INTERVENTIONS FOR IMPROVING EMPLOYMENT OUTCOMES FOR WORKERS WITH HIV: A COCHRANE SYSTEMATIC REVIEW

Rachel Kristin Robinson
Master’s Thesis
Public Health
School of Medicine
Faculty of Health Sciences
University of Eastern Finland
May 2015
UNIVERSITY OF EASTERN FINLAND, Faculty of Health Sciences, Public Health
ROBINSON, RACHEL K.: Interventions for improving employment outcomes for workers
with HIV: A Cochrane Systematic Review
Master’s Thesis. 66 pages, 3 attachments (94 pages).
Instructors: Jos Verbeek MD, PhD; Sohaib Khan MBBS, MPH, PhD
May 2015

Keywords: HIV, HIV/AIDS, Return to Work, interventions, employment, educational,
pharmacological, psychological, vocational, ART

INTERVENTIONS FOR IMPROVING EMPLOYMENT OUTCOMES FOR WORKERS
WITH HIV: A COCHRANE SYSTEMATIC REVIEW

HIV infection, specifically in the working age population, is a major public health and economic
problem. The objective of this review was to evaluate the effect of interventions aimed at
sustaining and improving employment in HIV+ persons. We conducted a comprehensive search
from 1981 until December 2014 in the following databases: Cochrane Central Register of
Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, OSH UPDATE databases
(CISDOC, HSELINE, NIOSHTIC, NIOSHTIC-2, RILOSH), and PsycINFO. We considered
for inclusion all randomized controlled trials (RCTs) or controlled before-after (CBA) studies
assessing the effectiveness of pharmacological, vocational and psychological interventions with
HIV+ working-aged (16 years or older) participants that had used indices of employment as
outcomes. Two review authors independently screened all potential references and final
selection of studies was determined by consensus. We performed data extraction and ‘Risk of
bias’ assessment with the Downs & Black checklist, in duplicate. We measured the treatment
effect using odds ratio (OR) for binary outcomes and mean difference (MD) for continuous
outcomes. We applied the GRADE approach to appraise the quality of the evidence. We found
one RCT with 174 participants and five CBAs with 48,058 participants assessing the
effectiveness of vocational training (n = 1) and antiretroviral therapy (ART) (n = 5). We found
no studies assessing psychological interventions. The one RCT was conducted in the United
States; the five CBA studies were conducted in South Africa, India, Kenya, and Uganda. For
vocational intervention, in one study we could not infer the intervention effect due to a lack of
data. For pharmacological interventions, due to differences in outcome measures, we could only
combine the results of two studies in a meta-analysis. Two studies compared employment
outcomes of HIV+ persons on ART therapy to healthy controls. One study found a MD of - 1.22
days worked per month (95% confidence interval (CI) -1.74 to -1.07) at 24-months follow-up.
The other study found that the likelihood of being employed steadily increased for HIV+ persons
compared to healthy individuals from ART initiation (OR 0.35, 95% CI 0.26 to 0.47) to three-
to five-years follow-up (OR 0.73, 95% CI 0.42 to 1.28). Three other studies compared HIV+
persons on ART to HIV+ persons not yet on ART. Two studies indicated an increased likelihood
of employment due to ART for HIV+ persons on ART (OR 1.75 95% CI 1.44 to 2.12). One
study found that the group on ART worked 12.1 hours (95% CI 6.99 to 17.21) more per week
at 24-months follow-up. The evidence was rated as very low quality for all comparisons due to
a high risk of bias. Overall, we found very low-quality evidence showing that ART interventions
may improve employment outcomes for HIV+ persons. We need more high-quality, preferably
randomized studies, to assess the effectiveness of RTW interventions for HIV+ persons.
# Table of Contents

ABBREVIATIONS ............................................................................................................. 6

1 INTRODUCTION ......................................................................................................... 7

2 LITERATURE REVIEW .............................................................................................. 7
   2.1 HIV/AIDS ............................................................................................................. 8
   2.2 Ramifications of the Disease ............................................................................. 8
   2.3 Employment ......................................................................................................... 8
      2.3.1 Needs ........................................................................................................... 9
      2.3.2 Barriers to Employment .......................................................................... 10
      2.3.3 Employer Costs ....................................................................................... 12
      2.3.4 Interventions and Studies on Return to Work ..................................... 13
      2.3.5 ART ............................................................................................................ 15
      2.3.6 International Legislation/Interventions ................................................. 16
   2.4 Why it is important to do this review? ............................................................. 16

3 MAIN OBJECTIVE .................................................................................................... 17

4 METHODS ................................................................................................................ 18
   4.1 Criteria for considering studies for this review ............................................ 18
      4.1.1 Types of studies ....................................................................................... 18
      4.1.2 Types of participants ............................................................................ 18
      4.1.3 Types of interventions ............................................................................. 18
      4.1.4 Types of outcome measures .................................................................. 19
   4.2 Search methods for identification of studies ................................................. 19
      4.2.1 Electronic searches .................................................................................. 19
      4.2.2 Searching other resources ..................................................................... 20
   4.3 Data collection and analysis ............................................................................. 20
      4.3.1 Selection of studies .................................................................................. 20
      4.3.2 Data extraction and management ............................................................. 21
      4.3.3 Assessment of risk of bias in included studies ..................................... 21
      4.3.4 Measures of treatment effect ................................................................. 22
      4.3.5 Unit of analysis issues ............................................................................. 22
      4.3.6 Dealing with missing data ....................................................................... 23
      4.3.8 Assessment of reporting biases ............................................................... 24
      4.3.9 Data synthesis ......................................................................................... 25
      4.3.10 Subgroup analysis and investigation of heterogeneity ...................... 26
      4.3.11 Sensitivity analysis .................................................................................. 26

5 RESULTS .................................................................................................................. 28
   5.1 Results of the search ......................................................................................... 28
      5.1.1. included studies ...................................................................................... 29
      5.1.2 Excluded studies ....................................................................................... 33
   5.2 Risk of bias in included studies ....................................................................... 33
      5.2.1 Allocation (selection bias) ....................................................................... 34
      5.2.2 Blinding (performance bias and detection bias) .................................... 36
      5.2.3 Incomplete outcome data (attrition bias) ............................................. 36
      5.2.4 Selective reporting (reporting bias) ...................................................... 37
B. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy ............... 86
C. EMBASE search strategy .......................................................................................... 90
D. OSH UPDATE search strategy .................................................................................. 94
ABBREVIATIONS

AIDS    Acquired Immune Deficiency Syndrome
ART     Antiretroviral Therapy
cART    combination Antiretroviral Therapy
CBA     Controlled Before-After study
HAART   Highly Active Antiretroviral Therapy
HIV     Human Immunodeficiency Virus
MD      Mean Difference
OR      Odds Ratio
PLWH    People Living with HIV¹
RCT     Randomized Control Trial
RR      Risk Ratio
RTW     Return to work
SMD     Standardized Mean Difference
TNFCCP  Tamil Nadu Family Care Continuum Program
WHO     World Health Organization

¹ The terminology ‘PLWH’ was used in a few publications, interchangeably with HIV+ persons. For the sake of readability, we will use ‘HIV+ persons’ throughout the majority of the thesis.
1 INTRODUCTION

Chronic illness is associated with unemployment leading to economic insecurity, as well as social isolation (Bartley & Plewis 2002, Bambra et al. 2004,). Long-term absences, inability to perform, loss of productivity, stigmatization, unpredictability of the disease, medications, and cognitive symptoms all contribute to unemployment in those with chronic illness (Linn et al. 1985, Braveman et al. 2006). HIV/AIDS (human immunodeficiency virus)/(acquired immune deficiency syndrome) is not impervious to these issues. HIV/AIDS made its medical appearance in the 1980s, setting the scene for over a decade of public confusion and the scientific community racing against the clock to find a cause and a solution. The debilitating effects of HIV/AIDS include rapidly declining health status, quality of life, and a significantly abbreviated lifespan. Not until the development of the first protease inhibitor, Saquinavir, the fatal prognosis of HIV improved to a manageable chronic disease. As life expectancy for HIV+ individuals lengthens with treatment, other issues, such as sustaining employment have become apparent. With the vast majority of HIV+ persons being adults of working age, unemployment and job loss due to HIV construct serious public health and economic concerns (Yelin et al. 1991; Braveman et al. 2006; Kaiser Family Foundation 2007).

A vast array of literature has examined the barriers for HIV+ persons in returning to work and the needs of HIV+ individuals in sustaining employment. However, research has implemented very few employment related interventions within the HIV/AIDS community. The current research evidence base focuses primarily on antiretroviral therapy (ART) as means of restoring the functioning of an individual. However, as the needs of the HIV+ person in returning to work (RTW) are not solely medication related, other interventions to support employment are also necessary.

The following thesis will discuss HIV/AIDS, employment, and access the current evidence regarding interventions to improve employment outcomes for persons living with HIV (PLWH) using a Cochrane Systematic Review.
LITERATURE REVIEW

2.1 HIV/AIDS

UNAIDS reports more than 78 million persons have been infected with HIV in the past three decades (UNAIDS 2014). As of 2013, the WHO reports that currently 35 million people are living with HIV worldwide. Globally, 0.8% of adults aged 15-49 are infected with HIV. Of those adults, 16 million are women. In the past three and half decades, over 39 million HIV/AIDS related deaths have occurred. Sub-Saharan Africa remains the highest impacted region of the world with 1 in every 20 adults living HIV of which, 59% are women (UNAIDS 2014, WHO 2014).

When a HIV+ person’s CD4 count falls below 200 cells per cubic millimeter of blood (200 cells/mm3), clinically, the disease has progressed to AIDS. A normal CD4 counts ranges between 500 and 1,600 cells/mm3. An AIDS diagnosis can also be made if the patient develops one or more opportunistic illnesses, regardless of CD4 count. Survival, without treatment for HIV/AIDS, is approximately 3 years. (CDC 2015)

2.2 Ramifications of the Disease

The UNAIDS Gap Report discusses four key components widening the gap between people living with HIV and people without HIV: 1) Human rights violations, stigmatization and discrimination, 2) Access to treatment and services, 3) Gender-based inequalities, 4) Criminalization and exclusion. The People Living with HIV Stigma Index reports that persons who are HIV + as well as belong to certain populations encounter compounded stigmatization and discrimination for their gender, sexual orientation, participation in sex work or drug use (The People Living with HIV Stigma Index 2014).

2.3 Employment

Current HIV literature indicates unemployment and job loss is correlated with HIV infection in individuals of working age, especially for women (Dray-Spira et al. 2006). HIV, similar to other chronic illnesses, also gives rise to diminished productivity, increased absenteeism from work,
escalated financial burden on employers, increased unemployment and loss of wages (Feeley et al. 2004, Fox et al. 2004, Sendi et al. 2004, Kaiser Family Foundation 2007). In the last decade, however, as modern treatment advances management of the disease, it is now possible for HIV+ persons to have a longer life expectancy and healthier lives, pushing employment retention and return to work (RTW) to the forefront of the HIV discussion.

UNAIDS published unemployment averages of 37.7% for HIV+ individuals, which is more than three times higher than the international average unemployment rate of 11.7%. Reasons reported for unemployment include stigma, discrimination, restrictive policies and practices and ill health. One in nine people living with HIV are denied employment due to their HIV positive status (UNAIDS 2014). In a study conducted by van Gorp et al. of 98 HIV+ persons, who were actively seeking employment, only 24% of participants had returned to part or full-time work within two years (van Gorp et al. 1999). Rabkin et al. noted a high level of interest in returning to work for PLWH, however, current evidence supports relatively few actually return to work. The longitudinal study reported multiple factors, which supports the need for RTW interventions for PLWH. The authors describe work as source of income, self-esteem, companionship, and satisfaction. Furthermore, returning to work can serve as a ‘normalizing function’, which helps to eliminate the patient identity (Rabkin et al. 2004). A study by Waddell and Burton (2006) and a systematic review (Rueda et al. 2012), have both documented the benefits of employment on the health and well-being working aged adults. Blalock et al. showed that employment in PLWH had a positive association with self-esteem, confidence and dignity, leading to an overall improvement in quality of life (Blalock et al. 2002). Linn et al. cited employment as having multifactorial benefits, beyond a solution to financial needs, which included the satisfaction of creative urges, and offered an opportunity for the development of self-awareness and amassing achievements, which could boost self-esteem. (Linn et al. 1985)

2.3.1 Needs

Extensive literature recognizes key needs in returning to work for HIV+ persons. In a 2006 comprehensive review of the literature on HIV/AIDS and return to work (RTW), Braveman and colleagues composed a summary of the most commonly identified needs for HIV+ person to return to work and maintain employment:
1. Mental health and emotional needs
2. Physical and other health needs
3. Identity needs
4. Financial needs
5. Training and educational needs

Braveman’s review also notes that current literature predominately focuses on HIV+ persons who are unemployed (Braveman et al. 2006). However, one study, (Timmons et al. 2004) examined the specific needs of HIV+ persons who are employed. Assistance in identifying and negotiating job accommodations was pinpointed by Timmons et al. as the principal need for employed HIV+ individuals to maintain employment.

In regards to mental health and emotional needs, repeated absenteeism or long-term absence from work proceeds to job loss and may result in financial instability, social isolation, and depression (Linn et al. 1985, Henderson et al. 2005). Linn and colleagues elaborate that the negative ramifications of unemployment may produce anxiety, depression, deteriorate self-esteem and generate negative physical health effects. The effect of these consequences on healthy individuals can be extensive, and are even further magnified in the sick population. Linn and colleagues explored psychological and physical health variables after job loss. Their findings showed that people who made more visits to their physicians, those who spent more time in bed and those who took more medications experienced greater somatization, depression, and decreased locus of control. All of which would be potentially increased for a HIV+ persons. (Linn 1985)

As unemployment effects mental health, HIV also displays a correlation to mental health status for HIV+ persons. In turn, mental health plays a role in determining employment, creating a cycle of unemployment. An Australian study identified suicidal ideation as a negative mental health variable related to HIV+ status in men (Kelly et al. 1998). The same study also linked unemployment to poor memory performance (Kelly et al. 1998, Rabkin et al. 2004). Research also highlights that HIV+ persons commonly suffer from fear of discrimination and stigmatization (Braveman 2003, Timmons et al. 2004, Braveman et al. 2006).

2.3.2 Barriers to Employment
When the aforementioned needs go unmet, barriers to employment are built. After diagnosis of HIV, RTW can be an extensive and arduous process, especially if the HIV+ person has been absent from work for extended intervals (Gorman et al. 2009). HIV literature pinpoints multiple dynamics, which act as barriers to RTW for HIV+ persons. Barriers include health concerns such as unpredictability of the disease, frequently associated with recurrent, prolonged periods of illness, resulting in physical and cognitive impairment, medication side effects, and anxiety surrounding loss of disability allowance following RTW (Braveman et al. 2006; Gorman et al. 2009). Additionally, patient’s fear of discrimination and stigmatization at the workplace, following disclosure of HIV/AIDS status, acts a as barrier to RTW, especially in seeking accommodations, which would likely improve the sustainability of employment. (Rabkin et al. 2004, Rao et al. 2008, Rodger et al. 2010).

Six barriers to return to work were also identified by Braveman’s comprehensive review (Braveman et al. 2006):

1. Health concerns
2. Fear of loss of public benefits
3. Employability and career development
4. Stigmatization
5. External perceptions and the ‘sick role’

Braveman et al. summarized health concerns into three predominant barriers: uncertainty of disease progression, cognitive/physical symptoms, and medications/scheduling (Braveman et al. 2006). Physical and cognitive symptoms may include side effects of opportunistic infections, as well as chronic symptoms such as fatigue, diarrhea, and wasting (Vitry-Henry et al. 1999, Rabkin et al. 2004).

Fears about RTW include anticipated stigmatization and discrimination, loss of benefits, and a lack of belief in one’s ability to perform. The impact of the loss of benefits is contextual and dependent upon the residency of the HIV+ persons, yet has been noted in at least 6 different studies. According to Braveman, beyond the fear of loss of benefits, HIV+ persons are concerned about the availability of HIV medications and services, which may not be covered
by their new employer’s medical plans. The potential loss of access deters HIV+ persons from re-entering the workforce (Braveman et al. 2006).

The vast number of ramifications due to HIV generates questions in the HIV discussion, such as “should an HIV+ person work?” Research shows a strongly divided answer to this question due to external perceptions and the belief in the ‘sick role’. Conyers (2004) documented that HIV+ persons receive external pressure from family members, social and medical providers, and the community to relinquish employment or to not seek re-employment after illness related job loss. The ‘sick role’ defines the HIV+ person as a compliant, passive medical object of care (De Moor et al. 2005).

