The Amagugu intervention to increase disclosure of maternal HIV to HIV-uninfected primary-school aged children in Southern Africa: A randomised controlled trial.

Dr Tamsen Jean Rochat, PHD trochat@hsrc.ac.za

1. Africa Health Research Institute, , KwaZulu-Natal, South Africa.
2. Human and Social Development Research Program, Human Science Research Council, South Africa.
3. MRC/Developmental Pathways to Health Research Unit, School of Community Medicine, Faculty of Health Sciences, University of the Witwatersrand, South Africa
4. Section of Child and Adolescent Psychiatry, Department of Psychiatry, Oxford University, United Kingdom

Professor Alan Stein, F.R.C.Psych alan.stein@psych.ox.ac.uk

4. Section of Child and Adolescent Psychiatry, Department of Psychiatry, Oxford University, United Kingdom
5. MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Professor Mario Cortina-Borja, PHD m.cortina@ucl.ac.uk

6. Population, Policy and Practice Programme, University College London Great Ormond Street Institute of Child Health, United Kingdom

Professor Frank Tanser, PHD ftanser@gmail.com

7. Africa Health Research Institute, School of Nursing & Public Health, University of KwaZulu-Natal, KwaZulu-Natal, South Africa.
8. Centre for the AIDS Programme of Research in South Africa – CAPRISA, University of KwaZulu-Natal, Congella, South Africa.

Dr Ruth Bland, MD ruth.bland@ggc.scot.nhs.uk

1. Africa Health Research Institute, KwaZulu-Natal, South Africa.

5. School of Public Health, Faculty of Health Sciences, University of Witwatersrand, South Africa
8. Institute of Health and Wellbeing and Royal Hospital for Sick Children, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, United Kingdom

Corresponding author: Tamsen Jean Rochat, Human and Social Development Programme, Human Sciences Research Council, 5th Floor, The Atrium, 430 Peter Mokaba Ridge Road, Durban, 4000, PO Box 37429, Overport, 4067 trochat@hsrc.ac.za +27 31 242 5544

www.hsrc.ac.za

Key words: Parental HIV, primary school-aged children, disclosure, Amagugu, RCT

Summary: 323

Research in context panel: 674

Manuscript body text: 4175

Tables and Figures: 3 Tables; 2 Figures;

Web extra material: 4 Figures; 2 Table

References: 30

Structured summary

Background:

As HIV preventive efforts improve, an increasing population of preadolescent HIV-exposed but uninfected children face significant developmental and health challenges, including disclosure of parental HIV. The aim of this research is to test the efficacy of the Amagugu intervention to increase maternal HIV-disclosure to HIV-uninfected children aged 6-10 years, leading to improvements in health care engagement and custody planning.

Methods:

Individually randomised efficacy trial in rural KwaZulu-Natal, South Africa; follow-up to nine months. We used computer-generated simple random sampling with blinded assessment. The Amagugu intervention included six home-based counselling sessions; the enhanced standard of care included one clinic-based counselling session. The primary outcome was maternal HIV-disclosure (full, partial, none) measured at 9-months using an intention to treat analysis (NIH trial registration: NCT01922882 www.clinicaltrials.gov status: closed).

Findings:

We consecutively approached 634 women at four primary health care clinics (July 2013-December 2014). 464 mothers were randomised (Amagugu intervention *n*=235; enhanced standard of care *n*=229); 428 (92%) completed the 9-month assessment (September 2015). The Amagugu intervention led to an increase in any disclosure (204/235 vs. 128/229 aOR 9.88 [5.55-17.57] $p<0.001$) and full disclosure using the words 'HIV' (150/235 vs. 98/229 aOR 4.13 [2.80- 6.11] $p<0.001$). Time to full disclosure was shorter in the intervention group (median 2.83 vs. ESC median 9.10 months [log-rank test $p<0001$]). More mothers in the intervention group took their child to a clinic visit (aOR 31.49 [17.51-56.61] $p<0.001$), discussed a care plan (aOR 3.56 [1.64-7.69] $p=0.001$), and appointed a guardian (aOR 22.22

[1.25-3.94] *p*=0.001). There were no treatment related deaths; but 21 unrelated adverse events (intervention group=17; enhanced standard of care group=6).

Conclusions and Relevance:

This trial of a psychological intervention, the first from a low-resource setting, demonstrated positive outcomes. The counsellor-driven intervention changed maternal behaviours achieving high rates of mother-led HIV disclosure, enhanced health education and custody planning. Longer term follow-up and effectiveness research is required.

Funding: National Institutes of Health

Research in context panel

Evidence before this study

Given widespread use of antiretroviral therapy and successful prevention of mother-to-child transmission, there is a growing population of HIV-negative children living with HIV-infected parents. The literature on parental HIV groups children by those who are *HIV-exposed* because their mothers were HIV-infected during their pregnancy resulting in biological exposure and impacts due to contextual and/or caregiving pathways; and those who are *HIV-affected* because their mother has become HIV-infected post birth, so while biologically unexposed they may still be *affected* through contextual/caregiving pathways.

We searched PubMed for English articles published up to 29 April 2017, using the terms "children" "parental HIV disclosure" "interventions" returning 47 articles. Besides prior publications on Amagugu, the vast majority focused on interventions for either adolescents or HIV-infected children, most from high-income settings. Several recent systematic reviews (5 published between 2013-2016) examine outcomes of HIV-infected, HIV-exposed and affected children, reporting associations between parental HIV, illness or death, and children's physical, cognitive, educational, social and emotional outcomes. There is some evidence that HIV-exposed/affected children may be at increased sexual and abuse victimisation risk. Reviews confirm benefits of parental disclosure for parents, children and families, reporting mostly observational research from high-income settings. The absence of parental disclosure, in particular in the primary school years, can have negative effects. Only a few qualitative studies report negative effects of disclosure, mostly related to unplanned disclosures or disclosure as a consequence of parental illness. The World Health Organisation (2012) guidelines recommend supporting HIV disclosures to exposed/affected children. Despite documented benefits, disclosure rates remain low, with a systematic review reporting

disclosure rates from as low as 5% to as high as 67% with a median rate of 41%. Higher rates of disclosure are noted in older age groups of children. There is a clear need for intervention studies to address this gap.

