

# Brief IPT for depression among people newly diagnosed with HIV/AIDS:

## Adaptation and evaluation using mixed methods

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### 1 Aim

To adapt and evaluate a brief Interpersonal Psychotherapy (Evaluate, Support, Triage- IPT-EST) designed to bridge the gap between initial screening and allocation of treatment for depression in primary care for use among newly diagnosed with HIV/AIDS in concentrated epidemic settings in low and middle income countries, with the aim of improving depressive symptoms and enhancing linkage to care.

### 2 Brief Background

#### 2.1 HIV & Depression

Depression has been identified as a problematic and common co-morbidity among people living with HIV/AIDS. Prevalence of depression is generally higher among people living with HIV/AIDS, as compared with the general population (Bing et al; Ciesla et al). Depression has been found to have an adverse impact upon a range of HIV outcomes, most notably: adherence; morbidity and mortality (Antelman 2007; Leserman 2003). Although the evidence is not completely consistent, most studies have concluded that depression is one of the predictors of poor adherence (Springer et al 2012). In response to the identification of depression as an important problem among people living with HIV/AIDS, there has been a proliferation of studies evaluating psychological interventions which aim to a) reduce depressive symptoms and b) improve HIV outcomes, most commonly, adherence. The association of sub-optimum adherence with both individual morbidity and the development of drug resistance has meant that adherence has become a key focus of research. Many of these studies reveal promising results in terms of reducing depressive symptoms (Sherr et al 2011; Safren et al 2009; 2012). However, very few have been able to demonstrate a secondary impact upon HIV-related outcomes and none have sought to have an impact upon initial engagement with care.

#### 2.2 Linkage to care

Linkage to care is defined as awareness of HIV status and receiving an initial HIV medical care visit and is an essential step towards people living with HIV/AIDS obtaining the benefits associated with treatment with ART. In generalised epidemic settings, research and policies are increasingly directed towards the integration of HIV testing and care into non-specialist health services, which will hopefully reduce the gap between diagnosis and initiation of care. However, in countries where there are concentrated epidemics, integration is likely to be limited. Late presentation for initial HIV care visits and delayed initiation of treatment are key contributory factors to the high levels of early mortality (25 percent) observed in the first year of treatment programmes for HIV/AIDS in sub-Saharan African settings (Lawn et al 2008, 2010). Despite increased availability of antiretroviral therapy around the world, a significant proportion of those diagnosed with HIV are not linked with care and consequently are not receiving treatment (Rosen et al 2011). In our study in Goa, India, we found that 67 percent of people who received a diagnosis linked with care (Mayston et al, *in press*).

#### 2.3 Common Mental Disorder and linkage to care

There is emerging evidence that common mental disorder may have an adverse impact upon linkage to care. In a US sample of people who had recently been diagnosed with HIV, depression was a borderline statistically significant predictor of not attending HIV treatment services within three months of follow-up (Bhatia et al 2011). In a recent

study carried out among newly diagnosed HIV-infected people in South Africa, a brief measure of psychological distress (the MHI-5), was associated with a small decreased risk in linkage to care (defined as obtaining a CD4 count).

In our study in Goa, India, although major depression (score of >10 on PHQ-9) was associated with non-attendance of post-test counselling, we found no evidence to support our a priori hypothesis that major depression would be associated with non-linkage to care. Upon closer investigation, we found that symptoms of depression and anxiety were associated with greatly reduced odds of linking with care (eg. scoring 5-9 on PHQ-9, adjusted odds ratio= 0.18 95% confidence interval=0.06-0.57) (Mayston et al, *in press*). Three quarters of those who did not attend the ART Centre had symptoms of depression and/or anxiety and a third of those with symptoms did not attend. Our findings suggest a need to consider the impact of symptoms of common mental disorder upon HIV outcomes beyond the relevant diagnostic categories.

