to 1 μg of DNA extract. Total viral DNA was quantified as previously described [5] and the same protocol was used for 2-LTR DNA quantification by adding Pr-2LTR-HIV1: FAM3′CTGGTGTGTAGTTCTGC CAATCAG5′TAMRA to the 2LTR-HIV1 primers for HIV-1 or Pr-2LTR-HIV2: FAM3′AGACCCTGGT CTGTTAGGACCCT5′TAMRA to the 2LTR-HIV2 primers for HIV-2 (annealing temperature 60°C).

Regardless of the PBMC's donor and the HIV-2 strain, a marked difference was found in the kinetics of HIV-1 and HIV-2 DNA production (Fig. 1). The total amount of viral DNA was lower with HIV-2 than with HIV-1, by 1.16 and 0.5 Log, respectively, between 6 and 96 h (HIV-1 NL4-3 versus HIV-2 ROD). After 96 h, total HIV-1 and HIV-2 DNA levels reached a plateau, and the difference was no longer appreciable. Whatever the PBMC donor, the amount of 2-LTR DNA was lower with HIV-2 than with HIV-1 for up to 48 h of culture, but then became higher throughout the remaining culture period (0.65 Log difference between HIV-1 NL4-3 and HIV-2 ROD at the two hundred and sixty-fourth hour). Comparison of MT4-CXCR4 and HeLa-CXCR4-CCR5 cells showed that the results were not influenced by the presence or absence of CCR5.

The time lag before 2-LTR HIV-2 DNA production was similar to that observed for total HIV-2 DNA, but the subsequent kinetic pattern was unexpected. Indeed, 2-LTR HIV-2 DNA levels, similar to 2-LTR HIV-1 DNA levels, increased rapidly but, in the plateau phase (at 168 h), 2-LTR circular forms represented only 2% of total HIV-1 NL4-3 DNA copies, compared with 21% and 18% with HIV-2 DNA ROD and MEN, respectively. This difference suggests that HIV-2 may integrate the host cell genome less efficiently than HIV-1, a possibility that would be compatible with the natural history of the two human infections.

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Impact of baseline health and community support on antiretroviral treatment outcomes in HIV patients in South Africa

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The importance of community support when scaling-up antiretroviral treatment (ART) in resource-limited settings is poorly understood. We assessed the impact of baseline health, patient characteristics and community support on ART outcomes at 6 and 12 months in a representative sample of 268 patients enrolled in the Free State public sector ART program (South Africa). Delayed ART initiation reduced ART response, whereas support from treatment buddies, community health workers and support groups significantly improved treatment outcomes.

Shortages of human resources in healthcare are often cited as the most important obstacle to successful scaling-up of antiretroviral treatment (ART) [1–3]. This is the case in South Africa [4,5] and in the Free State Province [6]. Under these circumstances, community involvement is

an essential prerequisite for a successful comprehensive AIDS strategy [7–9]. However, the potential capacity of these community support initiatives to address the overwhelming human resource challenges in HIV care is poorly understood [2] and a systematic assessment of these programs and activities is, therefore, urgently required [7].

Several studies [10–18] have indicated that the patient's age, sex, baseline CD4 cell count and baseline viral load are predictors of ART outcomes. The present study investigates how virological and immunological responses to ART, measured after 6 and 12 months of ART, were influenced by patient characteristics (age and sex), baseline CD4 cell count, baseline viral load and three different forms of community support (treatment buddy, community health worker (CHW) and HIV/AIDS support group). The study was based on a sample of HIV/AIDS patients enrolled in the Free State public sector ART program.

The participants included patients who were certified as medically ready to commence ART (CD4 cell count <200 cells/μl and/or WHO stage IV) in the first 2 months following the launch of the ART program. In order to detect a 5% difference in this population at the 95% confidence level, 268 patients were selected randomly, in proportion to the numbers of patients per clinic.