Despite Africa bearing the overwhelming burden of HIV across the globe, relatively little research emanates from the continent. Disclosure rates on the continent suggest that disclosure often takes place in adolescence, thus missing significant prevention and education opportunities in earlier childhood. Our search returned a recent systematic review of disclosure interventions in low and middle-income countries (LMIC) finding only thirteen studies, twelve of which targeted adults. The Amagugu intervention, reported on here, was the only disclosure intervention designed to support parental HIV disclosure to primary school-aged children in LMIC. Two other controlled studies supporting mothers to disclose to their children were conducted in the United States, targeting adolescents and preadolescent children. The latter was a pilot trial of the TRACK intervention with 80 families, which increased disclosure to 33% in the intervention versus 7.3% in the control.

A 2015 commentary on investments made over the last decade by National Institutes of Health (NIH) in parental HIV disclosure research globally identifies several funded protocols of controlled studies underway to support parental HIV disclosure. This includes research in LMIC (predominantly Asia) and one, besides Amagugu, in Africa focused on disclosure to HIV-infected children in Namibia. We conclude that this is the first randomised controlled trial to report on a psychological intervention to increase maternal HIV disclosure to HIV-exposed, uninfected preadolescent children in Africa.

Added value of this study

The Amagugu intervention is an established, locally developed conceptual model of a complex intervention. We demonstrate, for the first time in Africa, that Amagugu

significantly increases disclosure, parent-child communication about HIV and health, and promotes custody planning, and that it does not have negative effects for parental or child mental health.

Implications of all the available evidence

This parent-centred behavioural intervention, delivered by lay counsellors rather than nurses in a task-shifting model suited to low-resource settings, demonstrates significant success in changing the behaviour of HIV-infected parents towards disclosure. Given support, and specific educational guidance, parents are able to engage in HIV disclosure at much higher rates than previously reported. This efficacy trial finds Amagugu to be acceptable, effective in producing the intervention targets, and transferable. It has potential for wider scale implementation following effectiveness research, and may be adapted to other target populations and other diseases.

Background

Successful Prevention of Mother-to-Child Transmission programmes and HIV treatment access has changed the HIV landscape dramatically. There are fewer HIV-infected children, but increasing numbers of children living with HIV-infected parents[1] whose HIV can be successfully managed by antiretroviral treatment (ART).[2] These children face developmental,[3] health[4] and psychological challenges[5] particularly where stigma is high.[6] Risks are elevated when mothers become ill or die[7] or where there is instability in care[8]. Parental HIV may have negative effects on children's later sexual health, particularly where children face multiple cumulative risks,[9] potentially increasing children's risk of becoming HIV-infected.[10] The success of HIV programmes needs to be followed by public health strategies to improve children's life chances including safeguarding their health, ensuring ongoing care if their parents become ill, and minimising risks of HIV acquisition. This is critical as adolescents are the only population in whom HIV incidence is not decreasing globally.[11]

Parental HIV-disclosure to children offers a good starting point in improving the outcomes of HIV-exposed uninfected children. The World Health Organisation (WHO) recommends disclosure to children under 12 years of age.[8] Systematic reviews [4,6] consistently conclude that maternal HIV disclosure to children has benefits for mothers including improved HIV treatment adherence and compliance, improvements in parent-child and family relationships, mental health and lower stigma. For children, evidence suggests improvements in custody and care plans and, in high-income countries (HIC), of mental health improvements. Some qualitative studies report negative effects, particularly linked to unintended or unplanned disclosures.[12] Importantly, a lack of disclosure has been shown to have negative mental health impacts for children while for mothers lower disclosure is associated with non-

adherence[6]. Despite the reported benefits of maternal HIV disclosure,[12] rates of parental disclosure remain low globally[8] with few interventions appropriate to low-resource settings.[13]

Two clinical trials in HIC have tested parental HIV disclosure interventions, one with adolescents,[6] the other with children aged 6-12 years.[14] The latter trial (United States) randomised 80 families to an intervention comprising three home visits, telephone support and educational materials, finding mothers were almost five-fold more likely to disclose than controls (33% vs. 7%). In HIV prevalent settings interventions focused on younger children are particularly important because household HIV burden is high[12] and non-disclosure of HIV has been shown to have negative effects.[6] A recent systematic review of disclosure interventions in low-and-middle-income- countries (LMIC)s[13] found 13 interventions, 12 of which focused on adult disclosure to other adults, while only one, the Amagugu intervention being tested here, focused on children. Prior to this randomised controlled trial we conducted a pilot study[15] and a large scale uncontrolled evaluation including 281 families[16,17]. Amagugu is an IsiZulu word which directly translated means "treasures" referencing the importance of children and families in society.

The primary aim of this study was to test the efficacy of the Amagugu Intervention. Using a randomised controlled design we hypothesize that when compared to an enhanced standard of care which provided a once-off counselling session at a Primary Health Care (PHC) facility, the Amagugu intervention would significantly increase rates of maternal HIV disclosure to HIV-uninfected children aged 6-10 years, leading to secondary benefits, including improvements in health care engagement, custody planning and the parent-child relationship.

Methods

Trial Design

This trial was an individually randomised, efficacy trial, with blind assessment (2013-2015) with follow-up to nine months post baseline.

Participants

The trial was undertaken at the Africa Health Research Institute (previously known as the Africa Centre for Population Health) in a rural HIV-endemic region of KwaZulu-Natal, South Africa, with good HIV treatment coverage.[18] Participants were recruited from four PHC facilities with well-established HIV treatment programmes. To be eligible, mothers had to have tested HIV-positive at least 6 months previously; have initiated HIV treatment or be enrolled in pre-treatment HIV care; have an HIV-uninfected child (aged 6-10 years) resident in her household; have not disclosed to any children in the household under 10 years of age; have not participated in the previous Amagugu pilot or evaluation studies; and have mental capacity to consent. In the first six months, given a slower than expected recruitment rate, the upper age limit for inclusion of children was increased from nine to 10 years of age, and recruitment sites were expanded from one to four PHC facilities.

The Amagugu intervention

The Amagugu intervention conceptual framework (Supplementary Figures 1,2)[19] draw on well-established evidence that maternal avoidant coping and a lack of disclosure and communication can lead to psychological distress in children and increased pressure on the parenting role. The intervention aims to shift maternal parenting behaviours to an active coping style, and emphasises behavioural change towards parenting practices which address important issues linked to the children's wellbeing, including health education and custody planning.

