Outcomes of home visits for pregnant mothers and their infants: a cluster randomized controlled trial

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Objective: To evaluate the effect of home visits by community health workers (CHWs) on maternal and infant well being from pregnancy through the first 6 months of life for women living with HIV (WLH) and all neighborhood mothers.

Design and methods: In a cluster randomized controlled trial in Cape Town townships, neighborhoods were randomized within matched pairs to either standard care, comprehensive healthcare at clinics ($n = 12$ neighborhoods; $n = 169$ WLH; $n = 594$ total mothers); or Philani Intervention Program, home visits by CHWs in addition to standard care (PIP; $n = 12$ neighborhoods; $n = 185$ WLH; $n = 644$ total mothers). Participants were assessed during pregnancy (2% refusal) and reassessed at 1 week (92%) and 6 months (88%) postbirth. We analyzed PIP's effect on 28 measures of maternal and infant well being among WLH and among all mothers using random effects regression models. For each group, PIP's overall effectiveness was evaluated using a binomial test for correlated outcomes.

Results: Significant overall benefits were found in PIP compared to standard care among WLH and among all participants. Secondarily, compared to standard care, PIP WLH were more likely to complete tasks to prevent vertical transmission, use one feeding method for 6 months, avoid birth-related medical complications, and have infants with healthy height-for-age measurements. Among all mothers, compared to standard care, PIP mothers were more likely to use condoms consistently, breastfeed exclusively for 6 months, and have infants with healthy height-for-age measurements.

Conclusion: PIP is a model for countries facing significant reductions in HIV funding whose families face multiple health risks.

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Introduction

For the past 10 years, evidence has been mounting on the importance of integrating HIV care with care of other health risks [1]. In low-income and middle-income countries (LMICs), including South Africa, children's health is compromised not only by HIV, but also by the cumulative impact of poverty and related deficits from

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other infectious diseases, malnutrition, and maternal behaviors [2,3]. Yet, community health workers (CHWs) typically target single outcomes, such as HIV testing [4], tuberculosis (TB) adherence [5], securing a child grant [6], or maternal depression [7]. In some LMICs, two to three different CHWs visit a household, each targeting a different health risk, but also replicating some components of the intervention. HIV-identified CHWs are also more likely to be rejected, given the stigma surrounding HIV [8].

In contrast, we trained CHWs to address multiple health behaviors. A home visiting intervention strategy for new mothers has repeatedly been demonstrated efficacious in the United States with significant short- and long-term outcomes when delivered by nurses [9–12]. The current global shortage of healthcare personnel in LMICs requires task-shifting from professionals to CHWs [13,14]. This study, set in Cape Town townships, evaluates the ability of home visits by CHWs to improve the well being of mothers and infants from pregnancy to the first 6 months of life for women living with HIV (WLH) and for all mothers. CHWs were trained in foundational skills to support behavioral change [15], specifically for HIV, alcohol use, infant malnutrition, and general maternal and child health.

We hypothesized that, compared to the standard care, WLH and all mothers in the Philani Intervention Program (PIP) would have improved maternal and child health and well being in five domains: adherence to HIV-related preventive acts [for WLH, including the tasks to prevent mother-to-child transmission (PMTCT)]; child health and nutrition (including alcohol use during pregnancy and breastfeeding); healthcare and monitoring; mental health; and social support [16].

Methods

The Institutional Review Boards of the University of California, Los Angeles (UCLA), Stellenbosch University, and Emory University approved the study [16].

Standard care and Philani Intervention Program conditions

Standard care

The standard care condition consisted of access to healthcare at government clinics and hospitals, including rapid HIV testing and receipt of results. WLH were routinely offered HIV care, including testing for CD4 cell count; antiretroviral medication for WLH with low CD4 cell counts; maternal zidovudine (ZDV) from the 28th week of pregnancy and during delivery; nevirapine (NVP) for the mother during delivery and for the infant within 24 h of birth; and infant ZDV, formula tins, cotrimoxazole, and HIV PCR testing postbirth.

Philani Intervention Program

The PIP condition received antenatal and postnatal home visits by CHWs in addition to the clinic-based care that is standard care. CHWs were selected to have good social/communication skills, problem-solving skills, and thriving children (positive deviants). CHWs were trained for 1 month using an intervention manual, role-playing, and watching videotapes of common challenging situations that CHWs might face during home visits. All CHWs were trained in foundational skills in behavior change; application of key health information about HIV, alcohol use, malnutrition, and general maternal and child health; and coping with their own life challenges. CHWs worked 20 h weekly, and were paid R1250 a month (about 150 USD).

In accordance with standard procedures for an effectiveness trial, PIP was mounted by the local Philani Maternal, Child Health and Nutrition Program, a community-based organization. CHWs systematically visited every home in their assigned neighborhood, identified pregnant mothers, carried a scale to weigh infants, plotted weight on growth charts to identify underweight children, and transcribed outcomes from the government-issued Road-to-Health card. The antenatal messages concerned good maternal nutrition and preparing for breastfeeding; regular antenatal clinic attendance and danger signs; HIV testing, PMTCT tasks, and partner prevention strategies; and stopping alcohol use [17]. The postnatal messages were breastfeeding and growth monitoring; medical adherence (immunizations, prevention for HIV-exposed children); infant bonding; and securing the child grant. The home visits were monitored in two ways: CHW handwritten notes; and CHWs carried mobile phones that noted visit time, length, content covered, and perceived impact.

On average, CHWs made six antenatal visits (range, 1–27) and five postnatal visits between birth and 2 months postbirth (range, 1–12) per participant. Sessions averaged 31 min (SD = 20). Supervisors monitored implementation by reviewing charts and visit documentation on mobile phones, making random site visits once every 2 weeks, and providing monthly CHW in-service trainings.

Procedures

Neighborhood matching and randomization

Household randomization would have increased the intervention's stigma and resulted in substantial contamination; therefore, we randomized by neighborhood. Similar neighborhoods ($N = 40$) were selected based on analysis of aerial photos, field observations, brief street-intercept surveys, and systematic counting of the number of alcohol bars, informal shops, clinics, child care centers, schools, and formal and informal houses per neighborhood. On the basis of these data, we identified 13 matched pairs of similarly-sized neighborhoods

(450–600 households) with formal and informal housing, that were within 5 km of health clinics; had five to seven alcohol bars; were noncontiguous or separated by natural barriers; had similar numbers of child care centers, informal shops, and schools; and had households with similar length of residence. In a cluster randomized controlled design, the UCLA team randomized neighborhoods within matched pairs to PIP or standard care using simple randomization. One matched pair was eliminated after 6 months of recruitment due to low numbers of pregnant women (total $n = 10$ pregnant women), leaving 24 study neighborhoods [16].

