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A peer adherence support intervention to improve the antiretroviral treatment outcomes of HIV patients in South Africa: The moderating role of family dynamics

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ABSTRACT

Given the severe shortage of human resources in the healthcare sector in many countries with high HIV prevalence, community-based peer adherence support is being increasingly cited as an integral part of a sustainable antiretroviral treatment (ART) strategy. However, the available scientific evidence on this topic reports discrepant findings on the effectiveness of peer adherence support programmes. These conflicting findings to some extent can be attributed to the lack of attention to the social contexts in which peer adherence support programmes are implemented.

This study explores the potential moderating role of family dynamics by assessing the differential impact of peer adherence support in different types of families, based on the theoretical underpinnings of the family functioning framework. These relationships were explored with the aid of multivariate statistical analysis of cross-sectional, post-trial data for a sample of 340 patients interviewed as part of the Effectiveness of Aids Treatment and Support in the Free State (FEATS) study conducted in the public-sector ART programme of the Free State Province of South Africa.

The analysis reveals no significant overall differences in CD4 cell count between the intervention group accessing additional peer adherence support and the control group receiving standard care. When controlling for the potential moderating role of family dynamics, however, the outcomes clearly reveal a significant interaction effect between the adherence intervention and the level of family functioning with regard to treatment outcomes. Multi-group analysis demonstrates that peer adherence support has a positive effect on immunological restoration in well-functioning families, while having a negative effect in dysfunctional families.

The study outcomes stress the need for peer adherence interventions that are sensitive to the sub-optimal contexts in which they are often implemented. Generic, broad-based interventions do not necessarily facilitate the treatment adherence of the most vulnerable patient groups, particularly those without supportive family contexts. Tailoring interventions aimed at creating a health-enabling environment to the needs of these at-risk patients should therefore be a priority for both research and policy.

1. Background

The HIV/AIDS epidemic is one of the largest health problems of current times. The virus has already killed nearly 30 million people, and another 34 million are currently infected. In absolute figures, South Africa has been the most severely affected, with 5.6 million seropositive inhabitants (UNAIDS, 2012). Nevertheless, there is hope. In November 2003, the South African Cabinet announced the *Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa*, which aimed to initiate life-saving antiretroviral treatment (ART) and prevention of mother-to-child-transmission throughout the country (Department of Health (2003); Wouters et al., 2010). In subsequent years, the public-sector ART programme has become the largest and most costly

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public health programme ever introduced in the country, with approximately 1.9 million people currently receiving antiretroviral treatment (Pillay, 2012).

The short-to-mid-term results of this public-sector ART programme are promising. A review by Barth et al. (2010) demonstrates that the proportions of patients with on-treatment success after two years of first-line therapy are comparable to those from developed countries (Barth et al., 2010). Our own research efforts in the Free State Province (the setting of this study) correspondingly demonstrate that – after two years of public-sector treatment – more than three out of four patients could be classified as a treatment success (CD4 cell count > 200 cells/μL and viral load < 400 copies/mL). The survival rate was 88.4% (Wouters et al., 2009b). A recent study conducted in KwaZulu-Natal by Bor et al. (2013) reveals a gain of 11.3 years in adult life expectancy – increasing from 49.2 in 2003 to 60.5 years by 2011 – since the implementation of public-sector ART (Bor et al., 2013). These favourable outcomes have led medical sociologists to conclude that, even in the developing world, HIV/AIDS has undergone a transition from a terminal illness to a controllable chronic condition, at least for those accessing treatment (Russell and Seeley, 2010).

These preliminary outcomes do not warrant complacency. Merely initiating life-saving ART in all eligible HIV/AIDS patients is not sufficient. As a chronic illness, HIV/AIDS requires life-long treatment adherence – and thus sufficient attention to the psychosocial dimensions of chronic disease care (Russell and Seeley, 2010; Wouters et al., 2009a, 2009b) – in order to produce such favourable outcomes in a sustainable manner. Non-adherence leads to drug resistance, and the discontinuation of ART almost certainly leads to death (Bangsberg et al., 2001; Brinkhof et al., 2010). Without sufficient attention to additional support needed to durably adhere to treatment, it is thus highly unlikely that the favourable short-term results of the Southern African ART programmes can be replicated and sustained in the decades to come – when the region is likely to be dependent upon ART as its primary curative weapon for combating the HIV/AIDS epidemic.

However, against the daunting challenge of providing additional adherence support to continually growing patient groups, one could well ask: who will do the job? (Van Damme et al., 2008). The inadequate supply and poor retention of skilled health professionals has been implicated as the single most serious obstacle to the sustainable implementation of the national treatment plan in South Africa (Van Damme et al., 2008). In 2010, 42.7% of all health professional posts in South Africa were vacant (Day et al., 2011). This shortage of human resources prevents the provision of much-needed additional adherence support to patients who are enrolled in the public-sector ART programme. As indicated by Van Damme et al. (2008) and Hontelez et al. (2012), sustainable treatment strategies thus require the mobilisation of additional human resources (Hontelez et al., 2012).