## **2.4 Factors associated with Common Mental Disorder among people newly diagnosed with HIV/AIDS**

Little is known about risk factors for mental disorder among people newly diagnosed with HIV/AIDS. Research suggests that although many people will have a short-term affective response to a diagnosis, most will recover and have the skills to cope with navigating the continuum of care. However, a minority, perhaps those with underlying psychosocial issues or depression, may need additional support to ensure they derive the full benefits from treatment. It is therefore important to take into account factors associated with depression when designing interventions for this group.

In our study in Goa, associations between psychosocial variables and CMD resembled patterns that found elsewhere among community based samples and may be indicative of the close multidirectional relationships between psychosocial adversity (particularly poverty), HIV and CMD. In contrast to other studies (Steward, Chandy et al. 2011, Akena, Musisi et al. 2012, Charles, Jeyaseelan et al. 2012), we failed to find an association between CMD and stigma. The way in which we measured stigma may have contributed to this null finding. Items on the adapted scale aimed to measure internalised stigma but the scale was not validated in Goa. Studies have shown that the relationship between stigma and CMD among people living with HIV/AIDS is nuanced, with evidence to support associations between particular domains of stigma- we only measured one.

## **2.5 Interventions for depression among people living with HIV/AIDS**

A recent systematic review identified ninety quantitative research papers reporting on a depression intervention with a comparison or control group, of which four were set in low and middle income countries (Sherr et al 2011). It is important to note that sixty four percent of studies included in this review were carried out among male or mostly male samples, the extent to which findings from these studies are generalisable to women and/or low and middle income settings is unclear. On the basis of this review, evidence for the effectiveness of psychological interventions in improving depressive symptoms among people living with HIV/AIDS in high income settings is moderately strong. Psychological interventions identified by the review were diverse. Whilst the majority of interventions employed a cognitive behavioural approach, other interventions included: peer support, counselling group therapy, interpersonal psychotherapy, mood management, coping effectiveness training (Sherr et al 2011).

Evidence for the efficacy or effectiveness of interventions for depression among people living with HIV/AIDS in low and middle income countries is sparse. A further two recent RCTs (including one pilot study) published after Sherr et al's (2011) review and carried out in low or middle income countries were identified. Both of these studies found an improvement in depressive symptoms when comparing the intervention group with the control among completers, they also had a significant level of non-uptake of the intervention or drop-out (Petersen et al 2014; Kaaya et al). Reasons for drop-out/non-attendance included earning own income, family illness, work commitments and the prohibitive cost of transport to sessions. In addition to these RCTs, Chibanda et al's (2011) promising pilot study of a problem-solving therapy (up to six sessions delivered by lay workers via a "friendship bench" in primary care) had a

high level of participation and was effective in reducing depressive symptoms. However, there was no comparison group with which to compare these findings.

Evidence for the effectiveness of treatments for depression in improving HIV-related outcomes is unclear. Four out of twenty studies identified in a systematic review of cognitive behavioural interventions for mood and anxiety disorders among people living with HIV measured adherence and two of these found that the intervention had a (positive) effect. Both of these trials were led by Safren (2009; 2012) using a CBT approach (12 sessions) with an intensive focus on adherence support. Perhaps the largest trial of psychological intervention among people living with HIV/AIDS remains The Healthy Living Project, an RCT of a CBT intervention aimed at reducing transmission risk behaviours. Although the intervention was successful in reducing risk behaviours over the twenty-five month study period, there was no impact upon psychosocial adjustment (Carrico et al 2009).