Sample size calculations

Sample size calculations were conducted to determine the minimum number of pregnant women to be recruited per neighborhood to achieve 80% power to detect a standardized effect size of 0.40 between intervention conditions among WLH and among all women [16].

Participants

Recruitment and retention

Three separate teams conducted the study to reduce any potential bias in data collection (Stellenbosch), intervention implementation (the Philani Program), and analyses (UCLA). From May 2009 to September 2010, the Stellenbosch team hired local township mothers to recruit pregnant women who were at least 18 years old, living within the target neighborhood, and able to give informed consent. Each recruiter worked in one PIP and one standard care neighborhood to ensure that recruiter competence was similar across conditions. Pregnant women were recruited at an average 26 weeks of pregnancy (range, 3–40 weeks); only 2% of women refused participation. Initially, however, we identified 22% fewer pregnant women in standard care. By redeploying recruiters, we identified an additional 94 women in 10 of the 12 standard care neighborhoods who were pregnant during the recruitment period (median of seven late-entry participants per neighborhood; range, 3–24). These women were enrolled postbirth when their infants were a mean age of 9 months old (range, 1–18 months). The final sample ($n = 1238$) consisted of a median of 51 pregnant women per neighborhood (range, 23–72).

Figure 1 summarizes participant flow from recruitment to 6 months postbirth. Follow-up rates were similar across intervention conditions: 92% were reassessed postbirth (Mean = 1.9 weeks; SD = 2.1), 88% at 6 months (Mean = 6.2 months, SD = 0.7), and 88% were assessed at all three points. Due to delayed enrollment, late-entry participants were asked baseline, postbirth, and 6-month questions in one assessment.

Assessments

Township women were trained as interviewers, used mobile phones for data entry, and were routinely monitored and supervised. A driver transported all participants to a central assessment site, allowing interviewers to be blinded to condition. However, participants may have spontaneously talked about CHWs to interviewers.

Measures

HIV-related preventive acts

HIV-related preventive acts (self-reported) included asking partners to test for HIV; discussing HIV status with sexual partners in the past 3 months; and using condoms consistently (in 10 of the last 10 sexual episodes). All pregnant women reported whether they completed the rapid HIV test in the antenatal clinic, received their results, and completed a blood test to evaluate CD4 cell count. Among WLH, there were additional perinatal tasks that included knowledge of CD4 cell count and behaviors in the PMTCT cascade [18,19]: adherence to ZDV from the 28th week of pregnancy; ZDV during labor; NVP during labor; infant NVP postbirth; infant ZDV postbirth; infant HIV PCR testing at 6 weeks and retrieval of results; and maintenance of one feeding method (either breastfeeding or formula) for 6 months. We calculated the percentage of women completing each task and the percentage of women who cumulatively completed steps in the PMTCT cascade.

Child health and nutrition

Child health and nutrition was assessed by low birth weight (LBW, <2500 g) and by calculating z-scores based on WHO age-specific and sex-specific standards for weight, height/length, weight-for-height, and head circumference [20]. A z-score below −2 standard deviations was considered a serious growth deficit [21]. We monitored self-reports of months of breastfeeding (then dichotomized as longer than the sample median of 3 months), breastfeeding exclusively for 6 months, alcohol use the month before birth, and risky drinking postbirth, assessed by the Alcohol Use Disorders Identification Test-C (AUDIT-C) [22].

Healthcare

Healthcare was tracked by maternal reports of antenatal clinic visits, postbirth complications (heavy vaginal bleeding, malodorous discharge, fever, persistent cough, breast infection), and TB testing. The infant's Road-to-Health card reported immunizations, clinic visits, and results of HIV PCR testing and formula feeding (allowing us to validate maternal self-reports of HIV status).

Mental health

Mental health was measured by the Edinburgh Postnatal Depression Scale (EPDS), using a cut-off of more than 13 to indicate depressed mood [23,24].

Social support

Social support was assessed by the frequency of material, emotional, and child-rearing support from family

