

Review

Impact of Case Management on HIV Patients' Linkage to Care and Their Clinical Outcome: A Systematic Review of Randomized Clinical Trials

Siavash Jafari ^{1, *}, Mariko Vaughan ¹, Souzan Baharlou ², Pooria Ghadiri ³, Nazila Hassanabadi ⁴, Ashkan Nasr ⁵

1. Faculty of Medicine, University of British Columbia, Vancouver, BC V6T 1Z3, Canada; E-Mails: siavash.jafari@vch.ca; marikov@alumni.ubc.ca
2. British Columbia Children's Hospital, Vancouver, BC V6T 1Z3, Canada; E-Mail: souzan_baharlou@yahoo.com
3. Department of Family Medicine, McGill University, Montreal, QC, Canada; E-Mail: Pooria589@yahoo.com
4. Department of Medicine, Division of Experimental Medicine, McGill University, Montreal, QC, Canada; E-Mail: Nazila_med85@yahoo.com
5. Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; E-Mail: ashkan.nasr@nv.touro.edu

* **Correspondence:** Siavash Jafari; E-Mail: siavash.jafari@vch.ca

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Abstract

Objectives: The purpose of this systematic literature review is to investigate the impact of case management on the link between HIV/AIDS patients (HIV-infected persons) and HIV treatment, and to investigate the impact of case management on their morbidity and mortality.

Methods: We searched PubMed, Current Contents, Scopus, EMBASE, MEDLINE, the Effect Review Summary Database and the ACP Journal Club until May 2018. A randomized clinical trial examined the impact of case management on the association of PLHA with care and



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publications in English. After reviewing the title and abstract, the full text of the included study is retrieved for in-depth review. Two commentators reviewed the articles and extracted relevant information.

Results: Six randomized controlled trials were selected for inclusion in the systematic review. We found significant heterogeneity in the included studies. These studies use a wide range of definitions and provide a variety of services under case management services. One study found a statistically significant reduction in mortality and viral load reductions, but there was no difference in CD4 counts in the case management group. Two studies have found that case management patients are more closely linked to HIV care. Three studies found no difference in treatment initiation rates and treatment initiation time between the two groups. One study did not find an improvement in CD4 counts. One study reported an increase in viral load.

Conclusions: The results of this systematic review show mixed results on the impact of case management on the outcome of interest. The nature and level of case management services offered to participants varied significantly. Case management could improve the linkage to care among PLHA, improve their survival rate and reduce viral load however has no impact on CD4 levels.

Keywords

Access to care; adherence to care; linkage to care; HIV/AIDS; case management

1. Background

According to the estimates by the Centers for Disease Control and Prevention (CDC), approximately 37,000 new human immunodeficiency virus (HIV) infections occur each year in the United States [1, 2]. The seroprevalence rate is even higher in some populations: especially African Americans, Hispanics and men who have sex with men are severely hit by HIV/AIDS people [3]. It is estimated that 21% of infected people do not know their serostatus [4]. People do not know that their serum status is more likely to engage in risk-free health behaviors such as unprotected sex [5]. People living with HIV/AIDS (PLHA) do not know their identity, accounting for more than half of new infections [5]. Conversely, when people know their HIV status, they are less likely to spread the disease, and studies have shown that patients with antiretroviral therapy (ART) are less contagious [3]. Lack of awareness can also lead to advanced HIV disease: 35% to 45% of newly diagnosed HIV-infected people develop AIDS within one year of diagnosis, representing late-stage care [3]. PLHA entering health care at this time is often extremely impaired, immune system and AIDS-related complications [3].

In Canada, the number of people infected with HIV/AIDS in 2014 is estimated at 75,000 [6]. An estimated 2,300 to 4,500 new HIV infections were reported in the same year [7]. The most common types of exposure in epidemics include MSM (51%), IDU (17%), heterosexual/non-endemic (15%), heterosexual/local (12%) and MSM-IDU (MSM-IDU) 4% [7]. Heterosexual/non-endemic was defined as contact with a person who is either HIV-infected or at risk for HIV, or heterosexual as the only identified risk and heterosexual/endemic was defined as non-IDU

heterosexual with origin in a country where heterosexual sex is the predominant mode of HIV transmission and HIV prevalence is high (primarily countries in sub-Saharan Africa and the Caribbean).