## **3 Materials and Methods**

### **3.1 Interpersonal Psychotherapy: Evaluation, Support, Triage (IPT-EST)**

IPT-EST was designed to fill the gap in primary care between screening patients for depression and triaging patients to appropriate treatment and care (Weissman & Verdelli 2012). IPT-EST is itself a new adaptation of an IPT approach which is currently undergoing testing in trials in Israel, Brazil and Haiti. The originators of the therapy have published an introductory paper on the design of the intervention in order to encourage collaborators to test it. There is good evidence to support the efficacy of IPT for the treatment of depression in primary care (Schulberg et al 2007; Weissman et al 2007). The IPT-EST intervention uses IPT strategies and is “designed to provide comprehensive evaluation and support to patients who screen positive for depression in primary care and who have transient symptoms in relation to a current stressor” over the course of three sessions. The intervention provides guidance on support and triage of those patients with sustained depression who require “more intensive or continuing treatment”. IPT-EST was developed partly in recognition of the fact that, in practice, those who initiate/seek psychological therapies rarely receive long-term treatment or even complete the recommended dose (usually at least six sessions). The authors point out that chronic, enduring depression requiring long-term treatment can be difficult to differentiate from more short term depressive symptoms.

### **3.2 Rationale**

The rationale for the proposed modification and evaluation of IPT-EST among people newly diagnosed with HIV/AIDS is based upon the need to address existing gaps in the evidence base. In order to effectively manage common mental disorders in the context of HIV/AIDS, it may be important to develop and test new interventions targeted at different levels of symptom severity and delivered at different points in the continuum of care. So far, mental health interventions in the context of HIV have targeted people with major depression who are engaged with care. Our own research in Goa suggests that milder symptoms of depression and/or anxiety may disrupt essential early engagement with care. In other settings, brief interventions delivered at a critical time point have been found to be effective in enhancing continuity of care at a time when this is threatened by change. For example, a “critical time point” intervention delivered to men with severe mental disorders during the time they were transitioning from sheltered to community living was found to reduce episodes of homelessness beyond the time limited period of active intervention (Susser et al 1997). An intervention targeted broadly aimed at bolstering self-help, resilience positive adjustment to living with HIV may help to close the gap between diagnosis and accessing treatment, alleviate immediate distress and promote enduring positive effects beyond the duration of the intervention. Triage and brief intervention of all those with depression/anxiety symptoms would facilitate identification and further intervention for the minority of people living with HIV/AIDS may have pre-existing or enduring depressive symptoms that require more intense, longer-term treatment.

The small existing evidence base suggests that there may be serious challenges in terms of the acceptability of psychological interventions which are designed to run over several weekly sessions and therefore require a significant commitment from participants outside of their normal attendance of health services. There is a need for brief interventions which coincide with usual care pathways. There appears to be a complete lack of research in this area of mental health interventions in the context of HIV/AIDS.

### 3.3 Approach to adaption of the IPT-EST intervention for use among people newly diagnosed with HIV/AIDS

Our approach to adaptation and evaluation of the modified intervention will closely follow the guidance of the MRC Framework for development and evaluation of complex interventions (2008). We will move from theoretical work (formative qualitative research to understand how depression and other factors inhibit linkage to care) to inform modifications to modelling (focus group discussions and cases series) to piloting of the refined modified intervention.

### 3.4 Setting

The study would be carried out in Goa, where we previously conducted the Umeed cohort study in which we explored the impact of common mental disorder upon access to care for HIV/AIDS (Mayston et al 2013; Mayston et al *in press*). Goa, the smallest Indian state by area, is situated on the west coast between Maharashtra and Karnataka and has a population of 1.34 millions (Government of Goa, 2010). For HIV/AIDS surveillance, Goa is divided into two districts: the north is described as one of India's high prevalence districts, with more than one percent prevalence among women at antenatal care. The south is medium prevalence, with more than five percent prevalence found among those attending STI clinics (high risk group) (UNAIDS, 2008). The target group for this intervention for the proposed study would be people newly diagnosed with HIV/AIDS. Potential participants will be informed about the study at the time of attending for pre-test counselling and testing for HIV/AIDS in public testing centres (from which we recruited the sample for the Umeed study). We will aim to deliver the three IPT-EST sessions at times that coincide with clinic attendance (pre-test counselling and testing, post-test counselling, initial ART Centre visits- Initial assessment, visits for CD4 counts, CD4 results, adherence counselling). The timing of these sessions will depend on the results of formative research.

