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# A Systematic Review of Interventions by Healthcare Professionals to Improve Management of Physical Long-Term Conditions in Adults who are Homeless

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## Abstract

**Objective:** To identify, describe and appraise trials of interventions to manage physical long-term conditions (LTCs) in homeless adults delivered by healthcare professionals.

**Design:** Systematic review of Randomised Controlled Trials (RCTs), Non-randomised Controlled Trials and Controlled Before-After (CBA) studies. Interventions characterised using Effective Practice and Organisation of Care (EPOC) taxonomy. Quality assessed using EPOC Risk of Bias (ROB) criteria.

**Data sources:** Database searches (Medline, Embase, PsycINFO, Scopus, CINAHL, Assia, CENTRAL), hand searching reference lists, citation searches, Grey literature, and contact with study authors.

**Setting:** Community.

**Participants:** Adults (≥ 18 years) fulfilling European Typology of Homelessness (ETHOS) criteria.

**Intervention:** Delivered by healthcare professionals managing physical LTCs.

**Outcomes:** Unscheduled healthcare utilisation, mortality, biological markers of disease control, adherence to treatment and engagement in care, patient satisfaction, knowledge, self-efficacy, quality of life and cost-effectiveness.

**Results:** 11 studies were included (8 RCTs, 2 quasi-experimental, 1 feasibility) involving 9-520 participants (71-94% male, median age 37-48). Ten from USA, one from UK. Studies included various LTCs (n=3); or focused on one LTC: latent tuberculosis (n=4); HIV (n=2); Hepatitis C (n=1); or Type 2 Diabetes Mellitus (n=1). All interventions were complex with multiple components. Four described theories underpinning their intervention. Three assessed unscheduled healthcare utilization with none showing consistent evidence of reduction in hospitalization or emergency department attendance. Six assessed adherence to specific treatments, of which four showed improved adherence to latent TB therapy. Three concerned education case-management, all of which improved disease specific knowledge. No improvements were seen in biological markers of disease (two studies) and none assessed mortality.

**Conclusions:** Evidence for management of physical LTCs in homeless adults is sparse. Educational case-management interventions may improve knowledge and medication adherence. Large trials of theory-based, interventions, assessing health care utilization and outcomes as well as assessment of biological outcomes and cost-effectiveness, are needed.

**Abstract word count: 295**

**Strengths and Limitations of the Study**

- This is the first systematic review to focus on effects of physical long-term condition management interventions for adults who are homeless.
- A comprehensive search strategy was supplemented with hand searching, Grey literature searches and contact with study authors.
- Interventions are described using the Effective Practice and Organisation of Care (EPOC) Taxonomy
- Significant heterogeneity precluded meta-analysis, so a narrative synthesis is presented along with a Harvest Plot summarising study findings.
- Evidence available for high income countries only.

## INTRODUCTION

The prevalence of homelessness is increasing across high income countries.[1] The experience of homelessness is associated with increased morbidity and mortality.[2-4] Social exclusion and socio-economic deprivation,[5, 6] adversity over the life course,[7] as well as environmental and behavioral risk factors[8] typical of homelessness, contribute to an increased prevalence of a range of physical long-term conditions (LTCs) compared to the rest of the population.[1] Outcomes of physical LTCs are poorer among people who are homeless.[9, 10] Engagement with scheduled appointments, preventative health services and adherence to treatment are typically lower.[11-14] Barriers to access, conflicting priorities, physical and mental multimorbidity are thought to contribute to poorly coordinated use of healthcare services. [14] Consequently, there is a need for tailored services.[14-16] Healthcare delivery models for people experiencing homelessness include specialised or generalist primary care services ;[17] and integrated housing and health interventions. There is insufficient evidence of reach and effectiveness to favour one model over another.[18]The expanding role of non-medical healthcare professionals e.g. nurse and pharmacist prescribers, targeting physical LTCs,[19] offers a complementary model of healthcare for people who are homeless. Sharing clinical roles may be welcome given the increasing evidence of multimorbidity and polypharmacy.[20]

Controlled evaluations of models of healthcare for people who are homeless are relatively few and optimal delivery varies between different health and social care systems.[16] There have been calls to evaluate more interventions to improve the

health of people who are homeless,[21] including long-term prospective studies with economic analyses. [14]

Previous systematic reviews have identified the potential benefit of tailored interventions and strategies for addressing mental health and substance misuse.[22, 23] These have shown potential for monetary incentives to improve adherence for people who are homeless with latent tuberculosis,[22] and that provision of housing improved health outcomes in HIV.[23]However, to the authors' knowledge, no previous systematic reviews have focused specifically on the management of physical LTCs for people who are homeless.

**Aims**

This review aims to systematically identify, describe and appraise trials of interventions focusing on the management of physical LTCs, delivered by healthcare professionals for adults who are homeless. It addresses the following two research questions:

1. What are the key components of interventions aimed at optimising physical LTC management including theoretical underpinnings?
2. What outcome measures have been used in trials of interventions aimed at optimising physical LTC management and what effects, if any, have been reported?

This systematic review followed a pre-specified protocol [24](registered with PROSPERO, ID: CRD42016046183, available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046183) and is described according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[25]

**Eligibility Criteria**

Eligibility criteria and search process are described in detail in our published protocol paper,[24] and are outlined briefly below. Homelessness was defined according to the ETHOS criteria[26]. Eligible studies included adult participants who met the ETHOS defined homelessness criteria with one or more physical LTC or those concerning physical LTC management as part of a broader intervention (e.g. access to primary care). Delivery by a healthcare professional was required, either alone or as part of a wider team.

**Literature Search**

Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1966 (or inception) until October 2016. Our search strategy was “homelessness” AND “long-term condition or healthcare delivery terms” AND “trial or evaluation terms”. The full search terms for Medline are shown in Additional File 1 and were adapted for other databases. Database searches were supplemented by hand searching of reference lists of all eligible studies, hand

searching the Journal of the Poor and Underserved, and forward citation searches of included studies using Web of Science. A number of 'Grey Literature' sources were also searched, (Additional File 1). Grey literature and relevant conference abstracts were used to identify recently publishes studies.

Two reviewers (PH plus LY, RL or RE), using DistillerSR software, independently screened titles and abstracts of all records identified. Full texts of all potentially eligible studies were obtained and assessed independently by two reviewers (PH, LY or RE) against the eligibility criteria. At all levels disagreements were resolved by discussion, involving a third reviewer (RL or LY) when consensus could not be reached. Where studies included homeless participants but analysis of these participants was not presented separately, we contacted the study authors to request these data. Studies were excluded if these were not available. Using a standardised data extraction form, two reviewers (PH plus LY or LG) independently extracted data from each study eligible for inclusion. The components of each intervention were described according to the Cochrane Effective Practice and Organization of Care (EPOC) taxonomy.[27] Two reviewers independently assessed each study according to the criteria outlined in the Cochrane EPOC guidelines for assessing risk of bias (ROB) in RCTs, non-randomised controlled trials and CBA studies.[27] After grading each study a judgment of the overall risk of bias was made for each outcome, taking into account the relative importance of potential sources of bias to the outcome in question.

**Synthesis**

We assessed the clinical and methodological heterogeneity of the eligible studies. Few studies considered similar outcomes, and those that did had either different comparator groups,[28, 29] differing methods of assessing similar outcomes (e.g. survey vs. routine data for emergency department (ED) attendance)[30, 31] or concerned complex interventions, the diversity of which would limit the utility of a pooled analysis.[30, 32] Consequently, a meta-analysis was deemed inappropriate and we performed a narrative synthesis of the study findings. Studies were grouped by outcome and the strength of the body of evidence for each outcome was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.[33]

We constructed a Harvest Plot *post hoc* to display the results. Harvest plots use bars representing individual studies placed on a plot matrix to indicate whether the review intervention showed an overall positive, negative, or no consistent effect for the outcome in question. They enable data to be summarised when study designs and outcomes are diverse and heterogeneous.[34, 35] We used the following criteria to decide how each study should be displayed:

- Height of the bar represented the number of participants in the study;
- RCTs were displayed in bold with other designs in grey;
- The risk of bias for the outcome of each study was indicated as low, moderate or high using a coloured dot above the bar;
- Statistically significant differences were displayed as a positive effect if they favoured the intervention; negative if they favoured the comparator and neutral if not statistically significant;
- Where some, but not all, findings in a group of outcomes showed a positive or negative effect, bars were hatched to indicate inconsistency.

## RESULTS

### Study Selection

The results of abstract and full-text screening are shown in the PRISMA diagram in Figure 1. A full list of studies excluded at full-text level, along with reasons for exclusion, is shown in Additional File 2.

**FIGURE 1 – PRISMA DIAGRAM**

### Description of Studies

Sixteen papers were eligible for inclusion which described eleven unique studies.[28-32, 36-46] Ten studies were from the USA [28, 29, 31, 32, 36-46] and one from UK.[30] Three studies included a range of LTCs;[30-32] four studies concerned latent tuberculosis;[28, 29, 36-40] one concerned Hepatitis C;[45] two studies concerned HIV;[42-44, 46] and one concerned Type 2 Diabetes Mellitus.[41] Eight were RCTs, two quasi-experimental and one was a pilot study.

### Study Populations

Details of the study populations are summarised in table 1. Sample sizes ranged from 9 to 520. Median age ranged from 37 to 49 years. In all of the studies the majority of participants were male (percentage male participants ranged from 67% to 94% in the intervention groups). Age and sex distributions were consistent with previous literature on homelessness.[1] Six studies, all from the USA reported details of ethnicity.[28, 29, 36, 40, 42, 45] African American participants were the most prevalent in five of these.

Only two studies included any detail of comorbidities.[30, 36] Details of attrition are shown in Additional File 4.

**Quality Assessment**

Results of the EPOC Risk of Bias assessment for each of the included studies is shown in table 2. None of the included studies scored low risk for each of the criteria. These were used to inform outcome-level risk of bias assessment. These are displayed, along with justification, in Additional File 4.

**Intervention Components and Theoretical Underpinnings**

Each of the studies described interventions that were complex and included multiple components. These included changes to how, and where, care was delivered, the personnel delivering care, how care delivery was coordinated, and the provision of financial support. The components of the EPOC taxonomy relating to each of the interventions are shown in table 3, along with a summary of the intervention and control interventions. Descriptions of the specific aspects of each intervention relating to the taxonomy are shown in Additional File 3.

Four of the eleven studies reported an explicit theoretical framework underpinning the intervention (table 3). These included the Comprehensive Health Seeking and Coping Paradigm underpinning two of the studies, and Self-Efficacy Theory and the Health Belief Model each underpinning one intervention.

**Table 1: Summary of study populations**

| Study | Design | Location | Number of Participants | Age, mean (SD) | Sex (%) | Ethnicity (%) | Long-term Condition | Homelessness definition |
|---|---|---|---|---|---|---|---|---|
| Pilote 1996[40] | RCT | USA | 244<br><br>I[1]: 83<br>I[2]: 82<br>C: 79 | I[1]: median 40<br>I[2]: median 39<br>C: median 40 | I[1]: M (71%)<br>I[2]: M (67%)<br>C: M (66%) | African American (I[1]: 48%, I[2]: 57%, C: 54%)<br>White (I[1]: 33%, I[2]: 27%, C: 27%)<br>Hispanic (I[1]: 16%, I[2]: 11%, C: 13%) | Latent TB | Homeless: not further defined |
| Tulsky 2000[29] | RCT | USA | 118<br><br>I[1]: 43<br>I[2]: 37<br>C: 38 | Median 37 | M (89%) | African American (52%)<br>White (21%)<br>Hispanic (27%) | Latent TB | Homeless or marginally housed |
| Tulsky 2004[28] | RCT | USA | 141<br><br>I: 72<br>C: 69 | Median 41 (range 21-79) | M (85%) | African American (47%)<br>White (32%)<br>Other (20%) | Latent TB | Homeless or marginally housed |
| Samet 2005[46] | RCT | USA | 151 (34 homeless)<br><br>I: 19<br>C: 15 | Median 44 (range 26-60) | M (82%) | N.S. | HIV with alcohol problems | Homeless: not further defined |
| Ciaranello 2006[31] | Quasi-experi-mental | USA | 6 transitional housing facilities<br><br>I:219 sampled<br>C: 50 sampled | I: 41.6 (9.6)<br>C: 41.3 (10.4) | I: M (81%)<br>C: M (44%) | N.S. | Various | "Formerly homeless" residents of transitional housing |
| Nyamathi 2006[36] Nyamathi 2007[37] Schumann 2007[38] Nyamathi 2008[39] | RCT | USA | 520<br><br>I: 279<br>C: 241 | 41.5 (8.5) | M (79.6%) | African American (81%)<br>White (7.3%)<br>Hispanic (9.4%)<br>Other (2.3%) | Latent TB | Sleeping in homeless shelters |
| Tsai | RCT | USA | 137 | I: Median 44 | I: M (91%) | I: Caucasian (48%) | HIV with comorbid | "homeless or marginally |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2013[42]<br>Tsai 2013[43]<br>Grelotti 2016[44] | | | I: 66<br>C: 71 | (IQR: 37-53)<br>C: Median 42 (IQR: 37-79) | C: M (89%) | C: Caucasian (51%) | depression | housed" |
| Savage 2014[41] | Random-ised pilot/ feasibility | USA | 9<br><br>I: 6<br>C: 3 | N.S. | N.S. | N.S. | Type 2 diabetes | Living without shelter or adequate accommodation |
| Tyler 2014[45] | Random-ised quasi-experi-mental | USA | 107 (hepatitis C positive subset)<br><br>I: 46<br>C: 61 | Males: 44 (7.1)<br><br>Females: 45.3 (8.9) | M (79%) | African American (63%)<br>White (17%)<br>Latino (18%) | Hepatitis C | Homeless: not further specified |
| O'Toole 2015[32] | RCT | USA | 185<br><br>$I^1$: 39<br>$I^2$: 40<br>$I^{1+2}$: 44<br>C: 62 | 48.6 (10.8) | M (94%) | "Minority population" (43%) | Various | "lacking fixed, regular and adequate night-time residence." |
| Hewett 2016[30] | RCT | UK | 410 | I: 41.6 (12.1)<br>C: 42.5 (11.3) | I: M (81.6%)<br>C: M (81.4%) | N.S.<br>Nationality:<br>UK: I (69.4%), C (72.5%)<br>European union: I (22.3%), C (17.6%)<br>Other: I (8.3%) C (9.8%) | Various | No fixed residence on hospital discharge |

Table 2: Risk of bias within individual studies

| Criteria | Study | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ciaranello 2014 | Hewett 2016 | Nyamathi 2006, 2007, 2008 and Schumann 2007 | O'Toole 2015 | Pilote 1996 | Samet 2005 | Savage 2014 | Tsai 2013, 2013 and Grelotti 2016 | Tulsky 2000 | Tulsky 2004 | Tyler 2014 |
| Random sequence generation | High | Low | Unclear | Low | Unclear | Unclear | High | Low | Low | Low | High |
| Allocation concealment | High | Low | Low | Unclear | Unclear | Unclear | High | Low | Low | Low | Unclear |
| Blinding of participants/ personnel | High | High | High | High | High | High | High | High | High | Unclear | High |
| Similar baseline outcome measures | High | Low | Low | Low | Unclear | Low | Unclear | Low | Unclear | Unclear | Low |
| Similar baseline characteristics | High | Low | Low | Low | Low | Low | Unclear | Low | Low | Low | Low |
| Blinding of outcome assessment | High | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | High |
| Incomplete outcome data | High | High | Low | Low | Low | Low | High | Low | Low | Low | Low |
| Protection from contamination | High | Unclear | Low | Unclear | Low | Low | Unclear | Low | Low | Low | Low |
| Selective Outcome Reporting | Low | Low | Low | Low | Low | Low | High | Low | Low | Low | Low |
| Other bias | High | Low | Low | Low | Low | Low | High | Low | High | High | Low |

**Table 3: Intervention Components, Theoretical Underpinning, and Outcomes**

| Study | Components | Theory | Intervention | Comparator | Outcomes |
|---|---|---|---|---|---|
| Pilote 1996[40] | **How care is delivered:** Individual delivery<br>**Where care is delivered:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | None specified | Monetary incentive for TB clinic attendance (group 1). Peer health advisor assisting with clinic attendance (group 2). | Usual care (clinic appointment and tokens for travel expenses). | Attendance at initial TB clinic appointment. |
| Tulsky 2000[29] | **How care is delivered:** Individual delivery<br>**Where care is delivered:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | None specified | Monetary incentive for uptake of directly observed therapy (group 1). Peer-health advisor supporting directly observed therapy (group 2). | Usual care | Completion of 6 months isoniazid therapy |
| Tulsky 2004[28] | **How care is delivered:** Individual delivery<br>**Where care is delivered:** Transportation services<br>**Finance**: Incentives | None specified | Monetary incentive for uptake of directly observed therapy | Non-cash incentive of equal value (vouchers) | Completion of 6 months isoniazid therapy<br>Cost effectiveness |
| Samet 2005[46] | **How care is delivered:** Individual delivery.<br>**Where care is delivered:** Outreach services.<br>**Who delivers care:** Self-management.<br>**Coordination of care:** Disease management. | Health belief model and motivational interviewing. | Adherence support for antiretroviral treatment | Usual care (written instructions/advice regarding treatment adherence) | Adherence to antiretroviral treatment<br>CD4+ count<br>HIV viral load |
| Ciaranello 2006[31] | **How care is delivered:** Individual delivery.<br>**Where care is delivered:** Outreach services; changing site of service delivery.<br>**Who delivers care:** Self-management.<br>**Coordination of care:** Communication between providers; disease management; multidisciplinary teams. | None specified | Weekly visits including health assessment, education, referral and social support. | Transitional houses in a different area not receiving the intervention. | ED attendance<br>Hospital admission<br>Blood pressure<br>Satisfaction with care |
| Nyamathi 2006[36]<br>Nyamathi 2007[37]<br>Schumann 2007[38]<br>Nyamathi 2008[39] | **How care is delivered:** Group delivery.<br>**Where care is delivered:** Outreach services; transportation services.<br>**Who delivers care:** Self-management.<br>**Coordination of care:** Case management; disease management.<br>**Finance**: Incentives. | Comprehensive Health Seeking and Coping Paradigm. | Directly observed therapy plus 8 education sessions. Information provided on community resources and participants escorted to appointments. | Directly observed therapy plus 20 minute educational lecture | Completion of directly observed TB therapy<br>TB knowledge<br>HIV knowledge<br>Self-efficacy |
| Tsai 2013[42] | **How care is delivered:** Individual delivery | None specified | Directly observed fluoxetine and | Advice on sources of | Adherence to |

| | | | | | |
|---|---|---|---|---|---|
| Tsai 2013[43]<br>Grelotti 2016[44] | **Coordination of care:** Case management; disease management.<br>**Finance**: Incentives | | weekly psychiatric interview | mental health support | antiretroviral therapy<br>HIV viral load<br>Depression |
| Savage 2014[41] | **How care is delivered:** Individual delivery<br>**Who delivers care:** Self-management | Self-efficacy theory | Nurse led case-management and diabetes education | No intervention (usual care) | Self-efficacy |
| Tyler 2014[45] | **How care is delivered:** Group delivery<br>**Who delivers care:** Self-management<br>**Coordination of care:** Case management; communication between providers | Comprehensive Health Seeking and Coping Paradigm. | Case management with group sessions, self-management training and education. | Single, brief educational intervention | Hepatitis C knowledge |
| O'Toole 2015[32] | **How care is delivered:** Individual delivery.<br>**Where care is delivered:** Orientation to environment/facilities; outreach services; transportation services.<br>**Who delivers care:** Self-management.<br>**Coordination of care:** Case management; disease management. | None specified | Nurse-led brief health assessment with motivational interviewing (group 1). Guided orientation to primary care clinic facilities (group 2). Both interventions together (group 3). | Usual care (social work assessment and description of available services) | ED attendance<br>Hospital admission<br>Access to primary care |
| Hewett 2016[30] | **How care is delivered:** Individual delivery; Coordination of care providers.<br>**Who delivers care:** Role expansion; recruitment of specific professionals.<br>**Coordination of care:** Care pathways; communication between professionals; discharge planning; integration of services; shared care; multidisciplinary teams. | None specified | Nurse and GP led inpatient intervention. Goal setting. Discharge planning. Liaison and multiagency meetings | Initial meeting with nurse and signposting of services | ED attendance<br>Hospital readmission<br>Quality of Life |

### The Impact of Interventions on Healthcare Outcomes

The overall findings of the included studies for impact on unscheduled healthcare utilization, adherence or access to care, and knowledge of self-efficacy, are illustrated in the harvest plot shown in Figure 2. The text that follows synthesized these findings under each outcome.

**FIGURE 2 – HARVEST PLOT**

### Primary Review Outcomes

### Unscheduled Healthcare Utilisation

Three studies assessed the impact of interventions on hospital admissions and emergency department (ED) attendance.[30-32] None focused on a specific LTC, however participants reported a range of LTCs and each intervention included identification and engagement with medical, as well as wider needs. The highest quality evidence was from two RCTs, neither of which showed any significant reduction in unscheduled healthcare utilisation.[30, 32] One RCT evaluated a multidisciplinary, multicomponent intervention targeting patients in two inner-city hospitals involving goal setting, discharge planning, and liaising with community services.[30] Neither hospital admissions, nor ED attendance after one year, were significantly different compared with usual care. The other RCT was a four-arm trial comparing usual care; a brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health

assessment.[32]Hospital admissions and ED attendance were assessed at 6 months post intervention in a post-hoc analysis and showed no significant difference to usual care. A third study, with a quasi-experimental design and high risk of bias, concerned a 'comprehensive health assessment' delivered to residents at transitional housing facilities. ED attendances were reportedly lower at 18 month follow-up, but not at 6 months. There was no difference in hospitalization at either follow-up point.

Taken together the available evidence does not suggest that the multidisciplinary, multifaceted interventions described reduced rates of unscheduled healthcare utilisation. The overall confidence in the estimate of effect is low.

**Secondary Review Outcomes**

**Access to primary healthcare**

One RCT concerned access to primary healthcare.[32] A brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health assessment were compared to usual care. All three intervention groups showed higher uptake of primary healthcare services after 6 months with clinic orientation alone and in combination with a physical health assessment significantly improving primary care access in adjusted analyses.

**Adherence to specific treatment**

Six studies (7 papers) assessed adherence to treatment or attendance at appointments.[28, 29, 36, 40, 42, 43, 46] Four recruited patients with latent tuberculosis undergoing directly observed therapy (DOT)[28, 29, 36, 40], one included participants with HIV and alcohol problems,[46] and one (2 papers) concerned participants with HIV and co-morbid depression.[42, 43] Of the TB studies, three were conducted by the same research group and assessed the impact of monetary incentives (cash and/or voucher) on attendance at initial TB clinic follow up [40] or on completion of DOT with isoniazid.[28, 29] Clinic attendance and DOT completion rates were significantly higher with cash incentives compared with usual care or peer-health advisors.[29] There was no statistically significant difference in DOT completion between cash and voucher incentives.[28] Details of the availability to the participants of social security or other sources of financial support are not described in either study. Although the cash incentive and delivery of the intervention were similar in both studies assessing DOT completion, the completion rate in the intervention group differed widely between the two studies (44% and 89%, respectively).[28, 29] The authors speculate that the location of the clinic (the higher completion rate being in an area more accessible and frequented by people who are homeless) or alterations in the follow-up protocol for non-attendees may explain the differences.

The final study concerning TB evaluated the impact of a nurse-led case management intervention on completion of latent tuberculosis treatment and tuberculosis knowledge (described below under knowledge and self-efficacy).

They found odds of DOT completion were three times greater with the intervention compared with usual care.[36]

An RCT concerning people with HIV and comorbid depression compared fluoxetine prescription and weekly psychiatric evaluation with signposting to local psychology services without the prescription of fluoxetine. Both arms were given a weekly cash incentive for attending. Outcomes included rate of uptake of anti-retroviral treatment (ART), and adherence to ART (assessed by unannounced pill counts) for those receiving treatment. Neither outcome was significantly different between the groups despite an improvement in depression severity and remission in the fluoxetine group.[42, 43]

Finally an RCT aimed at supporting antiretroviral medication adherence among HIV positive participants with a history of alcohol dependence or harmful drinking showed no change in antiretroviral adherence.[46] Findings were similar to a secondary analysis of participants who described themselves as homeless (unpublished results).

Overall, there is a moderate level of evidence for interventions improving adherence to treatment for latent TB, including a case-management educational approach and provision of monetary incentives (cash or non-cash). However, the efficacy of such interventions may be dependent on the social and cultural context in which it is delivered (highlighted by variation in completion rates between evaluations of similar interventions), of which there is limited description in the available studies.

**Knowledge and Self-efficacy**

Three studies (5 papers) assessed the impact of interventions on TB, HIV, hepatitis and diabetes disease knowledge and self-efficacy.[36-38, 41, 45] Two were trials incorporating nurse-led case management (for patients with latent TB or hepatitis C, respectively) combined with a regular educational intervention focusing on self-management, self-esteem, communication skills and social support. One was an RCT focusing on DOT for latent TB and assessed the impact on TB knowledge in all participants.[36] The intervention also involved HIV education and the impact of this was evaluated in a subset judged to be 'at risk' of HIV (i.e. sexually active or known to be intravenous drug users). Two analyses using structural equation modeling showed that the nurse-led case management intervention was associated with greater improvement in TB knowledge [37] and in HIV knowledge in the 'at risk' subset.[38] The latter also showed improved self-efficacy for condom use.[38] The other evaluated a similar approach concerning Hepatitis education for participants enrolled in a Hepatitis A/B vaccination programme (only the Hepatitis C positive subset was included in this review).[45] The case-management group showed a greater improvement in Hepatitis C knowledge than the control group. However, the randomisation procedure was designed for the vaccine trial, not for the evaluation of the case-management intervention, and the statistical analysis was not designed to compare the intervention with control in the Hepatitis C subset alone.[45]

The third study reported improved knowledge in a small (n=9) pilot study using a self-efficacy based approach for Type 2 Diabetes Mellitus. However, the small

sample size meant there was insufficient power to detect any difference between groups and there was incomplete reporting of outcomes and no clear comparison is made between the intervention and comparator.[41]

Taken together, there is a moderate quality of evidence showing that an educational case-management approach can improve disease specific knowledge when delivered alongside wider interventions, such as DOT or a vaccine study. The available studies, however, do not assess the impact on behavioural outcomes or the retention of knowledge beyond the trial period.

