitoring of those already on ART. However, the subgroup analysis of mortality in cohort 1 should be interpreted with caution, because the difference in effects between subgroups was moderate, the intervention–subgroup interaction was marginally significant, and the subgroups defined by CD4 cell count were not precisely defined in advance.

Nurses in the intervention group had little trouble with task shifting of represcriptions from doctors, which relieved doctors of a heavy burden and enabled them to focus on referred patients who were seriously ill. Biological evidence that intervention patients received more effective treatment than did those in the control group included the large increase in CD4 cell count in both cohorts and weight gain in cohort 1. In cohort 1, patients in the intervention group were more likely to remain in the programme and to have tuberculosis identified than were those in control clinics, and in cohort 2, switching of regimens occurred more in intervention than control clinics, indicating that STRETCH training and guidelines improved the delivery of appropriate care. Increased regimen switching could have resulted from nurses having good awareness of adverse treatment effects or drug resistance, leading to referrals to doctors authorised to switch regimens.

Our trial is unique because we included and followed up patients who had not yet started ART, and because the intervention included nurse initiation of ART. In the two most similar trials of ART task shifting—the CIPRA trial in South Africa[4] and the Jinja trial in Uganda[3] (panel)—treatment was initiated by doctors but followed up by nurses and non-medical field officers, respectively. These trials[3,4] also provided substantially more training than we did in our trial, and patients who had not yet started ART were not followed up. However, our finding that outcomes were no worse in intervention than in control groups is in keeping with their results.

The high mortality of cohort 1 patients is of concern, although it is lower than the proportion who died within 1 year of enrolment in these clinics before 2008 (29%), and much lower than the proportion who died in the province before 2006 (87%),[5] continuing the trends of decreasing mortality in South African ART programmes over time.[24]

STRETCH is thus an effective and feasible method of rapidly expanding ART provision in South Africa and other countries where shortages of doctors restrict access to ART. The increased rates of clinic visits to both doctors and nurses in cohort 1 could constrain implementation, although the lower rates and duration of

***Panel:* Research in context**

Systematic review

We searched PubMed and Google Scholar for randomised trials assessing task shifting of antiretroviral therapy (ART) published at any time before Oct 31, 2011, with the search terms "antiretroviral", "task-shifting" or "nurse" or "community health worker", and "trial". We identified three randomised trials of ART task shifting: cluster-randomised trials from Uganda[3] and Kenya,[22] and the individually randomised CIPRA trial from South Africa.[4] Another trial from Uganda[23] was excluded because it investigated the addition of community-based follow-up to clinic-based care, and so did not entail task shifting as defined by WHO.[1] The Ugandan[3] and Kenyan[22] trials compared clinic-based with community-based ART follow-up. The CIPRA trial[4] compared ART follow-up by nurses with follow-up by doctors, both provided at clinics. After ART initiation in one clinic, the Ugandan study[3] was based in 44 geographical areas, but the Kenyan one[22] was in only one clinic and CIPRA[4] was in two. All three trials had similar outcomes (viral load suppression, CD4 cell counts, and loss to follow-up) for patients on ART. In the Ugandan[3] and South African[4] trials, ART was initiated by doctors. None of these trials enrolled patients who had not yet started ART but were eligible or would soon be eligible. All three trials showed no significant difference in outcomes.

Interpretation

Our results are in keeping with the Ugandan,[3] Kenyan,[22] and CIPRA[4] trials and support provision of ART follow-up care by non-physicians. The generalisability and feasibility of implementation of our programme are supported by its basis in many clinics throughout a province. The suppression of viral load in patients who were already receiving ART at enrolment is similar to that reported for the Ugandan trial.[3] However, our trial provides original evidence of the effectiveness of a nurse-led system on the clinically challenging task of ART initiation, including for patients recently or newly enrolled in the treatment programme. We have shown that expansion of nurses' roles to include ART initiation can be done safely and can improve health outcomes and quality of care, but that time to ART initiation or mortality did not change. Several observational studies support the role of non-physician clinicians in provision of ART care, but few are of programmes in which ART initiation is led by non-physician clinicians.[2] Taken together, our study and the others we have identified suggest that the present approach of non-physician clinicians expanding ART programmes in resource-constrained environments is safe and feasible.

admission in the intervention group than in the control group in cohort 1, and the task shifting of clinic visits from doctors to nurses in cohort 2, indicate that resources are used more efficiently with the programme than without. The cost-effectiveness of the intervention will be reported separately. The suitability of this approach in countries where access to physicians is even more restricted than in South Africa or is non-existent should be assessed in a separate trial. Our results are relevant to other countries in Africa because they show that non-physician health workers can provide comprehensive ART care, including ART initiation, after just four additional short training sessions. Our training methods and guideline design have been previously assessed and are already being implemented in The Gambia and Malawi.[25,26]

Contributors

LF, MOB, CL, MZ, AB, RCo, CvV, DS, and EB designed the protocol. LF, MOB, and RCh obtained funding. LF, KU, GF, and RCo developed and implemented the intervention. LF, VT, KU, and EK oversaw data collection, data cleaning, merging of datasets, and preparation of extracts for analysis. CL led the analysis with assistance from LF and MOB. All authors contributed to interpretation of findings and preparation of the report, and have approved the final version.

Conflicts of interest

The Knowledge Translation Unit of the University of Cape Town Lung Institute (to which LF, VT, KU, DG, GF, RCo, BD, and EB are affiliated) provides training in PALSA PLUS and STRETCH to the South African and Western Cape Departments of Health. The other authors declare that they have no conflicts of interest.

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Chapter 4

Task shifting and integration of HIV care into primary care in South Africa: The development and content of the streamlining tasks and roles to expand treatment and care of HIV (STRETCH) intervention

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Task shifting and integration of HIV care into primary care in South Africa: The development and content of the streamlining tasks and roles to expand treatment and care for HIV (STRETCH) intervention

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Abstract

Background: Task shifting and the integration of human immunodeficiency virus (HIV) care into primary care services have been identified as possible strategies for improving access to antiretroviral treatment (ART). This paper describes the development and content of an intervention involving these two strategies, as part of the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) pragmatic randomised controlled trial.

Methods: Developing the intervention: The intervention was developed following discussions with senior management, clinicians, and clinic staff. These discussions revealed that the establishment of separate antiretroviral treatment services for HIV had resulted in problems in accessing care due to the large number of patients at ART clinics. The intervention developed therefore combined the shifting from doctors to nurses of prescriptions of antiretrovirals (ARVs) for uncomplicated patients and the stepwise integration of HIV care into primary care services.

Results: Components of the intervention: The intervention consisted of regulatory changes, training, and guidelines to support nurse ART prescription, local management teams, an implementation toolkit, and a flexible, phased introduction. Nurse supervisors were equipped to train intervention clinic nurses in ART prescription using outreach education and an integrated primary care guideline. Management teams were set up and a STRETCH coordinator was appointed to oversee the implementation process.

Discussion: Three important processes were used in developing and implementing this intervention: active participation of clinic staff and local and provincial management, educational outreach to train nurses in intervention sites, and an external facilitator to support all stages of the intervention rollout.
The STRETCH trial is registered with Current Control Trials ISRCTN46836853.

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Background

South Africa has the largest human immunodeficiency virus (HIV) burden in the world, with an estimated 5.7 million infected people [1]. By the end of 2008, five years after the public sector antiretroviral treatment (ART) programme was launched, an estimated 700,500 people were accessing ART [2]. Although this represents an increase of 53% on the previous year, it constitutes only 40% of those estimated to be in need of ART [3]. Despite policy guidelines recommending that comprehensive HIV care be incorporated into existing primary care services [4], the initial public sector ART rollout in South Africa was implemented as a vertical (stand alone) programme with separate funding, facilities, staff, medical records, and reporting requirements [5]. There are several reasons to justify such an initial vertical approach to comprehensive HIV care, including the need for a rapid response in a weak health system and the need for highly skilled staff to implement a new, complex intervention [6,7]. There are, however, two equally powerful reasons for moving away from vertical HIV care programmes in high HIV-burden countries: that such vertical programmes will be unable to achieve universal ART access because of the sheer numbers of people needing treatment; and that they could draw away financial and human resources from already struggling public health systems in these countries [8,9].

In order to address these concerns, calls have been made to utilise the impetus of new financing, training, and infrastructural support, directed towards the acquired immunodeficiency syndrome (AIDS) epidemic, to strengthen broader health systems [10], and to incorporate current vertical ART programmes into these health systems–a strategy now termed the 'diagonal approach' [11]. Approaches to incorporating HIV care into general health systems include: the referral of patients stabilised on ART from ART clinics to primary care clinics where they could receive monthly supplies of treatment (sometimes referred to as 'down referral') [12,13]; task shifting of aspects of HIV care to lower cadres of healthcare workers [14,15]; setting up nurse-driven HIV care programmes [16]; and integration of HIV care into primary care services [17-19].

These types of interventions are complex, and there are two important research questions that need to be answered, particularly in low- and middle-income countries [20]: What should be the components of these interventions [21-23]? And are these interventions effective in improving access to ART? This article addresses the first question–it describes the content of the STRETCH (Streamlining Tasks and Roles to Expand Treatment and Care for HIV) intervention, including its components, the processes of change used, the conditions in the control clinics, and links to manuals used in the intervention, as suggested in the WIDER recommendations (Workgroup for Intervention Development and Evaluation Research) [24]. The development of the intervention was based on the educational outreach model and our practical experience of engaging with the Free State Department of Health in implementing an earlier nurse training programme called PALSA PLUS (Practical Approach to Lung Health and HIV/AIDS) in the Free State [25-27]. The second question is being addressed through a pragmatic cluster randomised controlled trial of the effects of the STRETCH intervention on access to ART conducted in 31 ART clinics randomised in nine strata in the Free State province [28]. This description will supplement the forthcoming trial results.

Context and setting: the Free State public sector ART rollout

The Free State, with a population of 2.8 million [29], has an estimated HIV prevalence of 18.5% among 15 to 49 year olds [30]. The province comprises five districts, divided into 20 local areas, with primary care services offered at 222 nurse-led clinics. The public sector ART rollout commenced in mid-2004 in designated nurse-led ART assessment sites situated in selected primary care clinics. Table 1 summarises the organisation of HIV care in health facilities in the initial rollout. Patients diagnosed as HIV positive in primary care clinics and hospitals are referred to ART assessment sites for further clinical care and assessment of eligibility for ART. Those eligible for ART receive drug readiness training and are then referred to ART treatment sites in local hospitals for initiation of treatment and for three- to six-month reviews of ART prescriptions by a doctor. National regulations require that antiretrovirals (ARVs) be dispensed by or under the direct supervision of a pharmacist. Where assessment sites do not have pharmacists, ARVs have to be dispensed at treatment sites into patient-named packets and transferred to assessment sites where nurses issue them monthly to patients. In some remote areas, assessment and treatment site functions were conducted by combined sites with the support of visiting doctors.

In the first three years of the rollout, achievements included: good patient outcomes amongst patients receiving ART [31,32], a reliable supply of drugs and other medical supplies, and increases in nurse posts [33]. These successes were tempered by high mortality rates among patients waiting for ART [31], increased vacancies in primary care services [34], and high levels of burnout among ART and primary care nurses [35]. Despite opening 57 ART sites, coverage by the end of

Table 1 Responsibilities for provision of aspects of HIV care at different facilities in the initial ART rollout compared with responsibilities for sites in the STRETCH trial

Type of facility	Responsibilities for HIV care in initial ART Rollout	Responsibilities for HIV care for sites in the STRETCH trial
Primary care services	• Voluntary counselling and testing	• Voluntary counselling and testing • Initial CD4 count • Routine HIV care (repeat CD4 counts, clinical staging and TB screening) for patients not requiring ART • Drug readiness training • Baseline bloods • Monthly ART follow-up and issuing of ARVs (after first six months for stable patients)
ART assessment sites	• Initial CD4 count • Routine HIV care (repeat CD4 counts, clinical staging and TB screening) for patients not requiring ART • Refer patients eligible for ART (Stage IV AIDS or CD4 <200 cells/mm3) to doctor at treatment site • Drug readiness training • Baseline bloods • Monthly ART follow-up and issuing of ARVs	• Initiate uncomplicated patients on ART • Monthly ART follow-up and issuing of ARVs for first six months • Six monthly review and repeat ART prescription for stable patients • Refer complicated patients for initiation and repeat of ART prescription to doctor at treatment site
ART treatment sites	• Initiation of patients on ART • Monthly review first three months • Six monthly review and repeat ART prescription	• Initiation of complicated patients on ART • Monthly review first three months of complicated patients • Six monthly review and repeat ART prescription for complicated patients

2007 remained disappointingly low. Only 25% of new patients estimated to be in need of ART that year were started on treatment [36].

In late 2008, while the STRETCH trial was ongoing, the Free State ART programme was forced to implement a three-month moratorium on selected adult ART initiations to ensure uninterrupted drug supplies for those already on treatment. This moratorium was due in part to chronic underfunding of the ART programme in all provinces, and resulted in a major review and increase in funds for the national ART programme. In early 2010, before the STRETCH trial was completed, the South African government commenced implementation of its accelerated AIDS plan in all provinces. This plan includes nurse prescription of ART and integration of ART into all primary care clinics in an attempt to rapidly scale-up ART access [37]

Developing the intervention

In 2005, Free State Department of Health managers expressed their concern about high mortality rates among patients waiting for ART, and about the dependence of the programme on doctors, who are in short supply, for ART prescription. Working in the Free State, the Knowledge Translation Unit of the University of Cape Town Lung Institute had piloted and evaluated a training programme for nurses in the use of integrated primary care guidelines covering the management of respiratory diseases and HIV–the PALSA PLUS initiative [25-27,38,39]. The provincial department thus requested that nurse prescription of ART be included in the PALSA PLUS guidelines, and that training be rolled out in the province. Because of widespread ambivalence about the ability of nurses to take on the clinical responsibility for ART prescription and the absence of clear national policy, it was decided to pilot the intervention and monitor its outcomes as a pragmatic randomised controlled trial in the province's ART clinics. Meetings were then held over eighteen months between researchers, managers, senior clinicians, and clinic staff to develop the intervention.

Meetings with senior managers and clinicians

In initial meetings with senior managers and clinicians from the ART programme, it was established that delays in people accessing ART were caused not only by the shortage of doctors but also the high caseload of ART nurses at ART assessment sites that were managing growing numbers of patients on ART as well as those not yet eligible for ART. The intervention was therefore designed to be a more complex task-shifting intervention with two main components: shifting ART prescription from doctors to ART nurses and shifting routine HIV care for patients not yet eligible for ART (pre-ART care), from ART nurses to primary care nurses at ART assessment sites.

Meetings with middle managers

Workshops were then held with district and local area managers to further develop the intervention. Managers expressed concern about the ability of nurses to assume these new clinical responsibilities and about how to implement the reorganisation of care required for this type of complex health intervention. It was agreed that in addition to providing nurse training, the intervention would be implemented in phases, and detailed

descriptions of the task and role changes needed at intervention clinics in each phase would be included in an implementation 'toolkit' to be developed by the researchers.

Meetings with clinic staff

To obtain feedback from clinic staff on the proposed intervention, the STRETCH coordinator (KU) visited all 31 nurse-led ART assessment clinics selected for the trial and held meetings with staff members. The staff raised a number of problems with functioning of the ART sites that were resulting in difficulties for patients accessing ART. These difficulties included increasing workload, drug transport and storage problems resulting from hospital-based ART dispensing, transport problems for patients, and lack of basic communication infrastructure such as telephones and fax machines (see Table 2). ART nurses were also struggling to cope with providing care for the growing numbers of patients accessing ART as well as those not yet eligible for ART. In one local area where primary care clinics did not offer HIV testing, ART staff had to provide this service too. However, in other districts, increasing workload had already prompted ART sites to integrate pre-ART care into the work of the surrounding primary care clinics. In one district, ART sites were already discussing the integration of drug readiness training, for patients eligible for ART, into primary care services.

Thus, in their comments on the proposed intervention and in order to address some of the problems outlined in Table 2, such as nurse workload and transport difficulties for patients, many of the staff felt that more elements of HIV care, including drug readiness training and monthly collection of ARVs, needed to be integrated into primary care services. Furthermore, these elements of care needed to be available not only within the ART clinic but also in surrounding primary care clinics referring patients to these ART sites. Task shifting of pre-ART care from ART nurses to primary care nurses at ART sites, as initially envisaged in discussions with management, was thus reformulated as a step-wise integration of the following six elements of comprehensive HIV care into all primary care services both within the ART clinics and those at clinics referring patients to the ART nurses at the ART sites: voluntary counselling and testing; initial CD4 count; routine HIV care for patients not yet eligible for ART; drug readiness training for patients initiating ART; baseline blood tests for patients initiating ART; and monthly ART care for stable patients. This 'decentralisation checklist' was included in the implementation toolkit.

A meeting was also held to gather the views of primary care nurses in the 16 ART sites. These nurses were concerned about the burden of HIV disease in their patients, were keen to be involved in the programme, and felt capable of providing comprehensive HIV care. However, they were also concerned about the increased workload this would create for healthcare providers in already overloaded and understaffed primary care services.

Table 2 Problems in delivery of care at ART sites, as identified in initial clinic meetings

Operational issues	• Increasing workload as patients on ART were required to attend monthly to obtain supplies of ARVs • Staff shortages and delays in filling vacant post in the ART programme • Antagonism of primary care nurses toward ART nurses on account of their different post structures and remuneration leading to refusal to assist (some clinics) • Long delays in taking of CD4 counts because of lack of capacity in primary care services in some areas to perform voluntary counselling and testing and CD4 counts • Lack of integration of primary care services for patients on ART leading to multiple visits to healthcare facilities
Drug supply issues	• Shortage of pharmacists and pharmacy assistants • ARVs classified as hospital level medication which could only be dispensed by pharmacist • Shortage of transport to deliver dispensed ARVs to assessment sites • Lack of storage space and systems for locating individual patient's dispensed ARVs at assessment sites • Difficulty looking for individual patient's pack of dispensed ARVs • Differing availability of cotrimoxazole and fluconazole at ART service points
Transport issues	• Patients unable to afford taxi fares to attend treatment sites for doctor's assessment • Regular clinic transport systems becoming overwhelmed by increasing numbers of ART patients needing to go to assessment sites for monthly supply of ARVs
Communication issues at assessment sites	• Few or no telephones • No fax machines or photocopy machines • No electricity (one clinic) • Shortage of computers or poor connectivity causing back log in data collection • Shortage of data clerks
Space issues	• Lack of sufficient consulting rooms • Lack of space for large drug readiness training classes • Lack of waiting room space for ART patients

Components of the intervention

The main components of the intervention are discussed below and are summarised in Table 3, where they are compared with standard of care support at control clinics.

The STRETCH coordinator

A provincial STRETCH coordinator (KU), a family medicine practitioner with experience in the management of HIV/AIDS and tuberculosis, was appointed and had the following responsibilities during the intervention: further developing the intervention in consultation with staff at management and clinic level; involvement in initial training and continuing support of nurse training at intervention sites; teaching in the Free State ART training programme alongside ART programme doctors; helping to provide clinical advice to all ART sites; providing extra support to nurses prescribing ART at the intervention sites; and facilitating the establishment of management teams to oversee the implementation of the intervention. The involvement of the STRETCH coordinator in teaching in the ART programme and helping to provide clinical advice to all ART sites was not initially envisaged as part of the intervention, but was included at the request of the province because of the shortage of doctors available to provide this support.

Regulatory changes

Although there was no official national policy prior to the trial on nurse prescription of ART, two pieces of national legislation supported such prescription [40,41]. The Free State Pharmaceutical and Therapeutics Committee gave permission for professional nurses in the province to initiate and repeat ART prescriptions for adults during the trial. This permission was conditional on these nurses completing appropriate training and

Table 3 Components of the intervention compared to standard care at control clinics

Intervention component	Intervention clinics (n = 16)	Control clinics (n = 15)
STRETCH Coordinator	• Teaching in the Free State ART training programme alongside ART programme doctors • Available for clinical advice for all staff in ART sites • Initial training and support of nurse trainers at intervention sites • Providing extra support to nurses prescribing ART at intervention sites • Facilitating the establishment of local management teams to implement the intervention	• Teaching in the Free State ART training programme alongside ART programme doctors • Available for clinical advice for all staff in ART sites
Regulatory environment for prescription of ART	• Pharmaceutical and Therapeutics Committee of the Free State Department of Health gave permission for professional nurses at intervention sites to initiate and repeat prescriptions of ART for adults identified as eligible for nurse management.	• Only doctors were allowed to initiate and repeat prescriptions three or six monthly for patients needing ART
Nurse Training	• All professional nurses completed two-week ART training and on-site training in PALSA PLUS guidelines–six to eight sessions in total • 16 PALSA PLUS trainers, one for each clinic, trained in use of STRETCH guidelines (TtTtT) • All professional nurses offered on-site training in the use of STRETCH guidelines to identify patients eligible for nurse management-four sessions in total	• All professional nurses completed two-week ART training and on-site training in PALSA PLUS guidelines-six to eight sessions in total
Patient management guidelines for nurses	• Special 2007 STRETCH Free State edition of PALSA PLUS guidelines with extra STRETCH guidelines for nurse initiation and repeat prescription of ARVs issued to all staff at intervention sites	• Standard 2006 edition of PALSA PLUS issued to all staff at control sites during training in 2006 or 2007
Management support	• STRETCH team established at each intervention site to manage the introduction of changes in clinic function during the intervention • Local area management support teams were set up to support the integration of aspects of comprehensive HIV care into the services of these primary care clinics referring patients to the intervention site	• Standard management support by clinic supervisor, district ART coordinator and local area manager
Implementation guideline	• STRETCH Toolkit issued to STRETCH teams at 16 intervention clinics to assist the teams in implementing the intervention	• None
Phased introduction	• Phase one: Training and establishment of STRETCH teams at each intervention site • Phase two: Nurse repeat prescription of ART for patients on ART for six months or more and eligible for nurse management • Phase three: Nurse initiation of ART for adults eligible for nurse management	• None

working at one of the 16 intervention clinics. Usual care continued at the 15 control clinics where only doctors were allowed to prescribe ART.

Nurse training

Table 4 summarises the characteristics of the ART training available to nurses in all clinics across the province and the training offered as part of the intervention. The details of these training programmes are described below.

Standard of care training in all clinics

Since 2005, the Free State Department of Health has been running a regular two-week ART training course for staff in ART and other primary care clinics. This course combines one week of lectures broadcast to classrooms throughout the province and a one-week placement at an existing ART site. Regular maintenance training is also conducted in the districts and in weekly lectures broadcast to staff in these classrooms. Clinical support was available to staff at all ART sites from doctors at treatment sites, specialists at a tertiary level AIDS clinic and the STRETCH coordinator.

At the time of the trial, PALSA PLUS training was being rolled out to all provincial primary care clinics, including all ART assessment sites [27]. This model of training involves equipping nurse managers to conduct outreach training for nurses at clinics in their area. Nurse managers are trained in a one week course known as Training the Trainer to Train (TtTtT) [25]. Adult education models are used to fully integrate experiential learning on how to facilitate small group training using case scenarios, while enabling the trainers to become familiar with the contents of the guideline. These nurse managers in turn conduct outreach training onsite, in short sessions over several weeks, using these case scenarios to facilitate nurses engaging with the PALSA PLUS guideline. This training has been shown to be effective in improving quality of care and minimises disruption to clinic services [26,27]. Thirty of the 31 ART sites in the STRETCH trial had completed PALSA PLUS training before the trial began and plans were made to train staff at the outstanding clinic.

Training at intervention clinics

The PALSA PLUS model of training was expanded to include extra training in nurse prescription of ART. One established PALSA PLUS trainer was identified for each of the 16 intervention clinics. All had been trained in ART, and three had experience working in ART sites. These trainers were either clinic supervisors or local programme coordinators regularly visiting these clinics in a supervisory capacity. They participated in a two and one-half-day training on: how to train nurses in the ART protocols contained in the STRETCH edition of the guidelines by using four case scenarios; and the staff role changes needed as part of the intervention, as described in the toolkit. We anticipated that nurse confidence might be severely compromised if patients who were started on ART by nurses developed severe side effects. The case scenarios were therefore also used to impart basic skills for trainers to debrief nurses. The

Table 4 Characteristics of various nurse trainings available as standard of care in all ART and primary care sites compared with training offered at intervention clinics during STRETCH intervention

	Free State Department of Health ART course (Standard training)	PALSA PLUS training (Standard training)	STRETCH Training (Additional training in intervention clinics)
Description	Two- week training course comprising one week of lectures and one week of practical training	One- to two-hour sessions weekly or fortnightly of case scenario-based interactive training in use of PALSA PLUS guidelines (six to eight sessions in total)	One- to two-hour sessions weekly or fortnightly of case scenario-based interactive training in use of PALSA PLUS STRETCH guidelines (four sessions in total)
Trainers	Senior doctors, pharmacists dieticians and social workers working in ART programme	Middle level nurse managers trained as PALSA PLUS trainers	Middle level nurse managers trained as PALSA PLUS and STRETCH trainers
Trainees	Doctors, professional nurses enrolled nurses pharmacists and social workers involved in providing primary care services at hospitals and clinics across the province	Professional and enrolled nurses and ancillary staff at all intervention and control clinics and primary care clinics throughout the province.	All professional nurses (whether appointed to ART or primary care posts) at 16 intervention sites only
Setting	Local classrooms located throughout the province to which lectures are broadcast. Local ART sites during practical training	Training sessions held at the clinic	Training sessions held at the clinic
Mode of delivery	Lectures broadcast live from central studio with limited telephone interaction. Face-to-face with staff at ART sites during practical training	Face-to-face small group facilitative work	Face-to-face small group facilitative work
Intensity and duration	Full day training for one week of lectures and one week of practical training	One to two hours once every week or two weeks for two to three months	One to two hours once every week for four weeks

training was led by three facilitators from the research team: two nurses experienced in adult and nurse education who had been involved in developing the PALSA PLUS training (GF and PM), and the STRETCH coordinator.

The trainers then trained all nurses at the 16 intervention clinics, including designated ART nurses and those working in primary care, commencing in August 2007. A minimum of four educational outreach trainings, one of which was supported by the STRETCH coordinator, were conducted at each clinic, and most of these sessions were completed by October 2007. The trainers continued to support the nurses and train those who were newly appointed or had not attended all the initial sessions, but the regularity of these visits varied and depended on their other supervisory responsibilities.

All doctors supporting the intervention sites were oriented by the STRETCH coordinator using the guidelines and case scenarios. Doctors working in the five combined sites were able to provide clinical support to the nurses. However, at the other eleven assessment sites, where doctors only worked at distant treatment sites, they were less able to provide support. Additional clinical support was also provided by the STRETCH coordinator via telephone or during clinic visits. These visits took place typically once every four months in the first twelve months of the trial and less frequently after that.

Patient management guidelines for nurses

Nurses working in all primary care clinics including all ART sites had access to and were receiving training in the use of the PALSA PLUS guidelines (see above). A STRETCH edition of the PALSA PLUS guideline, containing algorithms for nurse initiation and management of adults on ART, was distributed to all nurses in the 16 intervention clinics and used in outreach training by the STRETCH trainers. The algorithms were developed in consultation with clinicians in the province and with reference to the Integrated Management of Adolescent and Adult Illnesses guideline [42]. Thus, adults with a CD4 <50, Stage 4 HIV, previous ARV treatment, who were on tuberculosis (TB) or other chronic medication, were bedbound, or who were pregnant were identified as potentially complicated cases that needed to be initiated onto ART by a doctor. All other adults eligible for ART could be initiated by nurses. Similarly, a decreasing CD4 count, detectable viral load, or clinical problems in a patient already receiving ART were criteria for doctor management, while all other patients could be managed by a nurse. (The ART algorithms are included in Additional file 1)

Phased introduction

The intervention was implemented in phases to support logistical changes such as the dispensing of nurse ART prescriptions and to allow nurses to build confidence and skills in ART prescriptions. The three phases of implementing the intervention were: the training of nurses in ART prescription and setting up of management support teams; nurse re-prescription of ART for stable patients; and nurse initiation of ART for uncomplicated new patients. The timing of progress through the stages was determined by staff in the STRETCH teams at each individual clinic.

Implementation guideline

Because of the complexity of the intervention, the research team developed an implementation guideline called the STRETCH Toolkit and distributed copies to all intervention sites. The Toolkit contained the decentralisation checklist (as outlined above), descriptions of the different phases of the study, as well as details about the changing roles of all staff members in each phase and useful advice on communicating these changes to the community. It also contained important documents and information, such as contact numbers for doctors and nurse managers of all the clinics in the trial and relevant managers in the provincial department, along with copies of documents authorising nurse prescription of ART. (The STRETCH Toolkit is included in Additional file 2)

Management support

Standard support was provided to all ART sites by two to three monthly visits from district ART coordinators (who had district wide responsibility for the ART programme) and monthly visits from clinic supervisors (who were responsible for overall primary care services in a local group of clinics). Meetings between clinic managers (in charge of each clinic) and local area managers (who had overall responsibility for health services in that local area) are typically held at one- or two-month intervals.

During phase one of the intervention, STRETCH teams were convened by the STRETCH coordinator at each of the intervention clinics. These teams usually comprised the clinic manager, one clinic nurse representing ART services and one representing primary care, and the pharmacist or pharmacy assistant, as well as staff from the treatment site and the district ART coordinator. These teams were given copies of the STRETCH Toolkit and were tasked with implementing changes at the clinic during the intervention. One of these tasks, as outlined in the decentralisation checklist, was to assess the state of integration of comprehensive HIV care into primary care services, and which further elements of HIV care needed to be integrated into these services (Table 1).

Thirteen of the intervention clinics had patients referred for ART from other primary care clinics in their area. In four of these intervention clinics, local

management had already started implementing the integration of all six elements of HIV care into the primary care clinics. In the other nine intervention clinics, the STRETCH team identified the need to integrate further elements of HIV care into these referring clinics. Local area management teams were then convened for seven of the nine clinics. In the remaining two clinics management support was difficult to mobilise. These teams usually comprised the local area manager, the manager of the intervention site, facility managers of all referring primary care clinics, and the local ART pharmacist. They were able to evaluate capacity to integrate further elements of HIV care into the referring clinics by assessing staffing and training needs, space for drug readiness training classes, and ability to store and transport ARVs–all of which were the type of practical issues identified by staff (Table 2). The STRETCH coordinator's responsibility was to convene these management teams and assist at the first one or two meetings. It was then the team's responsibility to decide which elements of HIV care could be integrated at which primary care clinics and to implement these decisions.

Discussion

One of the distinctive features of this intervention was the participation of clinic staff and all levels of management in many stages of its development and implementation. First, the trial was set up at the request of senior management to address the problem of high mortality rates among patients eligible for ART and awaiting access to treatment. In the national environment of ambivalence to nurse ART-prescription that existed at the start of the trial, senior management support was crucial to developing and implementing the intervention. Second, senior management, middle management, and clinic staff were involved in an iterative process of assessing the barriers facing patients and staff with regard to accessing ART, and then tailoring the intervention to be relevant and implementable. Management concerns about the complexity of the intervention led to the development of an 'Implementation Toolkit.' The types of problems outlined by staff (Table 2) and their insight into possible solutions led to the reformulation of integration in the context of ART rollout as the flexible, progressive integration of pre-ART and ART care into all primary care services referring to intervention sites. Third, staff at local area and clinic level were involved in the teams tasked with implementing the intervention, with support from the STRETCH coordinator. STRETCH teams were tasked with assessing readiness for different phases of the intervention and with implementing the changes at clinic level. Local management teams assessed capacity and arranged for primary care services to take on aspects of pre-ART and ART care.

The strong participation of clinic staff and managers in intervention development and implementation could be seen as an example of how features of participatory action research can be integrated into trial intervention design and implementation. It has been suggested that this approach to intervention design may make complex health interventions both more effective and more easily reproducible in other settings [43]. This is congruent with evidence from a systematic review that suggests that interventions tailored to prospectively identified barriers have a greater likelihood of improving professional practice than interventions with no such tailoring [44]. However the review also notes that further work is needed on methods to identify barriers and tailor interventions to address them. The participatory approach used here is also in line with calls to involve the district health systems in efforts to deliver comprehensive HIV care [8,17,45]

One of the weaknesses of the development of this intervention is that, while staff at the ART sites were involved in initial discussions, staff at the primary care clinics referring patients to these sites were not. However, as part of the implementation, managers of these primary care clinics were included as members of local management teams and were then able to give their input, assess capacity issues, and make workable plans for the integration of HIV care into their clinic services.

A second change technique used to facilitate uptake of the intervention was educational outreach. This approach was the basis for the training of professional nurses in the intervention clinics. The PALSA PLUS training model, on which the STRETCH intervention was based, draws on adult education principles and the outreach education approach, and has been shown to be effective in changing nurse clinical practice in study setting and more widely [26,27,46]. The trainers chosen to implement this training were local staff members–another facet of active participation in the implementation. Many of the 16 STRETCH trainers were themselves clinic supervisors and had also been PALSA PLUS trainers. As part of this trial, they trained the professional nurses at the clinics for which they provided supervision.

The STRETCH coordinator also functioned as an 'agent of change' in this intervention, playing a role in facilitating the active participation of staff in, firstly, the process of developing and reformulating the intervention so that it was implementable and responsive to local conditions in the clinics and, secondly, in establishing local teams to implement the intervention actively. The coordinator was appointed by the research team but based in the provincial health department. This

allowed her to facilitate communication between the research team and provincial staff and act as a 'problem solver.' The coordinator was also able to provide ongoing support to nurses, doctors, and trainers because of her previous clinical experience. All of these roles have been acknowledged as important functions of external facilitation in the implementation of complex health interventions [47]. Models of implementation also acknowledge the overlap between outreach educators, which formed one component of this intervention, and facilitation, which formed another component. These models suggest that facilitators take on a wider range of roles than outreach educators, including the use of a greater range of enabling approaches to help support practice change and mediate between stakeholders [48].

Conclusion

This paper describes the development and content of the STRETCH intervention intended to improve access to ART. This complex intervention incorporates three processes: participatory action research, educational outreach, and external facilitation to change the practice of nurses in primary care settings in South Africa. The effects of the intervention are now being evaluated in a pragmatic randomised controlled trial. To evaluate the degree to which the intervention was implemented as intended [43,49], a qualitative process evaluation of the trial was conducted. In addition, the integration of HIV care into primary care services was monitored using a semi-quantitative questionnaire. The findings of these parallel studies will contribute to understanding the effects of the intervention described in this paper.

Additional material

Additional file 1: ART algorithms. Algorithms for initiation and management of patients on antiretroviral therapy included in the STRETCH edition of the PALSA PLUS guideline that was used in intervention clinics during the STRETCH trial.

Additional file 2: STRETCH Toolkit. STRETCH Implementation toolkit developed by the research team to assist clinic staff in implementing the STRETCH intervention.