2.3.3 Employer Costs

An important aspect in the HIV/AIDS discussion is not only whether an HIV+ person should return to work, but what are the employer cost of retaining HIV+ employees? A study conducted in South Africa and Botswana by Rosen and colleagues (2004) examined the costs of AIDS for businesses. The researchers constructed a four-part description of costs including direct, indirect, individual and organizational costs. The extensive list of direct costs include benefit payments, medical care, recruitment and training of a replacement worker, insurance premiums, accidents due to ill and inexperienced workers, and litigation over benefits. Indirectly, companies incur costs from reduced job productivity, increased absenteeism, supervisor’s time, vacancy, lower productivity during replacement’s start-up period, senior management time, production disruptions, loss of workforce morale, loss of experience and institutional memory, reduced returns to training investments, and deteriorating labor relations. (Rosen et al. 2004) A Ugandan study of two companies showed that HIV/AIDS employees received 120% and 185% of the annual pay/benefits for the average workers (Feely et al. 2004). Due to the high cost of HIV/AIDS on employers, it is advantageous for employers to be actively involved in interventions for improving employee health and employment outcomes. Feely et al. demonstrates this point by noting that a year of ART costs approximately 29,000 shillings per person, which is only 2-4.8% of the cost lost per worker. It may follow, that if a company provides ART for their HIV+ employees then, health will improve, labor productivity loss will be diminished and pay outs for benefits, retirement and death with be reduced. Rosen & Feely
highlight the need for further exploration of employer involvement in return to work interventions.

2.3.4 Interventions and Studies on Return to Work

The typical employment services offered by current HIV/AIDS service organizations are limited. Services usually include fact sheets pertaining to disability laws, help in preparing a resume, the benefits of returning to work. The aforementioned services do not adequately abolish the barriers present in returning to work for HIV+ persons (Kielhofner et al. 2004). Therefore, further employment interventions targeted at meeting the needs of HIV+ workers are necessary. Interventions that promote RTW for any sick person usually include all activities introduced to enhance the work capacity of the individual. These activities may include interventions directed at the employee, employer and the workplace.

Researchers have explored numerous interventions in hopes of sustaining employment in HIV+ persons. Kielhofner and colleagues (2004) conducted a three-year, psycho-educational and occupational therapy RTW program for HIV+ persons with a participatory research strategy. The authors surmised that a combination method such as this, addressed a comprehensive range of physical, psychosocial and environmental issues. The four phase vocational program, Employment Options, recruited 129 participants with 30% attrition due mainly to illness, unrealistic vocational goals, death, and substance abuse. Phase one focused on self-assessment, exploration of vocational choices, pertinent job skill development, and emotional support for returning to work. This consisted of weekly group sessions, which taught self-assessment, vocational planning, job skills, job searching strategies, tools for coping in the work place, disability benefits, and the economic impact of RTW. Furthermore, participants received individual therapy and occupational coaching. Phase two aimed to build confidence in one’s ability to manage a work routine through to taking part in volunteer positions, internships, and temporary work placement. Phase three concentrated on permanent work placement and successful return to employment. Additionally, phase three assisted participants in seeking reasonable work place accommodations, as well as providing employer education. The fourth and final phase focused on sustaining employment and long-term follow-up including group meetings and staff contact. At the end of the program, 60 participants had returned to work,
gained new employment, went back to school, or began an internship or volunteer position. The study reports history of mental illness as a strong indicator whether or not an individual will be successful in returning to work. In light of the correlation between history of mental illness and successful employment, Kielhofner and colleagues highlight the importance of narrative understanding in order to create successful return to work interventions. Another community based participatory research program was the Helping Overcome Problems Effectively (HOPE) intervention, which focused on employment and mental health in African American gay men living with HIV/AIDS. The participants were male, African American, identified as homosexual, 18 years of age or older, unemployed, and fluent in English. The pilot program included 7 participants attending 7 weekly 3-hour group sessions. Topics included understanding HIV/AIDS, working with medications, working with health care providers, HIV tests and treatments, lifestyle management, employment, and further job skills development. The researchers found better overall mental health and increased self-efficacy in job-seeking skills as at 3 months post intervention 3 men were actively seeking employment, 3 were enrolled in college courses, and 1 was employed part-time. Participants identified problem solving and goal setting as two key benefits of the HOPE intervention program. Participants also identified mock job interviews, resume assistance, career interests assessments, and peer support buddies as crucial elements of the intervention. (Hergenrather et al. 2013).

Numerous qualitative studies have examined different types of vocational and psychosocial rehabilitation interventions for optimizing return to work in HIV+ persons. Overall, the results have been positive. One vocational services intervention study targeted at HIV+ persons reported a positive impact on employment (Conyers 2004). The Matrix Research Institute (MRI) implemented the Kirk Employment Empowerment Project (KEEP) as a multi-dimensional intervention service approach program. KEEP services included job search assistance, disability management education, benefits and legal counseling, on-site job support, job related problem solving and skills training, referrals to and coordination with other service providers. The study concluded the vocational rehabilitation services improved employment outcomes for HIV+ persons (Escovitz & Donegan 2005). Additionally, a group counseling intervention aimed at boosting RTW in HIV+ persons reported a positive impact (Kohlenberg et al. 2003). Kohlenberg et al. researched a group counseling intervention to support RTW in HIV+ persons experiencing
physical and cognitive symptoms. The intervention predominately focused on the development of personal skills training and career plans.

Beyond behavioral and psychological interventions studies, interventions primarily concentrate on Antiretroviral Therapy (ART) in sustaining employment and workforce re-entry. Previous pharmacological interventions studies support the use of ART in improving employment related economic productivity for HIV+ persons (Bernell et al. 2005, Van der Borght et al. 2006, Van der Borght et al. 2010).

2.3.5 ART

The creation of Antiretroviral Therapy (ART) produced positive results for HIV patients including reduced mortality, improved immune function, declining viral load burdens, abbreviated symptoms, and overall enhanced quality of life (Martin et al. 2005). The Gap Report: People Living with AIDS published by UNAIDS states that only 38% or two out every five of the people infected with HIV, receive ART therapy. (UNAIDS 2014) A systematic review on economic and quality of life outcomes for ART in developing countries conducted by Beard et al. consisted of 21 quantitative and qualitative publications. The systematic review concluded that HIV+ persons on ART reported significant improvements in physical, emotional, and mental health resulting in better daily function. The review found that compared to HIV+ who were not yet on ART, ART patients had decreased absenteeism and enhanced work performance. Furthermore, the review concluded that in all cohorts analyzed, ART was associated with a reduction in dementia, anxiety, and depression. (Beard et al. 2009) Interestingly, the study notes that the mere qualification for ART treatment improved the individual’s self-perception of physical health and emotional well-being. Booysen et al. reported that after less than 1 month 77% of patients on ART indicated an overall health improvement (Booysen et al. 2007). The economic benefits of strongly support ART as an intervention. A study by Resch et al. reported a net economic benefit of $19 billion USD. The $34.2 billion USD gross, equals 240% of program costs for the Global Fund to Fight AIDS, Tuberculosis and Malaria which provides ART in low and middle income countries (Resch et al. 2011). The study reports that the mass delivery of ART through the Global Fund restores labor productivity in
workers with HIV/AIDS, reduces orphan care expenditures, and delays end of life costs associated with AIDS related deaths.

### 2.3.6 International Legislation/ Interventions

International interest groups and organizations have amassed substantial progress in eradicating workplace barriers associated with RTW for HIV+ persons. The International Labour Organisation (ILO), published the 'Recommendations concerning HIV and AIDS and the World of Work', (ILO 2010) and the 'Code of Practice on HIV/AIDS and the World of Work' (ILO 2001). Both documents set out recommendations and good practice for the workplace, which include employment principles such as: non-discrimination, promotion of retention in work of HIV+ PERSONS, respect for the human right and dignity, universal access to preventive measures, treatment, and support. The ILO’s two sets of guidelines are intended to form the foundation for policy development to respond to HIV in the workplace (ILO 2001; ILO 2010).

### 2.4 Why it is important to do this review?

The availability of up-to-date, evidence-based employment interventions for HIV+ persons, goes hand in hand with employer/employee co-operation, in order to sustain employment and promote RTW. Reviews of RTW interventions after chronic conditions, i.e. cancer (De Boer et al. 2011) and musculoskeletal disorders (Schaafsma et al. 2010) are present in literature. However, no systematic review has been conducted aimed at assessing interventions to promote RTW or employment retention for HIV+ persons, specifically.
3 MAIN OBJECTIVE

To carry out a Cochrane Systematic Review of all current research on interventions used to help HIV+ persons return to work, maintain employment and prevent job loss. Thereby, highlighting the most effective methods, which have been employed to improve job retention and shorten RTW times for HIV+ persons. The results from this review can then be utilized in work place policies, government & non-profit initiatives and within communities to improve the economic viability of individuals diagnosed as HIV+. 
4 METHODS

4.1 Criteria for considering studies for this review

4.1.1 Types of studies

We assessed all eligible randomized controlled trials (RCTs) for inclusion in this review. However, due to the complexity of conducting RCTs in work organizations, we also accepted cluster RCTs and controlled before-after (CBA) studies.

4.1.2 Types of participants

We included studies conducted with HIV+ persons aged 16 years and over who were employed or unemployed at the time of diagnosis, irrespective of the stage of disease at the time of diagnosis.

4.1.3 Types of interventions

We included studies that evaluated any intervention or arrangement aimed at sustaining work or employment in people living with HIV. We considered interventions that were targeted at the workplace or at the individual or groups of individuals within the workplace or community, including policies aimed at preserving employment in specific categories of workers. We categorized interventions as follows:

- Medical or pharmacological interventions such as provision of free ART or antidepressants.
- Vocational interventions such as vocational or occupational rehabilitation, workplace adjustments such as protected time for medication, change in work schedule or duties, modified work hours, or improved communication with or between managers, colleagues, and health professionals.
- Psychological interventions such as education, counseling, cognitive-behavioral interventions, training in coping skills, or group psychotherapy.
- A combination of any of the above.
4.1.4 Types of outcome measures

4.1.4.1 Primary outcomes

- RTW, measured either as the number of days to partial or full work resumption or as the number of days absent during follow-up.
- Job loss, measured as the number of people who lost their job during the time of follow-up. As the complement of job loss is being employed, we also included studies that had measured being employed or the amount of time spent at work.

4.1.4.2 Secondary outcomes

- Overall quality of life (physical and emotional).
- Cost of intervention programs and cost effectiveness of RTW or employment.

4.2 Search methods for identification of studies

4.2.1 Electronic searches

We searched for relevant studies in the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 12)
- MEDLINE (1980 to December 2014)
- EMBASE (1980 to December 2014)
- CINAHL (1983 to December 2014)
- OSH UPDATE databases (CISDOC, HSELINE, NIOSHTIC, NIOSHTIC-2, RILOSH; 1980 to December 2014)
- PsycINFO (1980 December 2014)

We have presented the search strategies for MEDLINE, CENTRAL, EMBASE, and OSH UPDATE as Appendix 3. We designed the strategies to include appropriate MeSH subject headings and text word terms, interventions under consideration, and included study designs.
We restricted the searches to years from 1981 onwards, reflecting the year when the first acquired immunodeficiency syndrome (AIDS) cases were reported in the United States. We imposed no language restrictions.

4.2.2 Searching other resources

We screened the reference lists of selected articles and reviews to locate additional potentially eligible studies. We considered articles and studies published in any language. We intended for relevant articles published in languages other than English to be translated, but we found no such articles. When we required further information to determine inclusion, we wrote to the corresponding authors.

4.3 Data collection and analysis

4.3.1 Selection of studies

We carried out the selection of eligible studies in two stages.

Stage 1: Three review authors [Rachel Robinson (RR), Emmanuel Okpo (EO), and Nomusa Mngoma (NM)] independently screened the titles and abstracts of studies the search strategy identified for relevance, that is whether the study assessed the effectiveness of an intervention aimed at sustaining employment in HIV- infected individuals and measured RTW. If the title and abstract provided sufficient information to determine that the study did not satisfy the criteria for inclusion, we excluded the study. Review authors resolved differences in opinion through discussion.

Stage 2: We retrieved full texts of all the studies selected in stage 1. Each review author then independently examined whether the selected studies met the inclusion criteria. At this stage, we documented the reasons for study exclusion. We resolved differences in opinion by discussion and consensus.

We have presented a PRISMA study flow diagram to describe the sequence of steps in the screening process and reasons for the exclusion of studies in Figure 1.
4.3.2 Data extraction and management

We designed a data extraction form specifically for this review that captured key elements such as study design, country, setting, socio-demographic characteristics of participants including ethnicity, interventions (content, duration, provider, context), follow-up, and all outcomes of interest, particularly RTW measures. Review authors (RR, EO, and NM) independently extracted data from the eligible studies.

4.3.3 Assessment of risk of bias in included studies

All three review authors (RR, EO, and NM) independently assessed the risk of bias of all the included studies by following the procedures described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins & Green 2011). We assessed RCTs and cluster RCTs against the six domains listed below. We rated studies as having 'low risk of bias' (plausible bias unlikely to seriously alter the results); 'high risk of bias' (plausible bias that seriously weakens confidence in the results); or 'unclear risk of bias' (plausible bias that raises some doubt about results).

- Sequence generation: Was the allocation sequence adequately described?
- Allocation concealment: Was allocation adequately concealed?
- Blinding of participants, personnel, and outcome assessors: Was knowledge of the allocation intervention adequately prevented during the study?
- Incomplete outcome data: Was incomplete outcome data adequately addressed?
- Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting?
- Other sources of bias: Did the study appear to be free of other problems that could put it at high risk of bias?

For non-randomized studies, we utilized the checklist developed by Downs and Black (1998) to measure the quality of the studies. The criteria consist of several scales, but our review team
used only the following two:

- Internal validity in terms of bias (seven items)
- Internal validity in terms of confounding and selection bias (six items)

We added an additional item on baseline comparability of intervention and control group, but we did not use the item on power of the study. We combined all items with the Cochrane ‘Risk of bias’ tool in the Characteristics of included studies section. For confounding and baseline comparability, we used the following factors that according to our judgment could increase or decrease employment: gender, age, socioeconomic status, migration status, disease severity.

Instead of the original score as ‘yes’, ‘no’, or ‘unable to determine’, we used ‘low’, ‘high’, and ‘unclear’ risk of bias to make the checklist compatible with the Cochrane ‘Risk of bias’ tool as implemented in RevMan (2014).

We determined blinding of participants to be ‘low risk’ for retrospective studies because participants were unaware of the intervention at the time. Conversely, we considered blinding of participants to be ‘high risk’ if study authors did not report having used blinding or if it was clear from the report that the study was unblinded. See point 14 in our ‘Risk of bias’ assessments in the Characteristics of included studies section.

### 4.3.4 Measures of treatment effect

We plotted the results of each study as point estimates. For binary outcomes, that is where the probability of an event occurring or not occurring is considered, we used risk ratios RRs as the measure of effect; if this was not reported, we used odds ratios ORs. For continuous outcomes, we plotted the results of individual studies using mean differences MDs. The reporting of effect sizes did not require the use of standardized mean difference as we found no studies using similar continuous outcome measures. When we could not plot the results, we described them in the text.

### 4.3.5 Unit of analysis issues

As we found no cluster RCTs to include in the review, we did not have to contend with unit of
analysis problems. If in future updates we encounter studies that employ a cluster-randomized design and that report sufficient data for us to include in the meta-analysis but do not make an allowance for the design effect, we will calculate the design effect based on a fairly large assumed intra-cluster correlation of 0.10. We based this assumption of 0.10 being a realistic estimate by analogy on studies about implementation research (Campbell et al. 2001). We will follow the methods stated in the Cochrane Handbook for Systematic Reviews of Interventions for the calculations (Higgins & Green 2011).

If in future updates we find studies with repeat observations on participants, we will compute an effect measure for each participant factoring in all the time points and will present this as trends over time or overall means, depending on the data.

4.3.6 Dealing with missing data

When the issue of missing data arose, we discussed the reasons why the data could be missing and determined a way of dealing with it accordingly. Where we suspected missing data due to a lack of publication, publication in obscure places, or data presented inappropriately, we did whatever was possible to contact the original authors of the studies.

If in future updates of this review we discover that participants are missing from the reported results, such as when analyses of randomized trials do not include all randomized participants (not intention-to-treat analyses), we will consider performing intention-to-treat analysis on the presented data. We will also consider:

- analyzing only the available data (i.e. ignoring the missing data);
- imputing the missing data with replacement values and treating these as if they were observed;
- imputing the missing data and accounting for the fact that these were imputed with uncertainty;
- using statistical models to allow for missing data while making assumptions about their
relationships with the available data.