**Biological markers of disease control**

Two studies (3 papers) assessed the impact of interventions on disease control outcomes. One RCT assessed the impact on HIV-1 viral load of directly observed fluoxetine in comorbid HIV and depression. There was no difference in viral suppression between intervention and comparator groups.[42-44] The other RCT found no difference in viral load or CD4+ count with adherence support for antiretroviral therapy in HIV infected individuals with a history of alcohol problems.[46]

**Cost effectiveness**

Only one study assessed the cost-effectiveness of the intervention. The quality of life cost of the 'Pathway' intervention involving a GP and nurse led inpatient service for people experiencing homelessness included goal setting, discharge

planning, and liaising with community services; was £26,000 per quality adjusted life year. The authors describe circumstances in which such intervention may be cost effective.[30]

## DISCUSSION

### Summary of findings

The available evidence from controlled trials of interventions by healthcare professionals managing physical LTCs in people who are homeless does not show any convincing effects on unscheduled healthcare utilisation.[30-32] The impact on mortality was not assessed, and evidence for the impact on biological markers of disease control is limited to a few studies on HIV, which did not show any evidence of benefit on viral load.[42, 43] Patient-centred interventions – incorporating case management, education, self-management support and social support – may improve disease specific knowledge in TB, HIV, and Hepatitis C; improve completion of DOT in latent TB; and increase access to primary care in combination with clinic orientation.[32, 36-38, 45] Cash and non-cash incentives, in the context of DOT for latent TB, may improve clinic attendance and treatment adherence; however treatment completion rates vary between different studies of similar interventions.[28, 29, 40] It is not clear if improvement in these intermediate outcomes impacts other clinical outcomes, or if effects are sustained beyond the course of treatment evaluated in these studies. There was only one study of cost effectiveness.

### Strengths and Limitations

The strengths of this review include a-priori methods with a robust process for study identificatuion, appraisal, data extraction and description.[24] The comprehensive search strategy included database searches supplemented by hand searching, forward citation searching, grey literature, and contact with study authors. All screening and data extraction was performed by two reviewers independently. We also described the components of each intervention using a previously defined taxonomy,[27] which is important when reviewing complex interventions such as those included.[47, 48] However, many of the findings, particularly those concerning adherence to treatment, were in the context of specific conditions (e.g. latent TB), included a time-limited course of treatment, and were conducted in a single centre. All but one of the included studies was from the USA. As such the findings may not be directly applicable to other disease areas or other health and social care contexts. Limitations in the existing evidence base also meant we were unable to undertake a formal meta-analyses.

This review is timely given the increasing number and complexity of physical LTCs among people who are homeless,[1] the pressure on healthcare services to address this burden, and the potentially expanding roles of various healthcare professionals to support physical LTC management.[19] However, by focusing on interventions by healthcare professionals this review may overlook evidence for housing or social interventions that may impact on physical LTCs.[49, 50]

**Implications for practice, policy and research.**

Despite the social complexity and exclusion that typify the experience of homelessness, a patient-focused case-management approach was shown to positively impact disease specific knowledge and self-efficacy in the management of physical LTCs.[36-38, 45]

It is not clear to what extent the findings presented here are generalisable to wider social or healthcare contexts. The evidence for improved adherence was predominantly in the context of DOT for latent TB. Further research would be required to establish whether these principles of adherence support are transferable to the long-term management of non-communicable diseases. Further research may benefit from being multicentre and having a longer duration of follow up. Furthermore, the potential efficacy of cash incentives will vary between societal contexts where access to, and the extent of, financial support varies widely. The application of such findings, derived from studies with short-term durations of follow up, to life-long treatment for other LTCs also has important implications for cost-effectiveness and future research. Finally, the available literature focuses mainly on the role of nurses and physicians, with little consideration of the potential role of other healthcare professionals e.g. pharmacists.

This review highlights a paucity of controlled trial evidence for the management of non-communicable diseases in people who are homeless. Two reports of quasi-experimental studies of specialist primary-care services for people who are homeless were excluded as they had only historical comparator groups.[51, 52] Both showed improvements in glycaemic control in diabetes, and improved

blood pressure and lipid profiles in Hypertension,[51, 52] however emergency department use and hospitalisations both increased. Few included studies concerned the impact on biological markers of disease control, and none evaluated mortality. The extent to which the improvements in knowledge or adherence that have been demonstrated may impact on physical or behavioural outcomes has not been evaluated. This raises the question of how such issues may be best addressed by future research. It is likely, given their apparent scarcity, that evaluation of complex interventions to address LTC management (including aspects of randomization, longer follow-up and consideration of broader outcomes) will inform practice. However, the intrinsic complexity of the experience of homelessness, and the impact this has on health, may require a broader methodological approach (e.g. realist synthesis) to understand the context and process of potential interventions in this area.

Finally, the higher use of emergency healthcare services by people who are homeless makes the reduction of unscheduled healthcare use a potential target for interventions aiming not only to improve the health of such individuals, but to ease pressure on healthcare services and reduce costs. The available evidence does not demonstrate a positive impact on these outcomes. There is a need to evaluate anticipatory interventions, aiming to prevent or pre-empt the development of health crises. Based on existing patterns of need and service utilisation, as well as the need to demonstrate effectiveness and cost-effectiveness of novel models of care, well designed and conducted studies following a framework for testing complex interventions [48] for people who are homeless are overdue.

## Conclusions

Trials of interventions delivered by healthcare professionals for the management of physical LTCs in people who are homeless do not show convincing evidence of the primary outcome measure for this review – an impact on unscheduled healthcare utilisation. A patient-centred case-management approach may improve knowledge and self-efficacy. These interventions, as well as incentives, may also improve adherence in specific contexts. The impact on biological outcomes and mortality remains largely unexplored, as does the economic impact of successful interventions. Future complex intervention evaluation research is needed to test innovative models of care, and expand those interventions showing promise, into diverse health and social care contexts.

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**Competing interests**

None declared

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**Data sharing**

Full details of the screening process are detailed in the supplementary appendices. Any additional detail will be available on request from the corresponding author.

**Contributions**

All authors listed fulfil the ICMJE criteria for authorship. All authors (PH, LY, LG, AEW, FM and RL) and RE contributed to the conception and design of the proposed study. PH, LY, AEW, FM and RL contributed to the development of data sources and search strategy. PH, LY, RE, AEW, FM and RL developed and refined the inclusion criteria. PH, LY, RE, LG, FM and RL developed the data extraction template which was piloted by PH, LY and LG. PH, LY, RE and RL screened titles,

abstract and full texts. PH, LY and LG completed data extraction and quality assessment on all included studies. PH wrote the first draft of the manuscript. All authors critically reviewed this and subsequent drafts of the manuscript and provided input into its content. All authors approved the final version of the manuscript to be published. RL is the guarantor of the review. All authors accept accountability for the accuracy of the findings presented.

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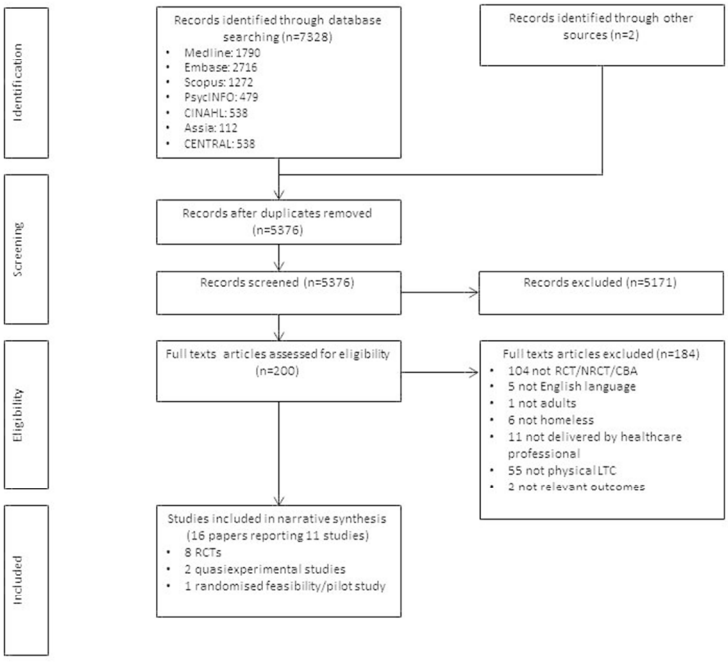


Figure 1: PRISMA diagram of search findings

254x190mm (96 x 96 DPI)

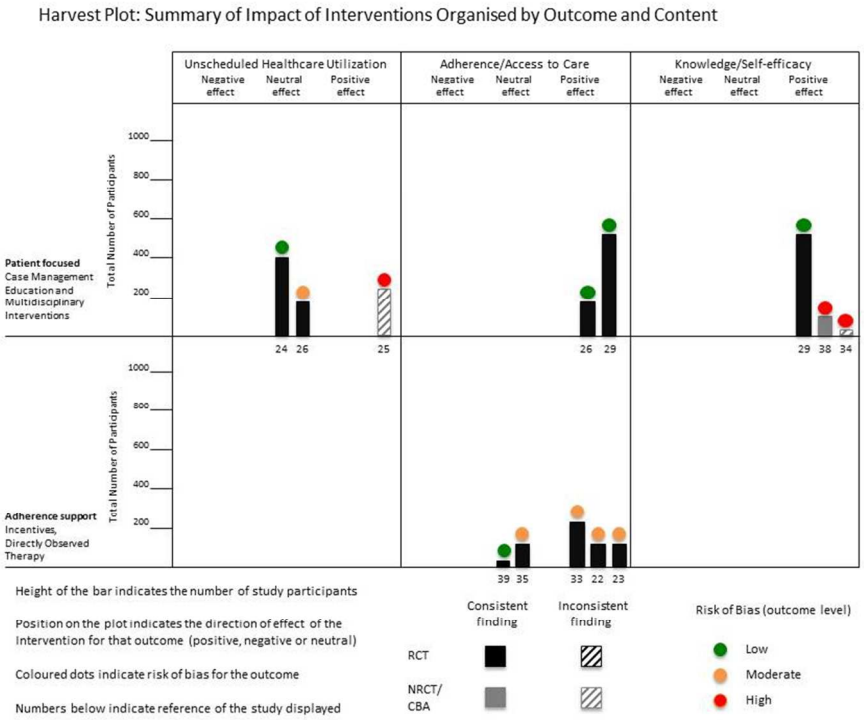


Figure 2: Harvest plot of findings of included studies

254x190mm (96 x 96 DPI)

| Inclusion Criteria and Search Strategy (adapted from protocol paper *Hanlon et al 2017 [1a]*) | |
|---|---|
| **PICOS component** | **Description** |
| Population | • Adults (≥ 18 years old)<br>• ETHOS criteria for homelessness*<br>• ≥1 physical LTC |
| Intervention | • Be delivered, in whole or in part, by a healthcare professional**<br>• Address the management of one or more physical LTC |
| Comparator | 'Usual care' or alternative intervention<br>Contemporaneous comparator only (exclude historical controls) |
| Outcomes | Primary outcome: Unscheduled use of healthcare services, including:<br>• Emergency department attendance<br>• Hospital admission<br>• Use of out-of-hours services<br>• Ambulance call-outs<br>Secondary outcomes:<br>• Physical health outcomes (e.g. mortality, disease specific markers of control)<br>• Quality of life<br>• Patient engagement (e.g. attendance at planned healthcare services, medication adherence)<br>• Behavioural or cognitive (e.g. self-efficacy, knowledge) changes related to health<br>• Emotional wellbeing, anxiety, and depression<br>• Satisfaction with care<br>• Cost effectiveness<br>• Changes to treatment or medication |
| Settings | Community: interventions delivered solely in non-community settings (e.g. hospitals, ) will be excluded |
| Study design | RCTs (including Cluster RCTs)<br>Non-randomised controlled trials/ quasi-experimental studies<br>CBAs |
| Databases | Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, Cochrane Central Register of Controlled Trials (CENTRAL) |
| Manual searching | Reference lists of all eligible studies.<br>Journal of the Poor and Underserved. |
| Grey literature | Websites of non-governmental organisations that aim to assist homeless persons: Department of Health England webpage; OpenGrey; WorldCat; Grey Literature Report; OAIster and WorldWideScience for reports and theses; British library and Zetoc; Research Councils UK information on publicly funded research; Repositories including Grey Guide and Open DOAR. Other related sites including UK health forum, St. Michael's hospital, and Grey Net. |
| Forward citations | Performed for all included studies (using Web of Science). |
| Contact with study authors | Where data pertaining to homeless participants were not presented separately, we attempted to contact study authors to request these data. |
| Restrictions | English language only |
| Dates | Database: Jan 1966 (or inception) to Oct 2016. Forward citation search completed Mar 2017 |
| * Studies including a broader population but including homeless participants will be included only if data pertaining to | |

homeless participants are considered separately.

** including, but not limited to, physicians, nurses, dentists, pharmacists, paramedics, mental health professionals, allied health professionals (e.g. physiotherapists, dieticians, clinical psychologists etc.), midwives.

(1a) Hanlon P, Yeoman L, Esiovwa R, Gibson L, Williamson AE, Mair FS, Lowrie R. Interventions by healthcare professionals to improve management of physical long-term conditions in adults who are homeless: a systematic review protocol. BMJ Open. 2017 Aug 21;7(8):e016756. doi: 10.1136/bmjopen-2017-016756.

**Medline Search Strategy***

1. Exp. Homeless Persons/
2. Home?less.mp
3. Roof?less.mp
4. House?less.mp
5. (home* adj2 lack).mp
6. (home* adj2 no).mp
7. (without adj2. Home*).mp
8. (lack adj2 hous*).mp
9. (no adj2 hous*).mp
10. (without adj2. hous*).mp
11. (lack adj2 roof*).mp
12. (no adj2 roof*).mp
13. (without adj2 roof*).mp
14. (inadequate* adj3 hous*).mp
15. (insecur* adj3 hous*).mp
16. (insecur* adj2 tenan*).mp
17. (unfit* adj2 hous*).mp
18. ((transition* or insecure or inadequate or substandard or substandard or sheltered or emergency or intermittent or transient or marginal* or problem*) adj (hous* or home* or accommodat*)).mp
19. (sheltered or unsheltered or shelters).mp
20. Vagran*.mp
21. Destitute.mp
22. Skid row.mp
23. (sleep* adj2 rough).mp
24. ("street person" or "street people"). Mp
25. Exp "Delivery of Health Care"/
26. Exp Primary Health Care/
27. Exp Community Health Services/
28. Exp Chronic Disease
29. ((chronic or long term) adj2 (disease or condition*)).mp
30. Exp Patient Care Management/
31. Intervention*.mp
32. Exp Pragmatic Clinical Trial/ or exp Clinical Trial/ or exp Randomized Controlled Trial/ or exp Controlled Clinical Trial/
33. Trial*.mp
34. Control*.mp
35. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
36. 25 or 26 or 27 or 28 or 29 or 30
37. 31 or 32 or 33 or 34
38. 35 and 36 and 37

*Adapted for other databases

**Additional File 2. Studies Excluded at Full-Text Assessment**

104 not RCT/NRCT/CBA (including those without contemporaneous comparator group) [1-104]

5 not published in English [105-109]

1 did not include adults [110]

6 participants were not homeless, or homeless participants were not considered separately [111-116]

11 intervention not delivered by a healthcare professional [117-127]

55 did not consider physical long-term conditions [128-182]

2 did not report relevant outcomes [183, 184]

**Not RCT/NRCT/CBA with contemporaneous control group**


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| Characterisation of Interventions by the Effective Practice and Organisation of Care (EPOC) Taxonomy | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study** | **How** care is delivered | | **Where** care is delivered | | | | **Who** and delivers care | | | **Coordination** of care | | | | | | | | **Finance** |
| | Group/ Individual deliver | Coordination of care providers | Orientation to environment/ facilities | Outreach services | Changing site of service delivery | Transportation services | Role expansion | Self-management | Recruitment of specific professionals | Care pathways | Case management | Communication between providers | Discharge planning | Disease management | Integration of services | Shared care | Multi-disciplinary teams | Incentives (monetary or not) |
| **Cianarello 2006** | Individual | | | Took place in transitional housing facility | Services delivered at transitional housing facilities | | | Health education a component of intervention | | | | Liaising with social work | | Diagnostic studies and medical referral carried out | | | Multidisciplinary model of service provision | |
| **Hewett 2016** | Individual | Liaising between inpatient and community services | | | | | GPs delivering ward-based care. Homeless-specific nurses | | Specialised "pathway" team | Focus of the intervention | | "Pathway" meeting with further liaising with community services | Focus of the intervention | | Liaising between inpatient and community services. Needs assessment | "pathway" and ward inpatient teams | MDT meeting key part of intervention | |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, and Nyamathi 2008** | Group | | | Tracking of non-attenders | | Escorted to appointments | | Education and self-management focus of the case-management sessions | | | Focus of intervention, given in addition to DOT for latent TV | | | In context of DOT | | | | Incentive to both groups when taking DOT. |
| **O'Toole 2014** | Individual | | Clinic orientation arm and combined arm. | Both arms | | Clinic orientation arm and combined arm. | | Health promotion within personal health assessment arm and combined arm. | | | Personal health assessment and combined arm | | | Personal health assessment and combined arm | | | | |
| **Pilote 1996** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Samet 2005** | Individual | | | Home visit at 3 weeks to reinforce intervention | | | | Motivational interviewing for behaviour change and adherence support | | | | | | Tailored support for antiretroviral treatment. | | | | |
| **Savage 2014** | Individual | | | | | | | Educational intervention | | | | | | | | | | |
| **Tsai 2013, Tsai 2013, Gerlotti 2014** | Individual | | | | | | | | | | Psychiatric evaluation and initiation of therapy | | | Treatment of comorbid depression | | | | Monetary incentive for treatment |
| **Tulsky 2000** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Tulsky** | Individual | | | | | Bus tokens to | | | | | | | | | | | | Both |

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| **2004** | | | | | | all groups | | | | | | | | | | | | study arms |
| **Tyler 2014** | Group | | | | | | | Health promotion and transmission prevention education | | | Case management on top of vaccination programme | Onward referral for medical or social needs | | | | | | |

| Study | Participants | Recruitment, retention and attrition | Intervention/Comparator (description) | Frequency, Duration and Intensity of intervention.<br><br>Length of Follow-up | Theoretical underpinning of intervention | Findings | Risk of bias (outcome level assessment – See Additional File 4 for study level assessment) |
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| **Ciaranello 2006**<br><br>(quasi-expieri-mental, non-equivalent comparator group) | **Sample:** 6 transitional housing facilities (I: 4, C: 2. Residents (I: ~200, C: ~50) randomly sampled at time points but not followed up individually)<br><br>**Sex:** I: 81% male at baseline, C: 44% male at baseline<br><br>**Age:** I: 41.6 (9.6), C: 41.3 (10.4)<br><br>**LTC:** Various<br><br>**Homeless definition:** Residents of transitional housing facilities, referred to as 'formerly homeless'. | Four transitional housing facilities selected from area in which intervention took place. Comparator was two transitional housing facilities in a different area, under control of a different authority.<br><br>Residents were sampled at baseline and 6 and 18 month follow-up points, however follow-up surveys included residents who had arrived in the intervening period, owing to the usual length of stay of less than 9 months. | **I:** 'Integrated service team' (medical director, nurse practitioner, medical clerk and social worker) made weekly visits to housing facilities. Performed 'comprehensive health assessment', health education, medical and dental referrals, brief psychotherapy, diagnostic studies, and social work services. Supplemented by 24 hour a day nurse telephone-advice line. Additional HIV and TB clinics.<br><br>**C:** 'Usual care'. Facilities under a different healthcare authority. No additional details given | Weekly visits and assessments<br><br>24 hour telephone advice service<br><br>Service delivered for 2 years.<br><br>Data collected by survey of residents at 6 and 18 months post initiation of intervention. | None described | **ED attendances (assessed by survey):** Significantly fewer residents in intervention facilities reporting ≥2 ED attendances in previous 6 months at compared with comparator group at 18 month follow-up (adjusted OR: 0.3, 95%CI 0.12 to 0.74). No significant difference at 6 month follow-up.<br><br>**Hospitalisation (assessed by survey):** No significant difference in adjusted OR of having ≥1 hospitalisation in previous 6 months between intervention or comparator facilities at 6 or 18 months follow-up | **High:** Survey data susceptible to recall bias (e.g. for ED use). Follow-up surveys included people who had arrived in the facility between initial and follow-up surveys. As such changed in outcome variable could be the result of a different sample, rather than changes in outcome relating to the intervention. Also no blinding, randomisation, protection from contamination. Differences in baseline outcomes. |
| | | | | | | **Diastolic blood pressure:** Adjusted mean lower in intervention group at 6 months (mean difference -6.4mmHg, SE 2.4, p=0.03) but not 18 months (mean difference 0.57mmHg, SE 2.3, p=0.80) | **High:** All biases above relalvant, particularly the inclusion of residents arriving between baseline and follow-up. Also unclear if participants were hypertensive as such validity of outcome measure is questionable |
| | | | | | | **Satisfaction with care:** No significant differences described between intervention and control based on survey data. Not further described. | **High:** Biases above also relevant for satisfaction data |
| **Hewett 2016**<br><br>RCT | **Sample:** I: 206, C: 204<br><br>**Sex:** I: 81.6% male, C: 81.4% male<br><br>**Age:** I: 41.6 (12.1), C: 42.5 (11.3)<br><br>**LTC:** Various (79.1% and 76.5% had 'long-term medication condition' in I and C groups, respectively)<br><br>**Homeless definition:** "Homeless" (i.e. no fixed | 1009 patients identified by ward team of whom 622 were eligible. 410 consented and were included in analysis.<br><br>3 month admission data routinely collected and was available for all 410.<br><br>Survey data collected using telephone follow-up and was only obtained for 110 participants (57 intervention, 53 | **I:** During hospital admission patients who were homeless were identified by ward teams. Nurse met completes interview including medical, mental health, drug and alcohol details, housing history, care needs and consideration of any goals on discharge.3x weekly GP led ward round reviewing goals, care plans, medial findings and discharge planning. Regular visit by homelessness nurse to provide community links including with social work and housing services. Weekly | 3-4 times weekly GP ward round during admission<br><br>Initial meeting by nurse followed by liaising with relevant services.<br><br>Weekly multiagency meetings<br><br>Questionnaire data obtained 6 (+/-4) weeks following discharge. | None explicitly described. Development of service was the result of quality improvement work based in the study site which has been published and described | **ED attendance:** no significant difference between standard or enhanced care at 12 months (adjusted mean difference -0.8, 95% CI -4.3 to 2.8)<br><br>**Hospital readmission:** No significant difference between standard or enhanced care at 30 or 90 days (adjusted OR 0.83 (95% CI 0.52 to 1.33) and 1.02 (95% CI 0.67 to 1.54), respectively) | **Low:** Data on readmission and attendance was routinely collected and complete data available for those who consented. Protection from contamination and adjustment for baseline imbalances made |
| | | | | | | **Quality of Life:** (EQ-5D-5L questionnaire) Non-statistically significant improvement with enhanced care over standard care at 6 week | **Moderate:** Based on survey data with poor response to follow-up. Potential for selection bias from those who |

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| | residence) | comparator).<br><br>Consent to longer term follow up (1 year) was a change in protocol. Consent obtained from 226 participants). | multiagency meeting in which housing manager, social workers, drug and alcohol workers, liason psychiatry, street outreach workers, hostel key workers and ward staff met with 'pathway' team to review discharge plans for all patients.<br><br>**C:** Visited once by homelessness nurse and given information leaflet detailing local services | Emergency department attendance assessed at 1 and 3 months, readmission at 3 months. | | follow-up (adjusted mean difference 0.09 (95% CI -0.03 to 0.22) | responded to follow-up. |
| | | | | | | **Cost effectiveness:** £26,000 per quality adjusted life year | **Moderate:** Based on survey data with poor response to follow-up. |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, Nyamathi 2008**<br><br>RCT | **Sample:** I: 279, C: 241<br><br>**Sex:** 79.6% male<br><br>**Age:** 41.5 (SD 8.5)<br><br>**LTC:** Latent TB (a subset of these judged at risk of HIV also identified)<br><br>**Homeless definition:** Individuals having spent the night prior to recruitment at one of the study shelters considered homeless and eligible for inclusion<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment by flyers in 12 homeless shelters.<br><br>3959 screened, 980 PPD positive. 25 refused CXR, 199 did not return for follow-up. 221 not eligible due to active TB, suspected TB or other medical indications.<br><br>520 randomised<br><br>Follow-up data on 494 | **I:** Delivered alongside Directly Observed Therapy (DOT) for latent TB. Research nurse and outreach worker delivered 8 1-hour TB education sessions. Focus was on self-esteem, TB and HIV risk, coping, self-management, problem solving and positive relationships and social networks to maintain behaviour change. Provided with community resourced and escorted to appointments. Participants not attending were tracked by the outreach worker.<br><br>**C:** 20 minute lecture and 10 minute discussion with study nurse in addition to DOT. | 8 1 hour sessions over a period of 6 months. | Comprehensive Health Seeking and Coping Paradigm. | **Completion of Directly Observed Therapy for Latent TB:** Nurse led case management with education, incentives and tracking associated with improved DOT completion (61.5% completion vs 39% with usual care, adjusted OR for completion 3.01 (95% CI 2.15 to 4.20). | **Low:** Complete outcome data available and adjusted for potential confounders in multivariate analysis. |
| | | | | | | **TB knowledge:** Latent variable analysis showed nurse-led case management predicted greater TB knowledge at 6 month follow-up. **HIV knowledge/self-efficacy:** Latent variable analysis of subgroup at risk of HIV showed nurse-led case management predicted greater HIV knowledge and greater self-efficacy for condom use at 6 month follow-up. | **Low:** two separate models used to control for numerous confounders and assess magnitude of the impact of inter intervention on knowledge. |
| **O'Toole 2015**<br><br>RCT | **Sample:** I: 123, C: 62<br><br>**Sex:** 94% male<br><br>**Age:** 48.5 (SD 10.8)<br><br>**LTC:** 72.7% reported at least one chronic medical problem, most commonly hypertension, arthritis/chronic pain, hepatitis/cirrhosis | Recruitment from 11 community sites (soup kitchens, transitional and emergency shelters, drop-in centres). Potential participants identified in common areas and provided with information about the study. No healthcare services offered at time of recruitment. | **I: Group 1**, (n=39), personal health assessment/brief intervention. Nurse led interview about medical history, health, risk behaviours, barriers to care, medications and self-identified needs. Cursory examination. Brief motivational interview and summary of findings highlighting unmet health needs. No clinic orientation performed **Group 2,** (n=40), clinic | Personal health assessment was a brief, one off, intervention. As described. Lasted 20-30 minutes.<br><br>Clinic orientation also a one off intervention. 15-20 minutes. Also transport to clinic. | None described | **ED attendance**: no significant difference between groups (ANOVA p=0.61) **Medical hospital admission:** no significant difference between groups (ANOVA p=0.07) | **Moderate:** Post-hoc analysis and very small number of events. High possibility of type 2 error. Randomised design, routinely collected data reduce potential bias. |
| | | | | | | **Access to primary care:** Cox regression using usual care as baseline showed clinic orientation alone (HR 2.64 (95% CI 1.54 to 4.53)) and physical health assessment in combination with clinic orientation (HR | **Low:** Primary outcome with design focused on assessing outcome. Participants all eligible for veterans' services and data on usage routinely collected and complete for |