In recent years, health-systems researchers have been increasingly exploring the potential benefits of involving community-based lay adherence supporters in providing the additional care that patients need in order to durably comply with treatment guidelines. In two recent review studies (Bärnighausen et al., 2011; Wouters et al., 2012b) researchers have systematically assessed the impact of adherence-support interventions on a wide range of ART outcomes in resource-limited settings characterised by a high prevalence of HIV. According to the review findings, emerging evidence suggests that the support provided by community-based adherence counsellors could significantly improve ART outcomes in settings in which the tasks of healthcare professionals are usually limited to medical-technical services. These results illustrate the potential contribution of the community level in addressing health issues at the individual level (Wouters et al., 2012b).

Despite a general positive trend, reviews of the growing number of impact evaluations of community-based peer adherence support programmes highlight the considerable variability in the effectiveness of such support in improving ART outcomes, ranging from non-significant effects to improvements of 20% and more (Bärnighausen et al., 2011; Wouters et al., 2012b). These discrepancies have not only been attributed to measurement bias or the dissimilar characteristics of the various adherence intervention types under study, but also to the social contexts in which community-based adherence supporters operate. This suggests the need for research that incorporates these social units in the assessment of adherence support interventions (Bärnighausen et al., 2011). Inspired by social ecological theory, the recently developed Individual-Family-Community (IFC) model integrates the different social contexts impacting on HIV/AIDS care in general and on ART interventions in particular: the IFC model indicates that the impact of HIV/AIDS and its associated treatment can be mitigated by interlinked factors on the (1) individual-, (2) family- and (3) community-level (Wouters, 2012). Based on this theoretical framework, the current study argues that exploring the potential contribution of community-based initiatives to the sustainable success of ART by linking *individual* patients to *community*-based adherence support inevitably omits a crucial mediating level: the *family* unit (Hosegood et al., 2007; Li et al., 2006; Wouters, 2012).

The effect of family dynamics on physical and mental health has been studied for many years, starting with Emile Durkheim, who concluded that family life has an impact on suicide rates (Durkheim, 1951; Dyer et al., 2012). One of the enduring research topics of family sociology and psychology is why some families respond positively or constructively to challenges, while others fail to cope well under similar circumstances (Black and Lobo, 2008). Theoretically, the *Resiliency Model of Family Stress, Adjustment and Adaptation* focuses on the significance of the family's relational processes – levels of family functioning – in explaining individual and family-level differences in responding to adversity (McCubbin and McCubbin, 1996). According to this framework, families create specific, recurring styles of functioning, which express the quality of the interactions among the family members. The resulting patterns have predictive power in explaining which families and individuals will adapt negatively and positively to health-related challenges (McCubbin et al., 1996). To date, however, the perspective that family dynamics can have either a positive or a negative influence on the effect of chronic illness and associated support interventions has found very little resonance in HIV/AIDS research. Only a few studies (conducted in the United States and Thailand) have explored the potential of better family functioning as a catalyst for improved health-related outcomes in families affected by HIV/AIDS (Dyer et al., 2012; Rotheram-Borus et al., 2010) – both supporting the beneficial role of constructive family dynamics in HIV care. This situation emphasises the need for research on the moderating role of family dynamics in translating community-based adherence interventions into beneficial health outcomes at the patient level, especially in resource-limited settings characterised by a high prevalence of HIV, in which this knowledge is most needed.

The current study aims to address this research gap by exploring the potential moderating role of family dynamics in explaining the differential impact on immunologic treatment outcomes of peer adherence support in different types of families, based on the theoretical underpinnings of the family functioning framework (McCubbin et al., 1996). These relationships are explored in a sample of 340 patients in the public-sector ART programme of the Free State Province of South Africa.

2. Methods

The current study aims to test the hypothesis of the moderating role of family dynamics in peer adherence support interventions by performing a secondary statistical analysis of post-trial data of the Effectiveness of Aids Treatment and Support in the Free State (FEATS) study conducted in the public-sector ART programme of the Free State Province of South Africa. In this section, we first describe key features of the FEATS study and of the dataset used in the multivariate statistical analyses. Next, we describe the main study variables, including the peer adherence support programme implemented as part of the study. Last, we outline the statistical methods employed in the secondary data analysis.