We explicitly state the assumptions of any methods used to cope with missing data and perform sensitivity analyses to assess how sensitive results are to changes in the assumptions.

4.3.7 Assessment of heterogeneity

We assessed clinical homogeneity based on similarity of the population, intervention, outcome, and follow-up. We considered populations as similar when they were people living with HIV aged 16 years and over irrespective of the stage of the disease at the time of diagnosis. We considered the various intervention categories (as outlined in Types of interventions) as different. We deemed the various outcome categories as different. For the RTW outcome, both the number of days to partial or full work resumption and number of days absent during follow-up had to be sufficiently similar to combine them as similar outcomes. We regarded follow-up times as different if they were less than three months, three months to one year, and more than one year.

In conducting meta-analyses, we considered the extent to which the results of studies are consistent by comparing confidence intervals for the results of individual studies and observing overlap as indication of the presence of statistical heterogeneity. We performed a \( \chi^2 \) test to further check for statistical heterogeneity. When the P value indicated that there was heterogeneity, we used the result of the I² measure to quantify the degree of heterogeneity. A percentage of 0% to 40% indicated that heterogeneity might not be important; 30% to 60% signified moderate heterogeneity; 50% to 90% substantial heterogeneity; and 75% to 100% considerable heterogeneity.

4.3.8 Assessment of reporting biases

We compared the outcomes listed in the methods section of an article with the reported results. We considered inadequately reported, non-significant results as a potential source of bias. We included published and unpublished data on the intervention under review to reduce publication bias. If sufficient data are available in future updates of this review, we will use funnel plots to detect reporting bias. We reduced the effect of reporting bias by including studies and not
publications in order to avoid the introduction of duplicated data (that is two articles could represent duplicate publications of the same study). Following the Cho (2000) statement on redundant publications, we extracted data only once for duplicate studies or if multiple articles reported on the same study. We prevented location bias by searching across multiple databases. Additionally, we prevented language bias by not excluding any article based on language.

4.3.9 Data synthesis

As this review includes different types of studies (randomized and non-randomized studies), we analyzed the data separately for the different study designs. We pooled suitably homogeneous data using Review Manager 5.3 software (RevMan 2014). The meta-analyses is presented in the Summary of findings for the main comparison.

When sufficient data was available, we performed meta-analyses for two studies. As the studies were statistically homogeneous, we used a fixed-effect model. We included 95% confidence interval (CI) for all estimates. In future updates of the review, if studies are heterogeneous, we will use a random-effects model. When using the random-effects model, we will conduct a sensitivity check by using the fixed-effect model to reveal differences in results.

We assessed the quality of evidence using the GRADE approach as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green 2011). See Appendix 2. We downgraded the quality of evidence for the RTW outcome based on the following factors:

- Limitations of the study design and implementation: allocation concealment, blinding, loss to follow-up, and selective reporting
- Indirectness of evidence: indirect population, intervention, control, and outcomes
- Inconsistency of results: subgroup analysis, heterogeneity, and inconsistent results
- Imprecision of results: wide confidence intervals
- Publication bias
We considered upgrading the quality of evidence for CBA studies based on the following factors:

- Magnitude of the effect
- Dose-effect relation
- All confounding excluded

The GRADE approach specifies four levels of quality (high, moderate, low, and very low).

### 4.3.10 Subgroup analysis and investigation of heterogeneity

Although we had planned to carry out a series of subgroup analyses, the included studies did not provide sufficient data to do so. In future updates, wherever possible, we will carry out subgroup analysis to account for differences in the primary outcome of RTW and disability rates between:

- gender, i.e. men versus women;
- different stages of the disease, e.g. clinically asymptomatic (WHO stages 1 and 2) versus symptomatic including AIDS (WHO stages 3 and 4);
- type of employment before diagnosis was made, e.g. health-related versus non-health-related employment;
- economic setting, e.g. low income, lower middle income, and upper middle income versus high income.

If we can conduct meta-analyses in future updates, we will quantify the degree of heterogeneity using the $I^2$ statistic, where an $I^2$ value of 30% to 60% indicates moderate heterogeneity, 50% to 90% substantial heterogeneity, and greater than 75% considerable heterogeneity (Higgins & Green 2011). We will investigate substantial heterogeneity further using meta–regression assuming that we have included an adequate number of studies.

### 4.3.11 Sensitivity analysis

In our protocol we planned to conduct a sensitivity analysis to monitor the robustness of the
results. However, our meta-analysis only includes two studies. Therefore, we did not conduct a sensitivity analysis.
5 RESULTS

5.1 Results of the search

We searched six key databases up to December 2014: the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, PsycINFO, and OSH Update (CISDOC, HSELINE, NIOSHTIC, NIOSHTIC 2, RILOSH). The initial search in 2012 yielded a total of 5799 studies. After removal of duplicate references, 4787 studies remained. In June 2013 and December 2014 we conducted updated searches of all aforementioned databases, resulting in an additional 460 and 331 references, respectively. We obtained a combined total of 5578 references for title and abstract inspection.

Evaluation of the reference titles and abstracts identified 29 studies for full-text examination. Nine studies did not meet the study design criteria of RCT or CBA studies. We disqualified two studies due to topic irrelevance. We excluded an additional five studies due to lack of a control group. We eliminated one final study that focused on chronic diseases and RTW because HIV-specific outcome data was unavailable (we requested raw data from the authors but they could not provide HIV-specific data). Ten studies remained for further consideration (Paul-Ward et al. 2005, Borwein et al. 2010, Popiel 2010, Thirumurthy et al. 2011, Bor et al. 2012, Baran 2012, Martin et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013).

We categorized four of these as 'Studies awaiting classification' (see Characteristics of studies awaiting classification); three due to a lack of full-text article and one because it was in progress in 2005, but we could not locate a final publication of outcome data. We requested full-text articles from the authors of these studies as well as unpublished raw outcome data, but we received none. The remaining six studies (one RCT and five CBA studies) formed the list of the final six included studies on which we performed data extraction and 'Risk of bias' assessment (Thirumurthy et al. 2011, Bor et al. 2012, Martin et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). For the search flow diagram, see Figure 1.
Figure 1. PRISMA study flow diagram

Search of Databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, OSH UPDATE databases, PsycINFO

Two review authors independently reviewed abstracts and titles for inclusion (n = 5143)

Did not meet inclusion criteria (n = 5112)

Full text requested for studies that potentially met inclusion criteria (n = 29)

Review authors’ judgments of included studies compared (n = 29)

Agreements (n = 26), Disagreements reviewed by third author (n = 3)

Excluded studies and justifications:
- No control group n = 5
- Wrong study design n = 8
- No employment outcome n = 1
- Not a primary study n = 5

Include (n = 6)
Exclude (n = 19)
Awaiting Classification (n = 4)

Included studies n = 6
Not contributing data n = 1

5.1.1. Included studies
See Characteristics of included studies. (Appendix 1A)

5.1.1.1 Study designs

We found one RCT (Martin et al. 2012) and five CBA studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). The RCT utilized a stratified randomization procedure; the researchers stratified participants of both control and index groups on education, CD4 count, and ethnic minority status to account for potential influence of these covariates. All five CBA studies were ART studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). Both Larson et al. 2013 and Bor et al. 2012 were retrospective analyses of cohorts. Linnemayr et al. 2013, Nannungi et al. 2013, and Thirumurthy et al. 2011 were prospective cohort studies.

5.1.1.2 Number of participants


5.1.1.3 Types of participants

The vocational therapy RCT conducted by Martin et al. 2012 recruited participants through advertisements at AIDS service organizations, community and mental health centers, HIV medical providers, gay and lesbian centers, community forums for HIV+ adults, and through advertisements in publications targeted at HIV+ persons in the United States.

Two studies analyzed HIV+ workers referenced against the non- HIV general work force (Bor et al. 2012, Larson et al. 2013). Larson et al. 2013 examined a cohort of tea pluckers in two major Kenyan tea plantations. Bor et al. 2012 used data from all inhabitants of Hlabisa sub-district in South Africa and combined employment data extracted from the Africa Centre for Health and Population Studies surveil- lance system with data on being HIV+ from the Hlabisa HIV Treatment and Care Program records.

Three studies compared HIV+ persons on ART to HIV+ persons not yet eligible for ART
(Thirumurthy et al. 2011, Linnemayr et al. 2013, Nunnungi et al. 2013). Linnemayr et al. 2013 and Nunnungi et al. 2013 examined participants from four Ugandan HIV treatment clinics, one rural (Kakira) and three urban (Kampala). Thirumurthy et al. 2011 compared HIV+ persons who had initiated ART with HIV+ persons who were classified as pre-ART and were a part of the Tamil Nadu Family Care Continuum (TNFCC) Program in Tamil Nadu, India. In all five CBA studies, participants were of working age (16 years or older) and were HIV+. Additionally, Thirumurthy et al. 2011 also included 67 children in their analysis as well as 54 caretakers.

5.1.1.4 Interventions

The included studies evaluated five pharmacological ART interventions and one mixed vocational and psychological intervention (Thirumurthy et al. 2011, Bor et al. 2012, Martin et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nunnungi et al. 2013). We found no psychological interventions. The vocational intervention consisted of 13 group sessions with at least 1 individual session, carried out over a 7 week period (Martin et al. 2012). The group sessions included presentations, brainstorming, discussions, role playing, and homework assignments regarding motivation and barriers to RTW, concerns of a HIV+ persons in the work force, skills for retaining a job, and “thinking like an employer” training.

The pharmacological intervention CBAs consisted of measuring employment outcomes prior to ART initiation, at the time of ART initiation, and at several follow-up intervals (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nunnungi et al. 2013). HIV+ persons in the Larson et al. 2013 study received free ART through their workplace hospitals and clinics. Participants in the Bor et al. 2012 study received free ART from the Hlabisa HIV Treatment and Care Program. In the Linnemayr et al. 2013 study, participants received basic HIV primary medical care and ART from two Joint Clinical Research Centre HIV clinics in Uganda, one rural (Kakira) and one urban (Kampala). The participants in Nunnungi et al. 2013 acquired HIV primary medical care and ART from two HIV clinics in urban Kampala, Uganda. Thirumurthy et al. 2011 participants received free ART from the TNFCC Program. Additionally, all of the Thirumurthy et al. 2011 participants received other clinical care services, nutritional supplements, and home-based care, which for the indexed participants involved ART adherence support.
5.1.1.5 Time period and location

All six included studies were conducted between 2000 and 2013. The studies were conducted in South Africa, the United States, India, Kenya, and Uganda.

5.1.1.6 Outcomes reported

RCT

The Martin et al. 2012 study measured employment as any type of employment in the past 6 months, job training class attendance, and active job searching in the past 30 days. Although Martin et al. 2012 reported having measured employment outcomes at 6, 12, 18, and 24 months post-ART initiation, only baseline data was published. We requested the 6, 12, 18, and 24 month follow-up outcome data from the authors, but we did not receive a response.

CBA

Bor et al. 2012 measured employment solely as employed versus unemployed. Employment was measured 24, 18, 12, and 6 months before beginning ART and 0, 6, 18, 24, and 30 to 60 months following ART initiation. The authors reported the ORs from logistic regression with T-values. We calculated the standard error needed for determining 95% CI by dividing the logOR by the reported T-value.

Larson et al. 2013 measured employment as days worked in the past month and stratified the results by gender. The researchers measured employment 24, 18, 12, and 6 months before beginning ART and 0, 6, 18, 24, and 30 to 60 months following ART initiation.

Linnemayr et al. 2013 measured employment status based on whether or not the HIV+ persons had participated in employment activity in the week prior to the interview. The researchers measured employment for all participants at 0, 6, and 12 months and reported as changes in employment status. The authors reported the ORs from logistic regression with T-values. We calculated the standard error needed for input into the data tables by dividing the logOR by the reported T-value. The authors graphically reported 0, 6, and 12 months outcomes for currently working, pain interference with work, health interference with work, and work self-efficacy.
We contacted the authors for the raw data of these outcomes, however, we did not receive a response.

Nannungi et al. 2013 measured employment status as a binary outcome based on whether or not the HIV+ persons had participated in employment activity in the week prior to the interview. The researchers measured employment for all participants at 0, 6, and 12 months.

Thirumurthy et al. 2011 measured employment as hours worked in the last week and stratified the results by gender. The researchers measured employment at 6, 12, 18, and 24 months following ART initiation. We contacted the authors for further explanation of Table 3, however, we did not receive a response.

None of the included studies, whether RCT or CBA, measured our secondary outcomes of quality of life or costs.

### 5.1.2 Excluded studies

We gave 19 studies particular consideration before exclusion as detailed in the Characteristics of excluded studies section. We excluded nine of these studies on the basis of irrelevant study design, that is they were not RCTs or CBA intervention studies (Rosolen et al. 2002, Martin et al. 2003, Rosen et al. 2004, Bernell & Shinogle 2005, Van der Borght 2006, Van der Borght 2010, Resch et al. 2011, Rueda et al. 2012, Thirumurthy et al. 2013). Six studies did not have control groups (Goldman & Bao 2004, Escovitz & Donegan 2005, Ajithkumar et al. 2007, Rosen et al. 2010, Hergenrather et al. 2013, Rosen et al. 2014). We excluded one purely qualitative study (Maticka-Tyndale et al. 2002). We excluded Herdt et al. 1999 due to lack of topic relevance. We excluded Lee & Chan 2005 due to a lack of specific HIV data. We excluded a summary of an ongoing study that was later published in 2012 (Martin et al. 2005, Martin et al. 2012). (Appendix 1B)

### 5.2 Risk of bias in included studies

See Figure 2 for an overall view of our assessment of the included studies’ risk of bias.
Figure 2: Risk of Bias Summary

5.2.1 Allocation (selection bias)

RCT

The researchers of the RCT reported adequate details on their randomization sequence generation (Martin et al. 2012). However, we judged their allocation concealment to be unclear. As the study recruited participants from multiple AIDS service organizations, community mental health centers, HIV medical providers, and gay/lesbian centers, some participant features may be disproportionately represented in index and reference groups. However, reported baseline demographics were similar between groups. We therefore determined the risk of population selection bias as unclear. We found no evidence of time selection bias, as recruitment of all participants occurred during the same time frame.

CBA
Neither of the retrospective studies reported the use of adequate sequence generation (Bor et al. 2012, Larson et al. 2013). The CBA studies did not use randomization or allocation concealment (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). Prior analysis predetermined allocation to reference and control groups in both retrospective cohort studies (Bor et al. 2012, Larson et al. 2013). None of the prospective cohort studies reported the use of adequate sequence generation or allocation concealment (Thirumurthy et al. 2011, Linnemayr et al. 2013, Nannungi et al. 2013). The participants’ CD4 counts and health status preordained allocation to index and reference groups in the prospective studies (Thirumurthy et al. 2011, Linnemayr et al. 2013, Nannungi et al. 2013). All HIV+ persons utilizing ART (CD4 count less than 250 cells/mm3) were assigned to the index group and all HIV+ persons pre-ART (CD4 count less than 400 cells/mm3 but greater than 250 cells/mm3) were assigned to the control group. We considered the risk of selection bias for the population as low in all five observational studies. Three studies’ use of HIV+ persons seeking care for both the index and reference groups reduces selection bias by eliminating the potential differences between people who choose to seek care and those who choose not to seek care (Thirumurthy et al. 2011, Linnemayr et al. 2013, Nannungi et al. 2013). Bor et al. 2012 gathered participants in both the index and reference groups from the Africa Center for Health and Population Studies’ population surveillance system. Bor et al. 2012 included all HIV+ people who were utilizing ART during the 10 year follow-up period of the Africa Centre for Health and Population Studies population surveillance study and who sought care through the Hlabsia HIV Treatment and Care Programme as index participants. Larson et al. 2013 collected all participants from the work forces of two Kenyan tea plantations. For index participants, Larson et al. 2013 used all HIV+ workers who visited the tea plantation hospitals and healthcare clinics. Linnemayr et al. 2013 used clinic staff to approach eligible clients for study participation at the appointment in which ART eligibility was assessed. Nannungi et al. 2013 enrolled consecutive new clinic clients who had recently been evaluated for ART eligibility. Thirumurthy et al. 2011 procured index and reference group participants from the Tamil Nadu Family Care Continuum Program. There was no randomization in any of the five studies, as all HIV+ persons who were utilizing ART were assigned to the index group out of physical necessity. However, we judged the studies as at low risk of selection bias, as all HIV+ persons using ART were assigned to the index group. Recruitment of index and reference participants occurred at the same time in all
five observational studies, showing no time-based selection bias.