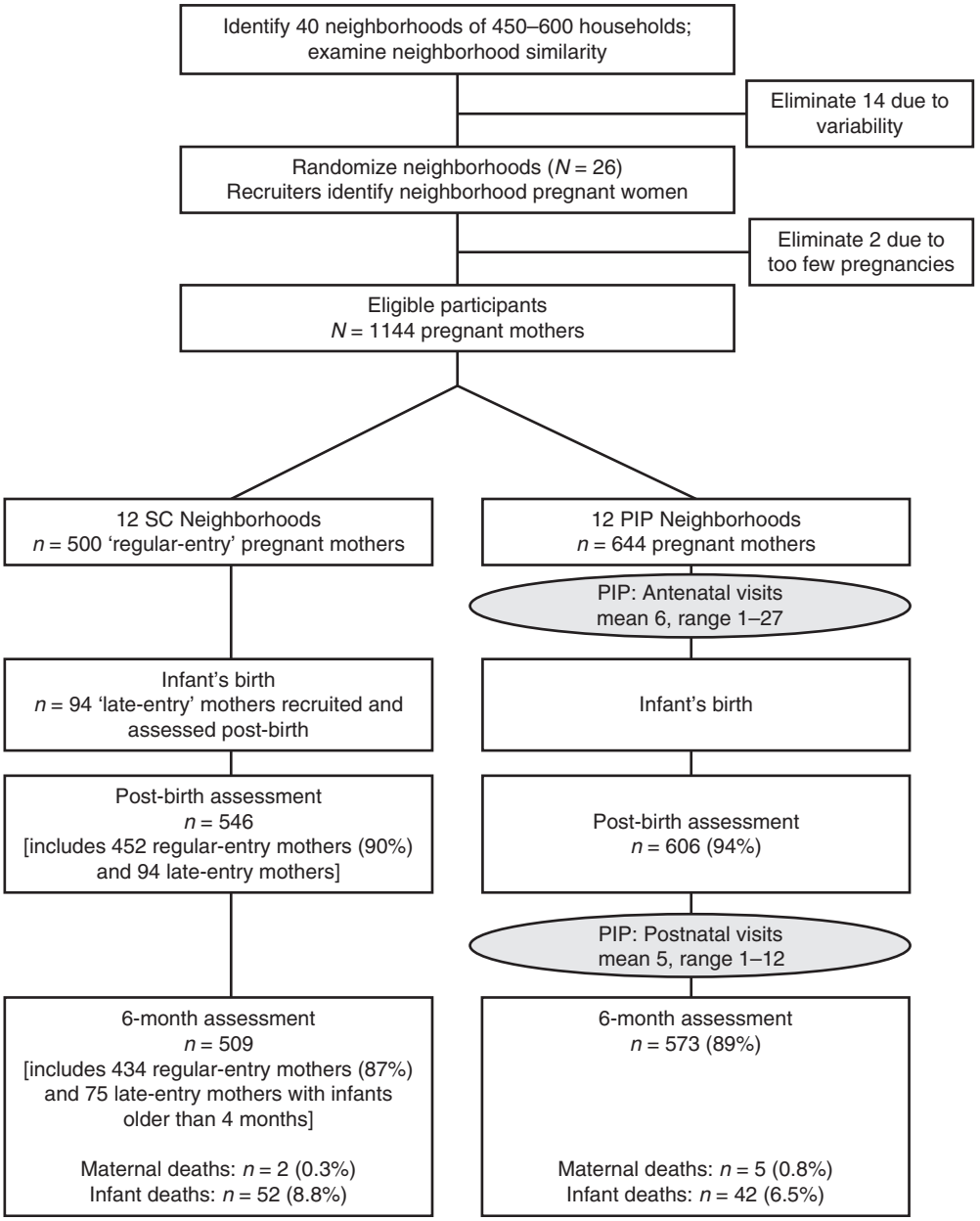


Fig. 1. Movement of participants through the trial at each assessment point for mothers in the standard care and the Philani Intervention Program. PIP, Philani Intervention Program; SC, standard care.

members, neighbors, and friends, and whether mothers applied for and received the child grant (R240/month, about 30 USD).

Analyses

Among WLH and among all mothers, we first looked for significant differences in baseline demographics between intervention conditions and between participants lost to follow-up vs. those reassessed at postbirth and 6 months. For WLH and for all mothers, our primary analysis of the impact of the intervention at 6 months compared women in PIP and standard care using a binomial test of the number of significant effects favoring PIP among our 28 measures. Our secondary analyses explored differences in individual outcomes between conditions among WLH and among all participants.

Primary analysis: binomial test for correlated outcomes

Comparisons between PIP and standard care on 28 binary outcomes were tested at a one-sided upper-tail α equal to 0.025 using logistic random effects regressions adjusting for neighborhood clustering in SAS PROC GENMOD (version 9.2; SAS Institute Inc., Cary, North Carolina, USA). All models included an indicator variable for

intervention status (1 = PIP, 0 = standard care). Among WLH, we controlled for baseline employment because it differed significantly between intervention conditions; among all participants, there were no significant baseline differences between conditions.

We can expect $28 \times 0.025 = 0.7$ significant tests (i.e. less than 1 of 28) on average if there are no differences between PIP and standard care. If outcomes are independent, the probability that there are three or fewer significant differences is 99.5%, leading to a type 1 error of 0.005. However, the outcomes are likely positively correlated, which does not affect the expected number of positive tests, but does affect the variance of the number of positive tests. To study the effects of global positive correlation among all outcomes on the number of positive tests assuming no intervention effect, we treated each of our 28 tests as a normal z-test (z-statistics were assumed to come from an equicorrelated multivariate normal distribution) and simulated 40 000 trials of the number of significant outcomes, for z-tests having mutual correlations ρ for ρ running from 0 to 0.9 in steps of 0.1. We declared significance for z more than 1.96. Simulations were performed in R (version 2.11.1).

Across the 10 correlations, using a decision rule of rejecting the null of no PIP treatment effect given four or more significant tests of 28, the worst situation was that we reject the null with probability 0.059 when $\rho = 0.7$. For more reasonable correlations of ρ equal to 0.1 or 0.2, the actual type 1 error is 0.021 and 0.037, respectively. We estimated the average absolute correlations among the outcomes; because variables included 'true dichotomies' (e.g. Asked partner to test for HIV) and indicators created by dichotomizing continuous outcomes (e.g. Weight-for-age z-score ≥ -2), we estimated both the Pearson and the tetrachoric correlations, planning to use whichever method produced higher average absolute correlations. If the correlations were found to be higher than 0.2, we would increase the needed number of significant results from four to five of 28 before declaring PIP's significance. This would keep the type 1 error below 0.05, no matter what the outcomes' correlations.

As we performed two binomial tests, one for WLH and one for all women, we examined the P values to see whether each was below $0.05/2 = 0.025$ to control for the family-wise error rate before declaring a significant result in favor of PIP.

Secondary analyses

We tested PIP's impact on individual outcomes at a two-sided α equal to 0.05 using the regressions described above. We used the same models to estimate PIP's effect on completing all tasks in the PMTCT cascade. We considered our secondary analyses to be exploratory and retained the model P values in lieu of a multiple-testing adjustment.

Late-entry participants with infants in the same age range as regular-entry participants' infants at a particular assessment were included in analyses, when possible. Overall, results were similar whether or not late-entry participants' data were included; results are available upon request.

Results

Baseline characteristics of overall sample

Table 1 summarizes the self-reports of PIP and standard care mothers at baseline. Women were similar across conditions on outcome-related measures, such as HIV testing, receiving HIV test results, asking partners to test, knowledge of partner HIV status, alcohol use in pregnancy, rates of prior LBW infants, depression, and social support measures; matching criteria, such as housing type, water source, and presence of flush toilet and electricity on premises; demographic characteristics, including age, marital status, education, employment status, and household income; and general health, including HIV and TB infection rates. One significant baseline difference between PIP and standard care was noted: among women who had been pregnant before, standard care had a higher mean number of previous births. There were no significant selection effects between mothers who were successfully reassessed over the 6 months postbirth and those who were not. There were no serious study-related adverse events. Over 6 months, less than 1% of mothers died, and about 8% of infants died, similar across conditions.

Postbirth and 6-month outcome measures

Women living with HIV

At the baseline interview, 295 women reported an HIV-positive serostatus. Between the baseline and 6-month assessments, 59 additional women disclosed an HIV-positive serostatus to the researchers ($n = 354$, 29%). About 20% of WLH were prescribed lifelong antiretroviral drugs. At 6 months, 2% of WLH's infants were HIV-positive.

The average absolute correlation between the 28 measures using the Pearson and the tetrachoric correlations was 0.088 and 0.202, respectively. As shown in Table 2, PIP outperformed standard care on six of 28 outcomes, resulting in PIP having significantly better overall maternal and infant well being over the first 6 months postbirth compared to standard care using the binomial test (correlation = 0.2, $P = 0.009$).