Early diagnosis and connection to care for people living with HIV have a significant impact on their morbidity and mortality. Early initiation of HIV treatment and long-term adherence can lead to better health outcomes and reduce the spread of infection. Therefore, shortly after the diagnosis of HIV, contact with care can be an important intervention to improve prognosis and prevent transmission. Many people living with HIV are not linked to care or are not cared for after HIV diagnosis [8, 9].

Case management was developed in the 1970s and it was adapted into HIV/AIDS care in 1980s. This is a multifaceted intervention to ensure timely access to and coordination of medical and psychosocial services for people living with HIV. Although there is no universal case management program, a case manager is usually assigned to people living with HIV to help them assess and prioritize needs such as health care, housing, finance, and social support. In this way, case management is considered to prevent hospitalization or long-term care from admission, and doing so helps control costs associated with health care. The goal of case management is to promote and support individual independence and self-sufficiency. Therefore, the case management process requires customers to actively participate in decision-making and support clients' self-determination, dignity and respect, non-discrimination, compassionate non-judgmental care, and culturally competent case management providers.

Regarding the impact of case management on the health outcomes of people living with HIV, there are publications such as CD4 levels, adherence to care, health-related quality of life, use of street drugs, admission rates, and participation in treatment options. However, the sample size of these studies was small, the study time was different, and the various results of interest were studied. A systematic review and a potential meta-analysis are needed to investigate the combined effects of case management on the medical and psychosocial outcomes of PLHA.

2. Objectives

The purpose of this systematic literature review is to investigate the impact of case management on the link between people living with HIV/AIDS (PLHA) and HIV care programs and to investigate the effect of case management for their overall morbidity and mortality.

3. Methods

3.1 Search Strategy

MEDLINE (1966 - May 2018), EMBASE (May 1980 - 2018), Impact Review Summary Database (May 1991 to 2018), PsychINFO (1988 to May 2018) and Web of Science (1961 to May 2018) a search was conducted to determine relevant studies. The initial search strategy was developed from the medical subject heading (MeSH) terminology case management and HIV in MEDLINE. We reviewed the titles related to this study and then adjusted and combined the topic titles and free-text terms. We searched for proceedings and conference abstracts through the databases PapersFirst (1993) and Proceedings First (1993) until May 2018. The author's name and the publication year of the main paper are entered into a reference search in the database Web of

Science. For any articles that may be missing, the references to the retrieved research and review articles are screened. We also searched for journals related to HIV, Case Management, Epidemiology, and hepatitis-related abstracts and books. The following Medical Subject Headings (MeSH) were used to search to identify the relevant publications: case management, case managers, HIV infections, HIV-infected patients, HIV long-term survivors, health services accessibility, patient acceptance of health care, health services/utilization, health services needs and demand, patient care/utilization, primary health care/utilization, patient compliance, health services needs and demand, randomized controlled trial, and RCT.

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to prepare this systematic review [10].

3.2 Selection Criteria

We included randomized controlled trials investigating the impact of case management on the linkage of PLHA to care and presenting odds ratios (OR) and their corresponding 95% confidence Interval (95% CI) or provided enough data to calculate these parameters. If a study was published at a different stage, or if the data was repeated in multiple publications, only the most recent study was included. We limit our research to articles that were published 1) in English; 2) were from the North America or Europe; and 3) had a randomized trial design. If the article was not fully published, we tried to contact the author to retrieve the full manuscript.

3.3 Data Extraction

We created a spreadsheet and recorded study characteristics, including author name, publication year, study country, study design, sample size, study population, mean age and/or age range, participant gender, risk factor type or adjusted confounding factors, interest outcomes, adjusted OR and 95% CI. Two reviewers independently (SJ and PG) conducted a comprehensive review of the articles included. For studies that provide multiple levels of exposure, each exposure is classified and analyzed in a designated subgroup. We collected data on factors such as CD4 counts, viral load and reduction in high-risk behavior as outcome measures to assess the potential impacts of linkage to care.

3.4 Quality Assessment

The included studies were assessed for the risk of quality and bias. The CONSORT Reporting Guide was used to evaluate the included studies. The Newcastle-Ottawa Scale was used to assess the quality of the included studies (Appendix S1).

4. Results

A total of 622 titles were reviewed, including 55 publications, in which six randomized controlled trials (RCTs) comprising of five from the United States, and one from Russia were included in the systematic reviews (see Figure 1).