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Ethical approval

Approval to conduct this study was obtained from the Head of the Department of Health in the Free State, and the study protocol was approved by the Human Research Ethics Committees of the Faculty of Health Sciences of the University of the Free State and the University of Cape Town.

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Authors' contributions

LF, SL, MB, MZ, CL, and EB were involved with initial conception, design and development of the trial and reviewing the manuscript. LF, KU, GF, and PM were involved in developing and implementing the intervention and writing the manuscript. DvR and WM were involved with writing and reviewing the manuscript. CC and DG reviewed the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Chapter 5

Integrating HIV care into primary care services: quantifying progress of an intervention in South Africa

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Integrating HIV Care into Primary Care Services: Quantifying Progress of an Intervention in South Africa

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Abstract

Background: Integration of human immunodeficiency virus (HIV) care into primary care services is one strategy proposed to achieve universal access to antiretroviral treatment (ART) for HIV-positive patients in high burden countries. There is a need for controlled studies of programmes to integrate HIV care with details of the services being integrated.

Methods: A semi-quantitative questionnaire was developed in consultation with clinic staff, tested for internal consistency using Cronbach's alpha coefficients and checked for inter-observer reliability. It was used to conduct four assessments of the integration of HIV care into referring primary care clinics (mainstreaming HIV) and into the work of all nurses within ART clinics (internal integration) and the integration of pre-ART and ART care during the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) trial in South Africa. Mean total integration and four component integration scores at intervention and control clinics were compared using one way analysis of variance (ANOVA). Repeated measures ANOVA was used to analyse changes in scores during the trial.

Results: Cronbach's alpha coefficients for total integration, pre-ART and ART integration and mainstreaming HIV and internal integration scores showed good internal consistency. Mean total integration, mainstreaming HIV and ART integration scores increased significantly at intervention clinics by the third assessment. Mean pre-ART integration scores were almost maximal at the first assessment and showed no further change. There was no change in mean internal integration score.

Conclusion: The questionnaire developed in this study is a valid tool with potential for monitoring integration of HIV care in other settings. The STRETCH trial interventions resulted in increased integration of HIV care, particularly ART care, by providing HIV care at referring primary care clinics, but had no effect on integrating HIV care into the work of all nurses with the ART clinic.

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Introduction

There is international agreement that universal access to treatment for people with human immunodeficiency virus (HIV) in high-burden countries will not be achieved by vertical or single disease approaches to delivering HIV care, but rather by providing HIV care within general health systems [1,2,3]. Calls have been made to use international funding and support for HIV care to strengthen general health systems, and broaden existing vertical HIV programmes so as to provide HIV care within general health systems – the so-called diagonal approach [4,5].Various strategies have been used in order to do this in countries with severe human resource shortages and struggling health care systems. These include shifting tasks from highly skilled to lower skilled and even lay health workers, mobilising community support and integrating HIV care into primary care services [3]. There are many reports of the effectiveness of task shifting [6,7,8,9,10,11], and community mobilisation [12,13] and guidelines have been published by the World Health Organization [14]. However, there are few clear recommendations on effective strategies to integrate HIV care into primary care services partly because there is still little evidence that integration of health care programmes does improve patient outcomes [15].

One of the problems is that integration is a broad concept. It has been defined as "a variety of managerial or operational changes to health systems to bring together inputs, delivery, management and organisation of particular service functions" [16].Integration may take place in all or any combination of a number of different health system functions including service

delivery, management, financing, governance and monitoring and evaluation [17]. In order to provide evidence of the effectiveness of integration, controlled studies of integration are urgently needed. Such studies would need to describe what functions are being integrated and what strategies are used, but would also need to develop tools to monitor and quantify integration in order to correlate integration with outcomes achieved and compare outcomes across different studies [18].

There have been reports of strategies to integrate HIV care into primary care services including: co-location of vertically run HIV services in primary care facilities [19] down referral of stable patients on antiretroviral treatment (ART) to primary care clinics [20] and the provision of outreach support to primary care clinics from existing ART sites [21]. Other programmes have reported on strategies to integrate HIV care into all primary care consultations. These included staff training, standardised protocols, combined medical records and waiting areas, and the inclusion of HIV testing into triage [22,23]. There are reports of improved access to ART with primary care driven models of HIV care [8,21,24,25]. However all of these reports were observational and none were able to link patient outcomes with the extent to which HIV care was integrated.

This paper describes the development of a questionnaire as a tool to quantify integration of HIV care into primary care services achieved during a controlled trial of a complex intervention in the Free State Province of South Africa. This was a trial of a task shifting and integration intervention, monitoring the outcome of patients needing ART, called Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) [26]. The STRETCH trial is registered at isrctn.org (ISRCTN46836853)

Methods

Ethics statement

Approval to conduct this study was obtained from the head of the Department of Health in the Free State. The protocol for this sub-study was approved by the ethics committee of the Faculty of Health Sciences of the University of the Free State. The main STRETCH trial protocol was approved by the ethics committees of the faculties of health sciences at the Universities of Cape Town and the Free State. Clinic managers provided written informed consent to take part in the trial. As the STRETCH trial was an educational and managerial intervention aimed at entire clinics and their staff, all patients in the intervention clinics would be exposed to the same intervention. Informed consent was not requested from individual patients. Patients in intervention clinics were given written information about the trial. Ethical principles for use of medical records for research without patients' consent were followed: the research had a clear public benefit, approval was obtained for the study from the lead doctors and nurses managing the programme, use of the data for research did not influence individuals' care, the data were already being used by the research team for programme evaluation on behalf of the provincial health department, and data confidentiality was strictly enforced. Only selected data managers had access to personal identifiers. Anonymised data were provided only to the principal investigators, the lead statistician and the health economist. This consent procedure was approved by both ethics committees.

Context of the study

The Free State province, with a population of 2.8 million [27], and an estimated HIV prevalence of 18.5% among 15–49 year olds [28], commenced the public sector rollout of ART in 2004 with a vertical approach to delivery of HIV care. Patients diagnosed as HIV-positive, by nurses from primary care clinics (who diagnose and treat common conditions) were referred for all further HIV care to designated ART nurses (also primary care nurses but appointed for the ART programme) at ART assessment sites located within selected primary care clinics. Patients eligible for ART (CD4 <200 cells/μl or Stage 4) had baseline bloods taken, received drug readiness training and then were referred for initiation of ART to doctors at ART treatment sites and subsequently fetched monthly supplies of ART at the assessment site. Those not yet eligible for ART continued to access care (CD4 counts through laboratory testing, staging, tuberculosis (TB) screening and cotrimoxazole prophylaxis) with ART nurses at the assessment site. By the end of 2007, 57 ART assessment and treatment sites were functioning [29]. However, the vast majority of primary care clinics in the province could not provide on-site access to HIV care but rather had to refer their patients to primary care clinics with ART assessment facilities. While patients on ART had good outcomes [30,31], estimated coverage was only 25% [29,32], the mortality rate amongst patients awaiting ART was high [30], and high rates of burnout in nurses working in ART clinics were recorded [33].

In order to assess strategies to improve access to ART, a pragmatic, cluster, randomised controlled trial, the STRETCH trial was conducted. All 31 existing ART assessment sites at the end of 2006, were randomised into 16 intervention and 15 control clinics within 9 clusters of between 2–7 clinics. Clinics in a cluster were usually under one local area or district management structure, or referred patients to doctors at the same ART treatment clinic, or both. The trial comprised two interventions: 1) nurse initiation and repeat prescription of ART and 2) integration of HIV care into primary care. The primary outcomes were survival of patients with CD4<350 and not yet on ART (patients eligible for ART or likely to become eligible during the trial) and 12 month viral load suppression rates for patients on ART [26,34].

The integration intervention was developed in consultation with staff at all 31 clinics [34]. They reported that the existing system of ART nurses providing all HIV care at designated ART assessment sites was overloading these ART nurses and was also cumbersome for patients. One example of this was that HIV-positive patients on ART and those not yet eligible for ART who needed cotrimoxazole prophylaxis, accessed HIV care from ART nurses at the ART assessment site but had to fetch cotrimoxazole from primary care nurses at their local primary care clinic as cotrimoxazole was supplied from the clinic's primary care budget. The aims of the intervention developed with the staff were twofold: 1) HIV care was to be integrated into the work of all primary care nurses (and not just the ART nurses) within the ART clinic so that patients could access HIV care from any nurse at that clinic (internal integration) and, 2) HIV care was to be provided by nurses at all surrounding primary care clinics referring patients to that ART clinic, so that patients could access HIV care from their local clinic (mainstreaming HIV care). Staff also identified six elements of HIV care that needed to be integrated: 1) voluntary counselling and testing (VCT); 2) initial CD4 count; and 3) routine care including cotrimoxazole prophylaxis for those not yet eligible for ART (three elements of pre-ART care); 4) baseline blood tests; 5) drug readiness training; and 6) monthly supply of ART for patients eligible for ART (three elements of ART care). It was noted during development of the intervention that integration of pre-ART care had already commenced at some ART clinics and their surrounding primary care clinics ("referring primary care clinics"). ART prescription and adherence counselling could not be integrated into all primary care services during the trial as

provincial authorisation of nurse ART prescription was limited to trained nurses in intervention clinics only.

The strategies used to implement the STRETCH interventions have been described elsewhere [34] and are summarised in Table 1. These included provincial training in diagnosis and care of TB, respiratory disease, sexually transmitted diseases and HIV at all primary care clinics using the PALSA PLUS primary care guidelines [35,36], and extra training in ART prescription at intervention clinics using a STRETCH edition of PALSA PLUS. Clinic based teams, consisting of key clinic staff, implemented changes within intervention clinics. Local management teams comprising the local area manager, ART pharmacist and PALSA PLUS trainer, and clinic managers from the intervention clinic and referring primary care clinics, supported mainstreaming of HIV care. The STRETCH coordinator (KU) provided clinical and organisational support and was involved in facilitating the management teams. An implementation toolkit with descriptions of the trial interventions and changing roles of clinic staff, was distributed to members of the clinic based teams. The intervention was implemented in three phases at a pace decided by clinic teams.

Integration questionnaire

Although provincial tools existed to monitor provision of HIV care (such as HIV tests and CD4 counts) at primary care clinics, there was no tool to assess whether HIV care was integrated into all consultations within clinics. Thus, a new questionnaire was developed in consultation with clinic staff (see Additional File S1 and a summary in Table 2). There were eleven questions on internal integration. These questions assessed the integration of care for HIV-positive patients into the consultations of all nurses within the ART clinic. There were four questions on the integration of HIV care for patients not yet eligible for ART (pre-ART care) (Q1,3,5 and 7); four on the integration of HIV care for patients eligible for and on ART (ART care) (Q12,14,16 and 18) and three questions on the integration of primary care services needed by patients on ART at that clinic (TB diagnosis, dispensing of cotrimoxazole and contraception) (Q9,10 and 11). There were eight questions on mainstreaming HIV care. These questions assessed the provision of HIV care by nurses at referring primary care clinics. There were four questions each on the provision of pre-ART (Q2,4,6 and 8) and ART care (Q13,15,17 and 19).

Based on the initial discussions with staff, each question had only two or three possible responses to describe integration. Answers were scored 0 for no integration, 2 for full integration and, in questions with three responses, 1 for partial integration. The scores for each question were combined to give a total integration score and four component integration scores. These different combinations of questions and the resulting integration scores are summarised in Table 2 and described below:

- *Total integration score* – total score for all 19 questions.
- *Pre-ART integration score* – total score for questions 1–8 on the provision of HIV care for patients *not yet eligible for ART* by all nurses (primary care and ART nurses) at the ART clinic *and* at referring primary care clinics
- *ART integration score* – total score for questions 12–19 on the provision of HIV care for patients *eligible for, and on ART* by all nurses (primary care and ART nurses) at the ART clinic *and* at referring primary care clinics
- *Internal integration score* – total score for questions 1,3,5,7,9,10,11,12,14,16 and 18 on the provision by all nurses within the ART clinic, of pre-ART and ART care and on the provision of three key primary care services for patients on ART
- *Mainstreaming HIV score* – total score for questions 2,4,6,8,13,15,17,and 19 on the provision of pre-ART and ART care by nurses at referring primary care clinics

Internal integration scores could be calculated for all 31 clinics throughout the trial. However, the other integration scores could only be calculated for 23 clinics (13 intervention and 10 control)

Table 1. Intervention and control clinic characteristics during STRETCH trial.

	Intervention ART clinics	Primary care clinics referring to intervention clinic	Control ART clinics	Primary care clinics referring to control clinic
Nurse training	6–8 sessions of PALSA PLUS training. Extra 4 sessions STRETCH training in initiating and monitoring adults on ART	6–8 sessions of PALSA PLUS training	6–8 sessions of PALSA PLUS training	6–8 sessions of PALSA PLUS training
Provincial authorisation of ART prescription	Trained professional nurses authorised to initiate and repeat prescriptions of ART for uncomplicated adults	Patients referred to intervention site for ART prescription	Patients referred to doctors at treatment clinics for ART prescription	Patients referred to control clinics and thence to doctors at treatment clinics for ART prescription
Patient management guidelines	STRETCH edition of PALSA PLUS including guidelines for initiation and repeat prescription of ART	Standard Free State edition of PALSA PLUS guidelines	Standard Free State edition of PALSA PLUS guidelines	Standard Free State edition of PALSA PLUS guidelines
Implementation toolkit	STRETCH toolkit issued to members of clinic based team			
Clinic based support team	Clinic based STRETCH team to implement integration of pre-ART and ART care into work of all professional nurses in clinic			
Local area management support team		Local area management team to implement integration of pre_ART and ART care into all primary care clinics referring to intervention clinic		

Elements of STRETCH trial intervention including nurse training, patient care guidelines, toolkit and support teams at intervention clinics and their referring primary care clinics compared to standard care at control clinics and their referring primary care clinics.
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Table 2. Component questions of the five different integration scores.

Integration score	Component questions contributing to score	Example question
Total integration score	All 19 questions	
Pre-ART integration score	Q1–8 on the provision of HIV care for patients not yet eligible for ART by 1)all nurses within the ART site and 2) the patients local referring primary care clinic	Q4. If a patient is diagnosed HIV-positive at one of your referring PHC clinics is it possible to access their initial CD4 count at that clinic?
ART integration score	Q12–19 on the provision of HIV care for patients eligible for ART by 1)all nurses within the ART site and 2) the patients local referring primary care clinic	Q14. When patients from your clinic are about to start ARVs and need Baseline bloods who takes these bloods?
Mainstreaming HIV score	Q2,4,6,8,13,15,17,19 on the provision of pre-ART and ART care by the patients local referring primary care clinic	Q19. Is it possible for patients from your referring PHC clinics who are on ARVs to fetch their repeat supply of ARVs from their own PHC clinic?
Internal integration	Q1,3,5,7,9,10,11,12,14,16,18 on the provision of pre-ART and ART care by all nurses within the ART clinic *and* the provision of three key primary care services for patients on ART	Q1. If a patient needs an HIV test at your clinic who is performing this test?

A summary describing which questions from the integration questionnaire contributed to each integration score during the four assessments of the trial. An example of the questions contributing to each integration score is also included. The full questionnaire is included in Additional File 1.
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that still had primary care clinics referring patients to that ART clinic throughout the trial. New ART assessment clinics were established by the Department of Health during the trial and consequently eight of the 31 trial clinics no longer had patients referred from other primary care clinics by the last assessment of the trial.

The questionnaire was administered at all four assessments by the trial coordinator (KU) with the clinic manager or senior ART nurse at the clinic and preferably the same person at each assessment, but this was not always possible. The answer that best described the level of integration was decided by the interviewee in discussion with the coordinator. The coordinator was involved in local management teams responsible for the implementation of integration and so had independent confirmation about the progress of integration in each clinic. The assessments were done at all 31 clinics, as it could not be assumed that integration would not take place at control clinics [37]. Integration of HIV care into primary care services at the 16 intervention clinics commenced in Phase 1 of the trial and six-monthly integration assessments were planned. The first two assessments were conducted six months apart during early trial support visits. The last two assessments, when support visits were less frequent, were conducted telephonically, and the interval was extended to nine months as the trial had been extended due to a delay in nurse initiation of ART in some clinics. Time taken to complete the questionnaire was short (10–15 minutes), but as the coordinator had to travel to each clinic, or phone the interviewees at a time convenient to conduct the questionnaire, each round of assessments took four to six weeks to complete. A mean date of assessment was assigned in order to plot changes in mean scores.

Consistency and reliability of the questionnaire

Internal consistency of the questionnaire was tested using Cronbach's alpha coefficients. These were calculated from scores at the first assessment for the entire questionnaire, and then the groups of questions on internal integration and mainstreaming HIV care, as well as the questions on pre-ART and ART integration.

In order to test for inter-observer reliability, the interview was repeated by a different interviewer at five clinics (three intervention and two control) in two districts, two months after the first assessments. These clinics were chosen by convenient sampling from the 23 clinics that had primary care clinics referring patients throughout the trial and could give scores for all 19 questions.

Statistical analysis

Differences in the mean values of total integration scores and in the four component integration scores at intervention and control clinics were analysed with one way analysis of variance ANOVA (SPSS version 16.0) and a non-parametric analysis, Mann-Whitney (SAS version 9.2). Repeated measures ANOVA was used to analyse changes in mean scores over time (SPSS version 16.0). The level of significance was chosen as a p value of <0.05.

Results

Internal consistency and reliability of the questionnaire

Cronbach's alpha coefficient was 0.85 for all 19 questions, 0.86 for the 8 questions on pre-ART integration, 0.68 for the 8 questions on ART integration, 0.73 for the eleven questions on internal integration and 0.69 for the eight questions on mainstreaming of HIV care.

The second observer, who conducted repeat interviews at 5 clinics, obtained the same integration score on all questions at two clinics, a one point difference on one question only at two other clinics and a total score of one point difference with three questions scoring differently at the fifth clinic. The mean total integration score was 23.5 (maximum possible score 38) for the two assessments at the 5 sampled clinics by both observers. The mean difference between the total integration scores at the 5 clinics done by the two different observers was -0.6, with a standard deviation of 0.55 giving 95% limits of agreement of -1.7 to 0.5.

Progress of integration

In an initial analysis of the changes in scores across all clinics for individual questions, the four questions that showed the largest absolute increases in integration scores (an increase of between 14–16 points) between the first and fourth assessments were questions 13,15,17 and 19 – all questions dealing with the mainstreaming of ART care. The questions that showed minimal variation in integration scores (absolute changes between 1–3 points) were questions 1–8 on mainstreaming and internal integration of pre-ART care.

The changes in mean integration scores for intervention and control clinics are plotted in Figures 1, 2, 3. As seen in Figure 1, mean total integration scores at the first assessment at intervention (25.7) and control clinics (25.4) were not significantly different. At the third assessment, conducted in the middle of the trial, the mean total integration score at intervention clinics (28.8) was significantly higher than at control clinics (23.7) (ANOVA, $p = 0.0174$; Mann-Whitney, $p = 0.0267$). The increase in mean total integration score at intervention clinics from the first (25.7) to the third assessment (28.8) was a significant change (rmANOVA, $p = 0.0198$). There was also a significant increase in mean total integration scores at control clinics that occurred late in the trial between the third (23.7) and fourth assessments (27.6) (rmANOVA, $p = 0.0283$). Consequently at the fourth assessment, there was no longer a significant difference between mean total integration scores at intervention and control clinics (ANOVA, $p = 0.4581$; Mann-Whitney, $p = 0.5342$).

In order to determine whether there was any change in which elements of HIV care had been integrated, differences in mean pre-ART and ART integration scores at intervention and control clinics and changes in these scores were analysed (see Figure 2). Mean pre-ART and ART integration scores at the first assessment at intervention clinics (14.4 and 6.2 respectively) and control clinics (15.4 and 5.1 respectively) were not significantly different. At the third assessment only, the mean ART integration score at intervention clinics (8.5) was significantly higher than at control clinics (3.8) (ANOVA, $p = 0.0015$; Mann-Whitney, $p = 0.0029$) and was significantly higher than at the first assessment (6.2) (rmANOVA, $p = 0.004$). However the mean pre-ART integration scores at intervention clinics were not significantly different from control clinics at any assessment, and there was no significant change at intervention or control clinics from the first assessment to the last assessment. Thus, integration of elements of ART care was the main contributor to the increased total integration scores at intervention clinics during the trial. The increase in mean total integration scores at control clinics late in the trial was likewise due to a significant increase in mean ART scores between the third (3.8) and fourth assessment (7.4) (rmANOVA, $p = 0.0078$). It was noted, however, that mean pre-ART integration scores were already close to the maximum possible score of 16 at the beginning of the trial and remained there throughout the trial.

In order to determine whether any significant change in integration at the two levels of primary care had taken place during the trial, differences in mean mainstreaming HIV and internal integration scores and changes in these scores were analysed (see Figure 3). Mean mainstreaming HIV and internal integration scores at the first assessment at intervention (9.7 and 16.1 respectively) and control clinics (8.8 and 17.1 respectively) were not significantly different. At the third assessment only, the mean mainstreaming HIV score at intervention clinics (11.3) was significantly higher than at control clinics (8.7) (ANOVA, $p = 0.0073$; Mann-Whitney, $p = 0.0158$) and significantly higher than at the first assessment (9.7) (rmANOVA, $p = 0.0023$). There were no significant differences in mean internal integration scores between intervention and control clinics at any assessment, and no significant changes in internal integration scores at intervention or control clinics from the first assessment to the last assessment. Mainstreaming of HIV care into primary care clinics was thus the main contributor to the level at which integration of HIV care into primary care took place at intervention clinics during the trial. The increase in mean total integration scores, late in the trial at control clinics, was also due to a significant increase in mean mainstreaming HIV scores occurring between the third (8.7) and fourth assessments (11.1) (rmANOVA, $p = 0.0059$).

Discussion

This assessment shows that the strategies employed during the STRETCH trial resulted in significant increases in total integration scores at intervention clinics. The specific areas in which the integration score increased were in providing HIV care in primary care clinics not previously involved in the ART programme (mainstreaming HIV score) and in the provision of elements of ART care, namely, the taking of baseline blood tests, drug readiness training and monthly supply of ART for patients eligible for ART (ART score). These findings have been independently

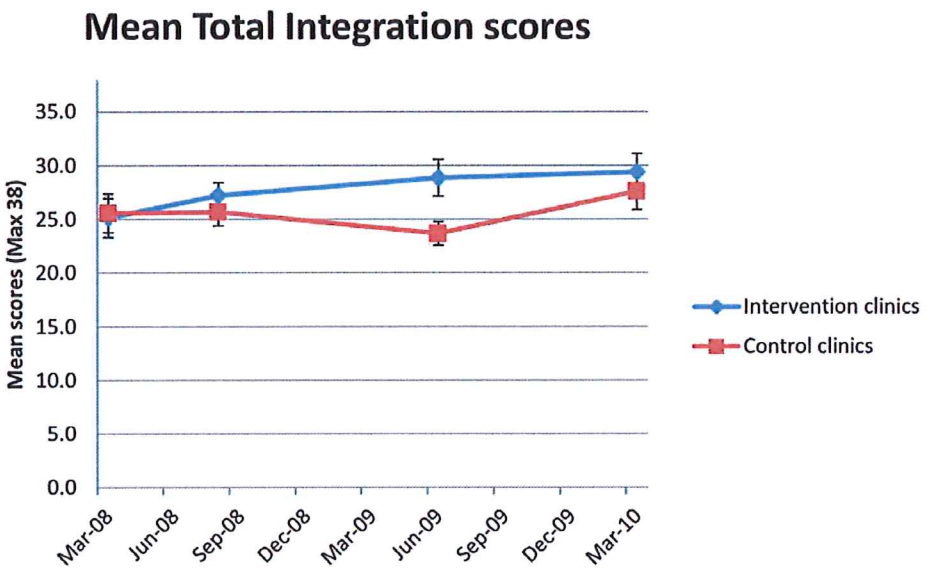

Figure 1. Progress of mean total integration scores during the STRETCH trial. Line graph of mean total integration scores at intervention and control clinics plotted against mean date of assessment, for four assessments during the STRETCH trail. Error bars depict standard error on the mean at each assessment.
doi:10.1371/journal.pone.0054266.g001

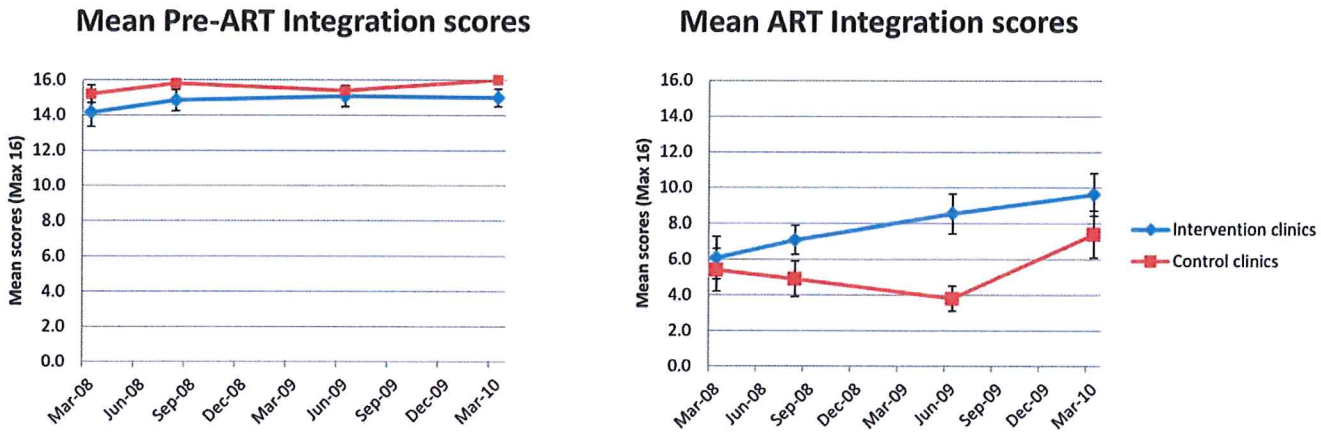

Figure 2. Progress of mean pre-ART and ART integration scores during the STRETCH trial. Two line graphs of mean pre-ART and ART integration scores at intervention and control clinics plotted against mean date of assessment, for four assessments during the STRETCH trial. Error bars depict standard error on the mean at each assessment.
doi:10.1371/journal.pone.0054266.g002

confirmed by a qualitative process evaluation of the STRETCH trial which found that patients and nurses appreciated the convenience of patients being able to access HIV care including ARVs at their local clinic instead of having to travel to an ART clinic [38]. There was no increase in mean pre-ART integration scores during the trial because these elements of HIV care, namely VCT, initial CD4 count and routine care for those not yet eligible for ART which had been identified by staff as critical elements of pre-ART needing integration, had already been substantially integrated into primary care services by local managers in the months leading up to the trial.

In contrast it appears that the strategies used in the STRETCH trial had no effect on internal integration scores at intervention clinics, with no significant shift towards patients being able to access HIV care from all nurses within the clinic. There may be other more effective strategies to achieve integration of HIV care into the work of all nurses within primary care clinics, or there may be factors that mitigate against internal integration. Topp et al described some strategies to integrate the provision of HIV care into the work of all nurses within two primary care clinics in Zambia [22]. These strategies included training of all staff in HIV care, as in the STRETCH trial, but also the use of other strategies not used in the STRETCH trial – combined medical records and waiting areas and the inclusion of HIV testing into triage of all patients. They did document increased uptake of HIV testing and good standards of HIV care. However, they also reported resistance on the part of nurses and patients to completely integrated ART services because of issues such as increased waiting times and the loss of informal support for patients on ART with the loss of ART waiting areas [22]. A synthesis of the findings of three qualitative studies on internal integration in Free State clinics conducted at the same time as the STRETCH trial found that administrative issues and patient and nurse preferences tended to mitigate against internal integration of HIV care (manuscript submitted for publication).

The increase in mean total integration, ARV and mainstreaming HIV scores by the fourth assessment late in the trial at control clinics, resulted from provincial implementation of a new national AIDS policy including nurse prescription of ART and the provision of ART in all primary care clinics – the two main

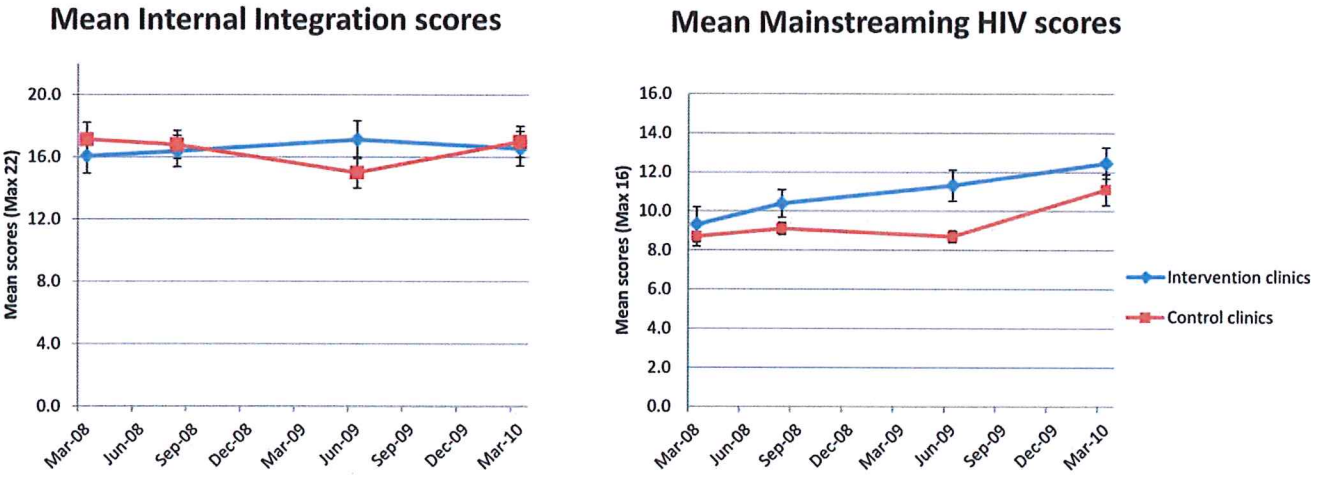

Figure 3. Progress of mean internal integration and mainstreaming HIV scores during the STRETCH trial. Two line graphs of mean internal integration and mainstreaming HIV scores at intervention and control clinics plotted against mean date of assessment, for four assessments during the STRETCH trial. Error bars depict standard error on the mean at each assessment.
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interventions of the trial [39]. The STRETCH trial was a pragmatic trial conducted under real conditions which include such policy changes. The research team was able to negotiate with the province that nurse initiation of ART would not be implemented in control clinics till after the trial, but was not able to delay integration of HIV care into primary care services in control clinics in the last few months of the trial.

One of the strengths of this study is that it is a prospective assessment using a new semi- quantitative tool to document integration of HIV care. The contents of this questionnaire were likely to be valid as the elements of HIV care and the need to integrate them at both levels were identified in consultation with staff at ART clinics. Internal consistency as shown by Cronbach's alpha was good. Real validity of the questionnaire was demonstrated in that it captured an increase in integration scores at control clinics as a result of the implementation of a new policy to integrate HIV care into primary care in the last months of the trial.

There were some potential limitations to this study. The first two interviews were conducted during clinic visits while the last two were conducted telephonically, interviews were not always conducted with the same staff member and data on services at referring primary care clinics were based on reports from staff at the ART site and not at the primary care clinic. However, all interviews were conducted by the trial coordinator who was well known to the clinic staff and involved in local management teams implementing integration and thus was able to independently confirm progress of integration as described by the interviewee at each clinic. Though there is a possibility that the coordinator may have influenced answers, the results of inter-observer reliability tests suggest that this was negligible. The lack of progress in internal integration compared with the progress in mainstreaming HIV, captured by the questionnaire, suggests that the interviewees were not unduly influenced to report integration where there was none. The integration questionnaire was developed to assess the integration of HIV care into primary care as it affected service delivery for patients and was therefore not able to assess the effects of integration of other areas of health system functioning. The questionnaire was not able to document the impact of integration of HIV care on the provision of other primary care services. This is an important area of research, and is the subject of a project currently being conducted in all primary care clinics in the Free State.

This questionnaire was validated in the specific context of the Free State and may need some further development, but it could be a valuable tool for assessing integration of HIV care into primary care clinics in other settings. The main results of the STRETCH trial showed that patient survival was not significantly different in intervention clinics compared with control clinics [40].The integration scores obtained in this study will be correlated with survival of patients with CD4 below 350 and not yet on ART, from the STRETCH trial to determine if integration of HIV care may have had an independent effect on patient survival. These results, together with the process evaluation and results of the STRETCH study, should be useful in identifying whether integration is an effective strategy to improve survival of HIV-positive patients in need of ART.

Conclusion

The integration questionnaire developed in this study is a valid tool with potential to monitor integration in other high HIV-burden countries. This study demonstrated an increase in total integration scores in clinics in the Free State province during the STRETCH trial. This was achieved by integrating ART care, particularly at primary care clinics not previously designated as ART clinics but there was no increase in integration of HIV care into all consultations. The scores documented in this intervention will be used to determine if integration is associated with an improvement in survival of patients needing ART.

Supporting Information

File S1 Survey of integration of HIV care in ARV clinics and their referring primary care clinics.
(DOC)

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Author Contributions

Conceived and designed the experiments: KEU GJ DHCJVR. Performed the experiments: KEU. Analyzed the data: KEU GJ EW. Wrote the paper: KEU GJ EW WFM DHCJVR.

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Chapter 6

Integration of HIV care into primary care services in South Africa: Effect on survival of patients needing antiretroviral treatment

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Integration of HIV care into primary care in South Africa: Effect on survival of patients needing antiretroviral treatment

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Introduction Integration of human immunodeficiency virus (HIV) care into primary care is a potential strategy to improve access to antiretroviral therapy (ART) in high-burden countries. This study was conducted to determine the effect of integration of HIV care on survival of patients needing ART.
Methods A questionnaire was used to measure integration of HIV care into primary care during a randomized controlled trial of task shifting and decentralization of HIV care in South Africa. Cox proportional hazard ratios were estimated for the effect of 5 different integration scores (total, pre-ART, ART, mainstreaming HIV and internal integration) on survival of patients with CD4≤350 cells/μl and not yet on ART.
Results A total of 9,252 patients were followed up for 12-18 months. Cox proportional hazards ratios adjusted for patient and clinic characteristics, showed decreased risk of mortality in clinics with high scores for total integration (HR 0.97; 95% CI 0.95-0.98; p<0.001); ART integration (HR 0.94; 95% CI 0.90-0.99; p=0.013) and internal integration (HR 0.97; 95% CI 0.95-1.00;p=0.041). Analysis of the effect of component scores adjusted for patient characteristics only, showed decreased risk of mortality in clinics with high scores for total integration (HR 0.97; 95% CI 0.94-1.00; p=0.032) pre-ART integration (HR 0.92; 95% CI 0.85-0.99; p=0.027) ART integration (HR 0.95; 95% CI 0.93-0.98; p=0.001) and mainstreaming HIV (HR 0.90; 95% CI 0.83-0.97; p=0.007).
Conclusion In a context of task shifting and decentralization of care, integration of HIV care into primary care is associated with improved survival of HIV positive patients needing ART.