On specific PMTCT tasks (Table 2), WLH were similar across conditions in the percentage of WLH adhering to antiretrovirals surrounding childbirth and seeking infant PCR testing. PIP WLH were more likely to administer infant NVP at birth (odds ratio, OR = 2.94; two-sided $P = 0.004$), correctly medicate infants with ZDV

Table 1. Baseline characteristics of sample ($N = 1238$) grouped by intervention condition: Philani Intervention Program (PIP, $N = 644$) vs. standard care ($N = 594$).[a]

	PIP ($N = 644$) *n* (%)	Standard care ($N = 594$) *n* (%)	Total ($N = 1238$) *n* (%)	*P* value[b]
Demographic characteristics				
Mean age (SD)	26.5 (5.5)	26.3 (5.6)	26.4 (5.5)	0.783
Mean highest education level (SD)	10.3 (1.8)	10.3 (1.8)	10.3 (1.8)	0.639
Married or lives with partner	377 (58.5)	324 (54.6)	701 (56.6)	0.524
Ever employed	129 (20.0)	104 (17.5)	233 (18.8)	0.341
Monthly household income >2000 Rand	280 (45.6)	279 (48.1)	559 (46.8)	0.484
Formal housing	197 (30.6)	191 (32.2)	388 (31.3)	0.958
Water on site	333 (51.7)	327 (55.1)	660 (53.3)	0.983
Flush toilet	340 (52.8)	343 (57.7)	683 (55.2)	0.923
Electricity	569 (88.4)	543 (91.4)	1112 (89.8)	0.843
Mother hungry past week	312 (48.4)	301 (50.7)	613 (49.5)	0.350
Children hungry past week	175 (27.2)	185 (31.1)	360 (29.1)	0.054
Maternal health				
Nonprimipara	422 (65.5)	394 (66.3)	816 (65.9)	0.714
Mean number of live births (SD)	1.5 (0.9)	1.7 (1.1)	1.6 (1.0)	0.005*
Antenatal clinic appointment	504 (78.3)	376 (75.2)	880 (76.9)	0.330
Tested for TB, lifetime	206 (32.0)	210 (35.4)	416 (33.6)	0.225
Test positive TB, lifetime	53 (8.2)	50 (9.4)	103 (8.8)	0.438
Mental health				
EPDS >13	238 (37.0)	195 (32.8)	433 (35.0)	0.265
HIV and reproductive health behavior				
Sexual partner, past 3 months	580 (90.1)	522 (87.9)	1102 (89.0)	0.284
Knowledge of partner HIV status				0.523
Partner HIV-positive	46 (7.9)	50 (9.6)	96 (8.7)	
Partner HIV-negative	325 (56.0)	296 (56.7)	621 (56.4)	
Partner serostatus unknown, or no response	209 (36.0)	176 (33.7)	385 (34.9)	
Request partner HIV test	391 (82.5)	355 (83.1)	746 (82.8)	0.790
Ever tested for HIV	590 (91.6)	550 (92.6)	1140 (92.1)	0.566
Received HIV test results	584 (99.0)	547 (99.5)	1131 (99.2)	0.399
Women living with HIV	149 (25.5)	146 (26.7)	295 (26.1)	0.649
Mean number people disclosed to (SD)	3.8 (4.5)	5.0 (7.2)	4.4 (6.0)	0.104
Sexual partner, past 3 months	127 (85.2)	125 (85.6)	252 (85.4)	0.947
Disclosed to partner	99 (73.9)	105 (82.7)	204 (78.2)	0.140
Knowledge of partner HIV status				0.260
Partner HIV-positive	42 (33.1)	50 (40.0)	92 (36.5)	
Partner HIV-negative	13 (10.2)	17 (13.6)	30 (11.9)	
Partner serostatus unknown, or no response	72 (56.7)	58 (46.4)	130 (51.6)	
Alcohol				
Drank any alcohol, month prior to pregnancy discovery	155 (24.1)	129 (25.8)	284 (24.8)	0.592
AUDIT-C >2, month prior to pregnancy discovery	113 (17.6)	101 (20.2)	214 (18.7)	0.323
Drank any alcohol after pregnancy discovery	56 (8.7)	49 (9.8)	105 (9.2)	0.540
AUDIT-C >2, after pregnancy discovery	41 (6.4)	24 (4.8)	65 (5.7)	0.385
Drank any alcohol, anytime during pregnancy	172 (26.7)	154 (25.9)	326 (26.3)	0.808
Low birth weight (LBW)				
Previous LBW infants, among nonprimiparous mothers	61 (14.5)	69 (17.5)	130 (15.9)	0.117

AUDIT-C, Alcohol Use Disorders Identification Test-C.
[a]Sample size for standard care includes 500 regular-entry controls and 94 late-entry controls.
[b]*P* values from linear (continuous variables), logistic (binary), or multinomial (categorical, >2 levels) random effects regressions, adjusted for neighborhood clustering.
*$P < 0.05$.

(OR = 2.95; $P = 0.028$), and practise one feeding method for the first 6 months (OR = 1.81; $P = 0.002$). Cumulative completion of the tasks in the PMTCT cascade (Fig. 2) was greater in PIP compared to standard care (OR = 1.95; $P < 0.001$). Furthermore, compared to standard care, PIP WLH were more likely to have infant height-for-age *z*-score at least −2 (OR = 1.63; $P = 0.013$), be free of postbirth complications (OR = 2.26; $P = 0.002$), and have the father acknowledge the infant to his family (OR = 4.66, $P = 0.007$). However, PIP WLH were less likely than standard care WLH to know their CD4 cell count (OR = 0.51, $P = 0.017$).

Overall sample

The average absolute correlation between the 28 measures among the full sample using the Pearson and the tetrachoric correlations was 0.075 and 0.173, respectively. As shown in Table 3, PIP outperformed standard care on seven of 28 outcomes; thus, using the binomial test, we can declare PIP to have resulted in significantly better overall maternal and infant well being over the first 6 months postbirth compared to standard care (correlation = 0.2, $P = 0.005$).

PIP and standard care mothers and infants differed significantly on individual outcomes. HIV prevention

Table 2. Postbirth and 6-month health and well being outcomes among women living with HIV ($N = 354$), grouped by intervention condition: Philani Intervention Program ($N = 185$) vs. standard care ($N = 169$).[a]