2.1. FEATS study

The 'Effective AIDS Treatment and Support in the Free State' (FEATS) study, a three-year prospective cohort study conducted by the Centre for Health Systems Research and Development of the University of the Free State (UFS) was approved by the Ethics Committee of the UFS Faculty of Health Sciences [ETOVS 145/07 DOH-27-0907-2025] and is registered in the trial register of the National Institutes of Health [NCT00821366]. The study has two aims, namely, (a) to investigate the benefits of ART to patients, to the family members of patients on ART, and to communities at large and (b) to investigate the impact of a peer adherence support and a nutritional intervention on measures of treatment success. A Zelen-type double randomised consent design was adopted in the RCT component of the study, which is appropriate where: blinding is not practicable or possible; the use of classical randomisation and informed consent procedures significantly threatens internal validity; the interventions are highly attractive; the control group receives standard care; the study focuses on a clinically relevant objective(s) and offers important new insights (Kaptchuk, 2001; MacLehose et al., 2001; Rains and Penzien, 2005). Within such design, study participants are only offered the treatment to which they are randomised and can accept or reject treatment.

In order to yield statistically significant outcomes, 653 study participants were recruited into the study from 12 public ART clinics across five districts in the Free State Province of South Africa in 2007/08. Inclusion criteria included a minimum age of 18 years, having commenced ART within the past five weeks and residing in the town or village in which the particular health facility was located. Data collection at pre-trial baseline (October 2007–October 2008) and at post-trial follow-up (April–October 2009 and again in March–June 2010), comprised a patient interview and a household interview, inclusive of an adult questionnaire, conducted by trained enumerators using a semi-structured questionnaire, in all cases only after informed consent was obtained from study participants. First and second follow-up yielded 498 and 422 completed interviews, respectively. Survey attrition was primarily due to mortality among study participants (42.4%) and unknown whereabouts (34.1%). A full description of the randomised controlled trial can be found in the CONSORT (CONsolidated Standards Of Reporting Trials) statement (including checklist and flowchart) of the overarching FEATS study added to the article as a Supplementary File.

2.2. Dataset

In addition to the interview data gathered in the context of the FEATS study, the current study also employs clinical data extracted from patient files at the healthcare facilities and from the electronic records of the National Health Laboratory Services after obtaining written consent from all of the patients, as well as authorisation from the Provincial Department of Health. However, the matching of these two data sources limited the sample size: the resulting dataset employed includes information for a sub-sample of 340 ART patients in the FEATS study which was (a) interviewed in the first round of follow-up interviews and (b) for whom CD4 counts collected from patient files and electronic patient records could be matched to interview data. The subsample only significantly differed from the remainder of the sample on three variables: patients in the subsample were less likely to be single, to have interrupted ART and had on average a slightly higher baseline CD4 cell count. The difficulties in matching the two types of data were caused by the fact that CD4 cell counts are only routinely captured every twelve months (after the first year of treatment) as well as by logistical and health system constraints, resulting in incomplete and/or inaccurate health records (Heunis et al., 2011a,b). We only employed data gathered at the first follow-up as the matching of interview and CD4 cell-count dates at follow-up 2 resulted in insufficient statistical power to test the required statistical models (Cohen, 1988; Soper, 2013).

2.3. Study variables

2.3.1. Peer adherence support

Peer adherence support comprised *bi-weekly visits by a trained community-based peer adherence supporter* who at recruitment had been on ART for at least 12 months. Recruited peer adherence supporters were provided with four days of theoretical and practical training on antiretroviral treatment and adherence support. Peer adherence supporters were paid a monthly stipend of ZAR 500 and were required to pay two visits each week to eight ART patients over a period of 18 months. The peer adherence supporters performed a wide range of adherence counselling tasks. Their activities included asking the patients about their primary complaints, talking to them about these complaints, improving their knowledge about HIV/AIDS/ART, referring them to the facility if needed, motivating them to adhere to treatment, performing a weekly pill-count to assess adherence and, if needed, providing counselling in order to address possible barriers to medication compliance.

2.3.2. Family functioning

In the current study, and in accordance with standard practice in national household surveys, a family is defined as the patient and those individuals who (a) lived under the same 'roof' or within the same structure at least four nights per week out of the past month, (b) share food from a common source when they are together, i.e. eat together, and (c) contribute to or share in the common resource pool.