Introduction

Although the prevalence of Acquired Immune Deficiency Syndrome (AIDS) is stabilizing and the number of people accessing antiretroviral treatment (ART) is increasing, the worldwide HIV/AIDS epidemic is still exacting a tremendous toll with an estimated 1.8 million deaths in 2010 [1]. In sub-Saharan Africa, 5 million people had been started on ART by the end of 2010, an estimated 49% of those in need [1]. Because of evidence of significant decreases in mortality in communities where universal ART coverage has been achieved [2],

the United Nations General Assembly has agreed on the importance of efforts to achieve universal ART coverage [3].

Given the problems in health infrastructure in sub-Saharan Africa, such as shortages of health care workers, underfunding, lack of drugs and poor laboratory services, the initial response in many countries was to set up vertical (stand-alone) HIV care programs with separate funding, staff and facilities [4-6] However, such vertical programs cannot reach the number of people needing ART in high-burden countries and there are reports they draw resources and staff away from general health programs [6, 7]. Vertical HIV care programs need to be broadened to provide HIV care within existing health systems in a manner that strengthens those health systems, the so-called diagonal approach [8].

Shortage of health care workers is one area that needs to be addressed. Van Damme and Kegels [9] pointed out the need to develop context specific models of HIV care delivery requiring less doctors and nurses in countries with such shortages. Many models of shifting HIV care from highly qualified to lower qualified health care workers (task-shifting or sharing) have been implemented in countries in sub-Saharan Africa and have demonstrated good patient outcomes [10-14]. However, as pointed out by Phillips et al [15], task-shifting is not a panacea. There is a need to support professional and lay health care workers, address health systems deficiencies, and identify sustainable strategies to integrate HIV care into these systems [6, 16].

One of the difficulties in identifying effective strategies to do this is that integration itself is a broad concept with a lot of overlap with the similar concept of decentralization. Integration has been defined as "a variety of managerial or operational changes to health systems to bring together inputs, delivery, management and organization of particular service functions" [17]. An even broader definition has been that integration is about providing the "right care" in the "right place"[18]. This difficulty in defining integration is one of the reasons there is a paucity of good evidence that integration does improve patient outcomes[19-21].

Many programs, described variously as decentralization or integration of HIV care, have reported significant progress towards universal access to ART. These include primary care-driven models of HIV care with either doctor support [22]or nurse ART prescription [10, 11, 23]; and models to provide HIV care within primary care services, such as the co-location of vertically run HIV services into existing primary care clinics [24], down-referral of patients from existing ART sites to primary care clinics [25, 26], or programs to support primary care

clinics by training and linkage with existing ART sites [23]. Other studies have reported on strategies to integrate HIV care into all primary care consultations, such as staff training, combined medical records, standardised protocols and regimens [27], combined waiting areas and the inclusion of HIV testing into triage [28]. Although all have reported good outcomes, none were conducted as controlled trials. This is thus a need for randomised controlled trials of the impact of integration on patient outcomes which describe what health system functions are being integrated [19-21]

The current study, part of a randomized controlled trial of the effect of task shifting and decentralization of care on patient outcomes in South Africa, the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH trial)[29] assesses the effect of integration of HIV care into primary care services on patient survival. The aim of the present study is to answer two specific questions: 1) Is there evidence that integrating HIV care into primary care services improves survival for patients with CD4≤350 cells/μL and not on ART? 2) If so, what level of integration of HIV care into primary care is important to improve patient survival? The STRETCH trial is registered at isrctn.org (ISRCTN46836853)

Methods

Context

The Free State Province, with a population of 2.8 million[30], has an estimated HIV prevalence of 18.5% among 15-49 year olds [31]. The public sector ART program commenced in the Free State in 2004 with a vertical approach to HIV care. Patients diagnosed as HIV-positive by nurses working in primary care clinics were referred to ART nurses (also primary care nurses but appointed for the ART program) at ART assessment clinics. ART nurses worked as a unit within certain existing primary care clinics from across the province which had been designated as ART assessment clinics. These ART nurses managed patients referred from the other primary care nurses within that clinic, and from surrounding clinics, and these patients received all further HIV care from these ART nurses. In one large urban area, even HIV testing was initially not available from primary care clinics and was only accessible through ART nurses.

All patients assessed by ART nurses as eligible for ART (CD4<200 cells/μl or Stage 4 AIDS), received drug readiness training, baseline blood tests and monthly ART supplies at that clinic, but were referred to ART treatment clinics in designated hospitals for doctors to

initiate ARVs and for monitoring and review of ARV prescriptions every 3-6 months. Those not yet eligible for ART were seen 6-12 monthly at the ART assessment clinic for CD4 counts, staging and TB screening. By mid-2007, a total of 57 ART assessment and treatment clinics were functioning [32], but the majority of the 222 primary care clinics in the province could not offer on-site access to ART. Patients who did receive ART had good outcomes [33, 34], but estimated coverage of those in need of ART was only 25% by 2007[32, 35], and the 12 month mortality rate amongst patients awaiting ART was 53% [34].

In order to assess strategies to improve access to ART, a pragmatic, cluster, randomized, controlled trial – the STRETCH trial – commenced in 2007. All 31 ART assessment clinics functioning by end 2006, were randomized into 16 intervention and 15 control clinics within nine clusters defined as groups of clinics referring to the same treatment site [36, 37]. The trial comprised two main interventions: 1) nurses at intervention clinics initiating and repeating ART prescriptions for uncomplicated adults and referring complicated patients to doctors at ART treatments sites and; 2) integrating elements of HIV care into primary care services to spread the workload amongst more nurses and facilities by enabling patients to access most elements of HIV care at primary care instead of at the ART assessment clinic.

The elements of HIV care that were to be integrated were: voluntary counseling and testing (VCT), initial CD4 counts, routine HIV care including co-trimoxazole prophylaxis, baseline bloods, drug readiness training and monthly ART supply for patients responding well to the first six months of ART at the intervention clinic. The integration of HIV care into primary care was to take place at two levels: firstly, into the package of services provided by primary care clinics, not designated as ART assessment clinics and which had been referring patients to intervention clinics (called mainstreaming HIV); and secondly, into consultations of all primary care nurses (not just ART nurses) within the intervention clinics (called internal integration). This was a complex health intervention and the details of the integration component particularly, were developed during extensive consultations with staff from the simpler principle of decentralization of routine HIV care to generalist nurses, as initially conceived by the researchers. This development process has already been described [37].

There were two primary outcomes: survival of patients in cohort 1 (CD4≤350 cells/μl and not on ART at enrolment) and 12 month viral load suppression rates of patients in Cohort 2 (on ART for six months or more at enrolment). The results showed no difference in patient survival overall in cohort 1 but significantly improved survival in a sub-group with CD4

between 200 and 350 and equivalent 12 month viral load suppression rates in cohort 2 [29]. This analysis looks at the effect of integration achieved during the STRETCH trial on survival of patients with CD4≤350 cells/μl and not on ART at enrolment (all patients in Cohort 1).

Integration questionnaire

During the trial a new instrument– a semi-quantitative questionnaire – was developed and validated [38]. This questionnaire was used to monitor integration in order to answer two questions: 1) Did integration of HIV services take place in intervention clinics during the trial? 2) Did integration have an independent effect on patient survival? Analysis of the results to answer the first question showed that integration scores at intervention and control clinics were similar at baseline and did progress by mid-trial in intervention clinics [38].

The instrument contained questions on the number of staff and referring primary care clinics as well as 19 questions on integration of elements of HIV care at both levels of primary care. There were (1) eight questions on the integration, at both levels, of VCT, initial CD4 counts and routine HIV care for those not yet eligible for ART (pre-ART care); (2) eight questions on the integration, at both levels, of baseline blood tests, drug readiness training, and monthly ART provision for patients eligible for ART (ART care); and (3) three questions on the integration of key primary care services (TB diagnosis, cotrimoxazole prophylaxis and contraception) for patients accessing ART at that site (see the full questionnaire in Appendix E).

Data collection

The questionnaire was administered at intervals during the trial by the trial coordinator (KU) to clinic managers or ART nurses at all intervention and control clinics (31 clinics). The trial was implemented in phases. Efforts to integrate HIV care into primary care services and the training of nurses in ART initiation began in September 2007. Patient enrolment in each clinic was commenced only on the date nurses at intervention clinics in that cluster started initiating patients on ART. The start date for patient enrolment in each cluster was staggered over a 10 month period from the end of January to the beginning of December 2008 as some clinics took longer than others to be ready to commence nurse initiation of ART. An assessment of integration conducted at all clinics between February and April 2008 was used

to determine if integration achieved between September 2007 and this first assessment affected subsequent survival of patients in Cohort 1.

Patients recruited into cohort 1 were monitored for a minimum of 12 and maximum 18 months and the primary outcome was survival [36]. Patient's age, sex, identity number and enrolment CD4 count and date of commencing ART were obtained from provincial electronic ART program medical records. Deaths were recorded by linkage to the national death register if the patient's national identity number was known. For patients with identity numbers missing, vital status at the end of follow-up was determined by checking for visits to health facilities after the period of follow-up. Data on the total number of patients accessing care at each clinic for the year 2009 were obtained from department of health statistics. The number of professional nurses at each clinic in mid-2009 was obtained from the integration questionnaire and a patient: staff ratio was calculated. Clinics in large multi-functional towns were classified as urban while those in small agricultural towns were classified as rural.

Each question had only two or three possible responses to depict integration of that element of care (see Supplemental digital content 1). Questions were scored as 0 for no integration, 2 points for full integration and, in the case of questions with three possible responses, 1 point for partial integration. For each clinic five integration scores were determined from different groupings of questions as follows:

- *Total integration score*-total score for all 19 questions.
- *Pre-ART integration score*- total score for questions 1-8 on the provision of HIV care for patients not yet eligible for ART by all nurses (primary care and ART nurses) at the ART clinic and at referring primary care clinics (Example: Q4. If a patient is diagnosed HIV-positive at one of your referring PHC clinics is it possible to access their initial CD4 count at that clinic?)
- *ART integration score*- total score for questions 12-19 on the provision of HIV care for patients eligible for, and on ART, by all nurses (primary care and ART nurses) at the ART clinic and at referring primary care clinics (Example: Q14. When patients from your clinic are about to start ARVs and need Baseline bloods who takes these bloods?)
- *Internal integration score*- total score for questions 1,3,5,7,9,10,11,12,14,16 and 18 on the provision by all nurses within the ART clinic, of pre-ART and ART care and

on the provision of three key primary care services for patients on ART (Example: Q1. If a patient needs an HIV test at your clinic, who is performing this test?)

- *Mainstreaming HIV score*- total score for questions 2,4,6,8,13,15,17,and 19 on the provision of pre-ART and ART care by nurses at referring primary care clinics (Example: Q19. Is it possible for patients from your referring PHC clinics who are on ARVs to fetch their repeat supply of ARVs from their own PHC clinic?)

Internal integration scores could be derived for all 31 clinics during the trial as this score assessed integration of HIV care within that clinic. However, the other integration scores could only be calculated for the 23 clinics (13 intervention and ten control clinics) that still had other primary care clinics referring patients for HIV care at the end of the trial. During the trial, the Free State department of health was establishing new ART clinics with emphasis on improving access for patients in rural areas. Primary care clinics, that used to refer patients to some clinics in the trial, became new ART clinics or started referring patients to new ART clinics and as a result eight trial clinics no longer had any patients referred from other clinics.

Data Analysis

For all patients in cohort 1, time from enrolment to death with follow-up censored at 18 months or at trial end-date if earlier, was analyzed using Cox proportional hazards models to determine if integration scores were associated with patient survival. This analysis was adjusted for cluster, arm of the study and patient and clinic characteristics known to affect survival or ascertainment of survival. These included age, sex, CD4 count at enrolment, whether the patient received ART and ascertainment of identity document (ID) number; and two clinic characteristics, patient to staff ratio and rural or urban clinic, known to affect survival of patients needing ART in Free State clinics [39]. As the integration intervention was likely to improve access to care by impacting patient to staff ratio (increasing the number of staff offering HIV care) and decreasing the distances patients travelled in rural areas (enabling them to access care at their nearest clinic), the analysis was then repeated without adjusting for these two clinic characteristics. All analyses were adjusted for intra clinic correlation of outcome, with Huber-White robust adjustment using Stata software. For all these calculations a p value of < 0.05 was considered to be significant.

Ethical considerations

Approval to conduct this study was obtained from the Head of the Department of Health in the Free State and the Human Research Ethics Committees of the Faculty of Health Sciences of the University of the Free State. As the STRETCH trial was an educational and managerial intervention aimed at entire clinics, written informed consent was obtained from clinic managers but not from individual patients. Patients in intervention clinics were given written information about the trial. Ethical principles for use of medical records for research without patients' consent were followed. Anonymized data were provided only to the principal investigators, the lead statistician and the health economist.

Results

Table 1 shows patient characteristics and outcomes in all 31 clinics and in the group of 23 clinics that still had patients referred from other primary care clinics. In Cohort 1, from all 31 clinics, 9252 patients were recruited: 58% at intervention clinics, 85.9% had a known identity number, 18.8% died during follow-up and 6% were lost to follow-up (last visit to clinic more than three months before end of trial and identity number unknown) and thus vital status could not be ascertained. Of the total number in Cohort 1, 8150 patients were in the 23 clinics: 60% at intervention clinics, 86% had a known identity number, 19% died during follow-up and 6% were lost to follow-up and vital status could not be ascertained. Table 2 shows the mean integration scores and clinic characteristics for all 31 clinics and the group of 23 clinics. Mean patient: staff ratio was similar in the 31 and 23 clinics but the percentage of rural clinics and patients at rural clinics was lower in the group of 23 clinics. This was probably due to provincial policy to establish ART sites in rural areas during the period of the trial. There was no difference in baseline patient characteristics in clinics with different integration scores. In the 23 clinics for which a total integration score was available, there was no correlation between integration scores at first assessment and patient characteristics at enrolment: mean CD4 (R^2 =0.05); mean age (R^2 =0.02) and male to female ratio (R^2 =0.04).

Table 3 shows the Cox proportional hazard ratios of the effect of the five integration scores on patient survival. Analysis of patient survival adjusted for cluster, arm of study and patient and clinic characteristics in the 23 clinics, showed a 3% decrease in mortality for every one point increase in total integration score (HR 0.97; 95% CI 0.95-0.98; p<0.001.). Hazard ratios without adjustment for patient to staff ratio and rural vs. urban clinics also showed a 3%

Table 1. STRETCH trial Cohort 1[#] patient characteristics and outcomes at all 31 clinics and at the 23 clinics that had referring primary care clinics till the end of the trial.

Patient characteristics and outcomes	All 31 clinics	23 clinics that had referring primary care clinics till end of trial
Median CD4 at enrolment(IQR)	139(70-199)	136(68-195)
% male	32.1%	32%
Median age (IQR)yrs	35(30-43)	36(30-43)
% with ID number known	85.9%	86%
% received ART during trial	66.3%	67%
% of patients at intervention clinic	58.3%	60%
Number of deaths/total number recruited (%)	1744/9252 (18.8%)	1542/8108 (19%)
Number of patients lost to follow-up[§] and vital status not ascertained (%)	559/9252 (6%)	476/8108(6%)

[#]CD4≤350 cells/μL and not on antiretroviral treatment at enrolment

[§]Lost to follow up defined as no visit to the clinic in the three months before end of trial and no identity number known

Table 2. STRETCH trial clinic characteristics and mean integration scores for the 31 clinics where only internal integration scores could be ascertained and the 23 clinics where all integration scores could be ascertained.

Clinic characteristics and mean integration scores	All 31 clinics	23 clinics that had referring primary care clinics till end of trial
Number of rural clinics/total (%)	19/31 (61%)	11/23 (48%)
% of patients at rural clinics	44.3%	36.4%
Median number patients seen in one year (2009) per nurse (Range)	6712 (1960-10679)	6595 (1960-9683)
Mean total integration score (range)	N/A	25.3 (12-34)
Mean pre-ART integration score (range)	N/A	14.6 (8-16)
Mean ART integration score (range)	N/A	5.8 (2-14)
Mean mainstreaming HIV score (range)	N/A	9 (4-16)
Mean internal integration score (range)	16.6(7-22)	16.3 (7-22)

Table 3. Effect of early trial clinic integration scores on time from enrolment to death in patients with CD4≤350 cells/μL and not on antiretroviral treatment at enrolment (Cox proportional hazard ratio; adjusted for cluster and arm of study, patient characteristics[#] and clinic characteristics*)

	Adjusted for cluster, arm of study, patient characteristics[#] and clinic characteristics*			Adjusted for cluster, arm of study and patient characteristics[#] only		
Integration scores	Hazard ratio	95% Confidence interval	Hazard ratio p value	Hazard ratio	95% Confidence interval	Hazard ratio p value
Total integration (23 clinics)	0.97	0.95-0.98	0.000	0.97	0.94-1.00	0.032
Pre-ART integration (23 clinics)	0.96	0.90-1.02	0.201	0.92	0.85-0.99	0.027
ART integration (23 clinics)	0.94	0.90-0.99	0.013	0.95	0.93-0.98	0.001
Mainstreaming HIV (23 clinics)	0.94	0.83-1.06	0.299	0.90	0.83-0.97	0.007
Internal integration (31 clinics)	0.97	0.95-1.00	0.041	0.97	0.93-1.01	0.108

[#]Patient characteristics were age, sex, CD4 at time of enrolment, whether patient received ART during trial, and presence of ID number.

*Clinic characteristics were patient: staff ratio and rural or urban clinic

decrease in mortality for every one point increase in total integration score (HR 0.97; 95%CI 0.94-1.00; p=0.032).

Analysis of the effect of component integration scores adjusted for strata, arm of study, patient and clinic characteristics in the 23 clinics, showed that there was a significant decrease in patient mortality of 6% for every one point increase in ART integration scores (HR 0.94; 95% CI 0.90-0.99; p=0.013). There was however, no significant difference in mortality related to pre-ART integration (HR 0.96; 95% CI 0.90-1.02; p=0.201) or mainstreaming HIV scores (HR 0.94; 95% CI 0.83-1.06; p= 0.299). In the 31 clinics, there was a significant decrease in mortality of 3% for every one point increase in internal integration scores (HR 0.97; 95%CI 0.95-1.00; p=0.041).

In order to determine whether the components of integration may have impacted survival by affecting patient to staff ratios and improving access for rural clinics, the analysis of hazard ratios was repeated without adjustment for these clinic characteristics. In the 23 clinics, there was a significant decrease in mortality of 8% for every one point increase in pre-ART integration scores (HR 0.92; 95% CI 0.85-0.99; p=0.027), 5% for every one point increase in ART integration scores (HR 0.95; 95% CI 0.93-0.98; p=0.001) and 10% for every one point increase in mainstreaming HIV scores (HR 0.90; 95% CI 0.83-0.97; p=0.007) but no difference in patient mortality in the 31 clinics with changes in internal integration scores (HR 0.97; 95%CI 0.93-1.01; p=0.108).

Discussion

These findings provide evidence that integration of HIV care into primary care services is associated with improved survival of patients with CD4≤350 cells/μL and not yet on ART, with every one point increase in total integration score associated with a 3% decrease in mortality hazard rate, independent of other patient and clinic factors known to impact survival. Various articles from Southern Africa have reported progress towards universal access to ART in communities where HIV and ART care has been provided within primary care services [10, 13, 22, 40] but have not linked these findings with data on patient survival. These results suggest that integration of HIV care into primary care services improves survival for HIV-positive people with CD4 counts ≤350. The possible mechanisms could include improved access to care, decreased stigma and improved confidentiality, continuity and comprehensiveness of care. Another mechanism may have been improved quality of care

with evidence from the STRETCH trial showing improved TB case detection, weight gain and increase in CD4 counts in intervention clinic patients [29]. Integration of HIV care into primary care services should thus be an important tool to achieve universal access to ART for people with CD≤350 cells/μl as currently recommended by the World Health Organization [41].

The findings also show that integration of HIV care at both levels of primary care assessed in this study is associated with improved patient survival. At the first level, there was a 10% decrease in patient mortality associated with every one unit increase in mainstreaming HIV score when adjusted for patient characteristics but no difference in outcome when adjusted also for patient to staff ratio and rural/urban. This suggests that the improved patient survival seen where HIV care was provided in all referring primary care clinics was most likely due to increasing the number of nurses able to offer this care and decreasing distances patients have to travel to access care. Providing HIV care in primary care clinics may only improve patient outcomes where attention is given to sufficient staffing. Integration, like task shifting, is unlikely to be a panacea [15, 18]. At the second level, integration of HIV care into all consultations within intervention clinics, there was a 3% decrease in patient mortality for every one point increase in internal integration score but only when adjusted for patient and clinic characteristics. The lack of impact of internal integration score on patient survival before adjustment for patient: staff ratio and rural/urban suggests that internal integration has an impact on survival, but in these 31 clinics with a larger percentage of rural clinics, it has a significant effect only when HIV care was available at all primary care clinics thus improving patient to staff ratios.

These results also provide evidence that the integration of ART care into primary care services significantly improves survival of patients with CD4≤350 cells/μl and not yet on ART. On the other hand, the analysis shows that integration of pre-ART care is associated with improved survival only before adjustment for patient:staff ration and rural/urban clinic. The group of patients needing pre-ART care generally had higher CD4 counts and thus a lower mortality rate and differences in survival may have been more difficult to demonstrate. Alternatively, the intervention may have impacted survival in this group primarily by improving distance travelled and patient:staff ratios. It appears from these results that the integration of many elements of HIV care ranging from testing to issuing of monthly ART supplies is associated with improved survival and the most likely mechanism is by improving access to care.

There are several strengths to this study. It was able to quantify integration of different elements HIV care and the levels at which integration took place with a tool that has already been validated [38], in the setting of a randomized controlled trial. The trial monitored patient survival by linkage with the national death register. The outcome of almost all patients at the end of follow-up was ascertained, with only 6% of patients lost to follow-up and identity number not known. The main STRETCH trial results showed a significant difference in survival only in patients with CD4 between 200 and 350 cells/μl[29]. This study, however, was able to demonstrate that one of the interventions in the STRETCH trial, namely integration of HIV care into primary care clinics was associated with improved survival of patients with CD4≤350 cells/μL. This is a relevant finding given that ART is currently being integrated into primary care services in South Africa as part of the new national AIDS policy.

One limitation of this study is that, although it took place as part of a randomized controlled trial, the analysis of integration was done on individual clinic scores. Adjustments were done for the arm of the study and for patient and clinic characteristics known to affect patient survival however there may have been residual confounding factors that were not identified. Another limitation is the integration questionnaire assessed only the integration of service delivery of elements of HIV care at two levels of primary care and not the effects of integration of other areas of health system functioning such as monitoring and evaluation.

This study is an important contribution to evidence about outcomes of programs to implement integration of HIV care into primary care services, showing that integration of HIV care into primary care is associated with improved survival of HIV positive patients in need of ART. Given mixed evidence of the outcomes of integration of other health programmes[20] further research is needed into the effect of different models of integration in primary care. These results are also of practical importance to policy makers in high HIV-burden countries and suggest that both pre-ART and ART care should be provided as part of the package of care provided in all primary care services and efforts should be made to integrate HIV care into all consultations within primary care.

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Chapter 7

Integrating HIV care into nurse-led primary health care services in South Africa: a synthesis of three linked qualitative studies

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Integrating HIV care into nurse-led primary health care services in South Africa: a synthesis of three linked qualitative studies

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Abstract

Background: The integration of HIV care into primary care services is one of the strategies proposed to increase access to treatment for people living with HIV/AIDS in high HIV burden countries. However, how best to do this is poorly understood. This study documents different factors influencing models of integration within clinics.

Methods: Using methods based on the meta-ethnographic approach, we synthesised the findings from three qualitative studies of the factors that influenced integration of HIV care into all consultations in primary care. The studies were conducted amongst staff and patients in South Africa during a randomised trial of nurse initiation of antiretroviral therapy (ART) and integration of HIV care into primary care services – the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) trial. Themes from each study were identified and translated into each other to develop categories and sub-categories and then to inform higher level interpretations of the synthesised data.

Results: Clinics varied as to how HIV care was integrated. Existing administration systems, workload and support staff shortages tended to hinder integration. Nurses' wanted to be involved in providing HIV care and yet also expressed preferences for developing expertise in certain areas and for establishing good nurse patient relationships by specialising in certain services. Patients, in turn, were concerned about the stigma of separate HIV services and yet preferred to be seen by nurses with expertise in HIV care. These factors had conflicting effects on efforts to integrate HIV care.

Conclusion: Local clinic factors and nurse and patient preferences in relation to care delivery should be taken into account in programmes to integrate HIV care into primary care services. The integration of medical records, monitoring and reporting systems would support clinic based efforts to integrate HIV care into primary care services.

Keywords: Integration, HIV care, Primary health care, Nurse specialisation, Stigma

Background

Despite substantial international progress towards achieving universal access to antiretroviral therapy (ART) for people living with human immunodeficiency virus (HIV), it was estimated that, by the end of 2010, only 47% of the 14.2 million people eligible for ART were receiving it [1]. Strategies to improve access to ART in low and middle income countries with health system constraints include task-shifting [2] and community mobilisation [3,4] as well as integration of HIV care, including the provision of ART, into primary care services in ways that strengthen health systems [5,6].

The integration of HIV care into primary care services is also seen as an important strategy to provide coordinated care for HIV/AIDS and other related health needs such as tuberculosis (TB) [7,8] and sexual health [9] and to generally support the provision of holistic care and

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counter the fragmentation that characterises single disease programmes [10]. This is not unique to HIV care: there have also been calls to integrate sexual and reproductive health [11] and mental health care [12] into primary care services. The debate on the merits of integrated compared to single disease approaches to primary care (the so-called horizontal versus vertical approach) has continued for many years [13,14], yet there are still few clear recommendations on the extent of integration of services that is needed or useful in primary care. Although the concept may be intuitively appealing, there is a lack of strong evidence that integration of services leads to improved health outcomes and therefore a need exists for more studies on the effectiveness of integrated health programmes [15].

One of the reasons behind the lack of clear guidelines and evidence is that integration is a very broad concept. It has been defined as "a variety of managerial or operational changes to health systems to bring together inputs, delivery, management and organisation of particular service functions" [13]. It can involve various health system functions including governance, planning, financing, monitoring and evaluation and service delivery [16]. In practice, there is wide organisational variety across different health programmes internationally and very few are fully integrated in all of these areas of health system functioning [17]. Given the broad nature of integration, any studies of the outcomes of programmes to integrate health services need to document clearly the levels of health system functioning that are being integrated so that evidence of outcomes can be compared across different interventions [17].

A range of strategies have been described in the specific area of the integration of HIV care into primary care services in South Africa and other low and middle income countries. These strategies have included co-location of vertically run HIV services within the same facilities as primary care services [18]; co-provision of ART within home based directly observed TB treatment programmes [19]; down referral of patients stabilised on ART from hospital-based ART clinics to primary care clinics [20,21]; and the provision of outreach support to primary care clinics from existing ART sites [22]. Other programmes have described strategies to integrate HIV care into all primary care consultations, for example through staff training, standardised protocols, combined waiting areas and medical records, and the inclusion of HIV testing in triage [7,23]. These reports have not commented on the degree of integration achieved in primary care, particularly within clinics, or on the barriers and facilitators to integration of HIV care.

This article responds to the need to document interventions to integrate HIV care into primary care services, to record outcomes of these interventions and to provide analytical insights to inform both programme management and further theoretical development of the area. We report on factors perceived to influence the integration of HIV care into primary care services at the level of service delivery during a randomised controlled trial of strategies to improve access to ART in South Africa: the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) trial [24]. Lessons learnt in the area of integration of HIV care may be useful in informing broader questions regarding the integration of programmes into service delivery in primary care.

Context: the Free State ART programme and the STRETCH trial

The Free State province of South Africa has an estimated HIV prevalence of 18.5% amongst 15–49 year olds [25]. The public sector ART rollout commenced in 2004 with a vertical approach to the delivery of HIV care. Patients diagnosed as HIV positive in primary care clinics were referred to ART nurses in ART assessment sites located within certain existing provincial primary care clinics for all further HIV care. Patients not yet eligible for ART were seen at 6–12 month intervals at these assessment sites for CD4 counts, staging and TB screening. Patients eligible for ART (CD4 < 200 or Stage 4 AIDS) accessed drug readiness training, baseline blood tests and monthly ART supplies at these assessment sites, but were referred to accredited ART treatment sites within designated hospitals for doctors to initiate and repeat ART prescriptions. By mid-2007, 57 ART assessment and treatment sites were functioning [26] but less than a quarter of the primary care clinics in the province were able to offer on-site access to ART services. By mid 2008, only an estimated 25% of those needing ART were receiving it in the Free State and this was the lowest coverage in South Africa with national coverage estimated at 40% [27].

The STRETCH trial, a pragmatic, cluster randomised, controlled trial, was conducted in the Free State from 2007 to 2010, to assess strategies to improve access to ART. Thirty one ART assessment sites were randomised into 16 intervention and 15 control sites [24]. The trial comprised two main interventions: nurse initiation and repeat prescription of ART for adults with uncomplicated HIV; and integration of HIV care into primary care services. Two salient features of the implementation of the integration interventions were: the role of the trial manager (KU) as an agent of change, and the involvement of local clinic staff in the development and implementation of the integration intervention [28].

The integration intervention that was developed and the existing system for delivering HIV care are compared in Table 1. Three elements of pre-ART care – voluntary

Table 1 Roles of primary care clinics with and without ART assessment sites in the delivery of elements of HIV care before and during the STRETCH intervention

	Primary care clinics without accredited ART site	Primary care clinics with accredited ART assessment site functioning within the clinic
Organisation of HIV care before the STRETCH trial		
Delivery of pre-ART care (voluntary counselling and testing, initial CD4, 6–12 monthly HIV care) and ART care (baseline bloods, drug readiness training and monthly issuing of ARVs)	• Primary care nurses identify and refer HIV positive patients to ART nurses at their referral primary care clinic with an accredited ART assessment site	• Primary care nurses identify and refer HIV positive patients to ART nurses working within that clinic • ART nurses provide pre-ART and ART care for all patients referred from primary care services • All patients needing ART initiation and re-prescription referred by ART nurses to doctors at ART treatment sites
Organisation of HIV care during the STRETCH trial (intervention clinics and their referring primary care clinics only)		
Delivery of pre-ART care (voluntary counselling and testing, initial CD4, 6–12 monthly HIV care)	**"Mainstreaming pre-ART care"** • Primary care clinic enabled to provide pre-ART care to their own patients	**"Internal integration of pre-ART care'** • All professional nurses (ART and primary care nurses) at intervention clinic encouraged to provide pre-ART care as part of routine consultations
Delivery of ART care (baseline bloods, drug readiness training and monthly issuing of ARVs)	**"Mainstreaming ART care"** • Primary care clinic enabled to provide ART care to their own patients	**"Internal integration of ART care"** • All professional nurses (ART and primary care nurses) at intervention clinic encouraged to provide ART care as part of routine consultations
Initiation and re-prescription of ART during STRETCH intervention	• All patients needing an ART prescription referred to ART nurses at intervention clinic	• All professional nurses (ART and primary care nurses) at intervention ART sites trained and authorised to initiate and repeat ART prescriptions • Complicated patients referred to doctor at ART treatment site

counselling and testing (VCT); initial CD4 counts; and 6-monthly routine HIV care – as well as three elements of ART care – baseline blood tests; drug readiness training; and monthly supply of ARVs – were to be integrated into primary care services at two different levels. The first level was integrating pre-ART and ART care into the routine consultations of all nurses within the intervention clinics (internal integration). The second level was to enable other primary care clinics, which before the trial were referring all their HIV positive patients to intervention clinics, to provide pre-ART and ART care to their own patients (mainstreaming HIV care). During the trial, training in HIV care was being rolled out to all primary care nurses but training and authorisation for nurses to initiate and repeat six month prescriptions of ARVs was limited to nurses at intervention ART sites only.

An integration questionnaire was developed and administered at intervals at all the clinics involved in the STRETCH trial in order to assess progress of the integration intervention. This assessment showed that there was significant progress made in the mainstreaming of HIV care but no significant progress made with internal integration [29]. The factors that may have contributed to this unexpected lack of progress in internal integration within intervention clinics in the STRETCH trial are the focus of this article. We report a synthesis of the findings of three qualitative studies conducted in the Free State during the time period of the STRETCH trial. This synthesis was undertaken in order to capture a broad picture of the factors that may have impacted on the integration of HIV care into all consultations in primary care.

Methods

In this paper we synthesise the findings from three separate but linked qualitative studies. Two were conducted as a part of a process evaluation of the STRETCH trial (KU, DG) [30] and the third explored primary care experiences of integration of HIV care in several primary care clinics (AG) [31], some of which were part of the STRETCH trial. The studies led by DG and AG included interviews and focus group discussions conducted within clinics with patients and staff from all services not only the ART services. This data collection was in English for the majority of staff and in a local language, seSotho, for patients and some staff, using interpreters. Interviews and focus groups followed a semi-structured approach, with efforts to explore specific themes but also responding to issues raised by respondents. Interview recordings were transcribed and analysed thematically. KU and AG also

conducted semi-structured observations, focused on understanding clinic activity around patient care, and participated in clinic meetings and other everyday interactions with staff and patients. Each study addressed different but related research questions, and each provides a rich account of how the integration of HIV care was experienced and implemented in primary care within the context of the STRETCH trial. Table 2 outlines the different focus, methods and data collected for each study. Although each study was conducted separately, there were common institutional links through the University of Cape Town and the investigators discussed these studies regularly during their implementation.

Insights from the three studies were combined based on the meta-ethnographic approach to synthesising qualitative data from published studies by different researchers in different settings [32]. We did not adhere to all seven steps of the meta-ethnographic approach as originally set out by Noblit and Hare and cited by Britten et al [33,34]. The first three steps of getting started, identifying focus of interest and then identifying and reading relevant studies are suitable for the synthesis of data from published qualitative studies identified as part of a review. For this study, where the focus and studies were already identified at the start, we based our synthesis around the final four steps of this approach: 1) identifying relations between the studies, 2) translating them in to one another, 3) synthesising these translations into higher order interpretations and then, lastly, 4) communicating the findings [33]. We consider that our approach conformed to the original intention of the meta-ethnographic approach through preserving the relationships between concepts or themes identified by the primary studies while facilitating comparison across the studies.

The process began with initial, unstructured discussion amongst the authors regarding the key issues identified by each study and the extent to which it would be useful to attempt to synthesise the findings of the three studies. KU, DG and AG then held a structured meeting during which the primary (participant understanding) and secondary (researcher interpretation) themes from the individual studies were presented, and common categories across these themes were identified. These were iteratively refined through further discussion into comprehensive categories and sub-categories. Translating the studies into each other involved developing these categories, with detailed data from each study added and used to elucidate and elaborate these common categories. Table 3 gives an illustrative view of this process. The synthesis into higher order interpretations grounded in the findings of the individual studies – the focus of our discussion below– was developed iteratively through discussion and writing, using these categories and sub-categories as a starting point.