	PIP ($N = 185$) *n* (%)	Standard care ($N = 169$) *n* (%)	Estimated odds ratio, PIP vs. standard care, (95% CI)[b]	Two-sided *P* value[b]	One-sided, upper tail *P* value[b]
HIV-related preventive acts					
Among mothers with a current sexual partner[c]					
Asked sexual partner to test for HIV	125 (91.9)	103 (91.2)	1.21 (0.57, 2.61)	0.619	0.309
Discussed HIV status with sexual partner	109 (80.1)	96 (85.0)	0.71 (0.34, 1.47)	0.360	0.820
Consistent condom use (used a condom in 10 of the last 10 sexual episodes)	82 (60.3)	61 (54.5)	1.19 (0.65, 2.19)	0.565	0.282
Mother knows last CD4 cell count	145 (89.5)	130 (92.9)	0.51 (0.30, 0.89)	0.017	0.992
PMTCT					
Mother took ZDV prior to labor, or full-ARVs[PB]	169 (94.4)	149 (93.7)	1.08 (0.42, 2.80)	0.868	0.434
Mother took ZDV during labor, or full-ARVs[PB]	164 (91.6)	147 (92.5)	0.87 (0.39, 1.95)	0.741	0.630
Mother took NVP tablet at onset of labor, or full-ARVs[PB]	166 (92.7)	142 (89.3)	1.52 (0.70, 3.31)	0.291	0.146
Infant given NVP syrup within 24 h of birth[PB]	171 (95.5)	141 (88.7)	2.94 (1.41, 6.13)	0.004	0.002*
ZDV dispensed for infant and medicated as prescribed[PB]	172 (96.1)	142 (89.3)	2.95 (1.12, 7.73)	0.028	0.014*
Took infant to 6-week HIV PCR test and fetched results	155 (96.9)	132 (94.3)	1.80 (0.62, 5.28)	0.282	0.141
One feeding method first 6 months: formula or breastfeeding	96 (55.8)	64 (42.1)	1.81 (1.26, 2.62)	0.002	0.001*
Child health and nutrition					
Birth weight $\geq$2500 g[PB]	156 (87.2)	123 (80.9)	1.27 (0.89, 1.82)	0.185	0.093
Weight-for-age *z*-score ≥ -2	163 (98.2)	147 (97.4)	– (–)	–	–[d]
Height-for-age *z*-score ≥ -2	146 (88.5)	118 (79.7)	1.63 (1.11, 2.39)	0.013	0.006*
Weight-for-height *z*-score ≥ -2	159 (95.8)	146 (98.0)	0.50 (0.13, 1.96)	0.321	0.840
Head-circumference-for-age *z*-score ≥ -2	163 (98.2)	138 (93.2)	– (–)	–	–[d]
Number of months breastfed exclusively > median of 3	8 (50.0)	9 (37.5)	1.62 (0.46, 5.73)	0.458	0.229
Exclusive breastfeeding first 6 months	4 (2.3)	2 (1.3)	1.93 (0.39, 9.61)	0.420	0.210
Drank no alcohol the month prior to giving birth[PB]	169 (91.4)	141 (91.0)	0.99 (0.46, 2.12)	0.970	0.515
No risky drinking at 6 months (AUDIT-C score $\leq$2)	152 (88.4)	139 (89.1)	0.85 (0.44, 1.66)	0.641	0.680
Healthcare and monitoring					
Four or more antenatal clinic visits (4 is standard practice)[PB]	142 (83.5)	136 (83.4)	0.98 (0.52, 1.85)	0.958	0.521
Mother free of postbirth complications through 6 months[e]	34 (18.4)	15 (8.9)	2.26 (1.34, 3.81)	0.002	0.001*
Mother tested for TB	23 (13.4)	19 (13.8)	0.84 (0.49, 1.43)	0.517	0.742
Number of immunizations > median of 11 (16 total)	57 (42.5)	61 (46.2)	0.91 (0.65, 1.27)	0.575	0.712
Mental health					
Not depressed (EPDS $\leq$ 13)	124 (72.1)	114 (73.1)	0.86 (0.57, 1.30)	0.474	0.763
Social support					
Number of close friends or relatives × frequency of contact > median of 20.5[f]	85 (49.4)	79 (50.6)	0.92 (0.55, 1.53)	0.739	0.631
Father acknowledged infant to family	162 (98.2)	141 (91.6)	4.66 (1.53, 14.19)	0.007	0.003*
Receiving child support grant	77 (65.8)	65 (62.5)	1.07 (0.61, 1.85)	0.822	0.411

ARV, antiretroviral; EPDS, Edinburgh Postnatal Depression Scale; NVP, nevirapine; PMTCT, prevention of mother-to-child transmission; ZDV, zidovudine.

[a]Sample size reflects participants available postbirth or at 6 months ($N = 354$). Postbirth outcomes are indicated using[PB]; other outcomes are from the 6-month assessment. Sample sizes for each assessment: postbirth assessment: PIP ($N = 185$), standard care ($N = 168$, including 145 regular-entry controls and 23 late-entry controls), total ($N = 353$). Six-month assessment: PIP ($N = 172$), standard care ($N = 156$, including 138 regular-entry controls and 18 late-entry controls with infants older than 4 months), total ($N = 328$).

[b]Random effects logistic regression, adjusted for neighborhood clustering, controlling for baseline employment. One-sided *P* value used in the binomial test; two-sided *P* value used in the secondary analysis of individual outcomes.

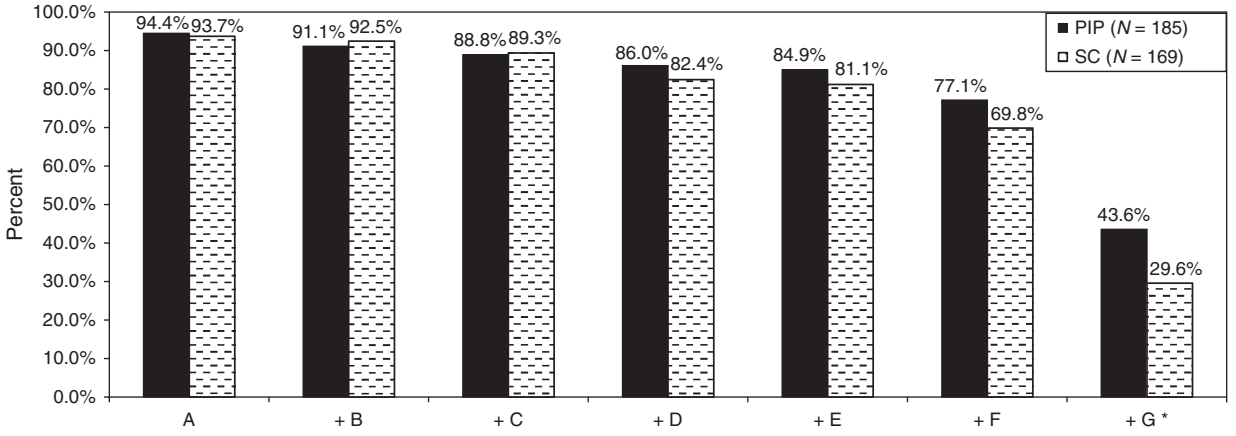
[c]Measures assessed for mothers with a current sexual partner: PIP ($N = 137$), standard care ($N = 113$), total ($N = 250$).

[d]Model failed to converge.

[e]Postbirth complications include heavy vaginal bleeding, malodorous discharge, fever, persistent cough, and breast infection.

[f]Median number of close friends or relatives: 2. Median frequency of contact in past month: 7.5.