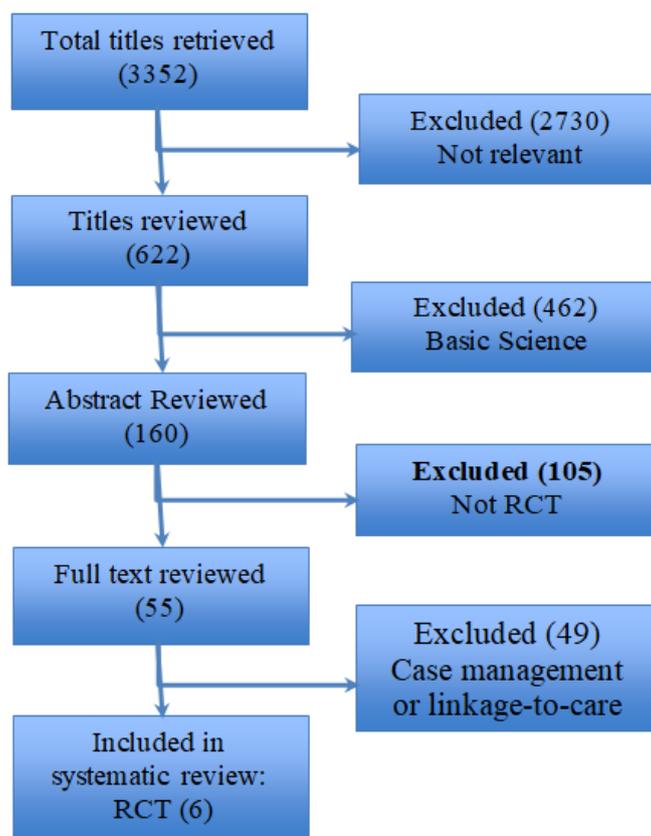


Figure 1 Selection of studies for inclusion in the systematic review and meta-analysis.

Table 1 summarize the results of the included studies. All included studies registered PLHIV in their study. PLHIV who were enrolled in Buchanan (2009) has been homeless for several months before enrollment, and are English speakers and HIV-seropositive [11]. Gardner (2005) included PLHIV who have used a care provider once in the past and have not taken ARVs [12]. Gordon (et al, 2017) included HIV-infected prisoners who have not received treatment within 30 days of enrolment [13]. Wohl (2011) recruited HIV-infected prisoners [14].

Wohl (2006) studied the effects of case management on the viral load and the linkage between care and treatment-naive PLHIV, and also, PLHIV with no more than one failed HAART experience in the past [15]. In 2017, Samet et al. investigated the impact of case management on the links between HIV-based care and HIV care using intravenous (IV) drugs.

Most studies provide detailed information about the age and gender of the participants. All studies included men and women. Most studies reported the age of participants aged 18 or older [12, 14]. However, in the study conducted by Buchanan 2009, Gordon 2017, Samet 2017 and Wohl 2006 [11, 13, 15, 16], the age of the participants was not clear. In the Wohl 2006 and Wohl 2011 studies, the study took 6 months, and in the 2005 Gardner and Buchanan, a 12-month 2009 to 18-month study by Gordon 2017. All studies reported two or more encounters during the study period. The sample size ranged from 105 participants in Buchanan 2009 to 349 participants in the Samet study in 2017. The quality of the included studies was assessed using a standard scale. The quality of studies varies from 12 to 13.

Table 1 List of included studies.

	Author	Country	Population of study	Sample size	Age and Gender	Follow up period	Intervention	Outcome of interest	Findings	Quality score (Max 16)
1	Buchanan 2009	USA	PLHIV	94.00	Male and female	Follow ups at 1, 3, 6, 9 and 12 months	Intensive Case Management vs. Usual Care	<ul style="list-style-type: none"> - Primary endpoint was survival with intact immunity - Secondary outcomes were CD4 counts, viral loads, and the fraction of patients with undetectable viral loads 	<ul style="list-style-type: none"> - After 1 year, 55% of the intervention and 34% of the usual care groups were alive and had intact immunity (P = .04). - 36% of intervention and 19% of usual care group had undetectable viral loads (P = .051). - No statistically significant differences in CD4 counts. 	13.00
2	Gardner 2005	USA	PLHIV	289.00	Male and female older than 18	Follow up visits at 6 and 12 months	ARTAS case management vs. Simple Referral	Linkage to care	<p>A higher proportion of the case-managed participants visited an HIV clinician:</p> <ul style="list-style-type: none"> - at least once within 6 months [(RR(adj)), 1.36; P = 0.0005) and - at least twice within 12 months [RR(adj), 1.41; P = 0.006)]. 	13.00
3	Gordon 2017	USA	PLHIV Inmate	100.00	Male and Female Adult	Follow up visits at 3, 6 and 12 months	<ul style="list-style-type: none"> i. Project Bridge (A team based model of care). ii. TAU MODEL iii. PB MODELS 	Rates of or time to treatment initiation	<ul style="list-style-type: none"> - No difference in rates of, or time to, treatment initiation when comparing the PB to TAU. - No difference between HIV medication regiment initiation by treatment condition 	13.00