Results

We identified three major categories in our synthesis of the factors that influenced integration of HIV care into all consultations: health systems issues; the way nurses perceived their work; and the influence of patients themselves on service organisation. These themes were identified in all three studies. The sub-categories within these three major categories had complex impacts on efforts to

Table 2 Summary of the methodology used in the three qualitative studies

Study focus	Study approach	Data collection method relevant for this synthesis	Detail of data collection
Study 1: STRETCH trial – trial of intervention to integrate HIV care into PHC and task shifting of initiation and prescription of ART to nurses	Randomised controlled trial, with participant observation by trial manager (KU)	Participant observation	170 visits of approximately two hours each to 31 clinics, conducted over four years while managing the trial; notes of visits kept in a diary
Study 2: STRETCH process evaluation – the evaluation explored all aspects of the intervention (training, managerial issues etc.) including issues of HIV care integration	Mixed-method qualitative evaluation (led by DG with SL and CC)	Focus group discussions	10 focus groups with nurses 6 focus groups with patients
		In-depth and key Informant Interviews	26 interviews with facility managers, doctors, trial manager, local/district/ provincial health managers and key stakeholders
		Observation	7 observations of support workshops for nurse-trainers and trial manager support visits to clinics
Study 3: Qualitative study to understand the organisation of PHC, following the integration of HIV care and task shifting in PHC shifting.	Mixed-methods study, based on ethnographic principles (AG, supervised by SL)	Observation	Observation in 4 clinics, including 2 STRETCH trial clinics, over a 15 month period. Emerging themes were explored in an additional 6 clinics, including 3 STRETCH trial clinics.
		Interviews	Interviews with 34 professional nurses, 6 other members of clinic staff and 21 patients

Table 3 Illustration of the process of aggregating themes and developing common categories

Primary and secondary themes from the individual studies	Common categories identified and further developed through reciprocal translation	
Study 1	**Category**	**Sub-category**
At one clinic patients accessing HIV treatment were sent to one nurse who had access to computer based records for HIV care	Health systems influence on service integration	Administration requirements with medical records, files, registers and monthly reporting specific to different programmes influences service integration
A clinic that initially integrated ART care into the work of all nurses experienced problems with recording of TB statistics and had to revert to more vertical delivery of care so that one nurse could concentrate on care of TB patients and collection of TB statistics		
Study 2		
Multiple registers for each programme require huge amounts of paperwork, which is one of the reasons why it is easier to have vertical programmes so each nurse has a specialty and the register to fill in for that specific condition.		
Because of the lack of resources, vertical approach simplifies and streamlines the large patient load (especially administration).		
Study 3		
Administrative demands on nurses to report on care provided and computer systems that require specific training and skills can support the separation of care.		

integrate HIV care: some factors facilitated integration of HIV care, others hindered integration, while still others tended to promote instead a more specialised or vertical approach to delivery of HIV care. Furthermore some factors appeared to have both facilitating and hindering effects on integration, depending on the setting.

Health systems factors

Our findings suggested that a range of systems level factors hindered the integration of care at the primary care level. These factors included: the plethora of medical records, registers and monthly reports specific to each programme; the shortage of support personnel; and the infrastructure of many clinics with separate waiting areas and buildings for different services. The high workload in many clinics had complex effects on integration while the smaller size and staff complement of some clinics appeared to promote integration of care.

Administrative and reporting requirements

The administrative work required of clinic staff tended to reinforce the existing organisation of care and thus to hinder integration in a number of ways. For example, some programmes had specific forms for each consultation to ensure that important clinical information was elicited and recorded within the patient's general file. In many clinics there were also separate medical files for HIV and other chronic diseases. In addition, many programmes had their own register in which the numbers of patients seen had to be recorded. These programme specific records tended to hinder efforts to integrate HIV care into all consultations within a clinic. For example in one clinic with many TB patients the former "TB nurse" struggled to cope with the addition of ART care on top of conducting the clinic's TB data collection and statistical reporting. The clinic manager therefore decided to revert to the system of ART patients accessing care only from ART nurses. In another clinic, nurses in the ART programme had, in theory, access to a computer to directly enter consultation details for ART patients. However, only one consultation room had a computer and other nurses had to send all HIV positive patients to the ART nurse in that room for their consultation details to be captured. However, separate administrative processes and structures did not always hinder integration. In one large clinic patients collected ART files from a separate reception area because the main reception was too small yet they accessed care from any nurse as the nurses in that clinic had decided they would all be involved in all HIV care.

Staff shortages hindered integration

The shifting of clinical tasks to nurses requires adjustments in the roles of other supporting staff, such as pharmacists. Within the context of the STRETCH trial, a shortage of support staff tended to hinder the integration of HIV care. For example, provincial regulations at the time limited ART dispensing to pharmacists only. In clinics where there was no pharmacist, ARVs were dispensed monthly by hospital pharmacists and sent in patient-named packets to the clinics. Where there were, in addition, no pharmacy assistants at the clinic to issue these packets from the dispensary, nurses often responded

by storing all the packets in one consultation room and having one nurse see, and issue drugs for, all patients on ART.

Physical infrastructure of clinics

The structure of clinics and the amount of space available also affected integration. Partly because of the history of separate service provision under different health programmes, a number of clinics had been built initially with different sections or had had extra sections built later, each with consulting and waiting rooms. Different programmes were allocated to separate sections and it was then difficult to integrate care. One STRETCH clinic, for instance, had two distinct parts within the building, each with separate waiting areas. Nurses referred to these as the 'ART side' and the 'mainstream side'.

Some clinics had been provided with prefabricated structures by the ART programme or by donors to increase the number of consulting and waiting rooms available. This also hindered integration as it was easier to locate specific programmes, usually the ART services, in these prefabricated structures. Nurses were, however, aware of the stigma of locating ART services in these separate buildings. In one PHC clinic that was due to start providing ART and had received a prefabricated structure to provide more space, the clinic manager did not want to locate only ART services there for this reason. However, the presence of adequate physical infrastructure was not sufficient on its own to ensure integration. For example, there were a number of clinics with one large waiting area where integration of care did not take place because of other factors, such as nurses preferring to specialise or attempting to cope with large workloads by task allocation (as discussed below).

High nurse workload

The high workload of nurses in most of the clinics had complex effects on integration. In some cases, workload hindered integration because nurses felt unable to spend sufficient time with patients to provide comprehensive care. Nurses reported they did not have time to provide comprehensive care in all consultations. Although workloads varied, nurses were under pressure to achieve a quota of having 40 patient consultations per day. This led to a general pressure to work quickly and address only a limited number of issues in any one consultation. Many nurses were troubled by this, saying they knew they were not providing quality care and were not always able to integrate HIV care into their consultations.

Another strategy adopted by many clinics with large patient numbers, was to allocate specific tasks to one nurse in order to streamline the work. In some clinics, all patients who needed TB investigations were sent to one nurse for sputum collection, partly for reasons of infection control, but also to save time and ensure that one nurse could be responsible for collating results. In another clinic, with a large number of patients on ART, all patients needing routine blood tests were sent to one nurse on arrival at the clinic so that all bloods would be ready for collection before the arrival of the laboratory transport officer.

Nurses also reported that HIV positive patients had more potential illnesses, side effects and emotional aspects to consider and thus required longer and more complicated consultations than for other chronic diseases. This affected their willingness to provide integrated care. Some nurses were willing to be involved in it while others found it too overwhelming.

In other cases, nurses responded differently to the pressure of workload. At one clinic, the high workload of patients needing ART care had prompted all nurses to want to respond to their patients' suffering. As a team, the nurses decided to reorganise delivery of care so that patients could access all HIV care from any nurse in that clinic. In another clinic, an ART nurse said that the high patient load meant she no longer had time to do all VCT and so all of the other nurses had become involved in VCT as well.

Clinic size

Large clinics with a large number of nurses tended to provide separate care under different programmes. The reasons underlying this were that, in most large clinics nurses would be allocated to one programme and be responsible for clinical care, reports and monthly statistics. Nurses could rotate through different programmes and gain comprehensive experience, but even so they tended to specialise in one programme and remain with that programme for extended periods of time. The possible extent of this separation is clear in one large clinic which had a "fast lane" for ART patients to go straight to the two ART nurses, without stopping at the clerks for their patient files. All other patients however could see any of the nurses for VCT and care before being referred to ART nurse for ARVs. However, large clinics did not always provide care separated into different programmes. One large clinic with 13 nurses provided fully integrated care. Patient files were uniform, there was one reception area and filing room, all waiting areas were integrated and patients were able to access any care from any nurse. This was reported to be due to the strong commitment of the clinic manager to integrated services.

In contrast, in clinics with only two or three nurses, each nurse had to be experienced in and responsible on a daily basis for caring for patients with health issues that spanned a number of programmes. In two clinics, each staffed by three professional nurses, patients could access integrated care from any nurse as there were

many days when only two nurses were present due to training, meetings or leave. In other small clinics, however, not all consultations were fully integrated despite nurses having experience in all programmes. In one clinic, with three nurses, two of the nurses referred patients who needed HIV testing or care to the ART nurse, reportedly because these nurses did not speak the same language as many of their patients and did not feel they could provide HIV care to their patients.

Nurses' and managers' beliefs and attitudes

Nurses often had a passion for developing specialist expertise in one area of care and also understood the importance of developing good nurse–patient relationships. Both of these factors tended to favour the separation of services by health condition (TB, HIV/AIDS) rather than integrated care. Nurse managers had mixed attitudes towards the integration of HIV care and this impacted significantly on efforts to integrate HIV care in their clinics.

Nurses' preferences for particular programmes

Across primary care, nurses expressed a preference for working on a particular service or programme. They described this as an 'interest' or 'passion' for this service, such as TB, child or HIV care. This passion for a particular service tended to promote separate rather than integrated provision of HIV care:

> I was saying that if people are not made to do this ARV thing comprehensively ... because some of the people have got passion ... like some of the sisters had passion for ARV, and the way they are with their clients you would say these people are friends. But when they were made to do child health some of them decided, no, I'm leaving this because I wanted to do this [ARV care]. This is my passion (STRETCH Nurse).

Although this desire to focus on a particular service was evident across primary care, there were also factors specific to HIV care. Providing HIV care, and ART in particular, often brought prestige and status to nurses. These nurses enjoyed being recognised by their community, with one clinic manager commenting that having ART in the clinic led to the community perceiving them as better nurses. In some cases, their colleagues felt that the prestige given to ART nurses, as well as their emotional attachment to ART care, made them reluctant to let other primary care nurses become involved. This issue led to sharp disagreement in one clinic between the ART and primary care nurses when HIV care was integrated into primary care services.

Some nurses noted that they did not have an interest in providing ART care. The commonest reasons for this were either that they would rather specialise in other areas of care or that they lacked the clinical confidence to provide ART care. This was related to the perceived complexity of providing ART and of delivering VCT. Similarly, ART nurses in some clinics raised concerns regarding whether all primary care nurses would be able to respond to this complexity and provide the same quality of care as they were able to. In a few clinics nurses reported that some of their colleagues did not want to provide ART care because they were afraid of HIV and stigmatised people living with this condition.

The effects of nurses' desire to specialise were offset in some clinics by a broad based enthusiasm to be involved HIV care provision which, in turn, tended to promote more integrated care. For example, in some clinics all of the primary care nurses wanted to gain experience in ART care as part of their professional development. In one clinic, nurses described personal motivations for providing HIV care. Because HIV had impacted the lives of friends or family, they wanted to help alleviate the suffering that they saw in their community. In this clinic all nurses provided ART care and it was integrated into all consultations.

Nurse–patient relationships and continuity of care

Some nurses felt that it was easier to establish and maintain good nurse–patient relationships in settings where nurses were allocated to a particular programme rather than to a fully integrated service, in which patients were seen by any nurse. This concern for relationships with patients was expressed not only in relation to HIV care but also for other illnesses. Some nurses argued that external managers who had decided that services must be integrated did not appreciate the potential benefits of separate programmes in promoting what nurses perceived as good relationships with patients. In a health system that does not support patients choosing which nurse they would like to see, nurse specialisation does allow patients to see the same nurse over a period of time, and therefore to develop a relationship with that nurse and benefit from continuity of care.

Attitudes of clinic managers towards integration

How clinic based nurse managers and local area managers, who had oversight of more than one clinic, exercised their leadership also influenced the implementation of integration. Their views and preferences influenced integration, but this was also modulated by individual nurse preferences and administrative factors that characterised the vertical ART rollout.

In one large clinic, the manager was strongly supportive of integration of care within all consultations. Despite concerns raised by some staff members about the competence of all nurses in providing HIV care, patients

in this clinic could access HIV care with any nurse in any consultation. In another clinic, a manager reported that, in order to implement her preference that HIV care be integrated into all consultations, she had to address significant resistance from some clinic nurses. One local area manager who supported integrated care explained some of the administrative obstacles:

> ...ARVs being handled like any other chronic disease. It must not be a special thing with special prescriptions and programmes on the computer, with special [ART] files and forms and those kinds of things. I want it handled like hypertension and diabetes (Local area manager).

Other managers were not supportive of full integration of HIV care into every consultation. One manager in an ART STRETCH clinic felt that it was beneficial for nurses to have a specialised focus in one area of primary care. Another clinic manager was not confident in providing HIV care herself and was not willing to integrate HIV care into all her consultations.

Patient preferences regarding delivery of care

Patient preferences had conflicting influences on the integration of HIV care. Patients preferred to receive services from a nurse with expertise in HIV care, and whom they knew and trusted. However, they also had concerns about the stigma of accessing HIV care in separate services.

Nurse–patient relationships

Patients preferred to be seen by a particular nurse either because they had established a relationship with that nurse or because they perceived the nurse to have developed expertise in ART care. This created pressure for separate care rather than integrated care:

> Again we want to have our own nurse. Sometimes we experience personal problems that we would like to discuss with our nurse but it is not easy if today you are seen by this one and next time is that one (Patient).

One group of patients reported concern when 'their' ART nurse left and they were moved from the ART side of the clinic and asked to wait with other patients and be seen by other nurses. They felt that these other nurses needed more training and did not have the same level of expertise as their ART nurse. Many ART patients were, or had been, very ill and were therefore reluctant to be seen by nurses other than the nurse they knew well and trusted. In one clinic, patients reportedly preferred waiting in their own area to see the ART nurse as this allowed them to share information with other patients on ART and to prevent other patients from pushing in. In one ART STRETCH clinic, nurses reported that ART patients had resisted efforts to integrate services by continuing to visit "their nurse".

The stigma of separate HIV services

Despite patients' desire to see a nurse with experience in ART care, they were also concerned about the stigma of accessing care through a specialised service. Many patients disliked the stigma of being identified in their community as 'ART patients' through their use of a separate section of the clinic, and through having their 'own' nurses. They claimed that they felt less HIV-related stigma when they were called from the main waiting room like any other patient. Even so, they continued to express a preference for seeing the nurse with whom they were familiar:

> We don't have a problem waiting with everyone but we want our files separated and our nurse should just call our names and we go to our specific room" (Patient).

Similarly, nurses in a number of clinics expressed concern that some patients resisted accessing treatment delivered through specialized HIV and ART nurses or specific waiting areas because of their fear of stigma. Nurses at one clinic reported that the number of patients tested for HIV increased markedly when all nurses were involved in providing HIV testing as well as other HIV care. Another ART clinic reportedly received increasing numbers of patients when they changed from having a separate ART waiting area to an integrated waiting area.

Discussion and conclusion

This synthesis of findings has identified three main categories of factors that affect efforts to integrate HIV care into primary care services. These are the characteristics of the health system itself; nurses' and managers' preferences regarding how to deliver care; and patients' preferences for how they would like to receive care. Factors hindering the integration of HIV care into all consultations included the existing organisation of clinical records and reporting; high workloads and shortages of support staff; and the structure and organisation of existing clinic buildings. Factors that promoted the delivery of HIV care as a separate programme included nurses' preferences to develop expertise and specialise in particular areas of care as well as the value that nurses and patients placed on nurse–patient relationships. On the other hand, factors that promoted the integration of HIV care into all consultations included: a widespread

concern amongst nurses to become involved in dealing with the HIV pandemic; and nurse and patient concerns about the stigma of separate HIV services.

Our findings show that even when efforts are made to integrate HIV care, the complex interaction of these three factors results in a variety of models of delivery of HIV care depending on local context –such as clinic size. These models varied on a spectrum from a fully integrated service, where patients accessed HIV care from any nurse, to a more separate delivery of care, with patients accessing care from an ART nurse. This variability in the outcome of efforts to integrate HIV care during the STRETCH trial –a complex intervention of task shifting – may have been one of the contributorsx to a lack of significant improvement at intervention clinics in survival of patients needing ART [35]. A quantitative study of integration conducted during the trial showed that patient survival was significantly improved in clinics with high integration scores [36].

These findings also suggest that as long as nurses are expected to manage high numbers of patients each day in primary care, HIV care is unlikely to be successfully integrated into service delivery. This finding is especially critical in countries like South Africa where criteria for ART eligibility have been widened and large numbers of people are now eligible for ART. Attention therefore needs to be given to the adequate resourcing and staffing of primary care services. A recent technical brief on integrated care from the WHO argues clearly that integrated care is not a solution to a shortage of health care workers [37]. Attention also needs to be paid to other areas of health system functioning [16,17]. The integration of HIV care into the governance, finance and planning of services would ensure that adequate staffing levels, and even new clinic design and the renovation of clinics, are planned and financed adequately and are aimed at the support of integrated service delivery. Full integration of administration, monitoring and evaluation of different programmes may not be possible or even desirable. However, serious efforts need to be made to have clear policies on the integration of services [38], to simplify and integrate patient records and registers and to provide supervision of and training in integrated care to support primary care nurses [7]. If these other areas of health system functioning are not coordinated in order to support integrated service delivery, nurses will continue to be frustrated in their attempts to provide integrated care.

It is also apparent from these findings that the model of integration of HIV care into primary care that is most preferred by patients and nurses may not always be the full integration of HIV care into all consultations. Some degree of specialisation of nurses, where they can be well trained and develop expertise may be desirable and this has been noted in a recent study of the barriers to integration of sexual and reproductive health services [38]. Both patients and nurses expressed their appreciation of the opportunity for nurses to develop expertise and specialise in certain areas of care, and noted the benefits of this for promoting nurse–patient relationships. Even where nurses and patients expressed concern about the stigma of separate HIV services, there was a certain tension with the wish to be seen by nurses with expertise and with whom they were familiar. A recent systematic review of the outcomes of integration of services into primary care noted evidence that integration of some services can lead to decreased utilisation and the need for studies of outcomes to document patient views of the desirability of integration [15]. The recent WHO technical brief on integration also comments that integration does not mean all services must be provided in one package but is rather about delivering the 'right care' in the 'right place', which is easy to access and achieves the desired results [37].

It may also be that the 'best model' for delivering HIV care in primary care varies according to local circumstances. This synthesis showed that the spectrum of integration within clinics in the STRETCH trial and the models of care that developed were at least in part influenced by the preferences of local staff, patients and managers. While this study does not assess the impacts of different models of integration of HIV care on patient outcomes, it does suggest that such integration is a process that takes time, needs support and needs to be responsive and adaptable to local conditions. The process evaluation of the STRETCH intervention also noted the positive impact of local support teams and external facilitators and the importance of mentoring in supporting task shifting [30].

The meta-ethnographic approach used in this study has allowed us to integrate findings from multiple studies and bring depth of insight to a number of issues surrounding the integration of HIV care into primary care services. Additional advantages of our approach are the team's deep knowledge of the study setting and their access to the full datasets for the studies, rather than the published papers only. One example of the usefulness of this rich dataset is that many of the factors identified had complex and even conflicting effects on integration in different contexts – these nuances may not have been identified through a review of less detailed data available from published papers. Although this study focussed on integration of HIV care, some of the findings are similar to those of a study on integration of sexual and reproductive health services in South African publicly funded clinics [38], and so are likely to be generalizable to other areas of integration in service delivery. One of the limitations is that the studies were not

designed together and methods and theoretical frameworks differed. Another potential limitation is that the nature of participant observations is that they may have been affected by the researchers involvement in the trial.

Based on our conclusions, we make three recommendations: firstly, the design, implementation and management of service integration should engage with and account for local variability and the active influence of nurses and patients, through closer, more dynamic approaches to management. Secondly, future research should explore which configurations of integration are best suited to different settings and should in particular explore patient and nurse preferences for integrated versus separate services, and how nurse–patient relationships can be maintained and supported within different models of care. Thirdly, the integration of management, administration, financing, planning and monitoring systems may help to support efforts to tailor the integration of HIV care into primary care at clinic level and further work in this area is needed.

Ethical approval

Permission to conduct these studies was obtained from the Head of the Free State Department of Health. Ethical approval of the protocols of these studies was obtained from the Human Research Ethics Committees of the London School of Hygiene and Tropical Medicine and the Faculty of Health Sciences of the University of Cape Town and the University of the Free State.

Abbreviations

AIDS: Acquired immune deficiency syndrome; ART: Antiretroviral therapy; ARVs: Antiretrovirals; HIV: Human immunodeficiency syndrome; TB: Tuberculosis; VCT: Voluntary counselling and testing; STRETCH: Streamlining tasks and roles to expand treatment and care for HIV.

Competing interests

The authors declare they have no competing interests.

Authors' contributions

KU was involved in developing the initial concept, data collection and synthesis and writing the manuscript. DG and AG were involved in developing the initial concept, data collection, analysis and synthesis and writing the manuscript. SL and CC were involved in the initial concept, data collection and analysis and reviewing the manuscript. All authors read and approved the final manuscript.

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Chapter 8

Main findings, conclusions and recommendations

1. The study in retrospect

There are three main justifications for both the STRETCH study and the focus on integration in this doctoral research. The first is the international emphasis on finding appropriate models to broaden the provision of HIV care in high-burden countries – such as those in southern Africa – in order to promote universal access to ART in ways that strengthen general health care systems. The second is the call for randomised controlled trials to determine whether there is any evidence that integration of HIV care into primary care services improves patient outcomes. The third is the need to describe the impact of strategies to integrate HIV care on clinic function at the primary care level.

This doctoral research, as well as the STRETCH study, attempted to supply answers to these three questions. Firstly, a review of the Free State public-sector ART programme highlighted the background for the STRETCH study – a pragmatic randomised controlled trial of task-shifting and integration of HIV care into primary care conducted in an effort to improve survival of people needing ART by improving access to care. Secondly, a detailed study was conducted of the development of the integration and task-shifting interventions in the STRETCH trial while a tool was developed and used to monitor the progress of integration during the trial. Thirdly, studies were conducted to determine the impact of integration on patient survival as well as on primary care services at the clinic level.

2. Main findings

2.1 Documenting the context of the study on integration

A retrospective review of achievements in the first four years (2004-2007) of the Free State public-sector ART programme showed increasing numbers of patients accessing ART, as well as increasing enrolment CD4 counts, suggesting that the programme was making significant inroads into the numbers of people needing ART. However it also confirmed the

limitations and constraints ascribed to vertical delivery of HIV in high-burden countries. Access to ART still remained low – by 2007, only 25% of those estimated to need ART in the Free State in that year had commenced on treatment – and patients in the Free State with CD4 counts ≤ 350 cells/μl and not yet on ART showed a 12 month mortality rate of 53% [1]. The ART programme was also draining staff from general health services while stringencies in national funding were becoming apparent. Two year projections showed that by 2009, even if staffing and funding allowed further expansion of the vertically implemented ART programme, only 39% of patients estimated to need ART in the Free State would be able to access such treatment.

The STRETCH trial was implemented in the Free State in response to this urgent need to accelerate access to ART in the face of a shortage of doctors which was one of the factors that constrained further expansion of the ART programme. This complex intervention which combined task shifting and integration of HIV care into primary care services was conducted in the setting of a public ART programme with real constraints including the shortage of doctors, nurses and other support staff and problems pertaining to resources. The pragmatic nature of the trial was illustrated by a three-month moratorium on new ART initiations imposed province-wide in the middle of the trial due to a shortage of ARV drugs resulting from a shortfall in national funding of the ART programme [2].

The main outcome of the STRETCH trial, determining patient survival, showed no significant difference between intervention and control clinics in survival of patients in Cohort 1 (CD4 ≤350 cells/μl and not yet on ART). This may have been due to a combination of factors, including: the time it took for nurses to develop confidence in initiating patients on ART; the appointment of more doctors to control clinics during the trial than to intervention clinics thus improving access to ART in control clinics; a three-month moratorium midway through the trial on initiating adults on ART; and the number of new ART clinics opened by the Free State Department of Health which would have decreased workload at all the clinics in the study. There was however a significant increase in survival in patients with CD4 counts between 200 and 350 cells/μl at intervention compared to control clinics, which may reflect that nurses were more confident to initiate ART in these relatively healthier patients when their CD4 did go below 200 cells/μl.

A process evaluation of the STRETCH trial found that nurses supported the interventions and were enthusiastic about being able to provide full HIV care including ART to patients in all

primary care services [3]. The nurses found the guidelines and training useful, although various constraints – such as workload, lack of supporting staff, problems with supply of ARVs at clinic level and insufficient mentoring support in some clinics – resulted in difficulties in some clinics and delays in fully implementing the intervention [3].

2.2 Developing and monitoring the integration intervention

The **first objective** of this study focussing on integration, was to develop and implement a practical strategy to integrate HIV care into primary care services as part of the STRETCH trial. The strategy developed was to integrate six elements of HIV care, namely: voluntary testing and counselling; initial CD4 counts; routine HIV care; baseline blood tests; drug readiness training; and monthly ART provision. These were to be integrated in a flexible, progressive manner both into the work of all primary care nurses in the intervention clinics and also into the work of primary care clinics referring patients to the intervention clinics.
In order to implement this strategy three important processes of change were employed during the trial.

The first process was participatory action research –a process of including staff in developing and implementing interventions that has been identified as an important change mechanism in any complex health intervention [4]. Staff members were involved at various levels. Senior management in the health department identified the need for an intervention and invited the researchers to conduct the trial. Managers at provincial and district levels and from the 31 trial clinics were involved in developing and implementing the intervention. Integration of HIV care into primary care was implemented specifically by clinic based teams and local management teams at a pace and in a manner responsive to local conditions, such as training needs, capacity of local facilities and staffing. Such tailoring of interventions and the incorporation of flexibility responsive to local conditions are thought to be important to delivering complex interventions which are both implementable and relevant to local needs [5, 6].

The second change process employed in the trial was educational outreach and was used to conduct training at both primary care clinics and in the intervention clinics in order to support nurses who provide basic HIV care as well as nurses initiating ART at the intervention clinics. This educational method has been shown to change nurse practice and improve patient outcomes [7].

The third change process was the work of an external facilitator acting as an agent of change during the trial. The author (KU) in her capacity as a member of the research team – yet based in the Department of Health – was able to function as a supporter of nurse training and of clinic and management teams, a facilitator of communication between clinics, management and researchers, a clinical advisor, and a problem solver. These varied roles have been acknowledged as important in the implementation of complex interventions [8].

The **second objective** of the study was to monitor the progress made in integration of HIV care into primary care services during the STRETCH trial. A new semi-quantitative questionnaire was developed, validated and used to document the progress in integration of HIV care during the trial. This questionnaire may also be useful in other settings to assess and monitor the integration of elements of HIV care into primary care services. The questionnaire was also able to document different aspects of integration with a total integration score as well as pre-ART and ART integration scores, mainstreaming HIV scores and internal integration scores. The results of monitoring showed that midway through the trial there had been significant increases in mean total integration, ART integration and mainstreaming HIV scores at intervention clinics in comparison with the control clinics. Mean pre-ART integration scores at intervention and control clinics were nearly at maximum at the first assessment and could therefore show no further significant increase, but mean internal integration scores showed no significant increases over the period of the trial.

2.3 Determining the impact of integration

The **third objective** of the study was to determine whether the integration of HIV care into primary care services during the STRETCH was associated with improved survival of patients in Cohort 1 (CD4≤350 cells/μl and not yet on ART). Cox proportional hazards analyses were conducted considering the impact of the clinic integration scores at the first assessment early in the trial on the subsequent survival of all patients in Cohort 1. These analyses were adjusted for patient and clinic characteristics known to have an impact on patient survival. It was found that there was a significant improvement in patient survival in clinics with high total integration scores. Patient survival was significantly improved in clinics with high pre-ART and ART integration scores demonstrating that integration of all elements of HIV care improved survival. Analysis also showed that both providing HIV care in primary care clinics (mainstreaming HIV) and integrating HIV care into all consultations within clinics (internal integration) improved survival, and in addition, that this may have

been mediated by and dependent on improvement in patient: staff ratios. Thus, although the main trial results failed to demonstrate that the STRETCH intervention significantly improved survival in the whole cohort, integration of HIV care did significantly improve survival of patients with CD4 < 350 cells/μl and not yet on ART.

The **fourth objective** of the study was to monitor the impact, at clinic level, of efforts to integrate HIV care into primary care. This is a very broad topic, and this study was not able to do a comprehensive evaluation of the impact of integration of HIV care on primary care services; it rather concentrated on one area – the barriers and facilitators to providing fully integrated HIV care within all nurse consultations. A meta-ethnographic approach was used to synthesise data from three related qualitative studies. It appeared that three major factors influenced integration of HIV care into all consultations: health system factors, nurse preferences and patient preferences for how care is delivered. Lack of integration of medical records, registers and monthly reporting, as well as heavy staff workloads at clinics are health system factors that tend to reinforce vertical approaches to delivering care. Similarly, nurse preferences to develop expertise in specific programmes as well as patient preferences to be seen by a nurse experienced in HIV care and whom they know well, also tended to promote specialisation amongst nurses, rather than a model of care where patients go to any nurse for HIV care. On the other hand, in some clinics the large number of patients needing HIV care prompted all nurses to want to develop expertise and provide HIV care; this, along with the stigma that patients experienced in accessing HIV care from ART nurses, prompted nurses and patients to promote the integration of HIV care into all consultations. These findings reinforce the calls for a pragmatic and flexible, rather than a rigid approach to integrated health services with the view to providing services that are user-friendly, easy to navigate and responsive to the expressed needs of both patients and staff – that is the development of service models that result in the "right care" in the "right place" [9].

3. Limitations of the study and areas for further research

The integration tool was developed and validated in the specific context of the ART programme in the Free State Province. It has the potential to be used as a tool for monitoring integration in other settings with a high burden of HIV disease as well, but may need to be adapted to other local contexts. Specifically the tool did not assess the integration of initiation and monitoring of ART into primary care services as this was still an experimental intervention limited only to intervention sites during the STRETCH trial. Given that initiation

and monitoring of ART by professional nurses in all primary care facilities is now part of national policy in South Africa [10], and is also part of many task shifting interventions in other Southern African countries, the tool would need to be adapted to include this element of ART care.

Although the current study on the impact of integration on patient survival was conducted as part of a randomised controlled trial, the analysis of the effect of integration was conducted on individual clinic integration scores. The finding that increased integration is associated with improved patient survival is an important finding, however, it does not prove causation. Although adjustment was done for other factors known to affect patient survival, there may have been other residual confounding factors. More research is needed to confirm the finding that integration does lead to improved patient survival.

The findings that the strategies used in the trial did not lead to increased integration of HIV care into all nurse consultations within the intervention clinics may reflect that the strategies used in the STRETCH trial did not adequately address health system barriers to integration, such as the multiplicity of forms and registers. However, the findings from the synthesis of qualitative data do suggest that there may be advantages for both staff and patients in some degree of specialisation amongst nurses in primary care. More research is needed on the best models of providing integrated HIV care at the clinic level, looking at ways to integrate management, administration and monitoring of health systems, as well as models of care that take into account nurse and patient preferences for good quality care to be delivered by nurses with expertise.

4. Recommendations

In the move towards universal coverage for people living with HIV, health programmes in countries with high HIV burdens need to firstly integrate HIV care into primary care services by providing all elements of HIV care at all primary care facilities and secondly investigate models of integrating HIV care into all primary care consultations. This would improve access to care and survival for people needing treatment for HIV, but only if efforts to integrate HIV care into primary care are accompanied by the following strategies:

Firstly, local management and clinic staff should be involved in programmes to integrate HIV care into primary care so as to develop a strategy that is flexible, implementable and relevant to local needs.

Secondly, training in the management and treatment of patients with HIV and clinical support should be available to all nurses working in primary care facilities.

Thirdly, attention needs to be given to integration of management, administration and monitoring and evaluation and medical records used in primary health care.

Fourthly, attention needs to be paid to adequate staffing and support of primary care facilities.

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Appendices

Appendix A

STRETCH trial protocol
Fairall LR, Bachmann MO, Zwarenstein M, Lombard C, Uebel K, Van Vuuren C, Steyn D, Boulle A, Bateman E. Streamlining tasks and roles to expand treatment and care for HIV; randomised trial protocol. *Trials* 2008, 9:21

Appendix B

STRETCH protocol guidelines for nurse initiation and monitoring patients on ART (ART algorithms)
Referred to in the article presented in Chapter 4 as Additional file 1.

Appendix C

STRETCH Toolkit
Referred to in the article presented in Chapter 4 as Additional file 2.

Appendix D

Protocol for sub-study on integration
As submitted to the Ethics Committee of the Faculty of Health Sciences, University of the Free State.

Appendix E

Integration questionnaire
Referred to in the article presented in Chapter 5 as Additional file 1 and in the article presented in Chapter 6 as Supplemental digital content 1.

Appendix F

Information sheet for Integration questionnaire

Appendix G

Consent form for Integration questionnaire

Appendix H

Copy of letter from the Ethics Committee, Faculty of Health Sciences, University of the Free State granting ethical permission to conduct the STRETCH trial

Appendix I

Copy of letter from the Head of the Free State Department of Health granting permission to conduct the sub-study on integration

Appendix J

Copy of letter from the Ethics Committee, Faculty of Health Sciences, University of the Free State granting ethical permission to conduct the sub-study on integration as an addendum to the STRETCH trial

Appendix A

STRETCH trial protocol

Fairall LR, Bachmann MO, Zwarenstein M, Lombard C, Uebel K, Van Vuuren C, Steyn D, Boulle A, Bateman E. Streamlining tasks and roles to expand treatment and care for HIV; randomised trial protocol. *Trials* 2008, 9:21

Trials

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Study protocol

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Streamlining tasks and roles to expand treatment and care for HIV: randomised controlled trial protocol

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Abstract

Background: A major barrier to accessing free government-provided antiretroviral treatment (ART) in South Africa is the shortage of suitably skilled health professionals. Current South African guidelines recommend that only doctors should prescribe ART, even though most primary care is provided by nurses. We have developed an effective method of educational outreach to primary care nurses in South Africa. Evidence is needed as to whether primary care nurses, with suitable training and managerial support, can initiate and continue to prescribe and monitor ART in the majority of ART-eligible adults.