5.2.2 Blinding (performance bias and detection bias)

RCT

As Martin et al. 2012 did not report blinding of participants or outcome assessors, we assessed the risk of bias due to blinding as high.

CBA

For two of the CBA studies, due to the retrospective comparisons of HIV+ persons on ART versus healthy people, we considered the participants to be blind to the idea of a special intervention, as they were not aware of the study at the time (Bor et al. 2012, Larson et al. 2013). For the prospective HIV+ persons on ART versus HIV+ persons pre-ART comparison, Linnemayr et al. 2013, Nannungi et al. 2013, and Thirumurthy et al. 2011 did not blind participants, as health status required knowledge of treatment. Nevertheless, due to the objective employment/unemployment outcome in all five CBA studies, we believe the lack of blinding has not biased the results. Blinding of the outcome assessors was unclear in all five CBA studies, however we believe that this lack of assessor blinding did not bias results due to objective administrative outcomes.

5.2.3 Incomplete outcome data (attrition bias)

RCT

Martin et al. 2012 did not report employment rates past the baseline and did not address attrition and reasons for missing data. We therefore assessed the risk of bias due to incomplete outcome data as high.

CBA

All five of the non-randomized CBAs addressed attrition rates of the index (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). Larson et al. 2013 missed data on 6% of index participants due to death, resignation, or retirement.
Larson et al. 2013 reported no attrition data on the control group. Bor et al. 2012 excluded data on 20% of index participants due to attrition, mortality, late cohort entry, and lack of employment information, but did not report attrition data for the reference group. Linnemayr et al. 2013 reported low attrition with approximately 95% retention of study participants and used an intention-to-treat analysis. However, Nannungi et al. 2013 reported 30% attrition at 6 months, which increased to 36% at 12 months. The high level of attrition in Nannungi et al. 2013 was evenly distributed between the ART and non-ART groups, at 37% and 35%, respectively. Thirumurthy et al. 2011 had an attrition of 34% and did not report any outcome data for controls.

Due to a lack of reporting of attrition for the controls in three studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013), we judged the risk of bias to be high for incomplete outcome data. Two studies reported no data for compliance to ART intervention (Bor et al. 2012, Larson et al. 2013). Neither Linnemayr et al. 2013 nor Nannungi et al. 2013 measured compliance with ART. Thirumurthy et al. 2011 provided ART adherence support but did not provide data for compliance. However, in all five ART intervention studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013), we can reasonably assume that compliance to ART medications would be high, as the health of the participant is highly dependent upon adherence. Martin et al. 2012 monitored compliance and conducted a dose-response analysis, but insufficiently reported the results and explanation.

We judged all five CBA studies to have an unclear risk of bias for compliance with the intervention, due to a lack of reporting of compliance measures combined with the necessity of ART for survival, which may encourage intervention compliance.

5.2.4 Selective reporting (reporting bias)

We judged Martin et al. 2012 to have a high risk of reporting bias due to complete lack of reporting of any follow-up outcome data. All five CBA studies, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013, and Thirumurthy et al. 2011, reported all of the original outcomes determined at the onset of the study for the index groups.

The two retrospective observational studies conducted retrospective unplanned subgroup analysis (Bor et al. 2012; Larson et al. 2013), whereas the single RCT is most likely guilty of
data dredging due to complete lack of outcome reporting and presenting results based on complicated and unjustified statistical analysis (Martin et al. 2012). We determined that the three prospective CBA studies did not indicate any unplanned retrospective subgroup analysis (Thirumurthy et al. 2011, Linnemayr et al. 2013, Nannungi et al. 2013).

5.2.5 Other potential sources of bias

RCT

The single RCT did not report any co-occurring interventions (Martin et al. 2012). Also, the authors did not account for ART utilization in the health status outcome, which could have influenced the results. Hence, we judged Martin et al. 2012 to have a high risk of other bias.

CBA

Baseline comparability assessment of the index and reference groups shows a high risk of bias for all five studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). As the studies inconsistently reported baseline characteristics, it is unclear if the baseline characteristics were appropriately comparable within comparisons. The baseline characteristics of intervention participants presented in the Linnemayr et al. 2013 study showed significantly fewer are working, higher levels of pain interfering with work, higher levels of health interfering with work, lower levels of self-efficacy, lower CD4 counts, lower levels of primary education, higher rates of depression, and lower overall physical function. The authors claim to have performed a sensitivity analysis restricting the control group to those with a similar health status as the intervention group, but for whom ART had been deferred. Linnemayr et al alleged that the results of the sensitivity analysis did not differ from the intention-to-treat analysis, meaning that the differences in health status at baseline did not affect the intervention effect. However, this data was not published. The Nannungi et al. 2013 study baseline characteristics showed a higher percentage of controls working at baseline with better overall health. The beneficial outcome reported may be confounded by the difference in disease severity at baseline between the pre-ART participants and the participants initiating ART. The health of HIV+ persons on ART may improve over time, while pre-ART participants’ health may decline, leading to an inflation of the intervention effect. The Linnemayr et al. 2013
study avoided similar inflation of the intervention effect by performing intention-to-treat analysis, keeping all participants in their original groups regardless of ART status at end of follow-up. However, the use of intention-to-treat analysis may have undermined the overall effect of the intervention. Once again, Linnemayr et al claim to have performed a second sensitivity analysis that excluded all participants in the control group who initiated ART during the study period. The analysis supposedly resulted in similar findings to the intention-to-treat analysis, therefore the authors did not provide the data and it cannot be verified within the text.

We assigned a high risk of bias to three of the observational CBA studies due to a lack of adjustment for confounding. Bor et al. 2012 adjusted for migration but did not adjust for age, sex, socioeconomic status, or disease severity. Larson et al. 2013 adjusted for gender but did not adjust for age, socioeconomic status, migration, or disease severity. Thirumurthy et al. 2011 adjusted for gender but did not adjust for age, socioeconomic status, migration, or disease severity. We deemed an unclear risk of bias for two of the prospective observational studies for adjustment for confounding, as they adjusted for some but not all potential confounders. Linnemayr et al. 2013 stratified data by gender and urban/rural and included physical and mental health confounders. Nannungi et al. 2013 adjusted for changes in physical health status, age, gender, education, relationship status, and CD4 count.

None of the five CBA studies reported possible co-interventions that may have influenced the employment outcome. Due to the file drawer phenomenon, bias often results in the publication of only positive-outcome studies. All studies included in this review provided positive intervention effects, leading to a possible artificially augmented effect. However, in regards to the ART intervention, the well-documented improvement in health status due to ART supports the positive findings.

5.2.6 Overall risk of bias in studies

RCT

We determined the overall risk of bias in the RCT based on allocation concealment/randomization, blinding, loss to follow-up, and selective reporting. We had decided a priori to consider studies to have a low risk of bias if all four items were graded as
low.

The above criteria resulted in a judgment of high overall risk of bias for Martin et al. 2012. The study had an unclear risk of allocation concealment and a high risk of bias due to a lack of blinding and selective reporting.

CBA

We determined the overall risk of bias in the CBA studies based on selection bias (items 21 and 22), adjustment for confounding (25), and baseline comparability using the Downs and Black (1998) checklist. We disregarded randomization and allocation concealment, as by definition the studies are non-randomized. We did not include blinding of outcome assessors, participants, and providers because the outcome is objectively obtained. We had decided a priori to consider a study to have a low overall risk of bias if all four items were graded as low.

See Figure 2 for an overall view of our assessment of the included studies’ risk of bias. Bor et al. 2012 had a high overall risk of bias. Study characteristics included a low risk of selection bias, a high risk of bias associated with adjustment for confounding, and a high risk of bias for baseline comparability.

Larson et al. 2013 had a high overall risk of bias. Study characteristics included low risk of selection bias, a high risk of bias due to a lack of adjustment for confounding, and a high risk of bias for baseline comparability.

Linnemayr et al. 2013 had a high overall risk of bias. Study characteristics included a high risk of population selection bias, an unclear risk of time selection bias, an unclear risk of bias for adjustment for confounding, and an unclear risk for baseline comparability. Nannungi et al. 2013 had a high overall risk of bias. Study characteristics included a high risk of population selection bias, a low risk of time selection bias, an unclear risk of bias due to adjustments for confounding, and a high risk of bias for baseline comparability. Thirumurthy et al. 2011 also had a high overall risk of bias. Study characteristics included a low risk of selection bias, a high risk of bias due to adjustment for confounding, and an unclear risk of bias for baseline comparability.
See Appendix 1 for Risk of Bias assessments for individual studies.

5.3 Effects of the interventions

5.3.1 Pharmacological interventions

5.3.1.1 HIV+ persons utilizing ART versus healthy (non-HIV+) individuals

Two CBA studies compared the effect of ART interventions in HIV+ persons on employment status to a control group of healthy, untreated participants (Bor et al. 2012, Larson et al. 2013). Both studies used existing data on health and employment outcomes before and after ART initiation. Bor et al. 2012 used retrospective data from a cohort from the Hlabisa Treatment and Care Program surveillance area in South Africa over 10 years. Larson et al. 2013 drew data from hospitals and employer records of two major Kenyan tea plantations. The studies defined employment status as employed/unemployed and as the number of days worked per month. As an employment measure, the number of days worked highlights the ability of the participant to maintain work in comparison to the healthy controls.

We could not combine the results of these studies in meta-analysis due to the use of different outcome measures and statistical methods within the studies.

Primary outcome: being employed

24 to 18 months before start of ART

Neither Bor et al. 2012 or Larson et al. 2013 found a statistically significant difference between HIV+ persons and healthy participants in employment status. Bor et al. 2012 found no difference in being employed or not, OR 0.79 (95% CI 0.61 to 1.02), whereas Larson et al. 2013 found no difference in number of days worked per month, MD -0.05 days (95% CI -0.50 to 0.40).

6 to 0 months before start of ART

Bor et al. 2012 and Larson et al. 2013 both found a significant decrease in employment 6 months prior to the start of ART for HIV+ persons in comparison to healthy participants in the workforce. Bor et al. 2012 reported the HIV+ person more likely to be unemployed, with an OR of
0.50 (95% CI 0.26 to 0.47). Similarly, Larson et al. 2013 found HIV+ persons to have worked significantly less, with a MD of -1.28 days (95% CI -1.65 to -0.91).

At ART initiation

At the time of ART initiation, both studies observed a continual downward trend, with the lowest levels of employment for HIV+ participants. Bor et al. 2012 found an OR 0.35 (95% CI 0.26 to 0.47), meaning a three-fold lower rate of employment in the HIV+ participants when compared to the healthy persons. The findings of Larson et al. 2013 were similar, with a MD of -8.49 (95% CI -9.57 to -7.41), translating to an 8 to 9 days’ difference in days worked per month between the index and reference groups.

6 months after ART initiation

Bor et al. 2012 reported an OR of 0.38 (95% CI 0.28 to 0.52), indicating that HIV+ persons were still less likely to be employed after 6 months on ART than the reference group. However, in Larson et al. 2013, the difference in employment between healthy participants and HIV+ persons decreased immediately after the start of ART. Larson et al. 2013 reported a MD of 0.08 days (95% CI 0.05 to 0.11), meaning that HIV+ persons on ART had worked only slightly less than participants of the healthy reference group.

18 to 24 months after ART initiation

Bor et al. 2012 reported an OR of 0.44 (95% CI 0.31 to 0.62), representing a significantly lower likelihood of being employed for HIV+ participants on ART when compared to the healthy work force.

Larson et al. 2013 reported a MD of -1.22 days (95% CI -1.74 to -1.07), meaning that the HIV+ persons had worked a little less per month than the healthy workers in the reference group.

36 to 60 months after ART initiation

Bor et al. 2012 found similar employment rates in both groups, with an OR of 0.73 (95% CI 0.42 to 1.28) at 36 to 60 months post-ART initiation. Additionally, Bor et al. 2012 measured “unemployment due to illness”, “job loss spells”, and “resides in surveillance area”; we did not
include these figures in our review due to their reciprocal nature to the employment outcomes measured above. We made this decision to prevent double counting of outcomes. The OR of 2.17 (95% CI 1.31 to 3.58) for unemployment due to illness at ART initiation declines to 0.70 (95% CI 0.32 to 1.55) by 18 to 24 months post-ART.

5.3.1.2 HIV+ persons utilizing ART versus HIV+ persons pre-ART

We found three CBA studies (2748 participants) comparing HIV+ persons on ART with HIV+ persons pre-ART. Thirumurthy et al. 2011 measured RTW by the number of hours worked in the past week. The study obtained follow-up data every 6 months, culminating at 24 months post-ART initiation. The authors used linear regression analysis and a dummy coding system that coded for either all workers at different follow-up or for those on ART only at follow-up. Thus the results are expressed as the number of hours that the group on ART worked more than the average cohort. Some of the participants got ART in between follow-up. The authors excluded these participants from the analysis.

Nannungi et al. 2013 and Linnemayr et al. 2013 measured RTW as a binary 'yes' or 'no' outcome, by whether or not the participant engaged in work activities in the last seven days prior to the interview. Nannungi et al. 2013 reported percentages of participants who had RTW who were not employed at baseline as a change in work status at 6 and 12 months. Linnemayr et al. 2013 reported the data graphically; we could not obtain raw data for this review. In future updates of this review, we will present the outcomes for participants currently working at baseline (0 months), 6 months, and 12 months, if we are able to obtain the raw data at that time. Additionally, Nannungi et al 2013 and Linnemayr et al 2013 also document the impact of ART over time.

Primary outcome: RTW

6 months after ART initiation

Participants who initiated ART worked 11.95 hours (95% CI 6.75 to 17.15) more per week than the average of the HIV+ cohort of ART and pre-ART persons, which was 3.7 hours (Thirumurthy et al. 2011).
Nannungi et al. 2013 reported that of those on ART not working at baseline (n = 88), 50.9% returned to work (n = 45). Of the pre-ART group unemployed at baseline (n = 57), 48.8% were at work at 6 months (n = 28).

Of those on ART working at baseline (n = 169), 81.4% were still working at 6 months (n = 138). In the pre-ART group, of those working at baseline (n = 168), 84.5% were still employed at 6 months (n = 142) (P value = 0.000). Overall, 53% of those on ART (n = 136) were working compared to 47% of those in the pre-ART group (n = 106) at 6 months. However, the pre-ART group had more favorable predictive factors.

**12 to 24 months after ART initiation**

Long-term follow-up indicated a 12.1 hour (95% CI 6.99 to 17.21) increase in hours worked per week at the end of 24 months for the baseline ART group compared to the average of the cohort, which was 21 hours (Thirumurthy et al. 2011). Nannungi et al. 2013 reported continued improvement in employment status at 12 months after ART initiation; of those on ART and not working at baseline (n = 88), 55.6% had returned to work (n = 49). Of those in the pre-ART group unemployed at baseline (n = 57), 50.0% had RTW at 12 months (n = 29). However, the pre-ART group had strong predictive characteristics for regaining employment compared to ART group. Of those on ART working at baseline (n = 169), 87.7% were still working at 12 months (n = 148). In the pre-ART group, of the 74.5% working at baseline (n = 168), 75% were still employed at 12 months (n = 126).

Overall, 46% of those on ART (n = 118) were working compared to 54% of those in the pre-ART group (n = 121) at 12 months. However, the pre-ART group had more males, better physical health functioning and higher CD4 count, which are the strongest predictors of employment. After adjusting for gender, age, physical health functioning, education, relationship status and CD4 count, the ART group was more likely to be employed than the pre-ART group (OR 1.56, 95% CI 1.15 to 2.12) at 12 months follow up. Linnemayr et al. 2013 found a greater likelihood of employment for the ART group compared to the pre-ART group (OR 1.88, 95% CI 1.47 to 2.41) at 12 months follow-up.

The meta-analysis for Linnemayr et al. 2013 and Nannungi et al. 2013 found an increased
likelihood of employment for those on ART (OR 1.75, 95% CI 1.44 to 2.12) (Analysis 1 and Table 1).