The Family Attachment and Changeability Index 8 (FACI-8), developed by McCubbin et al. (1996), was used to measure *family functioning* at the follow-up interviews – FACI-8 was not included in the baseline interview. According to the above-mentioned Resiliency Model, the outcomes of all family dynamics result in a certain degree of adaptation and functioning in the family. The culturally and ethnically sensitive FACI-8 is a 16-item scale designed especially to measure levels of family functioning, using two subscales to assess Attachment and Changeability (McCubbin et al., 1996). The Attachment subscale consists of eight items (e.g. "In our family, everyone goes his/her own way" and "We have difficulty thinking of things to do as a family"). The subscale was designed to ascertain the strength of the family members' attachment to each other. The Changeability subscale consists of eight items that determine the relative flexibility of family members in their relationships with each other (e.g. "Our family tries

new ways of dealing with problems" and "Each family member has input in major family decisions"). In accordance with the literature, confirmatory factor analysis was used to extract two first-order factors (representing Attachment and Changeability). These factors were subsequently analysed in order to extract a single second-order factor measuring *the latent construct Family Functioning (FACI-8)*. The internal reliability (Cronbach's alpha) of both subscales was good: 0.78 (Attachment) and 0.79 (Changeability). All factor loadings were highly significant, and all but items 12 (standardised factor loading = 0.319) and 14 (standardised factor loading = 0.376) loaded sufficiently on their respective factors (standardised factor loadings ranging from 0.477 to 0.708). These two items were omitted from the respective factors. The resulting first-order factors – Attachment (standardised factor loading = 0.945) and Changeability (standardised factor loading = 0.687) – displayed significant and sufficiently high loadings on the second-order latent construct, resulting in a reliable FACI-8 factor score (Cronbach's alpha = 0.81; Standard Deviation = 0.730). The overall measurement model displayed an acceptable fit to the data (Root Mean Square Error of Approximation = 0.53, Comparative Fit Index = 0.923 and Tucker Lewis Index = 0.908). The resulting factor scores were used in all subsequent multiple linear regression models.

In addition to the stepwise linear regression analyses (using the three above-described family-related confounders), the current study tests group-specific multiple linear regression models (see Statistical analyses). In order to allow such multi-group analysis, different family types were constructed, following the procedure described by McCubbin et al. (1996). The FACI-8 scores were used to compute *four different family types*: the Extreme Family type, characterised by dysfunctional dynamics; the slightly better functioning Moderate Family type; the even better functioning Mid-range Family type; and finally, the Balanced Family type, which is characterised by optimum functioning. These family types were used solely to perform multi-group analysis.

In order to assess the true effect of family functioning on ART outcomes, two additional family-related confounders, being single: represented by a dichotomous variable '*partner status*', which indicated whether the respondent had a partner (0) or was single (1); and household size, a continuous variable measuring *the total number of persons living in the household*, were included in the regression analysis.

2.3.3. ARV treatment outcomes

Treatment outcomes were assessed using the patients' *CD4 cell counts*, recorded closest to the date of the interview and extracted from the patients' files and electronic records. Diverse studies have demonstrated that CD4 monitoring is a reliable and valid strategy for monitoring ART (Bagchi et al., 2007).

2.3.4. Other study variables

In the statistical analysis, we adjust for the following confounders. We included three health-related measures that have been demonstrated to affect ART outcomes in previous studies (Battegay et al., 2006; Hogg et al., 2003): (1) baseline CD4 cell count, (2) intermittent use of ART and (3) treatment duration. Many previous studies have shown that baseline health significantly influences the chance of success during the initial period of ART (Wouters et al., 2009d; Heunis et al., 2011a,b). Conversely, poor baseline health is a strong predictor of AIDS or death (Battegay et al., 2006), even beyond the initial phase of treatment (Mills et al., 2012). We thus included *baseline CD4 cell count* (defined as CD4 cell count at ART initiation) in our analysis as a potential predictor of immunological restoration. As demonstrated by Hogg et al. (2003), the *intermittent use of ART* is significantly associated with increased mortality, even when adjusted for other prognostic factors (Hogg et al., 2003). We therefore included a dichotomous variable to measure whether patients had ever stopped treatment since starting ART. The last health-related variable is *treatment duration*, measured as the number of days between the initiation of ART and the interview date.

Finally, previous studies have identified various demographic, economic and psychological characteristics as predictors of ART outcomes (Hargreaves et al., 2007; Nattrass, 2006; Peltzer et al., 2010; Rueda et al., 2006). Demographic data include *age*, *sex* and *educational level*. Educational level was measured according to five categories: no education, primary education, some secondary education, matric education (grade 12) or tertiary/post-matric education. Economic status was assessed using two dummy variables: (1) being *employed* and (2) having *access to a disability grant*. These economic variables were measured at baseline in order to prevent potential endogeneity bias. The final control variable can be described as *psychological health*. Various studies have indicated that mental health problems (e.g. anxiety and depression) can have a negative impact on ART outcomes. We therefore included each patient's score on the Hospital Anxiety and Depression Scale (HADS). A recent study demonstrates the reliability of the translated version of this scale in South Africa (Wouters et al., 2012a).