4	Samet 2017	Russia	PLHIV	349.00	Male and Female	Follow up visits at 6 and 12 months	Case Management vs. Usual Care	Linkage to care and CD4 cell counts	-Within 6 months of enrollment, intervention groups better linkage to care compared to controls [aOR 2.20; 95% CI: 1.42-3.41 ; p= 0.0004]. - No differences in the mean CD4 count at 12 months between the intervention and the control groups.	13.00
5	Wohl 2006	USA	PLHIV	250.00	Male and female adults	Follow up visits at 6 month	Case management + (DAART effect on viral load) vs. ICAM Vs. Standard of Care	Viral load and immunologic response at 6 months.	No statistical differences were observed in the percentage of patients with an undetectable viral load between the groups	13.00
6	Wohl 2010	USA	PLHIV Inmate	89.00	Male and Female older than 18	Follow up visits at 6 month	Bridging case management versus Standard of care	health and social service utilization for HIV-infected individuals released from prison	- No differences in accessing care at 12, 24 and weeks. - The median time to entering into clinical care after release was 4 weeks for those in both study arms (P = 0.8)	12.00

*Quality score: the maximum expected score is 16. The higher the score is, the better the quality of the study is.

4.1 Interventions Offered in the Included Studies

In 2009, Buchanan examined the impact of permanent housing and intensive case management of homeless people hospitalized with a chronic medical illness. A year after, 55% of the interventions and 34% of conventional care groups survived and had complete immunity ($P = 0.04$). Seventeen (36%) individuals from the intervention and nine (19%) individuals from the conventional care group had an undetectable viral load ($P = 0.051$). The median viral load in the intervention group was 0.89 log lower ($P = 0.03$). There was no statistical difference in CD4 counts.

Gardner 2005 uses a strength-based case management to require clients to identify their interval strength as assets and apply those resources to obtain the required resources. An intervention manual was developed and the ARTAS case manager was trained as a team prior to client's registration. Participants were randomly divided into 2 groups. Those who only receive information and referred to as Standard of care (SOC) and are sent to the local HIV medical care provider. Participants in the intervention group were introduced to the case manager. The study found that a higher proportion of participants in the intervention group visited the HIV clinician (aRR 1.36; $P = 0.0005$) at least once within 6 months, at least twice within 12 months (aRR 1.41; $P = 0.006$).

In 2017, Gordon tested the project bridge model, a team-based care model that provides intensive case management for HIV patients as they transit from imprisonment to community. Gordon 2017 reported no difference in the rates of, or time to, treatment initiation between PB and TAU (both > 0.05), and there was no statistically significant difference between HIV treatment regimens under treatment conditions ($p > 0.05$).

In 2017, Samet found that 45% of the intervention group and 30% of the controls were linked to HIV care within 6 months after enrollment (aOR 2.20; 95% CI: 1.42-3.41; $p = 0.0004$). The mean CD4 counts at 12 months in the intervention and control groups were 340 and 372, respectively. (Adjusted mean difference: -20.2; 95% CI: -83.3, 42.9). They found no improvement in CD4 levels.

Wohl and colleagues [15] in their study found no difference in the linkage to care between the intervention group and the control group. There was no difference in the immune response between the two groups too. In the intent-to-treat analysis, they found no statistical difference in the percentage of patients who were unable to detect viral load at 6 months between the DAART group (54%), the IACM group (60%), and the SOC group (54%), P value = 0.05).

In another study, Wohl and colleagues [14] found that case management intervention to bridge incarceration and release were no more effective than a less intensive pre-release discharge planning program to support the health and social service utilization of people living with HIV who were released from prison.

4.2 Description of Case Management

In a Buchanan 2009 study, a case manager who was a social worker at the hospital saw patients in the intervention group. The person explained the intervention and provided a referral of temporary housing after discharge. Gardner 2005 describes case management as an attempt to establish relationships, identify and address clients' needs and health care barriers, and encourage contact with clinics. In Gordon 2017, the study case management team consisted of a masters-level social worker who served as the case manager and a social worker who served as an

outreach employee. Case Manager provided participants with many of their social and practical needs, with a focus on facilitating participation in HIV medical care. Case managers were responsible for overall case planning when conducting case reviews and conducting case conferences for all decisions that required clinical judgment.

