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Effects of integrated models of care for diabetes and hypertension in low- and middle-income countries. A systematic review

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Abstract

Objectives

To assess the effects of integrated models of care for people with multi-morbidity including at least diabetes or hypertension in low-and middle-income countries (LMICs) on health and process outcomes.

Design

Systematic review

Methods

We included randomised controlled trials (RCTs), non-RCTs, controlled before-after studies and interrupted time series (ITS) studies of people with diabetes and/or hypertension plus any other disease, in LMICs; assessing the effects of fully integrated care compared to partially or non-integrated care. We conducted a comprehensive search up to 12 December 2019. Two authors independently screened retrieved records; extracted data and assessed risk of bias. We conducted meta-analysis where possible or synthesised data narratively. We assessed the certainty of evidence using GRADE.

Results

We included five studies - two ITS studies and three cluster RCTs. Four studies conducted in Sub-Saharan Africa and one in India. Risk of bias was moderate. Integrated models of care compared to usual care (comparison 1) may make little or no difference to mortality, the number of people achieving blood pressure (BP) or diabetes control, and access to care; may increase the number of people who achieve both HIV and BP/diabetes control; and may have a very small effect on achieving HIV control. Interventions to promote integrated care compared to usual care (comparison 2) may make little or no difference to mortality, depression and quality of life, but the evidence is very uncertain. Interventions to promote integrated care compared to usual care may have little or no effect on HbA1c, systolic BP, and total cholesterol levels. Process outcomes were poorly reported.

Conclusions

Current evidence on the effects of integrated care on health outcomes is very uncertain. Programmes and policies on integrated care must consider context-specific factors related to health systems and populations.

PROSPERO registration: CRD42018099314

Strengths and limitations of this study

- We included study designs that are able to provide reliable evidence on the effects of integrated models of care on health and process outcomes
- We performed a comprehensive search for published and unpublished studies up to 12 December 2019, with no language restrictions.
- We assessed the certainty of evidence using the GRADE approach taking into consideration study limitations, inconsistency, imprecision, publication bias and indirectness when downgrading the certainty of evidence.

- Our review did not aim to answer questions on aspects linked to implementation of integrated models of care and barriers and facilitators to integrated models of care at individual and health-system level

Introduction

Low- and middle-income countries (LMICs) are facing an increasing burden of non-communicable diseases (NCDs).¹ A recent report of the World Health Organization (WHO) on NCDs indicates that 41 million people succumb to NCDs globally which is the equivalent of 71% of total global deaths. Fifteen million people die prematurely due NCDs every year (between the ages of 30 and 69 years) and 85% of these premature deaths occur in LMICs.^{1,2} Furthermore, NCDs are projected to exceed communicable, maternal, perinatal, and nutritional diseases as the most common causes of death by 2030.³ In LMICs, the vast majority of NCD deaths are caused by cardiovascular diseases (CVDs), mainly due to coronary artery diseases and stroke,⁴ diabetes, cancer and chronic respiratory diseases; and they account for 54% of NCD disability adjusted life years.^{1,5} Diabetes and hypertension are the major cardiovascular risk factors for target organ damage of brain, heart and kidney.¹

Currently, it is estimated that 425 million people in LMICs live with diabetes. This number is expected to increase up to 629 million in 2045.⁶ According to the International Society of hypertension (ISH), around 40% of people over age of 25 years have hypertension worldwide and two thirds of them live in LMICs.⁷ Due to the existing high burden of communicable diseases, especially HIV infection, in sub-Saharan Africa, a lot of people are living with multi-morbidity. Because of the progress made with scaling up of anti-retroviral therapy (ART), the life expectancy of people living with HIV (PLHIV) has increased substantially, putting them at risk of NCDs that are common in older people. In addition to the traditional risk factors for NCDs, such as smoking, poor diet and a sedentary lifestyle, PLHIV have an increased risk of NCDs (especially CVD, cervical cancer, depression and diabetes), related to HIV itself and to ART related side effects⁸⁻¹¹ According to a recent systematic review examining the prevalence of NCDs among PLHIV in LMICs,¹² the pooled prevalence estimate of hypertension was 21.2% (95%CI 16.3 to 27.1); while that of depression was 24.4% (95%CI 12.5 to 42.1%). The prevalence of diabetes among PLHIV was reported to be between 1.2 and 18% and authors ascribed the variation in the findings to actual differences in populations, as well as the lack of standardised diagnostic criteria for diabetes.

In LMICs, people with NCDs such as diabetes and hypertension are generally characterised by very poor outcomes due to various other factors such as limited access to reliable healthcare services.¹³ The chronic nature of NCDs puts strain on the already scarce resources of healthcare systems and affected individuals in LMICs.¹⁴ Hence there is a need to design effective interventions to address the increasing burden of NCDs such diabetes and hypertension, in particular in complex patients with comorbidities such as HIV infection and other CVDs. Provision of integrated care has been advocated by researchers and many international bodies such as the WHO as a way of tackling the rising burden of NCDs and strengthening the health systems particularly in LMICs.¹⁵⁻¹⁷ Recent studies from LMICs have assessed integration of HIV/AIDS and tuberculosis (TB) services at primary healthcare (PHC) level.¹⁸⁻²⁰ Based on these integrated models of care, we conceptualised integrated care either as partial integration or full integration as illustrated in Figure 1.²¹ Fully integrated care is seen as a “one-stop-shop” model whereby a patient receives all necessary care or services under one roof by one or more health-care professionals. In a partially integrated model of care, patients receiving treatment for one disease such as diabetes receive additional care related to either prevention, diagnosis or treatment of another disease, but do not receive the full package of care²¹.

There are only a few systematic reviews to assess the effectiveness of integrated models of care in people with diabetes or hypertension and any other comorbid disease. We previously conducted a

1
2 scoping review to assess the evidence base²² and did not identify any systematic review that included
3 studies conducted in LMICs. Furthermore, none of the included studies assessed integrated care for
4 diabetes or hypertension and communicable diseases (e.g. HIV). A subsequent systematic review by
5 Haldane and colleagues examined existing programmes of integrated healthcare delivery for
6 diabetes, hypertension or CVDs with HIV/AIDS.²³ However, included studies mostly described existing
7 programmes with no thorough evaluation of the effectiveness of these programmes. A descriptive
8 study from Cambodia looked at the management of HIV/AIDS, diabetes, and hypertension and found
9 that integration of services for these conditions was highly acceptable and led to good health
10 outcomes with improved CD4 count, glycated haemoglobin (HbA1c) and blood pressure levels.²⁴
11 Dudley and Garner²⁵ assessed the effectiveness of strategies to integrate PHC services in LMICs. They
12 included studies that integrated family planning into existing services; nutrition and infectious
13 disease interventions; and sexually transmitted infections (STIs), HIV/AIDS and TB treatment. None of
14 the included studies reported on NCDs.
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18 In light of limited information in existing reviews, we conducted this review to assess the effects of
19 integrated models of care at PHC level for people living in LMICs, with multi-morbidity, of which
20 diabetes or hypertension is one, compared to no integrated care on health and process outcomes.
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23 Methods

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25 Our systematic review followed the methods pre-specified in a published protocol.²¹ We followed the
26 PRISMA reporting guideline to report on the findings of our systematic review.
27

28 We included studies with adults and children attending PHC clinics, presenting with diabetes or
29 hypertension plus one or more other chronic diseases (multi-morbidity), or risk factors for other
30 chronic diseases in LMICs. We defined LMICs according to the World Bank.²⁶ Eligible interventions
31 were models of full or partial integration of services at PHC and community level. Partial integration
32 of services was defined as models where patients treated for diabetes, hypertension, or any other
33 chronic disease received part of the package of care (prevention, diagnosis, treatment) for another
34 disease. Full integration of service delivery was defined as models where patients (primarily treated
35 for diabetes, hypertension or any other disease) received the full package of care (prevention,
36 diagnosis and treatment) for diabetes or hypertension and any other chronic disease at the same
37 point of care by one or more healthcare professionals. In addition, we considered interventions that
38 promoted an integrated approach to providing care for multiple conditions. We considered studies
39 that compared fully integrated models of care to stand-alone care; partially integrated models of
40 care to stand-alone care; fully integrated models of care to partially integrated models of care; and
41 interventions that promoted integrated care compared to usual care. Randomised controlled trials
42 (RCTs), including cluster RCTs, controlled (non-randomised) clinical trials (CCTs) or cluster non-
43 randomised trials, interrupted time series (ITS) studies with at least three data points before and
44 after the intervention, and controlled before-and-after (CBA) studies were eligible for inclusion.
45 Cluster randomised, cluster non-randomised or CBA studies were only included if there were at least
46 two intervention sites and two control sites. We included studies that reported on either primary or
47 secondary outcomes, as defined and reported by primary study authors. Primary outcomes were all-
48 cause mortality, disease specific morbidity as reported in included studies (e.g. disease control
49 metrics), quality of life, glycated haemoglobin (HbA1c), systolic Blood pressure (SBP) and cholesterol
50 levels. Secondary outcomes were access to care, retention in care, adherence, continuity of care,
51 quality of care and cost of care.
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58 We searched MEDLINE (PubMed), EMBASE (Ovid), the Cochrane Central Register of Controlled Trials
59 (CENTRAL), LILACS, Africa-Wide Information (via EBSCO host), CINAHL, and Web of Science (Core
60 collection) (Date of last search: 12 December 2019). We searched the WHO International Clinical
Trials Registry Platform (ICTRP) and Clinicaltrials.gov for ongoing studies, as well as conference

1
2 abstracts from the International AIDS Society Online Resource Library, the HIV/AIDS Implementers'
3 Meetings and the NCDs Alliance meetings. Search terms included 'diabetes', 'hypertension',
4 'comorbidities', 'integrated health care delivery', 'low-and middle-income countries' and their
5 synonyms. The full search strategy for MEDLINE (Pubmed) is provided in Supplementary file 1. To
6 supplement the search of electronic databases, we screened reference lists of included studies and
7 reference lists of relevant systematic reviews, and contacted experts in the field and relevant
8 organisations (e.g. NCD Alliance) for unpublished studies. We did not have any restrictions related to
9 language or publication status.
10

11 Two authors (JUN and AR or a research assistant) independently screened titles and abstracts of
12 studies identified by the search, using Covidence software.²⁷ We retrieved full texts of potentially
13 eligible studies. Two authors (JUN and AR/TY/CMB) independently screened full texts for eligibility.
14 Discrepancies were resolved through discussion with a third author (JJM/IT). We classified studies as
15 included, excluded or ongoing and provided reasons for excluding studies.
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18 Two authors (JUN, AR and IT) independently extracted data for included studies using a pre-specified,
19 piloted data extraction form and assessed risk of bias. Discrepancies were resolved through
20 discussion or by consulting a third author (TY/JJM). We extracted data related to the study design,
21 participants, intervention, comparison, outcomes, setting, context and funding sources. We used the
22 template for intervention description and replication (TIDieR)²⁸ and the PRISMA-Complex
23 Interventions extension checklist²⁹ to guide data extraction and reporting related to the
24 interventions. We used guidance from Cochrane Effective Practice and Organisation of Care (EPOC)
25 to assess risk of bias for included studies³⁰. Risk of bias was assessed as low, high, or unclear for each
26 domain. For RCTs, non-randomised trials and CBA studies, we assessed the following nine domains:
27 1) random sequence generation, 2) allocation concealment, 3) baseline outcome measurements, 4)
28 baseline characteristics, 5) incomplete outcome data, 6) knowledge of allocated intervention
29 (blinding), 7) protection against contamination, 8) selective outcome reporting and 9) other risks of
30 bias. For cluster RCTs, we assessed additional risk of bias linked to recruitment, cluster baseline
31 differences, loss of clusters, incorrect analysis and compatibility with RCTs randomised by individuals,
32 as per the Cochrane handbook.³¹ For ITS studies, we assessed whether 1) the intervention was
33 independent of other changes, 2) the shape of the intervention effect was pre-specified, 3) the
34 intervention was unlikely to affect data collections, 4) knowledge of the allocated intervention was
35 adequately prevented during the study, 5) incomplete outcome data was likely to bias results, 6)
36 outcomes were reported selectively and 7) there were any other risks of bias.
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40 We extracted relevant data for each outcome per included study. For dichotomous outcomes, we
41 reported risk ratios (RR) and 95% confidence intervals (CI). For continuous outcomes, we reported
42 mean differences (MD) with 95% CI if outcomes were measured in the same way across studies, or
43 standardised mean differences (SMD) with 95% CI where outcomes were measured differently across
44 studies and where standard deviations (SD) were reported. For ITS studies, we reported beta
45 coefficients (β) with standard error (SE). We contacted study authors to request information on
46 missing data. We did not impute any data.
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50 All included cluster RCTs appropriately adjusted for the effects of clustering in their analysis, we thus
51 used these adjusted effect estimates and standard errors in our meta-analysis using the generic
52 inverse-variance method in Review Manager 5.³² We did not include studies with more than one
53 treatment arm in our review.
54

55 We explored clinical heterogeneity by clearly documenting study characteristics related to the
56 population, intervention, outcomes and context in table format. We assessed statistical
57 heterogeneity in each meta-analysis by inspecting forest plots and calculating Chi² test values and I²
58 statistics. We considered heterogeneity to be significant if the p-value of the Chi² test was < 0.10, and
59 the I² statistic was above 30%, as per the recommendations in the Cochrane handbook.³¹
60

1
2 We pooled data from individual studies if we judged them to be sufficiently homogeneous in terms
3 of design, population, intervention and comparator. As we anticipated some degree of
4 heterogeneity, we performed random-effects meta-analysis. We did not pool data from RCTs and
5 non-randomised studies in a single meta-analysis. Where we judged included studies to be too
6 heterogeneous to pool, we used narrative synthesis and presented data in tabular format. We did
7 not perform subgroup or sensitivity analysis, as only two studies contributed to the meta-analysis.
8 We were unable to examine reporting biases by means of funnel plots, as we only included two
9 studies in the meta-analysis.
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12 We assessed the certainty of the evidence using GRADE³³ for the following outcomes: mortality,
13 disease specific morbidity, quality of life, HbA1c, systolic BP, cholesterol levels and access to care. We
14 created a 'Summary of findings' table using GRADEpro software.³⁴ Our judgements to downgrade the
15 certainty of evidence were based on assessment of the following five domains: 1) study limitations,
16 2) inconsistency, 3) imprecision, 4) indirectness and 5) publication bias. We considered upgrading the
17 certainty of evidence for non-randomised studies if there was a large effect, a dose-response and
18 cases where all plausible residual confounding would reduce a demonstrated effect or would suggest
19 a spurious effect if no effect was observed. For each outcome, we described the certainty of
20 evidence as high, moderate, low or very low.³⁵
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23 Patient and public involvement

24 No patients were involved in this systematic review.
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28 Results

29 The results of the search are depicted in the PRISMA flow diagram (Figure 2). We screened titles and
30 abstracts of 7568 records. We obtained and screened full texts of 49 potentially relevant studies. We
31 included five studies,³⁶⁻⁴⁰ (Table 1) reported in six articles and excluded 37 articles with reasons
32 (Table 2). For one study⁴¹ that met eligibility criteria, we were only able to access the conference
33 abstract. We classified this study as 'awaiting assessment', as we are unable to definitively decide on
34 inclusion or exclusion until we have access to the full report. We identified five ongoing RCTs,⁴²⁻⁴⁵
35 investigating integrated care for depression and hypertension in China;⁴² integrated care for
36 depression and hypertension⁴³ or depression and diabetes/HIV⁴⁴ in South Africa; integrated care for
37 common mental disorders and hypertension, diabetes or ischemic heart disease in India;⁴⁵ and
38 diabetes and TB in India.⁴⁶
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Table 1: Summary of characteristics of included studies

Study ID	Study design	Country and Setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes ¹
<i>Integrated models of care</i>							
Ameh 2017 ³⁶	Controlled ITS study	South Africa: Primary health care (PHC) facilities, Ehlanzeni health district, Mpumalanga Province	Patients with chronic disease (HIV, diabetes or hypertension) n=878	Integrated chronic disease management (ICDM) model Clinics: n=7 Participants: n=435	Usual care in PHC facilities Clinics: n=5 Participants: n=443	30 months Pre-intervention: 6 months Post-intervention: 24 months	<ul style="list-style-type: none"> - Blood pressure (BP) control² - CD4 count control³ - Number of healthcare visits
Havlir 2019 ⁴⁰	Cluster RCT	Kenya and Uganda: Rural regions in south-western and eastern Uganda, and western Kenya	Clusters: Communities of 9000 to 11 000 people Participants: People residing in community n=150 395 (baseline)	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and streamlined, patient-centered care Clusters: n=16 Participants: n=79 818 (baseline)	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care (not integrated) Clusters: n=16 Participants: n=70 577 (baseline)	36 months	<ul style="list-style-type: none"> - Cumulative HIV incidence - Time to initiation of ART - Viral suppression - Death - Incident tuberculosis or death due to illness - Control of hypertension⁴ among HIV-infected persons - Control of diabetes⁵ or hypertension (NCD) among HIV infected persons - Control of HIV⁶ and hypertension - Control of HIV and NCDs⁷ - Control of hypertension in the overall population - Control of diabetes in the overall population

¹ Outcomes relevant to this review are in bold

² Defined as: BP <140/90mmHg

³ Defined as: CD4 count >350 cells/mm³

⁴ Defined as: At least one systolic BP measurement <140mmHg, and at least one diastolic measurement of <90mmHg

⁵ Defined as: Finger prick blood glucose ≤11 mmol/L

⁶ Defined as: Suppressed viral replication (<500 copies/ml)

⁷ Defined as: Control of all prevalent NCDs (hypertension or diabetes)

1 2 3 4 5 6 7 8 9 10 11 12	Rawat 2018 ³⁹	ITS study	South Africa: PHC clinics in the Free state Province	Patients attending PHC clinics (focus on diabetes and hypertension) n=not reported	Integration of HIV care into HC facilities n=131 clinics	No control group	48 months Pre-intervention: 12 months Post-intervention: 36 months	<ul style="list-style-type: none"> - Population level new diabetics on treatment - Clinic level new diabetics on treatment - Population-level new hypertensive on treatment - Clinic level new hypertensive on treatment - Total ART patients - New patients initiated on ART
13	<i>Interventions to promote integrated delivery of care</i>							
14 15 16 17 18 19 20 21 22 23 24 25 26 27	Fairall 2016 ³⁷	Cluster RCT	South Africa: Mostly rural PHC clinics in Eden and Overberg districts, Western Cape Province	Patients with one or more of the following: hypertension, diabetes, chronic respiratory disease, depression n=4393	Primary Care (PC) 101 management tool Clinics: n=19 Participants: n=2166	Usual care: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool Clinics: n=19 Participants: n=2227	14 months	<ul style="list-style-type: none"> - Treatment intensification for hypertension, diabetes and chronic respiratory disease - Depression - CVD risk - Systolic BP - HbA1C - Body Mass Index (BMI) - Smoking status - Health-related quality of life - Mortality - Healthcare utilisation
28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	Prabhakaran 2019 ³⁸	Cluster RCT	India: Community Health Centres (CHC) from 4 districts in Haryana and 2 districts in Karnataka	Patients with confirmed diagnosis or hypertension n=3698	mWellcare system CHCs: n=20 Participants: n=1842	Enhanced usual care CHCs: n=20 Participants: n=1856	12 months	<ul style="list-style-type: none"> - Mean change in systolic BP - Mean change in HbA1C - Mean change in fasting plasma glucose - Mean change in total cholesterol - Mean change in CVD risk - Mean change in Tobacco use - Mean change in BMI - Alcohol use - Depression score - Adherence - Perceived quality of care

Table 2: List of excluded studies

Studies excluded for wrong population	Studies excluded for wrong study design	Studies excluded for wrong intervention
Abrahams-Gessel 2018 ⁴⁷ Adomaviciute 2014 ⁴⁸ Alharbi 2014 ⁴⁹ Miao 2016 ⁵⁰ Myers 2018 ⁴⁴ Rakic 2011 ⁵¹ Sarrafzadegan 2006 ⁵² Spaak 2017 ⁵³	Ajay 2016 ⁵⁴ Al Asmary 2013 ⁵⁵ Garrib 2018 ⁵⁶ Germe 2017 ⁵⁷ Kwarisiima 2019 ⁵⁸ Li 2013 ⁵⁹ Mahomed 2014 ⁶⁰ Narayanan 2012 ⁶¹ Nigatu 2012 ⁶² Nyabera 2011 ⁶³ Patel 2018 ⁶⁴ Patel 2015 ⁶⁵ Rabkin 2018 ⁶⁶ Samb 2010 ⁶⁷ Sarraf-Zadegan 2003 ⁶⁸ Sushilkumar 2015 ⁶⁹ Tedjokusumo 2003 ⁷⁰ Tiam 2012 ⁷¹ Wasay 2009 ⁷²	Bachmann 2018 ⁷³ Hong 2013 ⁷⁴ Kowalski 2017 ⁷⁵ McKee 2011 ⁷⁶ Mendis 2010 ⁷⁷ Pibernik-Okanovic 2015 ⁷⁸ Saleh 2018 ⁷⁹ Sarrafzadegan 2009 ⁸⁰ Tourkmani 2018 ⁸¹ Wenxi 2017 ⁸²

Characteristics of included studies

We included three cluster RCTs and two ITS studies. One cluster RCT was conducted in South Africa,³⁷ one in India,³⁸ and the Sustainable East Africa Research in Community Health (SEARCH) trial was conducted in Uganda and Kenya.⁴⁰ The two ITS studies were both conducted in South Africa^{36 39} (Table 1). All studies were conducted in PHC facilities in mostly rural settings. All five studies assessed the effect of strategies for full integration of care compared to partial integration of care.

The two ITS studies^{36 39} and the SEARCH trial⁴⁰ assessed the effects of integrated models of care for chronic diseases (Table 3). Ameh and colleagues³⁶ conducted a controlled ITS study, comparing the integrated chronic disease management (ICDM) model to usual care over a period of 30 months. Rawat and colleagues³⁹ examined the effect of integrating HIV care into PHC clinics over a 48 months period. The SEARCH trial⁴⁰ assessed the effects of universal ART and streamlined, patient-centered care (integrated care) compared to usual care as per national guidelines. Interventions are described in more detail according to the TiDIER checklist in supplementary file 2.

The other two cluster RCTs^{37 38} assessed the effectiveness of interventions to promote integration of care (Table 3). Fairall and colleagues³⁷ introduced the Primary Care (PC) 101 clinical management tool to promote provision of comprehensive care for all symptoms including NCDs, HIV, TB, mental health and women's health, in PHC clinics randomised to the intervention, while the control clinics continued using the Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool, which did not cover all NCDs and was the standard of care at the time of the trial. Prabhakaran and colleagues³⁸ introduced the mWellcare system, a m-health based electronic decision support system, to promote integrated management of hypertension, diabetes, depression,

and alcohol and tobacco use in PHC centres randomised to the intervention. Control centres continued with usual care. Interventions are described in more detail in supplementary file 3.

Table 3: Key components of included interventions

Name and Study ID	Components related to provision of care in the clinic	Components related to provision of care in the community/at home	Training	Appointment reminders
Integrated chronic disease management (ICDM) model Ameh 2017	Facility reorganisation: designated chronic care area; supply of critical medicines; pre-packaging of medication Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral	Ward-based outreach teams to ensure individual responsibility and “assisted” self-management Health promotion and population screening	-	-
National policy to integrate HIV care into all PHC facilities Rawat 2018	Policy to integrate HIV care into PHC clinics Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for all diseases in single consultation room Additional staff to strengthen drug delivery systems	-	Training of nurses in comprehensive management of HIV: Nurse initiated Management of ART (NIMART) Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)	-
SEARCH intervention Havlir 2019	Patient-centered, integrated care for HIV, diabetes, hypertension: 3-month visit intervals; ART to all HIV positive participants; hypertension and diabetes treated according to standard algorithms	Community health campaigns (CHCs): Testing for HIV, diabetes and hypertension; counselling and clinic appointments; blood tests for HIV positive participants; transportation voucher for first clinic visit	-	Phone/SMS reminders about clinic visits

		Home-based testing for participants that did not attend CHCs		
		Appointments to initiate ART within 7 days for HIV positive participants not on ART; introductory phone call from clinic staff; support hotline available via phone or text message		
Primary Care (PC) 101 Fairall 2016	PC 101 guideline: Ring-bound, colour illustrated booklet Expanded prescribing provisions for nurses Desk pads with key messages	-	Training of facility trainers Educational outreach sessions by facility trainers	Letters and SMS reminders of follow-up visits
mWellcare Prabhakaran 2018	mWellcare system: m-Health-based electronic decision-support system Visible charts on the management of the conditions Onsite supervision and support	Pamphlets containing lifestyle advice	Training of physicians on current clinical management guidelines and orientation to mWellcare Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use	SMS reminders of follow-up visits and medication adherence

Risk of bias in included studies

For the two ITS studies, we judged risk of bias to be low or unclear in all domains (Figure 3). For the three cluster RCTs, we judged risk of selection bias to be low, risk of performance bias to be high, as blinding of participants and personnel was not possible due to the nature of the interventions, and risk of detection bias to be unclear for all three studies. We judged attrition bias to be low for two cluster RCTs^{37 38} and unclear for the SEARCH trial⁴⁰ (Figure 4). Detailed judgements for each included study are reported in supplementary file 4.

Integration of chronic disease services compared to usual care

We included three studies as part of this comparison.^{36 39 40} Results are summarised in the summary of findings table (Table 4) and forest plots are available in supplementary file 5.

Table 4: Summary of findings for integrated models of care compared to usual care for diabetes and hypertension in LMICs

For peer review only

Patient or population: Patients with multi-morbidity (diabetes and/or hypertension and other chronic conditions e.g. HIV) Setting: Low- and middle-income countries Intervention: Integrated care for hypertension, diabetes and HIV Comparison: Usual care						
Outcome	Effect			No of participants (studies)	Certainty of evidence (GRADE)	Comments
	Risk with usual care	Risk with integrated care	Relative effect (95% CI)			
Mortality	0.56 per 100 person-years	0.51 per 100 person-years	RR 0.90 (0.79 to 1.02)	171 431 (1 RCT)	⊕○○○ VERY LOW a,b,c	Integrated care compared to usual care may make little or no difference to the rate of death, but the evidence is very uncertain
BP control (number of people achieving BP control)	The RCT showed no effect, while the ITS study showed a very small effect			2319 (2 studies: 1 RCT, 1 ITS study)	⊕○○○ VERY LOW a,c,d,e,f	Integrated care compared to usual care may make little or no difference to achieving BP control but the evidence is very uncertain
BP or diabetes (NCD) control (number of people achieving NCD control)	There was no effect among PLHIV with prevalent NCD at baseline and at follow-up			1 RCT*	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may make little or no difference to achieving NCD control but the evidence is very uncertain
HIV control (CD4 count control)	The probability of CD4 count control was 6% greater in intervention clinics compared to control clinics			878 (1 ITS study)	⊕○○○ VERY LOW e,f	Integrated care may have a very small effect on achieving CD4 count control, but the evidence is very uncertain
BP and HIV control (number of people achieving both HIV viral suppression and BP control)	There was a small effect among PLHIV with prevalent hypertension at baseline and at follow-up			1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both BP and HIV control but the evidence is very uncertain
BP or diabetes (NCD) and HIV control (number of people achieving both HIV viral suppression and NCD control)	There was a small effect among PLHIV with prevalent hypertension at baseline and at follow-up			1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both NCD and HIV control but the evidence is very uncertain
Quality of life	-	-	-	-	-	Not reported
Systolic BP	-	-	-	-	-	Not reported
HbA1c	-	-	-	-	-	Not reported
Cholesterol levels	-	-	-	-	-	Not reported

<p>Access to care</p>	<p>There was no change in trend from pre- to post-intervention for population level new diabetics on treatment, clinic level new diabetics on treatment and clinic-level new hypertensive patients on treatment. There was a slight decrease in new hypertensive patients on treatment at population level at 36 months</p>	<p>1 ITS*</p>	<p>⊕○○○ VERY LOW e.g</p>	<p>Integrated care may make little or no difference to short term access to care and may result in a slight decrease in long-term access to hypertensive care, but the evidence is very uncertain.</p>
<p>CI: Confidence interval; RR: Risk ratio; MD: Mean difference; BP: Blood pressure; HIV: Human Immunodeficiency Virus; HbA1c: Glycated Haemoglobin; NCD: Non-communicable disease; RCT: Randomised controlled Trial; ITS: Interrupted time series</p> <p>*Sample size not reported</p> <p>High certainty: We are very confident that the true effect lies close to that of the estimate of the effect</p> <p>Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</p> <p>Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect</p> <p>Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect</p> <p><i>Footnotes: Explanation of GRADE certainty of evidence</i></p> <p>a) Downgraded by 1 due to high risk of performance bias and unclear risk of bias for other domains</p> <p>b) Downgraded by 1 due to indirectness: Results are based on number of participants at baseline, however authors did not report how many participants had HIV plus hypertension/diabetes at baseline. At 3-year follow-up, less than 1% of participants at follow-up had hypertension/diabetes and HIV infection (0.7% (694/103 777) in the control group and 0.6% (747/121 347) in the intervention group)</p> <p>c) Downgraded by 1 due to indirectness: Usual care comprised care according to national guidelines in Kenya and Uganda. Authors did not report what this entails. It is not clear to what extent care was integrated or not</p> <p>d) Downgraded by 1 due to imprecision: Small sub-sample with hypertension and HIV in the RCT with wide 95% confidence intervals</p> <p>e) Observational study, starting at low certainty evidence</p> <p>f) Downgraded by 1 due to indirectness: Intervention clinics experienced stock-outs of anti-hypertensive drugs and malfunctioning of BP machines. We are therefore not confident that the intervention was delivered as intended</p> <p>g) Downgraded by 1 due to indirectness: Study reported on population level new diabetics on treatment, clinic level new diabetics on treatment, population level new hypertensive patients on treatment and clinic level new hypertensive patients on treatment. This is an indirect measure of access to care</p>				

The SEARCH trial⁴⁰ reported the rate of all-cause mortality among baseline residents in included communities. Results suggest that integrated compared to usual care may make little or no difference to the mortality rate when compared to usual care but the evidence is very uncertain (RR 0.90 95%CI 0.79 to 1.02, n=171 431, 1 RCT, very low-certainty evidence).