Methods/design: This is a protocol for a pragmatic cluster randomised trial to evaluate the effectiveness of a complex intervention based on and supporting nurse-led antiretroviral treatment (ART) for South African patients with HIV/AIDS, compared to current practice in which doctors are responsible for initiating ART and continuing prescribing. We will randomly allocate 31 primary care clinics in the Free State province to nurse-led or doctor-led ART. Two groups of patients aged 16 years and over will be included: a) 7400 registering with the programme with CD4 counts of ? 350 cells/mL (mainly to evaluate treatment initiation) and b) 4900 already receiving ART (to evaluate ongoing treatment and monitoring). The primary outcomes will be time to death (in the first group) and viral suppression (in the second group). Patients' survival, viral load and health status indicators will be measured at least 6-monthly for at least one year and up to 2 years, using an existing province-wide clinical database linked to the national death register.

Trial registration: Controlled Clinical Trials ISRCTN46836853

Background

South African government health services started in 2004 to provide free ART to HIV-infected patients with CD4 counts ? 200 cells/μl or stage 4 AIDS, but by 2007 only a third of patients who need ART were receiving it [1]. Coverage is even lower in many other African and Asian countries [1]. The major bottleneck is due to reliance on doctors to prescribe ART, including starting treatment. Doctors are generally only available in hospitals and large urban health centres, whereas most public sector primary care clinics are staffed by nurses. Therefore better use of nurses is a compelling way to expand access and avoid delays in starting treatment. We urgently need to know whether most patients with HIV/AIDS can start and continue ART without doctors' involvement. If so, they could start treatment earlier, and thus avoid disease progression and death.

At present in South Africa only doctors may prescribe ART, in keeping with national guidelines. In the Free State province, where this trial is located, doctors initiate ART and repeat prescriptions when reviewing patients 6-monthly, with monthly visits to nurses in between. It is still widely assumed that ART is too difficult and risky to be entrusted to nurses because of drug side effects and resistance. But many eligible patients continue to die because of delays in starting ART. Our evaluation of the Free State province's ART programme to December 2005 found that, of 4570 patients followed for one year or until death, 53% died, 87% of them before they started ART [2]. However when ART was received it reduced mortality by 87%, during up to 19 months of follow up. Most patients with advanced HIV/AIDS have no contra-indications to ART, and can be managed by first line ART regimes (stavudine, lamivudine and efavirenz, or stavudine, lamivudine and nevirapine). It is thus likely that, with appropriate training and support, nurses can manage most patients effectively, leaving doctors to manage the minority at high risk or with complications.

We believe there is equipoise about whether a nurse-led system, based in primary care and with educational and managerial support, can be as effective as the current doctor-led system. On the one hand, nurses have less medical expertise than doctors and so may provide inferior care. On the other hand, if they can start treatment earlier they will probably obtain better outcomes.

A Cochrane review identified 16 randomised trials comparing primary care provided by doctors and nurses in other contexts and found that nurses could manage general medical conditions, including chronic diseases and cardiovascular risk factors, as effectively as doctors can [3]. However nurses were generally not more cost effective, because of lengthier consultations, more tests, and costs of medical supervision. None of these trials evaluated AIDS care, which is potentially more complex and risky than the types of care investigated by these trials. A Cochrane review on organisation and delivery of HIV/AIDS care highlighted the absence of trial evidence from developing countries [4]. Our own literature review found no randomised trials comparing ART care provided by doctors with ART care provided by nurses or other health workers. Recent studies from Africa [5,6] and other developed countries [7-9] described new roles for nurses in AIDS care, but they were not randomised trials and none compared doctors or nurses with other health workers.

The trial builds on two randomised trials we carried out in the same setting between 2003 and 2007. The first, Practical Approach to Lung Health in South Africa ("PALSA") trial, was a cluster randomised trial in the 40 largest primary care clinics in the Free State [10]. It evaluated a multifaceted method of educational outreach to clinic nurses based on syndromic algorithmic guidelines for integrated management of adult lung disease, building on a WHO initiative. It showed that the intervention was effective and cost effective in improving tuberculosis case detection and asthma treatment. The second, "PALSA PLUS", cluster randomised trial evaluated the extension of the guideline and training to cover HIV/AIDS care in the 15 clinics then providing ART. It demonstrated effectiveness in increasing cotrimoxazole prophylaxis and tuberculosis case detection among HIV/AIDS patients (paper submitted), which led to its adoption as a provincial programme. However at that time only doctors could initiate ART. We simultaneously conducted a cohort study of all 14267 patients enrolled on the HIV/AIDS programme to the end of 2005, discussed above [11]. These studies have demonstrated the effectiveness of our educational method and guidelines for improving quality of primary nursing care provided by nurses, the research value of these programme data, and the impact of our research on policy.

In another randomised trial in South Africa, which by April 2008 had ended recruitment but not yet reported results, patients receiving ART in two clinics were randomised to be monitored either by a HIV-trained doctor or either of two HIV-trained primary care nurses (ClinicalTrials.gov NCT00255840). Key differences between our current trial and that one are: a) our trial evaluates a complex intervention including training, staffing, and management support as well as professional substitution, and b) our trial includes all clinics and patients involved in an entire province's HIV/AIDS programme. Our search of randomised trial registers (Controlled Clinical Trials meta-register and linked registers) identified no other planned, ongoing or completed randomised trials comparing ART provision by doctors with ART provision by nurses or other health professionals.

The Free State health department has therefore decided to support this trial and to decide whether to implement nurse-led ART based on the trials' results. Despite national guidelines, its Provincial Pharmaceutical and Therapeutics Committee is legally authorised to permit nurses to prescribe Schedule 4 drugs such as antiretrovirals, and has done so for intervention clinics in this trial. The National Department of Health and the main patient advocacy group in South Africa, the Treatment Action Campaign, also support the trial and are keenly interested in the results. The timing of this trial is thus critical for policy making.

Methods/Design

Design

Pragmatic cluster randomised trial with clinics randomised to two parallel arms

Aims

To compare the effectiveness of a primary care system based on nurse-led ART, with the current system based on doctor-led ART.

Inclusion criteria

Clinics

All 31 nurse-staffed primary care clinics providing ART as part of the public-sector treatment program, in the Free State province, South Africa.

Patients

The study population will be two subgroups of HIV-infected patients aged ? 16 years and over enrolled with the Free State Comprehensive Care, Management and Treatment of HIV and AIDS Program. Children aged <16 are excluded because management by doctors is still considered necessary, because of complexities of drug dosages and detecting complications.

Subgroup 1

Patients with CD4 count ? 350 cells/μl and not yet receiving ART. These patients are either eligible for ART (CD4 ? 200) or likely to become eligible during the trial period (CD4 >200 – 350). The latter patients, with CD4s between 200 and 350 cells/μl, are included to assess the ability of nurses in intervention clinics to monitor patients up to the time they become eligible for ART and then to initiate ART promptly.

Subgroup 2

Patients who have already received ART for at least 6 months. This subgroup is included so as to enable evaluation of the effect of the intervention on longer term ART monitoring and re-prescriptions, while restricting the trial's follow-up period.

Interventions

Control clinics

Current practice will be followed: 1. Patients eligible for ART (with CD4 ? 200 or stage 4 AIDS) will be referred to a doctor who will initiate and repeat prescriptions for ART and review patients every six months. Between visits to doctors, patients will be seen monthly by nurses (who may not prescribe ART) and will collect their medication. 2. Nurses will continue to use PALSA PLUS algorithmic guidelines for management of HIV/AIDS, sexually transmitted infections, and tuberculosis, having been trained to do so. These guidelines state that nurses do not prescribe ART. 3. Clinics will continue to receive routine managerial support and monitoring.

Intervention clinics

STRETCH is a complex intervention, to be implemented in intervention clinics, that will differ from control clinics as follows.

1. Designated nurses in each clinic will be authorised to prescribe ART. In addition to the training provided to control clinic nurses, they will receive training at their clinics covering ART prescribing, drug effects and side-effects, and use of algorithmic clinical practice guidelines including criteria for identifying patients requiring referral to a doctor. Nurses will not initiate ART in patients meeting the following criteria criteria but will refer them to the doctor (CD4 < 50, Stage 4 AIDS, previous ART, bed- or wheelchair-bound, using drugs other than cotrimoxazole or vitamins, pregnant, weight < 40 kg or body mass index >28). Doctors will also receive training about the guidelines so that they can support the nurses. These "ART nurses" will prioritise assessment and ART initiation for ART-eligible patients and carry out most treatment monitoring. Non-ART-prescribing nurses working in the ART clinics and surrounding clinics, who have received the same training as control clinic nurses, will provide routine HIV care to patients not yet eligible for ART, and refer them to ART-prescribing nurses as soon as they meet criteria for treatment. To relieve the workload of ART prescribing nurses, supportive components of ART care (apart from ART prescribing) such as drug readiness training and serial CD4 monitoring prior to ART initiation, will be decentralised to other primary care clinics that have staff trained in these components of ART care. This is intended to relieve the workload on ART prescribing nurses.

2. Managerial decisions relating to ART will be delegated to clinic managers. Clinics will receive additional managerial support through regular clinic visits by designated STRETCH co-ordinators. These arrangements, which include managerial steps to be taken, definitions of new staff roles, tips on dealing with likely problems, contact

details of programme managers, and authorisation of nurse prescribing, are clearly described in the STRETCH Implementation Toolkit – a 30 page document provided to each clinic and trained nurse.

Randomisation

Clinics were randomised to either of two arms. Randomisation was stratified by referral hospital-based "treatment site", because differences between these sites may confound clinic level ART care. However stratification was not used in one district where assessment and treatment are combined. Randomisation was carried out by the trial statistician (Lombard) before the intervention and patient recruitment started. N-Query Advisor was used to generate the allocation codes.

Allocation concealment

Blinding and masking of patients and clinicians are not possible because, in each clinic, all eligible patients will be managed in the same way. However the trial statistician who carried out randomisation did not know the characteristics of the clinics being randomised, and the primary statistical analysis will be blinded to allocation.

Endpoints

Primary outcomes

Subgroup 1

Time from enrolment to death. Survival analysis will be censored 12 months after the last patient has been recruited. Mortality is the most important health outcome and it is common – currently 28% of enrolled ART-eligible patients die within a year or enrolment. Deaths will be identified from programme data and by linkage with the national mortality register [2,11]. Because it is routinely recorded independently of the programme, with most deaths occurring in hospital or at home, measurement is less dependent on clinic professionals' practice, unlike adverse clinical outcomes or side effects of treatment, which require clinical skills to detect. This outcome reflects both the effectiveness of the health system in initiating treatment, and the effectiveness of ART once started.

Subgroup 2

Undetectable viral load (<400 copies/mL) one year after recruitment. This demonstrates continuing ART effectiveness, including adherence and treatment monitoring. Excess detectable viral loads will show whether the additional burden on nurses of initiating ART undermines the effectiveness of treatment monitoring, including dealing with poor adherence or resistance. Mortality would be a less appropriate primary outcome in this subgroup because mortality on ART is lower (17% per year [2]) and because it would probably take more than a year for suboptimal monitoring to lead to death.

Secondary outcomes

Subgroup 1

Process measures

time from enrolment to starting ART; proportion of patients who started ART during the study period; proportion with sputa submitted for TB screening; proportion diagnosed with tuberculosis; proportion receiving cotrimoxazole prophylaxis; nurse and doctor visits to ART programme.

Health measures

proportion with viral loads <400 copies/mL; baseline CD4 count of patients starting ART; changes in CD4 and weight; hospital admissions.

Subgroup 2

Process measures

proportion lost to follow-up; proportion with sputa submitted for TB screening; proportion diagnosed with tuberculosis; proportion receiving cotrimoxazole prophylaxis; nurse and doctor visits to ART programme.

Health measures

time from recruitment to death; changes in CD4 and weight; hospital admissions.

Side effects: reporting and quantification

Adverse AIDS outcomes and adverse ART reactions are expected among some patients and will be monitored:

- Patients with evidence of adverse ART effects (severe rashes, lactic acidosis, severe anaemia) will be identified by the nurses and doctors monitoring them, who will record these events.

- Deaths known to ART providers will be recorded. Mortality will also be tracked by monthly linkage with deaths notified on the national population register.

- Hospital admissions, and reasons for admissions, will be continuously monitored by linkage with health department admissions data.

Statistical analysis plan

Sample size

For subgroup 1, patients newly enrolled on the programme, sample size is calculated for a superiority trial (2 sided), because we hope to show decreased mortality in the nurse-led arm owing to reduced delay to starting ART. We expect to recruit at least 7400 newly enrolled patients during the first 12 months of the trial, since 4000 eligible patients were enrolled in trial clinics between 1 September and mid-December 2007. Previous programme data show that 29% of patients followed for at least a year died within one year, with an intra-clinic correlation coeffi-

cient (ICC) of 0.01. A sample size of 6000 (3000 per arm) would provide 90% power to detect a 6% difference in one-year mortality (24% vs 30%) at the 5% significance level, assuming ICC = 0.01. To cater for a 10% dropout the sample size has to be increased to 7400 in total (6000/((1-0.1)^2). Furthermore, Cox regression of time to death will have more power than comparison of proportions dying within a year.

For subgroup 2, patients already receiving ART, sample size is calculated for an equivalence trial, because we hope to show that nurse-led ART will be just as effective in suppressing HIV. We expect to recruit at least 4000 such patients since 2000 eligible patients were identified in trial clinics between 1 September and mid-December 2007. Previous programme data show that 82% of patients who had received ART for 12 months had undetectable viral loads, with an intra-clinic correlation coefficient of 0.005. A sample size of 4000 (2000 in each arm) would provide 90% power to reject the null hypothesis of non-equivalence in favor of the alternative hypothesis that the proportions patients with undetectable viral load in the two groups are equivalent using a 6% equivalence limit (i.e. within 6% of 80% in either arm), at the 5% significance level, assuming ICC = 0.005. To cater for a 10% dropout the sample size has to be increased to 4900 in total (4000/((1-0.1)^2).

Types of analyses

Statistical analyses will be by intention to treat. For analysis of mortality, patients with only one clinic contact will be excluded; if the proportions of patients with only one contact differ between trial arms, these analyses will be adjusted for the clinic-level proportions with only one contact. The statistical methods will be:

- Time to death: Cox proportional hazards regression
- Proportion with undetectable viral load, proportion alive after one year and other binary outcomes: Logistic regression
- CD4 and body weight: Linear regression, adjusting for baseline values
- Time to new diagnosis of tuberculosis: Cox proportional hazards regression
- Health care utilisation rates, and sputa submitted to detect tuberculosis: Poisson regression

Analyses will be at patient level and account for the stratified randomisation and intra-clinic clustering of outcomes. In secondary analyses we will also adjust for baseline confounders, if present.

Subgroup analyses

Patients with different CD4 levels at entry into trial (eg >200, ? 200 and >100, ? 100 cells/μl) and, among subgroup 1 patients: patients on ART at end of follow-up, patients eligible for ART but not receiving it at end of follow-up, and patients not yet eligible for ART at end of follow-up.

Interim analyses, stopping rules and independent data monitoring committee

An independent data safety and monitoring committee, including a statistician, has been established. An interim analysis of the primary outcomes is planned one year after recruitment starts. The trial statistician (Lombard) will carry out the analysis, blinded to allocation, and report the results to the data safety and monitoring committee. If there is a highly significant ($p < 0.001$) difference in any primary outcome a panel comprising the researchers and Free State Department of Health managers will meet to discuss whether to terminate the trial.

Ethical issues

The protocol was approved by the Research Ethics Committees of the University of Cape Town and University of Free State Medical Schools.

Patients with HIV/AIDS are at risk of adverse outcomes. However the treatment programme aims to improve outcomes, and there is equipoise as to whether patients in either arm would be at greater risk. According to provincial health department policy the intervention would probably be implemented incrementally in any case. The effects of the proposed research will be to randomly allocated implementation, and to provide training, managerial support and evaluation to ensure optimal implementation.

Professionals and managers in each clinic have consented to their clinic taking part in the trial. However it is not feasible to obtain patients' consent to be randomised to intervention or control arms, because randomisation will be at clinic level. Intervention- and control-type care cannot be provided within the same clinic because of the practicalities of clinic staffing, training and management, and because within-clinic randomisation would severely contaminate the trial. Even if patients preferred doctor- or nurse-led care or did not consent to take part in the trial, they would still necessarily receive the type of care that the clinic was allocated to provide [12].

Patients will not be asked for their consent for their medical records to be used for this research because it is not feasible. That is, programme managers and health professionals have insisted that obtaining such consent from all eligible patients would be a serious obstacle to widening

access to HIV/AIDS care. This is because of a) the many procedures already involved in patient enrolment, b) current delays in providing effective treatment and c) the large scale of the programme, with over a thousand new enrolments per month.

However we will adhere to the ethical principles for use of medical records without patients' consent [13], as follows. The research has a clear public benefit. We have obtained approval for the study from the Research Ethics Committees of the Faculties of Health at the Universities of Cape Town and Free State, and from the lead doctors and nurses managing the programme. Use of the data for research will not influence decisions about individuals' care. The data are already being used by members of the research team for programme evaluation on behalf of the provincial health department, and for observational evaluation of ART effectiveness in the programme cohort. Only a small number of data managers have access to personal identifiers. Anonymised unlinked data (without names or national ID numbers) will be provided only to selected members of the research team – the principal investigators, the lead statistician, the data monitoring and ethics committee statistician and the health economist. There are hundreds of patients in each clinic so individuals cannot be identified from clinic names. Data with patient identifiers will be securely stored at the Lung Institute, University of Cape Town, and anonymised unlinked data will be securely stored at the University of East Anglia and the South African MRC.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed to the study design. LRF is the principal investigator. CJL is the trial statistician, and carried out the randomisation and sample size calculations. KU is the trial manager. All authors have read and approved the final manuscript.

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Appendix B

STRETCH protocol guidelines for nurse initiation and monitoring patients on ART (ART algorithms)

Referred to in the article presented in Chapter 4 as Additional file 1.

ENROLMENT IN THE ARV PROGRAMME

- ARVs prevent and treat AIDS. ARVs are for life.
- **Clients need ARVs if CD4 ≤ 200 or stage 4 HIV. If pregnant, client needs ARVs if CD4 ≤ 350 or stage 4 HIV.**
- All clients need routine HIV care (see page 17)
- At the first visit: - Assess eligibility for nurse-managed or doctor-managed ARVs (step 1)
  - Prepare all clients for ARVs with steps 2–6

Step 1. Assess eligibility for nurse-managed or doctor-managed ARVs

- CD4 51-200 and
- Stage 1, 2 or 3 HIV and
- ARV-naïve (no previous ARVs or ARVs ≤1 month) and
- Able to walk unaided and
- Only using co-trimoxazole ± multivitamins and
- Not pregnant and
- Weight > 40kg and BMI< 28

For nurse-managed ARVs

- CD4 ≤ 50 or
- Stage 4 HIV or
- Previous use of ARVs (>1 month) or
- Bed- or wheelchair-bound or
- Using medication other than co-trimoxazole and multivitamins or
- Pregnant (refer same week for Drug Readiness Training) or
- Weight < 40kg or BMI > 28

Refer for doctor-managed-ARVs (same week if CD4 ≤ 50 or pregnant)

Step 2. Exclude TB. Always look for TB symptoms.

Exclude TB
Go to page 6

Investigate for TB if any of the following are present:

- Cough • 2 weeks or
- Weight loss • 1.5kg in 4 weeks or
- Drenching night sweats or fever • 2 weeks or
- Chest pain or
- Blood stained sputum

} Send sputa for two smears
(see pages 6 - 8 for diagnosing TB)

If symptomatic, do not commence ARVs until TB has been excluded. If unsure, refer to doctor.

Step 3. Assess clinically

- ARVs are not an emergency treatment: HIV emergencies are usually due to opportunistic infections.
- Assess for opportunistic infections or other HIV-related diseases.
  - Refer the client with CD4 ≤ 50 or Kaposi's sarcoma same week to doctor for ARVs.
  - Look for and treat **acute severe illness** – stabilize the client before starting ARVs. (See pages 24-35)
  - Ask about • **peripheral neuropathy** (pain, burning/ 'heat' or tingling in the hands or feet). (See page 31)
    • **depression.** (See page 35)
    • **pregnancy** (refer to doctor for ARVs same week)
- Assess nutritional status, calculate BMI (see page 18)

Routine Care
Weight
Exclude TB
Review CD4
Update Stage
STI screen
Condoms
Pap

Step 4. Discuss contraception and safe sex

- Discuss your client's plans for a family. If required, advise reliable contraception (injectable contraceptive plus condoms).
- **Efavirenz causes birth defects. Women of child-bearing age must receive nevirapine instead.**
- Unsafe sex on ARVs can still transmit HIV and carries the risk of reinfection with different strains of HIV. This can lead to treatment failure.
- Encourage the use of condoms. Encourage your client to have only one partner.

Step 5. Assess blood results

- All clients need a baseline ALT.
- Normal range < 40 IU/ml. If result not within normal range, refer to doctor for assessment and to start ARVs

Step 6. Start Drug Readiness training at the same time as clinical work-up

One session per week for three weeks – clients must complete all three sessions before starting ARVs
If client is pregnant, she should complete drug readiness training within one to two weeks

- Session One: Disclosure and Positive Living
- Session Two: Basics of HIV, CD4 and viral load; Co-trimoxazole prophylaxis
- Session Three: Opportunistic Infections, ARV Treatment Plan, Adherence

Encourage attendance by treatment 'buddy' (friend or family member)

Step 7. Assess readiness to start treatment

ARVs are not an emergency treatment. Clients must be clinically stable, psychologically prepared and adherent before starting treatment.

Clinically ready?
Able to walk unaided
No TB symptoms
No acute illness
Normal baseline ALT

Adherent?
Takes co-trimoxazole/ multivitamins as instructed
Attends appointments reliably
Understands the importance of adherence
Plans for regular attendance and adherence

Socially ready?
Treatment buddy
Support group recommended
No alcohol abuse
Contraceptive/ condoms

If yes to all **the above, client is ready to start nurse-managed ARVs. If no to** any **of the above, refer for doctor-managed ARVs.**

Step 8. Start ARVs – Regimen 1

- The client must always receive 3 different ARVs. Prescribe 3TC and d4T and either:
  - nevirapine for all women of child-bearing age or
  - efavirenz for all men and women not of child-bearing age
- Counsel client about how to take ARVs
- Remind about possible side effects (see page 22)
- Draw baseline viral load
- Continue co-trimoxazole ± multivitamins.
- Schedule clinic follow-up after two weeks

Antiretroviral	Weight	Dose	Frequency
Lamivudine (3TC)	>40kg	150mg	12-hourly
Stavudine (d4T)	40-60kg	30mg	12-hourly
Nevirapine	>40kg	200mg	once daily for 2 weeks, then 12-hourly[1]
Efavirenz	>40kg	600mg	24-hourly - the same time every night

ver enzymes responsible for its own metabolism. Step-wise introduction helps to avoid sub-therapeutic levels and reduce the risk of skin rash and hepatitis.

MONITORING THE CLIENT ON ARVs

Routine Care
Weight
Exclude TB
Review CD4
Update Stage
STI screen
Condoms
Pap

Follow-up appointments for client on ARVs. ARVs are for life.

- Check for adherence and reliable attendance. Re-issue medication (ARVs, co-trimoxazole) monthly.
- Check safety bloods according to schedule below
- Monitor response to ARVs (see below)
- Look for ARV side-effects and review safety bloods results. (See page 22)

Week	2	4	8	12	24 (6 months)	48 (12 months)	6-monthly thereafter	12-monthly thereafter
Safety bloods per ARV	• ALT (NVP) • Increase **NVP to 12-hourly if client well**	• ALT (NVP) • FBC + diff (AZT)	• ALT (NVP) • FBC + diff (AZT)	• FBC + diff (AZT)	• ALT (NVP) • FBC + diff (AZT) • Fasting cholesterol and triglycerides (LPV/r)	• ALT (NVP) • FBC + diff (AZT) • Fasting Glucose (LPV/r)	• ALT (NVP) • FBC + diff (AZT)	• Fasting cholesterol & triglycerides (LPV/r) • Fasting glucose (LPV/r)

Monitoring response to ARVs

Response to ARVs is assessed clinically, virologically (with viral load, VL) and immunologically (with CD4)

Exclude TB
Go to page 6

Clinical

- After starting ARVs, opportunistic infections can occur, especially if CD4 < 100. Look for signs of infection, particularly TB, at each visit.
- Weight: - Investigate > 1.5kg weight loss.
  - Weight gain > 10kg or to BMI > 28 increases risk of lactic acidosis. Refer to doctor.

CD4

- Check 6-monthly.
- Response varies from client to client.
- Some CD4s may never rise.
- Refer for doctor review if CD4 falls and new opportunistic infections or VL > 400.
- If well and CD4 > 200 stop co-trimoxazole

Viral load

- Check 6-monthly.
- Should be < 400 or 'lower than detectable limits'.
- If > 400 refer to adherence counselor same day and refer to doctor for next ARV appointment.

Treatment failure

- Refers to a VL persistently > 400 with or without the occurrence of opportunistic infections.
- The client will need to change to a new ARV regimen, usually regimen 2.
- The most common cause of treatment failure is low adherence.

Regimen 2 ARVs	Weight	Dose	Frequency
Zidovudine (AZT)		300 mg	12-hourly
Didanosine (ddI)[1]	< 60 kg > 60 kg	250 mg 400 mg	Once a day
Lopinavir/ ritonavir (LPV/r)[2]		400/100 mg	12-hourly

Approach to low adherence (See page 44 for an approach to adherence counseling)

More than 95% of ARV doses must be taken to avoid development of resistance.

- Educate on the importance of adherence and dangers of resistance
- Re-explain treatment schedule (12-hourly doses including weekends)
- Consider adherence aids (pillboxes, diaries)
- Ask about drug-related side-effects or alcohol abuse
- Refer client to adherence counselor
- Insist on participation in a support group
- See the client more frequently (weekly instead of monthly)
- Arrange a home visit

Inform ARV site doctor and nurse of low adherence so that CD4 and VL can be interpreted accordingly.

[1] Dissolve at least 2 tablets in water. Take on an empty stomach 1 hour before food or medication.
[2] Take with food to improve absorption. Store in a cool, dry place. (< 25 °C)

Appendix C

STRETCH Toolkit

Referred to in the article presented in Chapter 4 as Additional file 2.

STRETCH

Streamlining Tasks and Roles to Expand Treatment and Care for HIV

Implementation Toolkit **2007**

Department of Health
Departement van Gesondheid
Lefapha La BopheloBo Botle

FOREWORD

The STRETCH intervention is an important pilot intervention in ARV clinics in the Free State and is aimed at increasing access to treatment for the many HIV-infected patients in our province who need antiretroviral therapy.

We recognise the tremendous work done so far by all our healthcare workers in rolling out ARVs across the province, but we also see that we need to get many more patients onto ARVs if we are going to make an impact on the toll HIV is taking in our communities.

To this end the STRETCH programme is one way of steamlining and increasing provision of HIV care by redefining the roles of different health care workers and reintegrating HIV care back into the primary healthcare system.

This is being done as a research pilot programme in partnership with the UCT Lung Institute, so that we can monitor the effect of this new programme to see if we can expedite access to ARVs for people who need them, without compromising standards of care.

I recommend this programme to you and support its implementation and look forward to seeing the results.

MS SRO KHOKHO
Acting Executive Manager
Strategic Health Programmes & Medical Support

Department of Health
Departement van Gesondheid
Lefapha La BopheloBo Botle

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WHAT IS STRETCH?

STRETCH is a multifaceted health systems intervention comprising:

- Algorithms to triage HIV patients eligible for ARVs for nurse- or doctor-managed care (included in a special edition PALSA PLUS guideline).
- PALSA PLUS educational outreach training in the new guideline.
- Expanded prescribing provisions to permit trained nurse practitioners[1] to prescribe ARVs.
- Re-defining roles of clinical staff
  - Primary healthcare services: pre-ARV HIV care.
  - ARV nurses: monitoring of stable ARV patients, ARV initiation in selected adults.
  - ARV doctors: manage complex cases and review problem cases.
- This system's toolkit: a handbook for managers on how to implement STRETCH.
- Provincial STRETCH co-ordinator.
- STRETCH facility support teams – to facilitate changes and provide support.
- Community awareness by community health workers.

STRETCH is *not* just nurse-initiated ART, nurses doing doctors' work, excluding doctors or a quick fix.

STRETCH aims to:

- Provide high quality HIV and ARV care while expanding ARV treatment access.
- Decentralise care and integrate HIV care into primary care.
- Consolidate care for most clients to the clinic/assessment site to reduce traveling between facilities and to avoid fragmented care.
- Enable doctors to see complex cases.
- Provide a sustainable model of care and support health workers working together to avoid burn-out.

STRETCH will be introduced in 3 phases:

1. Site preparation including decentralisation of HIV care according to provincial policy (e.g. rollout of CD4 staging).
2. Consolidation of decentralisation of HIV care to PHC services and ARV monitoring to ARV nurses.
3. Initiation of ARV treatment by nurses in selected cases.

[1] Only selected nurse practitioners at STRETCH facilities may prescribe ARVs. See page 5 for details.

HOW TO USE THIS TOOLKIT

- As a **handbook**! The organisation of care in a clinic depends on many factors including its size, location, distance from referral hospital and staffing. The recommendations in this toolkit ***must*** be tailored for each STRETCH clinic. Some clinics will have more changes to make than others to achieve integrated decentralised HIV care.

- To **inform others** including managers and clinic staff. The overview of the programme (pages 3-4) provides a useful summary, and descriptions of everyone's tasks and roles during each phase may also help provide clarity.

- As a **resource**. The toolkit includes useful checklists (pages 21-22), contact numbers (pages 27-29) and documents (pages 24-26) which you may need during your interactions with other mangers and clinical staff.

STRETCH OVERVIEW

Phase 1: Site preparation (3 months)

KEY ACTIVITIES

- PALSA PLUS training to all clinic nurses to ensure all equipped to manage HIV and TB.
- Convene support team for each STRETCH facility to initiate system changes for Phases 2 and 3.
- Start decentralisation of routine HIV care according to provincial policy (e.g. VCT and CD4s at local clinic).

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses (2 to 3 months)

KEY ACTIVITIES

- Consolidate efforts to decentralise routine HIV care to PHC services nurses.
- ARV monitoring decentralised to ARV nurses at STRETCH facilities.
- STRETCH support team to meet regularly (weekly for 3 weeks, thereafter 2 weekly) & PALSA PLUS training to continue.

Initial assessment by PHC services nurse with ***same day*** CD4 draw

CD4 result appointment with PHC services nurse

CD4 ≤ 200 and/or AIDS and not pregnant ***or***
Pregnant and CD4 ≤ 350 and/or AIDS

Refer to ARV nurse for ARVs. Fast-track if pregnant

Refer to doctor at treatment site for ARVs
Continue work-up for ARVs:
CD4 if not yet done, TB screen, RPR, Preg test, ALT, Pap etc.

Monitoring on ARVs
ARV nurse reissues/represcribes ARVs and other meds, draws **and** interprets all bloods, supports adherence, refers selected cases to doctor.
ARV doctor reviews cases referred by ARV nurse and, if appropriate, changes drugs.

CD4 ≥ 200 and no AIDS and not pregnant ***or***
Pregnant and CD4 > 350 and no AIDS

6 monthly review by PHC services nurse
Referral to PMTCT programme

Routine HIV care can prevent AIDS
PHC services nurse to monitor CD4
CD4 251 to 499: recheck 6 monthly
CD4 ≥ 500: recheck 12 monthly

Phase 3: Initiation of ARV treatment by nurses in selected cases

KEY ACTIVITIES

- ARV nurses triage all clients referred for ARVs & initiate treatment in selected cases. Others are referred to doctors at the treatment site as before.
- STRETCH support team to meet weekly for first 6 weeks, thereafter 2 weekly & PALSA PLUS training to continue.

Initial assessment by PHC services nurse with same day CD4 draw

CD4 result appointment with PHC services nurse

CD4 ≤ 200 and/or AIDS and not pregnant ***or***
Pregnant and CD4 ≤ 350 and/or AIDS

Refer to ARV nurse for ARVs. Fast-track if pregnant.

Triage clients according to PALSA PLUS guideline (STRETCH edition)
and work-up for ARVs
For nurse or doctor-managed ARVs?

For nurse-managed ARVs

Initiate ARVs and monitor according to guideline

For doctor-managed ARVs

Refer to doctor at treatment site for ARVs

Monitoring on ARVs
ARV nurse reissues/represcribes ARVs and other meds, draws and interprets all bloods, supports adherence, refers selected cases to doctor.
ARV doctor reviews cases referred by ARV nurse and, if appropriate, changes drugs.

CD4 ≥ 200 and no AIDS and not pregnant ***or***
Pregnant and CD4 > 350 and no AIDS

6 monthly review by PHC services nurse
Referral to PMTCT programme

Routine HIV care can prevent AIDS
PHC services nurse to monitor CD4:
CD4 251 to 499: recheck 6 monthly
CD4 ≥ 500: recheck 12 monthly

TIMELINES

- It is recommended that STRETCH be introduced over a period of 4 to 6 months in a clinic. This will depend on the number of changes that need to be made in a clinic to achieve integrated decentralised HIV care.
- Phase 1 has already started in all STRETCH clinics, but will need to be consolidated before proceeding to Phase 2.
- The duration of Phase 2 depends on the extent of verticalisation in the clinic, and the confidence of ARV nurses in monitoring clients on ARVs. A period of 2 to 3 months is recommended.
- Schedule activities (PALSA PLUS training, STRETCH support team meetings, start dates for phases 2 and 3, orientation workshops etc.) to ensure implementation proceeds smoothly. See page 20 for a suggested timeline.

PRESCRIBING/DISPENSING AND ISSUING OF ARVS DURING STRETCH

- Only nurses working in selected STRETCH clinics may be considered for prescribing ARVs until further notice.
- In order to prescribe ARVs nurses must fulfill **all** of the following criteria:
  - Professional/Senior Professional/Chief Professional nurse authorised to prescribe medication at the clinic.
  - Completed provincial ARV training.
  - Completed or receiving outreach training in the PALSA PLUS guideline (STRETCH edition).
- All nurses who fulfill these criteria must be registered with the STRETCH provincial co-ordinator in order to be able to prescribe ARVs. Fax certificates for above training to Dr Kerry Uebel at 051 4081961.
- These nurses may only prescribe ARVs according the clinical criteria in the PALSA PLUS guideline (STRETCH edition).
- Nurses may not dispense ARVs. Scripts should be faxed to pharmacists/pharmacy assistants at the treatment site or central pharmacy for dispensing. Once dispensed they will be sent to the clinic for issuing.
- Permission for nurses to prescribe ARVs under these conditions has been provided by the Free State Pharmaceutical and Therapeutics Committee (see page 26).