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| | **Homeless definition:** "lacking a fixed, regular and adequate night-time residence" plus eligible for Veterans Healthcare Services. Must have not been in receipt of primary healthcare services in previous 6 months | 221 enrolled, 36 removed as ineligible (6 duplicate enrolment, 15 not eligible for veterans' services, 14 receiving primary care in prev. 6 months, 1 did not adequately complete baseline assessment).<br><br>Follow-up for re-interview was 81% at 1 month and 71% at 6 months. | orientation, transported to clinic and introduced to clinic team. Orientated to services available. Usual care only following this.<br>**Group 3,** (n=44), physical health assessment plus clinic orientation.<br><br>**C:** Usual care, comprising social-worker administered assessment of homelessness and social needs, description of services available and how to access (verbal or written) | Follow-up at 1 and 6 months. | | 3.41 (95% CI 2.02 to 5.76)) were both significantly associated with improved primary care access. Unadjusted Chi-squared estimates were significant at both 4-weeks and 6-months with usual care showing lowest rates of access. | eligible participants. Potential bias from randomisation procedure for clinic orientation arm as randomised by calendar day based on attendance. |
| **Pilote 1996**<br><br>RCT | **Sample:** I1: 83, I2: 82, C: 79<br><br>**Sex:** I1: 71% male, I2: 67% male, C: 66% male<br><br>**Age:** Median: I1: 40, I2: 39, C: 40<br><br>**LCT:** Latent TB<br><br>**Homeless definition:** "homeless", not further defined<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | During a population based survey of TB and HIV, homeless people with positive purified protein derivative (PPD) were assessed approached for inclusion.<br><br>1608 interviewed, 1257 had skin tests and returned for evaluation. 441 PPD positive. 297 of these eligible (no recent follow-up). 244 agreed to participate. | **I1:** Monetary incentive. $5 incentive given on attendance to TB clinic follow-up in addition to appointment and bus tokens received by all participants.<br><br>**I2:** Peer health advisors: In addition to bus tokens and appointment, peer health advisors met participants in shelters, accompanied to appointment, helped with paper-work and orientation.<br><br>**C:** Usual care. Bus tokens and TB clinic appointment only. | One off payment for monetary incentive arm.<br><br>One off intervention in peer health advisor arm, as described. Included transport assistance and support in attendance. | None described | **Attendance at initial TB clinic follow-up:** Monetary incentive (84%) and peer health advisor (75%) groups more likely to attend appointment than usual care (53%) (p=<0.001 and p=0.004, respectively). Both interventions significant predictors of adherence in multivariate analysis. | **Moderate:** Details of randomisation not clear and blinding not possible, otherwise low risk of bias. |
| **Samet 2005**<br><br>RCT | **Sample:** I: 74 (15 homeless), C: 77 (19 homeless)<br><br>**Sex:** 84% male (homeless subset)<br><br>**Age:** Median: 43.6 (37.9-45.0) (homeless subset)<br><br>**LCT:** HIV<br><br>**Homeless definition:** | Participants were from a longditudinal cohort study (HIV Alcohol Longitudinal Cohort). Mostly recrtuied from Boston Medical Centre Clinic.<br><br>Of 74 randomised to intervention, 56 received complete intervention, 13 received partial intervention, 5 received | **I:** ADHERE intervention:<br>- Assessment and discussion of alcohol and substance use of readiness for behaviour change.<br>- A watch that served as a medication timer reminder.<br>- Enhancement of perceived efficacy of medications.<br>- Individualised HIV | Baseline visit at medical centre lasting 60 minutes.<br><br>Home visit within 3 weeks of intervention lasting 30-45 minutes.<br><br>1-month follow-up at assessment centre: 15-30 minutes.<br><br>3 month follow-up visit | Intervention used behavioural science theories using motivational interviewing to promote behaviour change and using principles of the Health Belief Model to support the benefit and need for therapy. | No separate analysis of homeless participants is provided in the published paper. Analyses were repeated on the homeless participants only using Generalised Estimating Equations as described in the original manuscript. Data were provided by the study authors and the analysis was performed by the review authors. Models were fit to analyse the overage intervention effect over time.<br><br>**Adherence to Antiretroviral** | **Low:** Objective assessment of outcomes and adjustment for baseline variables |

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| | "homeless" as a variable – not otherwise defined<br><br>**Inclusion/exclusion:** HIV positive participants with a history of alcohol problems (current or lifetime history of alcohol abuse or dependence – CAGE questionnaire or study clinician diagnosis). Participants also needed to be taking antiretroviral medication. | no intervention (could not be contacted). Homeless proportions of these numbers not available.<br><br>10 in total lost to follow-up (3 control, 7 intervention). Proportion of these who were homeless not stated. | counselling – ways to tailor medication use to specific circumstances.<br><br>**C:** Standard care. At study period this included verbal or written instructions regarding antiretroviral treatment and adherence strategies. | at medical centre: 15-30 minutes.<br><br>At follow-up visits all 4 components of the intervention were reassessed and reinforced. | | **treatment:** No significant improvement with intervention after controlling for baseline adherence (p=0.55) | |
| | | | | | | **CD4 count:** No significant change in CD4 count with the intervention after adjusting for baseline CD4 count (p=0.31)<br><br>**HIV1-RNA:** No significant reduction in viral load seen with intervention after adjusting for baseline laboratory estimates. (p=0.23) | **Low:** Objective assessment of outcomes and adjustment for baseline variables |
| **Savage 2014**<br><br>Randomised pilot/ feasibility study | **Sample:** I: 6, C: 3<br><br>**Sex:** Not specified<br><br>**Age:** Not specified<br><br>**LTC:** Type 2 diabetes mellitus<br><br>**Homeless definition:** Those living without adequate shelter or in temporary accommodation. | Convenience sample recruited from a homeless clinic. Unclear how those with type 2 diabetes were identified. 9 identified in total for participation in feasibility study. | **I:** Nursing case-management with diabetes self-management. Education sessions delivered alongside nursing case-management (6 sessions total).<br><br>**C:** No intervention | 6 sessions over 12 weeks. Each 45 minutes long. | Chronic disease self-management approach based on self-efficacy theory. | **Self-efficacy:** paper states "participants who attended the intervention had higher scores on some outcome variables, most notable in cognitive symptom management, which improved from a pre-intervention score of 1.3/5 to a post-intervention score of 2.75". Participants in comparison stated to have "similar scores" at baseline and 12 week follow-up. | **High:** Randomisation not clear. Incomplete outcome reporting. No assessment of baseline imbalances. Small sample size, incomplete recruitment. |
| **Tsai 2013, Tsai 2013, Grelotti 2016**<br><br>RCT | **Sample:** I: 66, C: 71<br><br>**Sex:** I: 91% male, C: 89% male<br><br>**Age:** I: 44 (37-53), C: 42 (37-49)<br><br>**LTC:** HIV<br><br>**Homeless definition:** "Homeless or marginally housed". Not further defined<br><br>**Inclusion/exclusion:** HIV positive, depression (DSM-IV). Excluded if self-report of alternative psychiatric diagnosis. | Participants identified from homeless shelters, free-lunch programmes, low-income single-room occupancy hotels, public HIV clinics and social service agencies.<br><br>Block randomisation.<br><br>1555 screened. 647 potentially eligible. Of these 190 met DSM-IV criteria for depression. | **I:** Psychiatric evaluation and prescription of fluoxetine. Directly observed therapy for 24 weeks. Psychiatric interview was carried out weekly. 25 dollar reimbursement given per week for all doses.<br><br>**C:** Advised of diagnosis of depression and advised to seek treatment at a public mental health clinic specialising in care of HIV positive persons. 25 dollar incentive for attending study site weekly for data collection. | Weekly dispensing and incentive. Weekly psychiatric evaluation.<br><br>Follow-up 6 months. | None stated | **Adherence to antiretroviral therapy:** Mixed-model analysis showed no statistically significant effects of the intervention on antiretroviral therapy update (adjusted OR 1.18 (95% CI (0.83 to 1.68)). Percentage of antiretroviral adherence was similar in intervention and comparator groups. | **Moderate:** Low risk from study design however unannounced pill-counts on a monthly basis may not be a robust method of assessing compliance with treatment. |
| | | | | | | **HIV-1 viral load:** No statistically significant difference in viral suppression between intervention and comparator group (adjusted OR 1.04 (95% CI 0.97 to 1.12). | **Low:** Good methodological rigour across study (Additional file 4) and objective measurement of outcome |
| | | | | | | **Depression:** Improved mood in both study arms. Statiscially significant treatment effect observed using with Ham-D and BDI-II scores to assess depression. | **Low:** Good methodological rigour across study (Additional file 4). Assessed as primary outcome with analysis designed around this. Two measured used and compared as sensitivity analysis. |

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| **Tulsky 2000**<br><br>RCT | **Sample:** I1: 43, I2: 37, C: 38<br><br>**Sex:** 89% male<br><br>**Age:** Median 37<br><br>**LTC:** Latent TB<br><br>**Homeless definition:** Either "literally homeless", staying in emergency shelter, street, car, or other shelter not designed for sleeping, or "maginally housed", staying in low-cost temporary accommodation.<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>Eligibility was positive TST and no TB follow-up in previous 6 months.<br><br>2158 screened. 618 positive TST. 89 refused randomisation. 199 ineligible as did not return or rsults, HIV infection, recent screening with chest x-ray or current isoniazid treatment. 330 randomised and attended clinic. Of these 121 prescribed isoniazid.<br><br>3 stopped due to toxicity. 118/121 analysed. | **I1:** Monetary incentive: $5 at each twice weekly visit for directly observed isoniazid. If a dose missed, attempts to contact participant made by letter or telephone call. Any onward referrals were made by TB clinic, not research assistants following up patients.<br>**I2:** Peer health adviser: Adviser provided and observed isoniazid twice weekly. Adviser accompanied participant for monthly refill appointments. If appointments missed, adviser spent an allotted amount of time looking for the participant.<br><br>**C:** Usual care: routine TB clinic care. Given 1 month supply of treatment and monthly drop in follow-up scheduled. Adherence monitored by TB charts. For non-attendance, standard follow-up or 3 letters or telephone calls. Treatment not directly observed. Protocol change during study due to low initial clinic attendance in usual care arm meant that the protocol was changed to offer all participants $5 at the initial visit. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion significantly higher in monetary incentive group (44%) than peer advisor (18%, p=0.01) and usual care (26%, p=0.04). No statistically significant difference between peer advisors and usual care. Multivariate analysis comparing monetary incentive to peer advisors and usual care considered together (i.e. single comparison group) showed monetary incentive arm significantly more likely to complete treatment (Adjusted OR 2.57 (95% CI 1.11 to 5.94)). | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |

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| **Tulsky 2004**<br><br>RCT | **Sample:** I: 72, C: 69<br><br>**Sex:** 85% male<br><br>**Age:** Median 41 (21-79)<br><br>**LTC:** Latent TB<br><br>**Homeless definition:** "true homeless", street or shelter dwelling, or "marginally housed", staying in low-cost temporary accommodation<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>2570 tested. 647 positive TST, 488 new or required further screening. 95% accepted referral. 353 attended initial appointment. 212 of these were not randomised (190 not prescribed isoniazid, 6 active TB, 16 refused). 141 randomised.<br><br>16 not prescribed isoniazid after diagnostic tests (4 cash, 12 non-cash). 6 censored (3 cash, 3 non-cash). | **I:** Cash incentive: $5 payment for keeping twice weekly appointment for directly observed isoniazid therapy. Tracking included names and addresses of family, friends and case workers. Missed appointments were followed up by letters, telephone calls, and using tracking information, following a protocol specifying a number of outreach attempts.<br><br>**C:** Non-cash incentive: A choice of fast-food or grocery coupons, phone cards or bus tokens with a value of $5 was offered from each kept appointment. Tracking and follow-up of missed appointment was identical to the cash incentive group. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion rates were 89% with monetary incentives and 81% with non-monetary incentives (no statistically significant difference, p=0.23) | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |
| **Tyler 2014**<br><br>Randomised quasi-experimental | **Sample:** I: 46, C: 61 (Hepatitis C positive subset only)<br><br>**Sex:** 79% male<br><br>**Age:** males 44 (7.1), females 45.3 (8.9)<br><br>**LTC:** Hepatitis C<br><br>**Homeless definition:** "homeless". Not further defined.<br><br>**Inclusion/exclusion:** Recruitment was to a vaccine study (Hep A/B). Data presented here | Recruitment view flyers in homeless shelters within the study area. | **I:** Case management in the context of a hepatitis A/B vaccination programme. Three 40 minute group sessions delivered by study nurse with education on hepatitis A, B, C and HIV diagnosis, prevention and transmission. Self-management training. Case management focusing on self-esteem, social, behavioural and communication skills. Behavioural education around blood-borne virus risk. Also included participant needs assessment and onward referral to address medical, mental health, food, shelter and transportation needs. | Total of 3 group session across study period in intervention group. Time-frame not specifically stated.<br><br>Outcomes assessed 6 months post-intervention | Based on the Comprehensive Health Seeking and Coping Paradigm (CHSCP) | **Hepatitis C knowledge:** Measured using a modification of an 18 item tool initially developed for tuberculosis. Greater improvement in the nurse case-managed group than the standard intervention in the hepatitis C positive subset. Statistical analysis of the significance of the difference between intervention and control groups not performed for the hepatitis C positive subset. | **High:** Randomisation was carried out according to a protocol to assess the vaccine efficacy, not that of the case-management/education intervention. Futhermore, while data on the hepatitis C positive subset are presented, the study design and analysis was not focused on a comparison of intervention and control intervention in this subset of participants. As such baseline imbalances and sequence of allocation could introduce bias for the outcome of hepatitis C knowledge. |

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| | pertain to hepatitis C positive subset | | **C:** Single brief 20 minute presentation around hepatitis A, B, C and HIV at baseline visit of vaccination programme. | | | | |

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7<br>Additional file 1 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 7-8<br>Additional file 1 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Additional file 1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8<br>Additional file 5 |

# PRISMA 2009 Checklist

| | | | |
|---|---|---|---|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 8 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 9 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 10 |



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 8<br>Additional file 4 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | n/a |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1, Page 11 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 11,12<br>Table 1 (page 13)<br>Additional file 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table 2 (page 15) |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 18-23 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | n/a (figure 2 summarises narrative synthesis) |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Figure 2, Additional |

# PRISMA 2009 Checklist

| | | | |
|---|---|---|---|
| | | | file 4, |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 24 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 25 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 28 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 29 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

BMJ Open

# A Systematic Review of Interventions by Healthcare Professionals to Improve Management of Physical Long-Term Conditions in Adults who are Homeless

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| Keywords: | Homelessness, chronic disease, long-term conditions, Complex interventions |
| | |

# A Systematic Review of Interventions by Healthcare Professionals to Improve Management of Physical Long-Term Conditions in Adults who are Homeless

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**Word Count: 3982 (Limit 4000)**

## Abstract

**Objective:** To identify, describe and appraise trials of interventions to manage physical long-term conditions (LTCs) in homeless adults delivered by healthcare professionals.

**Design:** Systematic review of Randomised Controlled Trials (RCTs), Non-randomised Controlled Trials and Controlled Before-After (CBA) studies. Interventions characterised using Effective Practice and Organisation of Care (EPOC) taxonomy. Quality assessed using EPOC Risk of Bias (ROB) criteria.

**Data sources:** Database searches (Medline, Embase, PsycINFO, Scopus, CINAHL, Assia, CENTRAL), hand searching reference lists, citation searches, Grey literature, and contact with study authors.

**Setting:** Community.

**Participants:** Adults (≥ 18 years) fulfilling European Typology of Homelessness (ETHOS) criteria.

**Intervention:** Delivered by healthcare professionals managing physical LTCs.

**Outcomes:** Primary outcome: unscheduled healthcare utilization. Secondary outcomes: mortality, biological markers of disease control, adherence to

treatment and engagement in care, patient satisfaction, knowledge, self-efficacy, quality of life and cost-effectiveness.

**Results:** 11 studies were included (8 RCTs, 2 quasi-experimental, 1 feasibility) involving 9-520 participants (71-94% male, median age 37-48). Ten from USA, one from UK. Studies included various LTCs (n=3); or focused on one LTC: latent tuberculosis (n=4); HIV (n=2); Hepatitis C (n=1); or Type 2 Diabetes Mellitus (n=1). All interventions were complex with multiple components. Four described theories underpinning their intervention. Three assessed unscheduled healthcare utilization with none showing consistent evidence of reduction in hospitalization or emergency department attendance. Six assessed adherence to specific treatments, of which four showed improved adherence to latent TB therapy. Three concerned education case-management, all of which improved disease specific knowledge. No improvements were seen in biological markers of disease (two studies) and none assessed mortality.

**Conclusions:** Evidence for management of physical LTCs in homeless adults is sparse. Educational case-management interventions may improve knowledge and medication adherence. Large trials of theory-based, interventions, assessing health care utilization and outcomes as well as assessment of biological outcomes and cost-effectiveness, are needed.

**Abstract word count: 299**

## Strengths and Limitations of the Study

- This is the first systematic review to examine effects of physical long-term condition management interventions for adults who are homeless.
- A comprehensive search strategy was supplemented with hand searching, Grey literature searches and contact with study authors.
- Interventions are described using the Effective Practice and Organisation of Care (EPOC) Taxonomy
- Significant heterogeneity precluded meta-analysis, so a narrative synthesis is presented along with a Harvest Plot summarising study findings.
- Evidence available is mostly limited to the USA, with one study from the UK.

## INTRODUCTION

The prevalence of homelessness is increasing across high income countries.[1] The experience of homelessness is associated with increased morbidity and mortality.[2-4] Social exclusion and socio-economic deprivation,[5 6] adversity over the life course,[7] as well as environmental and behavioral risk factors[8] typical of homelessness, contribute to an increased prevalence of a range of physical long-term conditions (LTCs) compared to the rest of the population.[1] This includes physical long-term conditions (LTCs). LTCs are conditions that require care and management over a prolonged priod of time.[9 10] We use the term physical LTCs to draw a distinction between conditions considered in this review and mental health conditions or addictions. Physical LTCs include non-communicable diseases[11] as well as specific communicable diseases (such as human immunodeficiency virus (HIV), tuberculosis (TB) and hepatitis C) which require long-term management and access to care. This review focusses on physical LTCs because, compared to interventions for mental health problems or addiction, the management of physical LTCs in the context of homelessness has not been synthesised in the systematic review literature.[12] Physical LTCs disproportionateley affect people who are homeless. They may also be amenable to effective prevention or treatment. Innovative models of care and expanded roles of healthcare professionals offer potential strategies to target physical LTCs. However, no previous systematic reviews have specifically focussed on the potential impact of healthcare professional or other intervention on physical LTCs for adults experiencing homelessness. This is despite calls for more

evdence for interventions for health problems that can be improved by equitable access to prevention and early intervention.[12]

Outcomes of physical LTCs are poorer among people who are homeless.[13 14] Engagement with scheduled appointments, preventative health services and adherence to treatment are typically lower.[15-18] Barriers to access, conflicting priorities, physical and mental multimorbidity are thought to contribute to poorly coordinated use of healthcare services. [18] Consequently, there is a need for tailored services.[18-20] Healthcare delivery models for people experiencing homelessness include specialised or generalist primary care services;[21] and integrated housing and health interventions. There is insufficient evidence of reach and effectiveness to favour one model over another.[22]The expanding role of various healthcare professionals e.g. nurse and pharmacist prescribers, targeting physical LTCs,[23] offers a complementary model of healthcare for people who are homeless. Sharing clinical roles may be welcome given the increasing evidence of multimorbidity and polypharmacy.[24]

Controlled evaluations of models of healthcare for people who are homeless are relatively few and optimal delivery varies between different health and social care systems.[20] There have been calls to evaluate more interventions to improve the health of people who are homeless,[25] including long-term prospective studies with economic analyses. [14]

Previous systematic reviews have identified the potential benefit of tailored interventions and strategies for addressing mental health and at-risk substance

use.[26 27] These have shown potential for monetary incentives to improve adherence for people who are homeless with latent tuberculosis,[26] and that provision of housing improved health outcomes in HIV.[27]However, to the authors' knowledge, no previous systematic reviews have focused specifically on the management of physical LTCs for people who are homeless.

**Aims**

This review aims to systematically identify, describe and appraise trials of interventions focusing on the management of physical LTCs, delivered by healthcare professionals for adults who are homeless. It addresses the following two research questions:

1. What are the key components of interventions aimed at optimising physical LTC management including theoretical underpinnings?
2. What impact has been demonstrated of trials of interventions aimed at optimising physical LTC management?

## METHODS

This systematic review followed a pre-specified protocol [28](registered with PROSPERO, ID: CRD42016046183, available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046183) and is described according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[29]

### Eligibility Criteria

Eligibility criteria and search process are described in detail in our published protocol paper,[28] and are outlined briefly below. Full details are given in Additional File 1. Homelessness was defined according to the ETHOS criteria[30]. Eligible studies included adult participants who met the ETHOS defined homelessness criteria with one or more physical LTC or those concerning physical LTC management as part of a broader intervention (e.g. access to primary care). Delivery by a healthcare professional (any professional trained to provide any form of health care, but excluding social workers and professionals without a health-related training) was required, either alone or as part of a wider team. We considered a range of pre-specified outcomes. Studies including any of our primary or secondary outcomes were eligible for inclusion. Unscheduled healthcare utilization was our primary outcome. Secondary outcomes included physical measures of disease control, quality of life, behavioural outcomes, emotional wellbeing, satisfaction with care and cost effectiveness. These are fully detailed in Additional File 1

**Literature Search**

Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1966 (or inception) until October 2016. The search was updated in November 2017. Our search strategy was "homelessness" AND "long-term condition or healthcare delivery terms" AND "trial or evaluation terms". The full search terms for Medline are shown in Additional File 1 and were adapted for other databases. Database searches were supplemented by hand searching of reference lists of all eligible studies, hand searching the Journal of the Poor and Underserved, and forward citation searches of included studies using Web of Science. A number of 'Grey Literature' sources were also searched, (Additional File 1). Grey literature and relevant conference abstracts were used to identify recently publishes studies.

Two reviewers (PH plus LY, RL or RE), using DistillerSR software, independently screened titles and abstracts of all records identified. Full texts of all potentially eligible studies were obtained and assessed independently by two reviewers (PH, LY or RE) against the eligibility criteria. At all levels disagreements were resolved by discussion, involving a third reviewer (RL or LY) when consensus could not be reached. Where studies included homeless participants but analysis of these participants was not presented separately, we contacted the study authors to request these data. Studies were excluded if these were not available. Using a standardised data extraction form, two reviewers (PH plus LY or LG) independently extracted data from each study eligible for inclusion. The components of each intervention were described according to the Cochrane

Effective Practice and Organization of Care (EPOC) taxonomy.[31] Two reviewers independently assessed each study according to the criteria outlined in the Cochrane EPOC guidelines for assessing risk of bias (ROB) in RCTs, non-randomised controlled trials and CBA studies.[31] After grading each study a judgment of the overall risk of bias was made for each outcome, taking into account the relative importance of potential sources of bias to the outcome in question.

**Synthesis**

We assessed the clinical and methodological heterogeneity of the eligible studies. Few studies considered similar outcomes, and those that did had either different comparator groups,[32 33] differing methods of assessing similar outcomes (e.g. survey vs. routine data for emergency department (ED) attendance)[34 35] or concerned complex interventions, the diversity of which would limit the utility of a pooled analysis.[34 36] Consequently, a meta-analysis was deemed inappropriate and we performed a narrative synthesis of the study findings. Studies were grouped by outcome and the strength of the body of evidence for each outcome was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.[37]

We constructed a Harvest Plot *post hoc* to display the results. Harvest plots use bars representing individual studies placed on a plot matrix to indicate whether the review intervention showed an overall positive, negative, or no consistent

effect for the outcome in question. They enable data to be summarised when study designs and outcomes are diverse and heterogeneous.[38 39] We used the following criteria to decide how each study should be displayed:

- Height of the bar represented the number of participants in the study;
- RCTs were displayed in bold with other designs in grey;
- The risk of bias for the outcome of each study was indicated as low, moderate or high using a coloured dot above the bar;
- Statistically significant differences were displayed as a positive effect if they favoured the intervention; negative if they favoured the comparator and neutral if not statistically significant;
- Where some, but not all, findings in a group of outcomes showed a positive or negative effect, bars were hatched to indicate inconsistency.

## RESULTS

### Study Selection

The results of abstract and full-text screening are shown in the PRISMA diagram in Figure 1. A full list of studies excluded at full-text level, along with reasons for exclusion, is shown in Additional File 2.

**FIGURE 1 – PRISMA DIAGRAM**

### Description of Studies

Sixteen papers were eligible for inclusion which described eleven unique studies.[32-36 40-50] Ten studies were from the USA [32 33 35 36 40-50] and one from UK.[34] Three studies included a range of LTCs;[34-36] four studies concerned latent tuberculosis;[32 33 40-44] one concerned Hepatitis C;[49] two studies concerned HIV;[46-48 50] and one concerned Type 2 Diabetes Mellitus.[45] Eight were RCTs, two quasi-experimental and one was a pilot study.

### Study Populations

Details of the study populations are summarised in table 1. Sample sizes ranged from 9 to 520. Median age ranged from 37 to 49 years. In all of the studies the majority of participants were male (percentage male participants ranged from 67% to 94% in the intervention groups). Age and sex distributions were consistent with previous literature on homelessness.[1] Six studies, all from the USA reported details of ethnicity.[32 33 40 44 46 49] African American participants

were the most prevalent in five of these. Only two studies included any detail of comorbidities.[34 40] Details of attrition are shown in Additional File 3.

**Quality Assessment**

Results of the EPOC Risk of Bias assessment for each of the included studies is shown in table 2. None of the included studies scored low risk for each of the criteria. These were used to inform outcome-level risk of bias assessment. These are displayed, along with justification, in Additional File 3.

**Intervention Components and Theoretical Underpinnings**

Each of the studies described interventions that were complex and included multiple components. These included changes to how, and where, care was delivered, the personnel delivering care, how care delivery was coordinated, and the provision of financial support. The components of the EPOC taxonomy relating to each of the interventions are shown in table 3, along with a summary of the intervention and control interventions. Descriptions of the specific aspects of each intervention relating to the taxonomy are shown in Additional File 4.