2.4. Statistical analyses

As stated in the Background section, the current article's objective is to explore the potential moderating role of family dynamics in the impact of peer adherence support on clinical treatment outcomes. We employed a two-step approach in order to achieve this objective. First, for the purpose of establishing a reference point for the interpretation of the results generated in the second stage (see discussion below), stepwise multiple linear regression analyses were used to examine differences between the treatment outcomes of patients receiving standard care and those of patients receiving the additional guidance of a peer adherence supporter. To assess the net gain of peer adherence support, four blocks of potentially confounding variables were tested for inclusion in the analyses: (1) demographic characteristics, (2) health-related characteristics, (3) economic characteristics and (4) psychological characteristics. In order to identify the best model, we compare the Akaike information criterion (AIC): the model with the smallest AIC has a better fit and fewer parameters relative to competing models (Kline and Santor, 1999). Standardised beta coefficients are provided for purposes of comparing the relative importance of the independent variables. Missing data was handled using listwise deletion, which resulted in a sample size of 244.

In the second step, we explored the potential moderating role of family dynamics by assessing the differential impact of peer adherence support in families with differing levels of family functioning in two ways, based on the theoretical underpinnings of the family functioning framework. We first introduced the family-related variables in the stepwise logistic regression analyses, including an interaction term between peer adherence support and the level of family functioning (peer adherence intervention * family functioning). In addition, and using multi-group analysis, four group-specific multiple linear regression models (one for each family type) were used to conduct an independent assessment of the impact of peer adherence support on treatment outcomes in the different family types. Here, listwise deletion resulted in a sample size of 228. All analyses were computed using the statistical software package Mplus, version 5 (Muthén and Muthén, 1998–2007).

Table 1
Means and distribution of the FACI-8 scores.

FACI-8	
Changeability (mean score, SD)	
- In our family it is easy for everyone to express his/her opinion	3.55 (1.54)
- Each family member has input in major family decisions	3.47 (1.57)
- Family members discuss problems and feel good about the solutions	3.62 (1.48)
- Family members consult other family members on their decisions	2.52 (1.58)
- Discipline is fair in our family	3.00 (1.75)
- Our family tries new ways of dealing with problems	3.15 (1.53)
- In our family, everyone shares responsibilities	3.71 (1.48)
- When problems arise, we compromise	2.53 (1.64)
Attachment (mean score, SD)	
- It is easier to discuss problems with people outside the family than with other family members	3.44 (1.57)
- In our family everyone goes his/her own way	4.06 (1.45)
- We have difficulty thinking of things to do as a family	3.61 (1.48)
- Family members feel closer to people outside the family than to other family members	3.82 (1.47)
- It is difficult to get a rule changed in our family	2.98 (1.60)
- Family members avoid each other at home	3.97 (1.42)
- Family members are afraid to say what is on their minds	3.80 (1.37)
- Family members pair up rather than do things as a total family	3.69 (1.54)

3. Results

3.1. Sample description

The median age of the ART patients in this sample was 37.0 years (SD = 9.1). The majority of the patients interviewed at follow-up one were female (77.4%). With regard to the highest level of education achieved, 3.1% of patients had no formal education, 26.9% had completed primary education, 46.9% had completed some secondary education, 20.0% had completed secondary education and only 3.1% had completed tertiary education. Health-related indicators showed that the majority of respondents had been severely ill at ART initiation: the median baseline CD4 cell count was 132.0 (SD = 112.1). After a median treatment duration of 504.7 days (SD = 85.9), immunological restoration had led to a median CD4 cell count of 309.5 (SD = 186.2) with 81.5% reaching the threshold of a CD4 cell count of 200 cells per μl blood. Only 40.0% of patients had CD4 cell counts above 350 cells per μl blood at Follow-up 1. Less than one out of ten respondents (8.9%) indicated having interrupted treatment at least once. With regard to the economic situation of the respondents at baseline, 25.1% had jobs, while nearly one out of five respondents (29.9%) was receiving a disability grant. With regard to family situation, the mean household consisted of 3.6 (SD = 2.1) members. The vast majority of the respondents had no partner (72.8%). Based on the FACI-8 scores for family type, 17.1% of the respondents' families could be classified as Extreme (low levels of changeability and attachment); 21.2% families could be categorised as Moderate, 35.1% as Mid-range and 26.7% as the optimal Balanced type (high levels of attachment and changeability). Table 1 shows the means and standard deviations of the FACI-8 items. Finally, we considered the psychosocial characteristics of our sample. Based on Zigmond and Snaith's (1983) original scoring method of the HADS, 15.1% of the patients presented with symptoms of moderate to severe anxiety, and the prevalence of moderate to severe depressive symptoms was 10.1% (Zigmond and Snaith, 1983).

