**Outcomes of PLHIV following hospital discharge: a systematic review**

**Contents**

1. **Protocol**
2. **Search strategies**
3. **Intervention Characteristics**
4. **Risk of Bias**
5. **GRADE Tables**
6. **References**
7. **Protocol**

**1. Background**

The identification and management of people with advanced HIV disease is a key component in the HIV response. Hospitalizations from complications relating to HIV infection, including co-infections associated with advanced HIV, remain substantial. A recent review found that AIDS-related infections and bacterial infections are leading causes of hospital admission. Low CD4 cell count and low antiretroviral coverage at admission are major contributors to this disease profile and associated mortality.1,2 People who are hospitalized are at a heightened risk of adverse outcomes, including readmission within 30 days and death.3 This heightened risk of mortality that may persist after hospital discharge,4 and people living with HIV who survive to hospital discharge have been described as a population with high mortality.5

We did this systematic review and meta-analysis to assess interventions to improve post-discharge outcomes of people living with HIV.

**2. Methods**

**2.1 Types of studies**

* Randomized and quasi-randomized controlled trials
* Comparative and non-comparative observational studies
* Other studies designs can be included if they contain relevant quantitative data

**2.2. Types of participants**

***Inclusions***

* HIV positive adults and children discharged from hospital

***Exclusions***

* Studies conducted before 1998
* Studies in which <20 patients were included
* Studies where outcomes could not be disaggregated according to HIV status

**2.3. Types of outcomes**

Primary outcomes post discharge:

* Number readmitted
* Number died
* Number successfully linked to care

**2.4. Databases**

The following databases will be searched from inception to 10 August 2024.

* Embase
* Medline via Pubmed
* Cochrane Database of Systematic Reviews

**2.5. Restrictions**

No date, language, or geographical exclusions will be applied.

**3.0. Risk of bias and evidence certainty**

Risk of bias will be assessed using the Cochrane risk of bias tool for randomized trials and an adapted Newcastle Ottawa score for observational studies. The certainty of the evidence will be assessed using the GRADE framework

**4.0. Quantitative synthesis**

If appropriate, outcome data will be pooled using the DerSimonian-Laird random-effects method following appropriate transformation of the raw proportions.6 Heterogeneity will be assessed through visual inspection of forest plots.

**Contact**

Nathan Ford, WHO, Geneva

Email: fordn@who.int

**References**

1. Ford N, Shubber Z, Meintjes G, et al. Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis. *Lancet HIV* 2015; **2**(10): e438-44.

2. Wajanga BM, Webster LE, Peck RN, et al. Inpatient mortality of HIV-infected adults in sub-Saharan Africa and possible interventions: a mixed methods review. *BMC health services research* 2014; **14**: 627.

3. Akinkuotu A, Roemer E, Richardson A, et al. In-hospital mortality rates and HIV: A medical ward review, Lilongwe, Malawi. *International Journal of STD and AIDS* 2011; **22**(8): 465-70.

4. Myer L, Smith E, Mayosi BM. Medical inpatient mortality at Groote Schuur Hospital, Cape Town, South Africa, 2002-2009. *S Afr Med J* 2012; **103**(1): 28-31.

5. Hoffmann CJ, Milovanovic M, Cichowitz C, Kinghorn A, Martinson NA, Variava E. Readmission and death following hospitalization among people with HIV in South Africa. *PLoS ONE* 2019; **14**(7).

6. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**(3): 177-88.