Four of the eleven studies reported an explicit theoretical framework underpinning the intervention (table 3). These included the Comprehensive Health Seeking and Coping Paradigm underpinning two of the studies, and Self-Efficacy Theory and the Health Belief Model each underpinning one intervention.

**Table 1: Summary of study populations**

| Study | Design | Location | Number of Participants | Age, mean (SD) | Sex (%) | Ethnicity (%) | Long-term Condition | Homelessness definition |
|---|---|---|---|---|---|---|---|---|
| Pilote 1996[44] | RCT | USA | 244<br><br>I[1]: 83<br>I[2]: 82<br>C: 79 | I[1]: median 40<br>I[2]: median 39<br>C: median 40 | I[1]: M (71%)<br>I[2]: M (67%)<br>C: M (66%) | African American (I[1]: 48%, I[2]: 57%, C: 54%)<br>White (I[1]: 33%, I[2]: 27%, C: 27%)<br>Hispanic (I[1]: 16%, I[2]: 11%, C: 13%) | Latent TB | Homeless: not further defined |
| Tulsky 2000[33] | RCT | USA | 118<br><br>I[1]: 43<br>I[2]: 37<br>C: 38 | Median 37 | M (89%) | African American (52%)<br>White (21%)<br>Hispanic (27%) | Latent TB | Homeless or marginally housed |
| Tulsky 2004[32] | RCT | USA | 141<br><br>I: 72<br>C: 69 | Median 41 (range 21-79) | M (85%) | African American (47%)<br>White (32%)<br>Other (20%) | Latent TB | Homeless or marginally housed |
| Samet 2005[50] | RCT | USA | 151 (34 homeless)<br><br>I: 19<br>C: 15 | Median 44 (range 26-60) | M (82%) | n/a | HIV with alcohol problems | Homeless: not further defined |
| Ciaranello 2006[35] | Quasi-experi-mental | USA | 6 transitional housing facilities<br><br>I:219 sampled<br>C: 50 sampled | I: 41.6 (9.6)<br>C: 41.3 (10.4) | I: M (81%)<br>C: M (44%) | n/a | Various* | "Formerly homeless" residents of transitional housing |
| Nyamathi 2006[40]<br>Nyamathi 2007[41]<br>Schumann 2007[42]<br>Nyamathi 2008[43] | RCT | USA | 520<br><br>I: 279<br>C: 241 | 41.5 (8.5) | M (79.6%) | African American (81%)<br>White (7.3%)<br>Hispanic (9.4%)<br>Other (2.3%) | Latent TB | Sleeping in homeless shelters |
| Tsai 2013[46] | RCT | USA | 137 | I: Median 44 | I: M (91%) | I: Caucasian (48%) | HIV with comorbid | "homeless or marginally |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Tsai 2013[47] Grelotti 2016[48] | | | I: 66<br>C: 71 | (IQR: 37-53)<br>C: Median 42 (IQR: 37-79) | C: M (89%) | C: Caucasian (51%) | depression | housed" |
| Savage 2014[45] | Random-ised pilot/ feasibility | USA | 9<br><br>I: 6<br>C: 3 | n/a | n/a | n/a | Type 2 diabetes | Living without shelter or adequate accommodation |
| Tyler 2014[49] | Random-ised quasi-experi-mental | USA | 107 (hepatitis C positive subset)<br><br>I: 46<br>C: 61 | Males: 44 (7.1)<br><br>Females: 45.3 (8.9) | M (79%) | African American (63%)<br>White (17%)<br>Latino (18%) | Hepatitis C | Homeless: not further specified |
| O'Toole 2015[36] | RCT | USA | 185<br><br>$I^{1}$: 39<br>$I^{2}$: 40<br>$I^{1+2}$: 44<br>C: 62 | 48.6 (10.8) | M (94%) | "Minority population" (43%) | Various** | "lacking fixed, regular and adequate night-time residence." |
| Hewett 2016[34] | RCT | UK | 410 | I: 41.6 (12.1)<br>C: 42.5 (11.3) | I: M (81.6%)<br>C: M (81.4%) | N.S.<br>Nationality:<br>UK: I (69.4%), C (72.5%)<br>European union: I (22.3%), C (17.6%)<br>Other: I (8.3%) C (9.8%) | Various*** | No fixed residence on hospital discharge |

* Included hypertension, otherwise not fully specified ** Asthma, COPD, hepatitis, cirrhosis, diabetes, hypertension, arthritis *** Categorised by organ system (included liver, pulmonary, musculoskeletal, central nervous system, cardiovascular system, endocrine, skin, gastrointestinal and haematological pathology). Causes for hospital attendance also categorised by aetiology, 35% related to cardiovascular disease, 15% to metabolic conditions

Table 2: Risk of bias within individual studies

| Criteria | Study | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ciaranello 2014 | Hewett 2016 | Nyamathi 2006, 2007, 2008 and Schumann 2007 | O'Toole 2015 | Pilote 1996 | Samet 2005* | Savage 2014 | Tsai 2013, 2013 and Grelotti 2016 | Tulsky 2000 | Tulsky 2004 | Tyler 2014 |
| Random sequence generation | High | Low | Unclear | Low | Unclear | Unclear | High | Low | Low | Low | High |
| Allocation concealment | High | Low | Low | Unclear | Unclear | Unclear | High | Low | Low | Low | Unclear |
| Blinding of participants/ personnel | High | High | High | High | High | High | High | High | High | Unclear | High |
| Similar baseline outcome measures | High | Low | Low | Low | Unclear | Low | Unclear | Low | Unclear | Unclear | Low |
| Similar baseline characteristics | High | Low | Low | Low | Low | Low | Unclear | Low | Low | Low | Low |
| Blinding of outcome assessment | High | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | High |
| Incomplete outcome data | High | High | Low | Low | Low | Low | High | Low | Low | Low | Low |
| Protection from contamination | High | Unclear | Low | Unclear | Low | Low | Unclear | Low | Low | Low | Low |
| Selective Outcome Reporting | High | Low | Low | Low | Low | Unclear | High | Unclear | Low | High | Unclear |
| Other bias | High | Low | Low | Low | Low | Low | High | Low | High | High | Low |

* Assessment based on methods and results as described in the original manuscript. Unpublished data were supplied by authors for secondary analysis of homeless study participants.

**Table 3: Intervention Components, Theoretical Underpinning, and Outcomes**

| Study | Components | Healthcare Professional delivering the intervention | Theory | Intervention | Comparator | Outcomes |
|---|---|---|---|---|---|---|
| Pilote 1996[44] | **How care is delivered:** Individual delivery<br>**Location/environment:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | Nurse plus peer health advisor | None specified | Monetary incentive for TB clinic attendance (group 1). Peer health advisor assisting with clinic attendance (group 2). | Usual care (clinic appointment and tokens for travel expenses). | Attendance at initial TB clinic appointment. |
| Tulsky 2000[33] | **How care is delivered:** Individual delivery<br>**Location/environment:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | Nurse, outreach worker, peer health advisor | None specified | Monetary incentive for uptake of directly observed therapy (group 1). Peer-health advisor supporting directly observed therapy (group 2). | Usual care | Completion of 6 months isoniazid therapy |
| Tulsky 2004[32] | **How care is delivered:** Individual delivery<br>**Location/environment:** Transportation services<br>**Finance**: Incentives | Nurse, outreach worker, peer health advisor | None specified | Monetary incentive for uptake of directly observed therapy | Non-cash incentive of equal value (vouchers) | Completion of 6 months isoniazid therapy<br>Cost effectiveness |
| Samet 2005[50] | **How care is delivered:** Individual delivery. Self-management.<br>**Location/environment:** Outreach services.<br>**Coordination of care:** Disease management. | Nurse | Health belief model and motivational interviewing. | Adherence support for antiretroviral treatment | Usual care (written instructions/advice regarding treatment adherence) | Adherence to antiretroviral treatment<br>CD4+ count<br>HIV viral load |
| Ciaranello 2006[35] | **How care is delivered:** Individual delivery. Self-management.<br>**Location/environment:** Outreach services; changing site of service delivery.<br>**Coordination of care:** Communication | Medical director, nurse practitioner, medical clerk, social worker | None specified | Weekly visits including health assessment, education, referral and social support. | Transitional houses in a different area not receiving the intervention. | ED attendance<br>Hospital admission<br>Blood pressure<br>Satisfaction with care |

| | | | | | | |
|---|---|---|---|---|---|---|
| | between providers; disease management; multidisciplinary teams. | | | | | |
| Nyamathi 2006[40] Nyamathi 2007[41] Schumann 2007[42] Nyamathi 2008[43] | **How care is delivered:** Group delivery. Self-management. **Location/environment:** Outreach services; transportation services. **Coordination of care:** Case management; disease management. **Finance**: Incentives. | Nurse and outreach worker | Comprehensive Health Seeking and Coping Paradigm. | Directly observed therapy plus 8 education sessions. Information provided on community resources and participants escorted to appointments. | Directly observed therapy plus 20 minute educational lecture | Completion of directly observed TB therapy<br>TB knowledge<br>HIV knowledge<br>Self-efficacy |
| Tsai 2013[46] Tsai 2013[47] Grelotti 2016[48] | **How care is delivered:** Individual delivery **Coordination of care:** Case management; disease management. **Finance**: Incentives | Psychiatrist and study nurse | None specified | Directly observed fluoxetine and weekly psychiatric interview | Advice on sources of mental health support | Adherence to antiretroviral therapy<br>HIV viral load<br>Depression |
| Savage 2014[45] | **How care is delivered:** Individual delivery Self-management | Nurse | Self-efficacy theory | Nurse led case-management and diabetes education | No intervention (usual care) | Self-efficacy |
| Tyler 2014[49] | **How care is delivered:** Group delivery Self-management **Coordination of care:** Case management; communication between providers | Nurse | Comprehensive Health Seeking and Coping Paradigm. | Case management with group sessions, self-management training and education. | Single, brief educational intervention | Hepatitis C knowledge |
| O'Toole 2015[36] | **How care is delivered:** Individual delivery. Self-management. **Location/environment:** Orientation to environment/facilities; outreach services; transportation services. **Coordination of care:** Case management; disease management. | Nurse | None specified | Nurse-led brief health assessment with motivational interviewing (group 1). Guided orientation to primary care clinic facilities (group 2). Both interventions together (group 3). | Usual care (social work assessment and description of available services) | ED attendance<br>Hospital admission<br>Access to primary care |
| Hewett 2016[34] | **How care is delivered:** Individual delivery; Coordination of care providers. Role expansion; recruitment of specific | General practitioner, specialist nurse | None specified | Nurse and GP led inpatient intervention. Goal setting. Discharge planning. Liaison and multiagency meetings | Initial meeting with nurse and signposting of services | ED attendance<br>Hospital readmission<br>Quality of Life |

| | | | | | | |
|---|---|---|---|---|---|---|
| | professionals.<br>**Coordination of care:** Care pathways; communication between professionals; discharge planning; integration of services; shared care; multidisciplinary teams. | | | | | |

**The Impact of Interventions on Healthcare Outcomes**

The overall findings of the included studies for impact on unscheduled healthcare utilization, adherence or access to care, and knowledge of self-efficacy, are illustrated in the harvest plot shown in Figure 2. The text that follows synthesized these findings under each outcome.

**FIGURE 2 – HARVEST PLOT**

**Primary Review Outcomes**

**Unscheduled Healthcare Utilisation**

Three studies assessed the impact of interventions on hospital admissions and emergency department (ED) attendance.[34-36] None focused on a specific LTC, however participants reported a range of LTCs and each intervention included identification and engagement with medical, as well as wider needs. The highest quality evidence was from two RCTs, neither of which showed any significant reduction in unscheduled healthcare utilisation.[34 36] One RCT evaluated a multidisciplinary, multicomponent intervention targeting patients in two inner-city hospitals involving goal setting, discharge planning, and liaising with community services.[34] Neither hospital admissions, nor ED attendance after one year, were significantly different compared with usual care. The other RCT was a four-arm trial comparing usual care; a brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health

assessment.[36]Hospital admissions and ED attendance were assessed at 6 months post intervention in a post-hoc analysis and showed no significant difference to usual care. A third study, with a quasi-experimental design and high risk of bias, concerned a 'comprehensive health assessment' delivered to residents at transitional housing facilities. ED attendances were reportedly lower at 18 month follow-up, but not at 6 months. There was no difference in hospitalization at either follow-up point.

Taken together the available evidence does not suggest that the multidisciplinary, multifaceted interventions described reduced rates of unscheduled healthcare utilisation. The overall confidence in the estimate of effect is low.

**Secondary Review Outcomes**

**Access to primary healthcare**

One RCT concerned access to primary healthcare.[36] A brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health assessment were compared to usual care. All three intervention groups showed higher uptake of primary healthcare services after 6 months with clinic orientation alone and in combination with a physical health assessment significantly improving primary care access in adjusted analyses. Overall

confidence in effect for improvement in this outcome was high, but limited to one study so should be interpreted with caution.

**Adherence to specific treatment**

Six studies (7 papers) assessed adherence to treatment or attendance at appointments.[32 33 40 44 46 47 50] Four recruited patients with latent tuberculosis undergoing directly observed therapy (DOT)[32 33 40 44], one included participants with HIV and alcohol problems,[50] and one (2 papers) concerned participants with HIV and co-morbid depression.[46 47] Of the TB studies, three were conducted by the same research group and assessed the impact of monetary incentives (cash and/or voucher) on attendance at initial TB clinic follow up [44] or on completion of DOT with isoniazid.[32 33] Clinic attendance and DOT completion rates were significantly higher with cash incentives compared with usual care or peer-health advisors.[33] There was no statistically significant difference in DOT completion between cash and voucher incentives.[32] Details of the availability to the participants of social security or other sources of financial support are not described in either study. Although the cash incentive and delivery of the intervention were similar in both studies assessing DOT completion, the completion rate in the intervention group differed widely between the two studies (44% and 89%, respectively).[32 33] The authors speculate that the location of the clinic (the higher completion rate being in an area more accessible and frequented by people who are homeless) or alterations in the follow-up protocol for non-attendees may explain the differences.

The final study concerning TB evaluated the impact of a nurse-led case management intervention on completion of latent tuberculosis treatment and tuberculosis knowledge (described below under knowledge and self-efficacy). They found odds of DOT completion were three times greater with the intervention compared with usual care.[40]

An RCT concerning people with HIV and comorbid depression assessed fluoxetine prescription and weekly psychiatric evaluation compared with the provision of information about how to access local psychology services without the prescription of fluoxetine. Both arms were given a weekly cash incentive for attending. Outcomes included rate of uptake of anti-retroviral treatment (ART), and adherence to ART (assessed by unannounced pill counts) for those receiving treatment. Neither outcome was significantly different between the groups despite an improvement in depression severity and remission in the fluoxetine group.[46 47]

Finally an RCT aimed at supporting antiretroviral medication adherence among HIV positive participants with a history of alcohol dependence or harmful drinking showed no change in antiretroviral adherence.[50] Findings were similar to a secondary analysis of participants who described themselves as homeless (unpublished results).

Overall, there is a moderate level of evidence for interventions improving adherence to treatment for latent TB, including a case-management educational approach and provision of monetary incentives (cash or non-cash). However, the

efficacy of such interventions may be dependent on the social and cultural context in which it is delivered (highlighted by variation in completion rates between evaluations of similar interventions), of which there is limited description in the available studies.

**Knowledge and Self-efficacy**

Three studies (5 papers) assessed the impact of interventions on TB, HIV, hepatitis and diabetes disease knowledge and self-efficacy.[40-42 45 49] Two were trials incorporating nurse-led case management (for patients with latent TB or hepatitis C, respectively) combined with a regular educational intervention focusing on self-management, self-esteem, communication skills and social support. One was an RCT focusing on DOT for latent TB and assessed the impact on TB knowledge in all participants.[40] The intervention also involved HIV education and the impact of this was evaluated in a subset judged to be 'at risk' of HIV (i.e. sexually active or known to be intravenous drug users). Two analyses using structural equation modeling showed that the nurse-led case management intervention was associated with greater improvement in TB knowledge [41] and in HIV knowledge in the 'at risk' subset.[42] The latter also showed improved self-efficacy for condom use.[42] The other evaluated a similar approach concerning Hepatitis education for participants enrolled in a Hepatitis A/B vaccination programme (only the Hepatitis C positive subset was included in this review).[49] The case-management group showed a greater improvement in Hepatitis C knowledge than the control group. However, the randomisation procedure was designed for the vaccine trial, not for the evaluation of the case-management

intervention, and the statistical analysis was not designed to compare the intervention with control in the Hepatitis C subset alone.[49]

The third study reported improved knowledge in a small (n=9) pilot study using a self-efficacy based approach for Type 2 Diabetes Mellitus. However, the small sample size meant there was insufficient power to detect any difference between groups and there was incomplete reporting of outcomes and no clear comparison is made between the intervention and comparator.[45]

Taken together, there is a moderate quality of evidence showing that an educational case-management approach can improve disease specific knowledge when delivered alongside wider interventions, such as DOT or a vaccine study. The available studies, however, do not assess the impact on behavioural outcomes or the retention of knowledge beyond the trial period.

**Biological markers of disease control**

Two studies (3 papers) assessed the impact of interventions on disease control outcomes. One RCT assessed the impact on HIV-1 viral load of directly observed fluoxetine in comorbid HIV and depression. There was no difference in viral suppression between intervention and comparator groups.[46-48] The other RCT found no difference in viral load or CD4+ count with adherence support for antiretroviral therapy in HIV infected individuals with a history of alcohol problems.[50]

### Cost effectiveness

Only one study assessed cost-effectiveness, within the hospital sector.[30] Using a parallel arm design, people who were homeless and admitted to hospital, received an intervention comprising thrice weekly GP and homelessness nurse led inpatient visits in addition to regular visits by the homelessness nurse, or standard in patient care (an information leaflet describing local services). Patients in the intervention group also had multiagency care plans devised before, and implemented after hospital discharge. Quality of life was a secondary outcome, with health gain measured by translating generic EQ-5D-5L index scores into generic quality adjusted life years (QALYs). EQ5D5L scores were completed by approximately one quarter of participants in both arms. There was a non statistically significant increase in EQ-5D-5L scores at follow up, and there was no impact of the intervention on inpatient costs, therefore the authors compared the costs of the intervention with the effect on health gain as measured by QALYs. On this basis the incremental cost effectiveness ratio was £26,000 with the authors describing circumstances in which the intervention may be cost effective, and an accompanying sensitivity analysis.[34]

## DISCUSSION

### Summary of findings

The available evidence from controlled trials of interventions by healthcare professionals managing physical LTCs in people who are homeless does not show any convincing effects on unscheduled healthcare utilisation.[34-36] The

impact on mortality was not assessed, and evidence for the impact on biological markers of disease control is limited to a few studies on HIV, which did not show any evidence of benefit on viral load.[46 47] Patient-centred interventions – incorporating case management, education, self-management support and social support – may improve disease specific knowledge in TB, HIV, and Hepatitis C; improve completion of DOT in latent TB; and increase access to primary care in combination with clinic orientation.[36 40-42 49] Cash and non-cash incentives, in the context of DOT for latent TB, may improve clinic attendance and treatment adherence; however treatment completion rates vary between different studies of similar interventions.[32 33 44] It is not clear if improvement in these intermediate outcomes impacts other clinical outcomes, or if effects are sustained beyond the course of treatment evaluated in these studies. There was only one study of cost effectiveness.

**Strengths and Limitations**

The strengths of this review include a-priori methods with a robust process for study identificatuion, appraisal, data extraction and description.[28] The comprehensive search strategy included database searches supplemented by hand searching, forward citation searching, grey literature, and contact with study authors. All screening and data extraction was performed by two reviewers independently. We also described the components of each intervention using a previously defined taxonomy,[31] which is important when reviewing complex interventions such as those included.[51 52] However, many of the findings, particularly those concerning adherence to treatment, were in the context of specific conditions (e.g. latent TB), included a time-limited course of

treatment, and were conducted in a single centre. All but one of the included studies was from the USA. As such the findings may not be directly applicable to other disease areas or other health and social care contexts. Limitations in the existing evidence base also meant we were unable to undertake a formal meta-analyses. Contacting study authors to obtain results pertaining to participants who were homeless (when not reported separately) contributed to the comprehensiveness of the review, however this strength needs to be balanced against the potential bias of performing *post-hoc* secondary analyses on existing trial data. Furthermore, in such circumstances studies are not specifically powered to assess outcomes in this subgroup.

This review is timely given the increasing number and complexity of physical LTCs among people who are homeless,[1] the pressure on healthcare services to address this burden, and the potentially expanding roles of various healthcare professionals to support physical LTC management.[23] However, by focusing on interventions by healthcare professionals this review may overlook evidence for housing or social interventions that may impact on physical LTCs.[53 54]

**Implications for practice, policy and research.**

Despite the social complexity and exclusion that typify the experience of homelessness, a patient-focused case-management approach was shown to positively impact disease specific knowledge and self-efficacy in the management of physical LTCs.[40-42 49]

It is not clear to what extent the findings presented here are generalisable to wider social or healthcare contexts. The evidence for improved adherence was predominantly in the context of DOT for latent TB and in some cases involved cash incentives. Further research would be required to establish whether these principles of adherence support are transferable to the long-term management of non-communicable diseases. Further research may benefit from being multicentre and having a longer duration of follow up. Furthermore, the potential efficacy of cash incentives will vary between societal contexts where access to, and the extent of, financial support varies widely. The application of such findings, derived from studies with short-term durations of follow up, to life-long treatment for other LTCs also has important implications for cost-effectiveness and future research. Finally, the available literature focuses mainly on the role of nurses and physicians, often alongside other ancillary staff (such as peer advisors, case-managers and care coordinators), with little consideration of the potential role of other healthcare professionals e.g. pharmacists.

Two reports of quasi-experimental studies of specialist primary-care services for people who are homeless were excluded as they had only historical comparator groups.[55 56] Both showed improvements in glycaemic control in diabetes, and improved blood pressure and lipid profiles in Hypertension,[55 56] however emergency department use and hospitalisations both increased. Few included studies concerned the impact on biological markers of disease control, and none evaluated mortality. The extent to which the improvements in knowledge or adherence that have been demonstrated may impact on physical or behavioural outcomes has not been evaluated. This raises the question of how such issues

may be best addressed by future research. It is likely, given their apparent scarcity, that further evaluation of complex interventions to address LTC management (including aspects of randomization, longer follow-up and consideration of broader outcomes) will be needed to inform practice. However, the intrinsic complexity of the experience of homelessness, and the impact this has on health, may require a broader methodological approach (e.g. realist synthesis) to understand the context and process of potential interventions in this area.

Finally, the higher use of emergency healthcare services by people who are homeless makes the reduction of unscheduled healthcare use a potential target for interventions aiming not only to improve the health of such individuals, but to ease pressure on healthcare services and reduce costs. There is a need to evaluate anticipatory interventions, aiming to prevent or pre-empt the development of health crises. Based on existing patterns of need and service utilisation, as well as the need to demonstrate effectiveness and cost-effectiveness of novel models of care, well designed and conducted studies following a framework for testing complex interventions [52] for people who are homeless are overdue.

## Conclusions

Trials of interventions delivered by healthcare professionals for the management of physical LTCs in people who are homeless do not show convincing evidence of the primary outcome measure for this review – an impact on unscheduled healthcare utilisation. A patient-centred case-management approach may

improve knowledge and self-efficacy. These interventions, as well as incentives, may also improve adherence in specific contexts. The impact on biological outcomes and mortality remains largely unexplored, as does the economic impact of successful interventions. Future complex intervention evaluation research is needed to test innovative models of care, and expand those interventions showing promise, into diverse health and social care contexts.

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**Competing interests**

None declared

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**Data sharing**

Full details of the screening process are detailed in the supplementary appendices. Any additional detail will be available on request from the corresponding author.

**Contributions**

All authors listed fulfil the ICMJE criteria for authorship. RL conceived the initial idea. All authors (PH, LY, RE, LG, AEW, FM and RL) contributed to the conception and design of the proposed study. PH, LY, RE, AEW, FM and RL contributed to the development of data sources and search strategy. PH, LY, RE, AEW, FM and RL developed and refined the inclusion criteria. PH, LY, RE, LG, FM and RL developed the data extraction template which was piloted by PH, LY and LG. PH,

LY, RE and RL screened titles, abstract and full texts. PH, LY and LG completed data extraction and quality assessment on all included studies. PH wrote the first draft of the manuscript. All authors critically reviewed this and subsequent drafts of the manuscript and provided input into its content. All authors approved the final version of the manuscript to be published. RL is the guarantor of the review. All authors accept accountability for the accuracy of the findings presented.