3.2. Peer adherence support

The stepwise regression analyses demonstrate that the community-based peer-adherence support intervention did not produce a significant impact on the treatment outcome. In addition, treatment outcome was not strongly associated with demographic characteristics. The sex of the respondent was the only factor to have a significant correlation with immunological outcome: being female resulted in a 0.13 standard deviation ($P > 0.05$) increase in CD4 cell count. None of the other demographic measures had a significant impact on CD4 cell count. Two health-related measures had a significant impact on immunological outcome. Patients who had interrupted treatment had a significantly lower CD4 cell count ($\beta = -0.14$, $P < 0.05$). Baseline CD4 cell count also had a significant impact on treatment outcome: even after almost 17 months of ART, a significant correlation remained between baseline health and immunological restoration. Patients with low baseline CD4 cell counts were at greater risk of immunological failure than were patients with high baseline CD4 cell counts ($\beta = 0.28$, $P < 0.001$). None of the economic or psychological measures was significantly related to CD4 cell count. (Table 2).

Table 2
Stepwise multiple linear regression of intervention on CD4 cell counts (standardized regression coefficients) (listwise deletion: $n = 244$).

Variables	Model 0	Model 1	Model 2	Model 3	Model 4
Intervention	0.076	0.061	0.003	0.004	0.002
Demographic characteristics					
Age		−0.125	−0.118	−0.123	−0.123
Education level		0.129	0.129	0.123	0.116
Female		0.132*	0.134**	0.133*	0.126*
Health-related measures					
Treatment duration			0.081	0.088	0.081
Intermittent use of ART			−0.136*	−0.140*	−0.139*
Baseline CD4 cell count			0.293***	0.289***	0.284***
Economic situation					
Employed				−0.014	−0.015
Disability grant				−0.002	−0.001
Psychological characteristics					
Anxiety/depression					−0.037
Variance explained (R^2)	0.006	0.067*	0.159**	0.153**	0.150**
AIC	3200.609	3086.671	2879.656	2734.055	2710.494
BIC	3211.101	3107.454	2910.239	2770.820	2750.486
Sample size adjusted BIC	3201.591	3088.436	2881.718	2735.967	2712.465

*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$.

3.3. Family functioning as a catalyst for adherence support

We hypothesised that the intermediate level of the family could potentially moderate the impact of community-level peer-adherence support on the health of individual ART patients. In order to account for the moderating role of family dynamics, a block of family-related variables was introduced into the regression models displayed in Table 3. The first model assesses the impact of the intervention, the patient's family characteristics and an interaction term between levels of family functioning and the adherence-support intervention. The aforementioned blocks of variables were then re-introduced into the stepwise multiple linear regression analyses.

In accordance with the regression models displayed in Table 2, the demographic, economic and psychological characteristics of the patients had only a very limited impact on their CD4 cell counts. Respondents' sex significantly predicted their CD4 cell count in models 1 to 3. The age of the patient was significantly associated with immunological restoration in models 2 and 3, with older patients displaying significantly smaller increases in CD4 cell count. Again, health-related measures significantly predicted treatment outcomes: patients who had ever stopped treatment since ART initiation displayed significantly worse treatment outcomes than did patients who had never stopped treatment ($\beta = -0.16$, $P < 0.05$). In this case as well, baseline CD4 cell count was significantly and positively associated with CD4 cell count at Follow-up 1. This result indicates that the patients' health status at ART initiation was still significantly associated with the CD4 cell count at Follow-up 1 ($\beta = 0.21$, $P < 0.01$).

As before, the intervention consistently failed to produce a significant impact on CD4 cell counts, meaning that the peer-adherence support provided in our RCT did not significantly improve the health of the patients in this sample. In addition, none of the family characteristics was significantly associated with immunological restoration. However, when we controlled for the significant impact of patients' baseline health, the interaction term between the intervention and family functioning emerged as the strongest predictor of CD4 cell count in all remaining models ($\beta = 0.29$, $P < 0.01$). This interaction effect indicates that the better the affected family functions, the stronger the positive effect of the intervention on the CD4 cell count will be. In other words, the positive impact of the intervention is moderated by the patient's family. Patients in well-functioning families benefit more from the support provided by the peer-adherence support intervention than do patients with poorly functioning families. In all, the final model explained 14.4% of the variability in CD4 cell count.