### 3.5 Theory

#### 3.5.1 Formative qualitative research

**Aim:** To identify potential areas for adaptation of the original IPT-EST format

**Objectives:**

1. To identify barriers and facilitators to linkage to care
2. To assess the role of depressive symptoms in determining help seeking, self care and linkage to care
3. To assess the feasibility and acceptability of delivering a brief intervention for depression among people newly diagnosed with HIV/AIDS
4. In particular, to begin to explore: who might deliver such an intervention; the context in which the intervention might take place; the timing of the intervention

Participants to be included formative research will include:

- People newly diagnosed with HIV/AIDS with co-morbid depression
- People living with HIV/AIDS who had poor linkage to care
- People living with HIV/AIDS who had good linkage to care
- HIV counsellors
- ART Centre physicians

- HIV-related NGO staff

**Participants:** will be recruited using a similar methodology to that which we used in our previous study in Goa- which we found to be feasible and acceptable. A Research Assistant will describe the study to people attending the testing centre for pre-test counselling. Those who consent will be screened for depression; cognitive impairment using a brief instrument such as the PHQ-9. Participants will be asked to consent to later follow-up by telephone. Those who consent will be contacted a few days after their expected date for receiving test results and asked if they would be willing to participate in a qualitative interview, at the location of their choice (or told that they will not be interviewed). People living with HIV/AIDS who had poor/good linkage to care will be identified with the assistance of the ART Centre physicians and NGO staff.

### 3.5.2 Synthesis of findings and adaptation of IPT-EST

Findings from the formative qualitative work will be synthesised and discussed with an expert panel consisting of local people living with HIV/AIDS, NGO staff members, local and regional policymakers etc. with the aim of identifying appropriate modifications to the IPT-EST intervention. Modifications to the IPT-EST manual will be carried out in response to formative findings and expert feedback.

## 3.6 Modelling

### Aims:

1. To assess the acceptability of delivering the modified intervention among people newly diagnosed with HIV/AIDS
2. To generate hypotheses on key working mechanisms for intervention package selected for initial evaluation (based on findings from systematic review and formative qualitative research)

### 3.6.1 Methods:

**Focus Group Discussions:** with people living with HIV/AIDS to assess the acceptability of intervention style/components among people newly diagnosed (Barley et al 2012). The adapted intervention package and materials (info sheet etc.) will be presented to participants. Our objectives would be to obtain detailed feedback on this, to assess whether revisions needed to be made- in order to reduce potential barriers to the intervention working. (I.e. feedback on the potential intervention components; acceptability of: group/individual; number/timing of sessions; who delivers the intervention etc.)

**Participants:** in these focus groups would be recruited from NGO support groups and possibly previous participants in qualitative interviews.

**Series of n=1 case studies:** We will employ an exploratory single-case quantitative-qualitative analysis design (as used by Jordans et al 2012 to investigate the mechanisms for impact of counselling upon children with depression and anxiety in Burundi). Quantitative methods will be used to analyse how outcomes change over time from baseline; during the intervention (weekly time points for the duration of the intervention) and after the intervention (at 4 weeks after completion). Changes in depressive symptoms, resilience, attitudes and behaviours related to treatment and care (indicators to be developed on the basis of findings from and formative research).

After each intervention session, participants will take part in short qualitative interviews with a research assistant. These will be designed to:

- Identify life events between measurements that may have had an impact upon outcome indicators
- Gain insight into the participant's perceptions of the session- description, reflection and evaluation

Intervention facilitators will be asked to record in a logbook the topics covered, strategies used and client progress.

### 3.7 Piloting

**Aim:** To examine the feasibility and acceptability of the modified IPT-EST intervention compared with treatment as usual for a sample of people newly diagnosed with HIV/AIDS and with co-morbid depressive symptoms. The methods of the trial will be tested to inform the development of a definitive trial.