The Amagugu intervention included six 1-2 hour sessions delivered to mothers at home, over an 8-12 week period. It included printed materials and activities supporting age-appropriate

disclosure, and addressing maternal preparation for children's emotional reactions and questions following disclosure.[15-17] A detailed description of the intervention and the content of each of the sessions are included in the supplementary materials (Supplementary Table 2). While structured, the intervention was flexible allowing mothers to adjust the content to suit their circumstances and their child's developmental needs. Mothers selected the level of disclosure they were comfortable with, either partial (using the word 'virus') or full (using the words 'HIV') disclosure. The female lay-counsellors, all high-school graduates with several years' counselling experience, did not intervene directly with children but supported the mother to communicate with her child independently, thus enabling skills transference. The two-week counsellor training used the Amagugu training materials, including practical exercises and competency testing. Counsellors were seen fortnightly for supervision and managed between 15-25 families concurrently.

The enhanced standard of care

There is no standard of care in the South African Department of Health (DOH) regarding parental HIV disclosure to HIV-uninfected children, beyond a recommendation to 'counsel-to-disclose'. After randomisation, participants in enhanced standard of care were offered a once-off counselling session, focused on disclosure, delivered at the PHC facility as part of routine HIV services, either immediately or at another more convenient time. Participants who deferred counselling were re-approached and reminded about the offer of counselling by telephone and at their regular clinic visits but no follow up or counselling was conducted outside the clinic facility, there was no follow up at home. The one hour session provided information on the benefits of disclosure, disclosure guidance using a short vignette, and encouraged mothers to bring their children to a clinic visit and undertake custody planning. Counselling took place in a private furnished room, however, unlike in the Amagugu intervention no intervention materials were provided. Counsellors delivering the enhanced

standard of care had equivalent qualifications and experience to those in the intervention arm, and participated in a one-day training workshop using a training manual, role-plays and competency testing. They were seen every two months for supervision.

Standardisation of clinic services and intervention fidelity

Clinic staff, including HIV treatment nurses and counsellors, participated in a half-day workshop on the benefits of HIV disclosure, and health care engagement and custody planning for HIV-exposed children.

Both the Amagugu intervention and the enhanced standard of care counsellors participated in case reviews and completed study specific fidelity checklists developed and tested during the evaluation study.[16,17] An experienced trainer (isiZulu-speaking PhD student) conducted fidelity observations (using study specific scoring sheets) with 10% of participants in both the Amagugu intervention and enhanced standard of care arms, observing all counsellors across all intervention sessions. Average fidelity scores were >90% over the trial duration.

The two counselling teams (enhanced standard of care and Amagugu intervention) operated completely independently of each other. Counsellors were line- managed by different individuals, used separate transport services, were supervised separately, had differing scopes work, and were based at different geographical locations. Case reviews, supervision, and all aspects of the two arms were operationalized separately, and contact between staff was minimised.

Outcomes

The primary outcome (disclosure) and some secondary outcomes (health care engagement and care/custody planning) were measured using study specific surveys (used previously[16,17]) at baseline and 3, 6 and 9 month follow-up. For disclosure, if participants reported partial disclosure at an early time point, the survey was repeated at all further assessments, or until

full disclosure was reported. No imputation procedure was implemented to deal with lost-to-follow-up in line with an intention-to-treat principle. Other secondary outcomes were measured using psychometric scales, in interview format, in isiZulu, all of which have been used previously either in the study population or in other research with similar South African populations. All measures had good reliability scores in this randomised controlled trial (see supplementary Table 2 for full description and references).

Maternal mental health: Patient Health Questionnaires Depression (PHQ-9) and Anxiety scales (GAD-7) at baseline, 3, 6, 9 months.

Health-related quality of life: Rand Health Medical Outcomes Study Short Form (MOS-36 SF) (General Health subscale) at baseline, 9 months.

Parenting and the parent-child relationship: Parenting Stress Index short form (PSI-36SF) at baseline, 3, 6, 9 months.

Child mental health: Child Behaviour Checklist (CBCL) at baseline, 6, 9 months.

Family functioning: McMaster Family Assessment Device (FAD) at baseline, 3, 6, 9 months.

Sample size

A sample size of 480 participants followed for 9 months was calculated to achieve 90% power to detect a difference of 30% versus 45% (probability of type-one error of 5%, two-tailed) amongst women who undertook HIV disclosure to children, allowing for a 20% loss to follow-up (i.e. final sample of 384 women).

Randomisation

Screening, enrolment, randomisation and data collection used the Mobenzi Mobile Researcher Platform (MRP) (Mobenzi www.mobenzi.com), previously validated and used in South Africa.[20] Assessments, conducted via mobile phone, were uploaded to the MRP (via

secure SMS data transfer). Simple random sampling was used. Randomisation was completed in the MRP with guidance from the trial's statistician, using a computer generated random numbers algorithm, to create a pre-randomised list of participant IDs linked to each of the four PCH facilities. The number of IDs randomised was based on the estimated maximum recruitment estimates. The interviewer informed the participant of their randomisation to either home or clinic counselling (Supplementary Figure 3). Participants were allocated to counsellors electronically (ensuring even distribution); counsellors were notified of their participant's contact details via SMS. Outcome measures were collected using follow-up surveys by independent interviewers, blind to participants' randomisation and counsellor allocation. The MRP automated system delivered surveys and contact details of participants to the interviewers' mobile phone one week prior to the assessment date. The data collection protocol allowed the 9 month outcome assessment to be completed for up to 60 days post its due date, thereafter participants were declared loss to follow up if they could not be traced. The majority of assessments were completed within 20 days of being due.

Research Ethics approval

Ethical permission was granted by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC) (BFC273/12), and the DOH Provincial Research Ethics Committee (HRKM078/13).

We established a Data Safety and Monitoring Board (DSMB) prior to recruitment and undertook four reviews during the trial. The MRP provided an automated weekly report identifying potential harms using follow-up assessment data, including measures of potential suicide ideation and adverse effects of disclosure. Serious adverse events were defined by a Terms of Reference approved by the DSMB and BREC, and reported to the DSMB and BREC within three, and seven days respectively. They included: maternal or child death,

illness requiring hospitalisation >5 days, severe psychological/psychiatric illness (including psychosis, suicide ideation), trauma, violence or stigma as a direct result of the intervention or control conditions.