	Initiate	**Renew same prescription**	**Change prescription**	**Dispense**	**Issue**
Definition	*Complete first prescription for ARVs*	*Renew same ARVs at same doses for a further period (usually 3 months)*	*Change regimen or dose of ARVs*	*Attach client's personal details to packets of medication*	*Supply client with dispensed medication*
Phase 1 	Doctor	Doctor	Doctor	Pharmacist Pharmacy Assistant	Pharmacist Pharmacy Assistant ARV or PHC services nurse
Phase 2 	Doctor	Doctor ARV nurse (selected cases)	Doctor	Pharmacist Pharmacy Assistant	Pharmacist Pharmacy Assistant ARV or PHC services nurse
Phase 3 	Doctor ARV nurse (selected cases)	Doctor ARV nurse (selected cases)	Doctor	Pharmacist Pharmacy Assistant	Pharmacist Pharmacy Assistant ARV or PHC services nurse

THE STRETCH SUPPORT TEAM

- The purpose of the STRETCH Support Team is to ensure that the multiple components of STRETCH (PALSA PLUS training, reversal of vertical HIV care, down-referral of stable ARV clients, initiation of ARVs in selected cases) are actually implemented at the STRETCH facility.
- Communication is key to successful implementation and requires that the STRETCH Support Team meet regularly.
- Each STRETCH facility requires its own team.

GETTING STARTED

Who should be in the team?

A provincial STRETCH co-ordinator will convene a group of stakeholders for each STRETCH facility comprising the following:

STAKEHOLDER	ROLE IN THE STRETCH TEAM?
• Facility manager	To oversee changes in client flow in facility and assist with logistical requirements.
• PHC services nurse representative	To re-assume responsibility for routine HIV care, as well as serial CD4 staging.
• ARV services nurse representative	To assume full responsibility for ARV monitoring and initiate ARVs in selected cases.
• ARV doctor	To support ARV nurses.
• ARV co-ordinator	To ensure logistical requirements are met, and report back to district ARV Task Team.
• PALSA PLUS trainer	To train all clinic nurses and support them as their clinical responsibility increases.
• Clinic pharmacist/pharmacy assistant	To ensure adequate supplies of essential drugs (ARVs, cotrimoxazole).
• ARV administrative clerk	To revise filing of records and schedule follow-ups with the appropriate health professional.
• ARV data capturer	To ensure that all relevant records from PHC and ARV nurses are captured.
• Community health worker	To facilitate community buy-in and co-operation.

Who should lead the team?

- If possible, the facility manager should lead the team.
- Effective leadership qualities include being passionate about improving HIV care and ARV access, communication skills, sound decision-making and problem-solving abilities, purposeful planning and effective time management.

- *Teams which get things done meet regularly.*
  - Weekly meetings will be required initially to ensure all the site preparation tasks are completed in Phase 1.
  - More frequent meetings may be required during critical periods (e.g. start of phases 2 and 3).
  - The team will need to downscale its support during the maintenance phase to ensure sustainability in the long-term.
- STRETCH is about consolidating care to the primary care facility. Since most team members come from the facility, it makes sense to hold meetings at the facility itself.

Phase 1: Site preparation and start decentralisation of HIV care

GOAL	ACTIVITIES
To *upskill all nurses* to provide quality HIV and TB care	**PALSA PLUS training** • All clinic nurses should be encouraged to attend on-site training sessions. • Key knowledge includes routine HIV care, interpretation of ARV monitoring bloods and work-up of clients for ARVs including initiation in selected cases.
To ensure *buy-in* of clinic staff, local managers and doctors	**Engage local managers** • Make contact with local managers and doctors through ARV co-ordinator/ District ARV Task Team (e.g. invite local managers/ doctors to a STRETCH team meeting). **Orientation workshop for the clinic** • Larger clinics may need a more structured process for raising awareness of STRETCH and ensuring buy-in. • See page 23 for suggested programme for a half-day orientation workshop.
To provide *equipment and supplies* necessary to support the decentralisation of HIV care	See **Equipment and Supplies Checklist** on page 22 • Ensure all equipment and supplies are in place before proceeding to Phase 2. e.g. fax machine for faxing prescriptions, adequate storage facilities for extra drugs, extra needles and blood tubes.
To *inform the community* about plans to increase access to HIV care	**Community liaison** • This is the responsibility of the clinic's community health workers. • Key messages for the community in this phase include: - The clinic is planning to increase access to HIV care. - More nurses are being equipped to provide routine HIV care. - In future nurses will start ARVs in uncomplicated adult patients at the clinic. - Complex cases will still be referred to doctors for management.
To *assess readiness* for Phase 2	Have all nurses received **PALSA PLUS training?** Are the necessary **equipment and supplies** in place? Assess progress towards **decentralising HIV care** (see page 21 for Decentralisation Checklist).

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

GOAL	ACTIVITIES
To consolidate *decentralisation of HIV care* to PHC services	**Review Decentralisation Checklist** (see page 21) • Assess progress towards targets for your facility.
To change *follow-up bookings for ARV clients*	**Co-ordinate with Treatment Site through District ARV Task Team/ARV co-ordinator** • Book all ARV follow-up clients from STRETCH clinics for follow-up at the clinic instead of at the Treatment Site (unless complications arise).
To *support clinic staff*	**PALSA PLUS training** • See page 19. **ARV nurse doctor partnerships** • The ARV nurse and doctor must work closely to ensure that care is provided at the appropriate level and problems referred without delay. • For this reason try to assign one or two doctors at the treatment site to support nurses at a STRETCH facility. The doctor and nurse should work out how complex cases will be seen (weekly at the clinic or at the treatment site, how to arrange urgent referrals etc). • Encourage feedback from the treatment site (e.g. on appropriateness of referrals, complex cases). • Facilitate access to **debriefings by psychologists** through Employee Assistance Programme (EAP). Your PALSA PLUS trainer is also equipped to conduct debriefings.
To *inform clients* about changes in the organisation of HIV care	**Community/client liaison** • Community health workers should inform clients in the waiting room that the organisation of HIV care in the clinic is changing. Daily briefings are suggested (after morning song/prayers). • Key messages for clients in this phase include: - The clinic is planning to increase access to HIV care. - More nurses are being equipped to provide routine HIV care. - Clients on ARVs will be followed-up at the clinic unless complications arise.
To *assess readiness* for Phase 3	Is **monitoring ARVs** at the clinic working? Are the ARV nurses feeling confident about monitoring clients on ARVs? Are **drug supplies** regular? Is there good communication with the treatment site **doctor**? Is she/he seeing complex cases? Are the necessary **equipment and supplies** in place?

Phase 3: Initiation of ARV treatment by nurses in selected cases

GOAL	ACTIVITIES
To consolidate *decentralisation of HIV care* to PHC services	**Review Decentralisation Checklist** (see page 21) • Assess progress towards targets for your facility.
To *decentralise initiation of ARVs in selected cases* to ARV nurses	**Set date and start ARV initiation at the clinic** • Avoid starting on a Monday or Friday. • Ensure necessary equipment (e.g. fax machine for faxing prescriptions) and supplies (e.g. drugs) are in place (see below). • Consider marking the first time clients start ARVs at the clinic with some form of celebration.
To *support clinic staff*	**PALSA PLUS training** • See page 19. **ARV nurse doctor partnerships** • Communication with the treatment site doctor is vital to support the ARV nurse during the first weeks of phase 3. Ensure that the nurse has the right phone numbers and sufficient phone access, including cellphone access, to contact the doctor when necessary. • Prime the ARV doctor to receive frequent calls from the ARV nurse during the first weeks when clients are expected to present with side-effects. • Facilitate access to **debriefings by psychologists** through Employee Assistance Programme (EAP). Your PALSA PLUS trainer is also equipped to conduct debriefings.
To ensure that the necessary *equipment and supplies* are in place.	See **Equipment and Supplies Checklist** on page 22.
To *inform clients* about changes in the organisation of HIV care	**Community/client liaison** • Community health workers should inform clients in the waiting room about nurses starting to initiate ARVs in selected cases. Daily briefings are suggested (after morning song/prayers). • Key messages for clients in this phase include: - The clinic is planning to increase access to HIV care. - Nurses may commence ARVs in selected adult clients. - Clients on ARVs will be followed-up at the clinic unless complications arise.

MAINTENANCE AND SUPPORT

GOAL	ACTIVITIES
To maintain *decentralisation of HIV care* to PHC services	**Review decentralisation monthly** (see Decentralisation Checklist on page 21) • Are all nurses providing routine HIV care? • Is ARV monitoring and initiation in selected cases being done by the ARV nurse?
To *support clinic staff*	**PALSA PLUS Training** • Follow-up support from PALSA PLUS trainers. PALSA PLUS trainers should revisit STRETCH facilities 4 to 6 weekly during the maintenance phase. See page 19. **ARV nurse doctor partnerships** • Maintain open communication channels and promote regular feedback (from ARV task team meetings, on specific clients). Regular **clinic/district meetings** to share the impact of STRETCH. The STRETCH team should reduce their meeting frequency to once a month to ensure sustainability in the long-term. Share **monthly managers' reports** (data on waiting lists etc). Facilitate access to **debriefings by psychologists** through Employee Assistance Programme (EAP). Your PALSA PLUS trainer is also equipped to conduct debriefings.
To ensure a continued supply of the necessary *equipment and supplies*	Assign responsibilities for various equipment and supplies to specific people in the clinic e.g. working fax machine to the admin clerk; drug supplies to the pharmacist/pharmacy assistant.
To manage *staff turnover*	**Orientate and provide training** • Assign one full day to an appropriate clinic staff member to orientate each new staff member. • If new nurse, arrange for provincial ARV training (if appropriate) and inform PALSA PLUS trainer.

TIPS ON STREAMLINING CARE

Address verticalisation

- Verticalisation of services means clients see several health professionals per visit. This means a longer clinic visit and increased patient load on staff.
- Integration of HIV services into primary care services is a key component of STRETCH. See Decentralisation Checklist on page 21.
- Examine client flow in your clinic: are clerks directing clients to the appropriate nurses?
- Examine drug dispensing in your clinic: can ARVs and other drugs be issued/ dispensed by the same pharmacist/ pharmacy assistant?

Avoiding "peaks" and setting targets

- When ARV initiation becomes available at your clinic, it may be tempting to start many clients on ARVs at once to cut your waiting list.
- This will result in large numbers of clients needing follow-up care all on the same day which may be overwhelming for staff.
- This can be avoided by planning initiation visits carefully:
  - Work out how many clients will need nurse-initiated ARVs each month (we estimate this is around 1/3 of those who qualify each month).
  - Book initiation visits throughout the course of the month (see Batching below for more ideas on planning initiation visits).

Batching

- ARV clients become naturally organised into groups through Drug Readiness Training. Take advantage of this when it comes to initiation and follow-up.
- Advise clients how to take their ARVs in groups (instead of one-on-one) and arrange clinical follow-up on the same day. This saves valuable nurse time and allows clients to develop long-term supportive relationships with others in their group.
- The group approach may not be suitable for clients who are not yet comfortable with disclosure or who wish to discuss sensitive issues in private (e.g. sexual practices, contraception etc.)

Drawing bloods and interpreting results

- Routine HIV care (before and on ARVs) follows a clear course with events at pre-defined periods (e.g. CD4 monitoring).
- It wastes time to see a client once to draw blood for a CD4/viral load/ALT and again to follow-up the result.
- Consider drawing blood at usual check-up and follow-up results the following month (e.g. draw viral load and CD4 at 6 month ARV visit, review results at 7 month visit).
- Alternatively consider pre-filling blood request forms and asking clients to return on an arranged day for only the blood draw, and later for a clinical consultation to discuss the result.
- Ensure a fast-track system for blood draws in is place so that clients don't have to wait long periods simply to have blood taken.

The right person for the right job

- Skilled health workers are a scarce resource. Ensure that your nurses are not doing jobs which could be done by others (e.g. Drug Readiness Training Sessions 1 and 2 by counsellors, admin work by admin clerks and data capturers). Save their valuable clinical skills for clinical work.

Mondays and Fridays

- It is a bad idea to start a new programme (or a new phase of STRETCH) on a day when the clinic is very busy (Mondays) or winding down (Fridays).
- When setting dates for starting different phases of STRETCH, also bear in mind public holidays and other disruptions e.g. polio campaign weeks.

TIPS ON MANAGING STAFF SHORTAGES

A shortage of staff in facilities is a common problem with many causes that results in frustration, low morale and an overwhelming case load. Several approaches may prove helpful depending on the cause in your clinic.

Supporting staff and managing burnout

- A major cause of staff shortages is psychological or physical ill-health. Burnout occurs frequently in clinics with high TB and HIV caseloads.
- Regular support by a middle manager (e.g. ARV co-ordinator, local area manager) comprising frequent visits, empathetic listening and efficient management of problems can engender a feeling of a supportive work environment.
- Consider counselling or psychological support for those staff (as a group or individually) who display signs of burnout. Professional debriefings by a psychologist are available through the Employee Assistance Programme. Your PALSA PLUS trainer is also equipped to conduct debriefings.

Rethinking the "morning clinic" culture

- Clinics tend to be extremely busy in the morning and either empty or close early in the afternoon. Staff are often exhausted by midday.
- Encourage staff to pace their work throughout the working day, taking tea and lunch breaks but working a full day.
- Clients may initially be resistant to this approach but will soon see the benefits of a calmer clinic environment and non-stressed nurses.

Co-ordination of staff leave and attendance at off-site training

- Plan leave together to minimise periods when more than one member of staff is away at the same time.
- Many staff are absent from their facilities as they are attending training workshops elsewhere.
- Plan attendance at off-site training courses and attempt to streamline the training courses attended by nurses.
- Try and avoid repetition of topic in different courses.
- Encourage on-site training.
- Agree on a maximum number of days allowed per nurse per year for attendance at these courses.

Prioritise the filling of vacant posts

- Know how many vacant posts you have at your clinic. This information is readily available from Human Resources.
- Encourage managers to fill vacant posts especially those for which there are usually several applicants e.g. admin clerks, data capturers.
- Spread the word – ask colleagues to keep their ears and eyes open for someone who may be suitable for a position at your clinic.

TASKS AND ROLES: PHC SERVICES NURSE (assessment/combined sites/local clinics)

Phase 1: Site preparation and start decentralisation of HIV care

Clinical responsibilities:

- Suspect and diagnose HIV.
- Stage HIV clients and draw CD4 the *same day*.
  - CD4 ≤ 200 and/or AIDS ***or*** pregnant with CD4 ≤ 350 and/or AIDS: Refer to ARV nurse (urgently if pregnant, CD4 <50, Kaposi's sarcoma).
  - CD4 ≥ 201 and no AIDS or pregnant with CD4 > 350 and no AIDS: Schedule follow-up visits incl. CD4 counts, arrange PMTCT referral.
- Provide routine HIV care especially: screening for TB, cotrimoxazole prophylaxis to those with Stage 3 or 4 HIV or CD4 Õ200.

Record-keeping:

First visit: *VOLUNTARY COUNSELLING & TESTING* or *HIV FOLLOW-UP: NOT YET ON ARVS.*

Subsequent visits: *HIV FOLLOW-UP: NOT YET ON ARVS.*

Training:

- PALSA PLUS: ensure you understand how to stage clients, interpret CD4 counts, diagnose TB in HIV positive client, start cotrimoxazole prophylaxis.
- HIV form training: ensure you understand how to complete: *VOLUNTARY COUNSELLING & TESTING, HIV FOLLOW-UP: NOT YET ON ARVS.*

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Clinical responsibilities:

- As before.

Record-keeping:

- As before.

Training:

- Attend PALSA PLUS support visits.

Phase 3: Initiation of ARV treatment by nurses in selected cases

Clinical responsibilities:

- As before.

Record-keeping:

- As before.

Training:

- Attend PALSA PLUS support visits.

TASKS AND ROLES: ARV NURSE (assessment/combined sites)

Phase 1: Site preparation and start decentralisation of care

Clinical responsibilities:

- Decide on further management of staged HIV clients:
  - CD4 ≤ 200 and/or AIDS ***or*** pregnant with CD4 ≤ 350 and/or AIDS: Refer to ARV doctor (urgently if pregnant, CD4 <50, Kaposi's sarcoma).
  - CD4 ≥ 201 and no AIDS ***or*** pregnant with CD4 > 350 and no AIDS: Schedule follow-up visits including CD4 counts with the PHC services nurse.
- Re-issue repeat ARVs to clients on treatment, support adherence, monitor side-effects, draw monitoring bloods, book doctor follow-ups.
- Provide routine HIV care especially: screening for TB, cotrimoxazole prophylaxis to those with Stage 3 or 4 HIV or CD4 Ō200.

Record-keeping:

- PHC services nurses now complete *VOLUNTARY COUNSELLING AND TESTING* and *HIV FOLLOW-UP: NOT YET ON ARVS.*
- Complete as required: *HIV FOLLOW-UP: NOT YET ON ARVS, ARV NURSE FOLLOW-UP, REFER TO TREATMENT SITE.*

Training:

- PALSA PLUS: ensure you understand how to interpret ARV monitoring bloods and when to refer ARV clients to a doctor.

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Clinical responsibilities:

- Manage HIV clients not yet on ARVs as before.
- Continue to re-issue repeat ARVs, support adherence and monitor side-effects.
- Draw and now also interpret monitoring bloods and represcribe ARVs according to PALSA PLUS guidelines (STRETCH edition). Refer ARV clients to the ARV doctor only if problems arise.
- Continue to provide routine HIV care.

Record-keeping:

- Complete these forms as required: *HIV FOLLOW-UP: NOT YET ON ARVS, ARV NURSE FOLLOW-UP, REFER TO TREATMENT SITE.*

Training:

- Continue PALSA PLUS training: ensure you understand when eligible clients are suitable for nurse-managed ARVs, how to work-up clients for ARVs and to initiate treatment.

Phase 3: Initiation of ARV treatment by nurses in selected cases

Clinical responsibilities:

- Evaluate clients eligible for ARVs, and initiate treatment in selected cases according to PALSA PLUS guidelines (STRETCH edition). Refer others to the ARV doctor.
- Continue follow-up of clients on ARVs, including interpretation of bloods and represcription of ARVs. Refer to a doctor only if problems arise.

Record-keeping:

- Complete these forms as required: *ARV BASELINE ASSESSMENT, DRUG READINESS TRAINING RECORD (INCL. ARV TREATMENT COMMENCED), ARV NURSE-FOLLOW-UP, REFER TO TREATMENT SITE.*

Training:

- Attend PALSA PLUS support visits in clinic.

TASKS AND ROLES: ARV DOCTOR (treatment site)

Phase 1: Site preparation and start decentralisation of HIV care

Clinical responsibilities:

- Baseline assessment of eligible patients including exclusion of active TB.
- Initial prescription of ARVs.
- Follow-up of ARV clients (5, 10 and 14 weeks, thereafter 3 monthly) including interpretation of CD4 and viral loads.
- Drug substitution (toxicity) and regimen changes (failure).

Record-keeping:

Unchanged.

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Clinical responsibilities:

- Continue baseline assessment of eligible patients and initial ARV prescription.
- Refer all stable ARV clients (from STRETCH clinics only) back to the ARV nurse for further follow-up.
- Continue to monitor all complex cases, and if appropriate substitute drugs or change regimens.

Record-keeping:

- Unchanged.

Training and support:

- Provide support to ARV nurses now assuming responsibility for monitoring of stable ARV clients. Be prepared to accept calls from nurses with queries, and provide feedback on referred cases.

Phase 3: Initiation of ARV treatment by nurses in selected cases

Clinical responsibilities:

- Continue baseline assessment of eligible patients and initial ARV prescription. Attempt to fast-track these cases as only complex or advanced cases are now referred for doctor assessment.
- Refer all stable ARV clients (from STRETCH clinics only) back to the ARV nurse for further follow-up.
- Continue to monitor all complex cases, and if appropriate substitute drugs or change regimens.

Record-keeping:

- As before.

Training and support:

- Provide support to ARV nurses now assuming responsibility for initiation of ARVs in selected clients. Be prepared to accept calls from nurses with queries, and provide feedback on referred cases. Consider visiting the ARV nurse at the clinic to offer support and discuss cases.

TASKS AND ROLES: PHARMACIST/PHARMACY ASSISTANT (treatment sites/assessment sites/combined sites)

Phase 1: Site preparation and start decentralisation of care

At assessment or combined sites:

- Ensure adequate supplies of cotrimoxazole are available.
- Assess storage facilities for ARVs:
  - Is it possible to integrate ARV storage/dispensing/issuing with the usual pharmacy services at the clinic?
  - Would extra shelving in the pharmacy/clinic help? (If yes, contact the provincial STRETCH co-ordinator to arrange.)
- Assess communication systems for Phases 2 and 3. Is a working fax machine in place? If not, contact the facility manager or ARV co-ordinator to arrange.
- Review filing system for ARVs. Suggest filing by ZU number to facilitate quick access when client returns to collect medication.
- Review system for identifying and returning uncollected medication. Are clients' details forwarded to the ARV nurse/community health workers for tracing?
- Review arrangements for transporting ARVs from treatment to assessment sites. How can these be streamlined?

At treatment sites:

- Assess communication systems for Phases 2 and 3. Is a working fax machine in place? If not, contact the facility manager or ARV co-ordinator to arrange.
- Review arrangements for transporting ARVs from treatment to assessment sites. How can these be streamlined?

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

At assessment or combined sites:

- As before. Your will need to accommodate larger numbers of ARVs as clients no longer collect any medication from the treatment site (unless problems arise.)

At treatment sites:

- As before. Once the central pharmaceutical depot for chronic medication, including ARVs, is running, pharmacists at treatment sites will integrate with existing services at that facility.

Phase 3: Initiation of ARV treatment by nurses in selected cases

At assessment or combined sites:

- As before. Storage space for ARVs will need to increase dramatically now as clients start treatment at the clinic, increasing the total number of clients receiving ARVs from that facility.

At treatment sites:

- As before.

TASKS AND ROLES: ADMIN CLERK (treatment/assessment/combined sites)

Phase 1: Site preparation and start decentralisation of care

HIV clients not yet on ARVs must be seen by PHC services nurses, and no longer the ARV nurse (unless referred).

At assessment/combined sites:

- Direct HIV clients not yet on ARVs to a PHC nurse (with their HIV folder).
- Completion and capturing of forms (and filing of folders afterwards!) must continue for HIV clients who are seen by PHC services nurses.
- Bookings:
  - for HIV clients not yet on ARVs: PHC services nurses, not the ARV nurse (unless referred).
  - for clients on ARVs: ARV nurse or treatment site as usual.
  - for baseline assessments: treatment site as usual.
- Encourage HIV clients to bring their ID books with them so that the ID number can be captured. This is useful for tracking deaths among clients on HIV, which are usually not reported to the clinic. NO ID BOOK DOES NOT MEAN NO CARE. Simply encourage those clients who have them to bring them in at subsequent visits.
- Review filing system:
  - Consider filing by ZU number to enable easy retrieval.
  - Are more filing cabinets needed? If yes, contact the facility manager or ARV co-ordinator to arrange.

At treatment sites:

- Continue as usual.

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Clients on ARVs will now be mainly followed-up by nurses (STRETCH facilities only) unless problems arise.

At STRETCH assessment/combined sites:

- As before but now book follow-up appointments for ARV clients with the ARV nurse, and not the treatment site unless specifically instructed.

At treatment sites:

- For clients from STRETCH clinics: ask the doctor to indicate clearly whether the next appointment should be at the treatment site or at the STRETCH clinic.
- Note: Clients from non-STRETCH clinics must continue with follow-up as usual (i.e. shared between the assessment and treatment sites).

Phase 3: Initiation of ARV treatment by nurses in selected cases

Selected clients will now be started on ARVs by the ARV nurse at STRETCH assessment/combined sites.

At STRETCH assessment/combined sites:

- Book initiation visits for clients selected for nurse-managed ARVs. Work out the number of clients who can be booked for initiation visits each day with the ARV nurse (see Avoiding "peaks" and setting targets on page 11).

At treatment sites:

- Note that clients referred from STRETCH clinics for baseline assessments are ill or have a co-morbid condition and should be seen by the doctor as soon as possible.

TASKS AND ROLES: DATA CAPTURER (treatment/assessment/combined sites)

Phase 1: Site preparation and start decentralisation of care

HIV clients not yet on ARVs must be seen by PHC services nurses, and no longer the ARV nurse (unless referred).

At assessment/combined sites:

- Completion and capturing of forms (and filing of folders afterwards!) must continue for HIV clients who are seen by PHC services nurses.
- Ensure adequate supplies of forms are provided to nurses as follows:
  - PHC services nurses: *VOLUNTARY COUNSELLING AND TESTING, HIV FOLLOW-UP: NOT YET ON ARVS*
  - ARV nurses: *VOLUNTARY COUNSELLING AND TESTING, HIV FOLLOW-UP: NOT YET ON ARVS, ARV NURSE FOLLOW-UP*
- ID numbers are useful for tracking deaths among clients on HIV, which are usually not reported to the clinic. Please ensure that they are carefully captured onto MediTech. Note that NO ID BOOK DOES NOT MEAN NO CARE.
- Address problems with MediTech and networks urgently. Don't allow backlogs to grow!

At treatment sites:

- Continue as usual.

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Clients on ARVs will now be mainly followed-up by nurses (STRETCH clinics only) unless problems arise.

At STRETCH assessment/combined sites:

- As before but arrange for supplies of *ARV BASELINE ASSESSMENT* forms to be delivered to the ARV nurse in preparation for Phase 3.

At treatment sites:

- As before.

Phase 3: Initiation of ARV treatment by nurses in selected cases

Selected clients will now be started on ARVs by the ARV nurse at STRETCH assessment/combined sites.

At STRETCH assessment/combined sites:

- As before.

At treatment sites:

- As before.

TASKS AND ROLES: PALSA PLUS TRAINER

PALSA PLUS training in STRETCH clinics will differ from usual PALSA PLUS training as follows:

- Extra outreach sessions over a longer time period timed to coincide with critical stages of STRETCH.
- The PALSA PLUS trainer for the STRETCH clinic will be included in that STRETCH clinic support team.
- The training will make use of the special STRETCH edition PALSA PLUS guideline which includes algorithms for classifying eligible HIV clients for nurse- or doctor-managed ARVs, and more detailed recommendations for ARV monitoring.
- The supportive component of the outreach training will be increased.
- Existing PALSA PLUS trainers will be equipped for training in STRETCH clinics during a 2 day STRETCH Training the Trainer to Train (TtTtT) workshop.

Phase 1: Site preparation and start decentralisation of care

Core knowledge:

- Ensure that all clinic nurses are familiar with the content of the PALSA PLUS guideline and that the management of routine HIV care and TB is embedded in practice. This is needed to facilitate the decentralisation of routine HIV care to PHC services nurses.
- Complete training in new STRETCH edition algorithms: Enrolment in the ARV programme (guideline page 19); Monitoring the client on ARVs (guideline page 21).

Support:

- Participate in the STRETCH clinic support team (see page 6).
- Allocate time during outreach training sessions to the effects of changes brought about by STRETCH: in the facility, in roles, in responsibility.

Phase 2: Decentralisation of HIV care to PHC services nurses and ARV monitoring to ARV nurses

Core knowledge:

- As before.

Support:

- Continue involvement in STRETCH support team and PALSA PLUS training of nurses.
- Continue to nurture a relationship of trust with all staff in the clinic.
- Set aside time to be with individual nurses to ensure implementation of Phase 2 changes (see pages 13 and 14).
- Schedule weekly PALSA PLUS contact. Alternate phonecalls with clinic visits.

Phase 3: Initiation of ARV treatment by nurses in selected cases

Core knowledge:

- As before. Develop and work through case scenarios (or ask staff to bring client folders to sessions) as this helps to embed knowledge.
- Around 6 to 12 months after initiation review recognition, screening and management of lactic acidosis (guideline pages 22, 25, 32, 34) as this is when clients tend to present with this side-effect.

Support:

- Provide sensitive support around initiation of ARVs.
- If required follow the debriefing process as trained during STRETCH TtTtT: within 12 hours of critical incident or as soon as possible, individually or in a group.

SUGGESTED TIMELINE OF ACTIVITIES

MONTH	WEEK	WEEK STARTING	STRETCH SUPPORT TEAM	PALSA PLUS TRAINING	OTHER
1	1		Team convened	Outreach training	
	2				
	3		Meeting	Outreach training	
	4				
2	5		Meeting	Outreach training	
	6				
	7		Meeting	Outreach training	
	8				Clinic orientation workshop
3	9		Meeting	Outreach training	
	10				Community meeting
	11		Meeting	Outreach training	
	12				Clinic meeting to assess readiness for Phase 2
4	13		Meeting	Outreach training	PHASE 2 STARTS, Brief clients in waiting room
	14		Meeting		Brief clients in waiting room
	15			Outreach training	Brief clients in waiting room
	16		Meeting		Brief clients in waiting room
5	17			Outreach training	
	18		Meeting		
	19			Outreach training	
	20		Meeting		
6	21		Meeting	Outreach training	PHASE 3 STARTS, Brief clients in waiting room
	22		Meeting	Outreach training	Brief clients in waiting room
	23		Meeting	Outreach training	Brief clients in waiting room
	24				

Assess current level of decentalisation of HIV care

Which of the following levels of HIV care are currently handled by Primary Health Care services?

- ☐ Voluntary Counselling and Testing
- ☐ Initial CD4 count
- ☐ Routine HIV care pre-ARVs: serial CD4 monitoring, screening for TB, cotrimoxazole prophylaxis to those with Stage 3 or 4 HIV or CD4 ≤200
- ☐ Drug Readiness Training
- ☐ ARV Baseline bloods
- ☐ Issuing of repeat ARVs

Further decentralisation of HIV care needed at this clinic

Which levels of HIV care *currently* done at the ARV site could be *realistically* decentralised to Primary Health Care services at *your* clinic to enable the ARV sisters to start Phase 2 (monitoring of ARVs) and Phase 3 (initiation of ARVs)?

- ☐ Voluntary Counselling and Testing
- ☐ Initial CD4 count
- ☐ Routine HIV care pre-ARVs: serial CD4 monitoring, screening for TB, cotrimoxazole prophylaxis to those with Stage 3 or 4 HIV or CD4 ≤200
- ☐ Drug Readiness Training
- ☐ ARV Baseline bloods
- ☐ Issuing of repeat ARVs

EQUIPMENT AND SUPPLIES CHECKLIST

Item	Assess	Y/N	Notes
Waiting room and admissions			
Waiting room	Does part of the ARV waiting area need to be re-incorporated back into the general waiting room?		
Stigmatising signage	Can any signs directing HIV clients to the ARV area be removed?		
Storage of records	Is it possible for HIV and other records to be stored in a single area? Consider filing HIV records by ZU number to ensure easy retrieval.		
Filing cabinets	Are additional cabinets required?		
Drug supplies and storage			
ARVs	Where are these drugs currently stored? Is there sufficient room to accommodate a large increase in supply? Would additional shelving help?		
Cotrimoxazole	Who orders drugs for the clinic? Do they know to expect increased demand for cotrimoxazole?		
Other supplies			
EDTA tubes/vacutainer needles	Who orders these? Do they know to order increased quantities?		
Pregnancy tests	Who orders these? Do they know to order increased quantities?		
Sputa jars	Who orders these? Do they know to order increased quantities?		
HIV/ARV forms	Who orders the HIV forms? Do they know to order increased quantities of: VOLUNTARY COUNSELLING AND TESTING, HIV FOLLOW-UP: NOT YET ON ARVS, ARV NURSE FOLLOW-UP and ARV BASELINE ASSESSMENT		
Pap smear equipment	Are speculae available at the clinic? Who orders slides and spatulae? Do they know to order increased quantities?		
Other			
Scale	Does the clinic have a scale in working order?		
Laboratory transport	How are bloods transported to the laboratory? By what time should the day's bloods be drawn?		
Laboratory results	How are results returned to the clinic? How are they filed? How do you contact the lab if results are missing?		
Phone	Does the ARV nurse have access to a phone to contact the ARV doctor? Can she/he dial cell numbers?		
Phone access	Does the ARV nurse have sufficient "airtime" to contact the doctor daily? Does this need to be upgraded?		
Fax/ photocopier	Does the clinic have these? Does local area manager know of needs?		
PALSA PLUS guidelines	Does every nurse in the clinic have a PALSA PLUS guideline (STRETCH edition) and materials?		
ARV Treatment guidelines	Does every ARV nurse have a copy of the National Antiretroviral Treatment guidelines (orange book)?		
TB Diagnostic Algorithms	Are these clearly displayed in clinic consulting rooms (not the TB room as this is post-diagnosis!)		

SUGGESTED PROGRAMME FOR ORIENTATION WORKSHOP

Consider holding a half-day orientation workshop in larger STRETCH clinics, about one month before Phase 2 is scheduled to begin.
Scheduling this one mid-week afternoon will limit disruption to clinical services and ensure maximal participation by the clinic.
Ensure the clinic is informed well in advance (3 weeks) so that staff avoid making other commitments for that day.

Who should be invited?
Be inclusive. Many non-health professionals play an important role in the organisation of care at a clinic particularly during staff shortages.
Remember to invite administrative staff, voluntary health workers and cleaners.
Prepare handouts (e.g. STRETCH overview – pages 3 and 4 and relevant task and role sheets – pages 13 to 18).

Introduce STRETCH
Ideally the Facility Manager (STRETCH Team Leader) should facilitate.
Start off by acknowledging that ARVs are working for clients in the Free State, but that too few clients are receiving them.
Highlight the verticalisation of HIV care and the logistical burden this imposes on clients (multiple visits, high transport costs etc.).
Explain what STRETCH stands for.
Describe the step-wise process for introducing STRETCH (see handout).
Explain that phase 1 has already started. Ask about PALSA PLUS training? How is it going? Is it useful?

Allow time for review and discussion
Allow 10 minutes of quiet time (not tea-time) for staff to review handouts. Allow plenty of discussion time.
Review needs equipment and supplies checklist, and actions taken, with clinic staff.
List any additional requirements identified.

Seek buy-in and commitment
Set dates for starting Phases 2 and 3 together. Avoid starting on a Monday or Friday.
Contain anxiety to rush hundreds of clients onto ARVs immediately. Highlight the need for sustainability and avoiding burnout.

Close
Honour the health care workers who have introduced ARVs and comprehensive HIV care under difficult circumstances.
Summarise key activities in Phase 2 and start date.

PROVINCIAL PERMISSION FOR STRETCH

FREE STATE PROVINCE

Knowledge Translation Unit
University of Cape Town Lung Institute
PO Box 34560
Groote Schuur
7937

Dear Dr Fairall

RE: APPROVAL FOR STRETCH (Streamlining Tasks and Roles to Expand Treatment and Care for HIV) PROJECT

The Free State Department of Health requires that it restructure its Comprehensive Care, Treatment and Management of HIV and AIDS Programme to urgently expand antiretroviral treatment access in the province and reduce waiting times between qualifying for and starting antiretroviral treatment.