Heterogeneity: Chi² = 0.87, df = 1 (P = 0.35); I² =0.0% Test for overall effect: Z = 5.70 (P < 0.00001)  Test for subgroup differences: Not applicable.
Table 1: Summary of Findings

Anti-retroviral therapy compared with no ART for HIV

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Assumed Likelihood</th>
<th>Corresponding Likelihood</th>
<th>Relative Effect (95% CI)</th>
<th>No. of Participants (studies)</th>
<th>Quality of evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed at 12 months follow-up</td>
<td>710 per 1000</td>
<td>811 per 1000</td>
<td>1.75 (1.44 to 2.12)</td>
<td>1084 (2)</td>
<td>Very low¹</td>
</tr>
</tbody>
</table>

¹The basis for the assumed likelihood (e.g. the median control group risk across studies) is provided in footnotes. The corresponding likelihood (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk Ratio; ART: Anti-retroviral therapy

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Downgraded the quality of evidence because of limitations in study design as a non-randomized studies, as well as a HIGH of bias for baseline comparability, UNCLEAR for incomplete outcome data due to a lack of reporting of attrition for controls, and HIGH for adjustment for confounding.

5.3.2 Vocational interventions

5.3.2.1 Vocational therapy versus no vocational therapy

Primary outcome: RTW

Martin et al. 2012 measured outcomes at 6 month intervals beginning at baseline and continuing at 6, 12, 18, and 24 months, however the authors did not report these follow-up results, only providing a table of “estimated transition rates” in and out of employment based on a Markov
model for the outcomes. We requested further information, but the authors did not provide it.

5.3.3 Grading of the evidence

We used the GRADE approach to assess the quality of the evidence. All three observational studies, that is Bor et al. 2012, Larson et al. 2013, and Thirumurthy et al. 2011, started with a low-quality evidence rating, and the RCT, that is Martin et al. 2012, began at high rating as prescribed by the GRADE approach protocol (Appendix 2).

5.3.3.1 HIV+ persons utilizing ART versus healthy participants

We rated the evidence in this comparison to be very low quality. We downgraded the quality of evidence based on a high risk of bias due to limitations in study design and implementation. We did not downgrade the quality of the evidence due to indirectness because we judged there to be no limitations due to the use of direct populations, comparable interventions with similar control groups, and no use of surrogate data. Unexplained heterogeneity or inconsistency in the results showed no limitations for further downgrading of the evidence. We downgraded the quality of the evidence further based on imprecision, which was due to wide confidence intervals in both studies. We did not find evidence to downgrade for publication bias.

We found no justification for upgrading the quality of evidence. The magnitude of effect was not large, there was no dose-effect relation, and the studies did not exclude all confounding.

5.3.3.2 HIV+ persons utilizing ART versus HIV+ persons pre-ART

We graded the quality of evidence for this comparison as very low. We found no reason to downgrade the quality of evidence because of problems in allocation concealment and blinding. We downgraded the quality of evidence for limitations in study design implementation due risk of bias for baseline comparability, lack of adjustment for confounding and incomplete attrition data. We did not find any reason to downgrade for the indirectness of the evidence in this comparison. We found no sign of indirect evidence or use of surrogate data in any study. There was no reason to downgrade the quality of the evidence based on unexplained heterogeneity or inconsistency in the results or for publication bias. We found no justification for upgrading the quality of evidence. The magnitude of effect was not large, there was no dose-effect relation,
and the studies did not exclude all confounding.

### 5.3.3.3 HIV+ utilizing vocational therapy versus HIV+ not utilizing vocational therapy

We graded the quality of evidence for this comparison as very low. We downgraded the quality of evidence based on limitations in study design and implementation, as the study had a high risk of bias due to a lack of reporting of allocation concealment and loss to follow-up. Furthermore, the study was unblinded and the use of selective reporting necessitated another downgrade of the quality of evidence. We also downgraded the quality of the evidence for indirectness of the evidence. The authors did not report any follow-up data. As only a single study provided evidence for this comparison, there was no need to downgrade the quality of the evidence because of unexplained heterogeneity or inconsistency in the results or because of publication bias. Imprecision of the results in the form of complicated, unjustified statistical analysis of unclear outcomes necessitated downgrading the quality of the evidence further.
6 DISCUSSION

6.1 Summary of main results

We found very low-quality evidence in five studies that ART for HIV+ persons improves ability to work and maintain employment. The magnitude of the intervention effect is unclear due to differing results between comparisons (HIV+ vs. Healthy; HIV+ on ART vs. HIV+ pre-ART). The studies indicated that ART does not fully restore work capacity in HIV+ persons compared to healthy individuals. Two years after the start of ART, HIV+ persons still worked fewer days than healthy people. Five years after the start of ART there was a 27% greater unemployment rate among HIV+ people. However, the studies comparing HIV+ persons on ART with HIV+ person not yet on ART, indicate that ART recipients are almost twice as likely to be employed than HIV+ person pre-ART. Based on two studies of 33,379 participants (Bor et al. 2012, Larson et al. 2013), very low-quality evidence showed that HIV+ people utilizing ART worked less prior to ART initiation and got increasingly employed after ART initiation. Although employment increased after ART initiation, neither study showed full recovery of employment for the HIV+ index group in comparison to the healthy reference group during the follow-up period.

Two studies showed a similar trend in outcomes over a four-year period (Bor et al. 2012, Larson et al. 2013). The HIV+ persons index and healthy control group showed no statistical difference at 24 months pre-ART initiation. However, for the HIV+ persons, likelihood of employment and number of days worked per month declined significantly by six months prior to the start of ART. At the start of ART, unemployment in HIV+ persons was high in comparison to the healthy reference group. Larson et al. 2013 reported that employment outcomes improved six months after ART initiation and continued to increase at 18 to 24 months after the start of ART. Although there was improvement, neither Bor et al. 2012 nor Larson et al. 2013 indicated a full recovery of employment outcomes by the HIV+ persons on ART. The rate of improvement varied between the two studies. At 18 to 24 months post-ART initiation, Larson et al. 2013 reported that HIV+ persons worked approximately one day less than healthy participants. However, at 18 to 24 months post-ART initiation, Bor et al. 2012 reported a likelihood of employment for HIV+ persons on ART as less than half that of the healthy reference group. Bor
et al. 2012 reported statistically significant differences between the employment outcomes of the index group and those of the reference group until 36 to 60 months post-ART initiation. The differences between the results of the two studies can be partially accounted for by their use of different outcome measures. Larson et al. 2013’s measure of number of days worked notes smaller improvements in labor outcomes, whereas Bor et al. 2012’s absolute outcomes of employed/unemployed restricted the intervention from showing smaller increases in labor productivity. Linnemayr et al. 2013 and Nannungi et al. 2013 both reported improved RTW outcomes in HIV+ persons on ART in Uganda over a 12 month period. At baseline, the ART group had higher unemployment than the pre-ART group. Both studies indicated the most significant improvement in employment outcomes in the first 6 months for HIV+ persons on ART. Similar to the findings of Bor et al. 2012 and Larson et al. 2013, the number of those employed continued to rise after 12 months on ART, although not as dramatically as in the first 6 months. Half of those who were unemployed at baseline returned to work at six months in both the ART and pre-ART groups in one study (Nannungi et al. 2013). Although, it is important to note that the characteristics of the pre-ART group were more favorable to employment, due to a higher number of males and better overall health. Thereby, underestimating the overall effect of the intervention. When the analysis was adjusted for gender and health status, the likelihood of being employed favored the ART group. Of those who were employed at baseline, a larger percentage of the ART group remained employed at 12 months follow up than in the pre-ART group. The meta-analysis indicated a higher likelihood of employment in the ART group when considering the impact of ART over time (Linnemayr et al. 2013, Nannungi et al. 2013). Thirumurthy et al. 2011 measured employment outcomes in hours worked per week, indicating improvement in employment outcomes after ART initiation over HIV+ people who were pre-ART. The results indicate an intervention effect for ART improving the number of hours worked per week. In the analysis, the combined group of those on ART and those pre-ART worked an average of 21 hours per week, where the ART group alone worked approximately 32 hours per week to 24 months follow up.

From the Bor et al. 2012 and Larson et al. 2013 studies, we know that without ART, unemployment rises considerably. Apart from ART, no other factors have been identified by the literature to support the increased labor productivity findings and employment outcomes of Linnemayr et al. 2013, Nannungi et al. 2013, and Thirumurthy et al. 2011. Martin et al. 2012
found no evidence of the effectiveness of vocational rehabilitation interventions. As our systematic search yielded no studies on psychological interventions, we cannot say if they help or not.

6.2 Overall completeness and applicability of the evidence

The importance of interventions to help HIV+ persons to RTW has been highly stressed. However, surprisingly few intervention studies have been conducted in this area. The studies we found had been conducted in countries with a high prevalence of HIV, that is South Africa, Kenya, and Uganda, as well as in countries with a lower prevalence of HIV that is India and the United States. There were no studies from Europe, Latin America, or Australia. Given the differences in social security legislation, it is unclear if the evidence applies to European countries. Furthermore, evidence from one study suggested that ART interventions conducted in rural settings show a stronger effect. This might be due to accessibility of employment for farmers who are self-employed or working in the informal sector, whereas urban participants may have greater difficulty reassessing previous employment, particularly in areas with higher formal-sector development (Linnemayr et al. 2013). Of the five included pharmacological studies, only one study, Linnemayr et al. 2013, identified rural participants (OR 2.91, P value less than 0.01, t-statistic 4.77) from urban participants (OR 1.40, P value less than 0.05, t-statistic 2.57) and analyzed the data separately. Two other studies identified mixed urban and rural residency among participant demographics, but did not perform subgroup analysis of the data (Bor et al. 2012; Rosen et al. 2010). Nannungi et al. 2013 used data from urban clinics. Larson et al. 2013 focused exclusively on tea plantation workers and therefore must be considered separately, as all the participants worked for the same employer. The lack of subgroup analysis between rural and urban groups hindered applicability of the evidence across different socioeconomic and geographical locations. Part and parcel of the rural/urban issue, the nature of employment, whether formal or informal, is not consistently distinguished throughout the studies, which may also contribute to a lack of applicability of the evidence by not providing a full picture of the effect of ART on different careers and their RTW outcomes.

Research suggests that women are at higher risk of unemployment overall than men. Dray-Spira (2006) highlighted the disproportionate loss of employment for women. In this review, only by
the study by Thirumurthy et al. 2011 supports this finding. Three studies stratified outcome data by gender (Thirumurthy et al. 2011, Larson et al. 2013, Linnemayr et al. 2013); however, the studies yielded conflicting results and were unable to fully account for the differences between sexes. Larson et al. 2013 and Linnemayr et al. 2013 reported potentially better employment outcomes for women. Larson et al. suggested that women’s improved employment outcomes could be due to the increased likelihood of transfer to less physically demanding work. However, Linnemayr et al. 2013’s statistically insignificant findings for males could be due to the small male sample size and therefore insufficient power to detect the actual effect. In contrast, Thirumurthy et al. 2011 reported better employment outcomes for males. Thirumurthy et al. 2011 hypothesized that discrimination among the sexes segregates employment opportunities in the KwaZulu-Natal Umkhanyakude District, and these differences could play a role in HIV+ peoples’ ability to maintain or return to employment. Therefore, the gender component of RTW outcomes needs further exploration. Interventions need to be tailored to suit the needs of each sex, confounding for different societal, cultural, economic, and physical factors specific to each gender within a specified population. The lack of these adjustments may diminish the confidence of the intervention effect.

Unfortunately, we could not include all potentially relevant studies in this review. Baran 2012 examined multiple ART therapies in relation to healthcare costs and economic productivity for employers. This data could contribute to understanding the cost-effectiveness of ART programs as a secondary outcome. However, AbbVie Pharmaceutical Group funded the study and would not approve the release of necessary unpublished data for our use. The study examined three different types of ART medications, highlighting the differences in outcomes for participants based on the specific ART medication combination they received (Baran et al. 2012). None of the pharmacological interventions in this review accounted for differences in medication combinations. Had researchers of the ART studies conducted subgroup analysis, intervention effects could have been associated with specific treatment regimens. Although the HIV+ participants were drawn from a single geographic area or treatment center where a specific ART medication combination may be most common, there is no evidence to indicate that participants received the same ART medication combinations or regimens. Therefore, research in regards to specific ART medication combinations, such as in the Baran et al. 2012 study, could have shown differences in employment outcomes based on different ART medication combinations. In
addition, we excluded a non-intervention, modeling study that examined the secondary outcome of cost-effectiveness of ART programs by comparing estimated total program costs with select economic benefits of ART (1. restored labor productivity among workers with AIDS, 2. orphan care expenditures avoided because of parent survival due to ART, 3. delayed end-of-life care costs associated with AIDS-related death). Resch et al. 2011 reported an estimated expenditure of USD 14.2 billion for ART from 2011 to 2020 for the South African cohort of 3.5 million people. The study estimated a return on investment of USD 12 billion to USD 34 billion through improved labor productivity, averted orphan care expenses, and deferred medical treatment for end-of-life care and opportunistic infections. (Resch et al. 2011)

One other prospective cohort study, which produced three-year and five-year follow-up publications, Rosen et al. 2010 and Rosen et al. 2014, examined the economic well-being of ART patients in South Africa. We excluded the study, as it did not meet our inclusion criteria due to a lack of a control group. However, the findings showed a continued increase in employment from 32% to 44% between the start of ART and the five-year follow-up. These findings support the findings in all five included CBA ART studies (Thirumurthy et al. 2011, Bor et al. 2012, Larson et al. 2013, Linnemayr et al. 2013, Nannungi et al. 2013). Of the 248 participants who were unemployed but looking for work at baseline, 39% (n = 96) RTW, and of the 96 participants who were unemployed at baseline and not seeking work, 30% (n = 29) RTW and 53% (n = 51) were now actively seeking employment. Furthermore, the study examined outcomes outside of our predetermined outcomes, including the probability of experiencing pain or fatigue in the last week, the probability of being able to perform normal activities over the previous five-day work week, and reliance on external support in the form of a caretaker. The data collected demonstrated a decrease in reporting pain in the previous week from 69% at baseline to 17% (P value less than 0.001) and a decrease in reporting fatigue in the previous week from 62% at baseline to 7% (P value less than 0.001) after five years. These health improvements coincide with findings by Larson et al. 2013, where the measure of number of days worked allowed for smaller improvements in labor outcomes to be noted. Therefore, reductions in pain and fatigue due to ART may incrementally improve a person’s capacity to work.

Three included ART studies examined strict dichotomous outcomes of employment or
unemployment (Bor 201, Linnemayr et al. 2013, Nannungi et al. 2013), whereas the other two ART studies examined reduction in the labor productivity of HIV+ persons without a definitive loss of employment or reemployment (Thirumurthy et al. 2011, Larson et al. 2013). The overall evidence did not account for specific reasons of unemployment but assumes loss of employment is solely attributable to HIV status. Therefore, a pharmacological intervention targeting loss of employment due to HIV would not produce the same effect on RTW outcomes for a HIV+ person whom lost their job for other reasons.

Two included studies evaluated the effects of CD4 counts or progression of the disease at initiation of the intervention (Linnemayr et al. 2013, Nannungi et al. 2013). Although the index group criteria in the Thirumurthy et al. 2011 study required participants to have a CD4 count less than 200, the analysis did not take into account varying levels of health status. Along the same vein, not all of the studies clearly distinguished HIV+ participants from participants with fully developed AIDS. Only two studies clearly indicated the use of World Health Organization (WHO) guidelines for diagnosis of HIV/AIDS and ART eligibility (Linnemayr et al. 2013, Nannungi et al. 2013). The differing levels of health status, by either CD4 counts or HIV versus AIDS, at initiation of the intervention could impact the outcomes.

In 2012, the WHO reported varying levels of HIV prevalence in working-age populations (15 to 49 years) among the countries examined in the pharmacological ART intervention studies: South Africa (17.9%), Kenya (6.1%), Uganda (7.4%), and India (0.3%) (WHO 2013a, WHO 2013b, WHO 2013c, WHO 2013d). Within these countries, the overall makeup of the HIV+ population varies. These statistics indicate diverse social and political environments for HIV within each population. ART coverage among HIV+ persons also varies between countries: South Africa (80%), Kenya (73%), Uganda (64%), and India (50%). Therefore, the ART environment, available knowledge, access to other HIV services, and individual perceptions may also influence employment outcomes within a specific population. The cultural, social, educational, political, and economic diversity of each of the countries included in this review should be considered when examining the effectiveness of the interventions by their location. Furthermore, none of the studies controlled for possible co-occurring interventions, which may have positively altered the intervention effect.
6.3 Quality of the evidence

See Appendix 2 for GRADE ratings of the quality of the evidence.

6.3.1 Pharmacological interventions

6.3.1.1 HIV+ persons utilizing ART versus healthy (non-HIV+) individuals

The very low-quality evidence GRADE rating for the two-study comparison did not encourage the acceptability of the results of a positive intervention effect (Bor et al. 2012, Larson et al. 2013).