1. **Search strategies**

PubMed

|  |  |  |
| --- | --- | --- |
| 1 | "Patient Discharge"1 OR post-hospitali\*[tiab] OR posthospital\*[tiab] OR "post discharge"[tiab:~5] OR "post discharged"[tiab:~5] OR postdischarg\*[tiab] OR after-discharge\*[tiab] OR "after hospitalization"[tiab:~2] OR following-discharg\*[tiab] OR following-hospitali\*[tiab] OR "discharged hospitalization"[tiab:~5] OR "patient discharge"[tiab:~3] OR "patients discharge"[tiab:~3] OR "discharged patient"[tiab:~3] OR "discharged patients"[tiab:~3] OR "discharged home"[tiab:~3] OR discharge-plan\*[tiab] OR recent-dischar\*[tiab] OR recent-hospital\*[tiab] OR discharge-follow-up\*[tiab] OR "hospital discharge"[tiab:~3] | 177,804  |
| 2 | ("HIV Infections"1 OR PLHIV[tiab] OR PWH[tiab] OR "HIV"1 OR "HIV Long-Term Survivors"1 OR hiv2 OR hiv12 OR hiv22 OR "human immunodeficiency virus"2 OR "human immunedeficiency virus"2 OR "human immuno-deficiency virus"2 OR "human immune-deficiency virus"2 OR ((human-immun\*) AND ("deficiency virus"2)) OR "acquired immunodeficiency syndrome"2 OR "acquired immunedeficiency syndrome"2 OR "acquired immuno-deficiency syndrome"2 OR "acquired immune-deficiency syndrome"2 OR ((acquired immun\*) AND ("deficiency syndrome"2)) OR AIDS-virus\*2) | 472,717  |
| 3 | ("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "randomised"[tiab] OR "randomized"[tiab] OR "placebo"[tiab] OR "drug therapy"[sh] OR "randomly"[tiab] OR "trial"[tiab] OR "groups"[tiab])  | 6,139,558 |
| 4 | “Epidemiologic Studies”1 OR “cohort study”[TIAB] OR “cohort analysis”[TIAB] OR “follow up study”[TIAB] OR “follow-up study”[TIAB] OR “observational study”[TIAB] OR longitudinal[TIAB] OR retrospective[TIAB]  | 3,826,293 |
| 5 | #3 OR #4  | 8,738,705 |
| 6 | #1 AND #2 AND #6  | 943 |

EMBASE

|  |  |  |
| --- | --- | --- |
| 1 | (post-hospitali\* OR posthospital\* OR postdischarg\* OR after-discharge\* OR following-discharg\* OR following-hospitali\* OR discharge-plan\* OR recent-dischar\* OR recent-hospital\* OR discharge-follow-up\* OR ((patient\* OR hospital\* OR home) NEAR/3 (discharge\*)) OR ((post) NEAR/5 (discharge\*)) OR (after NEAR/2 hospital\*)):ti,ab | 322.862 |
| 2 |  |  |
| 3 | ('Human immunodeficiency virus infection'/de OR 'Human immunodeficiency virus'/de OR (PWH OR PLHIV OR hiv OR hiv1 OR hiv2 OR human-immunodeficiency-virus OR human-immunedeficiency-virus OR human-immuno-deficiency-virus OR human-immune-deficiency-virus OR acquired-immunodeficiency-syndrome OR acquired-immunedeficiency-syndrome OR acquired-immuno-deficiency-syndrome OR acquired-immune-deficiency-syndrome OR (aids NEAR/3 virus\*) ):ti,ab) | 588.84 |
| 4 | ('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (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\*):de,ab,ti) | 6,139,558 |
| 5 | observational study'/exp OR 'cohort analysis'/exp OR (“cohort study” OR “cohort analysis” OR “follow up study” OR “follow-up study” OR “observational study” OR longitudinal OR retrospective ):ti,ab | 3,826,293 |
| 6 | #1 AND #2 AND #5 | 1,110 |

Cochrane Database of Systematic Reviews

|  |  |  |
| --- | --- | --- |
|  | MeSH descriptor: [Patient Discharge] explode all trees | 2718 |
|  | (post-hospitali\* OR posthospital\* OR postdischarg\* OR after-discharge\* OR following-discharg\* OR following-hospitali\* OR discharge-plan\* OR recent-dischar\* OR recent-hospital\* OR discharge-follow-up\* OR ((patient\* OR hospital\* OR home) NEAR/3 (discharge\*)) OR ((post) NEAR/5 (discharge\*)) OR (after NEAR/2 hospital\*)):ti,ab | 33977 |
|  | #1 OR #2 | 34,504 |
|  | MeSH descriptor: [HIV] explode all trees | 4,250 |
|  | MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees | 2,490 |
|  | PWH OR PLHIV OR hiv OR hiv1 OR hiv2 OR human-immunodeficiency-virus OR human-immunedeficiency-virus OR human-immuno-deficiency-virus OR human-immune-deficiency-virus OR acquired-immunodeficiency-syndrome OR acquired-immunedeficiency-syndrome OR acquired-immuno-deficiency-syndrome OR acquired-immune-deficiency-syndrome OR (aids NEAR/3 virus\*):ti,ab | 35,152 |
|  | #4 OR #5 OR #6 | 35152 |
|  | #3 AND #6 | 249 |