Integrated care compared to usual care may make little or no difference to achieving BP control, but the evidence is very uncertain. Results from the SEARCH trial⁴⁰ suggest that integrated care compared to usual care may make little or no difference to the number of PLHIV who achieve BP control with prevalent hypertension at baseline (RR 1.09, 95%CI 0.98 to 1.21, 1 RCT, very low-certainty evidence) and PLHIV with prevalent hypertension at follow-up (RR 1.16, 95%CI 0.99 to 1.36, n=1441, 1 RCT, very low-certainty evidence). Results of the controlled ITS study³⁶ suggest that integrated care compared to usual care may increase the probability of achieving BP control by 1%, but the evidence is very uncertain ($\beta=0.010$, 95%CI 0.003 to 0.016, n=878, 1 ITS study, very low-certainty evidence).

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2 Results from the SEARCH trial⁴⁰ suggest that integrated care compared to usual care may make little
3 or no difference to the number of PLHV who achieve NCD (diabetes and/or hypertension) control
4 with prevalent NCD at baseline (RR 1.06, 95%CI 0.88 to 1.27, 1 RCT, very low-certainty evidence) and
5 prevalent NCD at follow-up but the evidence is very uncertain (RR 1.13, 95%CI 0.97 to 1.32, 1 RCT,
6 very low-certainty evidence).
7

8 One ITS study³⁶ reported on HIV control in terms of CD4 count control. Results suggest that
9 integrated care compared to usual care may increase the probability of achieving CD4 count control
10 by 6%, but the evidence is very uncertain ($\beta=0.057$, 95%CI 0.056 to 0.058, n=878, 1 ITS study, very
11 low-certainty evidence).
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14 Results from the SEARCH trial⁴⁰ suggest that integrated care compared to usual care may increase
15 the number of PLHIV who achieve both HIV viral suppression (HIV control) and BP control with
16 prevalent hypertension at baseline (RR 1.22, 95%CI 1.08 to 1.37, 1 RCT, very low-certainty evidence)
17 and with prevalent hypertension at follow-up (RR 1.24, 95%CI 1.10 to 1.40, n=1441, 1 RCT, very low-
18 certainty evidence). Integrated care compared to usual care may make little or no difference to the
19 number of PLHIV who achieve both HIV viral suppression (HIV control) and NCD control with
20 prevalent NCD at baseline (RR 1.18, 95%CI 0.97 to 1.44, 1 RCT, very low certainty), but may result in a
21 slight increase in the number of PLHIV who achieve both HIV viral suppression (HIV control) and NCD
22 control with prevalent NCD at follow-up (RR 1.24, 95%CI 1.10 to 1.40, 1 RCT very low-certainty
23 evidence). However, the evidence is very uncertain for these outcomes.
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27 One ITS study reported on access to care³⁹ in terms of the change in post-integration trend compared
28 to pre-integration trend for population level new diabetics on treatment, clinic level new diabetics on
29 treatment, population-level new hypertensive patients on treatment, and clinic level new
30 hypertensive patients on treatment. Integrated care may make little or no difference to population
31 level new diabetics on treatment at 18 (1/100 000, Standard Error (SE)=2, p=0.50, very low certainty)
32 and 36 months (1/100 000, SE=3, p=0.61, very low-certainty evidence) post-integration; clinic level
33 new diabetics on treatment at 18 (0/100 000, SE=1; p=0.96, very low-certainty evidence) and 36
34 months post-integration; clinic level new hypertensive patients on treatment at 18 (0/100 000, SE=1;
35 p=0.78, very low-certainty evidence) and 36 months (0/100 000, SE=0; p-value=0.57, very low-
36 certainty evidence) post-integration, and population level new hypertensive patients on treatment at
37 18 months post-integration (-7/100 000, SE=4; p=0.08, very low-certainty evidence). Results suggest
38 that there was a slight decrease in population level new hypertensive patients on treatment at 36
39 months post-integration (-6/100 000; SE=3; p=0.02, very low-certainty evidence). However, the
40 evidence is very uncertain for these outcomes.
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45 Authors also reported on the total number of patients on anti-retroviral treatment (ART) and the
46 number of new patients initiated on ART. Overall, the number of patients for both outcomes
47 increased during each year of follow-up. No effect size was reported. No other secondary outcomes
48 were reported for this comparison.
49

50 Interventions promoting integrated care compared to usual care

51 We included two studies in this comparison.^{37 38} Results are summarised in the summary of findings
52 table (Table 5) and forest plots are available in supplementary file 4.
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55 Results from one cluster RCT³⁷ suggest that interventions to promote integrated care compared to
56 usual care may make little or no difference in mortality (RR 1.11; 95% CI 0.79 to 1.56; n=3393; 1 RCT,
57 very low-certainty evidence) when compared to usual care, but the evidence is very uncertain.
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59 Results from two RCTs^{37 38} suggest that interventions to promote integrated care compared to usual
60 care may make little or no difference to depression scores, but the evidence is very uncertain. Fairall

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2 2016 reported the change in depression scores from baseline to follow up using the 10-item Center
3 for Epidemiologic Studies Depression Scale and reported no difference between groups (MD -0.12;
4 95%CI -1.72 to 1.48; n=3976, very low-certainty evidence). Prabhakaran 2019 measured depression
5 scores at follow-up using the Patient Health Questionnaire-9 and reported no difference between
6 groups (MD -1.6; 95%CI -4.4 to 1.2; n=3324, very low-certainty evidence).
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9 Results from one RCT³⁷ suggest that interventions to promote integrated care compared to usual
10 care may make little or no difference to quality of life, but the evidence is very uncertain. The RCT
11 reported on the change in health-related quality of life from baseline to follow-up using the EuroQol-
12 5D visual analogue scale and the EuroQol-5D index score. There was no difference between groups,
13 neither for the Euro-Qol-5D visual analogue scale (MD 6.06; 95%CI -3.25 to 15.36; n=3969, very low-
14 certainty evidence) nor for the EuroQol-5D index score (MD 0.00; 95%CI -0.05 to 0.06; n=3969, very
15 low-certainty evidence).
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18 Table 5: Summary of findings for interventions to promote integrated care compared to usual care
19 for diabetes and hypertension in LMICs
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Patient or population: Patients with diabetes, hypertension and other chronic diseases Setting: Low- and middle-income countries Intervention: Strategies to promote integrated care Comparison: Usual care						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with Strategies to promote integrated care				
Mortality	29 per 1,000	32 per 1,000 (23 to 45)	RR 1.11 (0.79 to 1.56)	4393 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to the risk of death, but the evidence is very uncertain
Depression	One study reported change in depression scores using the 10-item Center for Epidemiologic Studies Depression Scale and the other study reported depression scores at follow-up using the Patient Health Questionnaire-9. Both studies showed no effect.		-	7293 (2 RCTs)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to depression scores, but the evidence is very uncertain
Change in quality of life (Euro-Qol-5D visual analogue scale)	Quality of life scores with usual care improved by a mean of 6.4 points	The mean change in quality of life with integrated care was 6.06 points higher (3.25 points lower to 15.36 points higher)	-	3969 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference in quality of life, but the evidence is very uncertain
Change in HbA1c	The mean change in HbA1c with usual care ranged from -0.58 to -0.2%	The mean change in HbA1c with integrated care was 0.11 % higher (0.2 lower to 0.42 higher)	-	1687 (2 RCTs)	⊕⊕○○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on HbA1c
Change in systolic BP	The mean change in systolic BP with usual care ranged from -13.7 to -1.1 mmHg	The mean change in BP with integrated care was 1.11 mmHg higher (1.14 lower to 3.35 higher)	-	4807 (2 RCTs)	⊕⊕○○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on systolic BP

Change in total cholesterol	The mean change in total cholesterol with usual care was 2.0 mg/dl	The mean change in total cholesterol with integrated care was 2.5 mg/dl lower (7.1 lower to 2.1 higher)	-	3324 (1 RCT)	 LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on total cholesterol levels
<p>*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).</p> <p>CI: Confidence interval; RR: Risk ratio; MD: Mean difference; BP: Blood pressure; HbA1c: Glycated haemoglobin; RCT: Randomised controlled trial</p> <p>High certainty: We are very confident that the true effect lies close to that of the estimate of the effect</p> <p>Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</p> <p>Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect</p> <p>Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect</p> <p><i>Footnotes: Explanation of GRADE certainty of evidence</i></p> <ol style="list-style-type: none"> Downgraded by 1 due to high risk of performance bias and unclear risk of bias in some other domains Downgraded by 1 due to imprecision: study not adequately powered for this outcome, small sample size and wide 95% CI Downgraded by 1 due to indirectness: The interventions comprised strategies to promote integrated care at clinic level, and not integrated models of healthcare delivery at health system level 						

Results from two cluster RCTs^{37 38} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in HbA1c from baseline to follow-up (MD 0.11%; 95%CI -0.20 to 0.42; n=1687; 2 RCTs, low-certainty evidence).

Results from two cluster RCTs^{37 38} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in systolic BP from baseline to follow-up (MD 1.11mmHg; 95%CI -1.41 to 3.35; n=4807; 2 RCTs, low-certainty evidence).

Results from one cluster RCT³⁸ suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in total cholesterol from baseline to follow-up (MD - 2.50mg/dl; 95%CI -7.10 to 2.10; n=3324; low-certainty evidence).

Fairall 2016 reported the number of clinic visits three months before the follow-up interview and found no difference between groups (incidence rate ratio 1.02; 95%CI 0.93 to 1.13; n=3121).

One cluster RCT reported absolute numbers for drug adherence during the past seven days.³⁸ Patients in the intervention group reported greater adherence for both hypertensive drugs (833/1027; 81.1% vs. 648/1119; 57.9%) and anti-hyperglycemic drugs (683/829; 82.4% vs. 570/827; 68.9%) compared to patients receiving usual care.

One cluster RCT³⁸ reported on perceived change in quality of care as a composite perception on availability of drugs, guidance from physicians, quality of care, frequency of blood pressure measurement, and care provided by NCD nurses. Perceived quality of care improved in both groups. Patients receiving integrated care (n=1637), reported that quality of care was slightly/much better (96.6%), about the same (3.3%) and somewhat/much worse (0.2%). Patients receiving usual care (n=1687) reported that quality of care was slightly/much better (95%), about the same (4.4%) and somewhat/much worse (0.5%).

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2 Neither of the two cluster RCTs included in this comparison reported on access to care, continuity of
3 care or cost of care.
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5 6 Discussion 7

8 We included five studies and two comparisons in this review. Three studies were conducted in South
9 Africa, one in India and one in Kenya and Uganda. Two ITS studies and one cluster RCT provided data
10 for the first comparison, integration of chronic disease services compared to usual care. Results
11 suggest that integrated models of care compared to usual care may make little or no difference to
12 mortality, the number of people achieving blood pressure (BP) or diabetes control, and access to
13 care; may increase the number of people who achieve both HIV and BP/diabetes control; and may
14 have a very small effect on achieving HIV control. However, the evidence for all outcomes is very
15 uncertain. Two cluster RCTs provided data for the second comparison, interventions promoting
16 integrated care compared to usual care. Results suggest that interventions to promote integrated
17 care compared to usual care may make little or no difference to mortality, depression and quality of
18 life, but the evidence is very uncertain. Interventions to promote integrated care compared to usual
19 care may have little or no effect on HbA1c, systolic BP, and total cholesterol levels. Process outcomes
20 were poorly reported across included studies, with none of the studies reporting on continuity of
21 care or cost of care.
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25 We followed a rigorous and systematic process according to standard systematic review methods.
26 We performed a comprehensive search of published and unpublished studies up to 12 December
27 2019, with no language restrictions. We assessed the certainty of evidence using the GRADE
28 approach across outcomes, taking into consideration study limitations, inconsistency, imprecision,
29 publication bias and indirectness when downgrading the certainty of evidence.
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32 Other systematic reviews that assessed the effects of integrated models of care on health outcomes
33 in LMICs had similar findings. Dudley and Garner²⁵ assessed strategies to integrate PHC services on
34 healthcare delivery and health status in LMICs. They found no evidence that integrated services
35 improved healthcare delivery or health status. However, none of the included studies assessed
36 integrated care for NCDs. Haldane and colleagues²³ described existing integrated models of care for
37 HIV and NCDs and assessed health outcomes, barriers and facilitators. However, most of the included
38 studies were descriptive or observational and health outcomes were poorly reported. Indeed, they
39 highlighted the need for rigorous research that includes long-term follow-up and the role of
40 incentives.
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43 Although we considered multi-morbidity in terms of diabetes and/or hypertension plus any other
44 disease, four out of five studies were conducted in sub-Saharan Africa and included people with
45 diabetes and/or hypertension (and other NCDs) and HIV. Due to successful transformation of the
46 health systems to deliver HIV programmes, sub-Saharan Africa is presented with a unique
47 opportunity to leverage the investments made in order to scale-up NCD services. This can be
48 achieved in various ways, such as integrating NCD services into facilities originally providing HIV care
49 only, integrating HIV care into PHC facilities that offer NCD care, or concurrent introduction of HIV
50 and NCD services.⁸ However, even though this is recognised, there are still questions linked to the
51 implementation of integrated models of care. In South Africa, the ICDM model, the intervention
52 evaluated in the ITS study by Ameh and colleagues,³⁶ is one example where the vertical HIV
53 programme was integrated into general PHC facilities. As part of the pilot programme, Ameh and
54 colleagues not only evaluated the impact on health outcomes, but also conducted a qualitative study
55 to explore the perspectives of healthcare providers and patients on the quality of care in the ICDM
56 model.⁸³ They found that PHC facilities experienced BP drug stock-outs, lack of functioning BP
57 machines and staff shortages, among others, which impacted on the delivery of care and indirectly
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2 therefore on the health outcomes. Integrated NCD and HIV care is implemented to a varying degree
3 in other sub-Saharan African countries. A study examining policies and programmes for integrated
4 HIV and NCD care in Malawi, Kenya, South Africa and Swaziland found that these countries still
5 experience challenges in implementing integrated care. Some of these are related to inadequate
6 data to determine the burden of NCDs among PLHIV at a local level, lack of evidence to support the
7 implementation of integrated care models, inadequate stakeholder engagement, lack of NCD care
8 capacity and other health system challenges.⁸⁴
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11 Our definition of integrated care was based on a “one-stop-shop” model whereby a patient receives
12 all necessary care or services under one roof by one or more health-care professional (Figure 1),
13 which is just one way of describing integrated care. Indeed, a narrative review by Njuguna, et al.⁸⁵
14 aimed to describe various models of integrated care for HIV and NCDs in sub-Saharan Africa. Based
15 on the definition by WHO, the authors defined integrated care as the “coordination, co-location, or
16 simultaneous delivery of HIV and NCD services to patients who need it, when they need it” and
17 identified five models. These include community-based integrated HIV and NCD screening in the
18 general population; screening for NCD risk factors among PLHIV; integrated care for HIV and NCDs in
19 healthcare facilities through leveraging the HIV infrastructure to manage NCDs; differential care for
20 people well-controlled HIV or NCDs, which includes longer follow-up periods for stable patients; and
21 population health for all patients with any need.⁸⁵ We included two cluster RCTs that aimed to
22 promote integrated care through clinical management tools, which is different from integrated care
23 at facility level. We discussed this within our team and concluded that the aim of these interventions
24 was to provide care in a holistic way and to address all the needs of an individual when s/he presents
25 to a healthcare facility, and thus met our eligibility criteria.
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31 Integration of care for NCDs and HIV or other diseases is complex, partly due to the complex nature
32 of health systems.⁸⁶ Our review focused on the effectiveness of integrating care for people with
33 diabetes, hypertension and other co-morbidities in terms of health outcomes, which is just one
34 question that needs to be answered. In other words, the question of our review focused on one
35 building block of health systems as described by the WHO.⁸⁶ Although we aimed to examine process
36 outcomes, these were limited to access to care, retention in care, adherence, continuity of care,
37 quality of care and cost of care; and were poorly reported across included studies. The scope of our
38 review did not include outcomes related to implementation or perspectives from health providers
39 and patients, which are important aspects to consider. Although the literature predominantly
40 highlights the need to integrate NCD and HIV care, integrating mental health services into existing
41 NCD and or HIV services is just as important. Four⁴²⁻⁴⁵ of the five ongoing studies that we identified
42 examine integration of mental health with NCDs.
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46 Conclusion

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48 The evidence on the effectiveness of integrated models of care for people with diabetes,
49 hypertension and other co-morbidities, on health outcomes is very uncertain. We therefore do not
50 know whether integrated models of care lead to better or worse outcomes, or may make no
51 difference at all among people with diabetes, hypertension and other chronic conditions. There is a
52 need to scale-up NCD services, particularly in LMICs. In the context of an increasing burden of NCDs
53 against a backdrop of other chronic diseases, and scarce health system resources, such as human
54 capacity and funding, policies and programmes need to promote integrated models of care and
55 holistic, patient-centred services. However, these need to take into consideration context-specific
56 factors related to the health system and the targeted population.
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60 Further rigorous studies assessing the effects of integrated models of care on health outcomes are
needed. These studies should include an adequate description of the integrated model of care,

1
2 assess long term health effects as well as patient important outcomes, and cost of care.
3 Furthermore, there is a need to conduct implementation research, economic evaluations as well as
4 qualitative research on the barriers and facilitators to integrated models of care at patient and
5 health-system level in order to guide policy makers in planning and allocation of resources in order to
6 maximise the potential benefits of integrated care as well strengthening the health systems in
7 achieving universal health coverage in LMICs.
8
9

10 Authors' contributions

11 All authors contributed to development of the review protocol. JUN and AR screened titles and
12 abstracts; JUN, AR, TY and CMB participated in full text screening; TY, JJM and IT helped to resolve
13 discrepancies. AR, JUN and IT extracted data and assessed risk of bias. AR and IT assessed certainty of
14 evidence with input from TY and JJM. TY and JJM provided overall methodological guidance. JUN
15 drafted the background section, AR drafted the rest of the manuscript. JUN, IT, TY, and CMB critically
16 read and revised the manuscript. All authors have approved the final version of the manuscript.
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19

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22 Ayele for statistical input, and Selvan Naidoo for assistance with screening titles and abstracts.
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26 Data sharing statement

27 Not applicable
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30 Funding statement

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40 Competing interests statement

41 All authors have no known conflict of interest.
42
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45 Protocol

46 Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension
47 in low- and middle-income countries (LMICs): Protocol for a systematic review. *Syst Rev*
48 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]
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52 Figures

53 Figure 1: Logic model of integrated care
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56 Figure 2: PRISMA flow diagram
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59 Figure 3: Risk of bias in ITS studies
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Figure 4: Risk of bias for cluster RCTs

Supplementary files

Supplementary file 1: MEDLINE (PubMed) search strategy

Supplementary file 2: Summary of interventions according to the TIDiER checklist: Integrated models of care

Supplementary file 3: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated management of care

Supplementary file 4: Risk of bias assessments for included studies

Supplementary file 5: Forest plots

For peer review only

References

1. WHO. Noncommunicable diseases, 2018.
2. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390(10100):1211-59. doi: 10.1016/S0140-6736(17)32154-2 [published Online First: 2017/09/19]
3. Alliance N. Tackling non-communicable diseases in workplace settings in low- and middle-income countries. A CALL TO ACTION AND PRACTICAL GUIDANCE. Non-Communicable diseases (NCD) Alliance, 2017.
4. WHO. Cardiovascular diseases (CVDs) 2017 [Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))].
5. WHO. Global status report on non-communicable diseases 2010. Description of the global burden of NCDs, their risk factors and determinants, 2010.
6. Federation ID. IDF diabetes Atlas 8th Edition. 8 ed 2017. Available from: <https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/134-idf-diabetes-atlas-8th-edition.html>.
7. Campbell NRC, Lackland DT, Niebylski ML. High Blood Pressure: Why Prevention and Control Are Urgent and Important-A 2014 Fact Sheet From the World Hypertension League and the International Society of Hypertension. *Journal of Clinical Hypertension* 2014;16(8):551-53. doi: 10.1111/jch.12372
8. Duffy M, Ojikutu B, Andrian S, et al. Non-communicable diseases and HIV care and treatment: models of integrated service delivery. *Tropical Medicine and International Health* 2017;22(8):926-37. doi: 10.1111/tmi.12901
9. Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African primary healthcare. *South African Medical Journal* 2015;105(2):134-38. doi: 10.7196/SAMJ.8696
10. Remais JV, Zeng G, Li G, et al. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *International Journal of Epidemiology* 2013;42(1):221-27. doi: 10.1093/ije/dys135
11. Rabkin M, Kruk ME, El-Sadr WM. HIV, aging and continuity care: strengthening health systems to support services for noncommunicable diseases in low-income countries. *AIDS* 2012;26
12. Patel P, Rose CE, Collins PY, et al. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis. *AIDS* 2018;32 Suppl 1:S5-S20. doi: 10.1097/QAD.0000000000001888 [published Online First: 2018/06/29]
13. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012 doi: 10.1016/S0140-6736(12)61728-0
14. Mbanya JCN, Motala AA, Sobngwi E, et al. Diabetes in sub-Saharan Africa, 2010.
15. Atun R, De Jongh T, Secci F, et al. A systematic review of the evidence on integration of targeted health interventions into health systems. *Health Policy and Planning* 2010;25(1):1-14. doi: 10.1093/heapol/czp053
16. Shigayeva A, Atun R, McKee M, et al. Health systems, communicable diseases and integration. *Health Policy and Planning* 2010;25(Suppl. 1):i4-i20. doi: 10.1093/heapol/czq060
17. WHO. Package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings.
18. Legido-Quigley H, Montgomery CM, Khan P, et al. Integrating tuberculosis and HIV services in low- and middle-income countries: A systematic review. *Tropical Medicine and International Health* 2013;18(2):199-211. doi: 10.1111/tmi.12029
19. Naidoo K, Gengiah S, Yende-Zuma N, et al. Addressing challenges in scaling up TB and HIV treatment integration in rural primary healthcare clinics in South Africa (SUTHI): A cluster randomized controlled trial protocol. *Implementation Science* 2017;12(1):1-12. doi: 10.1186/s13012-017-0661-1
20. Uyei J, Coetzee D, Macinko J, et al. Integrated delivery of HIV and tuberculosis services in sub-Saharan Africa: A systematic review. *The Lancet Infectious Diseases* 2011;11(11):855-67. doi: 10.1016/S1473-3099(11)70145-1

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 - 59
 - 60
21. Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension in low- and middle-income countries (LMICs) : Protocol for a systematic review. *Syst Rev* 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]
22. Yiu KC, Rohwer A, Young T. Integration of care for hypertension and diabetes: a scoping review assessing the evidence from systematic reviews and evaluating reporting. *BMC Health Serv Res* 2018;18(1):481. doi: 10.1186/s12913-018-3290-8 [published Online First: 2018/06/22]
23. Haldane V, Legido-Quigley H, Chuah FLH, et al. Integrating cardiovascular diseases, hypertension, and diabetes with HIV services: a systematic review. *AIDS Care* 2018;30(1):103-15. doi: 10.1080/09540121.2017.1344350 [published Online First: 2017/07/07]
24. Janssens B, Van Damme W, Raleigh B, et al. BulleJohnson, W., Onuma, O., Owolabi, M., & Sachdev, A. S. (2017AD). Bulletin of the World Health Organization Stroke: a global response is needed. Bulletin of the World Health Organization, 85(February), 660–667. <https://doi.org/10.2471/BLTtin> of the Worl. *Bulletin of the World Health Organization* 2007;85:880-85. doi: 10.2471/BLT
25. Dudley L, Garner P. Strategies for integrating primary health services in low- and middle-income countries at the point of delivery. *Cochrane Database of Systematic Review* 2011(7) doi: doi: 10.1002/14651858.CD003318.pub3.
26. Bank W. World Bank list of economies 2016 [Available from: Siteresources.worldbank.org/DATASTATISTICS/Resources/CLASS.XLS]
27. Covidence systematic review software [program]. Melbourne, Australia: Veritas Health Innovation
28. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687. doi: 10.1136/bmj.g1687 [published Online First: 2014/03/13]
29. Guise JM, Butler ME, Chang C, et al. AHRQ series on complex intervention systematic reviews- paper 6: PRISMA-CI extension statement and checklist. *J Clin Epidemiol* 2017;90:43-50. doi: 10.1016/j.jclinepi.2017.06.016 [published Online First: 2017/07/20]
30. (EPOC) CEPaOoC. Suggested risk of bias criteria for EPOC reviews. . EPOC Resources fo r review authors, 2017.
31. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019): Cochrane 2019. Available from: www.training.cochrane.org/handbook
32. Review Manager (RevMan) [program]. 5.3 version. Copenhagen: The Cochrane Collaboration, 2014.
33. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026 [published Online First: 2011/01/05]
34. GRADEpro GDT: GRADEpro Guideline Development Tool [Software] [program]: McMaster University, 2015.
35. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64(4):401-6. doi: 10.1016/j.jclinepi.2010.07.015 [published Online First: 2011/01/07]
36. Ameh S, Klipstein-Grobusch K, Musenge E, et al. Effectiveness of an Integrated Approach to HIV and Hypertension Care in Rural South Africa: Controlled Interrupted Time-Series Analysis. *Journal of acquired immune deficiency syndromes (1999)* 2017;75(4):472-79. doi: 10.1097/qai.0000000000001437
37. Fairall LR, Folb N, Timmerman V, et al. Educational Outreach with an Integrated Clinical Tool for Nurse-Led Non-communicable Chronic Disease Management in Primary Care in South Africa: A Pragmatic Cluster Randomised Controlled Trial. *PLoS medicine* 2016;13(11):e1002178. doi: 10.1371/journal.pmed.1002178
38. Prabhakaran D, Jha D, Prieto-Merino D, et al. Effectiveness of an mHealth-Based Electronic Decision Support System for Integrated Management of Chronic Conditions in Primary Care:

- 1
2 The mWellcare Cluster-Randomized Controlled Trial. *Circulation* 2018 doi:
3 10.1161/CIRCULATIONAHA.118.038192
- 4 39. Rawat A, Uebel K, Moore D, et al. Integrated HIV-Care into Primary Health Care Clinics and the
5 Influence on Diabetes and Hypertension Care: An Interrupted Time Series Analysis in Free
6 State, South Africa over 4 Years. *Journal of Acquired Immune Deficiency Syndromes*
7 2018;77(5):476-83. doi: <http://dx.doi.org/10.1097/QAI.0000000000001633>
- 8 40. Havlir DV, Balzer LB, Charlebois ED, et al. HIV Testing and Treatment with the Use of a Community
9 Health Approach in Rural Africa. *N Engl J Med* 2019;381(3):219-29. doi:
10 10.1056/NEJMoa1809866 [published Online First: 2019/07/18]
- 11 41. Integrated versus referred management of cardiovascular disease (CVD) risk factors for HIV-
12 positive patients on antiretroviral therapy in Swaziland 20th International Workshop on Co-
13 morbidities and Adverse Drug Reactions in HIV; 2018; New York, USA.
- 14 42. Chen S, Conwell Y, Xue J, et al. Protocol of an ongoing randomized controlled trial of care
15 management for comorbid depression and hypertension: the Chinese Older Adult
16 Collaborations in Health (COACH) study. *BMC geriatrics* 2018;18(1):124. doi:
17 10.1186/s12877-018-0808-1
- 18 43. Petersen I, Bhana A, Folb N, et al. Collaborative care for the detection and management of
19 depression among adults with hypertension in South Africa: study protocol for the PRIME-SA
20 randomised controlled trial. *Trials* 2018;19(1):192. doi: 10.1186/s13063-018-2518-6
- 21 44. Myers B, Lund C, Lombard C, et al. Comparing dedicated and designated models of integrating
22 mental health into chronic disease care: study protocol for a cluster randomized controlled
23 trial. *Trials* 2018;19(1) (no pagination) doi: 10.1186/s13063-018-2568-9
- 24 45. Srinivasan K, Mazur A, Mony PK, et al. Improving mental health through integration with primary
25 care in rural Karnataka: study protocol of a cluster randomized control trial. *BMC Fam Pract*
26 2018;19(1):158. doi: 10.1186/s12875-018-0845-z [published Online First: 2018/09/13]
- 27 46. Devarsetty P. Diabetes and Tuberculosis - Integrated management using the primary healthcare
28 infrastructure in India 2017 [Available from:
29 <http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=15771>
- 30 47. Abrahams-Gessel S, Beratarrechea A, Irazola V, et al. Using mHealth tools to improve access,
31 coverage and treatment of uninsured people with high cardiovascular disease risk in
32 Argentina: a study protocol for a pragmatic cluster randomised trial. *BMJ innovations*
33 2018;4(3):135-41. doi: 10.1136/bmjinnov-2017-000255
- 34 48. Adomaviciute S, Watt H, Soljak M, et al. Impact of the Integrated Care Pilot on HbA1c, cholesterol
35 and systolic blood pressure levels in patients with diabetes. *Diabetic Medicine*
36 2014;31(SUPPL. 1):175. doi: http://dx.doi.org/10.1111/dme.12378_2
- 37 49. Alharbi TJ, Tourkmani A, Alkhashan H, et al. Impact of integrated care program on glycemic
38 control and cardiovascular risk in patients with type 2 diabetes; Interventional controlled
39 study. *Diabetes Research and Clinical Practice* 2014;106(SUPPL. 1):S93-S94.
- 40 50. Miao Y, Zhang L, Sparring V, et al. Improving health related quality of life among rural
41 hypertensive patients through the integrative strategy of health services delivery: A quasi-
42 experimental trial from Chongqing, China. *International Journal for Equity in Health*
43 2016;15(1):132. doi: <http://dx.doi.org/10.1186/s12939-016-0421-x>
- 44 51. Rakic D, Jakovljevic D. [Integrated approach to prevention and control of cardiovascular diseases].
45 *Srpski arhiv za celokupno lekarstvo* 2011;139(5-6):304-10.
- 46 52. Sarrafzadegan N, Baghaei A, Sadri G, et al. Isfahan healthy heart program: Evaluation of
47 comprehensive, community-based interventions for non-communicable disease prevention.
48 *Prevention and Control* 2006;2(2):73-84. doi: <http://dx.doi.org/10.1016/j.precon.2006.10.003>
- 49 53. Spaak J, Brommels M, Kahan T, et al. Integrated, Multidisciplinary, Person-centered Care for
50 Patients With Complex Comorbidities: Heart, Kidney and Diabetes, 2017.
- 51 54. Ajay VS, Jindal D, Roy A, et al. Development of a Smartphone-Enabled Hypertension and Diabetes
52 Mellitus Management Package to Facilitate Evidence-Based Care Delivery in Primary
53 Healthcare Facilities in India: The mPower Heart Project. *Journal of the American Heart*
54 *Association* 2016;5(12) doi: 10.1161/jaha.116.004343
- 55
56
57
58
59
60

- 1
2 55. Al Asmary SM, Al-Harbi T, Tourkmani AM, et al. Impact of integrated care program on glycemic
3 control and cardiovascular risk in adult patients with type 2 diabetes. *Journal of Clinical*
4 *Outcomes Management* 2013;20(8):356-63.
- 5 56. Garrib A, Birungi J, Lesikari S, et al. Integrated care for human immunodeficiency virus, diabetes
6 and hypertension in Africa. *Transactions of the Royal Society of Tropical Medicine and*
7 *Hygiene* 2018 doi: 10.1093/trstmh/try098
- 8 57. Germe M, Zingwari J, Matji R, et al. Baseline assessment of high volume facility capacity to
9 provide integrated tuberculosis (TB) and diabetes (DM) services in South Africa. *Diabetes*
10 2017;66(Supplement 1):A460-A61.
- 11 58. Kwarisiima D, Atukunda M, Owaraganise A, et al. Hypertension control in integrated HIV and
12 chronic disease clinics in Uganda in the SEARCH study. *BMC Public Health* 2019;19(1):511.
13 doi: 10.1186/s12889-019-6838-6 [published Online First: 2019/05/08]
- 14 59. Li Q, Li L, Fan XL, et al. The values of evidence-based comprehensive care for patients with type 2
15 diabetes mellitus and cardiovascular diseases to improve the quality of life. *Heart*
16 2013;99(SUPPL. 3):A282-A83. doi: <http://dx.doi.org/10.1136/heartjnl-2013-304613.797>
- 17 60. Mahomed OH, Asmall S, Freeman M. An integrated chronic disease management model: a
18 diagonal approach to health system strengthening in South Africa. *Journal of health care for*
19 *the poor and underserved* 2014;25(4):1723-29. doi:
20 <http://dx.doi.org/10.1353/hpu.2014.0176>
- 21 61. Narayanan G, Prabhakaran D. Integrating mental health into cardiovascular disease research in
22 India. *National Medical Journal of India* 2012;25(5):274-80.
- 23 62. Nigatu T. Integration of HIV and noncommunicable diseases in health care delivery in low- and
24 middle-income countries. *Preventing chronic disease* 2012;9:E93.
- 25 63. Nyabera RA, Yonga G, Mwangemi F, et al. Evaluation of a project integrating cardiovascular care
26 into HIV programmes. *Cardiovascular Journal of Africa* 2011;22(3 SUPPL. 1):S17.
- 27 64. Patel P, Speight C, Maida A, et al. Integrating HIV and hypertension management in low-resource
28 settings: Lessons from Malawi. *PLoS medicine* 2018;15(3):e1002523. doi:
29 10.1371/journal.pmed.1002523
- 30 65. Patel V, Chatterji S. Integrating Mental Health In Care For Noncommunicable Diseases: An
31 Imperative For Person-Centered Care. *Health affairs (Project Hope)* 2015;34(9):1498-505.
32 doi: 10.1377/hlthaff.2015.0791
- 33 66. Rabkin M, Palma A, McNairy ML, et al. Integrating cardiovascular disease risk factor screening
34 into HIV services in Swaziland: lessons from an implementation science study. *Aids*
35 2018;32:S43-S46. doi: 10.1097/qad.0000000000001889
- 36 67. Samb B, Desai N, Nishtar S, et al. Chronic Diseases: Chronic Diseases and Development 4
37 Prevention and management of chronic disease: a litmus test for health-systems
38 strengthening in low-income and middle-income countries. *Lancet* 2010;376(9754):1785-97.
39 doi: 10.1016/s0140-6736(10)61353-0
- 40 68. Sarraf-Zadegan N, Sadri G, Malek Afzali H, et al. Isfahan Healthy Heart Programme: a
41 comprehensive integrated community-based programme for cardiovascular disease
42 prevention and control. Design, methods and initial experience. *Acta cardiologica*
43 2003;58(4):309-20. doi: 10.2143/ac.58.4.2005288
- 44 69. Sushilkumar PL, Mahendrakumar BJ, Suman B, et al. Implementation and evaluation of health
45 screening services to diabetic and hypertensive patients in a selected community pharmacy
46 at belgaum city. *Asian Journal of Pharmaceutical and Clinical Research* 2015;8(3):305-15.
- 47 70. Tedjokusumo R. Introducing the integrated cardiovascular services at Dr. Hasan Sadikini Hospital.
48 *Heart Lung and Circulation* 2003;12(SUPPL. 2):S82-384. doi:
49 <http://dx.doi.org/10.1046/j.1443-9506.2003.t01-4-x>
- 50 71. Tiam A, Oyebanji O, Nkonyana J, et al. Family health days: An innovative approach to providing
51 integrated health services for HIV and non-communicable diseases among adults and
52 children in hard-to-reach areas of Lesotho. *Journal of the International AIDS Society*
53 2012;15(SUPPL. 3):236. doi: <http://dx.doi.org/org/10.7448/IAS.15.5.18438>
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45
46
47
48
49
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51
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53
54
55
56
57
58
59
60
72. Wasay M, Jabbar A. Fight against chronic diseases (high blood pressure, stroke, diabetes and cancer) in Pakistan; cost-effective interventions. *JPMA The Journal of the Pakistan Medical Association* 2009;59(4):196-7.
73. Bachmann MO, Bateman ED, Stelmach R, et al. Integrating primary care of chronic respiratory disease, cardiovascular disease and diabetes in Brazil: Practical Approach to Care Kit (PACK Brazil): study protocol for randomised controlled trials. *Journal of Thoracic Disease* 2018;10(7):4667-77.
74. Hong T. Web-Based Collaborative Care for Patients With Diabetes and Depression. <https://clinicaltrials.gov/show/nct01985711> 2013
75. Kowalski AJ, Poongothai S, Chwastiak L, et al. The INtegrating DEPrEssioN and Diabetes treatment (INDEPENDENT) study: Design and methods to address mental healthcare gaps in India. *Contemporary clinical trials* 2017;60:113-24. doi: 10.1016/j.cct.2017.06.013
76. McKee MD, Fletcher J, Sigal I, et al. A collaborative approach to control hypertension in diabetes: outcomes of a pilot intervention. *Journal of primary care & community health* 2011;2(3):148-52. doi: 10.1177/2150131911401028
77. Mendis S, Johnston SC, Fan W, et al. Cardiovascular risk management and its impact on hypertension control in primary care in low-resource settings: a cluster-randomized trial. *Bulletin of the World Health Organization* 2010;88(6):412-9. doi: 10.2471/blt.08.062364
78. Pibernik-Okanovic M, Hermanns N, Ajdukovic D, et al. Does treatment of subsyndromal depression improve depression-related and diabetes-related outcomes? A randomised controlled comparison of psychoeducation, physical exercise and enhanced treatment as usual. *Trials* 2015;16:305. doi: 10.1186/s13063-015-0833-8
79. Saleh S, Farah A, Dimassi H, et al. Using Mobile Health to Enhance Outcomes of Noncommunicable Diseases Care in Rural Settings and Refugee Camps: Randomized Controlled Trial. *JMIR mHealth and uHealth* 2018;6(7):e137. doi: 10.2196/mhealth.8146
80. Sarrafzadegan N, Kelishadi R, Esmailzadeh A, et al. Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran. *Bull World Health Organ* 2009;87(1):39-50. doi: 10.2471/blt.07.049841
81. Tourkmani AM, Abdelhay O, Alkhashan HI, et al. Impact of an integrated care program on glycemic control and cardiovascular risk factors in patients with type 2 diabetes in Saudi Arabia: an interventional parallel-group controlled study. *BMC Fam Pract* 2018;19:10. doi: 10.1186/s12875-017-0677-2
82. Wenxi T, Yan Z, Liang Z. Effects of provider incentives in integrated healthcare delivery system reform: a quasiexperiment on patients with chronic diseases in rural China. *International Journal of Integrated Care (IJIC)* 2017;17(3):171-72. doi: 10.5334/ijic.3207
83. Ameh S, Klipstein-Grobusch K, D'Ambruoso L, et al. Quality of integrated chronic disease care in rural South Africa: user and provider perspectives. *Health Policy Plan* 2017;32(2):257-66. doi: 10.1093/heapol/czw118 [published Online First: 2017/02/17]
84. Matanje Mwagomba BL, Ameh S, Bongomin P, et al. Opportunities and challenges for evidence-informed HIV-noncommunicable disease integrated care policies and programs: lessons from Malawi, South Africa, Swaziland and Kenya. *AIDS* 2018;32 Suppl 1:S21-S32. doi: 10.1097/QAD.0000000000001885 [published Online First: 2018/06/29]
85. Njuguna B, Vorkoper S, Patel P, et al. Models of integration of HIV and noncommunicable disease care in sub-Saharan Africa: lessons learned and evidence gaps. *AIDS* 2018;32 Suppl 1:S33-S42. doi: 10.1097/QAD.0000000000001887 [published Online First: 2018/06/29]
86. WHO. Everybody's business: Strengthening Health Systems to improve Health Outcomes. WHO's Framework for Action. , 2007.

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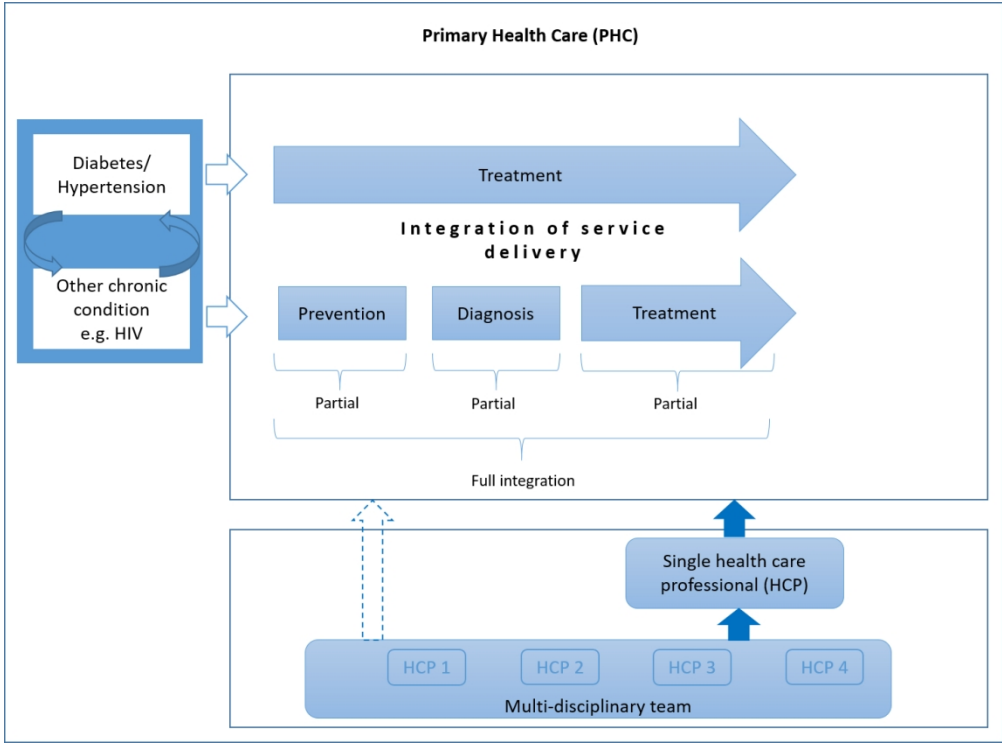


Figure 1: Logic model of integrated care

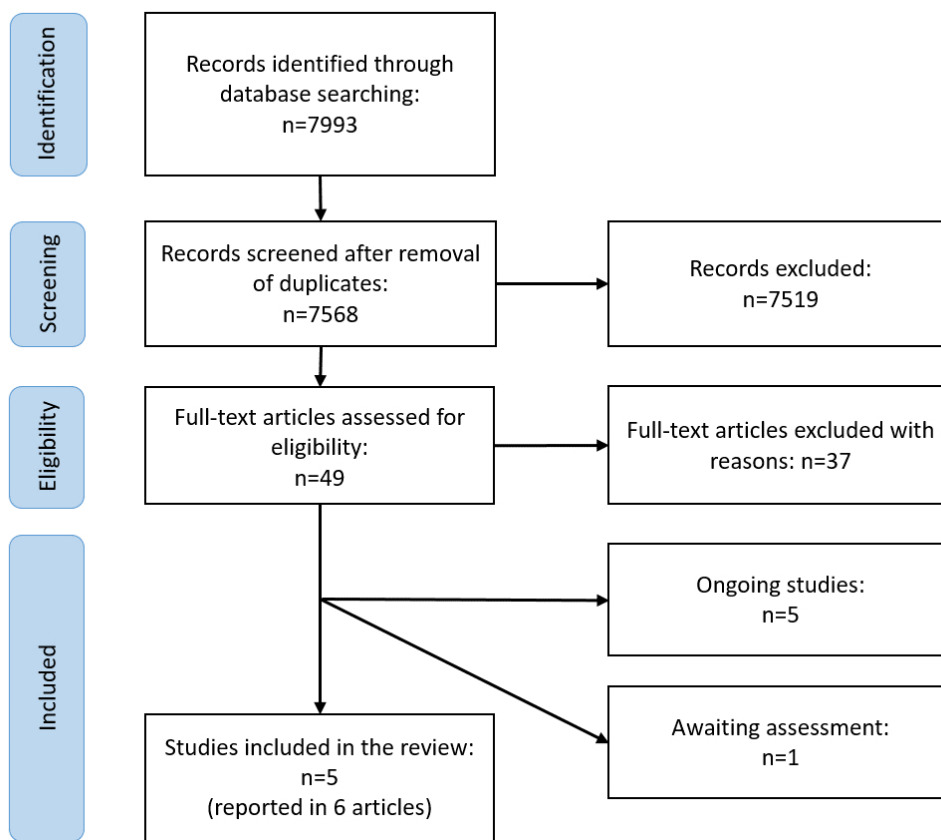


Figure 2: PRISMA flow diagram

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	Intervention was independent of other changes	The shape of the intervention was pre-specified	The intervention was unlikely to affect data collection	Knowledge of the allocated intervention adequately prevented during the study	Incomplete outcome data was likely to bias results	Outcomes were reported selectively	Other bias
Ameh 2017	+	+	?	?	+	+	+
Rawat 2018	+	?	+	+	?	+	+

Figure 3: Risk of bias in ITS studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data (attrition bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Protection against contamination	Selective reporting (reporting bias)	Recruitment bias	Baseline differences (clusters)	Loss of clusters	Incorrect analysis	Compatibility with RCTs randomised by individuals	Other bias	
Fairall 2016	+	+	+	?	+	-	?	?	+	+	+	+	+	+	+	?
Havlr 2019	+	+	?	+	?	-	?	?	?	+	?	+	?	+	+	?
Prabhakaran 2018	+	+	+	+	+	-	?	+	+	?	?	+	+	+	+	+

Figure 4: Risk of bias for cluster RCTs

Supplementary file 1: Medline (PubMed) search strategy

#1 "Hypertension"[Mesh] OR (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)[title/abstract]

#2 diabetes OR "diabetes mellitus"[title/abstract] OR "Diabetes Mellitus"[Mesh]

#3 #1 OR #2

#4 (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein)[title/abstract] OR "Dyslipidemias"[Mesh]

#5 (((HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR HIV/AIDS))) OR ((HIV infections [MeSH] OR HIV [MeSH]))

#6 (tuberculosis OR tuberculoses OR tb)[Title/Abstract] OR "tuberculosis"[Mesh]

#7 "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR NCD OR NCDs OR "Noncommunicable Diseases"[Mesh]

#8 (comorbid* OR co-morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity")[title/abstract] OR "Multimorbidity"[Mesh] OR "Comorbidity"[Mesh]

#9 multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring condition* OR cooccurring condition*

#10 chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle" OR "Multiple Chronic Conditions"[Mesh] OR "Chronic Disease"[Mesh]

#11 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 "Delivery of Health Care, Integrated"[Mesh] OR "delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "Comprehensive Health Care"[Mesh] OR "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "Continuity of Patient Care"[Mesh] OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "Patient-Centered Care"[Mesh] OR "patient centered care" OR "patient centred care"

#13 "Referral and Consultation"[Mesh] OR (referral AND consultation)

#14 integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR "integration of services" OR integrat* delivery OR integrat* management OR "integration of management"

#15 coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of services" OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat* management OR "coordination of management"

#16 co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes" OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-ordinat* management OR "co-ordination of management"

#17 horizontal care OR vertical care OR horizontal services OR vertical services OR horizontal programmes OR horizontal programs OR vertical programmes OR vertical programs OR horizontal service delivery OR vertical service delivery OR horizontal services OR vertical services OR horizontal delivery OR vertical management OR vertical management

#18 "multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR "multi delivery" OR multidelivery OR "multi management"

#19 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

#20 #3 AND #11 AND #19

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Supplementary file 2: Summary of interventions according to the TIDiER checklist: Integrated models of care

Study ID	Ameh 2017		Rawat 2018*	Havlir 2019	
Intervention groups	Intervention	Control	Intervention	Intervention	Control
Name of intervention	Integrated chronic disease management (ICDM) model	Standard care in clinics where ICDM model was not piloted	Implementation of national policy to integrate HIV care into all PHC facilities	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and patient-centered care	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care
Aim of the intervention	To improve management of patients with HIV, TB, hypertension, diabetes, COPD, asthma, epilepsy and mental health conditions at PHCs	Not reported	To provide comprehensive HIV care (prevention, diagnosis, treatment initiation and follow-up) at PHC facilities	To remove patient-level barriers and maximise the efficiency of the health system To overcome barriers of universal access to HIV treatment and to be able to reach UNAIDS goals	Not reported
Physical and informational materials used	Not reported	Not reported	Not reported	Treatment guidelines ART tablets SMS reminders	National treatment guidelines
Procedures, activities and processes used in the intervention	Facility reorganisation: designated chronic care area; supply of critical medicines; pre-packaging of medication	Not reported	Policy to integrate HIV care into PHC clinics Training of nurses in comprehensive management of HIV: Nurse initiated	Community health campaigns (CHCs): Multi-disease testing for HIV, diabetes and hypertension; counselling and clinic appointments for participants with positive tests; HIV	Community health campaigns: Multi-disease testing for HIV, diabetes and hypertension; counselling and clinic appointments for participants with positive tests; HIV positive

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	<p>Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral</p> <p>Ward-based outreach teams to ensure individual responsibility and "assisted" self-management</p> <p>Health promotion and population screening</p>		<p>Management of ART (NIMART)</p> <p>Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)</p> <p>Additional staff to strengthen drug delivery systems</p>	<p>positive participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>Home-based testing for participants that did not attend CHCs</p> <p>Linkage to ART: HIV positive participants not on ART received appointments to initiate ART within a maximum of 7 days; clinic staff introduce themselves in person or by mobile phone; participants could contact hotline via phone or text message for questions or support; phone/SMS reminders about clinic visits</p> <p>Patient-centered care for HIV, diabetes, hypertension: 3-month visit intervals; flexible clinic hours; reduced waiting time at clinics; welcoming staff; ART to</p>	<p>participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>ART, diabetes and hypertension treatment: provided in accordance with national guidelines</p>
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				<p>all HIV positive participants; if not eligible for ART according to national guidelines, trial provided Nevirapine; hypertension and diabetes treated according to standard algorithms</p>	
<p>Who provided the intervention</p>	<p>Nurses</p>	<p>Nurses</p>	<p>Nurses</p>	<p>CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya</p> <p>Patient-centered care: government clinics augmented by trial staff</p>	<p>CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya</p> <p>Care in clinics: Clinic staff, augmented by additional staff funded by trial to mitigate staff shortages</p>
<p>Modes of delivery</p>	<p>Not reported</p>	<p>Not reported</p>	<p>Practical implementation of policy varied across clinics: Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for all diseases in single consultation room</p>	<p>Face-to-face, via telephone or text message</p>	<p>Face-to-face</p>

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Location of the intervention	Primary healthcare facilities	Primary healthcare facilities	Primary healthcare clinics: 37 urban clinics 65 rural clinics 30 clinics from former homeland	CHCs: Under large tents in all communities, or home-based Patient-centered care: At clinics	CHC: Under large tents in all communities, or home-based ART, diabetes, hypertension care: At clinics
When and how much the intervention was delivered	Unstable HIV and hypertension patients: follow-up every month Stable HIV and hypertension patients: follow-up every 2-3 months Routine referral of all patients to doctor: Every 6 months	Not reported	Not reported	CHCs: lasted 2 weeks at baseline, annually and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: 3-month intervals	CHCs: lasted 2 weeks at baseline and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: not reported
Tailoring of the intervention	Not reported	Not reported	Modular structures and pharmacy renovations to address space concerns in some clinics	Not reported	Not reported
Modifications of the intervention	Not reported	Not reported	Not reported	The end point of the trial was reduced from 5 years to 3 years	Control clinics implemented ART guidelines that were specific to Uganda and Kenya; during the trial, the threshold for eligibility for ART in these countries expanded from a specific CD4+ T-cell count (ranging from <350

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					to <500) to universal treatment (regardless of CD4+ T-cell count)
Assessment of intervention adherence/fidelity	Not reported	Not reported	Not reported	Not reported	Not reported
Intervention delivered as planned	Not reported	Not reported	Not reported	Not reported	Not reported

*No control intervention described

HIV human immunodeficiency virus, TB tuberculosis, COPD chronic obstructive pulmonary disease, PHC primary healthcare clinics

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Supplementary file 3: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated management of care

Study ID	Fairall 2016		Prabhakaran 2018	
Intervention groups	Intervention	Control	Intervention	Control
Name of intervention	Primary Care (PC) 101	Usual care in for non-communicable and communicable diseases: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS)	mWellcare	Enhanced usual care
Aim of the intervention	To provide comprehensive care for all symptoms, including NCDs, HIV, TB, mental health conditions, women's health	To provide a user-friendly management tool that integrates and harmonises disease-specific guidelines and presents them in a simple format, aligned with patient presentation in primary health care settings, expanded nurses' scope of practice and prescribing (not covering all NCDs)	To facilitate integrated management of hypertension, diabetes, comorbid depression, and alcohol and tobacco use	Not reported
Physical and informational materials used	PC 101 guideline: a 101-page clinical management tool in form of a ring-bound, colour illustrated booklet Desk pads with key messages for priority conditions to facilitate booking of follow-up appointments	Latest version (2011/2012) of PALSA PLUS: clinical management tool	mWellcare system: m-Health-based electronic decision-support system that generates recommendations based on patient profile and risk level, used on Android tablet Visible charts on the management of the conditions	Nurses received a tablet to collect baseline data (without the mWellcare system) Visible charts on the management of the conditions Pamphlets containing lifestyle advice

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			Pamphlets containing lifestyle advice	
Procedures, activities and processes used in the intervention	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Expanded prescribing provisions for nurses</p> <p>Letters and SMS reminders of follow-up visits</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of physicians on current clinical management guidelines and orientation to mWellcare system</p> <p>Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use</p> <p>Onsite supervision and support</p> <p>SMS reminders of follow-up visits and medication adherence</p>	<p>Training of physicians on clinical management guidelines for hypertension and diabetes</p> <p>Training of NCD nurses in management of hypertension and diabetes mellitus</p>
Who provided the intervention	<p>Training of facility trainers: Experienced adult education practitioner with a background in nursing, family physician who lead the expansion of the clinical management tool</p> <p>Educational outreach sessions: Nurse trainers</p> <p>Care: Nurses</p>	<p>Training of facility trainers: not reported</p> <p>Educational outreach sessions: Nurse trainers</p> <p>Care: Nurses</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>

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Modes of delivery	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PC 101 to guide management, details not reported</p>	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PALS PLUS to guide management, details not reported</p>	<p>All training: face-to-face</p> <p>Care: Patient baseline data entered into mWellcare system which generated a decision support recommendation, lifestyle advice and suggested date for follow-up (printout). The recommendation was reviewed by the physician. Any changes to the recommended plan we captured in the mWellcare system. The nurse provided lifestyle advice and pamphlets</p>	<p>All training: face-to-face</p> <p>Care: According to clinical judgement of physician. Nurses provided and explained pamphlets on lifestyle advice</p>
Location of the intervention	In primary healthcare clinics	In primary healthcare clinics	Community Health Centres	Community Health Centres
When and how much the intervention was delivered	<p>Training of facility trainers: 5-days, in May 2011 and quarterly 1-day workshops</p> <p>Educational outreach sessions: Total of 155 educational outreach sessions, 8 sessions lasting 90 minutes at each of the 19 intervention clinics</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Educational outreach sessions: 90 minute sessions</p> <p>Follow-up sessions every year</p> <p>Distribution of updated tool every year</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Training for nurses using the mWellcare system: 3 days</p> <p>Onsite supervision: 2 days</p> <p>Care: follow-up visits according to the recommendation provided by the mWellcare system</p>	<p>Not reported</p> <p>Care: follow-up visits according to the discretion of the physician</p>
Tailoring of the intervention	Not reported	Not reported	Not reported	Not reported

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<p>Modifications of the intervention</p>	<p>Unexpected co-intervention by the district department of health: “Chronic Disease Season” (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p> <p>Facilitated group session to resolve tensions between nurses, doctors and pharmacists related to expanded prescribing provisions</p>	<p>Unexpected co-intervention by the district department of health: “Chronic Disease Season” (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p>	<p>None reported</p>	<p>None reported</p>
<p>Assessment of intervention adherence/fidelity</p>	<p>Nurse trainers were observed during 5-day workshop and quarterly 1-day workshops</p> <p>Two nurse trainers were interviewed and focus group discussions were held in four intervention clinics in December 2011</p>	<p>Not reported</p>	<p>Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source document examination, protocol adherence and recording of adverse events</p>	<p>Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source documents examination, protocol adherence and recording of adverse events</p>

			Site visits by investigators: monitor enrolment process, intervention delivery and protocol adherence	Site visits by investigators: to monitor enrolment process, intervention delivery and protocol adherence
Intervention delivered as planned	<p>Good uptake of nurse trainers, who completed all outreach sessions, and repeated some sessions to ensure that most staff could attend</p> <p>Due to absenteeism and shifts, not all nurses attended all the outreach sessions. In total, 18 nurses attended a median of six training sessions, five pharmacists and four doctors were trained</p> <p>Some variations in the uptake of the PC 101 tool were observed</p>	By 2011, 70% of nurses working in the relevant districts had received training in PALS PLUS.	Not reported	Not reported

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Supplementary file 4: Risk of bias assessments for included studies

Prabhakaran 2018

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	"An independent biostatistician performed central computer-based randomisation of CHCs stratified by states (Haryana and Karnataka) and within each state by the availability of NCD nurses recruited under NPCDCS." "using block randomisation (with a block size of 2)"
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study.
Baseline outcome measurements similar	Low risk	Measurement of outcomes was conducted in a standardised way. Outcomes were pre-defined and subjective
Baseline characteristics similar	Low risk	The EUC arm had a higher proportion of participants with peripheral vascular disease (4.4% versus 0.3%), self-reported tobacco use (17.5% versus 10.0%) and alcohol use (12.3% versus 7.8%), and higher mean SBP (157.0 mm Hg versus 152.5 mm Hg). Outcome measures adjusted for relevant baseline characteristics.
Incomplete outcome data	Low risk	No incomplete outcome data suspected. Number of participants in whom the outcomes were assessed were mentioned in a general manner.
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All/ "Given the nature of the cluster-randomized trial design, neither personnel nor participants were blinded to the intervention."
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All/ "Assessments at study end were carried out by independent outcome assessors" "It was difficult to blind independent assessors who carried out the end-of-study evaluations"
Protection against contamination	Low risk	Outcome group: All/ low possibility of contamination across clusters
Selective Outcome reporting	Low risk	Data on cost-effectiveness mentioned in protocol but not reported in full report of the study, because primary outcome do not differ substantially, otherwise all primary and secondary outcomes reported
Recruitment bias (<i>e.g. individuals are recruited to the trial after the clusters have been randomized</i>)	Unclear	Patients were recruited after randomisation. Of eligible participants, n=165 in the intervention group and n=193 in the control group were not enrolled in the trial.
Baseline differences clusters	Unclear	Characteristics of cluster not described
Loss of clusters	Low risk	No loss of clusters reported
Incorrect analysis	Low risk	Adjusted for clustering
Comparability (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search.