Statistical methods

The intention-to-treat principle was followed in the statistical analyses. We compared continuous variables using independent, two-sample *t*-tests and Wilcoxon-Mann-Whitney tests. Normality and homoscedasticity were assessed using the Shapiro-Wilk and Bartlett's tests, respectively. The interquartile range (IQR) was used as a measure of dispersion. We fitted logistic and ordinal (proportional odds) regression models adjusting for covariates where necessary to compare the main outcomes. Time to disclosure was analysed using Kaplan-Meier estimates and the log-rank test assessed differences in time to disclosure by study arm. Mixed-effects models with random effects in the intercept were fitted to account for the repeated measures resulting from the trial's protocol. Cox proportional hazard models were also fitted to analyse outcomes related to time to any and full disclosure. The assumption of proportional hazards was evaluated using the Therneau-Grambsch test.[21] Statistical analyses were performed using R version 3.2.1 and were undertaken by an independent trail statistican.

Role of funding source

The funder (National Institutes of Health) had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit.

Results

Recruitment

We consecutively approached 634 women attending HIV facilities (01 July 2013-01 December 2014); 482 met eligibility criteria: 18 (3.7%) declined participation; 464 mothers were randomised into enhanced standard of care (*n*=229) and Amagugu intervention (*n*=235) conditions, and 428 (92%) completed the 9-month end-point assessment (31st October 2015) (Figure 1 Trial Profile).

Non-completion rates of the 9-month assessment were 9.4% (22/235) in the Amagugu intervention group and 6.1% (14/229) in the enhanced standard of care group; these were not significantly different (Chi-squared p=0.39). In the enhanced standard of care arm 96 participants received counselling and 133 did not. Of these, 9, and 5, respectively were not followed-up to 9 months. The distribution of lost-to-follow-up in the three groups (intervention; standard of care treatment compliant; standard of care treatment non-compliant) was not significantly different (Chi-squared p=0.22).

Primary outcomes

As shown in Table 1, at baseline, significant differences between the Amagugu intervention and enhanced standard of care groups included that the intervention group had a higher number of boy children; higher levels of maternal employment and there were also significant differences in child age between the two groups, but the actual difference was small (median 7.7 vs. 7.9 years).

Adjusting for these three baseline differences, the intervention led to a nine-fold increase (p< 0.001) in any disclosure (including partial or full disclosure) and a four-fold increase (p<0.001) in full disclosure (using the words 'HIV' during disclosure) to children. These findings did not differ substantively from the unadjusted analysis (Table 2).

The intervention led to substantially higher rates of any disclosure (partial or full) in the intervention arm (204/221 or 92%, missing n=14), as compared to any disclosure in the standard of care (128/224 or 57%, missing n=5). When examining proportions of full disclosure only we show similarly higher rates in the intervention (150/221 or 68%) versus the standard of care group (98/224 or 44%).

Secondary outcomes

Unadjusted time to any disclosure was significantly shorter in the Amagugu intervention group (median 2.14 months) vs. enhanced standard of care (median 7.46 months, log rank test $p<0001$), as was time to full disclosure (intervention median 2.83 months vs. standard of care median 9.10 months, log-rank test $p<0001$) (see Kaplan Meier Curves of both times to disclosure in supplementary Figure 4). To account for the three covariates significantly associated with trial arm we fitted multivariable Cox -proportional hazard models to both times to disclosure; in both models the assumption of proportional hazards was not rejected. For time to any disclosure the adjusted hazard ratio (aHR) was 0.29 ($p<0.001$) and only the child's gender had a significant effect (aHR=1.25, $p=0.047$), indicating that participants in the enhanced standard of care arm had a 29% probability of completing disclosure compared with the Amagugu intervention arm, and that enhanced standard of care participants were 25% more likely to disclose if disclosure was to a girl child rather than to a boy child. For time to full disclosure the aHR between arms was 0.39 ($p<0.001$), whilst the only covariate with a significant effect was child age (AHR=1.12, $p=0.025$).

Amongst the 403 mothers with other children, we undertook some exploratory analysis into whether there were inter-arm differences in maternal disclosure to these children: 60/197

mothers in Amagugu intervention and 44/206 mothers in enhanced standard of care group disclosed to at least one other child (OR=1.61, p=0.041).

Compared to enhanced standard of care, many more mothers in Amagugu intervention took their child to a clinic visit (202/221, 91% versus 63/224, 28% p<0.001, missing n=14), completed a care plan (182/221, 82% versus 108/224, 48% p<0.001, missing n=5), and discussed the care plan with the child (Table 2). More mothers in Amagugu intervention appointed a guardian and did so earlier in the intervention.

There were no significant differences between the groups in terms of maternal or child mental health (although both groups showed improvements), or in family functioning, health-related quality of life, or overall parental stress. However, compared to the enhanced standard of care, mothers in the Amagugu intervention had significantly lower scores on the Parent-Child Dysfunctional Relationship subscale of the PSI-36SF (Table 3, Figure 2).

Adverse events

There were 17 adverse events reported in the Amagugu intervention: 5 Domestic Violence (expected/unrelated); 2 participant deaths (expected/unrelated); 2 Participant illness (requiring hospitalisation >5 days) (expected/unrelated); 3 Family member death (expected/unrelated); 1 Family illness (expected/unrelated); 4 sexual assault (3 participants 1 other family member) expected/unrelated.

There were 6 adverse events reported in the enhanced standard of care: 1 Domestic Violence (expected/unrelated); 1 participant death (expected/unrelated); 2 Participant illness (requiring hospitalisation >5 days) (expected/unrelated); 1 Serious psychiatric illness (participant child)

(unexpected/unrelated); 1 sexual assault (3 participants 1 other family member) expected/unrelated.

Discussion

This low-intensity intervention, delivered by lay counsellors, led to substantially increased rates of maternal HIV disclosure in a relatively short time period, with significant improvements in healthcare engagement and care planning for the child, and further disclosures to other children in the home. In the enhanced standard of care arm there were substantially lower rates of disclosure, health care engagement and care planning. We did not find significant differences between groups on psychological outcomes, although both groups showed marked improvements from baseline suggesting that disclosure did not lead to obvious negative mental health effects, and there was evidence for benefits in the quality of the parent-child relationship.