1. **Intervention Characteristics**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Country** | **Intervention** | **Cadre providing support post discharge** | **Written materials** | **Telephone follow up** | **Home visit** |
| **Pre discharge** | **Post discharge** |
| Giordano3  | USA | Peer support: 2 in person sessionsDischarge goalsBrochures  | Peer support: 5 post discharge telephone calls | Peer-provided  | Yes | Yes | No |
| Guzman Ramos4 | Spain | Risk stratification for readmission | 2 pharmacotherapeutic follow up visits, motivational interviewing, information leaflets on adherence, and SMS | Pharmaceutical follow up | Yes | Yes | No |
| Hoffmann5 | South Africa | Care referrals | home visit package with up to 6 home visits. Food for participants with food insecurity | Nurse clinician and counsellor | No | Yes | Yes |
| Peck6 | Tanzania | Intervention: first counselling session | Intervention: up to 5 sessions conducted by a social worker at hospital, home, and HIV clinic over a 3-month period.  | Social worker, nurse | Yes | Yes | Yes |
| Brizzi7 | USA | Review of medications | Pharmacist-driven ART stewardship; transitions of care (TOC) service; telephone follow up within 7 days for high-risk patients | Pharmacist; outreach worker | No | Yes | No |
| Claasen8 | Zambia | Discharge card: diagnoses, labs, medications, follow-up instructions | Community health worker visit within 7 days of discharge to check: vital signs, adherence, counselling, and referral as needed. Additional visits up to 3 months | Community health worker | No | No | Yes |
| Eaton9 | Canada | Goal setting with nurse; tailored meeting with a peer volunteer | 9 phone calls with peer volunteer over 7 weeks | Nurse, peer volunteer | Yes | Yes | No |
| Hill10 | USA | Medication counselling | Patient care navigators provide appointment reminders and assist with transport to discharge clinic; doctor, social workers counsellors address psychosocial needs. Pharmacists assist with medication reconciliation | Patient navigator | No | No | Yes |
| Khawcharoenporn\*11 | Thailand | Instructions about how to make a follow up appointment | Enhanced inpatient rounds, appointment reminders, and patient education, and telephone calls | Not stated | Yes | Yes | No |
| Nijhawan12  | USA | Review barriers to care, complete patient education and develop an individualized transitional care plan Multidisciplinary transitions team | Medical HIV consultation +/- transitional care nurse intervention | Multidisciplinary transition team & transitional care nurse | Yes | Yes | No |

\* intervention participants (where disaggregated)

**4. Risk of Bias**

**1. Randomized trials**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **D1** | **D2** | **D3** | **D4** | **D5** | **Overall** |
| Ramos | Some concerns | Some concerns | Low | Some concerns | Low | Some concerns |
| Hoffman | Some concerns | Low | Low | Some concerns | Low | Some concerns |
| Giordano | Low | Low | Low | Low | Low | Low |
| Peck | Low | Low | Low | Low | Low | Low |

D1: Bias arising from the randomization process. D2: Bias due to deviations from intended intervention. D3: Bias due to missing outcome data. D4: Bias in measurement of the outcome. D5: Bias in selection of the reported

**2. Observational studies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **D1** | **D2** | **D3** | **D4** | **D5** | **D6** | **D7** | **Overall** |
| Brizzi  | Moderate | Serious | Low | Low | Low | Low | Low | Moderate |
| Eaton | Moderate | Serious | Low | Low | Serious | Low | Moderate | Serious |
| Hill | Low | Moderate | Low | Low | Low | Low | Low | Moderate |
| Khawcharoenporn | Moderate | Moderate | Low | Low | Low | Moderate | Low | Moderate |
| Nijhawan | Moderate | Serious | Low | Low | Moderate | Low | Low | Serious |
| Claasens | Low | Moderate | Low | Low | Moderate | Low | Low | Moderate |