Fairall 2016

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention.”
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study. “Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention”
Baseline outcome measurements similar	Low risk	No differences between groups reported: Baseline BP and HbA1C similar
Baseline characteristics similar	Unclear	Baseline characteristics seem similar, but no statistical tests reported
Incomplete outcome data	Low risk	Loss to follow-up similar across groups and less than 20%
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All “Blinding of the intervention was not possible at the clinic level due to the nature of the intervention”
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All No blinding of outcome assessors reported Outcome assessors not blinded. This might have influenced BP readings, but not HbA1C (blood test)
Protection against contamination	Unclear	Outcome group: All Contamination of study arms unlikely. Control clinics might have had access to the guidelines although cluster randomisation took place
Selective Outcome reporting	Low risk	No selective outcome reporting suspected, all outcomes listed in the methods section are also reported in the results section – All pre-specified outcomes listed in the trial registration record reported on
Recruitment bias	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention” All patients were enrolled after the clusters were randomised. However, all eligible patients were included in the study.
Baseline differences (clusters)	Low risk	Control clinics had more nurses per clinic and more pharmacies on site compared to the intervention group, but patient load was also higher in the control clinics. Ratio of nurses to patients was similar in both groups
Loss of clusters	Low risk	All clinics completed the trial
Incorrect analysis	Low risk	Analysis conducted on individual level, but results adjusted for cluster effects. “The cluster randomisation design was accounted for using robust cluster variance-covariance estimates.”
Compatibility (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search
Other bias	Unclear	“Midway through the trial, the district health department launched a 3-mo campaign called Chronic Disease Season in all clinics to improve NCD recognition and care. Chronic Disease Season focused on hypertension and diabetes and involved both community and clinic health workers. The community-level interventions included several “health screening days” in which free blood pressure and finger-prick glucose measurements were offered at venues such as shopping centres and town halls” (Page 7, end)

Havliir 2019

Domain	Risk of bias	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate method – mix of methods used, including computer generated, coin tossing and drawing of lots See description in protocol (p45 version 2.0 (Nov 2012))
Allocation concealment (selection bias)	Low risk	Communities were matched and randomised within each pair. Method adequate to not be able to predict allocation
Baseline outcome measurements similar	Unclear	No baseline outcome measurements for HIV and hypertension control Page 25, online supplement to article
Baseline characteristics similar	Low risk	No obvious difference observed
Incomplete outcome data	Unclear	Unclear for HIV and Hypertension cohort, not clear how many at baseline.
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants and personnel due to the nature of the intervention. Can influence behaviour of both participants and personnel
Blinding of outcome assessment (detection bias)	Unclear	Not reported
Protection against contamination	Unclear	Distance from other potential trial communities taken into consideration as part of the eligibility criteria. Migration in and out of communities
Selective Outcome reporting	Unclear	Not clear whether dual control of HIV and Hypertension/NCDS was pre-specified
Recruitment bias	Low risk	Communities were recruited (selected) before randomisation. Participants were recruited after randomisation, but a household census and Community health campaigns to reach most people in community
Baseline differences (clusters)	Unclear	No description of clusters, but cluster pairs were matched for randomisation
Loss of clusters	Low risk	No loss of clusters
Incorrect analysis	Unclear	Not clear whether adequately adjusted for clustering
Compatibility (with RCTs randomised by individuals)	Low risk	No similar studies using individual randomisation found in our search
Other bias	Unclear	Primary endpoint should have been 5-year cumulative HIV incidence, but this was shortened to 3 years as the WHO recommendation on ART therapy changed

Rawat 2018

Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other intervention identified. Also, clinics were excluded if they were identified as 'priority sites' that were specifically designed to deliver ART.
The shape of the intervention effect was pre-specified	High risk	The shape of the intervention effect was not pre-specified.
The intervention was unlikely to affect data collections	Low risk	Data was collected from TIER.net (3 interlinked electronic registers) and the District Health Information System (DHIS) for data collected before and after the intervention.
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Low risk	Outcomes were based on indicators monitored by the Free State Department of Health. All outcomes are objective
Incomplete outcome data was likely to bias results	Unclear	Post-intervention data for diabetes outcomes only available for 18 months post intervention. For other outcomes there is data for 30 months.
Outcomes were reported selectively	Low risk	All outcomes reported in the methods section were reported in the results section
Other risks of bias	Low risk	No other risks of bias identified. As integration took place at various intervals, seasonality assumed not to have an effect.

Ameh 2017

Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other changes reported.
The shape of the intervention effect was pre-specified	Low risk	Point of analysis is the point of intervention
The intervention was unlikely to affect data collections	Unclear	It can be assumed that the re-organisation of care delivery also affected data collection in the intervention facilities
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Unclear	Knowledge of the allocated intervention hard to conceal because of an apparent change in care delivery. Outcomes were not assessed blindly.
Incomplete outcome data was likely to bias results	Low risk	No incomplete outcome data suspected. No attrition or missing cases reported, only data for diabetes patients was not reported because there were too few cases (n=4)
Outcomes were reported selectively	Low risk	No selective outcome reporting suspected. All outcomes reported in the methods section are reported in the results section
Other risk of bias	Low risk	No other sources of bias identified

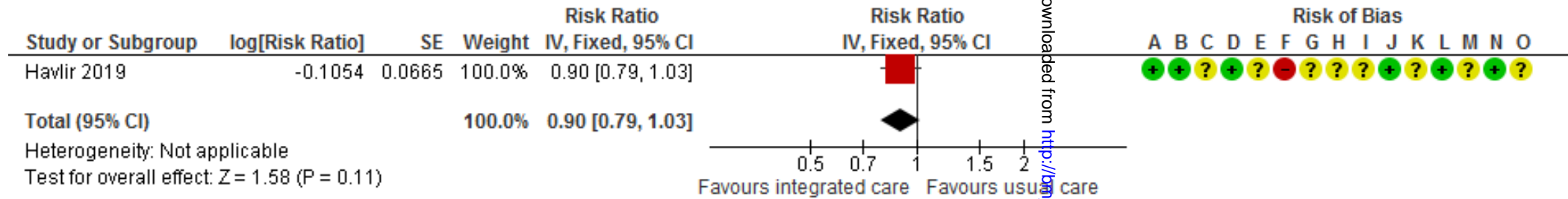
Supplementary file 5: Forest plots

For peer review only

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Comparison 1: Integrated models of care vs. usual care

Outcome: Mortality



Risk of bias legend

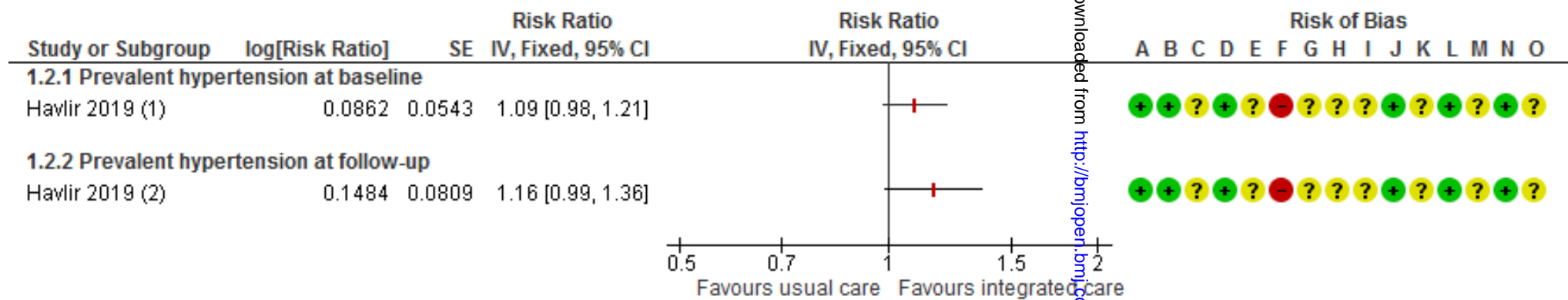
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 1: Integrated models of care vs. usual care

Outcome: BP control



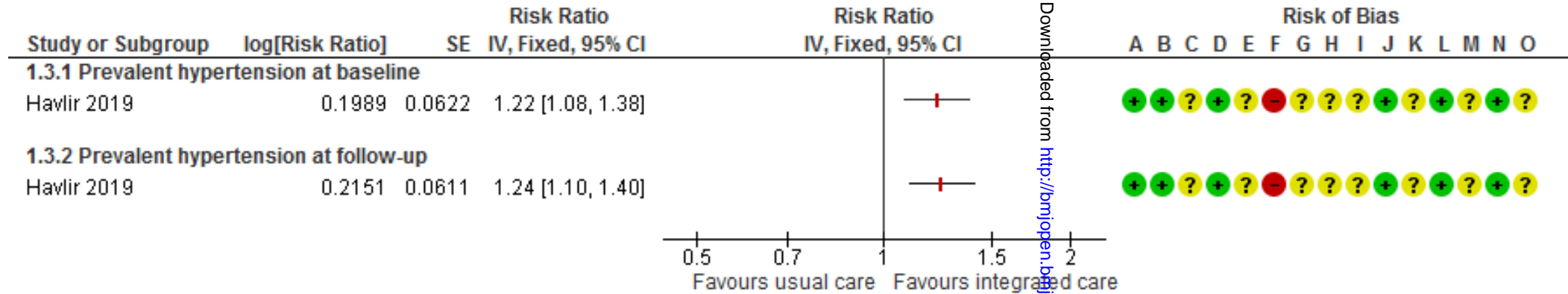
Footnotes

- (1) Among people living with HIV (PLHIV)
- (2) Among people living with HIV (PLHIV)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care
Outcome: BP and HIV control



Risk of bias legend

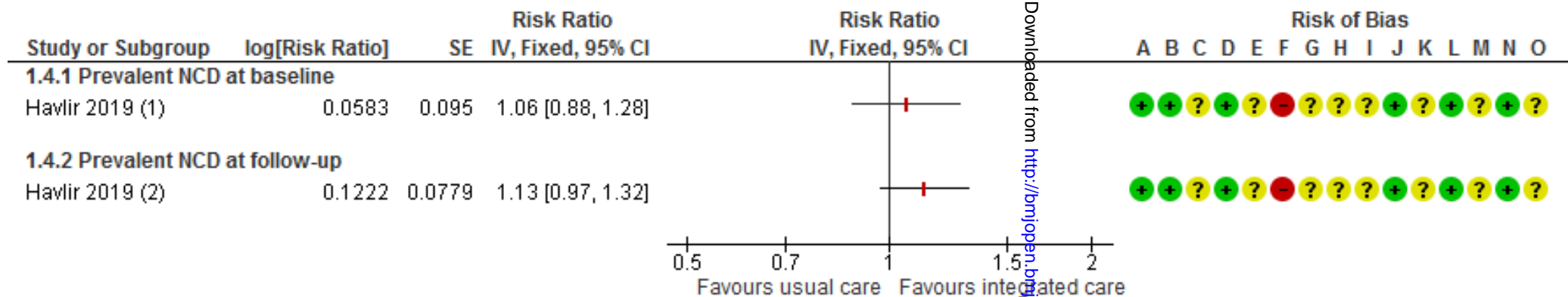
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 1: Integrated models of care vs. usual care

Outcome: NCD control



Footnotes

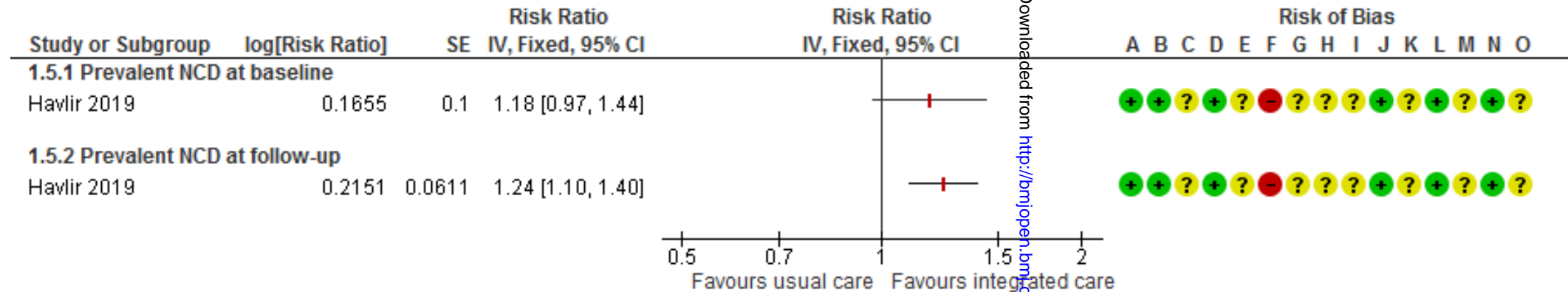
- (1) Among PLHIV
- (2) Among PLHIV

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care

Outcome: NCD and HIV control

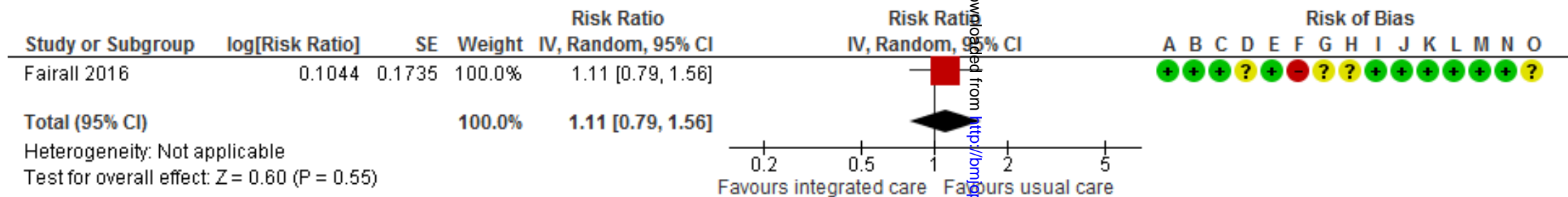


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
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- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Mortality

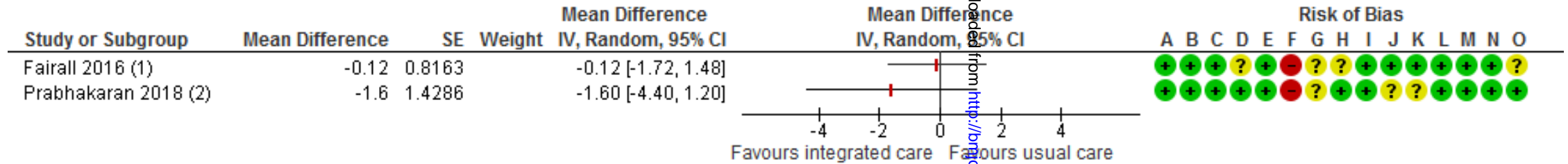


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Depression



Footnotes

- (1) Change from baseline to follow-up; 10-item Center for Epidemiologic Studies...
- (2) Value at follow-up; Patient Health Questionnaire-9

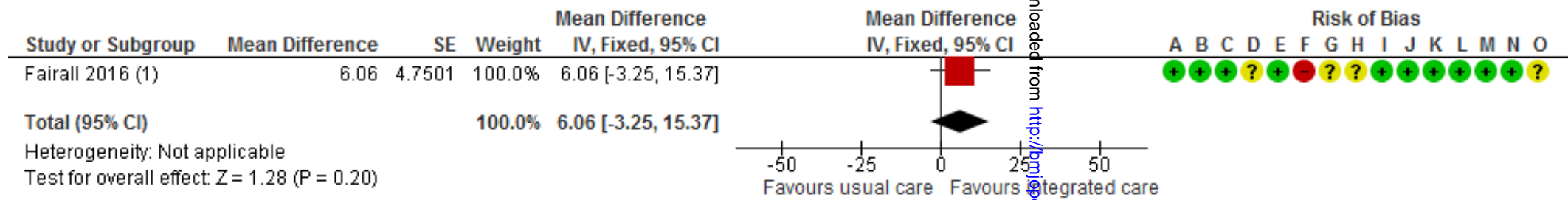
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCT randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Quality of life



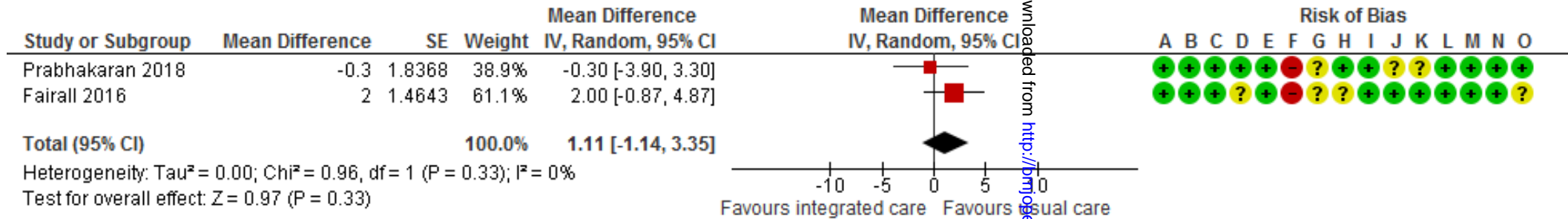
Footnotes

(1) Euro-Qol-5D visual analogue scale: 0=worst imaginable state of health,...

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Change in systolic BP



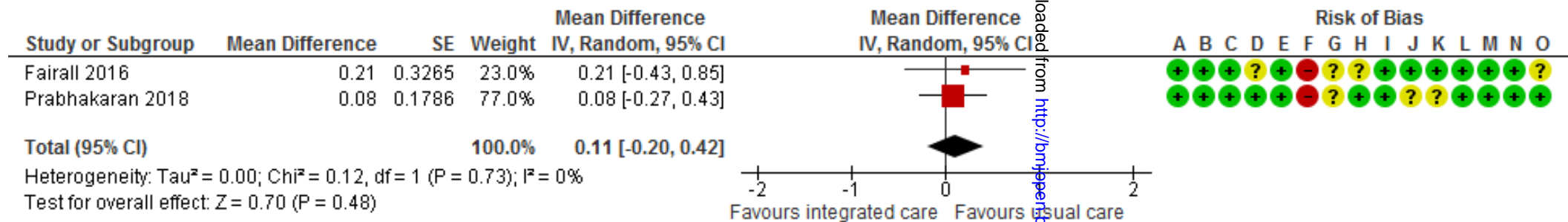
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
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- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Change in HbA1c

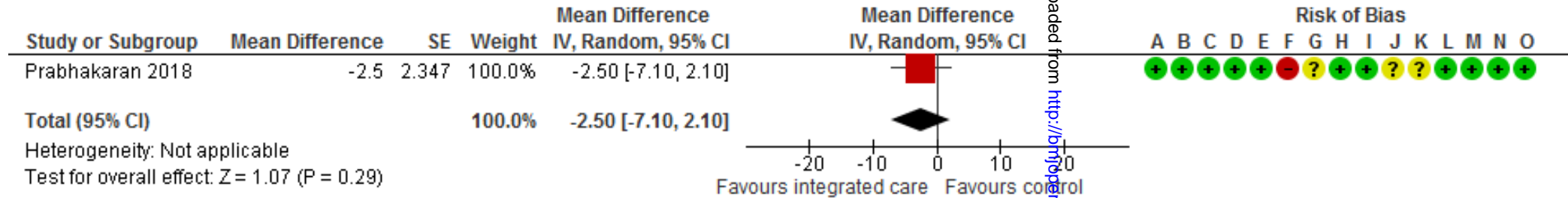


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Change in total cholesterol



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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PRISMA 2009 Checklist

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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
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4
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.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary 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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
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.	5



PRISMA 2009 Checklist

Page 1 of 2

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).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5
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.	6, Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO, follow-up period) and provide the citations.	7-9, Supplementary files 2 and 3
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).	11, Figure 3, 4 and supplementary file 4
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.	Supplementary file 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 4 and 5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
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).	19-20
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).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20-21
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.	21



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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

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Page 2 of 2

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Effects of integrated models of care for diabetes and hypertension in low-and middle-income countries. A systematic review and meta-analysis

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Effects of integrated models of care for diabetes and hypertension in low- and middle-income countries. A systematic review and meta-analysis

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Word count

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Keywords

Integrated care, diabetes, hypertension, low-and middle-income countries

Abstract

Objectives

To assess the effects of integrated models of care for people with multi-morbidity including at least diabetes or hypertension in low-and middle-income countries on health and process outcomes.

Design

Systematic review

Data sources

We searched MEDLINE, EMBASE, CENTRAL, LILACS, Africa-Wide, CINAHL, and Web of Science up to 12 December 2019.

Eligibility criteria

We included randomised controlled trials (RCTs), non-RCTs, controlled before-after studies and interrupted time series (ITS) studies of people with diabetes and/or hypertension plus any other disease, in LMICs; assessing the effects of integrated care.

Data extraction and synthesis

Two authors independently screened retrieved records; extracted data and assessed risk of bias. We conducted meta-analysis where possible and assessed certainty of evidence using GRADE.

Results

Of 7568 records, we included five studies - two ITS studies and three cluster RCTs. Studies were conducted in South Africa (n=3), Uganda/Kenya (n=1), and India (n=1). Integrated models of care compared to usual care may make little or no difference to mortality (very low certainty), the number of people achieving blood pressure (BP) or diabetes control (very low certainty), and access to care (very low certainty); may increase the number of people who achieve both HIV and BP/diabetes control (very low certainty); and may have a very small effect on achieving HIV control (very low certainty). Interventions to promote integrated delivery of care compared to usual care may make little or no difference to mortality (very low certainty), depression (very low certainty) and quality of life (very low certainty); and may have little or no effect on HbA1c (low certainty), systolic BP (low certainty), and total cholesterol levels (low certainty).

Conclusions

Current evidence on the effects of integrated care on health outcomes is very uncertain. Programmes and policies on integrated care must consider context-specific factors related to health systems and populations.

PROSPERO registration: CRD42018099314

Strengths and limitations of this study

- We included study designs that are able to provide reliable evidence on the effects of integrated models of care on health and process outcomes
- We performed a comprehensive search for published and unpublished studies up to 12 December 2019, with no language restrictions.

- We assessed the certainty of evidence using the GRADE approach taking into consideration study limitations, inconsistency, imprecision, publication bias and indirectness when downgrading the certainty of evidence.
- Our review did not aim to answer questions on aspects linked to implementation of integrated models of care and barriers and facilitators to integrated models of care at individual and health-system level

Introduction

Low- and middle-income countries (LMICs) are facing an increasing burden of non-communicable diseases (NCDs).¹ A recent report of the World Health Organization (WHO) on NCDs indicates that 41 million people succumb to NCDs globally which is the equivalent of 71% of total global deaths. Fifteen million people die prematurely due NCDs every year (between the ages of 30 and 69 years) and 85% of these premature deaths occur in LMICs.^{1,2} Furthermore, NCDs are projected to exceed communicable, maternal, perinatal, and nutritional diseases as the most common causes of death by 2030.³ In LMICs, the vast majority of NCD deaths are caused by cardiovascular diseases (CVDs), mainly due to coronary artery diseases and stroke,⁴ diabetes, cancer and chronic respiratory diseases; and they account for 54% of NCD disability adjusted life years.^{1,5} Diabetes and hypertension are the major cardiovascular risk factors for target organ damage of brain, heart and kidney.¹

Currently, it is estimated that 425 million people in LMICs live with diabetes. This number is expected to increase up to 629 million in 2045.⁶ According to the International Society of hypertension, around 40% of people over age of 25 years have hypertension worldwide and two thirds of them live in LMICs.⁷ Due to the existing high burden of communicable diseases, especially HIV infection, in sub-Saharan Africa and other LMICs, a lot of people are living with multi-morbidity. Because of the progress made with scaling up of anti-retroviral therapy (ART), the life expectancy of people living with HIV (PLHIV) has increased substantially, putting them at risk of NCDs that are common in older people. In addition to the traditional risk factors for NCDs, such as smoking, poor diet and a sedentary lifestyle, PLHIV have an increased risk of NCDs (especially CVD, cervical cancer, depression and diabetes), related to HIV itself and to ART related side effects⁸⁻¹¹ According to a recent systematic review examining the prevalence of NCDs among PLHIV in LMICs,¹² the pooled prevalence estimate of hypertension was 21.2% (95%CI 16.3 to 27.1); while that of depression was 24.4% (95%CI 12.5 to 42.1%). The prevalence of diabetes among PLHIV was reported to be between 1.2 and 18% and authors ascribed the variation in the findings to actual differences in populations, as well as the lack of standardised diagnostic criteria for diabetes.

In LMICs, people with NCDs such as diabetes and hypertension are generally characterised by very poor outcomes due to various other factors such as limited access to reliable healthcare services.¹³ The chronic nature of NCDs puts strain on the already scarce resources of healthcare systems and affected individuals in LMICs.¹⁴ Hence there is a need to design effective interventions to address the increasing burden of NCDs such diabetes and hypertension, in particular in complex patients with co-morbidities such as HIV infection and other CVDs. Provision of integrated care has been advocated by researchers and many international bodies such as the WHO as a way of tackling the rising burden of NCDs and strengthening the health systems particularly in LMICs.¹⁵⁻¹⁷ Recent studies from LMICs have assessed integration of HIV/AIDS and tuberculosis (TB) services at primary healthcare (PHC) level,¹⁸⁻²⁰ which is usually the first point of contact with health services for people living in LMICs. Based on these integrated models of care, we conceptualised integrated care either as partial integration or full integration as illustrated in Figure 1.²¹ Fully integrated care is seen as a “one-stop-shop” model whereby a patient receives all necessary care or services under one roof by one or more health-care professionals. In a partially integrated model of care, patients receiving treatment for one disease

1
2 such as diabetes receive additional care related to either prevention, diagnosis or treatment of
3 another disease, but do not receive the full package of care ²¹.