All clinical data were collected directly from patient files after written consent from all the patients had been obtained and with the authorization of the Provincial Department of Health. 'Baseline' (time 0, or after 0 days of ART) was defined as the date of ART initiation (baseline CD4 cell count and baseline viral load). In accordance with previous studies, we measured a combination of virological and immunological treatment outcomes after 6 (time 1) and 12 months of ART (time 2) [16,19,20]. We categorized patients as treatment successes [undetectable viral load (<400 copies/ml) and CD4 cell count ≥ 200 cells/μl], partial treatment successes (undetectable viral load or CD4 cell count ≥ 200 cells/μl) and treatment failures (detectable viral load and CD4 cell count <200 cells/μl). Data on age, sex and community support (CHW, support group and treatment buddy) were collected at times 1 and 2, when trained enumerators conducted face-to-face interviews using a standard questionnaire.

We used a fully cross-lagged regression analysis to study the impact of patient characteristics, baseline CD4 cell count and viral load on ART outcomes after 6 and 12 months of ART. The model also independently assessed the direct (within a wave) and cross-lagged (between adjacent waves) impacts of the three different forms of community support on ART outcomes. Patient characteristics, type of community support, treatment outcomes and the standardized parameter estimates for the cross-lagged model are shown in Table 1.

During the first 6 months of ART, treatment outcomes were significantly influenced by baseline viral load ($\beta = -0.19$, $P < 0.001$), baseline CD4 cell count ($\beta = 0.25$, $P < 0.001$), age ($\beta = 0.09$, $P < 0.01$) and all three community support initiatives. Patients with a treatment buddy ($\beta = 0.16$, $P < 0.001$) or an assigned CHW ($\beta = 0.12$, $P < 0.05$) reported significantly better treatment outcomes than patients without such support. Participating in a support group also had a significantly positive effect ($\beta = 0.12$, $P < 0.05$) on ART response.

Approximately 6 months later, baseline CD4 cell counts ($\beta = 0.06$, $P < 0.05$) and baseline viral loads ($\beta = -0.07$, $P < 0.05$) were still significantly related to treatment outcomes, but these measures of baseline health had a much weaker impact on antiviral efficacy at this stage of treatment. The importance of community support as a predictor of treatment outcomes increased significantly during treatment. The cross-lagged paths indicated that having a treatment buddy ($\beta = 0.12$, $P < 0.05$) or a CHW ($\beta = 0.10$, $P < 0.05$) at time 1 significantly increased a patient's chance of having a CD4 cell count of at least 200/μl and achieving viral suppression at time 2. At time 2, all three community support measures were positively associated with the 1-year treatment outcome. Treatment response was significantly higher ($\beta = 0.13$, $P < 0.01$) in patients with support from a treatment buddy ($\beta = 0.17$, $P < 0.001$), CHW ($\beta = 0.16$, $P < 0.01$) or HIV support group ($\beta = 0.13$, $P < 0.01$) compared with that of patients without such support.

To the best of our knowledge, this is one of the first studies to quantitatively assess the impact of different community support initiatives on public sector ART outcomes in a high-HIV-prevalence, resource-limited setting [8]. However, there were some limitations to our study. Although the analysis focused on the impact of community support on treatment outcomes, the regression model offered an incomplete explanation of ART outcomes. Patient characteristics were tested as predictors of treatment success but only baseline age was significantly related to treatment outcomes; other potentially relevant socio-behavioral factors were not available for this dataset. Further longitudinal research is therefore required to fully understand the complex interrelationships between community support and ART outcomes.

In summary, HIV/AIDS patients commencing ART with support from treatment buddies, CHWs and/or support groups had more favorable virological and immunological responses than those without such support. These findings have potentially important policy implications. The cross-lagged findings suggest a strategy for modulating the delicate balance between treatment success and failure: community support initiatives should initially target

Table 1. Baseline characteristics, community support and clinical outcomes and their impacts on treatment outcomes.