D1: Bias due to confounding. D2: Bias due to selection of participants. D3: Bias in classification of interventions. D4: Bias due to deviations from intended interventions. D5: Bias due to missing data. D6: Bias in measurement of outcomes. D7: Bias in selection of the reported

**5. GRADE Tables**

**1. Randomized controlled trials**

|  |  |  |
| --- | --- | --- |
| **Certainty assessment** | **Effect** | **Certainty** |
| **Outcome**  | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Relative risk** | **Risk difference (per 100)** |
| **Death** |
| 3 RCTs | Serious1 | Serious3 | Not serious | Serious6 | RR 0.98 (0.59-1.63) | 0(7 fewer to 6 more) | **LOW** |
| **Readmission** |
| 3 RCTs | Serious2 | Serious3 | Not serious | Serious6 | RR 0.82 (0.52-1.30) | 11 fewer33 fewer to 11 more | **LOW** |
| **Retention/linkage to care** |
| 2 RCTs | Not serious | Serious3,4 | Serious5 | Serious6 | RR 1.10 (0.95-1.27) | 66 fewer to 17 more | **LOW** |

1 Some concerns regarding randomization process and outcome measures

2 Some concerns regarding randomization process, deviation from intended intervention, and outcome measures.

3 Significant statistical heterogeneity (*I2*>40%)

4 Inconsistency in the outcomes measure

5 Linkage to care and retention in care combined; reported at different time points in the studies

6 Wide confidence intervals crossing the null including clinically relevant thresholds

**2. Observational studies**

|  |  |  |
| --- | --- | --- |
| **Certainty assessment** | **Effect** | **Certainty** |
| **Outcome** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Relative risk** | **Risk difference (per 100)** |
| **Death** |
| 2 studies | Serious1 | Not serious | Not serious | Serious4 | RR 1.00 (0.63-1.59) | 0(5 fewer to 6 more) | **LOW** |
| **Readmission** |
| 4 studies | Serious1 | Serious2 | Not serious | Serious4 | RR 0.77 (0.48-1.25) | 1 fewer(6 fewer to 3 more) | **LOW** |
| **Retention/linkage to care** |
| 3 studies | Moderate1 | Serious2,3 | Not serious | Serious5 | RR 1.42 (1.11-1.81) | 27 more (13 more to 41 more) | **LOW** |

1 Bias due to confounding and participant selection

2 Significant statistical heterogeneity (*I2*>40%)

3 Linkage to care and retention in care combined; reported at different time points in the studies

4 Wide confidence intervals crossing the null including clinically relevant thresholds

5 Wide confidence intervals including clinically relevant thresholds

**3. Combined studies**

|  |  |  |
| --- | --- | --- |
| **Certainty assessment** | **Effect** | **Certainty** |
| **Outcome** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Relative risk** | **Risk difference** **(per 100)** |
| **Death** |
| 3 RCTs and 2 observational studies | Serious | Serious | Not serious | Serious | RR 1.02 (0.79-1.32) | 0(3 fewer to 4 more) | **LOW** |
| **Readmission** |
| 3 RCTs and 3 observational studies | Serious | Serious | Not serious | Serious | RR 0.87 (0.69-1.09) | 2 fewer(7 fewer to 2 more) | **LOW** |
| **Retention/linkage to care** |
| 2 RCTs and 3 observational studies | Serious | Serious | Not serious | Serious | RR 1.24 (1.07-1.44) | 18 more(6 more to 30 more) | **LOW** |

**6. References**

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4. Guzman Ramos MI, Manzano Garcia M, Robustillo-Cortes MA, Gutierrez Pizarraya A, Morillo-Verdugo R. Influence of CMO pharmaceutical care model-based intervention on readmission rate in high risk HIV patients: the INFARDAR study. *Rev Esp Quimioter* 2021; **34**(5): 459-67.

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12. Nijhawan AE, Zhang S, Chansard M, Gao A, Jain MK, Halm EA. A Multicomponent Intervention to Reduce Readmissions Among People With HIV. *J Acquir Immune Defic Syndr* 2022; **90**(2): 161-9.