4
5 Although integrated models of care have been widely advocated, and various models and
6 programmes have been implemented and described, there is a lack of evidence on the effectiveness
7 of integrated care compared to other models of care in LMICs. We previously conducted a scoping
8 review to assess existing systematic reviews on the effectiveness of integrated models of care in
9 people with diabetes or hypertension and any other comorbid disease. ²² We found five reviews²³⁻²⁷
10 that met our inclusion criteria, but only one of these included studies conducted in LMICs.
11 Furthermore, none of the included studies assessed integrated care for diabetes or hypertension and
12 communicable diseases (e.g. HIV). A subsequent systematic review by Haldane and colleagues
13 examined existing programmes of integrated healthcare delivery for diabetes, hypertension or CVDs
14 with HIV/AIDS.²⁸ However, included studies mostly described existing programmes with no thorough
15 evaluation of the effectiveness of these programmes. A descriptive study from Cambodia looked at
16 the management of HIV/AIDS, diabetes, and hypertension and found that integration of services for
17 these conditions was highly acceptable and led to good health outcomes with improved CD4 count,
18 glycated haemoglobin (HbA1c) and blood pressure levels.²⁹ Dudley and Garner³⁰ assessed the
19 effectiveness of strategies to integrate PHC services in LMICs. They included studies that integrated
20 family planning into existing services; nutrition and infectious disease interventions; and sexually
21 transmitted infections (STIs), HIV/AIDS and TB treatment. None of the included studies reported on
22 NCDs.
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27 In light of limited information in existing reviews, we conducted this review to assess the effects of
28 integrated models of care at PHC level for people living in LMICs, with multi-morbidity, of which
29 diabetes or hypertension is one, compared to no integrated care on health and process outcomes.
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32 Methods

33 Our systematic review followed the methods pre-specified in a published protocol.²¹ We followed the
34 PRISMA reporting guideline to report on the findings of our systematic review.
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37 Criteria for considering studies for inclusion

38 *Types of study designs*

39 Randomised controlled trials (RCTs), including cluster RCTs, controlled (non-randomised) clinical trials
40 (CCTs) or cluster non-randomised trials, interrupted time series (ITS) studies with at least three data
41 points before and after the intervention, and controlled before-and-after (CBA) studies were eligible
42 for inclusion. Cluster randomised, cluster non-randomised or CBA studies were only included if there
43 were at least two intervention sites and two control sites.
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48 *Types of participants*

49 We included studies with adults and children attending PHC clinics, presenting with diabetes or
50 hypertension plus one or more other chronic diseases (multi-morbidity), or risk factors for other
51 chronic diseases in LMICs. We defined LMICs according to the 2016 classification of the World Bank,³¹
52 that defined low-income economies as those with a gross national income (GNI) per capita of \$1035
53 or less, lower middle income economies as those with a GNI per capita of \$1006 to \$3995, and upper
54 middle economies as those with a GNI per capita of \$3956 to \$12235.
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58 *Types of interventions*

59 Eligible interventions were models of full or partial integration of services at PHC and community
60 level. Full integration of service delivery was defined as models where patients (primarily treated for

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2 diabetes, hypertension or any other disease) received the full package of care (prevention, diagnosis
3 and treatment) for diabetes or hypertension and any other chronic disease at the same point of care
4 by one or more healthcare professionals. Partial integration of services was defined as models where
5 patients treated for diabetes, hypertension, or any other chronic disease received part of the
6 package of care (either prevention, diagnosis, or treatment) for another disease (see Figure 1).
7 Partially integrated models of care therefore refer to a lower level of integration compared to fully
8 integrated models of care. For example, with partially integrated care, patients receiving treatment
9 for hypertension would be tested for HIV and referred for treatment; whereas with fully integrated
10 care, patients receiving treatment for hypertension would be tested and treated for HIV during the
11 same clinic visit.
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14 Included studies did not provide adequate information for us to categorise interventions as fully
15 integrated models of care or partially integrated models of care and we thus categorised
16 interventions as integrated models of care and interventions that promoted integrated delivery of
17 care. Integrated models of care assessed the effect of integration of service delivery i.e. integration
18 of two previously separate models of delivery of care into one model of delivery of care, for example
19 integrating HIV services into general PHC services. We distinguished these interventions from
20 interventions that promoted an integrated approach to providing care in PHC facilities. In these
21 cases, services as such were not integrated, but healthcare workers were encouraged to provide
22 holistic patient care, for example through the provision and use of clinical management tools that
23 supported an integrated approach to care.
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27 *Types of comparisons*

28 We aimed to compare fully integrated models of care to stand-alone care; partially integrated
29 models of care to stand-alone care; and fully integrated models of care to partially integrated models
30 of care. However, for all included studies, comparisons were reported as standard or usual care and
31 authors did not provide an adequate description of what that entailed. Although these seemed to
32 refer to less integrated care, we unable to categorise them as partially integrated models of care or
33 stand-alone care. We therefore compared integrated models of care to usual care, and interventions
34 to promote integrated delivery of care to usual care.
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38 *Types of outcomes*

39 We included studies that reported on either primary or secondary outcomes, as defined by primary
40 study authors. Primary outcomes were all-cause mortality, disease specific morbidity as reported in
41 included studies (e.g. disease control metrics), quality of life, glycated haemoglobin (HbA1c), systolic
42 Blood pressure (SBP) and cholesterol levels. Secondary outcomes were access to care, retention in
43 care, adherence, continuity of care, quality of care and cost of care.
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47 *Search strategy*

48 We searched MEDLINE (PubMed), EMBASE (Ovid), the Cochrane Central Register of Controlled Trials
49 (CENTRAL), LILACS, Africa-Wide Information (via EBSCO host), CINAHL, and Web of Science (Core
50 collection) (Date of last search: 12 December 2019). We searched the WHO International Clinical
51 Trials Registry Platform (ICTRP) and Clinicaltrials.gov for ongoing studies, as well as conference
52 abstracts from the International AIDS Society Online Resource Library, the HIV/AIDS Implementers'
53 Meetings and the NCDs Alliance meetings. Search terms included 'diabetes', 'hypertension',
54 'comorbidities', 'integrated health care delivery', 'low-and middle-income countries', and their
55 synonyms. The full search strategies for all databases are provided in Supplementary file 1. To
56 supplement the search of electronic databases, we screened reference lists of included studies and
57 reference lists of relevant systematic reviews, and contacted experts in the field and relevant
58 organisations (e.g. NCD Alliance) for unpublished studies. We did not have any restrictions related to
59 language, date of publication or publication status.
60

Selection of studies

Two authors (JUN and AR or a research assistant) independently screened titles and abstracts of studies identified by the search, using Covidence software.³² We retrieved full texts of potentially eligible studies. Two authors (JUN and AR/TY/CMB) independently screened full texts for eligibility. Discrepancies were resolved through discussion with a third author (JJM/IT). We classified studies as included, excluded or ongoing and provided reasons for excluding studies.

Data extraction

Two authors (JUN, AR and IT) independently extracted data for included studies using a pre-specified, piloted data extraction form and assessed risk of bias. Discrepancies were resolved through discussion or by consulting a third author (TY/JJM). We extracted data related to the study design, participants, intervention, comparison, outcomes, setting, context and funding sources. We used the template for intervention description and replication (TIDieR)³³ and the PRISMA-Complex Interventions extension checklist³⁴ to guide data extraction and reporting related to the interventions.

Risk of bias assessment

We used guidance from Cochrane Effective Practice and Organisation of Care (EPOC) to assess risk of bias for included studies³⁵. Risk of bias was assessed as low, high, or unclear for each domain. For RCTs, non-randomised trials and CBA studies, we assessed the following nine domains: 1) random sequence generation, 2) allocation concealment, 3) baseline outcome measurements, 4) baseline characteristics, 5) incomplete outcome data, 6) knowledge of allocated intervention (blinding), 7) protection against contamination, 8) selective outcome reporting and 9) other risks of bias. For cluster RCTs, we assessed additional risk of bias linked to recruitment, cluster baseline differences, loss of clusters, incorrect analysis and compatibility with RCTs randomised by individuals, as per the Cochrane handbook.³⁶ For ITS studies, we assessed whether 1) the intervention was independent of other changes, 2) the shape of the intervention effect was pre-specified, 3) the intervention was unlikely to affect data collections, 4) knowledge of the allocated intervention was adequately prevented during the study, 5) incomplete outcome data was likely to bias results, 6) outcomes were reported selectively and 7) there were any other risks of bias.

Data analysis

We extracted relevant data for each outcome per included study. For dichotomous outcomes, we reported risk ratios (RR) and 95% confidence intervals (CI). For continuous outcomes, we reported mean differences (MD) with 95% CI if outcomes were measured in the same way across studies, or standardised mean differences (SMD) with 95% CI where outcomes were measured differently across studies and where standard deviations (SD) were reported. For ITS studies, we reported beta coefficients (β) with 95% CI or standard error (SE). We contacted study authors to request information on missing data. We did not impute any data.

All included cluster RCTs appropriately adjusted for the effects of clustering in their analysis, we thus used these adjusted effect estimates and standard errors in our meta-analysis using the generic inverse-variance method in Review Manager 5.³⁷ We did not include studies with more than one treatment arm in our review.

We explored clinical heterogeneity by clearly documenting study characteristics related to the population, intervention, outcomes and context in table format. We assessed statistical heterogeneity in each meta-analysis by inspecting forest plots and calculating Chi² test values and I² statistics. We considered heterogeneity to be important if the p-value of the Chi² test was < 0.10, and the I² statistic was above 30%, as per the recommendations in the Cochrane handbook.³⁶

1 We pooled data from individual studies if we judged them to be sufficiently homogeneous in terms
2 of design, population, intervention and comparator. As we anticipated some degree of
3 heterogeneity, we performed random-effects meta-analysis. We did not pool data from RCTs and
4 non-randomised studies in a single meta-analysis. Where we judged included studies to be too
5 heterogeneous to pool, we used narrative synthesis and presented data in tabular format. We did
6 not perform subgroup or sensitivity analysis, as only two studies contributed to the meta-analysis.
7 We were unable to examine reporting biases by means of funnel plots, as we only included two
8 studies in the meta-analysis.
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12 Certainty of evidence

13 We assessed the certainty of the evidence using GRADE³⁸ for the following outcomes: mortality,
14 disease specific morbidity, quality of life, HbA1c, systolic BP, cholesterol levels and access to care. We
15 created a 'Summary of findings' table using GRADEpro software.³⁹ Our judgements to downgrade the
16 certainty of evidence were based on assessment of the following five domains: 1) study limitations,
17 2) inconsistency, 3) imprecision, 4) indirectness and 5) publication bias. According to GRADE
18 guidance, non-randomised studies (such as CBAs and ITS studies) start at low certainty evidence. We
19 considered upgrading the certainty of evidence for non-randomised studies if there was a large
20 effect, a dose-response and cases where all plausible residual confounding would reduce a
21 demonstrated effect or would suggest a spurious effect if no effect was observed.
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25 For each outcome, we described the certainty of evidence as high, moderate, low or very low.⁴⁰ For
26 outcomes reported by both RCTs and non-randomised studies, we made separate GRADE
27 judgements for both types of studies. Where we arrived at the same level of certainty of evidence,
28 we summarised this in a single judgement per outcome. We interpreted the certainty of evidence
29 according to guidance provided by the GRADE working group, which takes into consideration the size
30 of the effect and the certainty of evidence.⁴¹
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33 Patient and public involvement

34 No patients were involved in the development of this systematic review.
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37 Results

38 The results of the search are depicted in the PRISMA flow diagram (Figure 2). We screened titles and
39 abstracts of 7568 records. We obtained and screened full texts of 49 potentially relevant studies. We
40 included five studies,⁴²⁻⁴⁶ (Table 1) reported in six articles and excluded 37 articles and reported
41 reasons for exclusion (Supplementary file 2). For one study⁴⁷ that met eligibility criteria, we were only
42 able to access the conference abstract. We classified this study as 'awaiting assessment', as we are
43 unable to definitively decide on inclusion or exclusion until we have access to the full report. We
44 identified five ongoing RCTs,⁴⁸⁻⁵¹ investigating integrated care for depression and hypertension in
45 China,⁴⁸ integrated care for depression and hypertension⁴⁹ or depression and diabetes/HIV⁵⁰ in South
46 Africa; integrated care for common mental disorders and hypertension, diabetes or ischemic heart
47 disease in India;⁵¹ and diabetes and TB in India.⁵²
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Table 1: Summary of characteristics of included studies

Study ID	Study design	Country and Setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes ¹
<i>Integrated models of care</i>							
Ameh 2017 ⁴²	Controlled ITS study	South Africa: Primary health care (PHC) facilities, Ehlanzeni health district, Mpumalanga Province	Patients with chronic disease (HIV, diabetes or hypertension) n=878	Integrated chronic disease management (ICDM) model Clinics: n=7 Participants: n=435 (Hypertension: n=210; Diabetes: n=2; HIV: n=141; Comorbidities: n=82)	Usual care in PHC facilities Clinics: n=5 Participants: n=443 (Hypertension: n=91; Diabetes: n=2; HIV: n=282; Comorbidities: n=68)	30 months Pre-intervention: 6 months Post-intervention: 24 months	<ul style="list-style-type: none"> - Blood pressure (BP) control² - CD4 count control³ - Number of healthcare visits
Havlir 2019 ⁴⁶	Cluster RCT	Kenya and Uganda: Rural regions in south-western and eastern Uganda, and western Kenya	Clusters: Communities of 9000 to 11 000 people Participants: People residing in community n=150 395 (baseline)	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and streamlined, patient-centered care Clusters: n=16 Participants: n=79 818 (baseline) (Hypertension in adults over 30 years: n=5953)	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care (not integrated) Clusters: n=16 Participants: n=70 577 (baseline)	36 months	<ul style="list-style-type: none"> - Cumulative HIV incidence - Time to initiation of ART - Viral suppression - Death - Incident tuberculosis or death due to illness - Control of hypertension⁴ among HIV-infected persons - Control of diabetes⁵ or hypertension (NCD) among HIV infected persons - Control of HIV⁶ and hypertension - Control of HIV and NCDs⁷

¹ Outcomes relevant to this review are in bold

² Defined as: BP <140/90mmHg

³ Defined as: CD4 count >350 cells/mm³

⁴ Defined as: At least one systolic BP measurement <140mmHg, and at least one diastolic measurement of <90mmHg

⁵ Defined as: Finger prick blood glucose ≤11 mmol/L

⁶ Defined as: Suppressed viral replication (<500 copies/ml)

⁷ Defined as: Control of all prevalent NCDs (hypertension or diabetes)

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					(Hypertension in adults over 30 years: n=5911)		<ul style="list-style-type: none"> - Control of hypertension in the overall population - Control of diabetes in the overall population
Rawat 2018 ⁴⁵	ITS study	South Africa: PHC clinics in the Free state Province	Patients attending PHC clinics (focus on diabetes and hypertension) n=not reported	Integration of HIV care into HC facilities n=131 clinics	No control group	48 months Pre-intervention: 12 months Post-intervention: 36 months	<ul style="list-style-type: none"> - Population level new diabetics on treatment - Clinic level new diabetics on treatment - Population-level new hypertensive on treatment - Clinic level new hypertensive on treatment - Total ART patients - New patients initiated on ART
<i>Interventions to promote integrated delivery of care</i>							
Fairall 2016 ⁴³	Cluster RCT	South Africa: Mostly rural PHC clinics in Eden and Overberg districts, Western Cape Province	Patients with one or more of the following: hypertension, diabetes, chronic respiratory disease, depression n=4393	Primary Care (PC) 101 management tool Clinics: n=19 Participants: n=2166 (Hypertension: n=1555; diabetes: n=851)	Usual care: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool Clinics: n=19 Participants: n=2227 (Hypertension: n=1672; diabetes: n=991)	14 months	<ul style="list-style-type: none"> - Treatment intensification for hypertension, diabetes and chronic respiratory disease - Depression - CVD risk - Systolic BP - HbA1C - Body Mass Index (BMI) - Smoking status - Health-related quality of life - Mortality - Healthcare utilisation
Prabhakaran 2019 ⁴⁴	Cluster RCT	India: Community Health Centres (CHC) from 4 districts in Haryana and 2 districts in Karnataka	Patients with confirmed diagnosis of diabetes or hypertension n=3698	mWellcare system CHCs: n=20 Participants: n=1842	Enhanced usual care CHCs: n=20 Participants: n=1856	12 months	<ul style="list-style-type: none"> - Mean change in systolic BP - Mean change in HbA1C - Mean change in fasting plasma glucose - Mean change in total cholesterol - Mean change in CVD risk - Mean change in Tobacco use - Mean change in BMI - Alcohol use

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								<ul style="list-style-type: none">- Depression score- Adherence- Perceived quality of care
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Characteristics of included studies

We included three cluster RCTs and two ITS studies. One cluster RCT was conducted in South Africa,⁴³ one in India,⁴⁴ and the Sustainable East Africa Research in Community Health (SEARCH) trial was conducted in Uganda and Kenya.⁴⁶ The two ITS studies were both conducted in South Africa^{42 45} (Table 1). All studies were conducted in PHC facilities in mostly rural settings. All five studies assessed the effect of strategies for full integration of care compared to partial integration of care.

The two ITS studies^{42 45} and the SEARCH trial⁴⁶ assessed the effects of integrated models of care for chronic diseases (Table 2). Ameh and colleagues⁴² conducted a controlled ITS study, comparing the integrated chronic disease management (ICDM) model to usual care over a period of 30 months. Rawat and colleagues⁴⁵ examined the effect of integrating HIV care into PHC clinics over a 48 months period. The SEARCH trial⁴⁶ assessed the effects of universal ART and streamlined, patient-centered care (integrated care) compared to usual care as per national guidelines. Interventions are described in more detail according to the TIDieR checklist in supplementary file 3.

The other two cluster RCTs^{43 44} assessed the effectiveness of interventions to promote integration of care (Table 2). Fairall and colleagues⁴³ introduced the Primary Care (PC) 101 clinical management tool to promote provision of comprehensive care for all symptoms including NCDs, HIV, TB, mental health and women's health, in PHC clinics randomised to the intervention, while the control clinics continued using the Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool, which did not cover all NCDs and was the standard of care at the time of the trial. Prabhakaran and colleagues⁴⁴ introduced the mWellcare system, a m-health based electronic decision support system, to promote integrated management of hypertension, diabetes, depression, and alcohol and tobacco use in PHC centres randomised to the intervention. Control centres continued with usual care. Interventions are described in more detail according to the TIDieR checklist in supplementary file 4.

Table 2: Key components of included interventions

Name and Study ID	Components related to provision of care in the clinic	Components related to provision of care in the community/at home	Training	Appointment reminders
Integrated chronic disease management (ICDM) model Ameh 2017	Facility reorganisation: designated chronic care area; supply of critical medicines; pre-packaging of medication Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral	Ward-based outreach teams to ensure individual responsibility and "assisted" self-management Health promotion and population screening	-	-

<p>National policy to integrate HIV care into all PHC facilities Rawat 2018</p>	<p>Policy to integrate HIV care into PHC clinics</p> <p>Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for all diseases in single consultation room</p> <p>Additional staff to strengthen drug delivery systems</p>	<p>-</p>	<p>Training of nurses in comprehensive management of HIV: Nurse initiated Management of ART (NIMART)</p> <p>Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)</p>	<p>-</p>
<p>SEARCH intervention Havir 2019</p>	<p>Patient-centered, integrated care for HIV, diabetes, hypertension: 3-month visit intervals; ART to all HIV positive participants; hypertension and diabetes treated according to standard algorithms</p>	<p>Community health campaigns (CHCs): Testing for HIV, diabetes and hypertension; counselling and clinic appointments; blood tests for HIV positive participants; transportation voucher for first clinic visit</p> <p>Home-based testing for participants that did not attend CHCs</p> <p>Appointments to initiate ART within 7 days for HIV positive participants not on ART; introductory phone call from clinic staff; support hotline available via phone or text message</p>	<p>-</p>	<p>Phone/SMS reminders about clinic visits</p>
<p>Primary Care (PC) 101 Fairall 2016</p>	<p>PC 101 guideline: Ring-bound, colour illustrated booklet</p> <p>Expanded prescribing provisions for nurses</p> <p>Desk pads with key messages</p>	<p>-</p>	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p>	<p>Letters and SMS reminders of follow-up visits</p>

<p>mWellcare Prabhakaran 2018</p>	<p>mWellcare system: m-Health-based electronic decision-support system</p> <p>Visible charts on the management of the conditions</p> <p>Onsite supervision and support</p>	<p>Pamphlets containing lifestyle advice</p>	<p>Training of physicians on current clinical management guidelines and orientation to mWellcare</p> <p>Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use</p>	<p>SMS reminders of follow-up visits and medication adherence</p>
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Risk of bias in included studies

For the two ITS studies, we judged risk of bias to be low or unclear in all domains (Figure 3). For the three cluster RCTs, we judged risk of selection bias to be low, risk of performance bias to be high, as blinding of participants and personnel was not possible due to the nature of the interventions, and risk of detection bias to be unclear for all three studies. We judged attrition bias to be low for two cluster RCTs^{43 44} and unclear for the SEARCH trial⁴⁶ (Figure 4). Detailed judgements for each included study are reported in supplementary file 5.

Integrated models of care compared to usual care

We included three studies as part of this comparison.^{42 45 46} Results are summarised in the summary of findings table (Table 3) and forest plots are available in supplementary file 6.

Table 3: Summary of findings for integrated models of care compared to usual care for diabetes and hypertension in LMICs

Patient or population: Patients with multi-morbidity (diabetes and/or hypertension and other chronic conditions e.g. HIV) Setting: Low- and middle-income countries Intervention: Integrated care for hypertension, diabetes and HIV Comparison: Usual care				
Outcome	Effect (95%CI)	No of participants (studies)	Certainty of evidence (GRADE)	Comments
Mortality	RR 0.90 (0.79 to 1.02) Risk with usual care: 0.56 per 100 person-years Risk with integrated care: 0.51 per 100 person-years	171 431 (1 RCT)	⊕○○○ VERY LOW a,b,c	Integrated care compared to usual care may make little or no difference to the rate of death, but the evidence is very uncertain
BP control (number of PLHIV achieving BP control)	RCT: Prevalent hypertension at baseline: RR 1.09 (0.98 to 1.21)	2319 (2 studies: 1 RCT, 1 ITS study)	⊕○○○ VERY LOW a,c,d,e,f	Integrated care compared to usual care may make little or no difference to achieving BP control but the evidence is very uncertain
	RCT: Prevalent hypertension at follow-up: RR 1.16 (0.99 to 1.36)			
	ITS study: $\beta=0.010$ (0.003 to 0.016)			
BP or diabetes (NCD) control (number of PLHIV achieving NCD control)	Prevalent NCD at baseline: RR 1.06 (0.88 to 1.27)	1 RCT*	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may make little or no difference to achieving NCD control but the evidence is very uncertain
	Prevalent NCD at follow-up: RR 1.13 (0.97 to 1.32)			
HIV control (CD4 count control)	$\beta=0.057$ (0.056 to 0.058)	878 (1 ITS study)	⊕○○○ VERY LOW e,f	Integrated care may have a very small effect on achieving CD4 count control, but the evidence is very uncertain
BP and HIV control (number of people achieving both HIV viral suppression and BP control)	Prevalent hypertension at baseline: RR 1.22 (1.08 to 1.37)	1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both BP and HIV control but the evidence is very uncertain
	Prevalent hypertension at follow-up: RR 1.24 (1.10 to 1.40)			
BP or diabetes (NCD) and HIV control (number of people achieving both HIV viral suppression and NCD control)	Prevalent NCD at baseline: RR 1.18 (0.97 to 1.44)	1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both NCD and HIV control but the evidence is very uncertain
	Prevalent NCD at follow-up: RR 1.24 (1.10 to 1.40)			
Quality of life	-	-	-	Not reported
Systolic BP	-	-	-	Not reported
HbA1c	-	-	-	Not reported
Cholesterol levels	-	-	-	Not reported

<p>Access to care</p>	<p>There was no change in trend from pre- to post-intervention for population level new diabetics on treatment, clinic level new diabetics on treatment and clinic-level new hypertensive patients on treatment. There was a slight decrease in new hypertensive patients on treatment at population level at 36 months</p>	<p>1 ITS*</p>	<p>⊕○○○ VERY LOW e.g</p>	<p>Integrated care may make little or no difference to short term access to care and may result in a slight decrease in long-term access to hypertensive care, but the evidence is very uncertain.</p>
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CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **BP:** Blood pressure; **HIV:** Human Immunodeficiency Virus; **HbA1c:** Glycated Haemoglobin; **NCD:** Non-communicable disease; **RCT:** Randomised controlled Trial; **ITS:** Interrupted time series

*Sample size not reported

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Footnotes: Explanation of GRADE certainty of evidence

Randomised controlled trials:

- a) Downgraded by 1 due to study limitations: high risk of performance bias and unclear risk of bias for other domains
- b) Downgraded by 1 due to indirectness: Results are based on number of participants at baseline, however authors did not report how many participants had HIV plus hypertension/diabetes at baseline. At 3-year follow-up, less than 1% of participants at follow-up had hypertension/diabetes and HIV infection (0.7% (694/103 777) in the control group and 0.6% (747/121 347) in the intervention group)
- c) Downgraded by 1 due to indirectness: Usual care comprised care according to national guidelines in Kenya and Uganda. Authors did not report what this entails. It is not clear to what extent care was integrated or not
- d) Downgraded by 1 due to imprecision: Small sub-sample with hypertension and HIV in the RCT with wide 95% confidence intervals

Interrupted time series studies:

- e) Observational study, starting at low certainty evidence
- f) Downgraded by 1 due to indirectness: Intervention clinics experienced stock-outs of anti-hypertensive drugs and malfunctioning of BP machines. We are therefore not confident that the intervention was delivered as intended
- g) Downgraded by 1 due to indirectness: Study reported on population level new diabetics on treatment, clinic level new diabetics on treatment, population level new hypertensive patients on treatment and clinic level new hypertensive patients on treatment. This is an indirect measure of access to care

All-cause mortality: The SEARCH trial⁴⁶ reported the rate of all-cause mortality among baseline residents in included communities. Results suggest that integrated compared to usual care may make little or no difference to the mortality rate when compared to usual care but the evidence is very uncertain (RR 0.90 95%CI 0.79 to 1.02, n=171 431, 1 RCT, very low-certainty evidence).