		Baseline	Time 1	Time 2
Demography				
Men (%)		33.3		
Age, mean (SD)		37.9 (8.6)		
Community support				
Treatment buddy (%)		–	51.5	50.7
CHW (%)		–	7.5	6.9
Support group (%)		–	14.8	17.5
Virologic and immunologic response				
CD4 cell count (cells/μl), mean (SD)		109 (68)	236 (158)	275 (140)
CD4 cell count gain (cells/μl), mean (SD)		–	+127 (130)	+39 (101)
<200 cells/μl (%)		95.9	44.8	30.3
≥200 cells/μl (%)		4.1	55.2	69.7
Viral load (copies/ml), mean (SD)		299 090 (628 028)	34 488 (221 029)	5833 (36 128)
<400 copies/ml (%)		3.3	83.5	84.7
≥400 copies/ml (%)		96.7	16.5	15.3
Treatment outcome				
Treatment failure (%)		–	9.6	8.5
Partial treatment success (%)		–	44.3	27.4
Treatment success (%)		–	46.1	64.1
Path		Path coefficient	*t*	*P*
Age	→ Treatment outcome (T1)	0.089	2.606	<0.01
Sex	→ Treatment outcome (T1)	−0.024	−0.498	NS
Baseline CD4 cell count (T0)	→ Treatment outcome (T1)	0.249	7.505	<0.001
Baseline viral load (T0)	→ Treatment outcome (T1)	−0.188	−5.236	<0.001
Treatment buddy (T1)	→ Treatment outcome (T1)	0.164	4.200	<0.001
Community health worker (T1)	→ Treatment outcome (T1)	0.118	2.450	<0.05
Support group (T1)	→ Treatment outcome (T1)	0.121	2.151	<0.05
R^2 (treatment outcome (T1))	0.19			
Age	→ Treatment outcome (T2)	0.030	0.849	NS
Sex	→ Treatment outcome (T2)	0.015	0.353	NS
Baseline CD4 cell count (T0)	→ Treatment outcome (T2)	0.057	2.016	<0.05
Baseline viral load (T0)	→ Treatment outcome (T2)	−0.067	−1.970	<0.05
Treatment buddy (T1)	→ Treatment outcome (T2)	0.123	2.378	<0.05
Community health worker (T1)	→ Treatment outcome (T2)	0.104	1.998	<0.05
Support group (T1)	→ Treatment outcome (T2)	0.042	0.974	NS
Treatment buddy (T2)	→ Treatment outcome (T2)	0.171	5.199	<0.001
Community health worker (T2)	→ Treatment outcome (T2)	0.156	2.673	<0.01
Support group (T2)	→ Treatment outcome (T2)	0.126	3.154	<0.01
R^2 [Treatment outcome (T2)]	0.21			
Test for fit		Model	Criteria for good fit	
RMSEA		0.0488	<0.05	
NFI		0.927	>0.90	
NNFI		0.916	>0.90	
Comparative fit index		0.931	>0.90	
PNFI		0.506		

Standardized regression coefficients (minus relative stability paths) and model summary of the fully cross-lagged model ($n = 268$). The goodness-of-fit statistics indicate that the model not only fits adequately, but also withstands the tests of parsimony. The squared multiple correlation coefficient, R^2, for the regression model predicting ART outcomes at T1 was 0.19. Approximately 6 months later (T2), the analysis explained 21.0% of the variance in ART outcomes. ART, antiretroviral treatment; CHW, community health worker; NFI, normed fit index; NNFI, nonnormed fit index; NS, not significant; PNFI, parsimony normed fit index; RMSEA, root mean square error of approximation.

patients with very low baseline CD4 cell counts and high baseline viral loads, because delayed ART initiation was associated with significantly reduced treatment responses. After 12 months of ART, baseline health only weakly predicted treatment outcomes, whereas the various community support initiatives became more important predictors of the ART response. These findings stress the importance of community support in achieving durable treatment success and indicate that health policy makers should acknowledge and strengthen the role of community support in the fight against HIV/AIDS.

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