*One-sided, upper tail $P < 0.025$.



Key: A. Maternal ZDV prior to labor, or full ARVs
B. Maternal ZDV during labor, or full ARVs
C. Maternal NVP at onset of labor, or full ARVs
D. Infant NVP within 24 hours of birth
E. Infant ZDV dispensed and medicating as prescribed
F. Infant HIV PCR test and results
G. One feeding method first 6 months

Note: "+" indicates that the behavior listed includes itself and all behaviors listed to the left: cumulative adherence.
*Estimated OR, PIP vs. SC (95% CI): 1.95 (1.36, 2.79); $p < 0.001$. From random effects logistic regression, adjusted for neighborhood clustering, controlling for baseline employment.

Fig. 2. Adherence to cumulative behaviors in the prevention of mother-to-child transmission cascade among women living with HIV ($N = 354$), by intervention condition. Philani Intervention Program (PIP; $N = 185$) vs. standard care (SC; $N = 169$). ARVs, antiretroviral drugs; NVP, nevirapine; ZDV, zidovudine.

differed by condition: consistent condom use was higher in PIP compared to standard care (OR = 1.52; two-sided $P = 0.002$), and, as described previously, there were significant differences in adherence to PMTCT tasks. Furthermore, PIP infants were more likely to have height-for-age z-score at least -2 (OR = 1.69; $P = 0.002$), breastfeed longer than the median number of 3 months (OR = 3.08; $P < 0.001$), and breastfeed exclusively for 6 months postbirth (OR = 3.59; $P < 0.001$). Healthcare, maternal depression, social support, and the percentage of mothers securing the child grant were similar across conditions.

Discussion

This study demonstrates the effectiveness of a CHW model for delivering home-based preventive care by addressing multiple health issues. We focused on the issues most salient in pregnancy in South Africa: HIV, alcohol use, and perinatal care. These were concurrently addressed with a model of pragmatic problem-solving with cognitive-behavioral intervention strategies. The South African government has begun to implement a similar model through a process they have termed 're-engineering primary healthcare' [25] and plans to deploy about 65 000 CHWs. We found significant benefits in overall maternal and infant well being for WLH and all neighborhood women and demonstrated the specific domains of improvement, especially for WLH. This model may be useful for countries that aim to promote task-shifting from professionals to CHWs in order to achieve HIV reduction and their Millennium Development Goals [1].

The gains for WLH and their children were broader than only adhering to PMTCT tasks. WLH and their children face life-long challenges, and home visits by CHWs create a vehicle for providing ongoing support to WLH and all community women. By having CHWs identified with a maternal, child health and nutrition program, much of the stigma associated with HIV is side-stepped. By focusing training on generic, common principles of behavior change and the specific health challenges of the local community, the potential exists to broadly diffuse the training model [26,27], allowing tailoring to the prevailing local diseases. Consistent with previous recommendations [28], the implementation was mounted by an agency with strong ties to community leaders, stakeholders, and clinical care sites; by CHWs who received a stipend to sustain the program; and following stringent supervision standards.

All neighborhoods (PIP and standard care) had nearby access to clinic and hospital services, which provided access to dual antiretroviral regimens for PMTCT. In the Cape Town area, PMTCT adherence rates are higher than in many parts of South Africa. In fact, the PMTCT adherence rates of WLH in standard care exceeded those observed in other studies of pregnant women in South Africa [29]. Yet, the odds of completing all PMTCT tasks were 1.95 times higher in PIP than standard care.

Table 3. Postbirth and 6-month health and well being outcomes among all participants ($N = 1157$), grouped by intervention condition: Philani Intervention Program ($N = 608$) vs. standard care ($N = 549$).[a]

	PIP ($N = 608$) *n* (%)	Standard care ($N = 549$) *n* (%)	Estimated odds ratio, PIP vs. standard care, (95% CI)[b]	Two-sided *P* value[b]	One-sided, upper tail *P* value[b]
HIV-related preventive acts					
Among mothers with a current sexual partner[c]					
Asked sexual partner to test for HIV	382 (87.8)	309 (83.5)	1.42 (0.96, 2.11)	0.078	0.039
Discussed HIV status with sexual partner	326 (74.9)	286 (77.3)	0.88 (0.65, 1.20)	0.412	0.794
Consistent condom use (used a condom in 10 of the last 10 sexual episodes)	189 (43.5)	124 (33.6)	1.52 (1.16, 1.99)	0.002	0.001*
Among HIV-positive mothers[d]					
Mother knows last CD4 cell count	145 (89.5)	130 (92.9)	0.51 (0.30, 0.89)	0.017	0.992
PMTCT					
Mother took ZDV prior to labor, or full-ARVs[PB]	169 (94.4)	149 (93.7)	1.08 (0.42, 2.80)	0.868	0.434
Mother took ZDV during labor, or full-ARVs[PB]	164 (91.6)	147 (92.5)	0.87 (0.39, 1.95)	0.741	0.630
Mother took NVP tablet at onset of labor, or full-ARVs[PB]	166 (92.7)	142 (89.3)	1.52 (0.70, 3.31)	0.291	0.146
Infant given NVP syrup within 24 h of birth[PB]	171 (95.5)	141 (88.7)	2.94 (1.41, 6.12)	0.004	0.002*
ZDV dispensed for infant and medicated as prescribed[PB]	172 (96.1)	142 (89.3)	2.95 (1.12, 7.73)	0.028	0.014*
Took infant to 6-week HIV PCR test and fetched results	155 (96.9)	132 (94.3)	1.80 (0.62, 5.28)	0.282	0.141
One feeding method first 6 months: formula or breastfeeding	96 (55.8)	64 (42.1)	1.81 (1.26, 2.62)	0.002	0.001*
Child health and nutrition					
Birth weight ≥ 2500 g[PB]	520 (90.1)	426 (87.1)	1.35 (1.00, 1.83)	0.051	0.025
Weight-for-age *z*-score ≥ -2	541 (97.8)	475 (97.5)	1.13 (0.59, 2.14)	0.715	0.357
Height-for-age *z*-score ≥ -2	496 (90.8)	414 (85.5)	1.69 (1.22, 2.34)	0.002	0.001*
Weight-for-height *z*-score ≥ -2	526 (95.6)	470 (97.1)	0.62 (0.36, 1.06)	0.079	0.961
Head-circumference-for-age *z*-score ≥ -2	537 (97.6)	462 (95.7)	1.88 (0.92, 3.81)	0.081	0.041
Number of months breastfed exclusively > median of 3	197 (49.5)	85 (23.9)	3.08 (2.17, 4.37)	<0.001	<0.001*
Exclusive breastfeeding first 6 months	59 (10.3)	15 (3.1)	3.59 (1.91, 6.75)	<0.001	<0.001*
Drank no alcohol the month prior to giving birth[PB]	566 (93.6)	443 (90.8)	1.50 (0.87, 2.58)	0.144	0.072
No risky drinking at 6 months (AUDIT-C score ≤ 2)	526 (91.8)	469 (92.1)	0.97 (0.60, 1.57)	0.893	0.553
Healthcare and monitoring					
Four or more antenatal clinic visits (4 is standard practice)[PB]	474 (82.7)	439 (82.7)	1.00 (0.74, 1.34)	0.992	0.504
Mother free of postbirth complications through 6 months[e]	127 (20.9)	102 (18.6)	1.16 (0.86, 1.57)	0.342	0.171
Mother tested for TB	72 (12.6)	57 (13.1)	0.95 (0.66, 1.36)	0.777	0.612
Number of immunizations > median of 11 (16 total)	179 (39.2)	185 (44.2)	0.81 (0.61, 1.09)	0.163	0.918
Mental health					
Not depressed (EPDS ≤ 13)	444 (77.5)	413 (81.1)	0.80 (0.59, 1.08)	0.148	0.926
Social support					
Number of close friends or relatives × frequency of contact > median of 16[f]	271 (47.3)	264 (51.9)	0.85 (0.62, 1.17)	0.318	0.841
Father acknowledged infant to family	536 (95.5)	475 (94.8)	1.17 (0.65, 2.13)	0.602	0.301
Receiving child support grant	233 (64.5)	213 (66.6)	0.92 (0.68, 1.23)	0.572	0.714