These findings are important because, notwithstanding access to lifesaving ART, HIV-infected mothers still face challenges including maintaining lifelong treatment, and negotiating possible periods of illness and hospitalisations, which impact on family life and caregiving.[7] Stigma is often high,[9] leaving parents and children socially isolated and stressed.[4] While parents often avoid disclosure about HIV in an effort to protect children,[6,16] by primary school-age children are likely to be aware of parental HIV, particularly in epidemic areas.[12,16,19] Rates of disclosure in the Amagugu intervention were higher than those recorded in other research across the globe, including in Africa: Uganda (50%); Asia: Thailand (35%); North America: Canada (31%) and Europe (11%). Likewise, participants were willing to disclose to children at younger ages than has generally evidenced in LMIC literature.[6] Developmental literature on parents with other life-threating diseases suggest the absence of communication about parental illness has negative effects on children.[22] With

438 millions of families affected by HIV in sub-Saharan Africa,[1] interventions which improve
439 family communication and planning[23], in the context of HIV,[4,7] have important potential
440 public health benefits.

441 Improved family communication and increased disclosure to children may hold longer term
442 benefits for mothers, given evidence that increased maternal disclosure to children is
443 associated with improved treatment adherence and compliance with clinical appointments.[6]
444 That the Amagugu intervention achieved a high level of behavioural change in the mother,
445 not only in HIV disclosure but also in engagement with a clinic visit and custody planning, in
446 a short time, is encouraging. There is evidence, from other parenting intervention work in
447 South Africa, to suggest that if programmes for HIV-infected parents and their children do
448 not target HIV disclosure directly, disclosure rates remain low, and that this non-disclosure is
449 associated with increased behavioural problems in children over time.[24,25] The primary and
450 secondary outcomes of this trial suggest that without the benefit of an intervention which
451 actively encourages parents to deal with communication about HIV, health education and
452 care planning, the rates of these remain low, which is concerning since the absence of these
453 are known to confer risks.[5,19]

454 We found that enhanced standard of care mothers were more likely to disclose to girls than
455 boys,[6,7] possibly linked to expectations that girls will assist with caregiving during illness.
456 HIV-infected parents face multiple stressors, including strained family relationships,
457 complicating care planning for children.[26] When HIV disclosure does not occur, or occurs
458 during periods of maternal illness, children are more likely to have emotional and behavioural
459 difficulties[6] and risk of neglect.[27] Timely maternal HIV-disclosure, with planning prior to
460 illness, may mitigate some of the effects of maternal HIV-related illness on children. Further,
461 given the evidence of increased sexual and reproductive health risks in this population in

adolescence, disclosure communication in earlier childhood may also provide opportunities to begin prevention early.[19]

A key aspect of the intervention was that primary school-aged children were given the opportunity to learn about HIV (or a virus), to become familiar with their local health care clinic, and to have input into their own care plan. The Amagugu model[19] (illustrated and described in supplementary materials) proposes that providing children with age-appropriate health and disease information[22,23] may have prevention effects, improving their ability to develop healthy practices and prevent longer-term risky behaviours.[28,29] We find that participants in the Amagugu intervention arm reported significant improvements in parent-child interactions. That Amagugu intervention mothers were more likely to take their child to clinic is encouraging as children would seldom accompany an adult to clinic in this context due to financial and time barriers. Early engagement of children in healthcare has demonstrated benefits both outside of , and in the context of, life threatening parental illness.[22]

Another key positive outcome was the increase in custody planning with the Amagugu intervention group. HIV-infected parents often express concerns about the future care of their children in the event of their own death.[26] Custody planning can decrease the likelihood of children being moved between households, separated from siblings, or placed in foster care.[5,7] Empirical studies on the adjustment of children orphaned by HIV highlight the importance of providing a supportive family environment and limiting the number of household moves during illness, or after a parent's death.[6,7] Therefore, custody planning can temper the potential detrimental effects of parental illness and possible death on the child.

Strengths and weaknesses

The limitations of this research include that there was an established HIV treatment programme in the study area, thus the results may not be generalizable to other parts of Sub-Saharan Africa with poor HIV treatment access. Further, the follow-up period was relatively short, and longer follow-up may be required to examine longer-term effects, including benefits for children's mental health. A potential limitation in the design includes that whilst every effort was made to ensure that counsellors did not meet or discuss participants, it was possible that this happened in a small number of cases. Likewise, whilst it was unlikely that mothers in the two arms met to discuss their counselling, there was a small chance this happened and may have led to contamination.

Strengths of this research include its focus on children aged 6-10 years who are particularly under researched in African contexts. Furthermore the Amagugu intervention specifically targeted mothers (as opposed to father and other caregivers) for training, a pragmatic decision since the majority of HIV-exposed children in Africa live with their mothers.[1] As reported elsewhere[19] the intervention is highly adaptable, allowing for inclusion of fathers and other family members in the disclosure process. An additional strength is that the intervention may be adaptable for other target populations, such as HIV -infected children. Intervention mothers were able to disclose to their children independently, and to other children in the household after the intervention, suggesting that skills gained through the intervention are transferable and effective for disclosure to younger children. While the Amagugu intervention is low intensity with only 6 sessions, compared to other interventions being tested with include between 14 and 24 sessions[30], it is possible that in future research some sessions may be combined to reduce intensity further, thus increasing scalability.

Conclusion

We demonstrate that a low intensity counsellor-driven intervention can change maternal behaviours towards communicating about HIV, achieving high rates of mother-led disclosure, enhanced health education, and care planning. Supporting parents to disclose to their preadolescent children (as recommended by the WHO) showed no evidence of negative impacts on children, and some evidence of improvements in parent-child relationship.

Globally adolescents are at high risk of HIV, and preventative interventions for that age group to date have shown little promise. HIV-exposed-uninfected children have heightened vulnerabilities and this, the first controlled study of a psychological intervention focused on HIV and targeting these children in LMIC, has demonstrated positive outcomes. It builds on existing evidence, mostly from HIC settings, which suggests that increased disclosure about parental life-threating illness, undertaken in a developmentally sensitive manner, improves parent-child communication about difficult-to-discuss health topics.