Samet 2017 applied strength-based case management (LINC). Wohl 2006 provided no explanation of the case management services. Wohl 2011 used the behavioral model of the health service for vulnerable populations. The case management strengths model focuses on identifying the client's talents, resources, and goals in an open, non-judgmental environment. Prior to recruitment, Bridging Case Managers (BCMrs) underwent a series of group training led by experts in the model, as well as structured self-study and continuous clinical supervision, to maintain BCMrs' ability and loyalty to the model.

Gardner 2005 and Samet 2017 found a significant improvement in the linkage to care, while Wohl 2006 and Wohl 2011 found no differences in the linkage to care between the intervention group and control group. Two studies showed no improvement in CD4 and viral load [11, 16]. Only one study investigated treatment initiation among PLHA inmates [13]. This study found no improvement in the initiation of treatment. Buchanan 2009 examined the impact of case management on the mortality of PLHA and found a lower mortality rate in the case management group.

5. Discussion

The results of this systematic review show mixed results on the impact of case management on the outcome of interest.

The nature and level of case management services offered to participants varied significantly. For example, a 90-day study yielded up to 5 contacts with a case manager [12]. Wohl et al. (2006) provided "Intensive Adherence Case Management" (IACM), in which participants met weekly with a case manager to overcome barriers to HAART compliance, including referrals to healthcare payments, accommodation, drug abuse treatment, legal advice, and nutritional support [15].

The National Case Management Network of Canada (NCMN) defines case management as "a collaborative, client-focused process for delivering quality health and support services through the effective and efficient use of resources" [17]. This network has introduced a set of case management practice standards that must be followed to ensure the success of such programs. Case management includes client intake, needs analysis, service planning, service plan implementation, service coordination, monitoring and follow-up, reassessment, case conferencing, crisis intervention and case closure. Case management activities are diverse; in addition to assisting clients in accessing and maintaining specific services, they may also include negotiation and advocacy of services, provider consultation, service system navigation, psychosocial support, supportive counseling, and general client education.

Several potential risk factors for failure to link to care have been identified, including African-American race, residence in a high-poverty area, lack of insurance or public insurance (vs. private insurance), lack of primary care prior to HIV diagnosis, substance use, History of injection drug use and longer waiting time for the first appointment [18-22]. Case management can overcome such barriers by trying to connect clients to relevant services, assessing clients for potential risk factors,

referring them to care providers, eliminating financial barriers, and reducing delays by simplifying appointments.

We used the Newcastle Ottawa Scale (NOS) to assess the quality of non-randomized studies in meta-analyses [23]. None of the studies provided the registration number of the clinical trial. We searched the Clinical Trial Registry and found no registration. In such research, the blinding of participants and researchers is impossible. All studies reported randomization process in their research.

In this systematic review, we were unable to perform a meta-analysis because the included studies examined a wide range of outcome measures and exhibited significant heterogeneity. However, detailed information on the methods and results of the included studies will allow us to use the results of this systematic review when considering case management as a potential service to PLHA. Based on the results of this systematic review, the Case Management PLHA offers some advantages. The extent of these benefits is not fully understood due to the heterogeneity and conflicting results of existing studies. Additional research is needed to clarify the benefits of case management for PLHA. Future research should be conducted using a clearer case management definition. A universal case management program would be ideal to enable better comparisons between studies.

Additional Materials

The following additional materials are uploaded at the web version of this paper.

Appendix S1: Consort 2010 checklist of information to include when reporting a randomised trial.

Author Contributions

Siavash Jafari: generated to original question and the idea of conducting a systematic review. He reviewed individual articles to decide on inclusion and exclusion. Also, he prepared the manuscript and all required editing. Mariko Vaughan, Souzan Baharlou, Pooria Ghadiri, Nazila Hassanabadi, and Ashkan Nasr performed articles search. They prepared the excel spread sheet and worked on data extraction. They are involved with deciding on inclusion and exclusion of articles. Mariko Vaughan and Pooria Ghadiri prepared the final graphs and table. Souzan Baharlou, Nazila Hassanabadi, and Ashkan Nasr assessed the quality of the studies.

Competing Interests

The authors have declared that no competing interests exist

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