Disease-specific morbidity (BP control): Integrated care compared to usual care may make little or no difference to achieving BP control, but the evidence is very uncertain. Results from the SEARCH trial⁴⁶ suggest that integrated care compared to usual care may make little or no difference to the number of PLHIV who achieve BP control with prevalent hypertension at baseline (RR 1.09, 95%CI 0.98 to 1.21, 1 RCT, very low-certainty evidence) and PLHIV with prevalent hypertension at follow-up (RR 1.16, 95%CI 0.99 to 1.36, n=1441, 1 RCT, very low- certainty evidence). Results of the controlled ITS study⁴² suggest that integrated care compared to usual care may increase the probability of

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2 achieving BP control by 1%, but the evidence is very uncertain ($\beta=0.010$, 95%CI 0.003 to 0.016,
3 $n=878$, 1 ITS study, very low-certainty evidence).
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5 **Disease-specific morbidity (NCD control):** Results from the SEARCH trial⁴⁶ suggest that integrated
6 care compared to usual care may make little or no difference to the number of PLHV who achieve
7 NCD (diabetes and/or hypertension) control with prevalent NCD at baseline (RR 1.06, 95%CI 0.88 to
8 1.27, 1 RCT, very low-certainty evidence) and prevalent NCD at follow-up but the evidence is very
9 uncertain (RR 1.13, 95%CI 0.97 to 1.32, 1 RCT, very low-certainty evidence).
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11 **Disease-specific morbidity (HIV control):** One ITS study⁴² reported on HIV control in terms of CD4
12 count control. Results suggest that integrated care compared to usual care may increase the
13 probability of achieving CD4 count control by 6%, but the evidence is very uncertain ($\beta=0.057$, 95%CI
14 0.056 to 0.058, $n=878$, 1 ITS study, very low-certainty evidence).
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17 **Disease-specific morbidity (HIV and BP control):** Results from the SEARCH trial⁴⁶ suggest that
18 integrated care compared to usual care may increase the number of PLHIV who achieve both HIV
19 viral suppression (HIV control) and BP control with prevalent hypertension at baseline (RR 1.22,
20 95%CI 1.08 to 1.37, 1 RCT, very low-certainty evidence) and with prevalent hypertension at follow-up
21 (RR 1.24, 95%CI 1.10 to 1.40, $n=1441$, 1 RCT, very low-certainty evidence).
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24 **Disease-specific morbidity (HIV and NCD control):** Integrated care compared to usual care may make
25 little or no difference to the number of PLHIV who achieve both HIV viral suppression (HIV control)
26 and NCD control with prevalent NCD at baseline (RR 1.18, 95%CI 0.97 to 1.44, 1 RCT, very low
27 certainty), but may result in a slight increase in the number of PLHIV who achieve both HIV viral
28 suppression (HIV control) and NCD control with prevalent NCD at follow-up (RR 1.24, 95%CI 1.10 to
29 1.40, 1 RCT very low-certainty evidence). However, the evidence is very uncertain for these
30 outcomes.
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33 **Access to care:** One ITS study reported on access to care⁴⁵ in terms of the change in post-integration
34 trend compared to pre-integration trend for population level new diabetics on treatment, clinic level
35 new diabetics on treatment, population-level new hypertensive patients on treatment, and clinic
36 level new hypertensive patients on treatment. Integrated care may make little or no difference to
37 population level new diabetics on treatment at 18 (1/100 000, Standard Error (SE)=2, $p=0.50$, very
38 low certainty) and 36 months (1/100 000, SE=3, $p=0.61$, very low-certainty evidence) post-
39 integration; clinic level new diabetics on treatment at 18 (0/100 000, SE=1; $p=0.96$, very low-
40 certainty evidence) and 36 months post-integration; clinic level new hypertensive patients on
41 treatment at 18 (0/100 000, SE=1; $p=0.78$, very low-certainty evidence) and 36 months (0/100 000,
42 SE=0; p -value=0.57, very low-certainty evidence) post-integration, and population level new
43 hypertensive patients on treatment at 18 months post-integration (-7/100 000, SE=4; $p=0.08$, very
44 low-certainty evidence). Results suggest that there was a slight decrease in population level new
45 hypertensive patients on treatment at 36 months post-integration (-6/100 000; SE=3; $p=0.02$, very
46 low-certainty evidence). However, the evidence is very uncertain for these outcomes.
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50 Authors also reported on the total number of patients on anti-retroviral treatment (ART) and the
51 number of new patients initiated on ART. Overall, the number of patients for both outcomes
52 increased during each year of follow-up. No effect size was reported. No other secondary outcomes
53 were reported for this comparison.
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56 Interventions to promote integrated delivery of care compared to usual care

57 We included two studies in this comparison.^{43 44} Results are summarised in the summary of findings
58 table (Table 4) and forest plots are available in supplementary file 6.
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2 **All-cause mortality:** Results from one cluster RCT⁴³ suggest that interventions to promote integrated
3 care compared to usual care may make little or no difference in mortality (RR 1.11; 95% CI 0.79 to
4 1.56; n=3393; 1 RCT, very low-certainty evidence) when compared to usual care, but the evidence is
5 very uncertain.
6

7 **Disease-specific morbidity (depression):** Results from two RCTs^{43,44} suggest that interventions to
8 promote integrated care compared to usual care may make little or no difference to depression
9 scores, but the evidence is very uncertain. Fairall 2016 reported the change in depression scores
10 from baseline to follow up using the 10-item Center for Epidemiologic Studies Depression Scale and
11 reported no difference between groups (MD -0.12; 95%CI -1.72 to 1.48; n=3976, very low-certainty
12 evidence). Prabhakaran 2019 measured depression scores at follow-up using the Patient Health
13 Questionnaire-9 and reported no difference between groups (MD -1.6; 95%CI -4.4 to 1.2; n=3324,
14 very low-certainty evidence).
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17 **Quality of life:** Results from one RCT⁴³ suggest that interventions to promote integrated care
18 compared to usual care may make little or no difference to quality of life, but the evidence is very
19 uncertain. The RCT reported on the change in health-related quality of life from baseline to follow-up
20 using the EuroQol-5D visual analogue scale and the EuroQol-5D index score. There was no difference
21 between groups, neither for the Euro-Qol-5D visual analogue scale (MD 6.06; 95%CI -3.25 to 15.36;
22 n=3969, very low- certainty evidence) nor for the EuroQol-5D index score (MD 0.00; 95%CI -0.05 to
23 0.06; n=3969, very low-certainty evidence).
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27 Table 4: Summary of findings for interventions to promote integrated delivery of care compared to
28 usual care for diabetes and hypertension in LMICs
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Patient or population: Patients with diabetes, hypertension and other chronic diseases Setting: Low- and middle-income countries Intervention: Strategies to promote integrated care Comparison: Usual care						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with Strategies to promote integrated care				
Mortality	29 per 1,000	32 per 1,000 (23 to 45)	RR 1.11 (0.79 to 1.56)	4393 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to the risk of death, but the evidence is very uncertain
Depression	10-item Center for Epidemiologic Studies Depression Scale: MD -0.12 (-1.72 to 1.48)		-	7293 (2 RCTs)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to depression scores, but the evidence is very uncertain
	Patient Health Questionnaire-9: MD -1.6 (-4.4 to 1.2)					
Change in quality of life (Euro-Qol-5D visual analogue scale)	Quality of life scores with usual care improved by a mean of 6.4 points	The mean change in quality of life with integrated care was 6.06 points higher (3.25 points lower to 15.36 points higher)	-	3969 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference in quality of life, but the evidence is very uncertain
Change in HbA1c	The mean change in HbA1c with usual care ranged from -0.58 to -0.2%	The mean change in HbA1c with integrated care was 0.11 % higher (0.2 lower to 0.42 higher)	-	1687 (2 RCTs)	⊕⊕○○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on HbA1c
Change in systolic BP	The mean change in systolic BP with usual care ranged from -13.7 to -1.1 mmHg	The mean change in BP with integrated care was 1.11 mmHg higher (1.14 lower to 3.35 higher)	-	4807 (2 RCTs)	⊕⊕○○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on systolic BP

<p>Change in total cholesterol</p>	<p>The mean change in total cholesterol with usual care was 2.0 mg/dl</p>	<p>The mean change in total cholesterol with integrated care was 2.5 mg/dl lower (7.1 lower to 2.1 higher)</p>	<p>-</p>	<p>3324 (1 RCT)</p>	<p>⊕⊕○○ LOW^{a,c}</p>	<p>Integrated care compared to usual care may have little or no effect on total cholesterol levels</p>
<p>*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; RR: Risk ratio; MD: Mean difference; BP: Blood pressure; HbA1c: Glycated haemoglobin; RCT: Randomised controlled trial High certainty: We are very confident that the true effect lies close to that of the estimate of the effect Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect <i>Footnotes: Explanation of GRADE certainty of evidence</i> a. Downgraded by 1 due to study limitations: high risk of performance bias and unclear risk of bias in some other domains b. Downgraded by 1 due to imprecision: study not adequately powered for this outcome, small sample size and wide 95% CI c. Downgraded by 1 due to indirectness: The interventions comprised strategies to promote integrated care at clinic level, and not integrated models of healthcare delivery at health system level</p>						

HbA1c: Results from two cluster RCTs^{43 44} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in HbA1c from baseline to follow-up (MD 0.11%; 95%CI -0.20 to 0.42; n=1687; 2 RCTs, low-certainty evidence).

Systolic BP: Results from two cluster RCTs^{43 44} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in systolic BP from baseline to follow-up (MD 1.11mmHg; 95%CI -1.41 to 3.35; n=4807; 2 RCTs, low-certainty evidence).

Total cholesterol: Results from one cluster RCT⁴⁴ suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in total cholesterol from baseline to follow-up (MD -2.50mg/dl; 95%CI -7.10 to 2.10; n=3324; low-certainty evidence).

Retention in care: Fairall 2016 reported the number of clinic visits three months before the follow-up interview and found no difference between groups (incidence rate ratio 1.02; 95%CI 0.93 to 1.13; n=3121).

Adherence: One cluster RCT reported absolute numbers for drug adherence during the past seven days.⁴⁴ Patients in the intervention group reported greater adherence for both hypertensive drugs (833/1027; 81.1% vs. 648/1119; 57.9%) and anti-hyperglycemic drugs (683/829; 82.4% vs. 570/827; 68.9%) compared to patients receiving usual care.

Quality of care: One cluster RCT⁴⁴ reported on perceived change in quality of care as a composite perception on availability of drugs, guidance from physicians, quality of care, frequency of blood pressure measurement, and care provided by NCD nurses. Perceived quality of care improved in both groups. Patients receiving integrated care (n=1637), reported that quality of care was slightly/much better (96.6%), about the same (3.3%) and somewhat/much worse (0.2%). Patients receiving usual

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2 care (n=1687) reported that quality of care was slightly/much better (95%), about the same (4.4%)
3 and somewhat/much worse (0.5%).
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5 Neither of the two cluster RCTs included in this comparison reported on access to care, continuity of
6 care or cost of care.
7

8 9 Discussion

10 11 Summary of main results

12 We included five studies and two comparisons in this review. Three studies were conducted in South
13 Africa, one in India and one in Kenya and Uganda. Two ITS studies and one cluster RCT provided data
14 for the first comparison, integrated models of care compared to usual care. Results suggest that
15 integrated models of care compared to usual care may make little or no difference to mortality, the
16 number of people achieving BP or diabetes control, and access to care; may increase the number of
17 people who achieve both HIV and BP/diabetes control; and may have a very small effect on achieving
18 HIV control. However, the evidence for all outcomes is very uncertain. Two cluster RCTs provided
19 data for the second comparison, interventions to promote integrated delivery of care compared to
20 usual care. Results suggest that interventions to promote integrated delivery of care compared to
21 usual care may make little or no difference to mortality, depression and quality of life, but the
22 evidence is very uncertain. Interventions to promote integrated delivery of care compared to usual
23 care may have little or no effect on HbA1c, systolic BP, and total cholesterol levels. Process outcomes
24 were poorly reported across included studies, with none of the studies reporting on continuity of
25 care or cost of care.
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30 31 Agreements and disagreements with other reviews

32 Other systematic reviews that assessed the effects of integrated models of care on health outcomes
33 in LMICs had similar findings. Dudley and Garner³⁰ assessed strategies to integrate PHC services on
34 healthcare delivery and health status in LMICs. They found no evidence that integrated services
35 improved healthcare delivery or health status. However, none of the included studies assessed
36 integrated care for NCDs. Haldane and colleagues²⁸ described existing integrated models of care for
37 HIV and NCDs and assessed health outcomes, barriers and facilitators. However, most of the included
38 studies were descriptive or observational and health outcomes were poorly reported. Indeed, they
39 highlighted the need for rigorous research that includes long-term follow-up and the role of
40 incentives.
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44 45 Overall completeness and applicability of evidence

46 Although we considered multi-morbidity in terms of diabetes and/or hypertension plus any other
47 disease, four out of five studies were conducted in sub-Saharan Africa and included people with
48 diabetes and/or hypertension (and other NCDs) and HIV. All studies were conducted in rural settings.
49 Due to successful transformation of the health systems to deliver HIV programmes, sub-Saharan
50 Africa is presented with a unique opportunity to leverage the investments made in order to scale-up
51 NCD services. This can be achieved in various ways, such as integrating NCD services into facilities
52 originally providing HIV care only, integrating HIV care into PHC facilities that offer NCD care, or
53 concurrent introduction of HIV and NCD services.⁸ However, even though this is recognised, there are
54 still questions linked to the implementation of integrated models of care. In South Africa, the ICDM
55 model, the intervention evaluated in the ITS study by Ameh and colleagues,⁴² is one example where
56 the vertical HIV programme was integrated into general PHC facilities. As part of the pilot
57 programme, Ameh and colleagues not only evaluated the impact on health outcomes, but also
58 conducted a qualitative study to explore the perspectives of healthcare providers and patients on the
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1
2 quality of care in the ICDM model.⁵³ They found that PHC facilities experienced BP drug stock-outs,
3 lack of functioning BP machines and staff shortages, among others, which impacted on the delivery
4 of care and indirectly therefore on the health outcomes. Integrated NCD and HIV care is
5 implemented to a varying degree in other sub-Saharan African countries. A study examining policies
6 and programmes for integrated HIV and NCD care in Malawi, Kenya, South Africa and Swaziland
7 found that these countries still experience challenges in implementing integrated care. Some of
8 these are related to inadequate data to determine the burden of NCDs among PLHIV at a local level,
9 lack of evidence to support the implementation of integrated care models, inadequate stakeholder
10 engagement, lack of NCD care capacity and other health system challenges.⁵⁴

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13 Our definition of integrated care was based on a “one-stop-shop” model whereby a patient receives
14 all necessary care or services under one roof by one or more health-care professional (Figure 1),
15 which is just one way of describing integrated care. Indeed, a narrative review by Njuguna, et al.⁵⁵
16 aimed to describe various models of integrated care for HIV and NCDs in sub-Saharan Africa. Based
17 on the definition by WHO, the authors defined integrated care as the “coordination, co-location, or
18 simultaneous delivery of HIV and NCD services to patients who need it, when they need it” and
19 identified five models. These include community-based integrated HIV and NCD screening in the
20 general population; screening for NCD risk factors among PLHIV; integrated care for HIV and NCDs in
21 healthcare facilities through leveraging the HIV infrastructure to manage NCDs; differential care for
22 people well-controlled HIV or NCDs, which includes longer follow-up periods for stable patients; and
23 population health for all patients with any need.⁵⁵

24 Strengths and limitations

25 We followed a rigorous and systematic process according to standard systematic review methods.
26 We performed a comprehensive search of published and unpublished studies up to 12 December
27 2019, with no language restrictions. We purposefully included study designs that are able to provide
28 reliable evidence on the effects of integrated care on health and process outcomes, and followed
29 guidance provided by Cochrane EPOC. We assessed the certainty of evidence using the GRADE
30 approach across outcomes, taking into consideration study limitations, inconsistency, imprecision,
31 publication bias and indirectness when downgrading the certainty of evidence.

32
33 Integration of care for NCDs and HIV or other diseases is complex, partly due to the complex nature
34 of health systems.⁵⁶ We aimed to compare fully integrated models of care to partially integrated
35 models of care or stand-alone care. However, it was difficult to classify interventions according to our
36 pre-specified definitions and we thus lumped interventions that integrated service delivery as
37 ‘integrated models of care’. We included two cluster RCTs that aimed to promote integrated delivery
38 of care through clinical management tools, which is different from integrated care at facility level.
39 We discussed this within our team and concluded that the aim of these interventions was to provide
40 care in a holistic way and to address all the needs of an individual when s/he presents to a healthcare
41 facility, and thus met our eligibility criteria. Furthermore, included studies did not provide adequate
42 information on the level of integration in comparisons, but rather referred to these as standard or
43 usual care. While these referred a lesser degree of integration compared to the interventions, we
44 were not able to categorise these as either partially integrated care or stand-alone care.

45
46 Our review focused on the effectiveness of integrating care for people with diabetes, hypertension
47 and other co-morbidities in terms of health outcomes, which is just one question that needs to be
48 answered. In other words, the question of our review focused on one building block of health
49 systems as described by the WHO.⁵⁶ Although we aimed to examine process outcomes, these were
50 limited to access to care, retention in care, adherence, continuity of care, quality of care and cost of
51 care; and were poorly reported across included studies. The scope of our review did not include
52 outcomes related to implementation or perspectives from health providers and patients, which are

1
2 important aspects to consider. Although the literature predominantly highlights the need to
3 integrate NCD and HIV care, integrating mental health services into existing NCD and or HIV services
4 is just as important. Four⁴⁸⁻⁵¹ of the five ongoing studies that we identified examine integration of
5 mental health with NCDs.
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8 Conclusion

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10 The evidence on the effectiveness of integrated models of care for people with diabetes,
11 hypertension and other co-morbidities, on health outcomes is very uncertain. We therefore do not
12 know whether integrated models of care lead to better or worse outcomes, or may make no
13 difference at all among people with diabetes, hypertension and other chronic conditions. There is a
14 need to scale-up NCD services, particularly in LMICs. In the context of an increasing burden of NCDs
15 against a backdrop of other chronic diseases, and scarce health system resources, such as human
16 capacity and funding, policies and programmes need to promote integrated models of care and
17 holistic, patient-centred services. However, these need to take into consideration context-specific
18 factors related to the health system and the targeted population.
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21 Further rigorous studies assessing the effects of integrated models of care on health outcomes are
22 needed. These studies should include an adequate description of the integrated model of care,
23 assess long term health effects as well as patient important outcomes, and cost of care.
24 Furthermore, there is a need to conduct implementation research, economic evaluations as well as
25 qualitative research on the barriers and facilitators to integrated models of care at patient and
26 health-system level in order to guide policy makers in planning and allocation of resources in order to
27 maximise the potential benefits of integrated care as well strengthening the health systems in
28 achieving universal health coverage in LMICs.
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33 Authors' contributions

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35 All authors contributed to development of the review protocol. JUN and AR screened titles and
36 abstracts; JUN, AR, TY and CMB participated in full text screening; TY, JJM and IT helped to resolve
37 discrepancies. AR, JUN and IT extracted data and assessed risk of bias. AR and IT assessed certainty of
38 evidence with input from TY and JJM. TY and JJM provided overall methodological guidance. JUN
39 drafted the background section, AR drafted the rest of the manuscript. JUN, IT, TY, and CMB critically
40 read and revised the manuscript. All authors have approved the final version of the manuscript.
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47 Ayele for statistical input, and Selvan Naidoo for assistance with screening titles and abstracts.
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50 Ethics approval

51
52 This systematic review does not involve human participants. All data included is in the public domain
53 and ethics approval was thus not sought.
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55 Data sharing statement

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57 All data relevant to the study are included in the article or uploaded as supplementary information.
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Competing interests statement

All authors have no known conflict of interest.

Protocol

Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension in low- and middle-income countries (LMICs): Protocol for a systematic review. *Syst Rev* 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]

Figures

Figure 1: Logic model of integrated care

Figure 2: PRISMA flow diagram

Figure 3: Risk of bias in ITS studies

Figure 4: Risk of bias for cluster RCTs

Supplementary files

Supplementary file 1: Search strategies for all databases

Supplementary file 2: Table of excluded studies

Supplementary file 3: Summary of interventions according to the TIDiER checklist: Integrated models of care

Supplementary file 4: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated delivery of care

Supplementary file 5: Risk of bias assessments for included studies

Supplementary file 6: Forest plots

References

1. WHO. Noncommunicable diseases, 2018.
2. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390(10100):1211-59. doi: 10.1016/S0140-6736(17)32154-2 [published Online First: 2017/09/19]
3. Alliance N. Tackling non-communicable diseases in workplace settings in low- and middle-income countries. A CALL TO ACTION AND PRACTICAL GUIDANCE. Non-Communicable diseases (NCD) Alliance, 2017.
4. WHO. Cardiovascular diseases (CVDs) 2017 [Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))].
5. WHO. Global status report on non-communicable diseases 2010. Description of the global burden of NCDs, their risk factors and determinants, 2010.
6. Federation ID. IDF diabetes Atlas 8th Edition. 8 ed 2017. Available from: <https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/134-idf-diabetes-atlas-8th-edition.html>.
7. Campbell NRC, Lackland DT, Niebylski ML. High Blood Pressure: Why Prevention and Control Are Urgent and Important-A 2014 Fact Sheet From the World Hypertension League and the International Society of Hypertension. *Journal of Clinical Hypertension* 2014;16(8):551-53. doi: 10.1111/jch.12372
8. Duffy M, Ojikutu B, Andrian S, et al. Non-communicable diseases and HIV care and treatment: models of integrated service delivery. *Tropical Medicine and International Health* 2017;22(8):926-37. doi: 10.1111/tmi.12901
9. Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African primary healthcare. *South African Medical Journal* 2015;105(2):134-38. doi: 10.7196/SAMJ.8696
10. Remais JV, Zeng G, Li G, et al. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *International Journal of Epidemiology* 2013;42(1):221-27. doi: 10.1093/ije/dys135
11. Rabkin M, Kruk ME, El-Sadr WM. HIV, aging and continuity care: strengthening health systems to support services for noncommunicable diseases in low-income countries. *AIDS* 2012;26
12. Patel P, Rose CE, Collins PY, et al. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis. *AIDS* 2018;32 Suppl 1:S5-S20. doi: 10.1097/QAD.0000000000001888 [published Online First: 2018/06/29]
13. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012 doi: 10.1016/S0140-6736(12)61728-0
14. Mbanya JCN, Motala AA, Sobngwi E, et al. Diabetes in sub-Saharan Africa, 2010.
15. Atun R, De Jongh T, Secci F, et al. A systematic review of the evidence on integration of targeted health interventions into health systems. *Health Policy and Planning* 2010;25(1):1-14. doi: 10.1093/heapol/czp053
16. Shigayeva A, Atun R, McKee M, et al. Health systems, communicable diseases and integration. *Health Policy and Planning* 2010;25(Suppl. 1):i4-i20. doi: 10.1093/heapol/czq060
17. WHO. Package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings.
18. Legido-Quigley H, Montgomery CM, Khan P, et al. Integrating tuberculosis and HIV services in low- and middle-income countries: A systematic review. *Tropical Medicine and International Health* 2013;18(2):199-211. doi: 10.1111/tmi.12029
19. Naidoo K, Gengiah S, Yende-Zuma N, et al. Addressing challenges in scaling up TB and HIV treatment integration in rural primary healthcare clinics in South Africa (SUTHI): A cluster randomized controlled trial protocol. *Implementation Science* 2017;12(1):1-12. doi: 10.1186/s13012-017-0661-1
20. Uyei J, Coetzee D, Macinko J, et al. Integrated delivery of HIV and tuberculosis services in sub-Saharan Africa: A systematic review. *The Lancet Infectious Diseases* 2011;11(11):855-67. doi: 10.1016/S1473-3099(11)70145-1

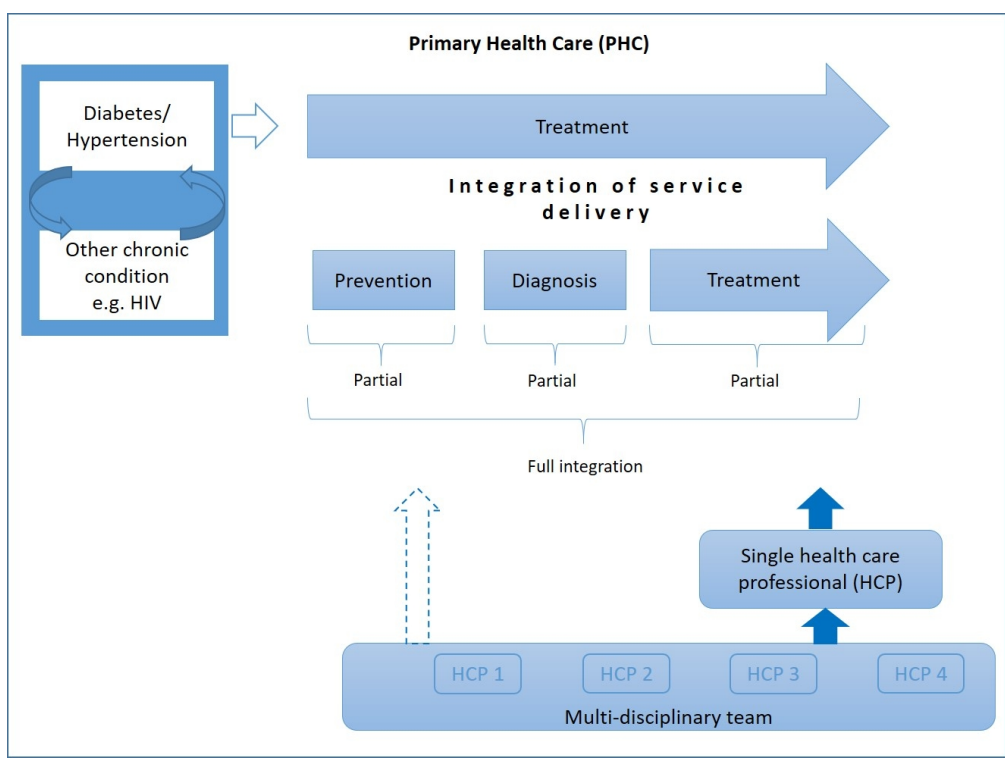
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21. Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension in low- and middle-income countries (LMICs) : Protocol for a systematic review. *Syst Rev* 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]
22. Yiu KC, Rohwer A, Young T. Integration of care for hypertension and diabetes: a scoping review assessing the evidence from systematic reviews and evaluating reporting. *BMC Health Serv Res* 2018;18(1):481. doi: 10.1186/s12913-018-3290-8 [published Online First: 2018/06/22]
23. Atlantis E, Fahey P, Foster J. Collaborative care for comorbid depression and diabetes: a systematic review and meta-analysis. *BMJ Open* 2014;4(4):e004706. doi: 10.1136/bmjopen-2013-004706 [published Online First: 2014/04/15]
24. Huang Y, Wei X, Wu T, et al. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. *BMC Psychiatry* 2013;13:260. doi: 10.1186/1471-244X-13-260 [published Online First: 2013/10/16]
25. Joshi R, Alim M, Kengne AP, et al. Task shifting for non-communicable disease management in low and middle income countries--a systematic review. *PLoS One* 2014;9(8):e103754. doi: 10.1371/journal.pone.0103754 [published Online First: 2014/08/15]
26. Smith SM, Wallace E, O'Dowd T, et al. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database Syst Rev* 2016;3:CD006560. doi: 10.1002/14651858.CD006560.pub3 [published Online First: 2016/03/16]
27. Watson LC, Amick HR, Gaynes BN, et al. Practice-based interventions addressing concomitant depression and chronic medical conditions in the primary care setting: a systematic review and meta-analysis. *J Prim Care Community Health* 2013;4(4):294-306. doi: 10.1177/2150131913484040 [published Online First: 2013/06/27]
28. Haldane V, Legido-Quigley H, Chuah FLH, et al. Integrating cardiovascular diseases, hypertension, and diabetes with HIV services: a systematic review. *AIDS Care* 2018;30(1):103-15. doi: 10.1080/09540121.2017.1344350 [published Online First: 2017/07/07]
29. Janssens B, Van Damme W, Raleigh B, et al. BulleJohnson, W., Onuma, O., Owolabi, M., & Sachdev, A. S. (2017AD). Bulletin of the World Health Organization Stroke: a global response is needed. Bulletin of the World Health Organization, 85(February), 660–667. <https://doi.org/10.2471/BLTtin> of the Worl. *Bulletin of the World Health Organization* 2007;85:880-85. doi: 10.2471/BLT
30. Dudley L, Garner P. Strategies for integrating primary health services in low- and middle-income countries at the point of delivery. *Cochrane Database of Systematic Review* 2011(7) doi: doi: 10.1002/14651858.CD003318.pub3.
31. Bank W. World Bank list of economies 2016 [Available from: [Siteresources.worldbank.org/DATASTATISTICS/Resources/CLASS.XLS](http://siteresources.worldbank.org/DATASTATISTICS/Resources/CLASS.XLS)]
32. Masquillier C, Wouters E, Mortelmans D, et al. On the road to HIV/AIDS competence in the household: building a health-enabling environment for people living with HIV/AIDS. *Int J Environ Res Public Health* 2015;12(3):3264-92. doi: 10.3390/ijerph120303264 [published Online First: 2015/03/21]
33. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687. doi: 10.1136/bmj.g1687 [published Online First: 2014/03/13]
34. Guise JM, Butler ME, Chang C, et al. AHRQ series on complex intervention systematic reviews- paper 6: PRISMA-CI extension statement and checklist. *J Clin Epidemiol* 2017;90:43-50. doi: 10.1016/j.jclinepi.2017.06.016 [published Online First: 2017/07/20]
35. (EPOC) CEPaOoC. Suggested risk of bias criteria for EPOC reviews. . EPOC Resources fo r review authors, 2017.
36. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0 (updated July 2019): Cochrane 2019. Available from: www.training.cochrane.org/handbook
37. Review Manager (RevMan) [program]. 5.3 version. Copenhagen: The Cochrane Collaboration, 2014.