**Design:** Randomised controlled trial with people recruited at the time of post-test counselling. The intervention is adapted IPT-EST (in addition to usual care (HIV post-test counselling) and the comparison group is enhanced usual care (HIV post-test counselling plus psychoeducation leaflet)).

**Sample size:** The estimation of a definite effect size is not the aim of this pilot trial. A sample of 70 participants (35 per group) has been recommended for external pilot trials, to enable the estimation of pooled standard deviation for a continuous outcome (Teare et al 2013). A total of 88 participants will be recruited in order to allow for a 25 percent drop-out.

**Recruitment:** Recruitment will take place in the largest testing and counselling centre in Goa, located at Goa Medical College. The study will be introduced to all those eligible who are attending for pre-test counselling. Potential participants will be asked for their consent to undergo screening for depression. Screening will be carried out by research assistants using the PHQ-9. Those who score more than 10 will be asked to consent to being approached at the time of post-test counselling regarding participation in the pilot trial. The timing of IPT-EST sessions will be determined in response to formative research findings.

**Randomisation:** Individual randomisation will be carried out independently by the Clinical Trials Unit at King's College London.

**Measures:** The primary outcome (depressive symptoms) will be measured using the PHQ-9 at baseline, at the end of three sessions of treatment and four weeks from the end of treatment. Secondary outcomes will include: initial visit to the ART Centre, subsequent visits to ART Centre (for CD4 count, CD4 count results, initiation of ART (if eligible), and adherence to medications (if prescribed)). Qualitative interviews will be carried out with a sub-sample of participants, clinic staff and intervention facilitators in order to assess the experience of the intervention from different perspectives and to further assess feasibility and acceptability.

**Blinding:** Although it will not be possible to blind participants as to their allocation to intervention or control, efforts will be made to blind the researchers carrying out outcome assessments (and extracting outcome data from clinical records).

### 3.8 Statistical treatment of results

**Formative qualitative interviews, focus group discussions, pilot qualitative interviews:** Framework analysis will be used to identify and code qualitative data relevant to the aims and objectives of the study.

**Series of n=1 case studies:** Trajectories of outcome variables will be presented on graphs for each participant. Two raters will independently visually inspect these graphs to identify parallel changes in multiple variables and abrupt changes on any outcome between two measurement points. Linear regression will be used to quantify change for agreed variables within cases. Content analysis of qualitative data will be carried out so that connections may be explored between potential treatment mechanisms, life events and salient features of quantitative data.

**Pilot RCT:** Descriptive analyses will be carried out and drop-out rate at each time point will be calculated. Linear mixed models will be used to assess the difference in PHQ-9 scores between the intervention and control arms at the three measurement points. Intention to treat analysis will be used.

### 3.9 Full justification of budget

It is estimated that the proposed body of work will take between twelve and eighteen months to complete. Please see attached RGA form and budget for full description of estimated costs. The total budget is £76,065.51. This includes the salary cost for Dr. Rosie Mayston for one day per week for a total of eighteen months (£23, 153). It is proposed that a large proportion of funds (£30, 891) would be subcontracted to Sangath, an established research non-governmental organisation led by Prof. Vikram Patel and where the researcher was previously based for her PhD project (the Umeed study). These sub-contracted funds would cover the cost of the salaries of local researchers, an administrator and project co-ordinator who would carry out the data collection, train intervention facilitators and manage the day-to-day running of the study. This part of the budget also includes the cost of local transport, computer equipment, communications, recording equipment and office costs. The budget for international travel and subsistence is £13,520. This includes the cost of four return flights from London to Goa so that Dr. Rosie Mayston and Prof. Martin Prince are able to travel to Goa. The budget includes six months subsistence funding for Dr. Rosie Mayston so that she is able to spend extended periods of time in Goa in order to oversee study development and data collection. Finally, we have included £8,500 for publications and conferences- this includes funds for the presentation of findings at one international conference and open access fees for three high impact publications.