STRETCH is a health system intervention which aims to decentralize HIV care, including monitoring of stable patients and initiation of antiretroviral treatment in selected cases, to primary care nurse practitioners without compromising treatment outcomes. Components of the intervention include PALSA PLUS (Practical Approach to Lung Health and HIV/AIDS in South Africa) educational outreach training, a clinical algorithm which stratifies patients as high or low risk and allows nurses to identify patients for nurse- or doctor-managed care, re-defining roles of generalist and ARV nurses and ARV doctors and the establishment of multidisciplinary facility support teams to support intervention facilities.

In order to ensure that the health service offer to patients is not compromised and that the revised clinical roles can be safely and efficiently assumed by health care workers, the STRETCH intervention will first be piloted in 16 of the province's 31 CCMT facilities. The intervention is structured in 3 phases. Phase 1 includes PALSA PLUS training and has already begun as part of provincial implementation of PALSA PLUS; phase 2 involves the decentralization of HIV care to generalist nurses, and ARV monitoring to ARV nurses and is scheduled to begin in July 2007; phase 3 involves the decentralization of ARV initiation to ARV nurses in selected cases and is scheduled to begin in August 2007.

The effectiveness of the STRETCH intervention on programme outcomes will be evaluated by means of a randomized controlled trial commencing in July 2007. After one year, an interim analysis will be completed and the results reported to the F

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State Department to decide whether or not to continue the trial, or stop the trial and rollout the intervention or withdraw it.

As accounting officer and acting Head of the Department of Health I grant approval subject to ethics Committee approval for the STRETCH project to proceed as described, including implementation in 16 pilot facilities, and evaluation by means of a randomized controlled trial. Ethics approval can be obtained at any University or Research Organisation.

Yours sincerely

RD Chapman

DR RD CHAPMAN
ACTING HEAD: HEALTH

DATE: 16/3/07

Department of Health • Departement van Gesondheid • Lefapha La Bophelo Bo Botle
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ETHICS PERMISSION FOR STRETCH TRIAL EVALUATION

UNIVERSITEIT VAN DIE VRYSTAAT
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Ms H Strauss 2007-05-24

DR L FAIRALL
HEAD: KNOWLEDGE TRANSLATION UNIT
UNIVERSITY OF CAPE TOWN LUNG INSTITUTE (PTY) LTD
P O BOX 34560
GROOTE SCHUUR
7937

Dear Dr Fairall

ETOVS NR 75/07
PRINCIPAL INVESTIGATOR: DR L FAIRALL
PROJECT TITLE: A CLUSTER RANDOMIZED CONTROLLED TRIAL OF AN EDUCATIONAL AND ORGANISATIONAL INTERVENTION TO EXPAND ANTIRETROVIRAL TREATMENT ACCESS IN PUBLIC-SECTOR PRIMARY CARE CLINICS IN SOUTH AFRICA: THE STRETCH (STREAMLINING TASKS AND ROLES TO EXPAND TREATMENT AND CARE FOR HIV) TRIAL – STUDY PROTOCOL REC NO IRB00001938.

- You are hereby informed that the following were approved by the Ethics Committee on 22 May 2007 subject to the approval of the Chief Professional Nurses to prescribe HAART:
  - ***Detailed Protocol***
  - ***Protocol Synopsis***
  - ***Information Sheet for Qualitative Evaluation***
  - ***Consent Form for Qualitative Evaluation***
  - ***Consent form for Economic Evaluation***
- The following documents are used by the Ethics Committee as guidance documents: Declaration of Helsinki, ICH, GCP and MRC guidelines on bio medical research. Clinical trial guidelines 2000 Department of Health RSA, Ethics in Health Research: Principles structure and processes Department of Health RSA 2004, the Constitution of the Ethics Committee of the Faculty of Health Sciences and the guidelines of the S.A. Medicines Control Council as well as laws and regulations with regard to the Control of Medicines.
- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
- The Committee must be informed of any serious adverse event and/or termination of the study.
- A progress report should be submitted within one year of approval of longterm studies and a final report at completion of both short term and long term studies.
- Please refer to the ETOVS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

for **PROF BB HOEK**
CHAIR: ETHICS COMMITTEE

PHARMACEUTICAL AND THERAPEUTICS COMMITTEE PERMISSION FOR EXPANDED PRESCRIBING PROVISIONS

MINUTES OF THE PROVINCIAL PHARMACEUTICAL AND THERAPEUTICS COMMITTEE HELD ON 7 MARCH 2007 AT 13H00 IN THE COMMITTEE ROOM (ROOM 3) NATIONAL HOSPITAL

1. **OPENING AND WELCOME**
Dr. Chapman, Acting Head of Health welcomed everyone present. Dr. Chapman apologized to members of the meeting for having to leave at 14h00 because of another important meeting at the Office of the Legislature. Dr. Chapman requested that Mrs Hettie Marais, Manager, Pharmaceutical Services act as chairperson in his absence.
Dr. Chapman thanked all the members of the meeting for their dedication. Dr. Chapman resigned with the Department of Health.
Me Marais and other members wished him well with his new appointment and assured him that he will be sorely missed.

2. **ATTENDANCE AND APOLOGIES**

Attendance

Dr. R.D. Chapman (Chairperson)	Head Office
Me H. M. Marais	Pharmaceutical Services
Me. M. Smith	Pharmaceutical Services
Me. B. Molongoana	RPM Plus
Me. T.P. Oosthuizen	Pharmaceutical Services
Me E.A. Schabort	District pharmacist, DC19
Dr. E.C. Wolmarans	Bethlehem
Dr. H. Dippenaar	Family Medicine
Prof. Odendaal	Dept. Anaesthetics (Pain clinic)
Dr. L. Keet	Dept. Paediatrics
Dr. M. Tshabalala	Treatment of HIV&AIDS Programme
Z. Loots	Pharmacy Universitas Hospital
Prof. Hoek	Department of Paediatrics,Universities
G.J. Kgasane	Pharmacist Pelonomi Hospital
Prof. D.K. Stones	Dept. Paediatrics
Prof. B.W.J. Van Rensburg	Dept. Internal Medicine, Nephrology
F. Gumbi	District Pharmacist, DC16

Apologies
Dr. M. Schoon

3. **CONFIRMATION OF AGENDA**
Agenda approved.

4. **APPROVAL OF MINUTES OF PREVIOUS MEETING**
Approved

5. **MATTERS ARISING FROM PREVIOUS MINUTES**

5.1 **Gadopentetic Acid/Magnevist**
Gadobotrol/Gadovist – Mrs Oosthuizen
The cheaper of the above 2 items can be used in future, depending on the contracts. **LEVEL - 4**

Gadobenic Acid (Gadobenate Dimeglumine = Multihance)
APPROVED – LEVEL 4

5.2 **Raloxifene – Dr. B.J. Van Rensburg**
Dr. Van Rensburg absent from meeting.
Standover for next meeting. (Presenters must be present at meetings to present products.)

5.3 **Teriparatide – Dr. B.J. Van Rensburg**
Dr. Van Rensburg absent from meeting.
Standover for next meeting. (Presenters must be present at meetings to present products.)

5.4 **Calcium Sandoz Eff Tablets**
APPROVED: LEVEL 3 – Tertiary hospital only. (For patients who has difficulty to swallow)

6. **FEEDBACK NEDL**

6.1 Prof Hoek stated that they are busy with the Tertiary list.

6.2 Me Marais stated that she sent a list of all specialist items to NEDLC.

6.3 Dr. Dippenaar stated that they already revised 4 of the Primary Care EDL Book chapters.

6.4 If there is a need for a drug which is included in the new EDL, but which was not previously included in the Free State Code list, a letter, addressed to the PTC is necessary from the relevant department. The letter should state clearly for what indication, the suggested prescribing level as well as the estimated usage.

6.5 If there is a need for another form of a drug which is included in these lists, only a letter is necessary from the relevant department as above.

7. **STRETCH IDEA: NURSE INISIATED ARV TREATMENT – Dr. M. Tshabalala**
The objectives of the presentation were the following:

- To motivate for the provision of antiretrovirals at the 16 STRECH intervention facilities within the context of a rigorous randomized controlled trail evaluation
- To motivate for trained nurse practitioners to initiate first-line antiretroviral treatment in eligible HIV positive adults, provided the conditions listed are met.
- To motivate for trained nurse practitioners to re-prescribe antiretroviral to adults already commenced on treatment provided the indications listed are met.
- To motivate for trained nurse practitioners to provide up to 3 months of ARV's to adults at a time once stabilized on treatment to reduce the burden imposed by follow-up visits to clinics.

The meeting took the following decisions:

PHARMACEUTICAL AND THERAPEUTICS COMMITTEE PERMISSION EXPANDED PRESCRIBING PROVISIONS

Bullet 1: That the normal distribution chain for Hospital level medicines in the province will also be used for antiretrovirals

The Bullets 2 and 3 were approved in principal subject to the following:

(i) Approval has to be obtained from the Ethics Committee to register the program as a trial (research)

(ii) The role of MCC plus the jurisdiction of National Department of Health and allocation of a number will be determined.

(iii) The following protocols must be included in the proposal to the ethics committees:

a) To motivate for trained nurse practitioners to initiate first-line antiretroviral treatment in eligible HIV positive adults provided the conditions listed are met.

b) To motivate for trained nurse practitioners to re-prescribe antiretrovirals to adults already commenced on treatment provided the indications listed are met.

Bullets 4 was not approved.

Nurses cannot dispense the medication as they need to be licensed

Three months medication will not be issued according to a previous decision taken by the PTC on 10 August 2006.

8. NEW MATTERS

8.1 Novo Seven – Dr. Marius Coetzee/Prof Stones
APPROVED – LEVEL 5 (Hematology)ONLY :
Off label emergencies with their approval.
(Universitas Hospital: Prof. Stones & Dr. Marius Coetzee)

8.2 Perfalgan (Paracetamol) IV Injection – Prof Odendaal
APPROVED – LEVEL 3 (ICU & Anaesthesiologists)
Note should be taken that Perfalgan should be infused over no longer than 15 minutes. It is less effective if infused over a longer period. It is safe and effective if infused over less than 15 minutes.
Dosage: Adults and Adolescents
Weight : > 50kg: 1g/administered up to 4x a day.
Minimum intervals between each administration are 4 hours.
Maximum daily dosage is 4 gram.
Prof Odendaal will write protocol

8.3 Losec Mups - Dr. Kriel/Keet
APPROVED – LEVEL 4 (Specialist Peadiatricians)
See pages 39,40,41 and 48 of EDL Paediatrics 2006.

9. CORRESPONDENCE

9.1 Captopril Tablets in the Treatment of Hypertensive Emergencies instead of Nefedipine - Dr. NSC Saidiya
NOT RECOMMENDED
Dr. Dippenaar will discuss the issue at NEDLC meeting and give feedback.

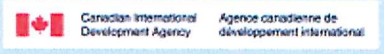
9.2 Melladerm Ointment 20 Gram (An addition) – Prof Sinclair

CONTACT LISTS

Clinic names and contact details for mangers and co-ordinators at the clinics involved in the trial have been removed to protect their confidentiality.

Compiled by the Knowledge Translation Unit, University of Cape Town Lung Institute
in partnership with the Free State Department of Health.

STRETCH has been developed with the aid of research grants from the
Canadian International Development Agency and Irish Aid.



Appendix D

Protocol for sub-study on integration

As submitted to the Ethics Committee of the Faculty of Health Sciences, University of the Free State

Protocol

Integrating HIV care into primary health care services in the Free State: process and impact.

Kerry Uebel MB BS (University of Sydney) BSc Med (University of Sydney) MFam Med (University of the Free State)
Knowledge Translation Unit, University of Cape Town Lung Institute, University of Cape Town, Cape Town, South Africa and
Free State Department of Health, Bloemfontein, South Africa

PhD student
Department of Internal Medicine
Faculty of Health Sciences
University of the Free State

Promoter Professor W. Mollentze
Co-Promoter Professor HCJ. van Rensburg

Summary

Background

South Africa has one of the largest burdens of HIV in the world and it is estimated that up to half a million new patients every year develop AIDS and will die unless they are given treatment. The South African Department of Health has been providing highly active antiretroviral treatment (HAART) to those with AIDS or CD4 $\leq$ 200 cells/μl since 2004. Vertical implementation has resulted in limited primary health care involvement and bottlenecks in the delivery of ARVs. Despite the best efforts of provincial departments less than 30% of those who need ARVs are receiving them. Innovative changes to the vertical nature of the programme and the roles of health care workers are needed to increase access to ARVs. A randomized controlled trial (the STRETCH trial) is currently being conducted amongst the 31 assessment sites in the Free State. The two main interventions are allowing nurses to prescribe ARVs for certain patients and promoting the integration of HIV and ARV care into PHC services to see if this can decrease the mortality among enrolled patients awaiting HAART while maintaining the quality of care for those already on treatment. It seems likely that integration of HIV care into PHC services may be a crucial factor in increasing access to ARVs.

Aim:

The aim of this study is to develop implement and evaluate the process of integration of HIV and ARV care into the PHC services that refer patients to the ARV clinics in the trial and to analyse the effect of this on the main outcomes of the STRETCH trial. This study will provide important information about how best to implement ARV delivery services to expand access to treatment for those who need it.

Methods/ design:

This study will concentrate on the integration of HIV and ARV services into PHC services. It will firstly explore develop and implement a practical means of integrating HIV and ARV care into primary health care services. Secondly it will develop and then pilot an evaluation tool which will then be used to evaluate the progress of this integration of HIV and ARV care during the STRETCH study. The results of this evaluation will then be compared with the outcomes of the study to see if integration of these services does indeed increase access to ARVs

Introduction

Worldwide, in 2007, 33.2 million people were estimated to be living with Human Immunodeficiency Virus (HIV) with 2.5 million acquiring new HIV infections and 2.1 million deaths due to Acquired Immunodeficiency Syndrome (AIDS). The global prevalence rate is estimated at 1% and this is thought to have peaked somewhere in the late 1990s. The largest burden of disease is in Sub-Saharan Africa with 22.5 million people living with HIV and an estimated prevalence of 5% which is also thought to have peaked in the late 1990s. Three countries in the region are showing signs of a recent decline in the prevalence rates Cote d'Ivoire, Kenya and Zimbabwe (UNAIDS 2007).One other country Uganda managed to achieve a remarkable decline in prevalence rates in the 1990s from 17% in the early 1990s to 6% in 2002 but their rate has remained stable since then. (Mugyenyi 2006)

Southern Africa is the worst hit region in the world. Thirty five percent of the world's population with HIV live in Southern Africa. Eight countries in Southern Africa (South Africa, her 6 neighbours and Zambia) all have adult prevalence rates above 15 %.(UNAIDS 2007). South Africa is the country with the largest number of people living with HIV estimated at 5.5 million (UNAIDS 2006) with a prevalence rate of 16.2% in people aged 15-49 as reported by UNAIDS. (UNAIDS 2007) South Africa's neighbours have similar high burdens with prevalence rates in this age group 15-49 years of 25.9% in Swaziland, 25.2% in Botswana, 23.5% in Lesotho, 18% in Zimbabwe (UNAIDS 2007)and 16% in Mozambique (UNAIDS 2006).

The only signs of a possible decline in the epidemic in South Africa come from the National HIV and Syphilis prevalence survey report from 2006. This survey of HIV and syphilis prevalence amongst pregnant women who attend public antenatal clinics showed a national prevalence of 29.1% in 2006 down from the 2005 figure of 30.2% but the downward trend needs to be checked against figures from 2007 which are yet to be released. (National HIV and Syphilis Prevalence Survey 2006)

There are marked variations across the nine provinces of South Africa with KwaZulu Natal, Free State and Mpumalanga the worst affected and the Western Cape the least affected. Estimated prevalence rates in 2005 in adults 15-49 years were Mpumalanga 23%, KwaZulu Natal 21.9% and Free State 19.2% with Western Cape 3.2% (HSRC 2005). The HIV prevalence in pregnant women across the provinces shows a similar trend with KwaZulu Natal the highest at 39.1%, Mpumalanga next highest at 32.1% and Free State at 31.1% and the Western Cape again the lowest at 15.1%. Eight of the nine provinces showed a decline in prevalence rates from the 2005 figures but the Free State antenatal prevalence rate increased from 30.3% in 2005 to 31.1% in 2006 .(National HIV and Syphilis Prevalence Survey 2006)

It is thought that 350,000 deaths in South Africa in 2006 were due to AIDS. (National Department of Health 2007) Although it is rarely recorded as the cause of death on death certificates, figures released by Statistics South Africa (Stats Online 2006) have shown that the death rates in women aged 20-39 have more than tripled from 1997-2004 and more than doubled in men aged 30-44. These increases have been attributed to AIDS. The Health Systems Trust has released estimated crude death rates per1000

in South Africa. These have almost tripled from 4.9 per 1000 in 1994 to 14.2 per1000 in 2005 (Health Systems Trust 2007).

There were increasing international calls in the early 2000s to rollout ARV programmes in resource poor countries to try and tackle the looming social and economic crises. These calls were accompanied by pledges of international funding, through funds such as the Global fund, and efforts to decrease drug prices. (Mukherjee 2003). There was also increasing discussion of the research priorities needed to inform such a huge international undertaking. The research priorities include exploring appropriate models of delivering ARV care whether through specialist centres, comprehensive primary health care centres or by using home based care models, exploring what laboratory monitoring is appropriate, how to support adherence and how to train and allocate different cadres of health care workers (Jaffar 2005)(Rabkin 2002). There were collaborative efforts in a few African countries such as Uganda to increase access to ARVs starting in 2001 and 2002 but the progress was slow with high prices of drugs proving a big barrier. (Mugyenyi 2006)
The South African National Department of Health finally published an Operational Plan in late 2003 to rollout ARVs in the public sector. The department cited falling drug prices and agreements with drug companies as the impetus for finally starting the rollout. In reality there had also been much civic pressure after protracted delays due to lack of political commitment and a government attitude of denialism about the link between HIV and AIDS and the effectiveness of ARVs versus alternative therapies (van Rensburg 2006). The Comprehensive Plan for the Care, Management and Treatment of HIV and AIDS (National Department of Health 2003)included provision of ARVs to adults with CD4 $\leq$ 200 cells/μl or AIDS and children with CD4<15% or stage 3. It set ambitious targets of having at least one ARV service point in every district health service by the end of the first year of the programme and achieving 100% coverage of all people who needed ARVs (an estimated 1.4 million people) after 5 years.
By late 2006, three years into the programme, the country's nine provincial health departments had established 273 accredited treatment facilities (Aids Law monitoring project 2006), but less than 30% of patients who needed ARVs were receiving them. (Dorrington et al 2006)(Hassan et al 2006) Many of the ARV service points had reached saturation as the demand for antiretroviral treatment had exceeded both the anticipated demand for HAART, and the capacity of health services. Although the operational plan's stated aim was to provide comprehensive HIV care in an integrated fashion the management and delivery of the rollout was done as a vertical programme. ARV service points had to be accredited by the National Department and had their own funding, staff, facilities and record keeping. These procedures were put in place by the National Department in an effort to ensure rapid rollout and good quality of care (National Department of Health 2003). There were good reasons to run it as a vertical program. AIDS is an epidemic, the treatment is specialised and is life long and requires high levels of adherence and patient education. All this was to be implemented urgently in a health system known to be under strain, all conditions which call for vertical programmes to try and ensure good quality rapid rollout (Victora et al 2004) The result is a well funded and well run service but one that is not

well integrated into the public health services. There have been concerns raised that such a vertical implementation threatens to undermine the public health system by drawing limited financial and human resources away from the public health system into the high profile HIV and AIDS programmes (van Rensburg 2006) (McCoy 2005) Victora and his colleagues have pointed out that even though vertical programme delivery has its place for rapid rollout in struggling health systems it is not an end in itself and has to be broadened into a more horizontal programme to be sustainable and to support comprehensive health systems (Victora et al 2004) There is also a realisation that South Africa will not be able to improve the coverage of people who need ARVs with the current model of ARV delivery. Analysis of projected patient numbers from a number of sites has shown that the current model cannot really increase enrolment of new patients and continue to care for those already on treatment. The Khayelitsha ARV programme which started in May 2001 is the oldest public ARV site in South Africa and has three clinics attached to community health centres in the township of Khayelitsha in Cape Town. In 2006 they were enrolling 1,500 new patients a year. But they estimate that there will be 3-4,000 new people a year in Khayelitsha for the next ten years, who will need to start ARVs. These services would have to more than double their enrolments per year and would accumulate four times the amount of patients in care. They do not have the capacity to do this unless the services are broadened to many more clinics in the area. (Boulle 2006) Similar patterns have been emerging from other sites. Barker (2007) reports that ARV service points in Mhlontlo district in the Eastern Cape reached capacity and were unable to enrol more than 20 patients a month whereas they estimated 100 people a month from their district needed to be enrolled.

The National Department of Health's Strategic plan for HIV and AIDS and STIs for South Africa 2007-2011 acknowledges that there are still many people with AIDS in South Africa who are not able to access treatment. In 2006 it was estimated that 230,000 adults and 25,300 children were on antiretrovirals but that 540,000 adults and 27,000 children were sick with AIDS and not yet on antiretroviral therapy (Dorrington et al 2006)(Hassan et al 2006) The Plan has set two main ambitious targets The first is to reduce new infections by 50% by 2011 and the second is to increase the number of new people accessing antiretrovirals each year incrementally to 420,000 per year or 80% of those who need it by 2011 (National Strategic Plan 2006) It acknowledges the need to provide "..universal access to a comprehensive package of treatment for HIV including ARVs therapy and integration of HIV and tuberculosis care." (National Strategic Plan 2006, page 57) The importance of integrating ARV therapy into the primary health care structure is underlined by the specific goal that 90% of care for HIV should be provided by PHC staff by 2011. The plan also specifically mentions task shifting including nurses initiating and monitoring ARV therapy and involving lay counsellors in pricking for HIV testing and support roles in the ARV programme. Their goals here are also ambitious. The plan aims to have 60% of patients initiated on ARVs by nurses and 70% on ARVs monitored by nurses by 2011.
Given the vertical nature of the programme so far and the saturation of the ARV service points, their ambitious goals can only be realised by reversing the vertical nature of the rollout and integrating HIV treatment and care services into the primary

health care services. There is evidence that such an approach can work. Ford et al (2006) reported on the work of Medicine san Frontier in the Lusikisiki area of the Eastern Cape where integrating ARV service, including initiation of ARVs, into primary health care clinics increased coverage of projected numbers of people needing ARVs to 95%. This was done while maintaining people in care and maintaining a 90% viral load suppression rate amongst patients enrolled at clinics.(Ford et al 2006) Barker (2007) reported on the experience in 2 rural areas Mhlontlo in the Eastern Cape and Umkhanyakude in KwaZulu Natal. Both districts initiated a programme of involving all primary health care clinics in the provision of HIV and ARV care services such as routine HIV care, ARV drug readiness training and chronic ARV care and both districts managed to improve coverage significantly with the Umkhanyakude district reaching their target of 500 new patients enrolling each month. (Barker 2007)

The Free State ARV Rollout

The ARV rollout began in the Free State in mid 2004 using the principles of the National Comprehensive Plan but with important modifications in that accredited ARV sites included:

- Treatment sites- These were doctor run sites usually at district hospitals where patients would be initiated and monitored on ARVs.
- Assessment sites-. These were nurse run sites usually at existing primary health care clinics or community health centres where patients would be screened and prepared for ARVs before and after referral to the doctor at the treatment site for initiation of ARVs, and have monthly follow-ups and be able to collect medication
- Combined sites- These were nurse run assessment sites where a doctor visited regularly to initiate and monitor patients on ARVs

These sites were connected with the so-called "walk-through-model" where patients could access HIV testing at PHC clinics then go to assessment sites for CD4 counts. If they needed ARVs they would then go to treatment sites for medical assessment then back to the assessment site for drug readiness training then back to treatment site for initiation of ARVs then back to the assessment site for monthly follow up and then back to the treatment site 6 monthly for monitoring of ARVs. Although the stated aim was to ground the programme in the clinics and have it nurse run the reliance on doctors to initiate and monitor ARVs made the system laborious for patients and staff alike. (van Rensburg 2006)

These modifications in the Free State were done to try and embed the provision of HIV care and treatment in the primary health care services by establishing a nurse driven service at certain accredited clinics at a primary health care level within district health services The establishment of combined sites was in an effort to provide accessible services particularly to rural areas especially Xhariep district where all 7 sites were combined sites (van Rensburg 2006)

Over the period 2004-2005 sites were accredited in two phases. In phase 1 by the end of 2004 four treatment sites 13 assessment sites and three combined sites had been set up. By the end of phase2 there were an additional four treatment sites and a satellite treatment site, six assessment sites and nine combined sites. Thus at the end of phase

2 there were eight treatment sites, a satellite treatment site, 19 assessment sites and 12 combined sites. ARV service points were established in 14 of the 20 municipalities of the Free State by the end of 2005. (van Rensburg 2006)
Despite the stated aim of the Operational Plan of 2003 that the provision of HIV care and treatment should be integrated into comprehensive primary health care, the programme was implemented in the Free State as well as nationally in a vertical fashion "In subsequent implementation ART indeed emerged as a vertical programme *par excellence,* separately and centrally financed, run by separate ARV personnel mainly or exclusively assigned to the task, conducted in physically separate areas or sections in facilities and with segregated filing, registering and recording systems" (van Rensburg 2006 page 60). The programme was implemented in a vertical fashion despite repeated calls by managers in the Free State to implement it in a comprehensive manner (van Rensburg 2006)

The effect of the vertical nature of the ARV rollout has been to isolate the provision of HIV health care within these assessment and treatment sites. Basic services for the care of patients such as HIV testing, CD4 counts and the provision of routine HIV care for those not yet needing ARVs, have not been widely available in PHC services apart from accredited clinics and even in these clinics was often restricted to ARV appointed nurses . Up till recently even an HIV test has, in some areas of the Free State, only been available in the assessment site and not in the Primary Health care clinics. Even so patients from many of the PHC clinics in the Free State who have been able to access HIV testing, have had to go to assessment sites to access CD4 counts and those who do not yet require ARVs either do not get follow-up routine care (6 monthly CD4s weight staging and TB screening) or have to go to the assessment site 6 monthly to do so.

Du Plooy (2006) comments that the ARV programme in the Free State has had both positive and negative effects on the patients, the staff and on other services provided by the clinics For the patients the treatment had offered improved health and hope but large numbers of patients being seen in inadequate facilities created huge space and equipment shortages. For the staff they benefited from the ARV training and saw they could now offer effective comprehensive treatment to their patients but there was increased workload both for the ARV nurses and for other nurses picking up the slack and trying to provide all the other clinic services. All this was happening in an environment of continuing staff shortages, moving of existing staff to ARV services, a perceived lack of support from management and lack of appropriate counselling services for staff. The nurses related that the ARV programme positively impacted other programmes because the care was now more comprehensive and integrated in one clinic and yet created more stress on non ARV nurses trying to run all the other services.

Looking at the impact of the ARV programme on patient outcome in the Free State much has been achieved but much still needs to be done. For those patients who do receive HAART their outcome is good. A recent marginal structural model analysis comparing survival among adult patients who did receive HAART in the programme with those who didn't shows that HAART, as provided by the Free State public-sector

programme, reduces mortality by as much as 86% (Fairall et al in press) However the programme has been overwhelmed by the demand for treatment, and many patients die after enrolling but before receiving treatment presumably because of the bottlenecks in the system. Of 4570 patients with CD4 counts <350 and not yet on ARVs followed for one year or until death, 53% died, the majority (87%) before receiving HAART (Fairall et al in press). Multiple factors are contributing to the high mortality rate among eligible patients not yet on HAART. Staff at assessment sites have been overwhelmed by the number of patients needing HIV testing, routine CD4 counts and HIV care, drug readiness training and monthly nurse follow-up for patients on ARVs. All of these services have at times been associated with long delays in appointments in various assessment sites. Even with this overwhelming uptake of the services, there are still patients who delay HIV testing until late when they are very ill, and they either do not have time to access treatment or die soon after starting. The vertical nature of the programme contributes to this delay by continuing the stigmatisation of HIV as patients have to go to the ARV clinic to access even basic HIV care services. The other major source of delays in appointments for eligible patients is the reliance on doctors to do all baseline assessments and initiation of ARVs as well as regular reviews (3 or 6 monthly) and repeat prescriptions on all patients. In many of the assessment sites there have been delays in getting appointments with the treatment site doctors particularly for new patients.

The vertical nature of the implementation of the ARV rollout in the Free State in concentrating HIV and ARV care in ARV sites provided by ARV staff has been successful in getting good quality ARV services started in the public sector. But it has been characterised by crowding of facilities, shortages of staff, pressures on other services in clinics and an inability to provide ARVs timeously to all the patients who are trying to access these facilities. With the high prevalence rate in South Africa, HIV is one of the commonest chronic diseases. Therefore services to treat HIV need to be as widely available as those for the other chronic diseases like diabetes mellitus and hypertension. The vertical programme needs to be urgently broadened and integrated into all existing health facilities in a way that strengthens these services. (McCoy et al 2005) (Victora 2004) HIV and ARV services such as VCT, routine CD4 counts and care for those not yet needing ARVs, Drug Readiness training and baseline bloods and issuing of repeat ARVs could be done by nurses and counsellors at all Primary Health Care clinics (Ford et al 2006) (Barker 2007). This would also go a long way to reducing the stigma that is still retarding our response to this epidemic. The continuation of a vertical, stigmatising model of provision of HIV services, is actually unsustainable.

The STRETCH Trial

STRETCH is an acronym for Streamlining Tasks and Roles to Expand Treatment and Care for HIV. It is a pragmatic trial being run in a partnership with the Free State Department of Health with the STRETCH coordinator (the researcher) based in the offices of the directorate responsible for the Free State ARV rollout and so results should be based on the real situation confronting the health system in Southern Africa. The results should therefore be relevant and applicable. (Walley et al 2007). The

motivation for the trial is to try and address some of the bottlenecks in the current ARV rollout and therefore increase access to ARVs for people who need them while at the same time evaluating the effectiveness of the interventions. This is in line with the goals of the National Department of Health's stated intentions to increase enrolment each year of new people needing ARVs to 80% by 2011 (National Department of Health 2006). The STRETCH trial is a pragmatic cluster randomized controlled trial currently in its early stages in the 31 phase 1 and phase 2 assessment sites in the Free State. The 24 clinics in 4 of the 5 districts were stratified by referral hospital-based treatment site and then randomised. The 7 combined sites in Xhariep were not stratified before randomisation as there are no centralised hospital based treatment sites in this district. There are 16 intervention clinics and 15 control clinics scattered evenly across the 5 districts of the Free State. There are 2 main experimental interventions:

1. Professional nurses at interventions sites to initiate and repeat ARV prescriptions for uncomplicated and stable patients
2. Routine HIV care to be decentralised to primary health care services

The STRETCH study aims to evaluate whether these interventions will decrease the number of patients dying before they can get ARVS while maintaining the quality of care given to patients who do receive ARVs. The primary outcomes are

1. Mortality of patients with CD4 counts < 350 and not yet on ARVs
2. Time to starting ARVs in patients who have a CD4< 200 or are in stage 4
3. Viral load suppression rates of patient on ARVs for 6 months or more.

Two cohorts of patients are being recruited to allow simultaneous evaluation of the effectiveness of the intervention on mortality among patients on the waiting list and on medium to longer term HAART treatment outcomes.
The first cohort includes all patients infected with HIV, and enrolled at the 31 assessment sites with CD4 levels under 350cells/μl and not yet on ARVs. People with CD4<350 in the Free State are known to have a high mortality rate and it is therefore this group whom the study could potentially affect.
The second cohort includes patients who have been on HAART for 6 months or more and are alive and in care at the start of the trial. In this group of patients quality of care will be monitored by viral load suppression rates.
The investigation and exclusion of TB in HIV positive patients by staff at ARV clinics is carried out by use of the TB algorithm included in PALSA Plus nurse guidelines in use at all ARV sites and currently being trained to nurses in primary health care clinics in the Free State. Regular CD4 counts and viral loads are taken as part of routine clinical care by clinic staff. Clinical data on patients such as weight and TB diagnosis are also routinely collected by clinic staff. This clinical information is routinely entered onto the provinces computerized information system (Meditech) and will be used for the analysis of the STRETCH study. South African national identity numbers are requested from patients and are used to link the clinical information with death registration details on the national population registry. The clinical information will also be linked with the province's electronic tuberculosis register and laboratory data. The STRETCH project is employing seven data clerks to help find missing

information on patients enrolled in STRETCH and will enter this data into the Meditech system

The STRETCH trial is being implemented in three phases.
Phase 1 The preparatory phase included setting up implementation teams in each clinic and training all Professional nurses at the 16 intervention clinics in the use of guidelines for enrolling and monitoring patients on ARVs and beginning the process of integrating HIV and ARV services into PHC clinics.
Phase 2 The professional nurses start monitoring patients and repeating ARV prescriptions for people who are responding well to ARVs and referring to the doctor only patients who are not doing well. Integration of HIV and ARV services into PHC services continues.
Phase 3 The Professional nurses start initiating and monitoring ARVs on patients they identify as being uncomplicated and referring to the doctor only patients who are potentially complicated. Integration of HIV and ARV services into PHC clinics continues.

The trial is currently in phase 3 in most clinics. The STRETCH project is being implemented by a provincial STRETCH coordinator (the researcher) working in partnership with the Free State Department of Health and particularly the ARV coordinators, and local and district managers responsible for the 31 assessment sites.

A qualitative study is also being conducted at the same time to assess the perceptions of staff managers and patients of the impact of STRETCH on the ARV programme

Complex Health Interventions
The STRETCH study is a complex health intervention as the intervention has several components. This can introduce difficulties in evaluating the intervention as these various components can be subject to more variations than in trials of drugs. (Campbell et al 2000). There can be difficulties in defining, developing, documenting and reproducing these components of complex interventions. Campbell et al (2000) recommend that in trials of complex health interventions there should be a phased approach to the development and implementation of the intervention. They describe theoretical formulation of the intervention followed by qualitative assessments of the context and opinions of stakeholders as to the applicability and acceptability of the theoretical intervention so that it can be reformulated before implementation of the intervention. Once these interventions are being implemented there is much to be gained in evaluating the process of how they are implemented. Oakley et al (2006) describe how such a process evaluation can add explanatory power and improve the reproducibility of the intervention.