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 - 60
38. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026 [published Online First: 2011/01/05]
39. GRADEpro GDT: GRADEpro Guideline Development Tool [Software] [program]: McMaster University, 2015.
40. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64(4):401-6. doi: 10.1016/j.jclinepi.2010.07.015 [published Online First: 2011/01/07]
41. Santesso N, Glenton C, Dahm P, et al. GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol* 2020;119:126-35. doi: 10.1016/j.jclinepi.2019.10.014 [published Online First: 2019/11/13]
42. Ameh S, Klipstein-Grobusch K, Musenge E, et al. Effectiveness of an Integrated Approach to HIV and Hypertension Care in Rural South Africa: Controlled Interrupted Time-Series Analysis. *Journal of acquired immune deficiency syndromes (1999)* 2017;75(4):472-79. doi: 10.1097/qai.0000000000001437
43. Fairall LR, Folb N, Timmerman V, et al. Educational Outreach with an Integrated Clinical Tool for Nurse-Led Non-communicable Chronic Disease Management in Primary Care in South Africa: A Pragmatic Cluster Randomised Controlled Trial. *PLoS medicine* 2016;13(11):e1002178. doi: 10.1371/journal.pmed.1002178
44. Prabhakaran D, Jha D, Prieto-Merino D, et al. Effectiveness of an mHealth-Based Electronic Decision Support System for Integrated Management of Chronic Conditions in Primary Care: The mWellcare Cluster-Randomized Controlled Trial. *Circulation* 2018 doi: 10.1161/CIRCULATIONAHA.118.038192
45. Rawat A, Uebel K, Moore D, et al. Integrated HIV-Care into Primary Health Care Clinics and the Influence on Diabetes and Hypertension Care: An Interrupted Time Series Analysis in Free State, South Africa over 4 Years. *Journal of Acquired Immune Deficiency Syndromes* 2018;77(5):476-83. doi: <http://dx.doi.org/10.1097/QAI.0000000000001633>
46. Havlir DV, Balzer LB, Charlebois ED, et al. HIV Testing and Treatment with the Use of a Community Health Approach in Rural Africa. *N Engl J Med* 2019;381(3):219-29. doi: 10.1056/NEJMoa1809866 [published Online First: 2019/07/18]
47. Integrated versus referred management of cardiovascular disease (CVD) risk factors for HIV-positive patients on antiretroviral therapy in Swaziland 20th International Workshop on Comorbidities and Adverse Drug Reactions in HIV; 2018; New York, USA.
48. Chen S, Conwell Y, Xue J, et al. Protocol of an ongoing randomized controlled trial of care management for comorbid depression and hypertension: the Chinese Older Adult Collaborations in Health (COACH) study. *BMC geriatrics* 2018;18(1):124. doi: 10.1186/s12877-018-0808-1
49. Petersen I, Bhana A, Folb N, et al. Collaborative care for the detection and management of depression among adults with hypertension in South Africa: study protocol for the PRIME-SA randomised controlled trial. *Trials* 2018;19(1):192. doi: 10.1186/s13063-018-2518-6
50. Myers B, Lund C, Lombard C, et al. Comparing dedicated and designated models of integrating mental health into chronic disease care: study protocol for a cluster randomized controlled trial. *Trials* 2018;19(1) (no pagination) doi: 10.1186/s13063-018-2568-9
51. Srinivasan K, Mazur A, Mony PK, et al. Improving mental health through integration with primary care in rural Karnataka: study protocol of a cluster randomized control trial. *BMC Fam Pract* 2018;19(1):158. doi: 10.1186/s12875-018-0845-z [published Online First: 2018/09/13]
52. Devarsetty P. Diabetes and Tuberculosis - Integrated management using the primary healthcare infrastructure in India 2017 [Available from: <http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=15771>
53. Ameh S, Klipstein-Grobusch K, D'Ambruoso L, et al. Quality of integrated chronic disease care in rural South Africa: user and provider perspectives. *Health Policy Plan* 2017;32(2):257-66. doi: 10.1093/heapol/czw118 [published Online First: 2017/02/17]
54. Matanje Mwangomba BL, Ameh S, Bongomin P, et al. Opportunities and challenges for evidence-informed HIV-noncommunicable disease integrated care policies and programs: lessons from

- 1
2 Malawi, South Africa, Swaziland and Kenya. *AIDS* 2018;32 Suppl 1:S21-S32. doi:
3 10.1097/QAD.0000000000001885 [published Online First: 2018/06/29]
4 55. Njuguna B, Vorkoper S, Patel P, et al. Models of integration of HIV and noncommunicable disease
5 care in sub-Saharan Africa: lessons learned and evidence gaps. *AIDS* 2018;32 Suppl 1:S33-
6 S42. doi: 10.1097/QAD.0000000000001887 [published Online First: 2018/06/29]
7
8 56. WHO. Everybody's business: Strengthening Health Systems to improve Health Outcomes. WHO's
9 Framework for Action. , 2007.
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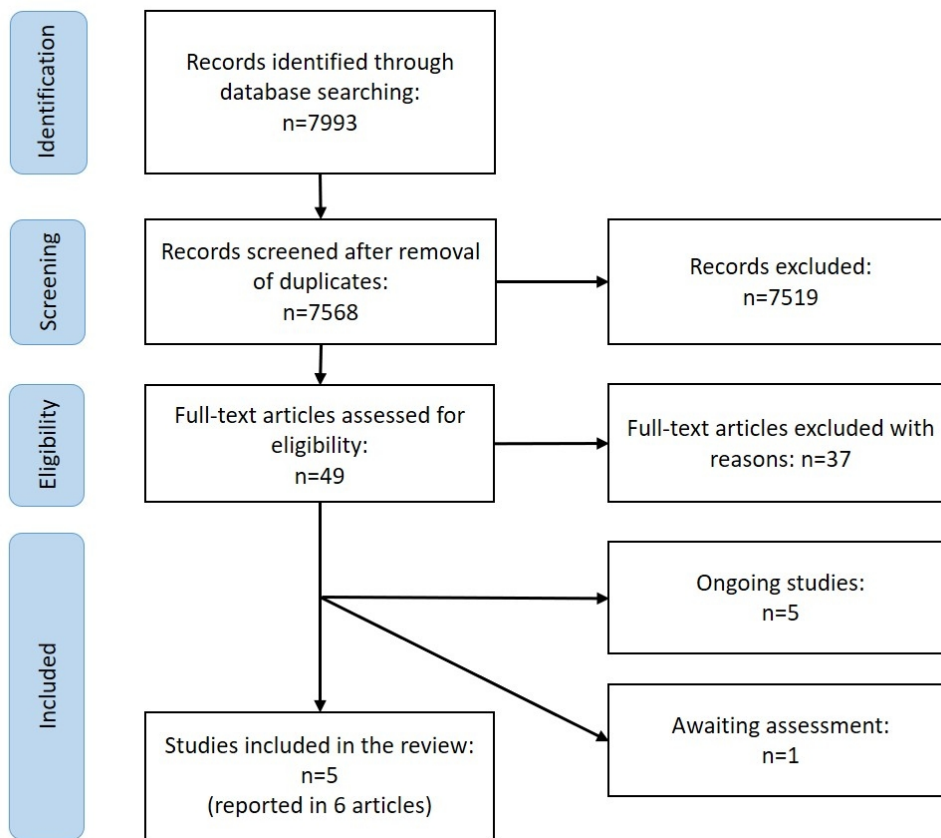
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	Intervention was independent of other changes	The shape of the intervention was pre-specified	The intervention was unlikely to affect data collection	Knowledge of the allocated intervention adequately prevented during the study	Incomplete outcome data was likely to bias results	Outcomes were reported selectively	Other bias
Ameh 2017	+	+	?	+	+	+	+
Rawat 2018	+	?	+	+	?	+	+

44x75mm (300 x 300 DPI)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data (attrition bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Protection against contamination	Selective reporting (reporting bias)	Recruitment bias	Baseline differences (clusters)	Loss of clusters	Incorrect analysis	Compatibility with RCTs randomised by individuals	Other bias
Fairall 2016	+	+	+	?	+	-	?	?	+	+	+	+	+	+	?
Havilir 2019	+	+	?	+	?	-	?	?	?	+	?	+	?	+	?
Prabhakaran 2018	+	+	+	+	+	-	?	+	+	?	?	+	+	+	+

98x73mm (300 x 300 DPI)

Supplementary file 1: Search strategies for electronic databases

1. Medline (PubMed) search strategy

#1 "Hypertension"[Mesh] OR (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)[title/abstract]

#2 diabetes OR "diabetes mellitus"[title/abstract] OR "Diabetes Mellitus"[Mesh]

#3 #1 OR #2

#4 (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein)[title/abstract] OR "Dyslipidemias"[Mesh]

#5 (((HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR HIV/AIDS))) OR ((HIV infections [MeSH] OR HIV [MeSH]))

#6 (tuberculosis OR tuberculoses OR tb)[Title/Abstract] OR "tuberculosis"[Mesh]

#7 "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR NCD OR NCDs OR "Noncommunicable Diseases"[Mesh]

#8 (comorbid* OR co-morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity")[title/abstract] OR "Multimorbidity"[Mesh] OR "Comorbidity"[Mesh]

#9 multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring condition* OR cooccurring condition*

#10 chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle" OR "Multiple Chronic Conditions"[Mesh] OR "Chronic Disease"[Mesh]

#11 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 "Delivery of Health Care, Integrated"[Mesh] OR "delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "Comprehensive Health Care"[Mesh] OR "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "Continuity of Patient Care"[Mesh] OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "Patient-Centered Care"[Mesh] OR "patient centered care" OR "patient centred care"

1
2 **#13** "Referral and Consultation"[Mesh] OR (referral AND consultation)

3
4 **#14** integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR
5 integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of
6 programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR
7 "integration of services" OR integrat* delivery OR integrat* management OR "integration of
8 management"

9
10 **#15** coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of services"
11 OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR
12 "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR
13 coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat*
14 management OR "coordination of management"

15
16 **#16** co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of
17 services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes"
18 OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service
19 delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-
20 ordinat* management OR "co-ordination of management"

21
22 **#17** horizontal care OR vertical care OR horizontal services OR vertical services OR horizontal
23 programmes OR horizontal programs OR vertical programmes OR vertical programs OR horizontal
24 service delivery OR vertical service delivery OR horizontal services OR vertical services OR horizontal
25 delivery OR vertical management OR vertical management

26
27 **#18** "multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR "multi
28 service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR "multi
29 delivery" OR multidelivery OR "multi management"

30
31 **#19** #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

32
33 **#20** #3 AND #11 AND #19

34
35 **#21** Developing Countries[Mesh:noexp] OR Africa[Mesh:noexp] OR Africa, Northern[Mesh:noexp] OR
36 Africa South of the Sahara[Mesh:noexp] OR Africa, Central[Mesh:noexp] OR Africa,
37 Eastern[Mesh:noexp] OR Africa, Southern[Mesh:noexp] OR Africa, Western[Mesh:noexp] OR
38 Asia[Mesh:noexp] OR Asia, Central[Mesh:noexp] OR Asia, Southeastern[Mesh:noexp] OR Asia,
39 Western[Mesh:noexp] OR Caribbean Region[Mesh:noexp] OR West Indies[Mesh:noexp] OR South
40 America[Mesh:noexp] OR Latin America[Mesh:noexp] OR Central America[Mesh:noexp] OR
41 Afghanistan[Mesh:noexp] OR Albania[Mesh:noexp] OR Algeria[Mesh:noexp] OR American
42 Samoa[Mesh:noexp] OR Angola[Mesh:noexp] OR "Antigua and Barbuda"[Mesh:noexp] OR
43 Argentina[Mesh:noexp] OR Armenia[Mesh:noexp] OR Azerbaijan[Mesh:noexp] OR
44 Bahrain[Mesh:noexp] OR Bangladesh[Mesh:noexp] OR Barbados[Mesh:noexp] OR
45 Benin[Mesh:noexp] OR Byelarus[Mesh:noexp] OR Belize[Mesh:noexp] OR Bhutan[Mesh:noexp] OR
46 Bolivia[Mesh:noexp] OR Bosnia-Herzegovina[Mesh:noexp] OR Botswana[Mesh:noexp] OR
47 Brazil[Mesh:noexp] OR Bulgaria[Mesh:noexp] OR Burkina Faso[Mesh:noexp] OR
48 Burundi[Mesh:noexp] OR Cambodia[Mesh:noexp] OR Cameroon[Mesh:noexp] OR Cape
49 Verde[Mesh:noexp] OR Central African Republic[Mesh:noexp] OR Chad[Mesh:noexp] OR
50 Chile[Mesh:noexp] OR China[Mesh:noexp] OR Colombia[Mesh:noexp] OR Comoros[Mesh:noexp] OR
51 Congo[Mesh:noexp] OR Costa Rica[Mesh:noexp] OR Cote d'Ivoire[Mesh:noexp] OR
52 Croatia[Mesh:noexp] OR Cuba[Mesh:noexp] OR Cyprus[Mesh:noexp] OR
53 Czechoslovakia[Mesh:noexp] OR Czech Republic[Mesh:noexp] OR Slovakia[Mesh:noexp] OR
54 Djibouti[Mesh:noexp] OR "Democratic Republic of the Congo"[Mesh:noexp] OR

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 2 Dominica[Mesh:noexp] OR Dominican Republic[Mesh:noexp] OR East Timor[Mesh:noexp] OR
 3 Ecuador[Mesh:noexp] OR Egypt[Mesh:noexp] OR El Salvador[Mesh:noexp] OR Eritrea[Mesh:noexp]
 4 OR Estonia[Mesh:noexp] OR Ethiopia[Mesh:noexp] OR Fiji[Mesh:noexp] OR Gabon[Mesh:noexp] OR
 5 Gambia[Mesh:noexp] OR "Georgia (Republic)"[Mesh:noexp] OR Ghana[Mesh:noexp] OR
 6 Greece[Mesh:noexp] OR Grenada[Mesh:noexp] OR Guatemala[Mesh:noexp] OR
 7 Guinea[Mesh:noexp] OR Guinea-Bissau[Mesh:noexp] OR Guam[Mesh:noexp] OR
 8 Guyana[Mesh:noexp] OR Haiti[Mesh:noexp] OR Honduras[Mesh:noexp] OR Hungary[Mesh:noexp]
 9 OR India[Mesh:noexp] OR Indonesia[Mesh:noexp] OR Iran[Mesh:noexp] OR Iraq[Mesh:noexp] OR
 10 Jamaica[Mesh:noexp] OR Jordan[Mesh:noexp] OR Kazakhstan[Mesh:noexp] OR Kenya[Mesh:noexp]
 11 OR Korea[Mesh:noexp] OR Kosovo[Mesh:noexp] OR Kyrgyzstan[Mesh:noexp] OR Laos[Mesh:noexp]
 12 OR Latvia[Mesh:noexp] OR Lebanon[Mesh:noexp] OR Lesotho[Mesh:noexp] OR Liberia[Mesh:noexp]
 13 OR Libya[Mesh:noexp] OR Lithuania[Mesh:noexp] OR Macedonia[Mesh:noexp] OR
 14 Madagascar[Mesh:noexp] OR Malaysia[Mesh:noexp] OR Malawi[Mesh:noexp] OR Mali[Mesh:noexp]
 15 OR Malta[Mesh:noexp] OR Mauritania[Mesh:noexp] OR Mauritius[Mesh:noexp] OR
 16 Mexico[Mesh:noexp] OR Micronesia[Mesh:noexp] OR Middle East[Mesh:noexp] OR
 17 Moldova[Mesh:noexp] OR Mongolia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR
 18 Morocco[Mesh:noexp] OR Mozambique[Mesh:noexp] OR Myanmar[Mesh:noexp] OR
 19 Namibia[Mesh:noexp] OR Nepal[Mesh:noexp] OR Netherlands Antilles[Mesh:noexp] OR New
 20 Caledonia[Mesh:noexp] OR Nicaragua[Mesh:noexp] OR Niger[Mesh:noexp] OR Nigeria[Mesh:noexp]
 21 OR Oman[Mesh:noexp] OR Pakistan[Mesh:noexp] OR Palau[Mesh:noexp] OR Panama[Mesh:noexp]
 22 OR Papua New Guinea[Mesh:noexp] OR Paraguay[Mesh:noexp] OR Peru[Mesh:noexp] OR
 23 Philippines[Mesh:noexp] OR Poland[Mesh:noexp] OR Portugal[Mesh:noexp] OR Puerto
 24 Rico[Mesh:noexp] OR Romania[Mesh:noexp] OR Russia[Mesh:noexp] OR "Russia (Pre-
 25 1917)"[Mesh:noexp] OR Rwanda[Mesh:noexp] OR "Saint Kitts and Nevis"[Mesh:noexp] OR Saint
 26 Lucia[Mesh:noexp] OR "Saint Vincent and the Grenadines"[Mesh:noexp] OR Samoa[Mesh:noexp] OR
 27 Saudi Arabia[Mesh:noexp] OR Senegal[Mesh:noexp] OR Serbia[Mesh:noexp] OR
 28 Montenegro[Mesh:noexp] OR Seychelles[Mesh:noexp] OR Sierra Leone[Mesh:noexp] OR
 29 Slovenia[Mesh:noexp] OR Sri Lanka[Mesh:noexp] OR Somalia[Mesh:noexp] OR South
 30 Africa[Mesh:noexp] OR Sudan[Mesh:noexp] OR Suriname[Mesh:noexp] OR Swaziland[Mesh:noexp]
 31 OR Syria[Mesh:noexp] OR Tajikistan[Mesh:noexp] OR Tanzania[Mesh:noexp] OR
 32 Thailand[Mesh:noexp] OR Togo[Mesh:noexp] OR Tonga[Mesh:noexp] OR "Trinidad and
 33 Tobago"[Mesh:noexp] OR Tunisia[Mesh:noexp] OR Turkey[Mesh:noexp] OR
 34 Turkmenistan[Mesh:noexp] OR Uganda[Mesh:noexp] OR Ukraine[Mesh:noexp] OR
 35 Uruguay[Mesh:noexp] OR USSR[Mesh:noexp] OR Uzbekistan[Mesh:noexp] OR Vanuatu[Mesh:noexp]
 36 OR Venezuela[Mesh:noexp] OR Vietnam[Mesh:noexp] OR Yemen[Mesh:noexp] OR
 37 Yugoslavia[Mesh:noexp] OR Zambia[Mesh:noexp] OR Zimbabwe[Mesh:noexp]

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 46 **#22** Macedonia[tw] OR Madagascar[tw] OR Malagasy Republic[tw] OR Malaysia[tw] OR Malaya[tw]
 47 OR Malay[tw] OR Sabah[tw] OR Sarawak[tw] OR Malawi[tw] OR Nyasaland[tw] OR Mali[tw] OR
 48 Malta[tw] OR Marshall Islands[tw] OR Mauritania[tw] OR Mauritius[tw] OR Agalega Islands[tw] OR
 49 Mexico[tw] OR Micronesia[tw] OR Middle East[tw] OR Moldova[tw] OR Moldovia[tw] OR
 50 Moldovian[tw] OR Mongolia[tw] OR Montenegro[tw] OR Morocco[tw] OR Ifni[tw] OR
 51 Mozambique[tw] OR Myanmar[tw] OR Myanma[tw] OR Burma[tw] OR Namibia[tw] OR Nepal[tw] OR
 52 Netherlands Antilles[tw] OR New Caledonia[tw] OR Nicaragua[tw] OR Niger[tw] OR Nigeria[tw] OR
 53 Northern Mariana Islands[tw] OR Oman[tw] OR Muscat[tw] OR Pakistan[tw] OR Palau[tw] OR
 54 Palestine[tw] OR Panama[tw] OR Paraguay[tw] OR Peru[tw] OR Philippines[tw] OR Philipines[tw] OR
 55 Phillipines[tw] OR Phillippines[tw] OR Poland[tw] OR Portugal[tw] OR Puerto Rico[tw] OR
 56 Romania[tw] OR Rumania[tw] OR Roumania[tw] OR Russia[tw] OR Russian[tw] OR Rwanda[tw] OR
 57 Ruanda[tw] OR Saint Kitts[tw] OR St Kitts[tw] OR Nevis[tw] OR Saint Lucia[tw] OR St Lucia[tw] OR
 58 Saint Vincent[tw] OR St Vincent[tw] OR Grenadines[tw] OR Samoa[tw] OR Samoan Islands[tw] OR

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2 Navigator Island[tw] OR Navigator Islands[tw] OR Sao Tome[tw] OR Saudi Arabia[tw] OR Senegal[tw]
3 OR Serbia[tw] OR Montenegro[tw] OR Seychelles[tw] OR Sierra Leone[tw] OR Slovenia[tw] OR Sri
4 Lanka[tw] OR Ceylon[tw] OR Solomon Islands[tw] OR Somalia[tw] OR Sudan[tw] OR Suriname[tw] OR
5 Surinam[tw] OR Swaziland[tw] OR Syria[tw] OR Tajikistan[tw] OR Tadjhikistan[tw] OR Tadjikistan[tw]
6 OR Tadjhik[tw] OR Tanzania[tw] OR Thailand[tw] OR Togo[tw] OR Togolese Republic[tw] OR
7 Tonga[tw] OR Trinidad[tw] OR Tobago[tw] OR Tunisia[tw] OR Turkey[tw] OR Turkmenistan[tw] OR
8 Turkmen[tw] OR Uganda[tw] OR Ukraine[tw] OR Uruguay[tw] OR USSR[tw] OR Soviet Union[tw] OR
9 Union of Soviet Socialist Republics[tw] OR Uzbekistan[tw] OR Uzbek OR Vanuatu[tw] OR New
10 Hebrides[tw] OR Venezuela[tw] OR Vietnam[tw] OR Viet Nam[tw] OR West Bank[tw] OR Yemen[tw]
11 OR Yugoslavia[tw] OR Zambia[tw] OR Zimbabwe[tw] OR Rhodesia[tw]

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14
15 **#23** Africa[tw] OR Asia[tw] OR Caribbean[tw] OR West Indies[tw] OR South America[tw] OR Latin
16 America[tw] OR Central America[tw] OR Afghanistan[tw] OR Albania[tw] OR Algeria[tw] OR
17 Angola[tw] OR Antigua[tw] OR Barbuda[tw] OR Argentina[tw] OR Armenia[tw] OR Armenian[tw] OR
18 Aruba[tw] OR Azerbaijan[tw] OR Bahrain[tw] OR Bangladesh[tw] OR Barbados[tw] OR Benin[tw] OR
19 Byelarus[tw] OR Byelorussian[tw] OR Belarus[tw] OR Belorussian[tw] OR Belorussia[tw] OR Belize[tw]
20 OR Bhutan[tw] OR Bolivia[tw] OR Bosnia[tw] OR Herzegovina[tw] OR Hercegovina[tw] OR
21 Botswana[tw] OR Brasil[tw] OR Brazil[tw] OR Bulgaria[tw] OR Burkina Faso[tw] OR Burkina Fasso[tw]
22 OR Upper Volta[tw] OR Burundi[tw] OR Urundi[tw] OR Cambodia[tw] OR Khmer Republic[tw] OR
23 Kampuchea[tw] OR Cameroon[tw] OR Camerons[tw] OR Cameroon[tw] OR Camerons[tw] OR Cape
24 Verde[tw] OR Central African Republic[tw] OR Chad[tw] OR Chile[tw] OR China[tw] OR Colombia[tw]
25 OR Comoros[tw] OR Comoro Islands[tw] OR Comores[tw] OR Mayotte[tw] OR Congo[tw] OR
26 Zaire[tw] OR Costa Rica[tw] OR Cote d'Ivoire[tw] OR Ivory Coast[tw] OR Croatia[tw] OR Cuba[tw] OR
27 Cyprus[tw] OR Czechoslovakia[tw] OR Czech Republic[tw] OR Slovakia[tw] OR Slovak Republic[tw] OR
28 Djibouti[tw] OR French Somaliland[tw] OR Dominica[tw] OR Dominican Republic[tw] OR East
29 Timor[tw] OR East Timur[tw] OR Timor Leste[tw] OR Ecuador[tw] OR Egypt[tw] OR United Arab
30 Republic[tw] OR El Salvador[tw] OR Eritrea[tw] OR Estonia[tw] OR Ethiopia[tw] OR Fiji[tw] OR
31 Gabon[tw] OR Gabonese Republic[tw] OR Gambia[tw] OR Gaza[tw] OR Georgia Republic[tw] OR
32 Georgian Republic[tw] OR Ghana[tw] OR Gold Coast[tw] OR Greece[tw] OR Grenada[tw] OR
33 Guatemala[tw] OR Guinea[tw] OR Guam[tw] OR Guiana[tw] OR Guyana[tw] OR Haiti[tw] OR
34 Honduras[tw] OR Hungary[tw] OR India[tw] OR Maldives[tw] OR Indonesia[tw] OR Iran[tw] OR
35 Iraq[tw] OR Isle of Man[tw] OR Jamaica[tw] OR Jordan[tw] OR Kazakhstan[tw] OR Kazakh[tw] OR
36 Kenya[tw] OR Kiribati[tw] OR Korea[tw] OR Kosovo[tw] OR Kyrgyzstan[tw] OR Kirghizia[tw] OR Kyrgyz
37 Republic[tw] OR Kirghiz[tw] OR Kirgizstan[tw] OR "Lao PDR"[tw] OR Laos[tw] OR Latvia[tw] OR
38 Lebanon[tw] OR Lesotho[tw] OR Basutoland[tw] OR Liberia[tw] OR Libya[tw] OR Lithuania[tw]

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44 **#24** "developing country"[tw] OR "developing countries"[tw] OR "developing nation"[tw] OR
45 "developing nations"[tw] OR "developing population"[tw] OR "developing populations"[tw] OR
46 "developing world"[tw] OR "less developed country"[tw] OR "less developed countries"[tw] OR "less
47 developed nation"[tw] OR "less developed nations"[tw] OR "less developed population"[tw] OR "less
48 developed populations"[tw] OR "less developed world"[tw] OR "lesser developed country"[tw] OR
49 "lesser developed countries"[tw] OR "lesser developed nation"[tw] OR "lesser developed
50 nations"[tw] OR "lesser developed population"[tw] OR "lesser developed populations"[tw] OR "lesser
51 developed world"[tw] OR "under developed country"[tw] OR "under developed countries"[tw] OR
52 "under developed nation"[tw] OR "under developed nations"[tw] OR "under developed
53 population"[tw] OR "under developed populations"[tw] OR "under developed world"[tw] OR
54 "underdeveloped country"[tw] OR "underdeveloped countries"[tw] OR "underdeveloped nation"[tw]
55 OR "underdeveloped nations"[tw] OR "underdeveloped population"[tw] OR "underdeveloped
56 populations"[tw] OR "underdeveloped world"[tw] OR "middle income country"[tw] OR "middle
57 income countries"[tw] OR "middle income nation"[tw] OR "middle income nations"[tw] OR "middle
58 income population"[tw] OR "middle income populations"[tw] OR "low income country"[tw] OR "low
59
60

income countries"[tw] OR "low income nation"[tw] OR "low income nations"[tw] OR "low income population"[tw] OR "low income populations"[tw] OR "lower income country"[tw] OR "lower income countries"[tw] OR "lower income nation"[tw] OR "lower income nations"[tw] OR "lower income population"[tw] OR "lower income populations"[tw] OR "underserved country"[tw] OR "underserved countries"[tw] OR "underserved nation"[tw] OR "underserved nations"[tw] OR "underserved population"[tw] OR "underserved populations"[tw] OR "underserved world"[tw] OR "under served country"[tw] OR "under served countries"[tw] OR "under served nation"[tw] OR "under served nations"[tw] OR "under served population"[tw] OR "under served populations"[tw] OR "under served world"[tw] OR "deprived country"[tw] OR "deprived countries"[tw] OR "deprived nation"[tw] OR "deprived nations"[tw] OR "deprived population"[tw] OR "deprived populations"[tw] OR "deprived world"[tw] OR "poor country"[tw] OR "poor countries"[tw] OR "poor nation"[tw] OR "poor nations"[tw] OR "poor population"[tw] OR "poor populations"[tw] OR "poor world"[tw] OR "poorer country"[tw] OR "poorer countries"[tw] OR "poorer nation"[tw] OR "poorer nations"[tw] OR "poorer population"[tw] OR "poorer populations"[tw] OR "poorer world"[tw] OR "developing economy"[tw] OR "developing economies"[tw] OR "less developed economy"[tw] OR "less developed economies"[tw] OR "lesser developed economy"[tw] OR "lesser developed economies"[tw] OR "under developed economy"[tw] OR "under developed economies"[tw] OR "underdeveloped economy"[tw] OR "underdeveloped economies"[tw] OR "middle income economy"[tw] OR "middle income economies"[tw] OR "low income economy"[tw] OR "low income economies"[tw] OR "lower income economy"[tw] OR "lower income economies"[tw] OR "low gdp"[tw] OR "low gnp"[tw] OR "low gross domestic"[tw] OR "low gross national"[tw] OR "lower gdp"[tw] OR "lower gnp"[tw] OR "lower gross domestic"[tw] OR "lower gross national"[tw] OR lmic[tw] OR lmic[tw] OR "third world"[tw] OR "lami country"[tw] OR "lami countries"[tw] OR "transitional country"[tw] OR "transitional countries"[tw]