6.3.1.2 HIV+ persons utilizing ART versus HIV+ persons pre-ART

The very low-quality evidence GRADE rating for the three-study comparison degraded the reliability of the positive intervention effect of ART (Thirumurthy et al. 2011, Linnemayr et al. 2013, Nannungi et al. 2013).

In both comparisons, a more definitive answer to the effectiveness of ART requires an improvement in the quality of the body of evidence.

6.3.2 Vocational interventions

6.3.2.1 HIV+ persons utilizing vocational therapy versus HIV+ persons not utilizing vocational therapy

The very low-quality evidence GRADE rating for the single-study comparison devalues the authenticity of the suggested positive intervention effect of mixed vocational and psychological rehabilitation (Martin et al. 2012).

To the best of our knowledge, no studies have produced evidence of a positive intervention effect that merits the use of mixed vocational and psychological interventions to improve employment outcomes. Therefore, justification for mixed vocational and psychological
interventions requires more, higher-quality studies.

6.4 Potential biases in the review process

We allowed the inclusion of studies with unemployed participants at time of intervention initiation, which required a relaxation of our predetermined inclusion criteria (Thirumurthy et al. 2011, Bor et al. 2012 Linnemayr et al. 2013, Nannungi et al. 2013). This decision may have potentially influenced the result.

Language bias is irrelevant in this review, as we excluded no studies on the basis of publication language.

6.5 Agreements and disagreements with other studies or reviews

To our knowledge, this is the first systematic review to analyze the effects of interventions designed to improve employment outcomes for HIV+ persons.
7 CONCLUSIONS

7.1 Implications for practice

We found very low-quality evidence for an increase in days worked and employment rates among HIV+ persons who were started on ART compared to healthy people to a level only a little under that of healthy workers. Additionally, we found very low-quality evidence for improvement in RTW outcomes for HIV+ persons on ART compared to HIV+ persons who are pre-ART. There was no evidence of the effectiveness of vocational rehabilitation. No studies supported psychological or other interventions.

7.2 Implications for research

Further research is required and should include more RCTs of vocational, psychological, educational, and support interventions. Researchers should account for all possible influences on employment outcomes, such as co-occurring interventions available within a treatment population. To improve the quality of the evidence, studies should fully report predetermined outcomes as well as account and compensate for attrition. All possible confounders (gender, age, socioeconomic status, migration, and disease severity) should be analyzed. Researchers should focus specifically on differences in employment outcomes by gender to help fine-tune the potency of interventions. Future pharmacological studies should clarify ART therapy regimens and differentiate between cART (combination antiretroviral therapy) prescriptions.

7.2.1 RCTs

More RCTs would improve the quality of evidence. Although the RCT study design is ideal for showing effectiveness, it is an unethical approach to conduct pharmacological ART interventions. However, RCTs can be effectively utilized for vocational and psychological interventions. Given the probably modest effect sizes and a large risk of confounding, RCTs with a follow-up of at least one year would be ideal.

7.2.2 CBA studies

CBA studies present a solution to the problem of studying ART interventions. However,
additional studies with higher-quality evidence are needed.

7.2.3 Blinding

All future studies should ensure blinding of outcome assessors, even if blinding of participants and personnel is not possible.

7.2.4 Other interventions

Although our comprehensive search criteria yielded only five pharmacological ART interventions and one mixed vocational and psychological counseling intervention, many other intervention possibilities exist. For example, income support interventions could possibly reduce the stress related to financial burden. Financial security may improve well-being and quality of life, whereas stress may potentially lead to expedited disease progression followed by job loss. Researchers could explore job or career field-specific intervention programs that focus on meeting the specific needs of the employee within the given profession. It is theorized that involvement in meaningful work improves one's sense of self-worth in addition to providing many other benefits. Caretaker or family educational interventions might encourage RTW by dispelling the myth that HIV+ people should not work and must play the 'sick role'. Educational interventions for caretakers or family could furthermore enhance the support system of the HIV+ individual, thereby boosting RTW outcomes. Educational interventions for employers could assist companies in mindfully accommodating HIV+ employees, retaining HIV+ employees, and decreasing absenteeism. The aforementioned list is not exhaustive of potential interventions, but merely suggests the current knowledge gap.

7.2.5 Reporting

All of the studies in our review indicated a high risk of bias due to incomplete outcome data and selective reporting. Future studies should employ all appropriate methods to reduce risk of bias, thereby improving the quality of evidence.
8 ACKNOWLEDGEMENTS

We would like to thank the Cochrane Occupational Safety and Health Review Group’s Trials Search Coordinator Leena Isotalo and Kaisa Neuvonen for developing the search strategy and Managing Editor Jani Ruotsalainen, Coordinating Editors Jos Verbeek and Sohaib Khan, for editing the text and providing helpful comments. We would like to thank Tawni Jaakola for her technical assistance and support. Also, we would like to acknowledge Elsie Rousseau, Matt, Mary and Mary Lou Robinson for their support. We would also like to thank Richard Othieno for his contributions to the protocol.

8.1 Contributions of authors

RR conducted the abstract appraisal, full-text review, data extraction, data analysis, and article write-up. We divided duplicate investigation of abstracts, full text, data, and article commentary evenly between EO and NM. RR is the guarantor of this review.

8.2 Declarations of interest

None known.

8.3 Publication

This Cochrane Review is published in the Cochrane Database of Systematic Reviews 2015. Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the Review. The reference is as follows:


The Protocol for this Cochrane Systematic Review:

9 DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The protocol for this review was published under the title, “Work arrangements for sustaining employment in workers with HIV”, however, we changed the title to “Interventions for improving employment outcomes for workers with HIV” as we considered this title to be more accurately describe the review.

We also included studies that allowed for participants to be unemployed at the time of diagnosis, in order to provide the most comprehensive picture of employment outcomes by accounting for job loss trends prior to diagnosis. This alteration accounts for the effects of HIV on employment being prior to diagnosis.
10 REFERENCE


Borwein A, Chan K, Parashar S, Druyts E, Palmer AK, Montaner JS, et al. Overcoming employment barriers: Health and Financial worries among a cohort of HIV positive Individuals on HAART. *Canadian Journal of Infectious Diseases and Medical Microbiology* 2010;21(3):84B.


Lee RKY, Chan CCH. Factors affecting vocational outcomes of people with chronic illness participating in a supported competitive open employment program in Hong Kong. Work 2005;25(4):359-68.


Maticka-Tyndale E, Adam BD, Cohen JJ. To work or not to work: combination therapies and HIV. *Qualitative Health Research* 2002;2013:362972.


Popiel M. HIV, employment and human rights in Canada: A workshop evaluation. *Canadian Journal of Infectious Diseases and Medical Microbiology* 2010;21(3):83B.


WHO. India Statistics Summary (2002-present). WHO2013b; http://apps.who.int/gho/data/node.country.country-IND.

WHO. South Africa Statistics Summary (2002-present). WHO 2013c; http://apps.who.int/gho/data/node.country.country-ZAF.


Appendix 1: CHARACTERISTICS OF STUDIES TABLES

A. Characteristics of included studies

Bor et al. 2012

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>CBA study (retrospective)</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>32,321 population cohort of all working-age (18-59) people who were members of a household in Africa Centre for Health and Population Studies’ population surveillance area during the 10-year follow-up period, excluding HIV+ persons not accessing ART. (South Africa)</td>
</tr>
<tr>
<td></td>
<td>Index group: 2027 HIV+ persons</td>
</tr>
<tr>
<td></td>
<td>Reference group: 30,294</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Intervention: Pharmacological, ART through the Hlabisa HIV Treatment and Care Program</td>
</tr>
<tr>
<td></td>
<td>Control: Drawn from the same population, but non-HIV, untreated, apparently healthy</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Employment: Employment status measured as ’yes’ or ’no’</td>
</tr>
<tr>
<td></td>
<td>Authors also assessed:</td>
</tr>
<tr>
<td></td>
<td>1) Unemployment due to illness,</td>
</tr>
<tr>
<td></td>
<td>2) Residence in surveillance area (migration indicator)</td>
</tr>
<tr>
<td></td>
<td>3) Physical function: Walk 5 km without stopping, carry heavy objects for 20 meters without stopping, participate in vigorous activities</td>
</tr>
<tr>
<td></td>
<td>4) Immunological status: CD4+lymphocyte count</td>
</tr>
</tbody>
</table>

| Notes | ART |

**Risk of Bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>14. Blinding (subjects)</strong></td>
<td>LOW</td>
<td>Retrospective data collected and cross-referenced from a cohort’s surveys of socio-demographics and health data. Participants were unaware they were under investigation for the specific intervention at the time of the cohort surveys</td>
</tr>
<tr>
<td><strong>15. Blinding (outcome assessors)</strong></td>
<td>LOW</td>
<td>Not blinded. Retrospective data collected and cross-referenced from a cohort’s surveys of socio-demographics and health data. Objective outcomes that should have been unaffected by blinding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>16. Retrospective unplanned sub-group analysis</td>
<td>UNCLEAR</td>
<td>Retrospective study, data dredging not clear.</td>
</tr>
<tr>
<td>17. Follow-up</td>
<td>LOW</td>
<td>Follow-ups conducted for both index and reference at 8-5 years, 5-3 years, 3-2.5 years, 2.5-2 years, 2-1.5 years, 1.5-1 years, 1-0.5 year both pre- and post-ART initiation</td>
</tr>
<tr>
<td>18. Statistical tests</td>
<td>LOW</td>
<td>Odds ratio, t-statistics, and hazards ratio</td>
</tr>
<tr>
<td>19. Compliance</td>
<td>UNCLEAR</td>
<td>Compliance to ART was not monitored or insured. ART adherence is required for survival, therefore compliance is highly likely</td>
</tr>
<tr>
<td>20. Outcome measures</td>
<td>LOW</td>
<td>All predetermined outcome measures were analyzed and reported</td>
</tr>
<tr>
<td>21. Selection Bias (population)</td>
<td>LOW</td>
<td>All participants were collected from South Africa’s Africa Centre population surveillance area in the Hlabisa subdistrict. The study used all HIV+ persons who were utilizing ART during the 10-year follow-up period of the Africa Centre’s population surveillance study</td>
</tr>
<tr>
<td>22. Selection Bias (time)</td>
<td>LOW</td>
<td>All individuals residing in the surveillance area were monitored between 2001-2010 and for inclusion in the study were required to have lived in the surveillance area 6 months prior to the establishment of the Hlabisa HIV Treatment and Care Program</td>
</tr>
<tr>
<td>24. Allocation Concealment</td>
<td>UNCLEAR</td>
<td>Retrospective study of a cohort. Participants were not assigned by the research team, but were predetermined by health status. Did not report the use of adequate sequence generation or allocation concealment techniques</td>
</tr>
<tr>
<td>26. Incomplete outcome data</td>
<td>HIGH</td>
<td>20.4% attrition in index group addressed. No data reported for control group</td>
</tr>
<tr>
<td>Baseline Comparability</td>
<td>HIGH</td>
<td>Differences in gender proportions: Index group 80.1% female and reference group 59.9% female. Age groups were disproportionate: (18-25 years) index 17.5%, reference 49.4%; (25-34 years) index 38.7%, reference 21%; (35-44 years) index 31%, reference 18.2% SES not specifically reported, but &gt; 12 years of school was also disproportionate between groups: index 33.9%, reference 45.1% Disease severity was incomparable in the index group (HIV+ persons) and reference group (healthy and undiagnosed, asymptomatic HIV+ people)</td>
</tr>
</tbody>
</table>

ART: antiretroviral therapy  
CBA: controlled before-after study
**Larson et al. 2013**

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>CBA study (retrospective)</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Intervention: Pharmacological, ART. Control: Healthy, untreated general work force.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Employment: 1. Total days working per month 2. Days spent plucking tea per month 3. Total kg of tea harvested per month 4. Total income per month</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>HIV</td>
</tr>
</tbody>
</table>

**Risk of Bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Blinding (subjects)</td>
<td>LOW</td>
<td>Participants were unaware of intervention.</td>
</tr>
<tr>
<td>15. Blinding (outcome assessors)</td>
<td>LOW</td>
<td>Not reported. Objective outcomes that should have been unaffected by blinding.</td>
</tr>
<tr>
<td>16. Retrospective unplanned sub-group analysis</td>
<td>UNCLEAR</td>
<td>Retrospective study, data dredging not clear.</td>
</tr>
<tr>
<td>17. Follow-up</td>
<td>LOW</td>
<td>Follow-ups conducted for both index and reference at 6-month intervals beginning 24 months pre-ART until 24 months post-ART</td>
</tr>
<tr>
<td>18. Statistical tests</td>
<td>LOW</td>
<td>Mean difference (95% confidence interval)</td>
</tr>
<tr>
<td>19. Compliance</td>
<td>UNCLEAR</td>
<td>Compliance to ART was not monitored or insured. ART adherence is required for survival, therefore compliance is highly likely</td>
</tr>
<tr>
<td>20. Outcome measures</td>
<td>LOW</td>
<td>All predetermined outcome measures were analyzed and reported</td>
</tr>
<tr>
<td>21. Selection Bias (population)</td>
<td>LOW</td>
<td>Study used all HIV+ persons who visited the tea plantation hospitals and healthcare clinics. All participants were employees of two tea plantations in the Kericho District of Kenya. However, it is important to note that some participants in the reference group were likely HIV+ but were undiagnosed or had not declared their HIV status as positive. This could have impacted the results.</td>
</tr>
<tr>
<td>22. Selection Bias (time)</td>
<td>LOW</td>
<td>All participants were monitored between 2006-2009.</td>
</tr>
<tr>
<td>23. Randomization</td>
<td>HIGH</td>
<td>No randomization for index group. Index group was matched with four references who were randomized into sub-estate groups.</td>
</tr>
<tr>
<td>24. Allocation Concealment</td>
<td>UNCLEAR</td>
<td>Retrospective, non-randomized study. Did not report the use of adequate sequence generation or allocation concealment techniques.</td>
</tr>
<tr>
<td>26. Incomplete outcome data</td>
<td>HIGH</td>
<td>6% attrition in index group addressed. No attrition data reported for controls. Data for workers in the general work force was incomplete due to a change in the management system resulting in the reassigning of employment identification numbers.</td>
</tr>
</tbody>
</table>

**Baseline Comparability**

| HIGH | No baseline demographics were reported for the reference group. The index group mean age for women was 39.4 (27.4-53) and for men was 39.5 (24.9-54.4). The average years of experience for women was 8.2 (1-24) years and for men was 7.7 (0.5-23) years. Median baseline CD4 counts for women were 178 (91-243) and for men were 153.3 (85-215). |

**ART:** antiretroviral therapy  
**CBA:** controlled before-after study
## Linnemayr et al. 2013

### Study Component Description

<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>CBA study (Longitudinal, prospective cohort)</th>
</tr>
</thead>
</table>
| **Participants** | 602 HIV+ treatment-naive clients, 18 years of age or older, who were newly evaluated for ART from 2 Joint Clinical Research Centres in Kampala (urban) and Kakira (rural), Uganda.  
Index: 300 HIV+ people initiating ART with CD4 count < 250 cells/mm³ (WHO disease stage III or IV) and had a 'treatment supporter'  
Control: 302 HIV+ people pre-ART with CD4 count < 400 cells/mm³ |
| **Intervention** | All participants underwent structured interview concerning background characteristics, physical and mental health status, and economic outcomes. Health data abstracted from patient medical records. Assessments taken at 0 and 12 months  
Index: ART provided by Joint Clinical Research Centre HIV Clinic, plus general HIV treatment  
Control: General HIV treatment, no ART |
| **Outcomes** | Employment:  
1. Work status in the week preceding interview  
Other health-related economic outcomes:  
2. Health interference with work (binary indicator of perceived health effect on work)  
3. Pain interference with work in last month (5-point scale from not at all’ to ’extremely’)  
4. Work-related self-efficacy (single visual analogue scale 0-10) |

### Notes
- Rand Corporation (California, USA)
- Joint Clinical Research Centre (Kampala, Uganda)
- Funding: The Rockefeller Foundation, Grant No. HE007; PIGWagner
- Participants received 5000 Uganda Shillings (~USD 2.50) for completion of each interview