3.4. Peer adherence support impact by family type

In order to quantify the effect of the peer-adherence support experiment in the four different family types, the final model (Model 4) was used for further group-specific regression analysis. The multi-group results indicate that the intervention had a significant positive effect in the most balanced families: patients undergoing the intervention displayed significantly better immunological outcomes ($\beta = 0.50$, $P < 0.001$) than did patients receiving standard care ($n = 40$). The peer-adherence support intervention did not produce any significant effects in Mid-range ($\beta = 0.01$, $P = 0.890$, $n = 70$) or Moderate ($\beta = -0.09$, $P = 0.474$, $n = 48$) families. In the most dysfunctional families (i.e. the Extreme family type), however, the intervention had a negative effect on treatment outcome. Patients receiving the peer-adherence support and residing in an Extreme family type had significantly lower CD4 cell counts ($\beta = -0.31$, $P < 0.05$) than did patients in similar familial circumstances who received no such adherence support ($n = 37$). These results thus suggest that the impact of the peer-adherence support intervention on patients' health is at least partially dependent upon the type of family in which it is implemented. The results of these group-specific analyses must be treated with extreme caution, however, as they are based on relatively small groups, thus limiting the accuracy of the estimates and the associated standard errors (Maas and Hox, 2005).

4. Discussion

The aim of the current study is to assess the moderating role of family dynamics in explaining the differential impact of peer adherence support interventions on treatment outcomes in previous studies. We hypothesised that the family might play a moderating role in the translation of peer adherence support into

Table 3
Stepwise multiple linear regression of family characteristics and intervention on CD4 cell counts (standardized regression coefficients) (listwise deletion: $n = 228$).

Variables	Model 0	Model 1	Model 2	Model 3	Model 4
Intervention	0.074	0.071	0.037	0.033	0.033
Family characteristics					
Family functioning	−0.137	−0.115	−0.200	−0.199	−0.217
Being single	−0.003	−0.029	−0.033	−0.040	−0.042
Total number of Household members	0.053	0.057	0.029	0.045	0.042
Interaction effect	0.212	0.168	0.256*	0.276*	0.292**
Demographic characteristics					
Age		−0.127	−0.139*	−0.141*	−0.143
Education level		0.107	0.093	0.090	0.075
Female		0.126*	0.124*	0.115*	0.105
Health-related measures					
Treatment duration			0.089	0.094	0.085
Intermittent use of ART			−0.158*	−0.161*	−0.160*
Baseline CD4 cell count			0.221**	0.219**	0.210**
Economic situation					
Employed				−0.001	−0.003
Disability grant				0.022	−0.025
Psychological characteristics					
Anxiety/Depression					−0.066
Variance explained (R^2)	0.025	0.075*	0.143**	0.142**	0.144**
AIC	2978.259	2909.081	2709.331	2576.901	2552.209
BIC	3002.264	2943.153	2752.719	2626.149	2604.577
Sample size adjusted BIC	2980.079	2911.461	2711.529	2578.629	2553.891

*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$.

beneficial treatment outcomes. Proceeding from the *Resiliency Model of Family Stress, Adjustment and Adaptation* (McCubbin and McCubbin, 1996), we explored whether differing levels of family functioning could render families more or less amenable to community-based adherence support. The study outcomes support our hypothesis by demonstrating a significant interaction effect between peer adherence support and levels of family functioning, while the peer adherence support intervention did not produce a significant direct impact in the overall sample. These findings build upon recent work by Rotheram-Borus et al. (2010), which associated better family functioning with better quality of life and better adherence levels in a sample of ART patients in Thailand (Rotheram-Borus et al., 2010). The present study extends the existing literature by providing additional insight into the crucial role of family dynamics in HIV/AIDS care, establishing a significant interaction effect between peer adherence support and family functioning in a resource-limited setting characterised by a high prevalence of HIV.

Subsequent multi-group analysis demonstrated that peer adherence support produced a strong positive effect on immunological restoration, but only in the Balanced family type. Only patients living in households displaying high levels of attachment and changeability were able to translate peer adherence support into better ART outcomes. Conversely, peer adherence support produced a negative effect on the treatment outcomes of patients living in the most vulnerable, dysfunctional families. In other words, families that form tight units and can easily adapt to external changes apparently form the ideal environment for community-based support initiatives, while dysfunctional families that have difficulty adapting to external changes are not able to translate the additional peer adherence support into better ART outcomes at the individual level. Even though the results of this multi-group analysis should be treated with caution, there are indications that the family context – ranging from well-functioning and amenable to outside support to dysfunctional and not yet ready for outside support – might well be a key factor explaining the widely differing impact of peer adherence support programmes in different research settings, as is evident from reviews of the impact of adherence support more generally and of peer adherence support in particular (Bärnighausen et al., 2011; Wouters et al., 2012b).