Increased communication and education of children about healthy behaviours, including HIV prevention before behaviours are established, may have potential to improve adolescent health behaviours among these high risk children as they mature. Longer term follow-up and effectiveness research is required.

Acknowledgements

We are grateful to all the mothers, children and their families who generously participated in the pilot, the evaluation research and the clinical trial. We acknowledge Samukelisiwe Dube, Megan Wight and Ntombizodumo Mkwanazi for their contribution to the implementation of the trial. We thank Kobus Herbst for assistance with data base design and management. We acknowledge our DSMB members: Professors Crick Lund (Chair), Nuala McGrath and Dr Conor Doherty and the chair of the BREC Professor Doug Wassenaar for their guidance during the course of the trial.

Interested readers may contact the corresponding author for information about access to the Amagugu intervention materials and protocol. Trial data is available on the Africa Health Research Institute data repository for researchers who meet the criteria for access to confidential data (www.africacentre.ac.za). For more information please contact the corresponding author or Dr Kobus Herbst, Deputy Director, Africa Health Research Institute. The authors have no conflict of interests to declare.

Author contributions

TR and RB contributed to conceptualisation, funding, supervision, acquisition, analysis and interpretation of data, drafted and made critical revisions to the manuscript. MC completed the statistical analysis of the trial and contributed to the interpretation and drafted and made critical revisions to the manuscript. AS and FT contributed to obtaining funding, acquisition, analysis and interpretation of data, and made critical revisions to the manuscript.

Funding sources

The randomized control trial received funding from the National Institutes of Health (RO1HD074267-01). The trial is registered on clinicaltrials.gov and can be assessed here (https://clinicaltrials.gov/ct2/show/record/NCT01922882) using the registration identifier

NCT01922882. The development of the Amagugu intervention and the evaluation study was funded by the Canadian International Development Agency (CIDA) (Grant No: ZA/A033520/3/8). The Africa Centre for Population Health, now called the Africa Health Research Institute (AHRI), where the research took place is funded by the Wellcome Trust (Grant Numbers: Previous Africa Centre 097410/Z/11/Z Current AHRI 201433/Z/16/Z).

Tamsen Rochat (AF160108) receives salary support from the Newton Advanced Fellowship Scheme. The UCL Great Ormond Street Institute of Child Health receives a proportion of funding from the Department of Health's National Institute for Health Research Biomedical Research Centre's funding scheme. The funding support of the Department of Science and Technology (DST) National Research Foundation (NRF) Centre of Excellence in Human Development at the University of the Witwatersrand towards the development of this manuscript is hereby acknowledged. Opinions expressed and conclusions arrived at, are those of the author and are not necessarily to be attributed to the Centre of Excellence in Human Development. Frank Tanser was supported by South African MRC Flagship (MRC-RFA-UFSP-01–2013/UKZN HIVEPI) and NIH grants (R01HD084233 and R01AI124389) as well as a UK Academy of Medical Sciences Newton Advanced Fellowship (NA150161).

References

1. Short SE, Goldberg RE. Children Living with HIV-Infected Adults: Estimates for 23 Countries in sub-Saharan Africa. *PloS one* 2015; **10**(11): e0142580.
2. Bekker L-G, Venter F, Cohen K, et al. Provision of antiretroviral therapy in South Africa: the nuts and bolts. *Antiviral therapy* 2014.
3. Rochat T, Houle B, Stein A, et al. Exclusive Breastfeeding and Cognition, Executive Function, and Behavioural Disorders in Primary School-Aged Children in Rural South Africa: A Cohort Analysis. *PLOS Medicine* 2016; **13(6): e1002044.** .
4. Goldberg RE, Short SE. What do we know about children living with HIV-infected or AIDS-ill adults in Sub-Saharan Africa? A systematic review of the literature. *AIDS care* 2016; **28**(sup2): 130-41.
5. Sherr L, Cluver L, Betancourt T, Kellerman S, Richter L, Desmond C. Evidence of impact: health, psychological and social effects of adult HIV on children. *AIDS* 2014; **28(Suppl 3)**: 251-9.
6. Qiao S, Li X, Stanton B. Disclosure of parental HIV infection to children: a systematic review of global literature. *AIDS Behav* 2013; **17**(1): 369-89.
7. Chi P, Li X. Impact of parental HIV/AIDS on children's psychological well-being: a systematic review of global literature. *AIDS and Behavior* 2013; **17**(7): 2554-74.
8. WHO. Guideline on HIV disclosure counselling for children up to 12 years of age. Geneva: World Health Organisation; 2011.
9. Cluver L, Orkin M, Boyes ME, Sherr L, Makasi D, Nikelo J. Pathways from parental AIDS to child psychological, educational and sexual risk: Developing an empirically-based interactive theoretical model. *Social science & medicine* 2013; **87**: 185-93.
10. Operario D, Underhill K, Chuong C, Cluver L. HIV infection and sexual risk behaviour among youth who have experienced orphanhood: systematic review and meta-analysis. *Journal of the International AIDS Society* 2011; **14**(1): 1.
11. Bekker L-G, Johnson L, Wallace M, Hosek S. Building our youth for the future. *Journal of the International AIDS Society* 2015; **18**(2Suppl 1).
12. Mkwanazi NB, Rochat TJ, Imrie J, Bland RM. Disclosure of maternal HIV status to children: considerations for research and practice in sub-Saharan Africa. *Future Virol* 2012; **7**(12): 1159-82.
13. Kennedy CE, Fonner VA, Armstrong KA, O'Reilly KR, Sweat MD. Increasing HIV serostatus disclosure in low and middle-income countries: a systematic review of intervention evaluations. *AIDS* 2015; **29**: S7-S23.
14. Murphy DA, Armistead L, Marelich WD, Payne DL, Herbeck DM. Pilot trial of a disclosure intervention for HIV+ mothers: the TRACK program. *J Consult Clin Psych* 2011; **79**(2): 203-14.
15. Rochat TJ, Mkwanazi N, Bland R. Maternal HIV disclosure to HIV-uninfected children in rural South Africa: a pilot study of a family-based intervention. *BMC Public Health* 2013; **13**(1): 147.
16. Rochat TJ, Arteche AX, Stein A, Mkwanazi N, Bland RM. Maternal HIV disclosure to young HIV-uninfected children: an evaluation of a family-centred intervention in South Africa. *AIDS* 2014; **28**: S331-S41.
17. Rochat TJ, Arteche AX, Stein A, Mitchell J, Bland RM. Maternal and child psychological outcomes of HIV disclosure to young children in rural South Africa: the Amagugu intervention. *AIDS* 2015; **29**: S67-S79.