In the STRETCH trial, work needs to be done to develop the most effective way to implement the integration of HIV and ARV care into primary health care services. This work can be done by the STRETCH coordinator (the researcher) in working with the Department of Health. A process evaluation of the implementation of this integration of care during the STRETCH trial should contribute valuable information

on effective strategies to improve access to ARVs. Because of anecdotal reports of the effect of integrating HIV and ARV care into PHC clinics on increasing the number of people accessing ARVs (Ford et al 2006) (Barker 2007), it is likely that this integration will be a significant factor in the outcomes of the trial i.e. whether the trial results in increasing access to ARVs. A process evaluation and analysis of correlation with increasing access to ARVs, such as proposed in this protocol, should provide valuable information about how to intervene in health systems to increase access to ARVs for patients in high HIV prevalence areas

Hypothesis

My hypothesis is that the integration of HIV and ARV care into the PHC services is crucial to increasing patient access to ARVs and that the primary outcomes of the STRETCH study will be positively affected by the progress made in integrating HIV and ARV care into PHC services both within that assessment site and amongst the PHC clinics that refer patients to that assessment site

Aims

The aim of this study is to develop, pilot, implement and evaluate a practical approach to integrating HIV and ARV care into the Primary Health care services and to analyse whether this integration improves access to ARVs

Objectives

The three main objectives of this study are:

1. To develop and implement in an effective manner the integration of HIV and ARV care into primary health care services as part of the STRETCH study
2. To evaluate the progress and levels of integration of HIV and ARV care into the PHC services
3. To monitor the impact of integrating these services into PHC services on staff patients and clinic functioning
4. To see if there is any correlation between levels of integration of HIV and ARV care into the PHC services and improved access to ARVs as defined by the primary outcomes of the STRETCH trial

Methods

Objective 1 Development of the intervention

There will be a phased approach to the development of the intervention. Steps 1-3 have already been completed and step 4 has begun.

Step 1 Theoretical formulation of the intervention.

The integration of HIV care into primary health care services was initially described in the protocol for the STRETCH study as decentralizing initial and 6 monthly CD4 counts from the ARV nurses in the assessment sites to generalist nurses in the assessment and referring PHC clinics. This initial proposal was based on the "walk through model" described for patients to access ARVs in the Free State (see Intro) According to this model all patients diagnosed as HIV positive at PHC clinics were to go to ARV nurses at assessment sites for initial and 6 monthly CD4 counts

Step 2 Exploration of the proposal.
The proposal to decentralise routine HIV care to generalist nurses needed to be discussed and introduced to staff at ARV sites to assess feasibility.

This exploration has already been done as part of phase 1 of the STRETCH study. In February 2007 the researcher visited all 31 assessment sites (control and intervention clinics) to discuss the project with staff and other stakeholders such as the district ARV coordinators. At that visit an assessment was done by the researcher of the practicalities of the STRETCH project and particularly the two main interventions. These site visits and discussions revealed that there was wide variation across the province with the levels of integration of HIV care and that the "walk through model" was not being used in all clinics. Some of the clinics had already routine HIV care and Drug readiness training into PHC clinics while other assessment sites were still doing HIV testing as well as all CD4 counts as none of their PHC services were even doing HIV tests. Staff feedback on the initial theoretical proposal to simply decentralise initial and 6 monthly CD4 counts was that a spectrum of HIV and ARV care, not just CD4 counts, needed to be integrated into primary health care clinics to free up staff at assessment sites and that this intervention needed to be practical, flexible and responsive to local context.

Step 3 Reformulation of the intervention
The proposal to decentralise routine HIV care to primary health care services needed to be reformulated in response to feedback from stakeholders.

This reformulation has already been done in continuing work in phase 1 by the researcher. A checklist was developed to be used by each of the 16 intervention sites (Appendix 1). In this checklist were included six components of HIV and ARV care that the staff had identified could be integrated into PHC services. These six were:

1. HIV testing
2. Initial CD4 counts
3. 6 monthly CD4 counts and routine HIV care pre ARVs
4. Drug readiness training
5. Baseline bloods for work-up for ARVs
6. Issuing of repeat monthly ARVs for stable patients

This checklist was included in a STRETCH toolkit which is an implementation guide developed by the STRETCH research team and distributed for use at each of the 16 STRETCH clinics.

The staffs at each STRETCH clinic were asked to assess which of these components of HIV and ARV care was currently available at PHC clinics. They were then asked to assess which other components, currently done at the ARV services, could be realistically integrated into the PHC services in their area as part of the STRETCH study. (Appendix 1)

Step 4
Implementation of the intervention
The checklist developed by the researcher needed to be implemented as part of the STRETCH trial

The implementation of this integration of HIV and ARV care has already begun as part of Phase 2 of the STRETCH trial. Staff at each of the 16 intervention clinics has identified components of HIV and ARV care they think could be integrated into PHC services. The process of integration is being implemented by clinic staff and managers, ARV coordinators, local area managers and district managers in the Department of health all working in conjunction with the researcher.

Objective 2 Evaluation of the process of integration of HIV and ARV care
This objective is also to be implemented in steps. Steps 1-2 have already been completed.

Step 1. Development of an evaluation tool
A quantitative evaluation tool needed to be designed.

This has already been done by the researcher during phase 1 of the trial. Information gathered during the first visit to the 31 clinics was used to design a set of questions for structured interviews. The aim of these interviews was to evaluate the level of integration in the clinic and amongst their referral PHC clinics. The 6 components of HIV and ARV care identified by clinic staff and other components of integrated care such as TB services and family planning were used to design questions to assess the level of integration of these services.

Step 2. Piloting of the evaluation tool
The evaluation tool needed to be piloted.
This has already been done by the researcher on a second round of visits to the 16 intervention clinics. Structured interviews were conducted by the researcher with the clinic manager or senior ARV nurse at these 16 intervention clinics during planned visits in July and August 2007 to assess readiness to start phase 2 of the STRETCH trial. The results of these pilot interviews helped to review the structured interview questions (Appendix 2) and will be used to give a baseline score for integration at these 16 clinics.

Step 3. Evaluation of the intervention
The structured interview questionnaire (Appendix 2) will be used to evaluate the implementation of the integration of HIV and ARV care.

Structured interviews will be conducted by the researcher at all 31 clinics i.e. both intervention and control clinics at 4 monthly intervals to assess the levels and progress of integration of HIV and ARV services into PHC clinics for the duration of the STRETCH trial. The interview will assess whether PHC staff at the assessment site and their referral PHC clinics can provide patients with HIV related health care such as VCT, CD4 counts, Drug Readiness Training and repeat supplies of medication such as ARVs and cotrimoxazole as well as TB diagnosis and family planning. Answers to each of these questions will be discussed and placed by consensus between the interviewer and interviewee in one of two or three categories which would indicate the service is not integrated, partially integrated or fully integrated. These answers will then be scored as either 0 (not integrated) 1 (partially integrated) or 2 (Fully integrated) these scores will be totalled to give each clinic a score for the level of integration of HIV care at each visit. The scoring system will be applied retrospectively to the pilot interviews done as part of the STRETCH study at the 16 intervention sites in phase1 referred to above, to allocate a baseline score for each intervention clinic.

There are possible limitations to the structured interviews. The information gathered will be the opinion of the clinic manager or senior ARV nurse at the assessment site who is being asked to give information on not only their clinic but clinics that refer patients to them. There will be no independent corroboration from the referring clinics. Another potential weakness is that the interviews will be done by the researcher who is also responsible for implementation of the STRETCH project and interviewees may be biased by this. Efforts will be made to corroborate the findings of the interviews during the work of the researcher with the relevant managers and coordinators as part of the work to implement the study with field notes made at time of clinic visits. The structured interview questions will be repeated at 5 clinics soon after the first interview by a second person familiar with the project in an attempt to validate the questionnaire.

<u>Objective 3 Monitoring the impact of integrating HIV and ARV care into PHC services on staff, patients and clinic functioning at PHC clinics</u>

This will be a sub study in the STRETCH qualitative study of the impact of the STRETCH project on the ARV programme overall.
Focus groups will be conducted with staff at 3 primary health care clinics where some integration of HIV and ARV care has taken place and at the STRETCH clinics that are referral assessment sites for these primary health care clinics. Individual interviews will be conducted with the local area managers responsible for these three pairs of clinics. A researcher from the team conducting the STRETCH qualitative study will conduct these focus groups and interviews.

Three primary health care clinics and their STRETCH assessment sites will be identified. They will each be from different districts and will be chosen to represent referring clinics from large (usually urban), medium sized and small ARV sites

(usually rural). The focus groups will explore the experience of staff at these clinics as to the impact of the integration of HIV and ARV care on the patients, the staff and clinic functioning. Notes of the findings will be taken and the discussion will be recorded. Interviews will explore the managers view of the impact of the integration of HIV and ARV care on the patients, the staff and clinic functioning. Transcripts and notes will be analysed for common themes by the researcher and the team from the STRETCH qualitative study

Objective 4 Compare levels of integration with outcomes of STRETCH study

Analysis of the results

Although this process of integrating HIV and ARV care into PHC services is only being actively facilitated at the 16 STRETCH intervention clinics, the process is not limited to these intervention clinics. The steps being taken to integrate HIV and ARV into primary health care clinics care are being made in the Free State Department of Health by managers and coordinators and are affecting control clinics as well. Therefore it is likely that some integration of HIV and ARV care will take place at primary health care clinics that refer patients to control clinics and that this may independently influence outcomes.

From the structured interviews the results of the baseline integration score, final integration score and the change in the score during the period of the study at all 31 clinics (intervention and control) will be compared to the three main outcomes to be used in the STRETCH study. If there is a range of scores for integration, these scores will be compared to outcomes at each clinic to see if there is any correlation. If however the integration scores are clustered clinics will be assigned to 4 groups based on their final integration score and their intervention or control status. These 4 will be:

1. Intervention clinic well integrated
2. Control clinic well integrated
3. Intervention clinic poorly integrated
4. Control clinic poorly integrated

The outcomes of the STRETCH study will be compared in each of these groups to see if the integration of HIV and ARV services was an independent factor in these outcomes.

Ethical considerations

The STRETCH study (both the Randomised controlled trial and the qualitative study) has received ethical approval from the University of Cape Town ethics committee (reference number 142/2007) and from the University of the Free State ethics committee (reference number ETOVS 75/07**).** The protocol for this study has been given ethical approval, as an addendum to the STRETCH trial, by the UFS ethics committee. This study is an observational study and written consent for the interviews will be obtained from the clinic managers of the 31 assessment sites involved (Appendix 3 & 4). Written approval has also been given by the senior management of the Free State Department of Health.

Time span

This study will run in parallel with the STRETCH study for between 12-24 months. The STRETCH study will run for 2 years from September 2007 but there will be an interim analysis at one year to assess if there are clear differences in outcomes for patient from STRETCH and control clinics. If outcomes are clearly worse in the intervention arm the study will be terminated. If however there are clear benefits the study will be terminated in the interests of rolling out the intervention to all assessment sites in the Free State. If there are no clear results at the interim analysis the study will run for the full 2 years.

Budget

This study will be run as a part of the STRETCH study and therefore costs for personnel and travel to the sites are already covered by funding for the STRETCH study. No extra travel is required as regular support visits are already planned to the 31 assessment sites. The only cost is for paper to make 3 copies of the structured interview and consents for each clinic~ R200.

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APPENDICES

Appendix 1
Integration checklist as included in STRETCH Toolkit for intervention clinics
This tool was developed by the researcher to help the clinic staff at intervention clinics to identify components of HIV and ARV care that could be realistically integrated into their referral PHC clinics as part of the STRETCH trial

ASSESS Current level of decentralisation of HIV Care

- ***Which of the following levels of HIV care are currently handled by the Primary Health Care services?***
  - ❑ ***Voluntary Counselling and Testing VCT***
  - ❑ ***Initial CD4 count on diagnosis of HIV***
  - ❑ ***6 or 12 monthly CD4 Pap, Staging and TB exclusion (CD4 >201 not yet needing ARVs) Routine HIV care***
  - ❑ ***Drug readiness training***
  - ❑ ***Baseline bloods***
  - ❑ ***Repeat supply of ARVs kept at PHC clinic***

ASSESS Further decentralisation of HIV care needed at this clinic

- ***Which levels of HIV care <u>currently</u> done at the ARV site could be <u>realistically</u> decentralised to Primary Health Care services at <u>your</u> clinic to enable the ARV sisters to start Phase 2 (monitoring of ARVs) and Phase 3 (initiation of ARVs)?***
  - ❑ ***Voluntary Counselling and Testing VCT***
  - ❑ ***Initial CD4 count on diagnosis of HIV***
  - ❑ ***6 or 12 monthly CD4 Pap, Staging and TB exclusion (CD4 >201 not yet needing ARVs) Routine HIV care***
  - ❑ ***Drug readiness training***
  - ❑ ***Baseline bloods***
  - ❑ ***Repeat supply of ARVs kept at PHC clinic***

Appendix E

Integration questionnaire

Referred to in the article presented in Chapter 5 as Additional file 1 and in the article presented in Chapter 6 as Supplemental digital content 1.

Survey of integration of HIV care in ARV clinics and their referral PHC clinics

Clinic and personal information

Name of clinic_____

Town/city_____ District_____

Date of interview_____

Interviewer_____

Job description of interviewee_____

Number of Professional nurses at clinic_____

Number of staff nurses at clinic_____

Number of enrolled nurse assistants at clinic_____

Number of ARV professional nurses at clinic_____

Number of ARV staff nurses at clinic_____

Number of lay counsellors_____

Number of referring PHC clinics in same town_____

Number of referring clinics in nearby towns_____

Number of mobile clinics from this clinic_____

Comments on clinic function_____

_____

_____

Diagnosis staging and routine HIV care

1. If a patient needs an HIV test at your clinic who is performing this test?
   - o ARV nurses at your clinic only
   - o PHC and ARV nurses at your clinic

2. If a patient needs an HIV test at one of your referral PHC clinics
   - o None of your referring clinics can do an HIV test
   - o Some of your referring PHC clinics can do an HIV test
   - o Most of your referring PHC clinics can do an HIV test

3. At your clinic who does the initial CD4 count for a newly diagnosed HIV positive patient
   - o ARV nurses at your clinic only
   - o PHC and ARV nurses at your clinic

4. If a patient is diagnosed HIV positive at one of your referring PHC clinics is it possible to access their initial CD4 count at that clinic?
   - o None of your referring clinics
   - o Some of your referring PHC clinics
   - o Most of your referring PHC clinics

5. If a patient at your clinic needs routine HIV care i.e. 6 or 12 monthly CD4, Pap and HIV Staging (for people with CD4 >200 not yet needing ARVs), who provides such care?
   - o ARV nurses at your clinic only
   - o PHC and ARV nurses at your clinic

6. Is it possible for a patient from one of your referring PHC clinics to access routine HIV care at that clinic?
   - o None of your referring clinics
   - o Some of your referring PHC clinics
   - o Most of your referring PHC clinics

7. If a patient at your clinic is stage 3 HIV but does not yet need ARVs, who can provide them with Cotrimoxazole prophylaxis
   - o ARV nurses at your clinic only
   - o ARV and TB nurses at your clinic only
   - o PHC and ARV and TB nurses at your clinic

8. If a patient from one of your referring PHC clinics needs Cotrimoxazole prophylaxis is it possible for them to get it at the PHC clinic?
   - o None of your referring PHC clinics
   - o Some of your referring PHC clinics
   - o Most of your referring PHC clinics

9. If patient at your clinic has symptoms of TB, who does the TB investigation)
   - o TB nurses at your clinic only
   - o TB and ARV nurses only
   - o PHC TB and ARV nurses at your clinic

Patients enrolling and on followup on ARVS

10. If a patient on ARVS at your clinic comes to fetch ARVs and needs family planning who can give it to them
    - o Family Planning nurse only?
    - o Any nurse at your clinic?

11. If a patient on ARVs is also on Cotrimoxazole prophylaxis do they fetch it
    - o At the same place that they fetch their ARVs?
    - o At your clinic but on the PHC side?
    - o At their own PHC clinic?

12. When patients at your clinic need to go to Drug Readiness Training who does the training?
    - o ARV site nurses do all three sessions
    - o ARV site nurses with Lay counselors assisting

13. When patients from your referring PHC clinics need to go to Drug Readiness Training who does the training?
    - o None of your referring PHC clinics
    - o The nurses or counselors at some of your referring PHC clinics
    - o The nurses or counselors at all of your referring PHC clinics

14. When patients from your clinic are about to start ARVs and need Baseline bloods who takes these bloods?
    - o ARV nurses only
    - o PHC and ARV nurses at your clinic

15. When patients needing ARVs from your referring PHC clinics need baseline bloods who can take these bloods
    - o None of your referring PHC clinics
    - o Some of your referring PHC clinics
    - o Most of your referring PHC clinics

16. When patients from your clinic on ARVs come for monthly follow-up nurse visits, who can see them
    - o ARV nurses only
    - o PHC and ARV nurses at your clinic

17. When patients on ARVs from one of your referring PHC clinics, need to come for monthly follow-up nurse visits, can they go to their PHC clinic?
    - o None of your referring PHC clinics
    - o Some of your referring PHC clinics
    - o Most of your referring PHC clinics

18. Where do patients from your clinic fetch their repeat supply of ARVs
    - o From ARV nurse
    - o From ARV pharmacy
    - o From main pharmacy at your clinic

19. Is it possible for patients from your referring PHC clinics who are on ARVs to fetch their repeat supply of ARVs from their own PHC clinic?
    - o None of your referring PHC clinics
    - o Some of your referring PHC clinics
    - o Most of your referring PHC clinics

Appendix F

Information sheet for Integration questionnaire

University of Cape Town
Lung Institute (Pty) Ltd

George Street
Mowbray, 7700
P O Box 34560
Groote Schuur 7937

Tel. No. (021) 406 6979
Fax No. (021) 406 6691

(Reg. No. 2006/000209/07)

Structured interviews to evaluate decentralization of HIV care as part of STRETCH trial
Information sheet for clinic managers

The objective of this research is to evaluate the progress of decentralization of HIV and ARV care to Primary health care services in your clinic and in clinics that refer patients to you. Decentralization of HIV and ARV care to primary health care services has been identified as a possible way of increasing patients access to ARVs and as such is one of the important components in the STRETCH study. We are requesting that you participate in this interview as a means to monitor this process of decentralization of HIV and ARV care so that we can find out if indeed it does improve access to ARVs.

The interview will take about twenty minutes and you will be asked to describe which levels of HIV and ARV care are available and in which clinics. Your name will be recorded on the notes of the interview but will not be used in reports of the findings.

This research has been formally approved by the University of the Free State Health Sciences Ethics Committee Contact Details 051 405 8512 email gndkhs.md@mail.uovs.ac.za

Contact details for the researcher:
Dr Kerry Uebel
084 900 1645
051 408 1707
uebelke@fshealth.gov.za

Appendix G

Consent form for Integration questionnaire

University of Cape Town
Lung Institute (Pty) Ltd

George Street
Mowbray, 7700
P O Box 34560
Groote Schuur 7937

(Reg. No. 2006/000209/07)

Tel. No. (021) 406 6979
Fax No. (021) 406 6691

Structured interviews to evaluate decentralization of HIV care as part of STRETCH trial
Consent form for clinic managers

REF no.: ETOVS 075/07

I agree to participate in a research project evaluating the effects of decentralizing HIV and ARV care to primary health care clinics to support the expansion of antiretroviral treatment services in the Free State. I have had an opportunity to ask questions and discuss this study with the research team and have received satisfactory answers to my questions. I have also read the subject information sheet provided to me.

I will participate in the study under the following conditions:

1. I will participate in interviews with the researcher to collect information about the functioning of this clinic and the clinics that refer to this clinic. I agree to allow the research team to use the information gained by my participation in the research in reports and research publications, but understand that my privacy and confidentiality will be protected.
2. I understand that I am free to withdraw from the study at any time without having to give a reason for withdrawing.

…… …… Date ……
(NAME IN BLOCK LETTERS) SIGNATURE

Manager/ARV nurse at……Clinic

The following should be signed by the Investigator responsible for obtaining consent:
As the Investigator responsible for this research or as a designated deputy, I confirm that I have explained to the participant named above, the nature and purpose of the study being *undertaken.*

…… …… Date ……
(NAME IN BLOCK LETTERS) SIGNATURE

Appendix H

Copy of letter from the Ethics Committee, Faculty of Health Sciences, University of the Free State granting ethical permission to conduct the STRETCH trial

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Direkteur: Fakulteitsadministrasie / Director: Faculty Administration
Fakulteit Gesondheidswetenskappe / Faculty of Health Sciences

Research Division
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Ms H Strauss

2007-05-24

DR L FAIRALL
HEAD: KNOWLEDGE TRANSLATION UNIT
UNIVERSITY OF CAPE TOWN LUNG INSTITUTE (PTY) LTD
P O BOX 34560
GROOTE SCHUUR
7937

Dear Dr Fairall

ETOVS NR 75/07
PRINCIPAL INVESTIGATOR: DR L FAIRALL
PROJECT TITLE: A CLUSTER RANDOMIZED CONTROLLED TRIAL OF AN EDUCATIONAL AND ORGANISATIONAL INTERVENTION TO EXPAND ANTIRETROVIRAL TREATMENT ACCESS IN PUBLIC-SECTOR PRIMARY CARE CLINICS IN SOUTH AFRICA: THE STRETCH (STREAMLINING TASKS AND ROLES TO EXPAND TREATMENT AND CARE FOR HIV) TRIAL – STUDY PROTOCOL REC NO IRB00001938.

- You are hereby informed that the following were approved by the Ethics Committee on 22 May 2007 subject to the approval of the Chief Professional Nurses to prescribe HAART:
  - ***Detailed Protocol***
  - ***Protocol Synopsis***
  - ***Information Sheet for Qualitative Evaluation***
  - ***Consent Form for Qualitative Evaluation***
  - ***Consent form for Economic Evaluation***
- The following documents are used by the Ethics Committee as guidance documents: Declaration of Helsinki, ICH, GCP and MRC guidelines on bio medical research. Clinical trial guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles structure and processes Department of Health RSA 2004, the Constitution of the Ethics Committee of the Faculty of Health Sciences and the guidelines of the S.A. Medicines Control Council as well as laws and regulations with regard to the Control of Medicines.
- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
- The Committee must be informed of any serious adverse event and/or termination of the study.
- A progress report should be submitted within one year of approval of longterm studies and a final report at completion of both short term and long term studies.
- Please refer to the ETOVS reference number in correspondence to the Ethics Committe secretariat.

Yours faithfully

for **PROF BB HOEK**
CHAIR: ETHICS COMMITTEE

Appendix I

Copy of letter from the Head of the Free State Department of Health granting permission to conduct the sub-study on integration

FREE STATE PROVINCE

TO:	**Dr Kerry Uebel** **STRETCH Coordinator**
RE:	**Permision to extend scope of STRETCH study in ARV clinics in the Free State**
DATE:	10 March 2008

Department of Health
Departement van Gesondheid
Lefapha La Bophelo Bo Botle
FREE STATE PROVINCIAL GOVERNMENT
A Healthy and Self-reliant Free State Community

Dr Uebel

Your letter dated 25 February 2008.

Receipt of the above mentioned letter is hereby acknowledged.

Kindly be informed that the Executive Management has granted approval to extend scope of STRETCH study in ARV clinics in the Free State Province.

The following conditions should be observed:

- The participants should give consent.
- Participation should be voluntary
- Study should not interfere with patient care.
- Participants should be protected.

Kind regards

Prof PL Ramela
Head: Health

HEAD: HEALTH
HOOF: GESONDHEID
2008 -03- 12
PROF P.L. RAMELA
P.O. BOX / POSBUS 227
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1st February 2008

Professor Ramela
Head of Department
Free State Department of Health
Bophelo House

Dear Professor Ramela,

Re Permission to extend scope of STRETCH study in ARV clinics in the Free State
Title: **Developing implementing and evaluating a practical approach to integrating HIV care into primary health care services in the Free State**

I would like to inform you of a research project, which is an extension of the scope of the STRETCH study, and ask your permission to conduct this study at clinics in the Free State ARV clinics which are currently involved in the STRETCH project. I am employed by the UCT Lung Institute in a partnership with the Free State Department of Health to implement and coordinate the STRETCH project which as you know is a randomized controlled trial to try and increase patients access to Antiretroviral therapy. There are two main interventions in the STRETCH project;
1 Training and allowing Professional nurses to initiate and monitor ARVs in selected patients
2. Decentralising some HIV and ARV services to Primary Health Care clinics.

I would like to do my study on the process of this decentralisation at each of the 31 ARV clinics involved in the STRETCH project. I have registered as a PhD student at the University of the Free State and am in the process of formalizing my protocol. I have approval from the Ethics committee of the University for this study as an addendum to the approval for the STRETCH study approval number is ETOVS 75/07.

To do this study I would like to conduct interviews with the clinic managers or ARV nurses at each of the 31 clinics in the STRETCH project at four monthly intervals to assess which HIV and ARV services have been decentralized to PHC clinics I have attached a copy of the interview questionnaire that I will use during the study.

The information from these interviews will be used to help analyse the results of the STRETCH trial and will be published in scientific journals. The results will help us to inform the Department of Health of effective ways to increase patients access to antiretroviral therapy which is one of the main goals of the National Strategic Plan of 2006

Thanking you

Dr Kerry Uebel
STRETCH Coordinator
Comprehensive HIV and AIDS Management Directorate
Free State Department of Health
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Appendix J

Copy of letter from the Ethics Committee, Faculty of Health Sciences, University of the Free State granting ethical permission to conduct the sub-study on integration as an addendum to the STRETCH trial

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Ms H Strauss

2008-02-14

DR KE UEBEL
COMPREHENSIVE HIV AND AIDS MANAGEMENT DIRECTORATE
FREE STATE DEPT OF HEALTH
BOPHELO HOUSE
CORNER OF CHARLES AND HARVEY STREETS
BLOEMFONTEIN
9301

Dear Dr Uebel

ETOVS NR 75/07
PROJECT TITLE: A CLUSTER RANDOMIZED CONTROLLED TRIAL OF AN EDUCATIONAL AND ORGANISATIONAL INTERVENTION TO EXPAND ANTIRETROVIRAL TREATMENT ACCESS IN PUBLIC-SECTOR PRIMARY CARE CLINICS IN SOUTH AFRICA: THE STRETCH (STREAMLINING TASKS AND ROLES TO EXPAND TREATMENT AND CARE FOR HIV) TRIAL – STUDY PROTOCOL REC NO IRB00001938.

- You are hereby informed that The Ethics Committee approved the following at the meeting held on 12 February 2008:

  **Addendum to the above-mentioned study: "Developing implementing and evaluating a practical approach to integrating HIV care into primary health care services in the Free State.*

- Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.

- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

- The Committee must be informed of any serious adverse event and/or termination of the study.

- A progress report should be submitted within one year of approval of longterm studies and a final report at completion of both short term and long term studies.

- Kindly refer to the ETOVS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

for .....
PROF BB HOEK
CHAIR: ETHICS COMMITTEE

List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANOVA	One way analysis of variance
ART	Antiretroviral therapy
ARVs	Antiretrovirals
AZT	Zidovudine
CI	Confidence Interval
DOH	Department of Health
FS	Free State
HIV	Human Immunodeficiency virus
HR	Hazard Ratio
ID	Identity Document
rmANOVA	Repeated measures one way analysis of variance
NHLS	National Health and Laboratory Service
NSP	National Strategic Plan
OP	Operational Plan
PALSA PLUS	Practical Approach to lung Health and HIV/AIDS
PHC	Primary Health Care
STRETCH	Streamlining tasks and roles to expand treatment and care for HIV
TAC	Treatment Action Campaign
TB	Tuberculosis
VCT	Voluntary Counselling and Testing
WHO	World Health Organization
WIDER	Workgroup for Intervention Development and Evaluation Research

Summary

HIV care programmes in many low and middle income countries were initially vertically run programmes with funding, facilities and staff designated only for HIV care. One of the strategies thought to be important in scaling up HIV care programmes to reach all people in need of treatment is to integrate HIV care into primary care services. There are many reports of approaches to the integration of HIV care into primary care services but there is little good quality evidence of its effectiveness in improving patient outcomes.

In the Free State Province of South Africa the first four years of the public antiretroviral treatment rollout, saw a vertical approach to ART delivery with incremental establishment of designated ART sites. Patients initiated on ART had good outcomes, but by 2007 only an estimated 25% of those needing ART in the province accessing treatment.

In an attempt to improve access to ART in the province, and provide evidence of effectiveness, two interventions were piloted in a randomised, controlled trial – the STRETCH trial – in all 31 nurse-run ART sites in the province. The interventions were: 1) nurse initiation and monitoring of ART; and 2) the integration of HIV care into primary care services. The main outcomes of the trial were survival of patients with CD4 $\leq$350 and not yet on ART and percentage viral suppression at 12 months for those on ART. The results showed no significant improvement in patient survival between intervention and control clinics and equivalent levels of viral suppression.

This PhD research, conducted by the STRETCH trial coordinator (KU), was a sub-study of the trial, on the integration of HIV care into primary health care services. The study aimed to describe the process of developing the intervention, monitor the level of integration achieved during the trial and determine its impact on patient survival and aspects of clinic functioning.

The integration intervention was developed during consultations with managers in the Department of Health and staff at all 31 clinics. Six elements of HIV care ranging from HIV testing to monthly supply of antiretrovirals were to be integrated into the consultations of all primary care nurses within ART assessment sites (internal integration) and into the services provided by primary care clinics that had been referring patients to the ART site for HIV care (mainstreaming HIV care). Integration was implemented during the trial by local teams with the assistance of the trial coordinator.

A questionnaire was developed in order to monitor the progress of integration in all 31 clinics. Five integration scores were determined – total integration, pre-ART and ART integration, mainstreaming HIV and internal integration. These assessments showed a significant increase in integration in intervention clinics during the trial but no progress in one area of integration, namely internal integration.

A Cox proportional hazards analysis showed that higher integration scores were significantly associated with improved patient survival. Integration of pre-ART and ART care at both levels (mainstreaming HIV and internal integration) improved survival.

The findings of three qualitative studies on internal integration of HIV care showed that some factors such as high patient workload inhibited integration, some factors such as nurse and patient preferences promoted specialised care rather than integration, while other factors such as many nurses wanting to provide HIV care for their patients, promoted integration of HIV care.

This study shows that HIV care can be integrated into primary health care services and this can lead to improved survival of patients needing ART. Integration of HIV care into all consultations within primary care services is more difficult to achieve and patient and nurse preferences for how HIV care is delivered need to be explored.

Key words

Integration, primary care, universal access to ART, HIV care, vertical programmes, task shifting

Opsomming

MIV-gesondheidsorg programme in talle lae- en middel-inkomste lande was aanvanklik vertikaal bedryf met befondsing, fasiliteite en personeel afgesonder uitsluitlik vir MIV-gesondheidsorg. Een van die strategieë wat as belangrik beskou word om MIV-gesondheidsorg programme uit te brei om dit binne die bereik te plaas van alle mense met 'n behoefte aan behandeling, is om MIV-gesondheidsorg te integreer met primêre gesondheidsorg dienslewering. Daar is talle voorbeelde van hoe die integrasie van MIV-gesondheidsorg met primêre gesondheidsorgdienste benader kan word, maar daar is 'n leemte aan goeie kwaliteit bewys van die effektiwiteit van sodanige integrasie om pasiënt uitkomste te verbeter.

Die eerste vier jaar van die openbare uitrol van antiretrovirale behandeling in die Vrystaat Provinsie van Suid-Afrika was gekenmerk deur 'n vertikale benadering tot die verskaffing van ARB met die vestiging, in inkremente, van geoormerkte ARB klinieke. Pasiënte wat ARB begin gebruik het, het goeie uitkomste gehad maar teen 2007 het slegs 'n geskatte 25% van diegene in die provinsie wat ARB benodig het, toegang tot behandeling gehad.

In 'n poging om die toeganklikheid tot ARB in die provinsie te verbeter en om bewys te kon lewer van die effektiwiteit van ARB, is twee intervensies in die vorm van 'n gerandomiseerde gekontroleerde proef – die sogenaamde STRETCH proef – van stapel gestuur in al 31 ARB klinieke in die provinsie wat onder beheer van verpleegkundiges was. Die intervensies was: 1) verpleegkundige-geïnisieerde ARB en monitering daarvan; en 2) die integrasie van MIV-gesondheidsorg met primêre gesondheidsorg dienste. Die hoofuitkomste van die proef was die oorlewing van pasiënte met 'n CD4<350 en wie nog nie op ARB was nie asook die persentasie waarmee die viruslading teen 12 maande by diegene op ARB mee onderdruk kon word. Die resultate het geen betekenisvolle verbetering getoon in pasiënt-oorlewing tussen die intervensie en die kontrole klinieke nie en die vlakke van virusonderdrukking in beide groepe het ooreengestem.

Hierdie PhD-navorsing uitgevoer deur die STRETCH proef koördineerder (KU), was 'n sub-studie van die proef gerig op die integrasie van MIV-gesondheidsorg met primêre gesondheidsorgdienste. Die doelwitte van die studie was om die proses rondom die ontwikkeling van die intervensie te beskryf, om die vlak van integrasie wat bereik is gedurende die proef te moniteer en om die impak daarvan op pasiëntoorlewing asook aspekte van kliniekfunksionering, te bepaal.

Die integrasie intervensie was ontwikkel gedurende konsultasies met bestuurders in die Departement van Gesondheid en die personeel by al 31 klinieke. Ses elemente van MIV-sorg wat gestrek het van MIV-toetsing tot die maandelikse voorsiening van antiretrovirale middels, moes geïntegreer word met die konsultasies van al die primêre gesondheidsorg-verpleegkundiges wat gesetel was in ARB beoordelings klinieke (interne integrasie) asook met die dienste voorsien deur primêre gesondheidsorg-klinieke wat pasiënte verwys het na die ARB klinieke vir MIV-sorg (hoofstroming van MIV-sorg). Integrasie gedurende die kliniese proef was geïmplementeer deur die plaaslike spanne met behulp van die proef koördineerder.

'n Vraelys was ontwikkel om die vordering met integrasie in al 31 klinieke te moniteer. Vyf integrasie-tellings was vasgestel – totale integrasie, pre-ARB en ARB integrasie, hoofstroming van MIV en interne integrasie. Hierdie waarnemings het 'n betekenisvolle toename in integrasie in intervensie klinieke gedurende die proef getoon, maar geen vordering kon in een area van integrasie naamlik interne integrasie, getoon word nie.

'n Cox proporsionele gevaar analise het getoon dat hoër integrasietellings betekenisvol geassosieer was met verbeterde pasiënt oorlewing. Integrasie van pre-ARB en ARB sorg op beide vlakke (hoofstroming van MIV en interne integrasie) het ook oorlewing verbeter.

Die resultate van die drie kwalitatiewe studies op interne integrasie van MIV-gesondheidsorg het getoon dat sommige faktore soos 'n hoë pasiënt werklading, integrasie belemmer het. Sommige faktore soos die voorkeure van verpleegkundiges en pasiënte het gespesialiseerde sorg bevorder eerder dan integrasie, terwyl ander faktore soos die talle verpleegkundiges wat HIV-gesondheidsorg graag aan pasiënte wou voorsien, het die integrasie van MIV-sorg bevorder.

Hierdie studie het getoon dat MIV-gesondheidsorg geïntegreer kan word met primêre gesondheidsorgdienste en dat dit kan lei tot die verbeterde oorlewing van pasiënte wat ARB benodig. Die integrasie van MIV-gesondheidsorg met al die konsultasies binne primêre gesondheidsorgdienste is moeiliker om te bewerkstellig en die voorkeure van die pasiënt sowel as die verpleegkundige oor hoe MIV-sorg gelewer behoort te word, moet ook benut word.