Possible explanations are to be found in the questionnaire items and subscales (attachment and changeability) included in the family-functioning scale. In families with low levels of *attachment*, personal issues and problems cannot be discussed, and family members tend to go their own way (McCubbin et al., 1996). In such a setting, home visits from peer adherence supporters are unlikely to increase the AIDS competence of the family unit as a whole. In tight-knit families, however, knowledge related to HIV/AIDS and treatment is likely to be absorbed by the family unit (Mfundsi et al., 2005), which can then provide additional support to the HIV patient in their midst. Families displaying low levels of *changeability* are less capable of adapting to challenges – such as a diagnosis of HIV infection or the initiation of ART – and outside influences – such as a community-based peer adherence intervention (McCubbin et al., 1996). In families characterised by unequal decision structures and closed communication styles, rigid family practices could hamper the ability of peer adherence supporters to bring about positive changes in treatment practices. In an extreme but not exceptional case, HIV/AIDS patients in such dysfunctional families are unable to disclose their health status to their family members (Wouters et al., 2009a; Wouters et al., 2009c), which renders them unable to take full advantage of any community-based peer adherence support that is offered. In such settings, home visits or even meetings with peer adherence supporters could pose serious challenges and cause additional stress, thereby hampering or even excluding potential positive effects of the intervention. These intricate inter-relationships between community-based adherence support, family dynamics and individual health behaviour stress the need for adherence interventions that are sensitive and thus adjusted to the familial contexts within which they are implemented.

The strengths of this study include its theoretical foundation in family sociology and the availability of information on family functioning for ART clients receiving peer adherence support as part of a randomised control trial, which allows an empirical investigation into the role of family context in moderating the impact of peer adherence support. To the best of our knowledge, ours is the first study to provide a quantitative assessment of the interaction between peer adherence support and family dynamics in predicting ART outcomes in a resource-limited setting characterised by a high prevalence of HIV. Our study is nevertheless subject to several limitations. First, although cross-lagged regression would have been more appropriate, the study was limited to cross-sectional analyses, as family functioning was not measured at baseline. Second, the results of the group-specific analyses employed to determine the moderating role of family type in explaining differential impacts of peer adherence support must be treated with extreme caution as they are based on relatively small groups, thus limiting the accuracy of the estimates and the associated standard errors (Maas and Hox, 2005). Finally, the statistical analysis conducted here, should not be interpreted as a test of the impact on treatment outcomes and of the effectiveness of the Effective Aids Treatment and Support in the Free State (FEATS) study's peer adherence support intervention. This paper (a) does not employ the standard statistical tools, most notably intent-to-treat analysis, used to assess the impact of interventions implemented as part of randomised control trials, (b) suffers from attrition bias insofar as CD4 counts could not be matched to survey data for all patients, and (c) does not make use of data on longer-term treatment outcomes observed in the second round of follow-up interviews insofar as CD4 counts could only be matched to patient data for a small number of observations. The CONSORT statement does contain an intent-to-treat analysis employing all available data which shows a statistically significant impact of peer adherence support on CD4 cell count.

Several important insights have emerged from this study, with implications for both theory and practice. From a theoretical point of view, the interaction effect between family functioning and peer adherence support on immunological restoration draws attention to the role of positive family dynamics in promoting adherence to ART. In addition to patient-level factors, future research activities should also incorporate the moderating role of the family context, as the efficacy of community-based adherence support is interconnected with family dynamics. The current study thus expands the theoretical and conceptual scope by indicating the need to acknowledge the family aspects and dynamics of HIV/AIDS and its associated treatment. Second, the findings call for caution when considering the available evidence on the impact of adherence-support interventions on treatment outcomes, as our randomised controlled study revealed no significant positive impact within the overall sample. We strongly stress the need to produce context-specific interpretations regarding the outcomes of peer adherence interventions. Our findings suggest that the discrepant findings reported in the literature are most likely due to differences in the degree of compatibility between peer adherence interventions and the contexts in which they are implemented (Bärnighausen et al., 2011). Further evaluation of the contribution of peer adherence support initiatives to HIV/AIDS care programmes in different contexts should therefore be an important research priority, including

studies in various settings and employing alternative research designs.

The study findings also have important implications for public health policy and practice. The fact that peer adherence support produced significant positive results only in well-functioning families stresses the need for peer adherence interventions that are sensitive to the suboptimal contexts in which they must often be implemented. The results clearly indicate that generic, broad-based interventions do not necessarily facilitate treatment adherence within the most vulnerable patient groups, particularly those without supportive family contexts. Exploring ways to ensure the training of peer adherence supporters enable them to adequately tailor their activities to different family contexts, including training in family counselling and in family skills, should thus be a priority for both research and policy. In our study, however, we did not investigate *how* or *why* family functioning is associated with the impact of peer adherence support on treatment outcomes in a positive or negative manner. Additional longitudinal studies and qualitative research is therefore needed in order to provide full clarification of the mechanisms by which family dynamics hamper or facilitate the impact of peer adherence support programmes on antiretroviral treatment outcomes.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.socscimed.2014.05.020.

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