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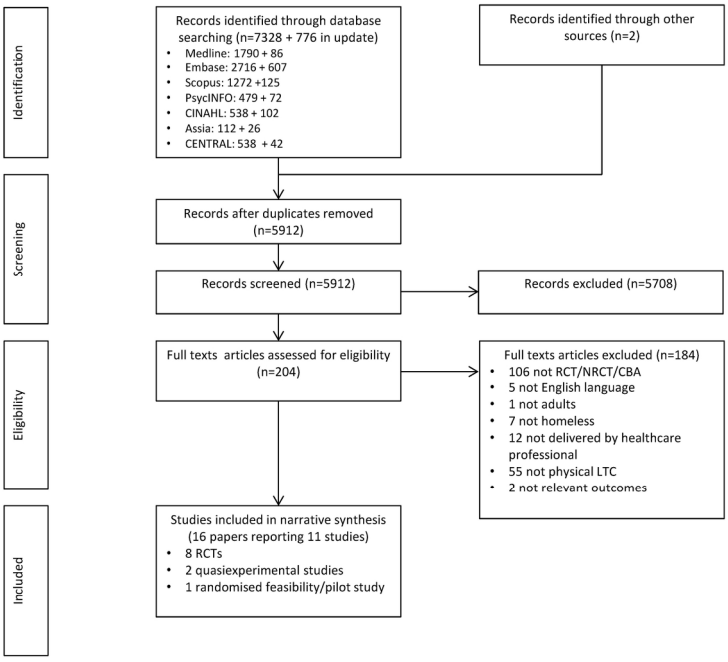


Figure 1: PRISMA diagram of search results and screening

190x142mm (300 x 300 DPI)

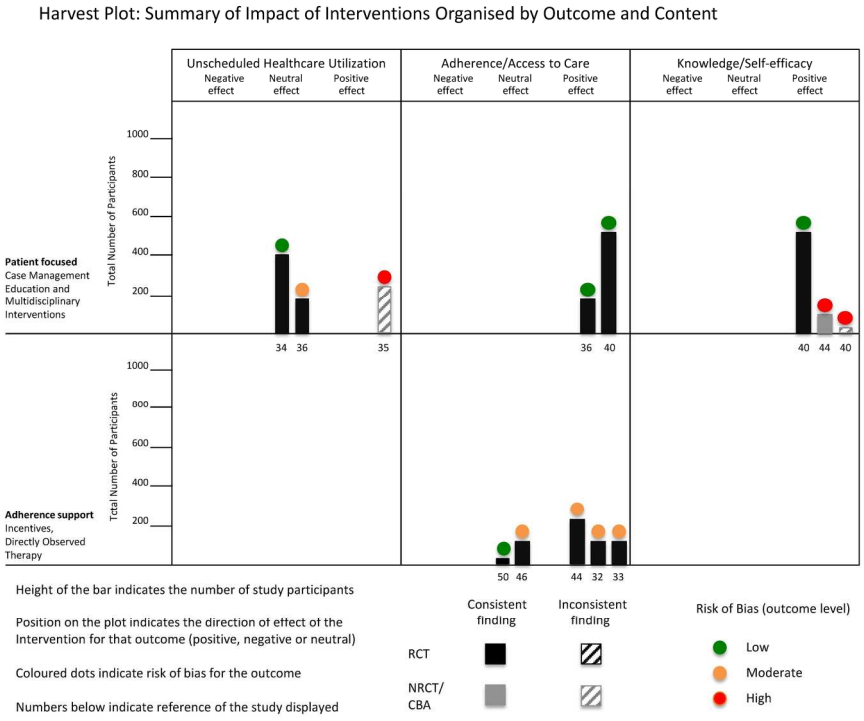


Figure 2: Harvest Plot of findings of included studies

190x142mm (300 x 300 DPI)

| Inclusion Criteria and Search Strategy (adapted from protocol paper *Hanlon et al 2017 [1a]*) | |
|---|---|
| **PICOS component** | **Description** |
| Population | • Adults (≥ 18 years old)<br>• ETHOS criteria for homelessness*<br>• ≥1 physical LTC |
| Intervention | • Be delivered, in whole or in part, by a healthcare professional**<br>• Address the management of one or more physical LTC |
| Comparator | 'Usual care' or alternative intervention<br>Contemporaneous comparator only (exclude historical controls) |
| Outcomes | Primary outcome: Unscheduled use of healthcare services, including:<br>• Emergency department attendance<br>• Hospital admission<br>• Use of out-of-hours services<br>• Ambulance call-outs<br>Secondary outcomes:<br>• Physical health outcomes (e.g. mortality, disease specific markers of control)<br>• Quality of life<br>• Patient engagement (e.g. attendance at planned healthcare services, medication adherence)<br>• Behavioural or cognitive (e.g. self-efficacy, knowledge) changes related to health<br>• Emotional wellbeing, anxiety, and depression<br>• Satisfaction with care<br>• Cost effectiveness<br>• Changes to treatment or medication |
| Settings | Community: interventions delivered solely in non-community settings (e.g. hospitals, ) will be excluded |
| Study design | RCTs (including Cluster RCTs)<br>Non-randomised controlled trials/ quasi-experimental studies<br>CBAs |
| Databases | Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, Cochrane Central Register of Controlled Trials (CENTRAL) |
| Manual searching | Reference lists of all eligible studies.<br>Journal of the Poor and Underserved. |
| Grey literature | Websites of non-governmental organisations that aim to assist homeless persons: Department of Health England webpage; OpenGrey; WorldCat; Grey Literature Report; OAlster and WorldWideScience for reports and theses; British library and Zetoc; Research Councils UK information on publicly funded research; Repositories including Grey Guide and Open DOAR. Other related sites including UK health forum, St. Michael's hospital, and Grey Net. |
| Forward citations | Performed for all included studies (using Web of Science). |
| Contact with study authors | Where data pertaining to homeless participants were not presented separately, we attempted to contact study authors to request these data. |
| Restrictions | English language only |
| Dates | Database: Jan 1966 (or inception) to Oct 2016, updated Nov 2017. Forward citation search completed Mar 2017 |

* Studies including a broader population but including homeless participants will be included only if data pertaining to homeless participants are considered separately.

** any professional trained to provide any form of health care, but excluding social workers and professionals without a health-related training , including, but not limited to, physicians, nurses, dentists, pharmacists, paramedics, mental health professionals, allied health professionals (e.g. physiotherapists, dieticians, clinical psychologists etc.), midwives.

(1a) Hanlon P, Yeoman L, Esiovwa R, Gibson L, Williamson AE, Mair FS, Lowrie R. Interventions by healthcare professionals to improve management of physical long-term conditions in adults who are homeless: a systematic review protocol. BMJ Open. 2017 Aug 21;7(8):e016756. doi: 10.1136/bmjopen-2017-016756.

**Medline Search Strategy***

1. Exp. Homeless Persons/
2. Home?less.mp
3. Roof?less.mp
4. House?less.mp
5. (home* adj2 lack).mp
6. (home* adj2 no).mp
7. (without adj2. Home*).mp
8. (lack adj2 hous*).mp
9. (no adj2 hous*).mp
10. (without adj2. hous*).mp
11. (lack adj2 roof*).mp
12. (no adj2 roof*).mp
13. (without adj2 roof*).mp
14. (inadequate* adj3 hous*).mp
15. (insecur* adj3 hous*).mp
16. (insecur* adj2 tenan*).mp
17. (unfit* adj2 hous*).mp
18. ((transition* or insecure or inadequate or substandard or substandard or sheltered or emergency or intermittent or transient or marginal* or problem*) adj (hous* or home* or accommodat*)).mp
19. (sheltered or unsheltered or shelters).mp
20. Vagran*.mp
21. Destitute.mp
22. Skid row.mp
23. (sleep* adj2 rough).mp
24. ("street person" or "street people"). Mp
25. Exp "Delivery of Health Care"/
26. Exp Primary Health Care/
27. Exp Community Health Services/
28. Exp Chronic Disease
29. ((chronic or long term) adj2 (disease or condition*)).mp
30. Exp Patient Care Management/
31. Intervention*.mp
32. Exp Pragmatic Clinical Trial/ or exp Clinical Trial/ or exp Randomized Controlled Trial/ or exp Controlled Clinical Trial/
33. Trial*.mp
34. Control*.mp
35. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
36. 25 or 26 or 27 or 28 or 29 or 30

| |
|---|
| 37. 31 or 32 or 33 or 34<br>38. 35 and 36 and 37 |
| *Adapted for other databases |

**Additional File 2. Studies Excluded at Full-Text Assessment**

104 not RCT/NRCT/CBA (including those without contemporaneous comparator group) [1-104]

5 not published in English [105-109]

1 did not include adults [110]

6 participants were not homeless, or homeless participants were not considered separately [111-116]

11 intervention not delivered by a healthcare professional [117-127]

55 did not consider physical long-term conditions [128-182]

2 did not report relevant outcomes [183, 184]

**Not RCT/NRCT/CBA with contemporaneous control group**

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| Details of included studies | | | | | | | |
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| **Study** | **Participants** | **Recruitment, retention and attrition** | **Intervention/Comparator (description)** | **Frequency, Duration and Intensity of intervention.**<br><br>**Length of Follow-up** | **Theoretical underpinning of intervention** | **Findings** | **Risk of bias (outcome level assessment –** See Additional File 4 for study level assessment**)** |
| **Ciaranello 2006**<br><br>(quasi-expieri-mental, non-equivalent comparator group) | **Sample:** 6 transitional housing facilities (I: 4, C: 2. Residents (I: ~200, C: ~50) randomly sampled at time points but not followed up individually)<br><br>**Sex:** I: 81% male at baseline, C: 44% male at baseline<br><br>**Age:** I: 41.6 (9.6), C: 41.3 (10.4)<br><br>**LTC:** Various<br><br>**Homeless definition:** Residents of transitional housing facilities, referred to as 'formerly homeless'. | Four transitional housing facilities selected from area in which intervention took place. Comparator was two transitional housing facilities in a different area, under control of a different authority.<br><br>Residents were sampled at baseline and 6 and 18 month follow-up points, however follow-up surveys included residents who had arrived in the intervening period, owing to the usual length of stay of less than 9 months. | **I:** 'Integrated service team' (medical director, nurse practitioner, medical clerk and social worker) made weekly visits to housing facilities. Performed 'comprehensive health assessment', health education, medical and dental referrals, brief psychotherapy, diagnostic studies, and social work services. Supplemented by 24 hour a day nurse telephone-advice line. Additional HIV and TB clinics.<br><br>**C:** 'Usual care'. Facilities under a different healthcare authority. No additional details given | Weekly visits and assessments<br><br>24 hour telephone advice service<br><br>Service delivered for 2 years.<br><br>Data collected by survey of residents at 6 and 18 months post initiation of intervention. | None described | **ED attendances (assessed by survey):** Significantly fewer residents in intervention facilities reporting ≥2 ED attendances in previous 6 months at compared with comparator group at 18 month follow-up (adjusted OR: 0.3, 95%CI 0.12 to 0.74). No significant difference at 6 month follow-up.<br><br>**Hospitalisation (assessed by survey):** No significant difference in adjusted OR of having ≥1 hospitalisation in previous 6 months between intervention or comparator facilities at 6 or 18 months follow-up | **High:** Survey data susceptible to recall bias (e.g. for ED use). Follow-up surveys included people who had arrived in the facility between initial and follow-up surveys. As such changed in outcome variable could be the result of a different sample, rather than changes in outcome relating to the intervention. Also no blinding, randomisation, protection from contamination. Differences in baseline outcomes. |
| | | | | | | **Diastolic blood pressure:** Adjusted mean lower in intervention group at 6 months (mean difference -6.4mmHg, SE 2.4, p=0.03) but not 18 months (mean difference 0.57mmHg, SE 2.3, p=0.80) | **High:** All biases above relalvant, particularly the inclusion of residents arriving between baseline and follow-up. Also unclear if participants were hypertensive as such validity of outcome measure is questionable |
| | | | | | | **Satisfaction with care:** No significant differences described between intervention and control based on survey data. Not further described. | **High:** Biases above also relevant for satisfaction data |
| **Hewett 2016**<br><br>RCT | **Sample:** I: 206, C: 204<br><br>**Sex:** I: 81.6% male, C: 81.4% male<br><br>**Age:** I: 41.6 (12.1), C: 42.5 (11.3)<br><br>**LTC:** Various (79.1% and 76.5% had 'long-term medication condition' in I and C groups, respectively)<br><br>**Homeless definition:** | 1009 patients identified by ward team of whom 622 were eligible. 410 consented and were included in analysis.<br><br>3 month admission data routinely collected and was available for all 410.<br><br>Survey data collected using telephone follow-up and was only obtained for 110 participants (57 | **I:** During hospital admission patients who were homeless were identified by ward teams. Nurse met completes interview including medical, mental health, drug and alcohol details, housing history, care needs and consideration of any goals on discharge.3x weekly GP led ward round reviewing goals, care plans, medial findings and discharge planning. Regular visit by homelessness nurse to provide community links including with social work and | 3-4 times weekly GP ward round during admission<br><br>Initial meeting by nurse followed by liaising with relevant services.<br><br>Weekly multiagency meetings<br><br>Questionnaire data obtained 6 (+/-4) weeks following | None explicitly described. Development of service was the result of quality improvement work based in the study site which has been published and described | **ED attendance:** no significant difference between standard or enhanced care at 12 months (adjusted mean difference -0.8, 95% CI -4.3 to 2.8)<br><br>**Hospital readmission:** No significant difference between standard or enhanced care at 30 or 90 days (adjusted OR 0.83 (95% CI 0.52 to 1.33) and 1.02 (95% CI 0.67 to 1.54), respectively) | **Low:** Data on readmission and attendance was routinely collected and complete data available for those who consented. Protection from contamination and adjustment for baseline imbalances made |
| | | | | | | **Quality of Life:** (EQ-5D-5L questionnaire) Non-statistically significant improvement with enhanced | **Moderate:** Based on survey data with poor response to follow-up. Potential for |

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| | "Homeless" (i.e. no fixed residence) | intervention, 53 comparator).<br><br>Consent to longer term follow up (1 year) was a change in protocol. Consent obtained from 226 participants). | housing services. Weekly multiagency meeting in which housing manager, social workers, drug and alcohol workers, liason psychiatry, street outreach workers, hostel key workers and ward staff met with 'pathway' team to review discharge plans for all patients.<br><br>**C:** Visited once by homelessness nurse and given information leaflet detailing local services | discharge.<br><br>Emergency department attendance assessed at 1 and 3 months, readmission at 3 months. | | care over standard care at 6 week follow-up (adjusted mean difference 0.09 (95% CI -0.03 to 0.22) | selection bias from those who responded to follow-up. |
| | | | | | **Cost effectiveness:** £26,000 per quality adjusted life year | **Moderate:** Based on survey data with poor response to follow-up. |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, Nyamathi 2008**<br><br>RCT | **Sample:** I: 279, C: 241<br><br>**Sex:** 79.6% male<br><br>**Age:** 41.5 (SD 8.5)<br><br>**LTC:** Latent TB (a subset of these judged at risk of HIV also identified)<br><br>**Homeless definition:** Individuals having spent the night prior to recruitment at one of the study shelters considered homeless and eligible for inclusion<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment by flyers in 12 homeless shelters.<br><br>3959 screened, 980 PPD positive. 25 refused CXR, 199 did not return for follow-up. 221 not eligible due to active TB, suspected TB or other medical indications.<br><br>520 randomised<br><br>Follow-up data on 494 | **I:** Delivered alongside Directly Observed Therapy (DOT) for latent TB. Research nurse and outreach worker delivered 8 1-hour TB education sessions. Focus was on self-esteem, TB and HIV risk, coping, self-management, problem solving and positive relationships and social networks to maintain behaviour change. Provided with community resourced and escorted to appointments. Participants not attending were tracked by the outreach worker.<br><br>**C:** 20 minute lecture and 10 minute discussion with study nurse in addition to DOT. | 8 1 hour sessions over a period of 6 months. | Comprehensive Health Seeking and Coping Paradigm. | **Completion of Directly Observed Therapy for Latent TB:** Nurse led case management with education, incentives and tracking associated with improved DOT completion (61.5% completion vs 39% with usual care, adjusted OR for completion 3.01 (95% CI 2.15 to 4.20). | **Low:** Complete outcome data available and adjusted for potential confounders in multivariate analysis. |
| | | | | | **TB knowledge:** Latent variable analysis showed nurse-led case management predicted greater TB knowledge at 6 month follow-up. **HIV knowledge/self-efficacy:** Latent variable analysis of subgroup at risk of HIV showed nurse-led case management predicted greater HIV knowledge and greater self-efficacy for condom use at 6 month follow-up. | **Low:** two separate models used to control for numerous confounders and assess magnitude of the impact of inter intervention on knowledge. |
| **O'Toole 2015**<br><br>RCT | **Sample:** I: 123, C: 62<br><br>**Sex:** 94% male<br><br>**Age:** 48.5 (SD 10.8)<br><br>**LTC:** 72.7% reported at least one chronic medical problem, most commonly hypertension, arthritis/chronic pain, | Recruitment from 11 community sites (soup kitchens, transitional and emergency shelters, drop-in centres). Potential participants identified in common areas and provided with information about the study. No healthcare services offered at time | **I: Group 1**, (n=39), personal health assessment/brief intervention. Nurse led interview about medical history, health, risk behaviours, barriers to care, medications and self-identified needs. Cursory examination. Brief motivational interview and summary of findings highlighting unmet health needs. No clinic orientation performed | Personal health assessment was a brief, one off, intervention. As described. Lasted 20-30 minutes.<br><br>Clinic orientation also a one off intervention. 15-20 minutes. Also transport to clinic. | None described | **ED attendance**: no significant difference between groups (ANOVA p=0.61) **Medical hospital admission:** no significant difference between groups (ANOVA p=0.07) | **Moderate:** Post-hoc analysis and very small number of events. High possibility of type 2 error. Randomised design, routinely collected data reduce potential bias. |
| | | | | | | **Access to primary care:** Cox regression using usual care as baseline showed clinic orientation alone (HR 2.64 (95% CI 1.54 to 4.53)) and physical health assessment in | **Low:** Primary outcome with design focused on assessing outcome. Participants all eligible for veterans' services and data on usage routinely |

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| | hepatitis/cirrhosis<br><br>**Homeless definition:** "lacking a fixed, regular and adequate night-time residence" plus eligible for Veterans Healthcare Services. Must have not been in receipt of primary healthcare services in previous 6 months | of recruitment.<br><br>221 enrolled, 36 removed as ineligible (6 duplicate enrolment, 15 not eligible for veterans' services, 14 receiving primary care in prev. 6 months, 1 did not adequately complete baseline assessment).<br><br>Follow-up for re-interview was 81% at 1 month and 71% at 6 months. | **Group 2,** (n=40), clinic orientation, transported to clinic and introduced to clinic team. Orientated to services available. Usual care only following this. **Group 3,** (n=44), physical health assessment plus clinic orientation.<br><br>**C:** Usual care, comprising social-worker administered assessment of homelessness and social needs, description of services available and how to access (verbal or written) | Follow-up at 1 and 6 months. | | combination with clinic orientation (HR 3.41 (95% CI 2.02 to 5.76)) were both significantly associated with improved primary care access. Unadjusted Chi-squared estimates were significant at both 4-weeks and 6-months with usual care showing lowest rates of access. | collected and complete for eligible participants. Potential bias from randomisation procedure for clinic orientation arm as randomised by calendar day based on attendance. |
| **Pilote 1996**<br><br>RCT | **Sample:** I1: 83, I2: 82, C: 79<br><br>**Sex:** I1: 71% male, I2: 67% male, C: 66% male<br><br>**Age:** Median: I1: 40, I2: 39, C: 40<br><br>**LCT:** Latent TB<br><br>**Homeless definition:** "homeless", not further defined<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | During a population based survey of TB and HIV, homeless people with positive purified protein derivative (PPD) were assessed approached for inclusion.<br><br>1608 interviewed, 1257 had skin tests and returned for evaluation. 441 PPD positive. 297 of these eligible (no recent follow-up). 244 agreed to participate. | **I1:** Monetary incentive. $5 incentive given on attendance to TB clinic follow-up in addition to appointment and bus tokens received by all participants.<br><br>**I2:** Peer health advisors: In addition to bus tokens and appointment, peer health advisors met participants in shelters, accompanied to appointment, helped with paper-work and orientation.<br><br>**C:** Usual care. Bus tokens and TB clinic appointment only. | One off payment for monetary incentive arm.<br><br>One off intervention in peer health advisor arm, as described. Included transport assistance and support in attendance. | None described | **Attendance at initial TB clinic follow-up:** Monetary incentive (84%) and peer health advisor (75%) groups more likely to attend appointment than usual care (53%) (p=<0.001 and p=0.004, respectively). Both interventions significant predictors of adherence in multivariate analysis. | **Moderate:** Details of randomisation not clear and blinding not possible, otherwise low risk of bias. |
| **Samet 2005**<br><br>RCT | **Sample:** I: 74 (15 homeless), C: 77 (19 homeless)<br><br>**Sex:** 84% male (homeless subset)<br><br>**Age:** Median: 43.6 (37.9-45.0) (homeless subset)<br><br>**LCT:** HIV | Participants were from a longditudinal cohort study (HIV Alcohol Longitudinal Cohort). Mostly recrtuied from Boston Medical Centre Clinic.<br><br>Of 74 randomised to intervention, 56 received complete intervention, 13 received partial | **I:** ADHERE intervention:<br>- Assessment and discussion of alcohol and substance use of readiness for behaviour change.<br>- A watch that served as a medication timer reminder.<br>- Enhancement of perceived efficacy of medications. | Baseline visit at medical centre lasting 60 minutes.<br><br>Home visit within 3 weeks of intervention lasting 30-45 minutes.<br><br>1-month follow-up at assessment centre: 15-30 minutes. | Intervention used behavioural science theories using motivational interviewing to promote behaviour change and using principles of the Health Belief Model to support the benefit and need for therapy. | No separate analysis of homeless participants is provided in the published paper. Analyses were repeated on the homeless participants only using Generalised Estimating Equations as described in the original manuscript. Data were provided by the study authors and the analysis was performed by the review authors. Models were fit to analyse the overage intervention effect over time. | **Low:** Objective assessment of outcomes and adjustment for baseline variables |

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| | **Homeless definition:** "homeless" as a variable – not otherwise defined<br><br>**Inclusion/exclusion:** HIV positive participants with a history of alcohol problems (current or lifetime history of alcohol abuse or dependence – CAGE questionnaire or study clinician diagnosis). Participants also needed to be taking antiretroviral medication. | intervention, 5 received no intervention (could not be contacted). Homeless proportions of these numbers not available.<br><br>10 in total lost to follow-up (3 control, 7 intervention). Proportion of these who were homeless not stated. | - Individualised HIV counselling – ways to tailor medication use to specific circumstances.<br><br>**C:** Standard care. At study period this included verbal or written instructions regarding antiretroviral treatment and adherence strategies. | 3 month follow-up visit at medical centre: 15-30 minutes.<br><br>At follow-up visits all 4 components of the intervention were reassessed and reinforced. | | **Adherence to Antiretroviral treatment:** No significant improvement with intervention after controlling for baseline adherence (p=0.55) | |
| | | | | | | **CD4 count:** No significant change in CD4 count with the intervention after adjusting for baseline CD4 count (p=0.31)<br><br>**HIV1-RNA:** No significant reduction in viral load seen with intervention after adjusting for baseline laboratory estimates. (p=0.23) | **Low:** Objective assessment of outcomes and adjustment for baseline variables |
| **Savage 2014**<br><br>Randomised pilot/ feasibility study | **Sample:** I: 6, C: 3<br><br>**Sex:** Not specified<br><br>**Age:** Not specified<br><br>**LTC:** Type 2 diabetes mellitus<br><br>**Homeless definition:** Those living without adequate shelter or in temporary accommodation. | Convenience sample recruited from a homeless clinic. Unclear how those with type 2 diabetes were identified. 9 identified in total for participation in feasibility study. | **I:** Nursing case-management with diabetes self-management. Education sessions delivered alongside nursing case-management (6 sessions total).<br><br>**C:** No intervention | 6 sessions over 12 weeks. Each 45 minutes long. | Chronic disease self-management approach based on self-efficacy theory. | **Self-efficacy:** paper states "participants who attended the intervention had higher scores on some outcome variables, most notable in cognitive symptom management, which improved from a pre-intervention score of 1.3/5 to a post-intervention score of 2.75". Participants in comparison stated to have "similar scores" at baseline and 12 week follow-up. | **High:** Randomisation not clear. Incomplete outcome reporting. No assessment of baseline imbalances. Small sample size, incomplete recruitment. |
| **Tsai 2013, Tsai 2013, Grelotti 2016**<br><br>RCT | **Sample:** I: 66, C: 71<br><br>**Sex:** I: 91% male, C: 89% male<br><br>**Age:** I: 44 (37-53), C: 42 (37-49)<br><br>**LTC:** HIV<br><br>**Homeless definition:** "Homeless or marginally housed". Not further defined<br><br>**Inclusion/exclusion:** HIV positive, depression (DSM-IV). Excluded if self-report of alternative | Participants identified from homeless shelters, free-lunch programmes, low-income single-room occupancy hotels, public HIV clinics and social service agencies.<br><br>Block randomisation.<br><br>1555 screened. 647 potentially eligible. Of these 190 met DSM-IV criteria for depression. | **I:** Psychiatric evaluation and prescription of fluoxetine. Directly observed therapy for 24 weeks. Psychiatric interview was carried out weekly. 25 dollar reimbursement given per week for all doses.<br><br>**C:** Advised of diagnosis of depression and advised to seek treatment at a public mental health clinic specialising in care of HIV positive persons. 25 dollar incentive for attending study site weekly for data collection. | Weekly dispensing and incentive. Weekly psychiatric evaluation.<br><br>Follow-up 6 months. | None stated | **Adherence to antiretroviral therapy:** Mixed-model analysis showed no statistically significant effects of the intervention on antiretroviral therapy update (adjusted OR 1.18 (95% CI (0.83 to 1.68)). Percentage of antiretroviral adherence was similar in intervention and comparator groups. | **Moderate:** Low risk from study design however unannounced pill-counts on a monthly basis may not be a robust method of assessing compliance with treatment. |
| | | | | | | **HIV-1 viral load:** No statistically significant difference in viral suppression between intervention and comparator group (adjusted OR 1.04 (95% CI 0.97 to 1.12). | **Low:** Good methodological rigour across study (Additional file 4) and objective measurement of outcome |
| | | | | | | **Depression:** Improved mood in both study arms. Statiscially significant treatment effect observed using with Ham-D and BDI-II scores to assess depression. | **Low:** Good methodological rigour across study (Additional file 4). Assessed as primary outcome with analysis designed around this. Two measured used and compared |

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| | psychiatric diagnosis. | | | | | | as sensitivity analysis. |
| **Tulsky 2000**<br><br>RCT | **Sample:** I1: 43, I2: 37, C: 38<br><br>**Sex:** 89% male<br><br>**Age:** Median 37<br><br>**LTC:** Latent TB<br><br>**Homeless definition:** Either "literally homeless", staying in emergency shelter, street, car, or other shelter not designed for sleeping, or "maginally housed", staying in low-cost temporary accommodation.<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>Eligibility was positive TST and no TB follow-up in previous 6 months.<br><br>2158 screened. 618 positive TST. 89 refused randomisation. 199 ineligible as did not return or rsults, HIV infection, recent screening with chest x-ray or current isoniazid treatment. 330 randomised and attended clinic. Of these 121 prescribed isoniazid.<br><br>3 stopped due to toxicity. 118/121 analysed. | **I1:** Monetary incentive: $5 at each twice weekly visit for directly observed isoniazid. If a dose missed, attempts to contact participant made by letter or telephone call. Any onward referrals were made by TB clinic, not research assistants following up patients.<br>**I2:** Peer health adviser: Adviser provided and observed isoniazid twice weekly. Adviser accompanied participant for monthly refill appointments. If appointments missed, adviser spent an allotted amount of time looking for the participant.<br><br>**C:** Usual care: routine TB clinic care. Given 1 month supply of treatment and monthly drop in follow-up scheduled. Adherence monitored by TB charts. For non-attendance, standard follow-up or 3 letters or telephone calls. Treatment not directly observed. Protocol change during study due to low initial clinic attendance in usual care arm meant that the protocol was changed to offer all participants $5 at the initial visit. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion significantly higher in monetary incentive group (44%) than peer advisor (18%, p=0.01) and usual care (26%, p=0.04). No statistically significant difference between peer advisors and usual care. Multivariate analysis comparing monetary incentive to peer advisors and usual care considered together (i.e. single comparison group) showed monetary incentive arm significantly more likely to complete treatment (Adjusted OR 2.57 (95% CI 1.11 to 5.94)). | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |

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| **Tulsky 2004**<br><br>RCT | **Sample:** I: 72, C: 69<br><br>**Sex:** 85% male<br><br>**Age:** Median 41 (21-79)<br><br>**LTC:** Latent TB<br><br>**Homeless definition:** "true homeless", street or shelter dwelling, or "marginally housed", staying in low-cost temporary accommodation<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>2570 tested. 647 positive TST, 488 new or required further screening. 95% accepted referral. 353 attended initial appointment. 212 of these were not randomised (190 not prescribed isoniazid, 6 active TB, 16 refused). 141 randomised.<br><br>16 not prescribed isoniazid after diagnostic tests (4 cash, 12 non-cash). 6 censored (3 cash, 3 non-cash). | **I:** Cash incentive: $5 payment for keeping twice weekly appointment for directly observed isoniazid therapy. Tracking included names and addresses of family, friends and case workers. Missed appointments were followed up by letters, telephone calls, and using tracking information, following a protocol specifying a number of outreach attempts.<br><br>**C:** Non-cash incentive: A choice of fast-food or grocery coupons, phone cards or bus tokens with a value of $5 was offered from each kept appointment. Tracking and follow-up of missed appointment was identical to the cash incentive group. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion rates were 89% with monetary incentives and 81% with non-monetary incentives (no statistically significant difference, p=0.23) | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |
| **Tyler 2014**<br><br>Randomised quasi-experimental | **Sample:** I: 46, C: 61 (Hepatitis C positive subset only)<br><br>**Sex:** 79% male<br><br>**Age:** males 44 (7.1), females 45.3 (8.9)<br><br>**LTC:** Hepatitis C<br><br>**Homeless definition:** "homeless". Not further defined.<br><br>**Inclusion/exclusion:** Recruitment was to a vaccine study (Hep A/B). Data presented here | Recruitment view flyers in homeless shelters within the study area. | **I:** Case management in the context of a hepatitis A/B vaccination programme. Three 40 minute group sessions delivered by study nurse with education on hepatitis A, B, C and HIV diagnosis, prevention and transmission. Self-management training. Case management focusing on self-esteem, social, behavioural and communication skills. Behavioural education around blood-borne virus risk. Also included participant needs assessment and onward referral to address medical, mental health, food, shelter and transportation needs. | Total of 3 group session across study period in intervention group. Time-frame not specifically stated.<br><br>Outcomes assessed 6 months post-intervention | Based on the Comprehensive Health Seeking and Coping Paradigm (CHSCP) | **Hepatitis C knowledge:** Measured using a modification of an 18 item tool initially developed for tuberculosis. Greater improvement in the nurse case-managed group than the standard intervention in the hepatitis C positive subset. Statistical analysis of the significance of the difference between intervention and control groups not performed for the hepatitis C positive subset. | **High:** Randomisation was carried out according to a protocol to assess the vaccine efficacy, not that of the case-management/education intervention. Futhermore, while data on the hepatitis C positive subset are presented, the study design and analysis was not focused on a comparison of intervention and control intervention in this subset of participants. As such baseline imbalances and sequence of allocation could introduce bias for the outcome of hepatitis C knowledge. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | pertain to hepatitis C positive subset | | **C:** Single brief 20 minute presentation around hepatitis A, B, C and HIV at baseline visit of vaccination programme. | | | | |

| Characterisation of Interventions by the Effective Practice and Organisation of Care (EPOC) Taxonomy | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study** | **How** care is delivered | | **Where** care is delivered | | | | **Who** and delivers care | | | **Coordination** of care | | | | | | | | **Finance** |
| | Group/ Individual deliver | Coordination of care providers | Orientation to environment/ facilities | Outreach services | Changing site of service delivery | Transportation services | Role expansion | Self-management | Recruitment of specific professionals | Care pathways | Case management | Communication between providers | Discharge planning | Diagnostic and treatment services | Integration of services | Shared care | Multi-disciplinary teams | Incentives (monetary or not) |
| **Cianarello 2006** | Individual | | | Took place in transitional housing facility | Services delivered at transitional housing facilities | | | Health education a component of intervention | | | | Liaising with social work | | Diagnostic studies and medical referral carried out | | | Multidisciplinary model of service provision | |
| **Hewett 2016** | Individual | Liaising between inpatient and community services | | | | | GPs delivering ward-based care. Homeless-specific nurses | | Specialised "pathway" team | Focus of the intervention | | "Pathway" meeting with further liaising with community services | Focus of the intervention | | Liaising between inpatient and community services. Needs assessment | "pathway" and ward inpatient teams | MDT meeting key part of intervention | |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, and Nyamathi 2008** | Group | | | Tracking of non-attenders | | Escorted to appointments | | Education and self-management focus of the case-management sessions | | | Focus of intervention, given in addition to DOT for latent TV | | | In context of DOT | | | | Incentive to both groups when taking DOT. |
| **O'Toole 2014** | Individual | | Clinic orientation arm and combined arm. | Both arms | | Clinic orientation arm and combined arm. | | Health promotion within personal health assessment arm and combined arm. | | | Personal health assessment and combined arm | | | Personal health assessment and combined arm | | | | |
| **Pilote 1996** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Samet 2005** | Individual | | | Home visit at 3 weeks to reinforce intervention | | | | Motivational interviewing for behaviour change and adherence support | | | | | | Tailored support for antiretroviral treatment. | | | | |
| **Savage 2014** | Individual | | | | | | | Educational intervention | | | | | | | | | | |
| **Tsai 2013, Tsai 2013, Gerlotti 2014** | Individual | | | | | | | | | | Psychiatric evaluation and initiation of therapy | | | Treatment of comorbid depression | | | | Monetary incentive for treatment |
| **Tulsky 2000** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Tulsky** | Individual | | | | | Bus tokens to | | | | | | | | | | | | Both |

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2004** | | | | | | all groups | | | | | | | | | | | | study arms |
| **Tyler 2014** | Group | | | | | | | Health promotion and transmission prevention education | | | Case management on top of vaccination programme | Onward referral for medical or social needs | | | | | | |

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7<br>Additional file 1 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 7-8<br>Additional file 1 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Additional file 1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8<br>Additional file 5 |

# PRISMA 2009 Checklist

| | | | |
|---|---|---|---|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 8 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 9 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 10 |



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 8<br>Additional file 4 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | n/a |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1, Page 11 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 11,12<br>Table 1 (page 13)<br>Additional file 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table 2 (page 15) |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 18-23 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | n/a (figure 2 summarises narrative synthesis) |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Figure 2, Additional |

# PRISMA 2009 Checklist

| | | | |
|---|---|---|---|
| | | | file 4, |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 24 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 25 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 28 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 29 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

BMJ Open

# A Systematic Review of Interventions by Healthcare Professionals to Improve Management of Non-communicable Diseases and Communicable Diseases Requiring Long-term Care in Adults who are Homeless



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|---|---|
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| Secondary Subject Heading: | General practice / Family practice |
| Keywords: | Homelessness, chronic disease, long-term conditions, Complex interventions |
| | |

# A Systematic Review of Interventions by Healthcare Professionals to Improve Management of Non-communicable Diseases and Communicable Diseases Requiring Long-term Care in Adults who are Homeless

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**Word Count: 4618**

## Abstract

**Objective:** Identify, describe and appraise trials of interventions delivered by healthcare professionals to manage non-communicable diseases (NCD) and communicable diseases requiring long-term care (LT-CDs), excluding mental health and substance use disorders, in homeless adults.

**Design:** Systematic review of Randomised Controlled Trials (RCTs), Non-randomised Controlled Trials and Controlled Before-After studies. Interventions characterised using Effective Practice and Organisation of Care (EPOC) taxonomy. Quality assessed using EPOC Risk of Bias (ROB) criteria.

**Data sources:** Database searches (Medline, Embase, PsycINFO, Scopus, CINAHL, Assia, CENTRAL), hand searching reference lists, citation searches, Grey literature, and contact with study authors.

**Setting:** Community.

**Participants:** Adults (≥ 18 years) fulfilling European Typology of Homelessness (ETHOS) criteria.

**Intervention:** Delivered by healthcare professionals managing NCD and LT-CDs.

**Outcomes:** Primary outcome: unscheduled healthcare utilization. Secondary outcomes: mortality, biological markers of disease control, adherence to

treatment, engagement in care, patient satisfaction, knowledge, self-efficacy, quality of life, cost-effectiveness.

**Results:** 11 studies were included (8 RCTs, 2 quasi-experimental, 1 feasibility) involving 9-520 participants (71-94% male, median age 37-48). Ten from USA, one from UK. Studies included various NCDs (n=3); or focused on latent tuberculosis (n=4); HIV (n=2); Hepatitis C (n=1); or Type 2 Diabetes (n=1). All interventions were complex with multiple components. Four described theories underpinning intervention. Three assessed unscheduled healthcare utilization: none showed consistent reduction in hospitalization or emergency department attendance. Six assessed adherence to specific treatments, of which four showed improved adherence to latent TB therapy. Three concerned education case-management, all of which improved disease specific knowledge. No improvements in biological markers of disease (two studies) and none assessed mortality.

**Conclusions:** Evidence for management of NCD and LT-CDs in homeless adults is sparse. Educational case-management interventions may improve knowledge and medication adherence. Large trials of theory-based interventions are needed, assessing healthcare utilization and outcomes as well as assessment of biological outcomes and cost-effectiveness.

**Abstract word count: 300**

## Strengths and Limitations of the Study

- This is the first systematic review to explicitly focus on NCD and LT-CD management for adults who are homeless.
- A comprehensive search strategy was supplemented with hand searching, Grey literature searches and contact with study authors.
- Interventions are described using the Effective Practice and Organisation of Care (EPOC) Taxonomy
- Significant heterogeneity precluded meta-analysis, so a narrative synthesis is presented along with a Harvest Plot summarising study findings.
- Evidence available is mostly limited to the USA, with one study from the UK.

## INTRODUCTION

The prevalence of homelessness is increasing across high income countries.[1] The experience of homelessness is associated with increased morbidity and mortality.[2-4] Social exclusion and socio-economic deprivation,[5 6] adversity over the life course,[7] and environmental and behavioral risk factors[8] typical of homelessness, contribute to an increased prevalence of a range of health problems compared to the rest of the population.[1] This review focuses on both non-communicable diseases (NCD) and communicable diseases that require long-term care or treatment (LT-CDs), excluding mental health and substance use disorders. We take this focus because, compared to interventions for mental health disorders or substance use disorders, the management of NCD and LT-CDs in the context of homelessness has not been synthesised in the systematic review literature.[9] Such conditions disproportionateley affect people who are homeless (e.g. TB rates between 20 times higher than general population, generally pooprer control of diabetes and hypertension and higher cardiovascular mortality).[1] Innovative models of care and expanded roles of healthcare professionals offer potential strategies to target NCDs and LT-CDs.

Outcomes of both NCDs and LT-CDs are poorer among people who are homeless.[10 11] Engagement with scheduled appointments, preventative health services and adherence to treatment are typically lower.[12-15] Barriers to access, conflicting priorities, physical and mental multimorbidity are thought to contribute to poorly coordinated use of healthcare services. [15] Consequently, there is a need for tailored services.[15-17] Healthcare delivery models for people

experiencing homelessness include specialised or generalist primary care services;[18] and integrated housing and health interventions. There is insufficient evidence of reach and effectiveness to favour one model over another.[19] The expanding role of various healthcare professionals e.g. registered nurses and pharmacists, targeting NCD/LT-CDs,[20] offers a complementary model of healthcare for people who are homeless. Sharing clinical roles may be welcome given the increasing evidence of multimorbidity and polypharmacy.[21]

Controlled evaluations of models of healthcare for people who are homeless are relatively few and optimal delivery varies between different health and social care systems.[17] There have been calls to evaluate more interventions to improve the health of people who are homeless,[22] including long-term prospective studies with economic analyses.

Previous systematic reviews have identified the potential benefit of tailored interventions for addressing mental health disorders and at-risk substance use.[23] [24] These have shown potential for monetary incentives to improve adherence for people who are homeless with latent tuberculosis,[23] and that provision of housing improved health outcomes in HIV.[24] However, to the authors' knowledge, no previous systematic reviews have specifically focussed on the potential impact of healthcare professional or other intervention on NCDs and LT-CDs for adults experiencing homelessness.

**Aims**

This review aims to systematically identify, describe and appraise trials of interventions focusing on the management of NCD and LT-CDs, delivered by healthcare professionals for adults who are homeless. It addresses the following two research questions:

1. What are the key components of interventions delivered by healthcare professionals aimed at improving management of NCD and LT-CDs including theoretical underpinnings?
2. What impact has been demonstrated by trials of interventions delivered by healthcare professionals aimed at improving management of NCD and LT-CDs?

## METHODS

This systematic review followed a pre-specified protocol [25](registered with PROSPERO, ID: CRD42016046183, available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046183) and is described according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[26]

### Eligibility Criteria

Eligibility criteria and search process are described in detail in our published protocol paper,[25] and are outlined briefly below. Full details are given in Additional File 1. Homelessness was defined according to the ETHOS criteria[27]. Eligible studies included adult participants who met the ETHOS defined homelessness criteria with one or more NCD or LT-CDs or those concerning management of these conditions as part of a broader intervention (e.g. access to primary care). We considered any change to the organization or delivery of care to be an intervention. Delivery by a healthcare professional was required, defined as a person with professional training or registration to provide healthcare. Peer-health advisors (lacking professional training) and social workers (lacking health-specific training) were not considered healthcare professionals, however interventions involving a wider range of roles were eligible for inclusion if a healthcare professional was involved in delivery as part of a wider team.

We considered a range of pre-specified outcomes. Studies including any of our primary or secondary outcomes were eligible for inclusion. Unscheduled healthcare utilization was our primary outcome. Secondary outcomes included physical measures of disease control, quality of life, behavioural outcomes, emotional wellbeing, satisfaction with care and cost effectiveness. These are fully detailed in Additional File 1

**Literature Search**

Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1966 (or inception) until October 2016. The search was updated in November 2017. Our search strategy was "homelessness" AND "NCD/LT-CDs or healthcare delivery terms" AND "trial or evaluation terms". The full search terms for Medline are shown in Additional File 1 and were adapted for other databases. Database searches were supplemented by hand searching of reference lists of all eligible studies, hand searching the Journal of the Poor and Underserved, and forward citation searches of included studies using Web of Science. A number of 'Grey Literature' sources were also searched, (Additional File 1). Grey literature and relevant conference abstracts were used to identify recently publishes studies.

Two reviewers (PH plus LY, RL or RE), using DistillerSR software, independently screened titles and abstracts of all records identified. Full texts of all potentially eligible studies were obtained and assessed independently by two reviewers (PH, LY or RE) against the eligibility criteria. At all levels disagreements were

resolved by discussion, involving a third reviewer (RL or LY) when consensus could not be reached. Where studies included homeless participants but analysis of these participants was not presented separately, we contacted the study authors to request these data. Studies were excluded if these were not available. Using a standardised data extraction form, two reviewers (PH plus LY or LG) independently extracted data from each study eligible for inclusion. The components of each intervention were described according to the Cochrane Effective Practice and Organization of Care (EPOC) taxonomy.[28] Two reviewers independently assessed each study according to the criteria outlined in the Cochrane EPOC guidelines for assessing risk of bias (ROB) in RCTs, non-randomised controlled trials and CBA studies.[28] After grading each study a judgment of the overall risk of bias was made for each outcome, taking into account the relative importance of potential sources of bias to the outcome in question.

**Synthesis**

We assessed the clinical and methodological heterogeneity of the eligible studies. Few studies considered similar outcomes, and those that did had either different comparator groups,[29 30] differing methods of assessing similar outcomes (e.g. survey vs. routine data for emergency department (ED) attendance)[31 32] or concerned complex interventions, the diversity of which would limit the utility of a pooled analysis.[31 33] Consequently, a meta-analysis was deemed inappropriate and we performed a narrative synthesis of the study findings. Studies were

grouped by outcome and the strength of the body of evidence for each outcome was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.[34]

We constructed a Harvest Plot *post hoc* to display the results. Harvest plots use bars representing individual studies placed on a plot matrix to indicate whether the review intervention showed an overall positive, negative, or no consistent effect for the outcome in question. They enable data to be summarised when study designs and outcomes are diverse and heterogeneous.[35 36] We used the following criteria to decide how each study should be displayed:

- Height of the bar represented the number of participants in the study;
- RCTs were displayed in bold with other designs in grey;
- The risk of bias for the outcome of each study was indicated as low, moderate or high using a coloured dot above the bar;
- Statistically significant differences were displayed as a positive effect if they favoured the intervention; negative if they favoured the comparator and neutral if not statistically significant;
- Where some, but not all, findings in a group of outcomes showed a positive or negative effect, bars were hatched to indicate inconsistency.

## RESULTS

### Study Selection

The results of abstract and full-text screening are shown in the PRISMA diagram in Figure 1. A full list of studies excluded at full-text level, along with reasons for exclusion, is shown in Additional File 2.

**FIGURE 1 – PRISMA DIAGRAM**

### Description of Studies

Sixteen papers were eligible for inclusion which described eleven unique studies.[29-33 37-47] Ten studies were from the USA [29 30 32 33 37-47] and one from UK.[31] Eight were RCTs, two quasi-experimental and one was a pilot study.

Three studies included a range of NCDs.[31-33] None of these studies included specific diagnoses as inclusion criteria, but rather recruited at hospital admission or from homeless accommodation targeting access to community health services. It was not specified if participants included also had LT-CDs. The three studies including a range of NCDs each focused on access to care and services. Identification and management of health needs were included in this, however the interventions did not target specific conditions or management strategies. With the exception of one small (n=9) pilot study in type 2 diabetes, all other studies focusing on management of specific conditions concerned LT-CDs: four

studies concerned latent tuberculosis;[29 30 37-41] one concerned Hepatitis C;[46] two studies concerned HIV.[43-45 47]

**Study Populations**

Details of the study populations are summarised in table 1. Sample sizes ranged from 9 to 520. Median age ranged from 37 to 49 years. In all of the studies the majority of participants were male (percentage male participants ranged from 67% to 94% in the intervention groups). Age and sex distributions were consistent with previous literature on homelessness.[1] Six studies, all from the USA reported details of ethnicity.[29 30 37 41 43 46] African American participants were the most prevalent in five of these. Only two studies included any detail of comorbidities.[31 37] Details of attrition are shown in Additional File 3.

**Quality Assessment**

Results of the EPOC Risk of Bias assessment for each of the included studies is shown in table 2. None of the included studies scored low risk for each of the criteria. These were used to inform outcome-level risk of bias assessment. These are displayed, along with justification, in Additional File 3.

**Intervention Components and Theoretical Underpinnings**

Multidisciplinary teams including both a physician and nurse working alongside social workers delivered two of the interventions.[31 32] The nine remaining interventions were delivered primarily by a nurse, alone[46 47] or alongside psychiatrists,[43] peer health advisors,[29 30 41] or outreach workers.[37]

Each of the studies described interventions that were complex and included multiple components. These included changes to how, and where, care was delivered, the personnel delivering care, how care delivery was coordinated, and the provision of financial support. The components of the EPOC taxonomy relating to each of the interventions are shown in table 3, along with a summary of the intervention and control interventions. Descriptions of the specific aspects of each intervention relating to the taxonomy are shown in Additional File 4.

Four of the eleven studies reported an explicit theoretical framework underpinning the intervention (table 3). These included the Comprehensive Health Seeking and Coping Paradigm underpinning two of the studies, and Self-Efficacy Theory and the Health Belief Model each underpinning one intervention.

**Table 1: Summary of study populations**

| Study | Design | Location | Number of Participants | Age, mean (SD) | Sex (%) | Ethnicity (%) | Condition | Homelessness definition |
|---|---|---|---|---|---|---|---|---|
| Pilote 1996[41] | RCT | USA | 244<br><br>I[1]: 83<br>I[2]: 82<br>C: 79 | I[1]: median 40<br>I[2]: median 39<br>C: median 40 | I[1]: M (71%)<br>I[2]: M (67%)<br>C: M (66%) | African American (I[1]: 48%, I[2]: 57%, C: 54%)<br>White (I[1]: 33%, I[2]: 27%, C: 27%)<br>Hispanic (I[1]: 16%, I[2]: 11%, C: 13%) | Latent TB | Homeless: not further defined |
| Tulsky 2000[30] | RCT | USA | 118<br><br>I[1]: 43<br>I[2]: 37<br>C: 38 | Median 37 | M (89%) | African American (52%)<br>White (21%)<br>Hispanic (27%) | Latent TB | Homeless or marginally housed |
| Tulsky 2004[29] | RCT | USA | 141<br><br>I: 72<br>C: 69 | Median 41 (range 21-79) | M (85%) | African American (47%)<br>White (32%)<br>Other (20%) | Latent TB | Homeless or marginally housed |
| Samet 2005[47] | RCT | USA | 151 (34 homeless)<br><br>I: 19<br>C: 15 | Median 44 (range 26-60) | M (82%) | n/a | HIV with alcohol problems | Homeless: not further defined |
| Ciaranello 2006[32] | Quasi-experi-mental | USA | 6 transitional housing facilities<br><br>I:219 sampled<br>C: 50 sampled | I: 41.6 (9.6)<br>C: 41.3 (10.4) | I: M (81%)<br>C: M (44%) | n/a | Various* | "Formerly homeless" residents of transitional housing |
| Nyamathi 2006[37]<br>Nyamathi 2007[38]<br>Schumann 2007[39]<br>Nyamathi 2008[40] | RCT | USA | 520<br><br>I: 279<br>C: 241 | 41.5 (8.5) | M (79.6%) | African American (81%)<br>White (7.3%)<br>Hispanic (9.4%)<br>Other (2.3%) | Latent TB | Sleeping in homeless shelters |
| Tsai 2013[43] | RCT | USA | 137 | I: Median 44 | I: M (91%) | I: Caucasian (48%) | HIV with comorbid | "homeless or marginally |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Tsai 2013[44] Grelotti 2016[45] | | | I: 66<br>C: 71 | (IQR: 37-53)<br>C: Median 42 (IQR: 37-79) | C: M (89%) | C: Caucasian (51%) | depression | housed" |
| Savage 2014[42] | Random-ised pilot/ feasibility | USA | 9<br><br>I: 6<br>C: 3 | n/a | n/a | n/a | Type 2 diabetes | Living without shelter or adequate accommodation |
| Tyler 2014[46] | Random-ised quasi-experi-mental | USA | 107 (hepatitis C positive subset)<br><br>I: 46<br>C: 61 | Males: 44 (7.1)<br><br>Females: 45.3 (8.9) | M (79%) | African American (63%)<br>White (17%)<br>Latino (18%) | Hepatitis C | Homeless: not further specified |
| O'Toole 2015[33] | RCT | USA | 185<br><br>$I^1$: 39<br>$I^2$: 40<br>$I^{1+2}$: 44<br>C: 62 | 48.6 (10.8) | M (94%) | "Minority population" (43%) | Various** | "lacking fixed, regular and adequate night-time residence." |
| Hewett 2016[31] | RCT | UK | 410 | I: 41.6 (12.1)<br>C: 42.5 (11.3) | I: M (81.6%)<br>C: M (81.4%) | N.S.<br>Nationality:<br>UK: I (69.4%), C (72.5%)<br>European union: I (22.3%), C (17.6%)<br>Other: I (8.3%) C (9.8%) | Various*** | No fixed residence on hospital discharge |

* Included hypertension, otherwise not fully specified ** Asthma, COPD, hepatitis, cirrhosis, diabetes, hypertension, arthritis *** Categorised by organ system (included liver, pulmonary, musculoskeletal, central nervous system, cardiovascular system, endocrine, skin, gastrointestinal and haematological pathology). Causes for hospital attendance also categorised by aetiology, 35% related to cardiovascular disease, 15% to metabolic conditions

Table 2: Risk of bias within individual studies

| Criteria | Study | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ciaranello 2014 | Hewett 2016 | Nyamathi 2006, 2007, 2008 and Schumann 2007 | O'Toole 2015 | Pilote 1996 | Samet 2005* | Savage 2014 | Tsai 2013, 2013 and Grelotti 2016 | Tulsky 2000 | Tulsky 2004 | Tyler 2014 |
| Random sequence generation | High | Low | Unclear | Low | Unclear | Unclear | High | Low | Low | Low | High |
| Allocation concealment | High | Low | Low | Unclear | Unclear | Unclear | High | Low | Low | Low | Unclear |
| Blinding of participants/ personnel | High | High | High | High | High | High | High | High | High | Unclear | High |
| Similar baseline outcome measures | High | Low | Low | Low | Unclear | Low | Unclear | Low | Unclear | Unclear | Low |
| Similar baseline characteristics | High | Low | Low | Low | Low | Low | Unclear | Low | Low | Low | Low |
| Blinding of outcome assessment | High | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | High |
| Incomplete outcome data | High | High | Low | Low | Low | Low | High | Low | Low | Low | Low |
| Protection from contamination | High | Unclear | Low | Unclear | Low | Low | Unclear | Low | Low | Low | Low |
| Selective Outcome Reporting | High | Low | Low | Low | Low | Unclear | High | Unclear | Low | High | Unclear |
| Other bias | High | Low | Low | Low | Low | Low | High | Low | High | High | Low |

* Assessment based on methods and results as described in the original manuscript. Unpublished data were supplied by authors for secondary analysis of homeless study participants.