### Risk of Bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Blinding (subjects)</td>
<td>UNCLEAR</td>
<td>No blinding, however due to a dichotomous outcome of employed or unemployed in past 7 days, this should not have affected the results.</td>
</tr>
<tr>
<td>15. Blinding (outcome assessors)</td>
<td>LOW</td>
<td>No blinding, objective outcomes should have been unaffected by lack of outcome assessor blinding.</td>
</tr>
<tr>
<td></td>
<td><strong>Retrospective unplanned sub-group analysis</strong></td>
<td>LOW</td>
</tr>
<tr>
<td>---</td>
<td>-----------------------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td><strong>Follow-up</strong></td>
<td>LOW</td>
</tr>
</tbody>
</table>
|   | **Statistical tests**                        | LOW | Two-tailed t-test, Chi2 test (has statistically low power when study has small sample size (n = 602)) Performed 2 sensitivity analyses:  
1. Excluded control-group participants who began ART treatment but were kept in the control group due to intention-to-treat study design analysis.  
2. Restricted control group to members of a similar health status. |
|   | **Compliance**                               | UNCLEAR | ART adherence is required for survival, therefore compliance, although not monitored, is highly likely. Eligibility for the index group required the HIV+ persons have a ’treatment supporter’ for adherence. |
|   | **Outcome measures**                         | LOW | All predetermined outcome measures were analyzed and reported. |
|   | **Selection Bias (population)**              | UNCLEAR | Eligible patients were approached by clinic staff when ART eligibility was assessed. No randomization. Intention-to-treat analysis was utilized to avoid control-group members changing to the index group. |
|   | **Selection Bias (time)**                   | UNCLEAR | Recruitment timeline not specified. 2008? |
|   | **Randomization**                            | UNCLEAR | Non-randomized. Participants were predetermined to index and reference groups by ART eligibility status. |
|   | **Allocation Concealment**                  | UNCLEAR | Non-randomized. Did not report the use of adequate sequence generation or allocation concealment techniques. |
|   | **Adjustment for confounding**              | UNCLEAR | Stratified data by gender and included physical health and mental health confounders. Did not account for age, SES, or education. |
|   | **Incomplete outcome data**                 | LOW | < 5% attrition, and all outcome data reported. |
|   | **Baseline Comparability**                  | UNCLEAR | Baseline health differences between the index and reference groups due to disease progression and need for treatment. Authors claim to have performed a sensitivity analysis and reported that the overall results did not change. However, data was not presented in the publication. |
### Study Component

**Methods**

RCT study

**Participants**

174 HIV+ persons aged 18-65 who had stopped working due to disability, were receiving disability services, and who were contemplating rejoining the workforce. (USA)

Index group: 83

Control group: 91

**Intervention**

**Intervention:**
- 1-hour individual counseling sessions conducted in the beginning, middle, and end of the 7-week group session period
- 13 group sessions over a period of 7 weeks

**Control:**
- 1 group session in which participants were given community referrals to assist in RTW

**Outcomes**

**Employment:**
1. Full-time, part-time, temporary, or under-the-table paid employment in the past 6 months and average hours per week
2. Unpaid volunteer work in the past 6 months and average hours per week
3. Attendance at job training classes in the past 6 months and average hours per week
4. Active job search for a period of 30 days or longer in the past 6 months

Authors also assessed:
1. Demographics in past 6 months
2. Current health status

**Notes**

Contacted authors for additional information. None provided.

### Risk of Bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Blinding (subjects)</td>
<td>HIGH</td>
<td>No blinding of participants or personnel.</td>
</tr>
<tr>
<td>15. Blinding (outcome assessors)</td>
<td>HIGH</td>
<td>Not reported.</td>
</tr>
<tr>
<td>16. Retrospective unplanned sub-group analysis</td>
<td>UNCLEAR</td>
<td>Only baseline data was reported. No follow-up outcomes provided.</td>
</tr>
<tr>
<td>17. Follow-up</td>
<td>LOW</td>
<td>Follow-ups conducted for both index and reference groups at 6, 12, 18, and 24 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>18. <strong>Statistical tests</strong></td>
<td>UNCLEAR</td>
<td>Unable to determine appropriateness due to unjustified, complex data analysis and unreported follow-up outcome.</td>
</tr>
<tr>
<td>19. <strong>Compliance</strong></td>
<td>HIGH</td>
<td>Compliance not insured. Dose-response analysis conducted but results uninterruptible.</td>
</tr>
<tr>
<td>20. <strong>Outcome measures</strong></td>
<td>LOW</td>
<td>All predetermined outcome measures were reported.</td>
</tr>
<tr>
<td>21. <strong>Selection Bias</strong> (population)</td>
<td>UNCLEAR</td>
<td>Participants were recruited from multiple AIDS service organizations, community mental health centers, HIV medical providers, and gay and lesbian centers, and may be disproportionate between index and reference groups, although reported baseline demographic characteristics were uniform between groups. Recruited at same time. Randomized.</td>
</tr>
<tr>
<td>22. <strong>Selection Bias</strong> (time)</td>
<td>LOW</td>
<td></td>
</tr>
<tr>
<td>23. <strong>Randomization</strong></td>
<td>LOW</td>
<td>Stratified randomization procedure on education, CD4 count, and ethnic minority status.</td>
</tr>
<tr>
<td>24. <strong>Allocation Concealment</strong></td>
<td>UNCLEAR</td>
<td>Not reported.</td>
</tr>
<tr>
<td>25. <strong>Adjustment for confounding</strong></td>
<td>HIGH</td>
<td>Not adjusted for gender; only 9-10% female in both groups.</td>
</tr>
<tr>
<td>26. <strong>Incomplete outcome data</strong></td>
<td>HIGH</td>
<td>All follow-up outcome data missing. Only baseline data provided with generalized summaries in results section.</td>
</tr>
</tbody>
</table>

**ART:** antiretroviral therapy  
**RCT:** randomized control trial
Nannungi et al. 2013

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>CBA study (Longitudinal, prospective cohort)</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>482 participants were recruited (July 2008 to August 2009) as consecutive, new clinic patients recently evaluated for ART from 2 HIV clinics in Kampala, Uganda (ReachOut Mbuya and Mulago Immune Suppression Syndrome Clinic) Index: 257 HIV+ persons initiating ART with CD4 count &lt; 250 cells/mm3 (WHO disease stage III or IV) Control: 225 HIV+ persons pre-ART with CD4 count &lt; 400 cells/mm3</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>All participants received HIV primary medical care (monitoring and treatment of infections and prescription of prophylactic medications) Index: ART plus HIV primary medical care Control: HIV primary medical care</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>All participants underwent structured interview concerning background characteristics, physical and mental health status, and economic outcomes. Health data abstracted from patient medical records and Medical Outcomes Study HIV Health Survey. Assessments taken at 0, 6, and 12 months. Employment: 1. Work status; having engaged in work activity in previous 7 days (binary yes or no) 2. Weekly income; last payment and number of weeks worked for this payment Other health-related economic outcomes: 3. Health interference with ability to work in last month (4-point scale from 'never' to 'most of the time')</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Infectious Diseases Institute Makerere University (Kampala, Uganda) Uganda National Council of Science and Technology (Uganda) Rand Corporation (CA, USA) Participants received 6000 Uganda Shillings (~USD2.50) for completion of each assessment</td>
</tr>
</tbody>
</table>

**Risk of Bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Blinding (subjects)</td>
<td>UNCLEAR</td>
<td>No blinding, however due to a dichotomous outcome of employed or unemployed in past 7 days, this should not have affected the results.</td>
</tr>
<tr>
<td>15. Blinding (outcome assessors)</td>
<td>LOW</td>
<td>No blinding, objective outcomes should have been unaffected by lack of outcome assessor blinding.</td>
</tr>
<tr>
<td>16. Retrospective unplanned sub-group analysis</td>
<td>LOW</td>
<td>No evidence of retrospective unplanned subgroup analysis.</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>17. Follow-up</td>
<td>UNCLEAR</td>
<td>Follow-up conducted at 0, 6, and 12 months. 36% attrition.</td>
</tr>
<tr>
<td>18. Statistical tests</td>
<td>LOW</td>
<td>Two-tailed t-tests, Chi2 tests, paired t-test, McNemar’s test.</td>
</tr>
<tr>
<td>19. Compliance</td>
<td>UNCLEAR</td>
<td>As ART adherence is required for survival, compliance, although not monitored, is highly likely</td>
</tr>
<tr>
<td>20. Outcome measures</td>
<td>LOW</td>
<td>All predetermined outcome measures were reported.</td>
</tr>
<tr>
<td>21. Selection Bias (population)</td>
<td>LOW</td>
<td>Non-randomized, non-blinded recruitment of consecutive new clinic clients recently evaluated for ART</td>
</tr>
<tr>
<td>22. Selection Bias (time)</td>
<td>LOW</td>
<td>All participant recruitment July 2008 to August 2009.</td>
</tr>
<tr>
<td>23. Randomization</td>
<td>LOW</td>
<td>Non-randomized, ART group and control group predetermined by health status and WHO stages of disease criteria</td>
</tr>
<tr>
<td>24. Allocation Concealment</td>
<td>HIGH</td>
<td>Non-randomization. Did not report the use of adequate sequence generation or allocation concealment techniques</td>
</tr>
<tr>
<td>25. Adjustment for confounding</td>
<td>UNCLEAR</td>
<td>Study adjusted for changes in physical, health status, age, gender, education, relationship status, and CD4 count. However, did not account for SES or mental health confounders</td>
</tr>
<tr>
<td>26. Incomplete outcome data</td>
<td>UNCLEAR</td>
<td>36% attrition, analysis included attrition weights for dropouts derived from study completion and baseline measures associated with ART</td>
</tr>
</tbody>
</table>

Baseline Comparability | HIGH | As expected, baseline health differences were present between the index and reference groups due to disease progression and need for treatment. Higher percentage of index group was married or in a committed relationship than control group. Higher percentage of control group working and higher weekly income at baseline than index group. Analysis adjusted for change in physical health status |

ART: antiretroviral therapy
CBA: controlled before-after study
<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>CBA study</td>
</tr>
</tbody>
</table>
| **Participants**| 1543 adult HIV+ persons, plus 54 caretakers and 67 children (Tamil Nadu, India)  
Index Group: 515  
Control Group: 723  
A total of 1238 participants were included in the final analysis |
| **Intervention**| Intervention: Pharmacological, ART and home visits for ART adherence support  
- Clinical care: routine medical care, diagnosis, and treatment of opportunistic infections  
- Nutritional supplement: nutritional assessment, counseling, macronutrient/micronutrient supplements  
- Home-based care: home visits for encouraging participants to make monthly hospital visits, social service connection for income-generating activities, legal services, and housing  
Control: All of the above except for ART and home visits for ART adherence support because CD4 counts were above 200 and ART was not indicated |
| **Outcomes**    | Employment:  
1. Whether participants took part in economic activities during the week prior to interview  
2. Number of hours they worked during the week prior to interview  
3. Individual income earned in the past 30 days  
4. Individual income earned in the past 6 months  
Health status:  
1. Body mass index  
2. CD4 cell count  
3. ART initiation date |
| **Notes**       | ***Participants were not required to be employed at the time of the study, however the study measured economic outcomes related to ART |
| **Risk of Bias**| Authors’ judgement  
Low, High, Unclear  
Support for judgement  
14. Blinding (subjects) LOW  
No blinding, however due to a dichotomous outcome of employment or non-employment, this should not have affected the results.  
15. Blinding (outcome assessors) LOW  
No blinding, objective outcomes should have been unaffected by lack of outcome assessor blinding.  
16. Retrospective unplanned sub-group analysis LOW  
No evidence of retrospective unplanned subgroup analysis. |
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>17. Follow-up</td>
<td>LOW</td>
<td>Same time period. 68.66% present for interviews at 24 months</td>
</tr>
<tr>
<td>18. Statistical tests</td>
<td>UNCLEAR</td>
<td>Possibly MD and SE for ART group and entire HIV+ cohort</td>
</tr>
<tr>
<td>19. Compliance</td>
<td>UNCLEAR</td>
<td>Compliance to ART was not reported. However, ART participants did receive home visits to encourage ART adherence. ART adherence is required for survival, therefore compliance, although not monitored, is likely</td>
</tr>
<tr>
<td>20. Outcome measures</td>
<td>LOW</td>
<td>All predetermined outcome measures were reported.</td>
</tr>
<tr>
<td>21. Selection Bias (population)</td>
<td>LOW</td>
<td>Selected from same population. (Tamil Nadu Family Continuum Care Program)</td>
</tr>
<tr>
<td>22. Selection Bias (time)</td>
<td>LOW</td>
<td>Recruited at the same time.</td>
</tr>
<tr>
<td>23. Randomization</td>
<td>HIGH</td>
<td>Non-randomized study. Participants were predetermined by health status and CD4 counts</td>
</tr>
<tr>
<td>24. Allocation Concealment</td>
<td>UNCLEAR</td>
<td>Non-randomization. Did not report the use of adequate sequence generation or allocation concealment techniques</td>
</tr>
<tr>
<td>26. Incomplete outcome data Baseline Comparability</td>
<td>UNCLEAR</td>
<td>34.34% attrition in index group addressed. No attrition data reported for controls Female percentage was 42% in the index group and 65% in the reference group. Percentage of those who completed secondary education was 28% in the index group and 27% in the reference group. CD4 counts at baseline were 128.2 for the index group and 465.6 for the reference group</td>
</tr>
</tbody>
</table>

ART: antiretroviral therapy
CBA: controlled before-after study
### B. Characteristics of Excluded Studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajithkumar 2007</td>
<td>No control group</td>
</tr>
<tr>
<td>Bernell 2005</td>
<td>Not a RCT or CBA study</td>
</tr>
<tr>
<td>Escovitz 2005</td>
<td>Kirk Employment Empowerment Project. No control group.</td>
</tr>
<tr>
<td>Goldman 2004</td>
<td>No control group</td>
</tr>
<tr>
<td>Herdt 1999</td>
<td>Study about AIDS prevention, not an HIV employment intervention study</td>
</tr>
<tr>
<td>Hergenrather 2013</td>
<td>No control group</td>
</tr>
<tr>
<td>Lee 2005</td>
<td>We sought unpublished raw data specific to HIV from the author but received none. The published data on general chronic diseases was not relevant to the other studies in the review</td>
</tr>
<tr>
<td>Martin 2003</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Martin 2005</td>
<td>Summary of ongoing study later published as Martin et al. 2012</td>
</tr>
<tr>
<td>Maticka-Tyndale 2002</td>
<td>All results were qualitative.</td>
</tr>
<tr>
<td>Resch 2011</td>
<td>Modeling study; not an intervention study</td>
</tr>
<tr>
<td>Rosen 2004</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Rosen 2010</td>
<td>No control group</td>
</tr>
<tr>
<td>Rosen 2014</td>
<td>No control group</td>
</tr>
<tr>
<td>Rosolen 2010</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Rueda 2012</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Thirumurthy 2013</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Van der Borght 2006</td>
<td>Not a RCT or CBA study</td>
</tr>
<tr>
<td>Van der Borght 2010</td>
<td>Not a RCT or CBA study</td>
</tr>
</tbody>
</table>

CBA: controlled before-after study

RCT: randomized controlled trial
C. Characteristics of Studies Awaiting Assessment [ordered by study ID]

### Baran et al. 2012

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>CBA study</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>196,350 employees &gt;18 years of age (USA)</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Pharmacological, ART</td>
</tr>
</tbody>
</table>
| **Outcomes**    | Employment:  
|                 | 1. Sick leave  
|                 | 2. Short-term disability  
|                 | 3. Long-term disability  
| **Notes**       | Poster presentation only. Contact author for full text and further unpublished outcome data. However, the author responded that he was unable to provide any unpublished data without the specific permission of AbbVie Pharmaceutical Group. AbbVie was contacted for authorization. Richard from AbbVie group is investigating my request. AbbVie would not release data for external publication or use |

### Borwein et al. 2010

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Not known</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Not known</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Not known</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Not known</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Original search produced only abstract. Contacted author but received no response. Additionally NM sought hard copies in Canada, and only poster abstracts were located from the <em>Canadian Journal of Infectious Diseases &amp; Medical Microbiology</em>. Study was still in progress in 2010, but no further publication has been made.</td>
</tr>
</tbody>
</table>
### Paul-Ward 2005

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Not known</td>
</tr>
<tr>
<td>Participants</td>
<td>48 HIV+ people from supportive living facilities (USA)</td>
</tr>
<tr>
<td>Interventions</td>
<td>ESD program</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Not known</td>
</tr>
</tbody>
</table>

**Notes**
Study still in progress as of 2005. No later publication found. Contacted author but received no response.

---

### Popiel 2010

<table>
<thead>
<tr>
<th>Study Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Not known</td>
</tr>
<tr>
<td>Participants</td>
<td>Not known</td>
</tr>
<tr>
<td>Interventions</td>
<td>Not known</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Not known</td>
</tr>
</tbody>
</table>