ARV, antiretroviral; AUDIT-C, Alcohol Use Disorders Identification Test-C; NVP, nevirapine; ZDV, zidovudine.

[a]Sample size reflects participants available postbirth or at 6 months ($N = 1157$). Postbirth outcomes are indicated using[PB]; other outcomes are from the 6-month assessment. Sample sizes for each assessment: Postbirth assessment: PIP ($N = 606$), standard care ($N = 546$, including 452 regular-entry controls and all 94 late-entry controls), total ($N = 1152$). Six-month assessment: PIP ($N = 573$), standard care ($N = 509$, including 434 regular-entry controls and 75 late-entry controls with infants older than 4 months), total ($N = 1082$).

[b]Random effects logistic regression, adjusted for neighborhood clustering. Models for outcomes among HIV-positive mothers control for baseline employment. One-sided *P* value used in the binomial test; two-sided *P* value used in the secondary analysis of individual outcomes.

[c]Measures assessed for mothers with a current sexual partner: PIP ($N = 437$), standard care ($N = 372$), total ($N = 809$).

[d]Measures assessed for HIV-positive mothers: PIP ($N = 185$), standard care ($N = 169$), total ($N = 354$).

[e]Postbirth complications include heavy vaginal bleeding, malodorous discharge, fever, persistent cough, and breast infection.

[f]Median number of close friends or relatives: 2. Median frequency of contact in past month: 7.

*One-sided, upper tail $P < 0.025$.

The gains from our study are significant, but modest. However, small gains often become magnified over time. Pregnancy and infancy are critical developmental phases with lifelong consequences; small changes that become habits can have substantial impact over a lifetime [10,30]. As our trial's primary endpoint is 18 months, we are continuing to monitor outcomes and will report final results when the trial is complete.

A universal goal in crafting interventions is sustainability. CHWs visited families on average six times during pregnancy and five times between birth and 2 months postbirth. This is substantially more intensive than most vertical, single-disease-targeted interventions that have been implemented in South Africa and globally. However, PIP has been ongoing since the 1990s and CHWs' salaries and experience are in line with South African government guidelines [31,32] and would, therefore, be sustainable. In addition to sustainability, home visits offer a viable strategy to circumvent challenges associated with obtaining healthcare from clinics. Clinic appointments are difficult to schedule; waiting lines are long; transport is expensive; and mothers must coordinate their own and infants' care across multiple clinics [32,33]. A CHW approach grounded in cognitive-behavioral skills, with locally tailored content addressing local health risks, may be a strategy that is scalable globally.

A noteworthy innovation was the use of mobile phones for data collection, and monitoring and supporting CHW [34]. Supervision and field support have often been major barriers to consistent, sustained CHW performance [35]. Mobile phones provided a tool for routine feedback in our study, and proved to be an effective supervisory tool, especially when combined with in-person supervision.

More than 1 million additional professional healthcare workers are required to meet existing health demands [36]. Task-shifting from healthcare professionals to CHWs has the potential to address this need [13]. PIP provided both task-shifting and site-shifting (from clinics to communities). It allows governments to leverage the investments in HIV to address concurrent health issues. PIP offers an intervention model and evaluation strategy for building sustainable, locally tailored CHW home visiting programs.

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Conflicts of interest

No authors have any competing interests. All authors have completed the Authorship Responsibility, Financial Disclosure, and Copyright Transfer form and declare no conflicts of interest: no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years, no other relationships or activities that could appear to have influenced the submitted work.

References

1. World Health Organization. *Millennium development goals*. http://www.who.int/topics/millennium_development_goals/en/. [Accessed 31 July 2012].
2. Grantham-McGreggor S, on behalf of the International Committee on Child Development Committee. **Correspondence: early child development in developing countries.** *Lancet* 2007; **369**:824.
3. USAID. *Maternal health in South Africa*. http://www.usaid.gov/our_work/global_health/mch/mh/countries/southafrica.html. [Accessed 14 December 2011].
4. Alamo S, Wabwire-Mangen F, Kenneth E, Sunday P, Laga M, Colebunders RL. **Task-shifting to community health workers: evaluation of the performance of a peer-led model in an antiretroviral program in Uganda.** *AIDS Patient Care STDS* 2012; **26**:101–107.