**Table 3: Intervention Components, Theoretical Underpinning, and Outcomes**

| Study | Components | Healthcare Professional delivering the intervention | Theory | Intervention | Comparator | Outcomes |
|---|---|---|---|---|---|---|
| Pilote 1996[41] | **How care is delivered:** Individual delivery<br>**Location/environment:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | Nurse plus peer health advisor | None specified | Monetary incentive for TB clinic attendance (group 1). Peer health advisor assisting with clinic attendance (group 2). | Usual care (clinic appointment and tokens for travel expenses). | Attendance at initial TB clinic appointment. |
| Tulsky 2000[30] | **How care is delivered:** Individual delivery<br>**Location/environment:** Orientation to environment/facilities; transportation services<br>**Finance**: Incentives | Nurse, outreach worker, peer health advisor | None specified | Monetary incentive for uptake of directly observed therapy (group 1). Peer-health advisor supporting directly observed therapy (group 2). | Usual care | Completion of 6 months isoniazid therapy |
| Tulsky 2004[29] | **How care is delivered:** Individual delivery<br>**Location/environment:** Transportation services<br>**Finance**: Incentives | Nurse, outreach worker, peer health advisor | None specified | Monetary incentive for uptake of directly observed therapy | Non-cash incentive of equal value (vouchers) | Completion of 6 months isoniazid therapy<br>Cost effectiveness |
| Samet 2005[47] | **How care is delivered:** Individual delivery. Self-management.<br>**Location/environment:** Outreach services.<br>**Coordination of care:** Disease management. | Nurse | Health belief model and motivational interviewing. | Adherence support for antiretroviral treatment | Usual care (written instructions/advice regarding treatment adherence) | Adherence to antiretroviral treatment<br>CD4+ count<br>HIV viral load |
| Ciaranello 2006[32] | **How care is delivered:** Individual delivery. Self-management.<br>**Location/environment:** Outreach services; changing site of service delivery.<br>**Coordination of care:** Communication | Medical director, nurse practitioner, medical clerk, social worker | None specified | Weekly visits including health assessment, education, referral and social support. | Transitional houses in a different area not receiving the intervention. | ED attendance<br>Hospital admission<br>Blood pressure<br>Satisfaction with care |

| | | | | | | |
|---|---|---|---|---|---|---|
| | between providers; disease management; multidisciplinary teams. | | | | | |
| Nyamathi 2006[37] Nyamathi 2007[38] Schumann 2007[39] Nyamathi 2008[40] | **How care is delivered:** Group delivery. Self-management. **Location/environment:** Outreach services; transportation services. **Coordination of care:** Case management; disease management. **Finance**: Incentives. | Nurse and outreach worker | Comprehensive Health Seeking and Coping Paradigm. | Directly observed therapy plus 8 education sessions. Information provided on community resources and participants escorted to appointments. | Directly observed therapy plus 20 minute educational lecture | Completion of directly observed TB therapy<br>TB knowledge<br>HIV knowledge<br>Self-efficacy |
| Tsai 2013[43] Tsai 2013[44] Grelotti 2016[45] | **How care is delivered:** Individual delivery **Coordination of care:** Case management; disease management. **Finance**: Incentives | Psychiatrist and study nurse | None specified | Directly observed fluoxetine and weekly psychiatric interview | Advice on sources of mental health support | Adherence to antiretroviral therapy<br>HIV viral load<br>Depression |
| Savage 2014[42] | **How care is delivered:** Individual delivery Self-management | Nurse | Self-efficacy theory | Nurse led case-management and diabetes education | Usual care | Self-efficacy |
| Tyler 2014[46] | **How care is delivered:** Group delivery Self-management **Coordination of care:** Case management; communication between providers | Nurse | Comprehensive Health Seeking and Coping Paradigm. | Case management with group sessions, self-management training and education. | Single, brief educational intervention | Hepatitis C knowledge |
| O'Toole 2015[33] | **How care is delivered:** Individual delivery. Self-management. **Location/environment:** Orientation to environment/facilities; outreach services; transportation services. **Coordination of care:** Case management; disease management. | Nurse | None specified | Nurse-led brief health assessment with motivational interviewing (group 1). Guided orientation to primary care clinic facilities (group 2). Both interventions together (group 3). | Usual care (social work assessment and description of available services) | ED attendance<br>Hospital admission<br>Access to primary care |
| Hewett 2016[31] | **How care is delivered:** Individual delivery; Coordination of care providers. Role expansion; recruitment of specific | General practitioner, specialist nurse | None specified | Nurse and GP led inpatient intervention. Goal setting. Discharge planning. Liaison and multiagency meetings | Initial meeting with nurse and signposting of services | ED attendance<br>Hospital readmission<br>Quality of Life |

| | | | | | | |
|---|---|---|---|---|---|---|
| | professionals.<br>**Coordination of care:** Care pathways; communication between professionals; discharge planning; integration of services; shared care; multidisciplinary teams. | | | | | |

## The Impact of Interventions on Healthcare Outcomes

The overall findings of the included studies for impact on unscheduled healthcare utilization, adherence or access to care, and knowledge of self-efficacy, are illustrated in the harvest plot shown in Figure 2. The text that follows synthesizes these findings under each outcome.

**FIGURE 2 – HARVEST PLOT**

## Primary Review Outcomes

### Unscheduled Healthcare Utilisation

Three studies assessed the impact of interventions on hospital admissions and emergency department (ED) attendance.[31-33] None focused on a specific conditions, however participants reported a range of NCD and each intervention included identification and engagement with medical, as well as wider needs. The highest quality evidence was from two RCTs, neither of which showed any significant reduction in unscheduled healthcare utilisation.[31 33] One RCT evaluated a multidisciplinary, multicomponent intervention targeting patients in two inner-city hospitals involving goal setting, discharge planning, and liaising with community services.[31] Neither hospital admissions, nor ED attendance after one year, were significantly different compared with usual care. The other RCT was a four-arm trial comparing usual care; a brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health

assessment.[33]Hospital admissions and ED attendance were assessed at 6 months post intervention in a post-hoc analysis and showed no significant difference to usual care. A third study, with a quasi-experimental design and high risk of bias, concerned a 'comprehensive health assessment' delivered to residents at transitional housing facilities. ED attendances were reportedly lower at 18 month follow-up, but not at 6 months. There was no difference in hospitalization at either follow-up point.

Taken together the available evidence does not suggest that the multidisciplinary, multifaceted interventions described reduced rates of unscheduled healthcare utilisation. The overall confidence in the estimate of effect is low. There were no studies targeting specific NCD or LT-CDs.

**Secondary Review Outcomes**

**Access to primary healthcare**

One RCT, including a range of NCDs, concerned access to primary healthcare.[33] A brief nurse-led physical health needs assessment; a guided orientation to clinical facilities with introduction to staff; and clinic orientation in combination with the physical health assessment were compared to usual care. All three intervention groups showed higher uptake of primary healthcare services after 6 months with clinic orientation alone and in combination with a physical health assessment significantly improving primary care access in adjusted analyses. Overall

confidence in effect for improvement in this outcome was high, but limited to one study so should be interpreted with caution.

**Adherence to specific treatment**

Six studies (7 papers), all of which concerned LT-CDs, assessed adherence to treatment or attendance at appointments.[29 30 37 41 43 44 47] Four recruited patients with latent tuberculosis undergoing directly observed therapy (DOT),[29 30 37 41] one included participants with HIV and alcohol problems,[47] and one (2 papers) concerned participants with HIV and co-morbid depression.[43 44] Of the TB studies, three were conducted by the same research group and assessed the impact of monetary incentives (cash and/or voucher) on attendance at initial TB clinic follow up [41] or on completion of DOT with isoniazid.[29 30] Clinic attendance and DOT completion rates were significantly higher with cash incentives compared with usual care or peer-health advisors.[30] There was no statistically significant difference in DOT completion between cash and voucher incentives.[29] Details of the availability to the participants of social security or other sources of financial support are not described in either study. Although the cash incentive and delivery of the intervention were similar in both studies assessing DOT completion, the completion rate in the intervention group differed widely between the two studies (44% and 89%, respectively).[29 30] The authors speculate that the location of the clinic (the higher completion rate being in an area more accessible and frequented by people who are homeless) or alterations in the follow-up protocol for non-attendees may explain the differences.

The final study concerning TB evaluated the impact of a nurse-led case management intervention on completion of latent tuberculosis treatment and tuberculosis knowledge (described below under knowledge and self-efficacy). They found odds of DOT completion were three times greater with the intervention compared with usual care.[37]

An RCT concerning people with HIV and comorbid depression assessed fluoxetine prescription and weekly psychiatric evaluation compared with the provision of information about how to access local psychology services without the prescription of fluoxetine. Both arms were given a weekly cash incentive for attending. Outcomes included rate of uptake of anti-retroviral treatment (ART), and adherence to ART (assessed by unannounced pill counts) for those receiving treatment. Neither outcome was significantly different between the groups despite an improvement in depression severity and remission in the fluoxetine group.[43 44]

Finally an RCT aimed at supporting antiretroviral medication adherence among HIV positive participants with a history of alcohol dependence or harmful drinking showed no change in antiretroviral adherence.[47] Findings were similar to a secondary analysis of participants who described themselves as homeless (unpublished results).

Overall, there is a moderate level of evidence for interventions improving adherence to treatment for latent TB, including a case-management educational approach and provision of monetary incentives (cash or non-cash). However, the

efficacy of such interventions may be dependent on the social and cultural context in which it is delivered (highlighted by variation in completion rates between evaluations of similar interventions), of which there is limited description in the available studies.

**Knowledge and Self-efficacy**

Three studies (5 papers) assessed the impact of interventions on disease specific knowledge and self-efficacy.[37-39 42 46] Two (4 papers) concerned LT-CDs (TB, HIV and hepatitis) and one concerned type 2 diabetes. Two were trials incorporating nurse-led case management (for patients with latent TB or hepatitis C, respectively) combined with a regular educational intervention focusing on self-management, self-esteem, communication skills and social support. One was an RCT focusing on DOT for latent TB and assessed the impact on TB knowledge in all participants.[37] The intervention also involved HIV education and the impact of this was evaluated in a subset judged to be 'at risk' of HIV (i.e. sexually active or known to be intravenous drug users). Two analyses using structural equation modeling showed that the nurse-led case management intervention was associated with greater improvement in TB knowledge [38] and in HIV knowledge in the 'at risk' subset.[39] The latter also showed improved self-efficacy for condom use.[39] The other evaluated a similar approach concerning Hepatitis education for participants enrolled in a Hepatitis A/B vaccination programme (only the Hepatitis C positive subset was included in this review).[46] The case-management group showed a greater improvement in Hepatitis C knowledge than the control group. However, the randomisation procedure was designed for the vaccine trial, not for the evaluation of the case-management intervention, and the statistical

analysis was not designed to compare the intervention with control in the Hepatitis C subset alone.[46]

The third study reported improved knowledge in a small (n=9) pilot study using a self-efficacy based approach for Type 2 Diabetes Mellitus. However, the small sample size meant there was insufficient power to detect any difference between groups and there was incomplete reporting of outcomes and no clear comparison is made between the intervention and comparator.[42]

Taken together, there is a moderate quality of evidence showing that an educational case-management approach can improve disease specific knowledge in the context of specific LT-CDs when delivered alongside wider interventions, such as DOT or a vaccine study. The available studies, however, do not assess the impact on behavioural outcomes or the retention of knowledge beyond the trial period.

**Biological markers of disease control**

Two studies (3 papers) concerning LT-CDs assessed the impact of interventions on disease control outcomes. One RCT assessed the impact on HIV-1 viral load of directly observed fluoxetine in comorbid HIV and depression. There was no difference in viral suppression between intervention and comparator groups.[43-45] The other RCT found no difference in viral load or CD4+ count with adherence support for antiretroviral therapy in HIV infected individuals with a history of alcohol problems.[47]

### Cost effectiveness

Only one study, including participants with a range of conditions including NCDs, assessed cost-effectiveness, within the hospital sector.[31] Patients in the intervention group also had multiagency care plans devised before, and implemented after hospital discharge. Quality of life was a secondary outcome, with health gain measured by translating generic EQ-5D-5L index scores into generic quality adjusted life years (QALYs). EQ5D5L scores were completed by approximately one quarter of participants in both arms. There was a non-statistically significant increase in EQ-5D-5L scores at follow up, and there was no impact of the intervention on inpatient costs, therefore the authors compared the costs of the intervention with the effect on health gain as measured by QALYs. On this basis the incremental cost effectiveness ratio was £26,000 with the authors describing circumstances in which the intervention may be cost effective, and an accompanying sensitivity analysis.[31]

## DISCUSSION

### Summary of findings

The available evidence from controlled trials of interventions by healthcare professionals improving access to care for people with NCDs who are homeless does not show any convincing effects on unscheduled healthcare utilisation.[31-33] There is also a lack of evidence to inform the management of specific NCDs in

this context. One multidisciplinary intervention did demonstrate improved access to primary healthcare.

Seven interventions were identified targeting specific LT-CDs. All of these involved a nurse primarily delivering the intervention, sometimes with support of peer-health advisors. Patient-centred interventions – incorporating case management, education, self-management support and social support – may improve disease specific knowledge in TB, HIV, and Hepatitis C; improve completion of DOT in latent TB; and increase access to primary care in combination with clinic orientation.[33 37-39 46] Cash and non-cash incentives, in the context of DOT for latent TB, may improve clinic attendance and treatment adherence; however treatment completion rates vary between different studies of similar interventions.[29 30 41] It is not clear if improvement in these intermediate outcomes impacts other clinical outcomes, or if effects are sustained beyond the course of treatment evaluated in these studies. The impact on mortality was not assessed, and evidence for the impact on biological markers of disease control is limited to a few studies on HIV, which did not show any evidence of benefit on viral load.[43 44] There was only one study of cost effectiveness.

**Strengths and Limitations**

The strengths of this review include a-priori methods with a robust process for study identificatuion, appraisal, data extraction and description.[25] The comprehensive search strategy included database searches supplemented by hand searching, forward citation searching, grey literature, and contact with

study authors. All screening and data extraction was performed by two reviewers independently. We also described the components of each intervention using a previously defined taxonomy,[28] which is important when reviewing complex interventions such as those included.[48 49] However, many of the findings, particularly those concerning adherence to treatment, were in the context of specific conditions (e.g. latent TB), included a time-limited course of treatment, and were conducted in a single centre. All but one of the included studies was from the USA. As such the findings may not be directly applicable to other disease areas or other health and social care contexts. Limitations in the existing evidence base also meant we were unable to undertake a formal meta-analyses. Contacting study authors to obtain results pertaining to participants who were homeless (when not reported separately) contributed to the comprehensiveness of the review, however this strength needs to be balanced against the potential bias of performing *post-hoc* secondary analyses on existing trial data. Furthermore, in such circumstances studies are not specifically powered to assess outcomes in this subgroup.

This review is timely given the increasing number and complexity of health problems among people who are homeless,[1] the pressure on healthcare services to address this burden, and the potentially expanding roles of various healthcare professionals to support management of NCDs and LT-CDs.[20] However, by focusing on interventions by healthcare professionals this review may overlook evidence for housing or social interventions that may impact on such conditions.[50 51]

**Implications for practice, policy and research.**

Despite the social complexity and exclusion that typify the experience of homelessness, a patient-focused case-management approach was shown to positively impact disease specific knowledge and self-efficacy in the management of selected LT-CDs.[37-39 46] These interventions were primarily delivered by a study nurse, with or without peer-health advisors, adopting a case-management approach.

It is not clear to what extent the findings presented here are generalisable to wider social or healthcare contexts, or to other conditions. The evidence for improved adherence was predominantly in the context of DOT for latent TB and in some cases involved cash incentives. Further research would be required to establish whether these principles of adherence support are transferable to the management of NCDs. Furthermore, the potential efficacy of cash incentives will vary between societal contexts where access to, and the extent of, financial support varies widely. Finally, the available literature focuses mainly on the role of nurses and physicians, often alongside other ancillary staff (such as peer advisors, case-managers and care coordinators), with little consideration of the potential role of other healthcare professionals e.g. pharmacists.

The extent to which the improvements in knowledge or adherence that have been demonstrated may impact on physical or behavioural outcomes has not been evaluated. This raises the question of how such issues may be best addressed by future research. It is likely, given their apparent scarcity, that

further evaluation of complex interventions to address both NCD and LT-CDs management (including aspects of randomization, longer follow-up and consideration of broader outcomes) will be needed to inform practice. Based on existing patterns of need and service utilisation, as well as the need to demonstrate effectiveness and cost-effectiveness of novel models of care, well designed and conducted studies following a framework for testing complex interventions [49] for people who are homeless are overdue.

However, the intrinsic complexity of the experience of homelessness, and the impact this has on health, may require a broader methodological approach (e.g. realist synthesis) to understand the context and process of potential interventions in this area.

**Conclusions**

Trials of interventions delivered by healthcare professionals targeting NCD in people who are homeless do not show convincing evidence of the primary outcome measure for this review – an impact on unscheduled healthcare utilisation. Despite their high prevalence and associated morbidity and mortality, little evidence was identified to inform the management of specific NCDs.

In the context of specific LT-CDs (HIV, TB and hepatitis C), patient-centred case-management interventions may improve knowledge and self-efficacy. Available evidence supports interventions delivered by a nurse and incorporating peer-health advisors. These interventions, as well as incentives, may also improve adherence in specific contexts. The impact on biological outcomes and mortality

remains largely unexplored, as does the effectiveness of alternative models of care involving different professions. The economic impact of successful interventions is also largely unexplored. Future complex intervention evaluation research is needed to test innovative models of care, and expand those interventions showing promise, into diverse health and social care contexts.

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**Competing interests**

None declared

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**Data sharing**

Full details of the screening process are detailed in the supplementary appendices. Any additional detail will be available on request from the corresponding author.

**Contributions**

All authors listed fulfil the ICMJE criteria for authorship. RL conceived the initial idea. All authors (PH, LY, RE, LG, AEW, FM and RL) contributed to the conception and design of the proposed study. PH, LY, RE, AEW, FM and RL contributed to the development of data sources and search strategy. PH, LY, RE, AEW, FM and RL developed and refined the inclusion criteria. PH, LY, RE, LG, FM and RL developed the data extraction template which was piloted by PH, LY and LG. PH, LY, RE and RL screened titles, abstract and full texts. PH, LY and LG completed

data extraction and quality assessment on all included studies. PH wrote the first draft of the manuscript. All authors critically reviewed this and subsequent drafts of the manuscript and provided input into its content. All authors approved the final version of the manuscript to be published. RL is the guarantor of the review. All authors accept accountability for the accuracy of the findings presented.

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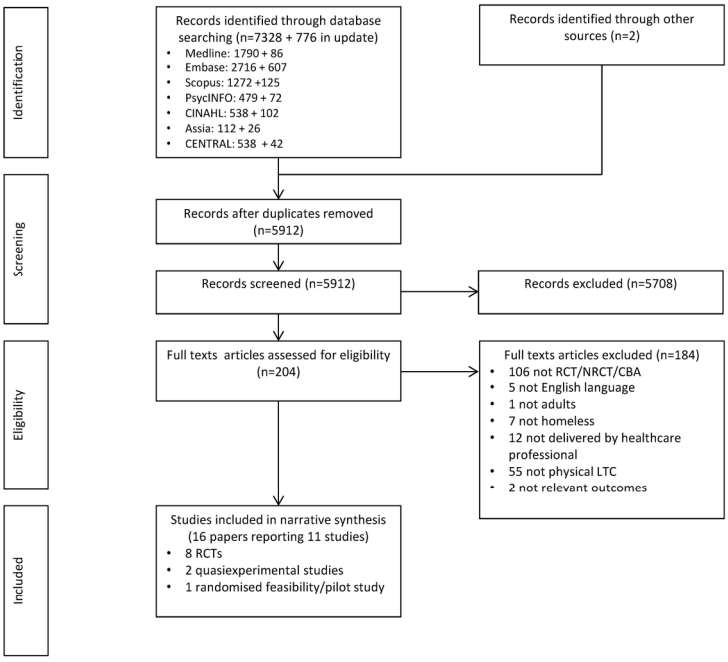


Figure 1: PRISMA diagram of search results and screening

190x142mm (300 x 300 DPI)

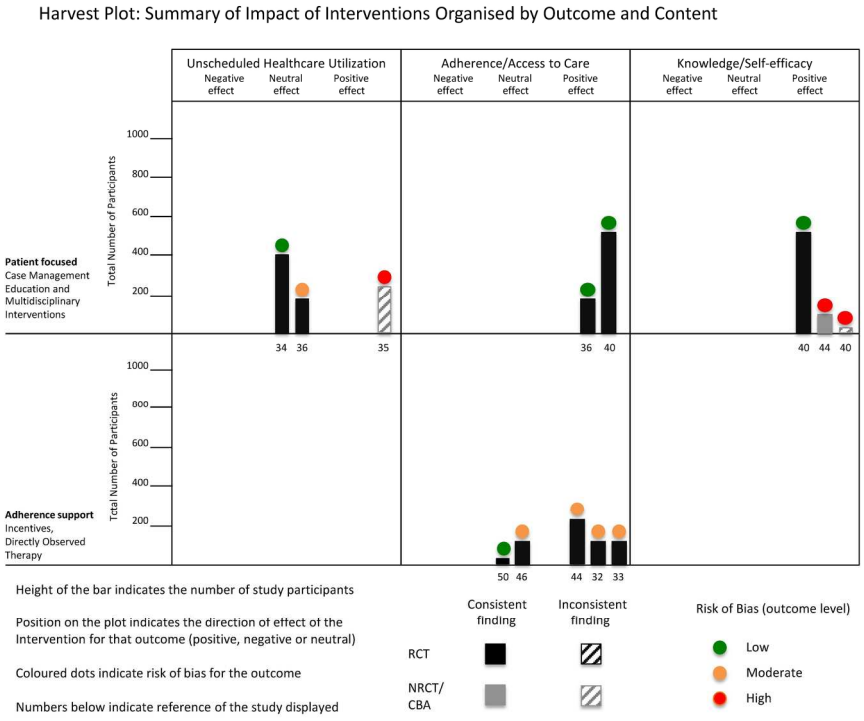


Figure 2: Harvest Plot of findings of included studies

190x142mm (300 x 300 DPI)

| Inclusion Criteria and Search Strategy (adapted from protocol paper *Hanlon et al 2017 [1a]*) | |
|---|---|
| **PICOS component** | **Description** |
| Population | • Adults (≥ 18 years old)<br>• ETHOS criteria for homelessness*<br>• ≥1 non-communicable disease (NCD) or communicable disease requiring long-term care (LT-CD) |
| Intervention | • Be delivered, in whole or in part, by a healthcare professional**<br>• Address the management of one or more NCD or LT-CD |
| Comparator | 'Usual care' or alternative intervention<br>Contemporaneous comparator only (exclude historical controls) |
| Outcomes | Primary outcome: Unscheduled use of healthcare services, including:<br>• Emergency department attendance<br>• Hospital admission<br>• Use of out-of-hours services<br>• Ambulance call-outs<br>Secondary outcomes:<br>• Physical health outcomes (e.g. mortality, disease specific markers of control)<br>• Quality of life<br>• Patient engagement (e.g. attendance at planned healthcare services, medication adherence)<br>• Behavioural or cognitive (e.g. self-efficacy, knowledge) changes related to health<br>• Emotional wellbeing, anxiety, and depression<br>• Satisfaction with care<br>• Cost effectiveness<br>• Changes to treatment or medication |
| Settings | Community: interventions delivered solely in non-community settings (e.g. hospitals, ) will be excluded |
| Study design | RCTs (including Cluster RCTs)<br>Non-randomised controlled trials/ quasi-experimental studies<br>CBAs |
| Databases | Medline, EMBASE, Scopus, PsycINFO, CINAHL, Assia, Cochrane Central Register of Controlled Trials (CENTRAL) |
| Manual searching | Reference lists of all eligible studies.<br>Journal of the Poor and Underserved. |
| Grey literature | Websites of non-governmental organisations that aim to assist homeless persons: Department of Health England webpage; OpenGrey; WorldCat; Grey Literature Report; OAlster and WorldWideScience for reports and theses; British library and Zetoc; Research Councils UK information on publicly funded research; Repositories including Grey Guide and Open DOAR. Other related sites including UK health forum, St. Michael's hospital, and Grey Net. |
| Forward citations | Performed for all included studies (using Web of Science). |
| Contact with study authors | Where data pertaining to homeless participants were not presented separately, we attempted to contact study authors to request these data. |
| Restrictions | English language only |
| Dates | Database: Jan 1966 (or inception) to Oct 2016. Forward citation search completed Mar 2017 |

* Studies including a broader population but including homeless participants will be included only if data pertaining to homeless participants are considered separately.

** any professional trained to provide any form of health care, but excluding social workers and professionals without a health-related training , including, but not limited to, physicians, nurses, dentists, pharmacists, paramedics, mental health professionals, allied health professionals (e.g. physiotherapists, dieticians, clinical psychologists etc.), midwives.

(1a) Hanlon P, Yeoman L, Esiovwa R, Gibson L, Williamson AE, Mair FS, Lowrie R. Interventions by healthcare professionals to improve management of physical long-term conditions in adults who are homeless: a systematic review protocol. BMJ Open. 2017 Aug 21;7(8):e016756. doi: 10.1136/bmjopen-2017-016756.