**Notes**
Original search produced only abstract. Contacted author but received no response. Additionally NM sought hard copies in Canada, and only abstracts were located from the *Canadian Journal of Infectious Diseases & Medical Microbiology.*
**Appendix 2: GRADE RATINGS FOR DETERMINING THE QUALITY OF THE LEVEL OF EVIDENCE**

<table>
<thead>
<tr>
<th>Comparison (No. of Studies)</th>
<th>HIV+ ART vs. Healthy (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limitations (Risk of bias in studies)</strong></td>
<td>HIGH risk of bias. Non-randomized retrospective studies of cohort data. Non-blinded but should not affect the results of the study as outcomes are objective. Low risk of selection bias. Low rate of attrition for index groups. High risk of bias for adjustments for confounding. Lack of attrition data for the control group. High risk of bias for baseline comparability. <strong>DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Directness of evidence</strong></td>
<td>No limitations. Populations in comparison: Kenyan tea workers (predominate employer in district) &amp; South African general population in subdistrict. Direct populations, direct ART interventions delivered through clinics, and healthy control group received no intervention. No surrogate data was used. <strong>NO DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Consistency between studies</strong></td>
<td>Results consistent in both studies. Subgroup analysis was not applicable. <strong>NO DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Precision of effect size</strong></td>
<td>Wide confidence intervals. <strong>DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Publication bias</strong></td>
<td>Not applicable; only two studies. <strong>NO DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Considerations for upgrading observational studies</strong></td>
<td>Small intervention participant numbers potentially inflate the magnitude of the effect. Dose-effect relation was explored as no data on dosage was provided. No analysis for confounders. <strong>NO UPGRADE</strong></td>
</tr>
<tr>
<td><strong>Level of Evidence</strong></td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparison (No. of Studies)</th>
<th>HIV+ ART vs. HIV+ Pre-ART (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limitations (Risk of bias in studies)</strong></td>
<td>HIGH risk of bias. Nonrandomized prospective cohort studies. No blinding, however results should be unaffected due to objective, dichotomous outcomes. Low risk of selection bias. Low rate of attrition for index. Unclear risk for a lack of attrition data for the control groups. High risk of bias for baseline comparability. <strong>DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Directness of evidence</strong></td>
<td>No outlying, indirect evidence. Control groups received standard care. No surrogate data used in any study. <strong>NO DOWNGRADE</strong></td>
</tr>
<tr>
<td><strong>Consistency between studies</strong></td>
<td>Results consistent in all 3 studies. <strong>NO DOWNGRADE</strong></td>
</tr>
</tbody>
</table>
**Precision of effect size**  
0% Heterogeneity.  
**NO DOWNGRADE**

**Publication bias**  
All 3 studies produced evidence of the positive effect of ART on employment, however we did not judge this to be biased to file drawer phenomenon. None of the studies had pharmaceutical funding or any known conflicts of interest.  
**NO DOWNGRADE**

**Considerations for upgrading observational studies**  
Small intervention participant numbers potentially inflate the magnitude of the effect.  
Dose-effect relation was not explored as no data on dosage was provided.  
Incomplete analysis for confounders. Studies individually adjusted for different and limited confounders.  
**NO UPGRADE**

<table>
<thead>
<tr>
<th><strong>Level of Evidence</strong></th>
<th><strong>VERY LOW</strong></th>
</tr>
</thead>
</table>

**Comparison (No. of Studies)**  
**Vocational Intervention vs. None (1)**

**Limitations (Risk of bias in studies)**  
High risk of bias. Allocation concealment and loss to follow-up not reported. No blinding and evidence of selective reporting.  
**DOWNGRADE**

**Directness of evidence**  
No outlying, indirect evidence due to single-study comparison. Control group received standard care. Outcome data limitations due to missing follow-up data and complex, confusing reporting.  
**DOWNGRADE**

**Consistency between studies**  
Only study, complete homogeneity.  
**NO DOWNGRADE**

**Precision of effect size**  
Poorly reported, minimal outcome data.  
**DOWNGRADE**

**Publication bias**  
No evidence of publication bias.  
**NO DOWNGRADE**

**Considerations for upgrading observational studies**  
Randomized study. Not applicable.  
**NO UPGRADE**

| **Level of Evidence** | **VERY LOW** |
Appendix 3: SEARCH STRATEGIES

A. MEDLINE (Pubmed) search strategy

14 March 2012 (by Leena Isotalo)


#4 #1 AND (#2 OR #3)


#7 #4 AND #5

#8 #4 AND #6

#9 #7 OR #8

Updated Search 9 December 2014 (by Kaisa Neuvonen)

Search Query  Items found
#10 #9 AND ("2013/11/06"[Date - Entrez] : "3000"[Date - Entrez]) 154
#9 #7 OR #8 3 249
#8 #4 AND #6 3 018
#7 #4 AND #5 1 033
#1 AND (#2 OR #3)

(work[ti] OR worker*[tw] OR worksite*[tw] OR occupation*[tw] OR 
"Occupational Groups"[Mesh]) AND ("disability management"[tw] OR 
"Rehabilitation"[Mesh:NoExp] OR 
"rehabilitation" [Subheading] OR "psychological intervention"[tw] OR "psychological interventions"[tw] OR 
"motivational interviewing" [tw] OR "self management"[tw] OR "behaviour change"[tw] OR "Occupational 
Therapy"[Mesh]) OR "work accommodation"[tw] OR "work modification"[tw]

#2

#3
B. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

9 October 2012 (by Leena Isotalo)

#1

hiv or "hiv-1*" or "hiv-2*" or hiv1 or hiv2 or "hiv infect*" or "human immunodeficiency virus" or "human immunedeficiency virus" or "human immuno-deficiency virus" or "human immune-deficiency virus":ti,ab,kw (Word variations have been searched)

#2

MeSH descriptor: [HIV] explode all trees

2250

#3

MeSH descriptor: [HIV Infections] explode all trees

6728

#4

("human immun*" and "deficiency virus") or "acquired immunodeficiency syndrome" or "acquired immunedeficiency syndrome" or "acquired immuno-deficiency syndrome" or "acquired immune-deficiency syndrome" or ("acquired immun*" and "deficiency syndrome") or "HIV/AIDS"

2340

#5

#1 or #2 or #3 or #4

9863

#6

MeSH descriptor: [Absenteeism] explode all trees

370

#7

MeSH descriptor: [Sick Leave] explode all trees

334

#8

MeSH descriptor: [Employment] explode all trees

958
MeSH descriptor: [Unemployment] explode all trees

MeSH descriptor: [Occupational Health] explode all trees

MeSH descriptor: [Occupational Health Services] explode all trees

MeSH descriptor: [Occupational Medicine] explode all trees

MeSH descriptor: [Rehabilitation, Vocational] explode all trees

absenteeism or "work disability" or "sick leave" or "sickness absence" or employment or "re-employment" or unemployment or unemployed or employability or employable or employee* or "work capacity" or "return to work" or "retirement" or "work status" or "job satisfaction" or "work ability" or workability or "work activity" or "work retention" or "job retention" or "job loss" or "job performance" or "work rehabilitation"

MeSH descriptor: [Occupational Groups] explode all trees

MeSH descriptor: [Rehabilitation] this term only
Any MeSH descriptor with qualifier(s): [Rehabilitation - RH] in all MeSH products

11494

MeSH descriptor: [Occupational Therapy] explode all trees

452

work*:ti (Word variations have been searched)

4338

worker* or worki* or workplace* or worksite* or occupation*

16400

"psychological intervention" or "psychological interventions" or "motivational interviewing" or "self management" or "behaviour change" or accommodation or modification

12075

"disability management"

18

"disability management"

18

#23 and #25
3171

#27

#15 or #26

9556

#28

#5 and #27

245

limited to:

Cochrane Central Register of Controlled Trials (Central)

80
C. EMBASE search strategy

20 September 2012 (by Leena Isotalo)

(#1)

'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus'/exp OR hiv:ab,ti OR 'hiv-1':ab,ti OR 'hiv-2':ab,ti OR 'human immunodeficiency virus':ab,ti OR 'human immuno-deficiency virus':ab,ti OR 'human immunodeficiency virus':ab,ti OR 'acquired immune-deficiency syndrome':ab,ti OR 'acquired immunodeficiency syndrome':ab,ti OR 'acquired immuno-deficiency syndrome':ab,ti OR 'acquired immunodeficiency syndrome':ab,ti OR 'hiv/aids':ab,ti

364,281

(#2)

'absenteeism'/de OR 'medical leave'/de OR 'work disability'/de OR 'employment'/exp OR 'unemployment'/de OR 'work capacity'/de OR 'occupational health'/de OR 'employability'/de OR 'job accommodation'/de OR 'vocational rehabilitation'/de OR 'occupational health service'/de OR 'occupational health nursing'/de OR 'occupational medicine'/de OR 'industrial medicine'/de OR 'job adaptation'/de OR 'retirement'/de OR 'job satisfaction'/de OR 'job performance'/de OR absenteeism:ab,ti OR 'work disability':ab,ti OR 'sick leave':ab,ti OR 'sickness absence':ab,ti OR employment:ab,ti OR 're-employment':ab,ti OR unemployment:ab,ti OR unemployed:ab,ti OR employability:ab,ti OR 'work capacity':ab,ti OR 'occupational health services':ab,ti OR 'return to work':ab,ti OR 'vocation':ab,ti OR 'work status':ab,ti OR 'job satisfaction':ab,ti OR 'work ability':ab,ti OR 'workability':ab,ti OR 'work activity':ab,ti OR 'work retention':ab,ti OR 'job retention':ab,ti OR 'job loss':ab,ti OR 'job performance':ab,ti OR 'vocational rehabilitation':ab,ti OR 'work rehabilitation':ab,ti OR 'work accommodation':ab,ti OR 'work modification':ab,ti

238,611

(#3)

work*:ab,ti OR occupation*:ab,ti OR 'work environment'/de OR 'work'/de OR 'workplace'/exp OR 'occupation and occupation related phenomena'/de OR 'occupation'/exp OR 'occupational health'/exp AND ('disability management':ab,ti OR rehabilitation:de,ab,ti OR 'psychological intervention':ab,ti OR 'psychological interventions':ab,ti OR 'motivational interviewing':ab,ti OR 'self management':ab,ti OR behavio* NEAR/3 chang* OR 'occupational therapy')

52,567

(#4)

#1 AND (#2 OR #3)

5,044

(#5)

random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind OR assign* OR allocat* OR volunteer* OR 'crossover procedure'/de OR 'double-blind procedure'/de OR 'single-blind procedure'/de OR 'randomized controlled trial'/de

1,405,159

(#6)

effect* OR control* OR evaluation* OR program* OR 'cohort analysis'/de OR 'intervention study'/de OR 'comparative study'/de OR 'comparative effectiveness'/de OR 'intermethod comparison'/de OR 'follow up'

12,732,170
(#7)
#4 AND #5
456
(#8)
#4 AND #6
3,435
(#9)
#7 OR #8
3,497
(#10)
'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it OR 'nonhuman'/de
5,767,119
(#11)
#9 NOT #10
3,228
(#12)
#11 AND [embase]/lim
2,110

Updated Search 9 December 2014 (by Kaisa Neuvonen)

(#13)
#11 AND [embase]/lim AND [6-11-2013]/sd NOT [9-12-2014]/sd
354
(#12)
#11 AND [embase]/lim
2,519
(#11)
#9 NOT #10
3,434
'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it OR 'nonhuman'/de
6,412,344

(#9)
#7 OR #8
3,686

(#8)
#4 AND #6
3,588

(#7)
#4 AND #5
575

(#6)
effect* OR control* OR evaluation* OR program* OR 'cohort analysis'/de OR 'intervention study'/de OR 'comparative study'/de OR 'comparative effectiveness'/de OR 'intermethod comparison'/de OR 'follow up'
12,986,661

(#5)
random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind OR assign* OR allocat* OR volunteer* OR 'crossover procedure'/de OR 'double-blind procedure'/de OR 'single-blind procedure'/de OR 'randomized controlled trial'/de
1,674,549

(#4)
#1 AND (#2 OR #3)
5,936

(#3)
work*:ab,ti OR occupation*:ab,ti OR 'work environment'/de OR 'work'/de OR 'workplace'/exp OR 'occupation and occupation related phenomena'/de OR 'occupation'/exp OR 'occupational health'/exp AND ('disability management':ab,ti OR rehabilitation:de,ab,ti OR 'psychological intervention':ab,ti OR 'psychological interventions':ab,ti OR 'motivational interviewing':ab,ti OR 'self management':ab,ti OR behavio* NEAR/3 chang* OR 'occupational therapy')
61,328

(#2)
'absenteeism'/de OR 'medical leave'/de OR 'work disability'/de OR 'employment'/exp OR 'unemployment'/de OR 'work capacity'/de OR 'occupational health'/de OR 'employability'/de OR 'job accommodation'/de OR 'vocational rehabilitation'/de OR 'occupational health service'/de OR 'occupational health nursing'/de OR 'occupational medicine'/de OR 'industrial medicine'/de OR 'job adaptation'/de OR 'retirement'/de OR 'job satisfaction'/de OR 'job performance'/de OR absenteeism:ab,ti OR 'work disability':ab,ti OR 'sick leave':ab,ti OR 'sickness absence':ab,ti OR 'employment':ab,ti OR 're-employment':ab,ti OR 'unemployment':ab,ti OR 'unemployed':ab,ti OR 'employability':ab,ti OR 'employable':ab,ti OR 'employee*':ab,ti OR 'work capacity':ab,ti OR 'occupational health services':ab,ti OR 'return to work':ab,ti OR 'retirement':ab,ti OR 'work status':ab,ti OR 'job satisfaction':ab,ti OR 'work ability':ab,ti OR 'workability':ab,ti OR 'work activity':ab,ti OR 'work retention':ab,ti OR 'job retention':ab,ti OR 'job loss':ab,ti OR 'job performance':ab,ti OR 'vocational rehabilitation':ab,ti OR 'work rehabilitation':ab,ti OR 'work accommodation':ab,ti OR 'work modification':ab,ti

262,028

(#1)

'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus'/exp OR 'hiv':ab,ti OR 'hiv-1':ab,ti OR 'hiv-2':ab,ti OR 'human immunodeficiency virus':ab,ti OR 'human immuno-deficiency virus':ab,ti OR 'human immunodeficiency virus':ab,ti OR 'human immunodeficiency virus':ab,ti OR 'acquired immune-deficiency syndrome':ab,ti OR 'acquired immunodeficiency syndrome':ab,ti OR 'acquired immunodeficiency syndrome':ab,ti OR 'acquired immuno-deficiency syndrome':ab,ti OR 'hiv/aids':ab,ti

404,528
D. OSH UPDATE search strategy

25 September 2012 (by Leena Isotalo)

#1 3152 GW {hiv OR "hiv-1*" OR "hiv-2*" OR hiv1 OR hiv2 OR "HIV/AIDS" OR HUMAN IMMUNODEFICIENCY VIRUS OR HUMAN IMMUNEDEFICIENCY VIRUS OR HUMAN IMMUNE-DEFICIENCY VIRUS OR HUMAN IMMUNO-DEFICIENCY VIRUS OR HUMAN IMMUN* DEFICIENCY VIRUS OR ACQUIRED IMMUNODEFICIENCY SYNDROME OR ACQUIRED IMMUNEDEFICIENCY SYNDROME OR ACQUIRED IMMUNE-DEFICIENCY SYNDROME OR ACQUIRED IMMUNO-DEFICIENCY SYNDROME OR ACQUIRED IMMUN* DEFICIENCY SYNDROME}

#2 89805 GW {absenteeism OR work disability OR sick leave OR sickness absence OR employment OR re-employment OR unemployment OR unemployed OR employability OR employable OR employee* OR work capacity OR occupational health service* OR return-to-work OR retirement OR work status OR job satisfaction OR work ability OR workability OR work activity OR work retention OR job retention OR job loss OR job performance OR vocational rehabilitation OR work rehabilitation}

#3 47230 GW {disability OR rehabilitation OR psycholog* OR motivational OR self management OR behaviour OR behavior OR therapy OR work accommodation OR work modification}

#4 87611 GW {workplace* OR worksite* OR work place* OR work site* OR organisation* OR organization*}

#5 19111 GW {occupation OR occupations}

#6 392334 GW {random* OR trial* OR groups OR effect* OR effic* OR control* OR evaluat* OR program* OR cohort* OR intervention* OR compar* OR follow-up}

#7 732455 DC {OUCISD OR OUHSEL OR OUNIOC OR OUNIOS OR OURILO}

#8 193459 #2 OR #3 OR #4 OR #5

#9 1355 #1 AND #8

#10 970 #9 AND #6

#11 764 #10 AND #7