18. Tanser F, Bärnighausen T, Grapsa E, Zaidi J, Newell M-L. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science* 2013; **339**(6122): 966-71.
19. Rochat T, Mitchell J, Stein A, Mkwanazi N, Bland R. The Amagugu Intervention: A conceptual framework for increasing HIV disclosure and parent-led communication about health and HIV prevention among HIV-infected parents with HIV-uninfected primary school-aged children. *Frontiers in Public Health* 2016; **4**(183).
20. Van Heerden A, Norris S, Tollman S, Richter L, Rotheram-Borus MJ. Collecting maternal health information from HIV-positive pregnant women using mobile phone-assisted face-to-face interviews in Southern Africa. *Journal of medical Internet research* 2013; **15**(6): e116.
21. Therneau TM, Grambsch PM. Modeling survival data: extending the Cox model: Springer Science & Business Media; 2000.
22. Christ GH, Christ AE. Current approaches to helping children cope with a parent's terminal illness. *CA: A Cancer Journal for Clinicians* 2006; **56**(4): 197-212.
23. Stein A, Ramchandani P, Murray L. Impact of parental psychiatric disorder and physical illness. Rutter's Child and Adolescent Psychiatry, Fifth Edition: Wiley-Blackwell; 2008: 407-20.
24. Allen AB, Finestone M, Eloff I, et al. The role of parenting in affecting the behavior and adaptive functioning of young children of HIV-infected mothers in South Africa. *AIDS and behavior* 2014; **18**(3): 605-16.
25. Eloff I, Finestone M, Makin JD, et al. A randomized clinical trial of an intervention to promote resilience in young children of HIV-positive mothers in South Africa. *AIDS* 2014; **28**: S347-S57.
26. Mason S. Custody Planning with Families Affected by HIV. *Health and Social Work* 2007; **32**(2): 143-6.
27. Cluver L, Boyes M, Orkin M, Sherr L. Poverty, AIDS and child health: Identifying highest-risk children in South Africa. *SAMJ: South African Medical Journal* 2013; **103**(12): 910-5.
28. Wilson EK, Dalberth BT, Koo HP, Gard JC. Parents' perspectives on talking to preteenage children about sex. *Perspectives on Sexual and Reproductive Health* 2010; **42**(1): 56-63.
29. Bastien S, Kajula L, Muhwezi WW. A review of studies of parent-child communication about sexuality and HIV/AIDS in sub-Saharan Africa. *Reprod Health* 2011; **8**(25): 1-17.
30. Rochat T, Netsi E, Redinger S, Stein A. Parenting and HIV. *Current Opinion in Psychology* 2017; **15**: 155-61.

Legends:

Figure 1: Trial profile showed randomised participants, lost to follow up and serious adverse events, by arm.

Figure 2: Changes in the Parent-Child Relationship Dysfunction Subscale by arm

Table 1: Sample characteristics by group (Intervention and Enhanced standard of care)

Table 2: Primary outcome (disclosure) and secondary outcomes of health care engagement, care and custody planning

Table 3: Secondary outcomes for parent-child relationships, maternal and child mental health, and family functioning

Supplementary materials include:

Figure 1: Non-disclosure as a pathway to risks for children of HIV-infected mothers

Figure 2: The Amagugu intervention model

Table 1: Description of Amagugu Intervention content

Table 2: Description of psychological measures used for secondary outcomes with references

Figure 3: Overview of the study design

Figure 4: Kaplan Meyer Curves for time to ‘any’ and ‘full’ disclosure, by arm

Table 1 Sample characteristics by group (Amagugu intervention and enhanced standard of care)

Characteristics	Total (*n* = 464) *n* (%)	Amagugu intervention (*n* = 235) *n* (%)	Enhanced standard of care (*n* = 229) *n* (%)	*p*-value
Maternal age *median (IQR)in years*	33 (29-39)	32 (29-39)	34 (29-39)	0.633
Maternal duration of ART *median (IQR) in years*	2.58 (1.29-4.66)	2.60 (1.29-5.02)	2.50 (1.29-4.33)	0.649
Maternal education				
None	25 (5)	18 (8)	7 (3)	0.071
Some Primary	74 (16)	31 (13)	43 (19)	
Grade 5 (Primary complete)	102 (22)	47 (20)	55 (24)	
Some Secondary	143 (31)	78 (33)	65 (28)	
Grade 12 (Secondary complete)	115 (25)	57 (24)	58 (25)	
Tertiary	5 (1)	4 (2)	1 (<1)	
Maternal employment				
Yes	111 (24)	67 (29)	44 (19)	**0.022**
No	353 (76)	168 (71)	185 (80)	
Maternal HIV treatment				
Yes	416 (90)	207 (88)	209 (91)	0.367
No	49 (10)	28 (12)	21 (9)	
Maternal health perceptions (MOS)				
Excellent	87 (19)	47 (20)	40 (17)	0.726
Very good	150 (32)	75 (32)	75 (33)	
Good	134 (29)	63 (27)	71 (31)	
Fair	74 16)	41 (17)	33 (14)	
Poor	20 (4)	9 (4)	11 (5)	
Maternal relationship status				
Not in a relationship	63 (13)	34 (14)	29 (13)	0.612
In a relationship with child's father	185 (40)	89 (38)	97 (42)	