5. Ospina JE, Orcau A, Millet JP, Sánchez F, Casals M, Caylà JA. **Community health workers improve contact tracing among immigrants with tuberculosis in Barcelona.** *BMC Public Health* 2012; **12**:158.
6. Community Agency for Social Inquiry. *Phasing in the child support grant: a social impact study*. http://www.case.org.za/~caseorg/images/docs/child_support_grant.pdf. Published July 2000. [Accessed 31 July 2012].
7. Peacock S, Konrad S, Watson E, Nickel D, Muhajarine N. **Effectiveness of home visiting programs on child outcomes: a systematic review.** *BMC Public Health* 2013; **13**:17.
8. Young SD, Hlavka Z, Modiba P, Gray G, Paeds FC, Van Rooyen H, *et al*. **HIV-related stigma, social norms, and HIV testing in Soweto and Vulindlela, South Africa: National Institutes of Mental Health Project Accept (HPTN 043).** *J Acquir Immune Dec Syndr* 2010; **55**:620–624.
9. Olds DL, Robinson J, Pettitt L, Luckey DW, Holmberg J, Ng RK, *et al*. **Effects of home visits by paraprofessionals and by nurses: age 4 follow-up results of a randomized trial.** *Pediatrics* 2004; **114**:1560–1568.
10. Olds DL, Kitzman H, Cole R, Robinson J, Sidora K, Luckey DW, *et al*. **Effects of nurse home-visiting on maternal life course and child development: age 6 follow-up results of a randomized trial.** *Pediatrics* 2004; **114**:1550–1559.
11. Olds D, Hill P, Rumsey E. Prenatal and early childhood nurse home visitation. Juvenile Justice Bulletin No. NCJ-172875. Washington DC, Office of Juvenile Justice and Delinquency Prevention. https://www.ncjrs.gov/html/ojjdp/172875/contents.html. [Accessed 14 December 2001].
12. Olds DL, Robinson J, O'Brien R, Luckey DW, Pettitt LM, Henderson CR Jr, *et al*. **Home visiting by paraprofessionals and by nurses: a randomized, controlled trial.** *Pediatrics* 2002; **110**:486–496.
13. World Health Organization. Treat Train Retrain. *Task shifting: rational redistribution of tasks among health workforce teams*. Global recommendations and Guidelines, Geneva 2008. http://www.who.int/healthsystems/TTR-TaskShifting.pdf. [Accessed 24 October 2012].
14. Haines A, Sanders D, Lehmann U, Rowe AK, Lawn JE, Jan S, *et al*. **Achieving child survival goals: potential contribution of community health workers.** *Lancet* 2007; **369**:2121–2131.
15. Meichenbaum D. *Cognitive behavioral therapy: an integrative approach*. New York: Plenum Behaviour Therapy Series; 1977.
16. Rotheram-Borus MJ, le Roux IM, Tomlinson M, Mbewu N, Comulada WS, le Roux K, *et al*. **Philani Plus (+): a randomized controlled trial of Mentor Mother home visiting program to improve infants' outcomes.** *Prev Sci* 2011; **12**:372–388.
17. O'Connor MJ, Whaley SE. **Brief intervention for alcohol use by pregnant women.** *Am J Pub Health* 2007; **97**:252–258.
18. South Africa National Department of Health. *Policy and guidelines for the implementation of the PMTCT programme*. http://southafrica.usembassy.gov/root/pdfs/2008-pmtct.pdf. Published 11 February 2008. [Accessed 17 October 2012].
19. Marcos Y, Ryan Phelps B, Bachman G. **Community strategies that improve care and retention along the prevention of mother-to-child transmission of HIV cascade: a review.** *J Int AIDS Soc* 2012; **15 (Suppl 2)**:17394.
20. WHO Multicentre Growth Reference Study Group. *WHO Child Growth Standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age – methods and development*. Geneva: World Health Organization; 2006.
21. Cogill B. *Anthropometric indicators measurement guide*. Washington DC: Food and Nutritional Technical Assistance Project; 2003.
22. Dawson DA, Grant BF, Stinson FS. **The AUDIT-C: screening for alcohol use disorders and risk drinking in the presence of other psychiatric disorders.** *Compr Psychiatry* 2005; **46**:405–416.
23. Chibanda D, Mangezi W, Tshimanga M, Woelk G, Rusakaniko P, Stranix-Chibanda L, *et al*. **Validation of the Edinburgh Postnatal Depression Scale among women in a high HIV prevalence area in urban Zimbabwe.** *Arch Womens Ment Health* 2010; **13**:201–206.
24. Hartley M, Tomlinson M, Greco E, Comulada WS, Stewart J, le Roux I, *et al*. **Depressed mood in pregnancy: prevalence and correlates in two Cape Town peri-urban settlements.** *BMC Reprod Health* 2011; **8**:9.
25. Mohapi MC, Basu D. **PHC re-engineering may relieve overburdened tertiary hospitals in South Africa.** *S Afr Med J* 2012; **102**:79–80.
26. Rotheram-Borus MJ, Swendeman D, Chorpita B. **Disruptive innovations for designing and diffusing evidence-based interventions..** *Am Psychol* 2012; **67**:463–476.
27. Chaudhary N, Mohanty PN, Sharma M. **Integrated management of childhood illness (IMCI) follow-up of basic health workers.** *Indian J Pediatr* 2005; **72**:735–739.
28. Nyonator FK, Awoonor-Williams JK, Phillips JF, Jones TC, Miller RA. **The Ghana Community-based Health Planning and Services Initiative for scaling up service delivery innovation.** *Health Policy Plan* 2005; **20**:25–34.
29. Rollins N, Coovadia HM, Bland RM, Coutsoudis A, Bennish M, Patel D, *et al*. **Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa.** *J Acquir Immune Defic Syndr* 2007; **44**:321–328.
30. Martorell R, Horta BL, Adair LS, Stein AD, Richter L, Fall CHD, *et al*. **Weight gain in the first two years of life is an important predictor of schooling outcomes in pooled analyses from five birth cohorts from low- and middle-income countries.** *J Nutr* 2010; **140**:348–354.
31. Magongo B. *Community health workers in Gauteng: context and policy 2004*. http://www.cadre.org.za/files/PolicyCHWs.pdf. [Accessed 9 August 2012].
32. University of the Western Cape. *Re-engineering primary healthcare for South Africa: focus on ward based primary healthcare outreach teams*. http://www.uwc.ac.za/usrfiles/users/280639/CHW_symposium-NationalPHC_Reenginnering.pdf. Published 7 June 2012. [Accessed 1 August 2012].
33. Sprague C, Chersich MF, Black V. **Health system weakness constrain access to PMTCT and maternal HIV services in South Africa: a qualitative overview.** *AIDS Res Therap* 2011; **8**:10.
34. Tomlinson M, Solomon W, Singh Y, Doherty T, Chopra M, Ijumba P, *et al*. **The use of mobile phones as a data collection tool: a report from a household survey in South Africa.** *BMC Med Inform Decis Mak* 2009; **9**:51.
35. Lewin S, Babigumira SM, Bosch-Capblanch X, Aja G, van Wyk B, Glenton C, *et al*. Lay health workers in primary and community healthcare: a systematic review of trials. Norwegian Knowledge Centre for the Health Services for the International Dialogue on Evidence-informed Action to Achieve Health goals in developing countries (IDEAHealth), Oslo (2006). http://www.who.int/rpc/meetings/LHW_review.pdf. [Accessed 24 October 2012].
36. Kenenchukwu M, Llewleyn M. **Compensation for the brain drain from developing countries.** *Lancet* 2009; **373**:1665–1666.