**Medline Search Strategy***

1. Exp. Homeless Persons/
2. Home?less.mp
3. Roof?less.mp
4. House?less.mp
5. (home* adj2 lack).mp
6. (home* adj2 no).mp
7. (without adj2. Home*).mp
8. (lack adj2 hous*).mp
9. (no adj2 hous*).mp
10. (without adj2. hous*).mp
11. (lack adj2 roof*).mp
12. (no adj2 roof*).mp
13. (without adj2 roof*).mp
14. (inadequate* adj3 hous*).mp
15. (insecur* adj3 hous*).mp
16. (insecur* adj2 tenan*).mp
17. (unfit* adj2 hous*).mp
18. ((transition* or insecure or inadequate or substandard or substandard or sheltered or emergency or intermittent or transient or marginal* or problem*) adj (hous* or home* or accommodat*)).mp
19. (sheltered or unsheltered or shelters).mp
20. Vagran*.mp
21. Destitute.mp
22. Skid row.mp
23. (sleep* adj2 rough).mp
24. ("street person" or "street people"). Mp
25. Exp "Delivery of Health Care"/
26. Exp Primary Health Care/
27. Exp Community Health Services/
28. Exp Chronic Disease
29. ((chronic or long term) adj2 (disease or condition*)).mp
30. Exp Patient Care Management/
31. Intervention*.mp
32. Exp Pragmatic Clinical Trial/ or exp Clinical Trial/ or exp Randomized Controlled Trial/ or exp Controlled Clinical Trial/
33. Trial*.mp
34. Control*.mp
35. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
36. 25 or 26 or 27 or 28 or 29 or 30

| |
|---|
| 37. 31 or 32 or 33 or 34<br>38. 35 and 36 and 37 |
| *Adapted for other databases |

**Additional File 2. Studies Excluded at Full-Text Assessment**

104 not RCT/NRCT/CBA (including those without contemporaneous comparator group) [1-104]

5 not published in English [105-109]

1 did not include adults [110]

6 participants were not homeless, or homeless participants were not considered separately [111-116]

11 intervention not delivered by a healthcare professional [117-127]

55 did not consider physical long-term conditions [128-182]

2 did not report relevant outcomes [183, 184]

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| Details of included studies | | | | | | | |
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| **Study** | **Participants** | **Recruitment, retention and attrition** | **Intervention/Comparator (description)** | **Frequency, Duration and Intensity of intervention.**<br><br>**Length of Follow-up** | **Theoretical underpinning of intervention** | **Findings** | **Risk of bias (outcome level assessment –** See Additional File 4 for study level assessment**)** |
| **Ciaranello 2006**<br><br>(quasi-expieri-mental, non-equivalent comparator group) | **Sample:** 6 transitional housing facilities (I: 4, C: 2. Residents (I: ~200, C: ~50) randomly sampled at time points but not followed up individually)<br><br>**Sex:** I: 81% male at baseline, C: 44% male at baseline<br><br>**Age:** I: 41.6 (9.6), C: 41.3 (10.4)<br><br>**Condition:** Various<br><br>**Homeless definition:** Residents of transitional housing facilities, referred to as 'formerly homeless'. | Four transitional housing facilities selected from area in which intervention took place. Comparator was two transitional housing facilities in a different area, under control of a different authority.<br><br>Residents were sampled at baseline and 6 and 18 month follow-up points, however follow-up surveys included residents who had arrived in the intervening period, owing to the usual length of stay of less than 9 months. | **I:** 'Integrated service team' (medical director, nurse practitioner, medical clerk and social worker) made weekly visits to housing facilities. Performed 'comprehensive health assessment', health education, medical and dental referrals, brief psychotherapy, diagnostic studies, and social work services. Supplemented by 24 hour a day nurse telephone-advice line. Additional HIV and TB clinics.<br><br>**C:** 'Usual care'. Facilities under a different healthcare authority. No additional details given | Weekly visits and assessments<br><br>24 hour telephone advice service<br><br>Service delivered for 2 years.<br><br>Data collected by survey of residents at 6 and 18 months post initiation of intervention. | None described | **ED attendances (assessed by survey):** Significantly fewer residents in intervention facilities reporting ≥2 ED attendances in previous 6 months at compared with comparator group at 18 month follow-up (adjusted OR: 0.3, 95%CI 0.12 to 0.74). No significant difference at 6 month follow-up.<br><br>**Hospitalisation (assessed by survey):** No significant difference in adjusted OR of having ≥1 hospitalisation in previous 6 months between intervention or comparator facilities at 6 or 18 months follow-up | **High:** Survey data susceptible to recall bias (e.g. for ED use). Follow-up surveys included people who had arrived in the facility between initial and follow-up surveys. As such changed in outcome variable could be the result of a different sample, rather than changes in outcome relating to the intervention. Also no blinding, randomisation, protection from contamination. Differences in baseline outcomes. |
| | | | | | | **Diastolic blood pressure:** Adjusted mean lower in intervention group at 6 months (mean difference -6.4mmHg, SE 2.4, p=0.03) but not 18 months (mean difference 0.57mmHg, SE 2.3, p=0.80) | **High:** All biases above relalvant, particularly the inclusion of residents arriving between baseline and follow-up. Also unclear if participants were hypertensive as such validity of outcome measure is questionable |
| | | | | | | **Satisfaction with care:** No significant differences described between intervention and control based on survey data. Not further described. | **High:** Biases above also relevant for satisfaction data |
| **Hewett 2016**<br><br>RCT | **Sample:** I: 206, C: 204<br><br>**Sex:** I: 81.6% male, C: 81.4% male<br><br>**Age:** I: 41.6 (12.1), C: 42.5 (11.3)<br><br>**Condition:** Various (79.1% and 76.5% had 'long-term medication condition' in I and C groups, respectively)<br><br>**Homeless definition:** | 1009 patients identified by ward team of whom 622 were eligible. 410 consented and were included in analysis.<br><br>3 month admission data routinely collected and was available for all 410.<br><br>Survey data collected using telephone follow-up and was only obtained for 110 participants (57 | **I:** During hospital admission patients who were homeless were identified by ward teams. Nurse met completes interview including medical, mental health, drug and alcohol details, housing history, care needs and consideration of any goals on discharge.3x weekly GP led ward round reviewing goals, care plans, medial findings and discharge planning. Regular visit by homelessness nurse to provide community links including with social work and | 3-4 times weekly GP ward round during admission<br><br>Initial meeting by nurse followed by liaising with relevant services.<br><br>Weekly multiagency meetings<br><br>Questionnaire data obtained 6 (+/-4) weeks following | None explicitly described. Development of service was the result of quality improvement work based in the study site which has been published and described | **ED attendance:** no significant difference between standard or enhanced care at 12 months (adjusted mean difference -0.8, 95% CI -4.3 to 2.8)<br><br>**Hospital readmission:** No significant difference between standard or enhanced care at 30 or 90 days (adjusted OR 0.83 (95% CI 0.52 to 1.33) and 1.02 (95% CI 0.67 to 1.54), respectively) | **Low:** Data on readmission and attendance was routinely collected and complete data available for those who consented. Protection from contamination and adjustment for baseline imbalances made |
| | | | | | | **Quality of Life** (EQ-5D-5L questionnaire). Non-statistically significant improvement with enhanced | **Moderate:** Based on survey data with poor response to follow-up. Potential for |

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| | "Homeless" (i.e. no fixed residence) | intervention, 53 comparator).<br><br>Consent to longer term follow up (1 year) was a change in protocol. Consent obtained from 226 participants). | housing services. Weekly multiagency meeting in which housing manager, social workers, drug and alcohol workers, liason psychiatry, street outreach workers, hostel key workers and ward staff met with 'pathway' team to review discharge plans for all patients.<br><br>**C:** Visited once by homelessness nurse and given information leaflet detailing local services | discharge.<br><br>Emergency department attendance assessed at 1 and 3 months, readmission at 3 months. | | care over standard care at 6 week follow-up (adjusted mean difference 0.09 (95% CI -0.03 to 0.22) | selection bias from those who responded to follow-up. |
| | | | | | **Cost effectiveness:** £26,000 per quality adjusted life year | **Moderate:** Based on survey data with poor response to follow-up. |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, Nyamathi 2008**<br><br>RCT | **Sample:** I: 279, C: 241<br><br>**Sex:** 79.6% male<br><br>**Age:** 41.5 (SD 8.5)<br><br>**Condition:** Latent TB (a subset of these judged at risk of HIV also identified)<br><br>**Homeless definition:** Individuals having spent the night prior to recruitment at one of the study shelters considered homeless and eligible for inclusion<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment by flyers in 12 homeless shelters.<br><br>3959 screened, 980 PPD positive. 25 refused CXR, 199 did not return for follow-up. 221 not eligible due to active TB, suspected TB or other medical indications.<br><br>520 randomised<br><br>Follow-up data on 494 | **I:** Delivered alongside Directly Observed Therapy (DOT) for latent TB. Research nurse and outreach worker delivered 8 1-hour TB education sessions. Focus was on self-esteem, TB and HIV risk, coping, self-management, problem solving and positive relationships and social networks to maintain behaviour change. Provided with community resourced and escorted to appointments. Participants not attending were tracked by the outreach worker.<br><br>**C:** 20 minute lecture and 10 minute discussion with study nurse in addition to DOT. | 8 1 hour sessions over a period of 6 months. | Comprehensive Health Seeking and Coping Paradigm. | **Completion of Directly Observed Therapy for Latent TB:** Nurse led case management intervention with education, incentives and tracking associated with improved DOT completion (61.5% completion vs 39% with usual care, adjusted OR for completion 3.01 (95% CI 2.15 to 4.2) | **Low:** Complete outcome data available and adjusted for potential confounders in multivariate analysis. |
| | | | | | **TB knowledge:** Latent variable analysis showed nurse-led case management predicted greater TB knowledge at 6 month follow-up.<br>**HIV knowledge/self-efficacy:** Latent variable analysis of subgroup at risk of HIV showed nurse-led case management predicted greater HIV knowledge and greater self-efficacy for condom use at 6 month follow-up. | **Low:** two separate models used to control for numerous confounders and assess magnitude of the impact of inter intervention on knowledge. |
| **O'Toole 2015**<br><br>RCT | **Sample:** I: 123, C: 62<br><br>**Sex:** 94% male<br><br>**Age:** 48.5 (SD 10.8)<br><br>**Condition:** 72.7% reported at least one chronic medical problem, most commonly hypertension, | Recruitment from 11 community sites (soup kitchens, transitional and emergency shelters, drop-in centres). Potential participants identified in common areas and provided with information about the study. No healthcare services offered at time | **I: Group 1**, (n=39), personal health assessment/brief intervention. Nurse led interview about medical history, health, risk behaviours, barriers to care, medications and self-identified needs. Cursory examination. Brief motivational interview and summary of findings highlighting unmet health needs. No clinic orientation performed | Personal health assessment was a brief, one off, intervention. As described. Lasted 20-30 minutes.<br><br>Clinic orientation also a one off intervention. 15-20 minutes. Also transport to clinic. | None described | **ED attendances:** no significant difference between groups (ANOVA p=0.61)<br>**Medical hospital admission:** no significant difference between groups (ANOVA p=0.07) | **Moderate:** Post-hoc analysis and very small number of events. High possibility of type 2 error. Randomised design, routinely collected data reduce potential bias. |
| | | | | | | **Access to primary care:** Cox regression using usual care as baseline showed clinic orientation alone (HR 2.64 (95% CI 1.54 to 4.53)) and physical health assessment in | **Low:** Primary outcome with design focused on assessing outcome. Participants all eligible for veterans' services and data on usage routinely |

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| | arthritis/chronic pain, hepatitis/cirrhosis<br><br>**Homeless definition:** "lacking a fixed, regular and adequate night-time residence" plus eligible for Veterans Healthcare Services. Must have not been in receipt of primary healthcare services in previous 6 months | of recruitment.<br><br>221 enrolled, 36 removed as ineligible (6 duplicate enrolment, 15 not eligible for veterans' services, 14 receiving primary care in prev. 6 months, 1 did not adequately complete baseline assessment).<br><br>Follow-up for re-interview was 81% at 1 month and 71% at 6 months. | **Group 2,** (n=40), clinic orientation, transported to clinic and introduced to clinic team. Orientated to services available. Usual care only following this. **Group 3,** (n=44), physical health assessment plus clinic orientation.<br><br>**C:** Usual care, comprising social-worker administered assessment of homelessness and social needs, description of services available and how to access (verbal or written) | Follow-up at 1 and 6 months. | | combination with clinic orientation (HR 3.41 (95% CI 2.02 to 5.76)) were both significantly associated with improved primary care access. Unadjusted Chi-squared estimates were significant at both 4-weeks and 6-months with usual care showing lowest rates of access. | collected and complete for eligible participants. Potential bias from randomisation procedure for clinic orientation arm as randomised by calendar day based on attendance. |
| **Pilote 1996**<br><br>RCT | **Sample:** I1: 83, I2: 82, C: 79<br><br>**Sex:** I1: 71% male, I2: 67% male, C: 66% male<br><br>**Age:** Median: I1: 40, I2: 39, C: 40<br><br>**Condition:** Latent TB<br><br>**Homeless definition:** "homeless", not further defined<br><br>**Inclusion/exclusion:** Positive PPD without active TB and with no TB follow-up or prevention in previous 6 months | During a population based survey of TB and HIV, homeless people with positive purified protein derivative (PPD) were assessed approached for inclusion.<br><br>1608 interviewed, 1257 had skin tests and returned for evaluation. 441 PPD positive. 297 of these eligible (no recent follow-up). 244 agreed to participate. | **I1:** Monetary incentive. $5 incentive given on attendance to TB clinic follow-up in addition to appointment and bus tokens received by all participants.<br><br>**I2:** Peer health advisors: In addition to bus tokens and appointment, peer health advisors met participants in shelters, accompanied to appointment, helped with paper-work and orientation.<br><br>**C:** Usual care. Bus tokens and TB clinic appointment only. | One off payment for monetary incentive arm.<br><br>One off intervention in peer health advisor arm, as described. Included transport assistance and support in attendance. | None described | **Attendance at initial TB clinic follow-up:** Monetary incentive (84%) and peer health advisor (75%) groups more likely to attend appointment than usual care (53%) (p=<0.001 and p=0.004, respectively). Both interventions significant predictors of adherence in multivariate analysis. | **Moderate:** Details of randomisation not clear and blinding not possible, otherwise low risk of bias. |
| **Samet 2005**<br><br>RCT | **Sample:** I: 74 (15 homeless), C: 77 (19 homeless)<br><br>**Sex:** 84% male (homeless subset)<br><br>**Age:** Median: 43.6 (37.9-45.0) (homeless subset)<br><br>**Condition:** HIV | Participants were from a longditudinal cohort study (HIV Alcohol Longitudinal Cohort). Mostly recrtuied from Boston Medical Centre Clinic.<br><br>Of 74 randomised to intervention, 56 received complete intervention, 13 received partial | **I:** ADHERE intervention:<br>- Assessment and discussion of alcohol and substance use of readiness for behaviour change.<br>- A watch that served as a medication timer reminder.<br>- Enhancement of perceived efficacy of medications. | Baseline visit at medical centre lasting 60 minutes.<br><br>Home visit within 3 weeks of intervention lasting 30-45 minutes.<br><br>1-month follow-up at assessment centre: 15-30 minutes. | Intervention used behavioural science theories using motivational interviewing to promote behaviour change and using principles of the Health Belief Model to support the benefit and need for therapy. | No separate analysis of homeless participants is provided in the published paper. Analyses were repeated on the homeless participants only using Generalised Estimating Equations as described in the original manuscript. Data were provided by the study authors and the analysis was performed by the review authors. Models were fit to analyse the overage intervention effect over time. | **Low:** Objective assessment of outcomes and adjustment for baseline variables |

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| | **Homeless definition:** "homeless" as a variable – not otherwise defined<br><br>**Inclusion/exclusion:** HIV positive participants with a history of alcohol problems (current or lifetime history of alcohol abuse or dependence – CAGE questionnaire or study clinician diagnosis). Participants also needed to be taking antiretroviral medication. | intervention, 5 received no intervention (could not be contacted). Homeless proportions of these numbers not available.<br><br>10 in total lost to follow-up (3 control, 7 intervention). Proportion of these who were homeless not stated. | - Individualised HIV counselling – ways to tailor medication use to specific circumstances.<br><br>**C:** Standard care. At study period this included verbal or written instructions regarding antiretroviral treatment and adherence strategies. | 3 month follow-up visit at medical centre: 15-30 minutes.<br><br>At follow-up visits all 4 components of the intervention were reassessed and reinforced. | | **Adherence to Antiretroviral treatment:** No significant improvement with intervention after controlling for baseline adherence (p=0.55) | |
| | | | | | | **CD4 count:** No significant change in CD4 count with the intervention after adjusting for baseline CD4 count (p=0.31)<br><br>**HIV1-RNA:** No significant reduction in viral load seen with intervention after adjusting for baseline laboratory estimates. (p=0.23) | **Low:** Objective assessment of outcomes and adjustment for baseline variables |
| **Savage 2014**<br><br>Randomised pilot/ feasibility study | **Sample:** I: 6, C: 3<br><br>**Sex:** Not specified<br><br>**Age:** Not specified<br><br>**Condition:** Type 2 diabetes mellitus<br><br>**Homeless definition:** Those living without adequate shelter or in temporary accommodation. | Convenience sample recruited from a homeless clinic. Unclear how those with type 2 diabetes were identified. 9 identified in total for participation in feasibility study. | **I:** Nursing case-management with diabetes self-management. Education sessions delivered alongside nursing case-management (6 sessions total).<br><br>**C:** No intervention | 6 sessions over 12 weeks. Each 45 minutes long. | Chronic disease self-management approach based on self-efficacy theory. | **Self-efficacy:** Paper states "participants who attended the intervention had higher scores on some outcome variables, most notable in cognitive symptom management, which improved from a pre-intervention score of 1.3/5 to a post-intervention score of 2.75". Participants in comparison stated to have "similar scores" at baseline and 12 week follow up. | **High:** Randomisation not clear. Incomplete outcome reporting. No assessment of baseline imbalances. Small sample size, incomplete recruitment. |
| **Tsai 2013, Tsai 2013, Grelotti 2016**<br><br>RCT | **Sample:** I: 66, C: 71<br><br>**Sex:** I: 91% male, C: 89% male<br><br>**Age:** I: 44 (37-53), C: 42 (37-49)<br><br>**Condition:** HIV<br><br>**Homeless definition:** "Homeless or marginally housed". Not further defined<br><br>**Inclusion/exclusion:** HIV positive, depression (DSM-IV). Excluded if self-report of alternative | Participants identified from homeless shelters, free-lunch programmes, low-income single-room occupancy hotels, public HIV clinics and social service agencies.<br><br>Block randomisation.<br><br>1555 screened. 647 potentially eligible. Of these 190 met DSM-IV criteria for depression. | **I:** Psychiatric evaluation and prescription of fluoxetine. Directly observed therapy for 24 weeks. Psychiatric interview was carried out weekly. 25 dollar reimbursement given per week for all doses.<br><br>**C:** Advised of diagnosis of depression and advised to seek treatment at a public mental health clinic specialising in care of HIV positive persons. 25 dollar incentive for attending study site weekly for data collection. | Weekly dispensing and incentive. Weekly psychiatric evaluation.<br><br>Follow-up 6 months. | None stated | **Adherence to antiretroviral therapy:** Mixed-model analysis showed no statistically significant effects of the intervention on antiretroviral therapy update (adjusted OR 1.18 (95% CI (0.83 to 1.68)). Percentage of antiretroviral adherence was similar in intervention and comparator groups. | **Moderate:** Low risk from study design however unannounced pill-counts on a monthly basis may not be a robust method of assessing compliance with treatment. |
| | | | | | | **HIV-1 viral load:** No statistically significant difference in viral suppression between intervention and comparator group (adjusted OR 1.04 (95% CI 0.97 to 1.12). | **Low:** Good methodological rigour across study (Additional file 4) and objective measurement of outcome |
| | | | | | | **Depression:** Improved mood in both study arms. Statistically significant treatment effect observed using with Ham-D and BDI-II scores to assess depression. | **Low:** Good methodological rigour across study (Additional file 4). Assessed as primary outcome with analysis designed around this. Two measured used and compared |

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| | psychiatric diagnosis. | | | | | | as sensitivity analysis. |
| **Tulsky 2000**<br><br>RCT | **Sample:** I1: 43, I2: 37, C: 38<br><br>**Sex:** 89% male<br><br>**Age:** Median 37<br><br>**Condition:** Latent TB<br><br>**Homeless definition:** Either "literally homeless", staying in emergency shelter, street, car, or other shelter not designed for sleeping, or "maginally housed", staying in low-cost temporary accommodation.<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>Eligibility was positive TST and no TB follow-up in previous 6 months.<br><br>2158 screened. 618 positive TST. 89 refused randomisation. 199 ineligible as did not return or rsults, HIV infection, recent screening with chest x-ray or current isoniazid treatment. 330 randomised and attended clinic. Of these 121 prescribed isoniazid.<br><br>3 stopped due to toxicity. 118/121 analysed. | **I1:** Monetary incentive: $5 at each twice weekly visit for directly observed isoniazid. If a dose missed, attempts to contact participant made by letter or telephone call. Any onward referrals were made by TB clinic, not research assistants following up patients.<br>**I2:** Peer health adviser: Adviser provided and observed isoniazid twice weekly. Adviser accompanied participant for monthly refill appointments. If appointments missed, adviser spent an allotted amount of time looking for the participant.<br><br>**C:** Usual care: routine TB clinic care. Given 1 month supply of treatment and monthly drop in follow-up scheduled. Adherence monitored by TB charts. For non-attendance, standard follow-up or 3 letters or telephone calls. Treatment not directly observed. Protocol change during study due to low initial clinic attendance in usual care arm meant that the protocol was changed to offer all participants $5 at the initial visit. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion significantly higher in monetary incentive group (44%) than peer advisor (18%, p=0.01) and usual care (26%, p=0.04). No statistically significant difference between peer advisors and usual care. Multivariate analysis comparing monetary incentive to peer advisors and usual care considered together (i.e. single comparison group) showed monetary incentive arm significantly more likely to complete treatment (Adjusted OR 2.57 (95% CI 1.11 to 5.94)). | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |

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| **Tulsky 2004**<br><br>RCT | **Sample:** I: 72, C: 69<br><br>**Sex:** 85% male<br><br>**Age:** Median 41 (21-79)<br><br>**LTC:** Latent TB<br>**Condition Homeless definition:** "true homeless", street or shelter dwelling, or "marginally housed", staying in low-cost temporary accommodation<br><br>**Inclusion/exclusion:** Positive TST without active TB and with no TB follow-up or prevention in previous 6 months | Recruitment from emergency shelters, free meal lines and low cost residential hostels. Participants were interviewed and screened with a tuberculin skin testing (TST) using Mantoux method.<br><br>2570 tested. 647 positive TST, 488 new or required further screening. 95% accepted referral. 353 attended initial appointment. 212 of these were not randomised (190 not prescribed isoniazid, 6 active TB, 16 refused). 141 randomised.<br><br>16 not prescibred isoniazid after diagnostic tests (4 cash, 12 non-cash). 6 censored (3 cash, 3 non-cash). | **I:** Cash incentive: $5 payment for keeping twice weekly appointment for directly observed isoniazid therapy. Tracking included names and addresses of family, friends and case workers. Missed appointments were followed up by letters, telephone calls, and using tracking information, following a protocol specifying a number of outreach attempts.<br><br>**C:** Non-cash incentive: A choice of fast-food or grocery coupons, phone cards or bus tokens with a value of $5 was offered from each kept appointment. Tracking and follow-up of missed appointment was identical to the cash incentive group. | Twice weekly attendance at TB clinic over 6 months in all participants. Interventions were on top of this, with the same frequency and duration.<br><br>6 month follow-up | None described | **Completion of 6 months isoniazid therapy:** Completion rates were 89% with monetary incentives and 81% with non-monetary incentives (no statistically significant difference, p=0.23) | **Moderate:** Randomisation/allocation procedure not clear. Method of assessment of adherence to isoniazid differed between directly observed group and usual care (former directly observed, latter assessed by percentage pick up of prescriptions). If anything, however, this would lead to underestimation of the effect size of the intervention. |
| **Tyler 2014**<br><br>Randomised quasi-experimental | **Sample:** I: 46, C: 61 (Hepatitis C positive subset only)<br><br>**Sex:** 79% male<br><br>**Age:** males 44 (7.1), females 45.3 (8.9)<br><br>**Condition:** Hepatitis C<br><br>**Homeless definition:** "homeless". Not further defined.<br><br>**Inclusion/exclusion:** Recruitment was to a vaccine study (Hep A/B). Data presented here | Recruitment view flyers in homeless shelters within the study area. | **I:** Case management in the context of a hepatitis A/B vaccination programme. Three 40 minute group sessions delivered by study nurse with education on hepatitis A, B, C and HIV diagnosis, prevention and transmission. Self-management training. Case management focusing on self-esteem, social, behavioural and communication skills. Behavioural education around blood-borne virus risk. Also included participant needs assessment and onward referral to address medical, mental health, food, shelter and transportation needs. | Total of 3 group session across study period in intervention group. Time-frame not specifically stated.<br><br>Outcomes assessed 6 months post-intervention | Based on the Comprehensive Health Seeking and Coping Paradigm (CHSCP) | **Hepatitis C knowledge:** Measured using a modification of an 18 item tool initially developed for tuberculosis. Greater improvement in the nurse case-managed group than the standard intervention in the hepatitis C positive subset. Statistical analysis of the significance of the difference between intervention and control groups not performed for the hepatitis C positive subset. | **High:** Randomisation was carried out according to a protocol to assess the vaccine efficacy, not that of the case-management/education intervention. Futhermore, while data on the hepatitis C positive subset are presented, the study design and analysis was not focused on a comparison of intervention and control intervention in this subset of participants. As such baseline imbalances and sequence of allocation could introduce bias for the outcome of hepatitis C knowledge. |

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| | pertain to hepatitis C positive subset | | **C:** Single brief 20 minute presentation around hepatitis A, B, C and HIV at baseline visit of vaccination programme. | | | | |

| Characterisation of Interventions by the Effective Practice and Organisation of Care (EPOC) Taxonomy | | | | | | | | | | | | | | | | | | |
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| **Study** | **How** care is delivered | | **Where** care is delivered | | | | **Who** and delivers care | | | **Coordination** of care | | | | | | | | **Finance** |
| | Group/ Individual deliver | Coordination of care providers | Orientation to environment/ facilities | Outreach services | Changing site of service delivery | Transportation services | Role expansion | Self-management | Recruitment of specific professionals | Care pathways | Case management | Communication between providers | Discharge planning | Diagnostic and treatment services | Integration of services | Shared care | Multi-disciplinary teams | Incentives (monetary or not) |
| **Cianarello 2006** | Individual | | | Took place in transitional housing facility | Services delivered at transitional housing facilities | | | Health education a component of intervention | | | | Liaising with social work | | Diagnostic studies and medical referral carried out | | | Multidisciplinary model of service provision | |
| **Hewett 2016** | Individual | Liaising between inpatient and community services | | | | | GPs delivering ward-based care. Homeless-specific nurses | | Specialised "pathway" team | Focus of the intervention | | "Pathway" meeting with further liaising with community services | Focus of the intervention | | Liaising between inpatient and community services. Needs assessment | "pathway" and ward inpatient teams | MDT meeting key part of intervention | |
| **Nyamathi 2006, Nyamathi 2007, Schumann 2007, and Nyamathi 2008** | Group | | | Tracking of non-attenders | | Escorted to appointments | | Education and self-management focus of the case-management sessions | | | Focus of intervention, given in addition to DOT for latent TV | | | In context of DOT | | | | Incentive to both groups when taking DOT. |
| **O'Toole 2014** | Individual | | Clinic orientation arm and combined arm. | Both arms | | Clinic orientation arm and combined arm. | | Health promotion within personal health assessment arm and combined arm. | | | Personal health assessment and combined arm | | | Personal health assessment and combined arm | | | | |
| **Pilote 1996** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Samet 2005** | Individual | | | Home visit at 3 weeks to reinforce intervention | | | | Motivational interviewing for behaviour change and adherence support | | | | | | Tailored support for antiretroviral treatment. | | | | |
| **Savage 2014** | Individual | | | | | | | Educational intervention | | | | | | | | | | |
| **Tsai 2013, Tsai 2013, Gerlotti 2014** | Individual | | | | | | | | | | Psychiatric evaluation and initiation of therapy | | | Treatment of comorbid depression | | | | Monetary incentive for treatment |
| **Tulsky 2000** | Individual | | Peer health advisor arm only | | | Bus tokens to all groups | | | Peer health advisors recruited and trained (not HCPs) | | | | | | | | | Monetary incentive arm only |
| **Tulsky** | Individual | | | | | Bus tokens to | | | | | | | | | | | | Both |

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| **2004** | | | | | | all groups | | | | | | | | | | | | study arms |
| **Tyler 2014** | Group | | | | | | | Health promotion and transmission prevention education | | | Case management on top of vaccination programme | Onward referral for medical or social needs | | | | | | |

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 7 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7<br>Additional file 1 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 7-8<br>Additional file 1 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Additional file 1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8<br>Additional file 5 |

# PRISMA 2009 Checklist

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| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 8 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 9 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 10 |



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 8<br>Additional file 4 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | n/a |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1, Page 11 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 11,12<br>Table 1 (page 13)<br>Additional file 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table 2 (page 15) |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 18-23 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | n/a (figure 2 summarises narrative synthesis) |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Figure 2, Additional |

# PRISMA 2009 Checklist

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| | | | file 4, |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 24 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 25 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 28 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 29 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.