In relationship with new partner	216 (47)	112 (48)	104 (45)	
Mother living with partner				
Yes	132 (28)	63 (27)	69 (30)	0.595
No	270 (58)	138 (59)	132 (57)	
Not in relationship (n/a)	63 (14)	34 (14)	29 (13)	
Mother knows partner HIV status				
Yes	151 (33)	78 (33)	73 (32)	0.903
No	119 (26)	60 (26)	59 (26)	
Not applicable	195 (42)	97 (41)	98 (42)	
Mother's partner's HIV status				
Positive	117 (25)	64 (27)	53 (23)	0.444
Negative	31 (7)	13 (6)	18 (8)	
Indeterminate	2 (<1)	1 (<1)	1 (<1)	
Declined to answer	1 (<1)	0 (<1)	1 (<1)	
Not applicable	314 (68)	157 (67)	157 (68)	
Mother disclosed to partner				
Yes	210 (45)	107 (46)	103 (45)	0.99
No	60 (13)	31 (13)	29 (12)	
Not applicable	195 (42)	97 (41)	98 (43)	
Level of disclosure to partner				
Full (using the words HIV)	204 (44)	102 (43)	102 (44)	0.213
Partial (using the words virus)	6 (1)	5 (2)	1 (<1)	
No disclosure/ not applicable	255 (55)	128 (55)	127 (55)	
Child's father alive				
Yes	363 (78)	177 (75)	186 (81)	0.199
No	94 (20)	52 (22)	42 (18)	
Don't know	8 (2)	6 (3)	2 (1)	
Child age *median (IQR)in years*	7.90 (6.98-8.92)	7.78 (6.86-8.76)	7.97 (7.19-9.05)	**0.021**
Child gender				
Male	232 (50)	131 (56)	101 (44)	**0.009**

Female	233 (50)	104 (44)	129 (56)	

Table 2: Primary outcome (disclosure) and secondary outcomes of health care engagement, care and custody planning.

Outcome	**Total (*n* = 464)**	**Amagugu intervention (*n* = 235)**	**Enhanced standard of care (*n* = 229)**	**OR [95%CI]**	**aOR [95%CI]**
PRIMARY OUTCOME					
Disclosed					
Yes	332 (75)	204 (92)	128 (57)	9.00 [5.14-15.77]	9.88 [5.55-17.57]
No	113 (25)	17 (8)	96 (43)		
Missing	19	14	5		
Level of disclosure					
Full disclosure	248 (56)	150 (68)	98 (44)	3.67 [2.52-5.35]	4.13 [2.80-6.11]
Partial disclosure	84 (19)	54 (24)	30 (13)		
No disclosure	113 (25)	17 (8)	96 (43)		
Missing	19	14	5		
SECONDARY OUTCOMES					
Took child to clinic visit					
Yes	265 (60)	202 (91)	63 (28)	27.17 [15.63-47.24]	31.49 [17.51-56.61]
No	180 (40)	19 (9)	161 (72)		
Missing	19	14	5		
Completed care plan for child					
Yes	290 (65)	182 (82)	108 (48)	5.01 [3.25-7.74]	5.55 [3.53-8.71]
No	155 (35)	39 (18)	116 (52)		
Missing values	19	14	5		
Discussed care plan with child					
Yes	255 (57)	168 (76)	87 (39)	2.90 [1.40-5.98]	3.56 [1.64-7.69]

No	35 (8)	14 (6)	21 (9)		
No care plan completed	155 (35)	39 (18)	116 (52)		
Missing	19	14	5		
Legal guardian appointed					
Yes	382 (86)	200 (90)	182 (81)	2.20 [1.25-3.85]	2.22 [1.25-3.94]
No	63 (14)	21 (10)	42 (19)		
Missing values	19	14	5		
Timing of guardian appointment					
3m	223 (50)	139 (63)	84 (38)	0.39 [0.26-0.59]	0.40 [0.26-0.61]
6m	121 (27)	47 (21)	74 (33)		
9m	38 (9)	14 (6)	24 (11)		
No guardian appointed	63 (14)	21 (10)	42 (19)		
Missing	19	14	5		

Table 3 Secondary outcomes for parent-child relationships, maternal and child mental health, and family functioning

Outcome	Baseline		9 month follow up		Unadjusted [c]	Adjusted [d]
	Intervention *n*=235	**Enhanced standard of care *n*=229**	**Intervention *n*=213[e]**	***Enhanced standard of care n=215[e]***		
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	***p*-value**	***p*-value**
MOTHER						
General Health Subscale (MOS-36) [a]	63.3 (12.6)	64.1 (11.6)	67.3 (19.8)	66.7 (20.9)	0.357	0.514
Depression (PHQ-9)	5.6 (5.0)	6.0 (5.7)	4.9 (4.7)	5.0 (4.9)	0.535	0.521
Anxiety (GAD-7)	4.5 (4.5)	5.0 (5.0)	3.1 (4.0)	3.3 (4.0)	0.334	0.542
Parenting Stress Total (PSI-36)	86.9 (26.1)	84.9 (24.0)	75.6 (29.5)	77.7 (25.4)	0.312	0.124
Parental Distress Subscale	34.7 (12.8)	34.7 (12.5)	27.6 (12.9)	28.4 (11.5)	0.595	0.495
Parent-child Relationship Dysfunction Subscale	**24.7 (8.8)**	**22.8 (7.5)**	**23.1 (10.6)**	**23.2 (9.5)**	**0.025**	**0.044**
Difficult Child Subscale	27.4 (8.6)	27.5 (8.6)	24.9 (9.8)	26.1 (8.8)	0.946	0.185
CHILD						
Child Behaviour Total problems (CBCL) [b]	52.9 (9.1)	52.0 (8.9)	47.1 (10.5)	47.1 (9.8)	0.319	0.268
Internalising	53.7 (9.8)	53.0 (9.5)	47.0 (10.5)	47.3 (9.9)	0.382	0.321
Externalising	51.9 (10.8)	51.9 (9.9)	46.4 (11.6)	46.1 (10.8)	0.845	0.754
FAMILY						
General Functioning Subscale (FAD)	2.5 (0.3)	2.5 (0.3)	2.4 (0.3)	2.4 (0.3)	0.650	0.242

a. *p-values result from a t-test for difference between 9 months and baseline by arms;*
b. *p-values are for main effects of differences between 9 months and baseline by arm adjusting for maternal employment, gender, and age; the models included an interaction term between time point and arm (interaction model).*
c. *General Health Subscale of the MOS - higher scores = better health related quality of life;*
d. *CBCL RTS - test developer norming software produces a standardised t-score by disorder; higher scores = more problem*
e. *Analysis based on complete cases at 9 months, using all available data, excluding loss to follow up in intervention (n=22) and enhanced standard of care (n=14)*