#25 #21 OR #22 OR #23 OR #24

#26 #20 AND #25

2. CENTRAL

#1 MeSH descriptor: [Hypertension] explode all trees

#2 hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic

#3 diabetes OR "diabetes mellitus"

#4 MeSH descriptor: [Diabetes Mellitus] explode all trees

#5 #1 OR #2 OR #3 OR #4

#6 dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR "low density lipoprotein" OR "high density lipoprotein" OR "low-density lipoprotein" OR "high-density lipoprotein"

#7 MeSH descriptor: [Dyslipidemias] explode all trees

#8 HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR "hiv infection" OR "hiv infections" OR "human immunodeficiency virus" OR "human immune deficiency virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus"

#9 (human immun*) AND (deficiency virus)

#10 "acquired immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-deficiency syndrome" OR "acquired immune-deficiency syndrome"

- 1
2 #11 (acquired immun*) AND (deficiency syndrome)
3
4 #12 HIVAIDS
5
6 #13 MeSH descriptor: [HIV Infections] explode all trees
7
8 #14 MeSH descriptor: [HIV] explode all trees
9
10 #15 tuberculosis OR tuberculoses OR tb
11
12 #16 MeSH descriptor: [Tuberculosis] explode all trees
13
14 #17 "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable
15 disease" OR "non-communicable diseases" OR NCD OR NCDs
16
17 #18 MeSH descriptor: [Noncommunicable Diseases] explode all trees
18
19 #19 comorbidity OR comorbidities OR comorbid OR co-morbid OR co-morbidity OR co-
20 morbidity OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity"
21
22 #20 MeSH descriptor: [Multimorbidity] explode all trees
23
24 #21 MeSH descriptor: [Comorbidity] explode all trees
25
26 #22 multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-
27 condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple
28 syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent
29 illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing
30 illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing
31 condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR
32 cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-
33 occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring
34 condition* OR co occurring condition* OR cooccurring condition*
35
36 #23 chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle"
37
38 #24 MeSH descriptor: [Multiple Chronic Conditions] explode all trees
39
40 #25 MeSH descriptor: [Chronic Disease] explode all trees
41
42 #26 #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
43 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
44
45 #27 MeSH descriptor: [Delivery of Health Care, Integrated] explode all trees
46
47 #28 "delivery of care" OR "delivery of health" OR "delivery of healthcare"
48
49 #29 MeSH descriptor: [Comprehensive Health Care] explode all trees
50
51 #30 "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health"
52
53 #31 MeSH descriptor: [Continuity of Patient Care] explode all trees 23230
54
55 #32 "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity
56 of healthcare"
57
58 #33 MeSH descriptor: [Patient-Centered Care] explode all trees
59
60 #34 "patient centered care" OR "patient centred care"
#35 MeSH descriptor: [Referral and Consultation] explode all trees

1
2 #36 referral AND consultation

3
4 #37 integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR
5 integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of
6 programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR
7 "integration of services" OR integrat* delivery OR integrat* management OR "integration of
8 management"

9
10 #38 coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of
11 services" OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR
12 "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR
13 coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat*
14 management OR "coordination of management"

15
16 #39 co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of
17 services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes"
18 OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service
19 delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-
20 ordinat* management OR "co-ordination of management"

21
22 #40 "horizontal care" OR "vertical care" OR "horizontal services" OR "vertical services" OR
23 "horizontal programmes" OR "horizontal programs" OR "vertical programmes" OR "vertical
24 programs" OR "horizontal service delivery" OR "vertical service delivery" OR "horizontal services" OR
25 "vertical services" OR "horizontal delivery" OR "vertical management" OR "vertical management"

26
27 #41 "multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR
28 "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR
29 "multi delivery" OR multidelivery OR "multi management"

30
31 #42 #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR
32 #39 OR #40 OR #41

33
34 #43 #5 AND #26 AND #42

35
36 #44 (Africa or Asia or Caribbean or "West Indies" or "South America" or "Latin America" or
37 "Central America")

38
39 #45 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia
40 or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
41 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
42 Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or "Burkina
43 Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or
44 Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or
45 Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or
46 Congo or "Republic of Congo" or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or
47 Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic")

48
49 #46 (Djibouti or "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or
50 "East Timur" or "Timor Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or
51 Eritrea or Estonia or Ethiopia or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia
52 or Georgian or Ghana or "Gold Coast" or Greece or Grenada or Guatemala or Guinea or Guam or
53 Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or
54 "Isle of Man" or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or

1
2 Kyrgyzstan or Kirghizia or "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or
3 Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania)
4

5 #47 (Macedonia or Madagascar or "Malagasy Republic" or Malaysia or Malaya or Malay or Sabah
6 or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius
7 or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldavia or Moldovan
8 or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or
9 Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or
10 "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or
11 Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or
12 "Puerto Rico")
13
14

15 #48 (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts"
16 or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or
17 Samoa or "Samoa Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi
18 Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka"
19 or Ceylon or "Solomon Islands" or Somalia or Sudan or South-sudan or Suriname or Surinam or
20 Swaziland or Syria or Tajikistan or TadzhiKistan or Tadjikistan or Tadjhik or Tanzania or Thailand or
21 Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or
22 Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist
23 Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet
24 Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia)
25
26
27

28 #49 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle
29 income" or low* NEXT income or underserved or "under served" or deprived or poor*) NEXT
30 (countr* or nation* or population* or world)
31

32 #50 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle
33 income" or low* NEXT income) NEXT (economy or economies)
34

35 #51 low* NEXT (gdp or gnp or "gross domestic" or "gross national")
36

37 #52 (low NEAR/3 middle NEAR/3 countr*)
38

39 #53 (Imic or Imics or "third world" or "lami country" or "lami countries")
40

41 #54 ("transitional country" or "transitional countries")
42

43 #55 #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54
44

45 #56 #43 AND #55
46

47 3. Embase

48
49 1 integrated health care system/ or integrated health care.mp.
50

51 2 *patient care/
52

53 3 ("comprehensive healthcare" or "comprehensive care" or "Continuity of Patient Care" or
54 "continuity of care" or "continuity of healthcare" or "Patient-Centered Care").ti.
55

56 4 ("comprehensive healthcare" or "comprehensive care" or "Continuity of Patient Care" or
57 "continuity of care" or "continuity of healthcare" or "Patient-Centered Care").ab.
58

59 5 (referral and consultation).mp.
60

- 1
2 6 ((integrated or integration) adj2 (care or services or program* or delivery or management)).ab.
3
4 7 ((integrated or integration) adj2 (care or services or program* or delivery or management)).ti.
5
6 8 ((coordination or coordinated) adj2 (care or services or program* or delivery or management)).ti.
7
8 9 ((coordination or coordinated) adj2 (care or services or program* or delivery or
9 management)).ab.
10
11 10 ((horizontal or vertical) adj2 (care or services or program* or delivery or management)).ab.
12
13 11 ((horizontal or vertical) adj2 (care or services or program* or delivery or management)).ti.
14
15 12 (Multiteam or multi-team or multi-care or multicare or multiclinic or multiservice or multi-
16 program* or multidelivery or multi-management).ti. or (Multiteam or multi-team or multi-care or
17 multicare or multiclinic or multiservice or multi-program* or multidelivery or multi-management).ab.
18
19 13 *health care delivery/
20
21 14 (delivery adj2 healthcare).mp.
22
23 15 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
24
25 16 hypertension.mp. or *hypertension/
26
27 17 (hypertension or hypertention or "blood pressure" or "arterial pressure" or systolic or
28 diastolic).ti. or (hypertension or hypertention or "blood pressure" or "arterial pressure" or systolic or
29 diastolic).ab.
30
31 18 diabetes.mp. or diabetes mellitus/
32
33 19 exp Neoplasms/
34
35 20 cardiovascular disease/
36
37 21 "heart disease".ti. or "heart disease*".ab.
38
39 22 *kidney disease/
40
41 23 ("kidney failure" or "renal failure" or "chronic kidney disease" or "renal disease").ti. or ("kidney
42 failure" or "renal failure" or "chronic kidney disease" or "renal disease").ab.
43
44 24 (dyslipidaemia or dyslipidemia or cholesterol or LDL or HDL or triglyceride or triglycerides or low
45 density lipoprotein or high density lipoprotein or low-density lipoprotein or high-density
46 lipoprotein).ti. or (dyslipidaemia or dyslipidemia or cholesterol or LDL or HDL or triglyceride or
47 triglycerides or low density lipoprotein or high density lipoprotein or low-density lipoprotein or high-
48 density lipoprotein).ab.
49
50 25 HIV infection.mp. or Human immunodeficiency virus infection/
51
52 26 tuberculosis/
53
54 27 non-communicable diseases.mp. or non communicable disease/
55
56 28 comorbidity.mp. or comorbidity/
57
58 29 multimorbidity.mp. or multiple chronic conditions/
59
60 30 (multi-disease* or multidisease* or multi disease* or multiple condition* or multi-condition* or
multi condition* or multiple illness* or multi-illness* or multi illness* or multiple syndrome* or
multi-syndrome* or multi syndrome* or concurrent condition* or concurrent illness* or concurrent

1
2 disease* or co-existing disease* or coexisting disease* or co-existing illness* or coexisting illness* or
3 co-existing syndrome* or coexisting syndrome* or co-existing condition* or coexisting condition* or
4 co-occurring disease* or co occurring disease* or cooccurring disease* or co-occurring illness* or co
5 occurring illness* or cooccurring illness* or co-occurring syndrome* or co occurring syndrome* or
6 cooccurring syndrome* or co-occurring condition* or co occurring condition* or cooccurring
7 condition*).ti.

8
9
10 31 (multi-disease* or multidisease* or multi disease* or multiple condition* or multi-condition* or
11 multi condition* or multiple illness* or multi-illness* or multi illness* or multiple syndrome* or
12 multi-syndrome* or multi syndrome* or concurrent condition* or concurrent illness* or concurrent
13 disease* or co-existing disease* or coexisting disease* or co-existing illness* or coexisting illness* or
14 co-existing syndrome* or coexisting syndrome* or co-existing condition* or coexisting condition* or
15 co-occurring disease* or co occurring disease* or cooccurring disease* or co-occurring illness* or co
16 occurring illness* or cooccurring illness* or co-occurring syndrome* or co occurring syndrome* or
17 cooccurring syndrome* or co-occurring condition* or co occurring condition* or cooccurring
18 condition*).ab.

19
20
21 32 (chronic disease* or lifestyle disease*).mp.

22
23 33 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32

24
25 34 15 and 33

26
27 35 developing countries.mp. or developing country/

28
29 36 (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central
30 America).mp.

31
32 37 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or
33 Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
34 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
35 Herzegovina or Hercegovina or Botswana or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or
36 Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or
37 Camerons or Cameroon or Camerons or Cape Verde or Central African Republic or Chad or Chile or
38 China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa
39 Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Czechoslovakia or Czech Republic
40 or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or
41 East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or
42 Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia
43 Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea
44 or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or
45 Iran or Iraq or Isle of Man or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea
46 or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or
47 Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or
48 Madagascar or Malagasy Republic or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or
49 Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or
50 Mexico or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia or
51 Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or
52 Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern
53 Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru
54 or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Puerto Rico or
55 Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts
56 or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan
57
58
59
60

1
2 Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia or
3 Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or
4 Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadjhikistan or
5 Tadjikistan or Tadjhik or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or
6 Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR
7 or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New
8 Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or
9 Zimbabwe or Rhodesia).mp.
10
11

12 38 ((developing or less* developed or under developed or underdeveloped or middle income or
13 low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or
14 population? or world)).ab.
15

16 39 ((developing or less* developed or under developed or underdeveloped or middle income or
17 low* income) adj (economy or economies)).ab. or ((developing or less* developed or under
18 developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti.
19

20 40 ((developing or less* developed or under developed or underdeveloped or middle income or
21 low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or
22 population? or world)).ti.
23
24

25 41 (low* adj (gdp or gnp or gross domestic or gross national)).ti. or (low* adj (gdp or gnp or gross
26 domestic or gross national)).ab.
27

28 42 (low adj3 middle adj3 countr*).ti. or (low adj3 middle adj3 countr*).ab.
29

30 43 (Imic or Imics or third world or lami countr*).ti. or (Imic or Imics or third world or lami
31 countr*).ab.
32

33 44 transitional countr*.ti. or transitional countr*.ab.
34

35 45 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44
36

37 46 34 and 45
38

39 4. Web of Science (Core collection) 40

41
42 TOPIC: (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR
43 diastolic OR diabetes OR "diabetes mellitus") AND TOPIC: (dyslipidaemia OR dyslipidemia OR
44 cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high
45 density lipoprotein OR low-density lipoprotein OR high-density lipoprotein OR HIV OR hiv-1 OR hiv-2*
46 OR hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency
47 virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired
48 immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-
49 deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS OR tuberculosis OR
50 tuberculoses OR tb OR "noncommunicable disease" OR "noncommunicable diseases" OR "non-
51 communicable disease" OR "non-communicable diseases" OR NCD OR NCDs OR comorbid* OR co-
52 morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity" OR multi-
53 disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi
54 condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-
55 syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent
56 disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness*
57 OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting
58 condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-
59
60

1
2 occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co
3 occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring
4 condition* OR cooccurring condition* OR chronic disease* OR lifestyle disease* OR "diseases of
5 lifestyle" OR "disease of lifestyle" OR "Multiple Chronic Conditions") AND TOPIC: ("delivery of care"
6 OR "delivery of health" OR "delivery of healthcare" OR "Comprehensive Health Care" OR
7 "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "Continuity of
8 Patient Care" OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR
9 "continuity of healthcare" OR "Patient-Centered Care" OR "patient centered care" OR "patient
10 centred care" OR "Referral and Consultation" OR integrat* care OR "integration of care" OR integrat*
11 services OR "integration of services" OR integrat* programmes OR integrat* programs OR
12 "integration of programmes" OR "integration of programs" OR integrat* service delivery OR
13 "integration of service delivery" OR integrat* services OR "integration of services" OR integrat*
14 delivery OR integrat* management OR "integration of management" OR coordinat* care OR
15 "coordination of care" OR coordinat* services OR "coordination of services" OR coordinat*
16 programmes OR coordinat* programs OR "coordination of programmes" OR "coordination of
17 programs" OR coordinat* service delivery OR "coordination of service delivery" OR coordinat*
18 services OR "coordination of services" OR coordinat* delivery OR coordinat* management OR
19 "coordination of management" OR co-ordinat* care OR "co-ordination of care" OR co-ordinat*
20 services OR "co-ordination of services" OR co-ordinat* programmes OR co-ordinat* programs OR
21 "co-ordination of programmes" OR "co-ordination of programs" OR co-ordinat* service delivery OR
22 "co-ordination of service delivery" OR co-ordinat* services OR "co-ordination of services" OR co-
23 ordinat* delivery OR co-ordinat* management OR "co-ordination of management" OR horizontal
24 care OR vertical care OR horizontal services OR vertical services OR horizontal programmes OR
25 horizontal programs OR vertical programmes OR vertical programs OR horizontal service delivery OR
26 vertical service delivery OR horizontal services OR vertical services OR horizontal delivery OR vertical
27 management OR vertical management OR "multi team" OR multiteam "multi care" OR multicare OR
28 "multi clinic" OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram
29 OR "multi programme" OR "multi delivery" OR multidelivery OR "multi management") AND TOPIC:
30 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or
31 Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
32 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
33 Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or "Burkina
34 Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or
35 Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or
36 Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or
37 Congo or "Republic of Congo" or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or
38 Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic" OR Djibouti or
39 "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or "East Timur" or "Timor
40 Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or Eritrea or Estonia or Ethiopia
41 or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia or Georgian or Ghana or "Gold
42 Coast" or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or
43 Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or "Isle of Man" or Jamaica or
44 Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or
45 "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or Lebanon or Lesotho or
46 Basutoland or Liberia or Libya or Lithuania OR Macedonia or Madagascar or "Malagasy Republic" or
47 Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or
48 "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or
49 "Middle East" or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni
50 or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or
51 "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat

1
2 or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or
3 Phillipines or Phillippines or Poland or Portugal or "Puerto Rico" OR Romania or Rumania or
4 Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint
5 Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoa Islands" or
6 "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or
7 Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands"
8 or Somalia or Sudan or South-Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or
9 Tadhikistan or Tadjikistan or Tadhik or Tanzania or Thailand or Togo or "Togolese Republic" or
10 Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine
11 or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek
12 or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or
13 Yugoslavia or Zambia or Zimbabwe or Rhodesia OR "developing country" OR "gross domestic" OR
14 "gross national" OR "low income" OR "low-income" OR "middle income" OR "middle-income" OR
15 LMIC OR LMICs OR "transitional country" OR "transitional countries" OR "third world" OR "lami
16 country" OR "lami countries" OR "under developed" OR underdeveloped OR under-developed)

21 5. CINAHL

22
23
24 **S1** MW hypertension OR ((hypertension OR hypertention OR "blood pressure" OR "arterial pressure"
25 OR systolic OR diastolic)) OR ((diabetes OR "diabetes mellitus")) OR MW "Diabetes Mellitus"
26 [320,859]

27
28
29 **S2** ((dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides
30 OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density
31 lipoprotein)) OR MW Dyslipidemias OR MW HIV OR MW HIV infections OR ((HIV OR hiv-1 OR hiv-2*
32 OR hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency
33 virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired
34 immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-
35 deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS)) OR ((tuberculosis
36 OR tuberculoses OR tb)) OR MW tuberculosis OR (("noncommunicable disease" OR
37 "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR
38 NCD OR NCDs)) OR MW "noncommunicable diseases" OR ((comorbid* OR co-morbid* OR "co
39 morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity")) OR MW multimorbidity OR
40 MW comorbidity [282,133]

41
42
43
44 **S3** ((multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition*
45 OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome*
46 OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR
47 concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR
48 coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR
49 coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR
50 co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR
51 co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring
52 condition* OR cooccurring condition*)) OR ((chronic disease* OR lifestyle disease* OR "diseases of
53 lifestyle" OR "disease of lifestyle")) OR MW "Multiple Chronic Conditions" OR MW "Chronic Disease"
54 [141,677]

55
56
57 **S4** S2 OR S3 [399,117]

58
59 **S5** MW "Delivery of Health Care, Integrated" OR MW "Comprehensive Health Care" OR MW
60 "Continuity of Patient Care" OR MW "Patient-Centered Care" [38488]

S6 (("delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "patient centered care" OR "patient centred care") OR ((referral AND consultation)) OR MW ("Referral and Consultation") OR ((integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR "integration of services" OR integrat* delivery OR integrat* management OR "integration of management")) OR ((coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of services" OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat* management OR "coordination of management")) OR ((co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes" OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-ordinat* management OR "co-ordination of management")) OR ((horizontal care OR vertical care OR horizontal services OR vertical services OR horizontal programmes OR horizontal programs OR vertical programmes OR vertical programs OR horizontal service delivery OR vertical service delivery OR horizontal services OR vertical services OR horizontal delivery OR vertical management OR vertical management)) OR (("multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR "multi delivery" OR multidelivery OR "multi management")) [145,695]

S7 S5 OR S6 [145,695]

S8 "((developing country" OR "gross domestic" OR "gross national" OR "low income" OR "low-income" OR "middle income" OR "middle-income" OR LMIC OR LMICs OR "transitional country" OR "transitional countries" OR "third world" OR "lami country" OR "lami countries" OR "under developed" OR underdeveloped OR under-developed)) OR ("low- and middle-income") OR ("low and middle income")" [32,715]

S9 S1 AND S4 AND S7 AND S8 [71]

S10 PY 2019 [381,913]

S11 PY 2018 [419,274]

S12 S10 OR S11 [801,187]

S13 S9 AND S12 [17]

6. Africa-Wide Information (via EBSCO host)

S1 SM hypertension OR (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)) OR ((diabetes OR "diabetes mellitus") OR SM "Diabetes Mellitus"

1
2 **S2** (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR
3 low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density
4 lipoprotein) OR SM Dyslipidemias OR SM HIV OR SM HIV infections OR (HIV OR hiv-1 OR hiv-2* OR
5 hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency
6 virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired
7 immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-
8 deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS) OR (tuberculosis
9 OR tuberculoses OR tb) OR SM tuberculosis OR ("noncommunicable disease" OR
10 "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR
11 NCD OR NCDs) OR SM "noncommunicable diseases" OR (comorbid* OR co-morbid* OR "co
12 morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity") OR SM multimorbidity OR SM
13 comorbidity

14
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17 **S3** (multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition*
18 OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome*
19 OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR
20 concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR
21 coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR
22 coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR
23 co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR
24 co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring
25 condition* OR cooccurring condition*) OR (chronic disease* OR lifestyle disease* OR "diseases of
26 lifestyle" OR "disease of lifestyle") OR SM "Multiple Chronic Conditions" OR SM "Chronic Disease"

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30 **S4** S2 OR S3

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32 **S5** AB "Delivery of Health Care, Integrated" OR AB "Comprehensive Health Care" OR AB "Continuity
33 of Patient Care" OR AB "Patient-Centered Care"

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35 **S6** ("delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "comprehensive
36 healthcare" OR "comprehensive care" OR "comprehensive health" OR "continuity of patient care" OR
37 "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "patient centered
38 care" OR "patient centred care") OR ((referral AND consultation)) OR SM ("Referral and
39 Consultation") OR (integrat* care OR "integration of care" OR integrat* services OR "integration of
40 services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR
41 "integration of programs" OR integrat* service delivery OR "integration of service delivery" OR
42 integrat* services OR "integration of services" OR integrat* delivery OR integrat* management OR
43 "integration of management") OR (coordinat* care OR "coordination of care" OR coordinat*
44 services OR "coordination of services" OR coordinat* programmes OR coordinat* programs OR
45 "coordination of programmes" OR "coordination of programs" OR coordinat* service delivery OR
46 "coordination of service delivery" OR coordinat* services OR "coordination of services" OR
47 coordinat* delivery OR coordinat* management OR "coordination of management") OR (co-
48 ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of services" OR
49 co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes" OR "co-
50 ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service delivery" OR
51 co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-ordinat*
52 management OR "co-ordination of management") OR (horizontal care OR vertical care OR
53 horizontal services OR vertical services OR horizontal programmes OR horizontal programs OR
54 vertical programmes OR vertical programs OR horizontal service delivery OR vertical service delivery
55 OR horizontal services OR vertical services OR horizontal delivery OR vertical management OR
56 vertical management) OR (("multi team" OR multiteam "multi care" OR multicare OR "multi clinic"

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2 OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi
3 programme" OR "multi delivery" OR multidelivery OR "multi management")
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5 **S7** S5 OR S6
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7 **S8** "(developing country" OR "gross domestic" OR "gross national" OR "low income" OR "low-
8 income" OR "middle income" OR "middle-income" OR LMIC OR LMICs OR "transitional country" OR
9 "transitional countries" OR "third world" OR "lami country" OR "lami countries" OR "under
10 developed" OR underdeveloped OR under-developed) OR ("low- and middle-income") OR ("low
11 and middle income")"
12

13 **S9** S1 AND S4 AND S7 AND S8
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15 7. LILACS

16 (Words: hypertension OR "high blood pressure" OR systolic OR diastolic OR diabetes) AND
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18 (Words: dyslipidemia OR cholesterol OR HIV OR tuberculosis OR multimorbidity OR comorbidity OR
19 non-communicable disease) AND
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21 (Words: LMIC OR low income OR middle income OR low-income OR middle-income OR developing
22 country OR developing countries)
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Supplementary file 2: List of excluded studies and reasons for exclusion

Studies excluded for wrong population	Studies excluded for wrong study design	Studies excluded for wrong intervention
Abrahams-Gessel 2018 ¹ Adomaviciute 2014 ² Alharbi 2014 ³ Miao 2016 ⁴ Myers 2018 ⁵ Rakic 2011 ⁶ Sarrafzadegan 2006 ⁷ Spaak 2017 ⁸	Ajay 2016 ⁹ Al Asmary 2013 ¹⁰ Garrib 2018 ¹¹ Germe 2017 ¹² Kwarisiima 2019 ¹³ Li 2013 ¹⁴ Mahomed 2014 ¹⁵ Narayanan 2012 ¹⁶ Nigatu 2012 ¹⁷ Nyabera 2011 ¹⁸ Patel 2018 ¹⁹ Patel 2015 ²⁰ Rabkin 2018 ²¹ Samb 2010 ²² Sarraf-Zadegan 2003 ²³ Sushilkumar 2015 ²⁴ Tedjokusumo 2003 ²⁵ Tiam 2012 ²⁶ Wasay 2009 ²⁷	Bachmann 2018 ²⁸ Hong 2013 ²⁹ Kowalski 2017 ³⁰ McKee 2011 ³¹ Mendis 2010 ³² Pibernik-Okanovic 2015 ³³ Saleh 2018 ³⁴ Sarrafzadegan 2009 ³⁵ Tourkmani 2018 ³⁶ Wenxi 2017 ³⁷

1. Abrahams-Gessel S, Beratarrechea A, Irazola V, et al. Using mHealth tools to improve access, coverage and treatment of uninsured people with high cardiovascular disease risk in Argentina: a study protocol for a pragmatic cluster randomised trial. *BMJ innovations* 2018;4(3):135-41. doi: 10.1136/bmjinnov-2017-000255
2. Adomaviciute S, Watt H, Soljak M, et al. Impact of the Integrated Care Pilot on HbA1c, cholesterol and systolic blood pressure levels in patients with diabetes. *Diabetic Medicine* 2014;31(SUPPL. 1):175. doi: <http://dx.doi.org/10.1111/dme.12378>
3. Alharbi TJ, Tourkmani A, Alkhashan H, et al. Impact of integrated care program on glycemic control and cardiovascular risk in patients with type 2 diabetes; Interventional controlled study. *Diabetes Research and Clinical Practice* 2014;106(SUPPL. 1):S93-S94.
4. Miao Y, Zhang L, Sparring V, et al. Improving health related quality of life among rural hypertensive patients through the integrative strategy of health services delivery: A quasi-experimental trial from Chongqing, China. *International Journal for Equity in Health* 2016;15(1):132. doi: <http://dx.doi.org/10.1186/s12939-016-0421-x>
5. Myers B, Lund C, Lombard C, et al. Comparing dedicated and designated models of integrating mental health into chronic disease care: study protocol for a cluster randomized controlled trial. *Trials* 2018;19(1) (no pagination) doi: 10.1186/s13063-018-2568-9
6. Rakic D, Jakovljevic D. [Integrated approach to prevention and control of cardiovascular diseases]. *Srpski arhiv za celokupno lekarstvo* 2011;139(5-6):304-10.
7. Sarrafzadegan N, Baghaei A, Sadri G, et al. Isfahan healthy heart program: Evaluation of comprehensive, community-based interventions for non-communicable disease prevention. *Prevention and Control* 2006;2(2):73-84. doi: <http://dx.doi.org/10.1016/j.precon.2006.10.003>

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8. Spaak J, Brommels M, Kahan T, et al. Integrated, Multidisciplinary, Person-centered Care for Patients With Complex Comorbidities: Heart, Kidney and Diabetes, 2017.
9. Ajay VS, Jindal D, Roy A, et al. Development of a Smartphone-Enabled Hypertension and Diabetes Mellitus Management Package to Facilitate Evidence-Based Care Delivery in Primary Healthcare Facilities in India: The mPower Heart Project. *Journal of the American Heart Association* 2016;5(12) doi: 10.1161/jaha.116.004343
10. Al Asmary SM, Al-Harbi T, Tourkmani AM, et al. Impact of integrated care program on glycemic control and cardiovascular risk in adult patients with type 2 diabetes. *Journal of Clinical Outcomes Management* 2013;20(8):356-63.
11. Garrib A, Birungi J, Lesikari S, et al. Integrated care for human immunodeficiency virus, diabetes and hypertension in Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2018 doi: 10.1093/trstmh/try098
12. Germe M, Zingwari J, Matji R, et al. Baseline assessment of high volume facility capacity to provide integrated tuberculosis (TB) and diabetes (DM) services in South Africa. *Diabetes* 2017;66(Supplement 1):A460-A61.
13. Kwarisiima D, Atukunda M, Owaraganise A, et al. Hypertension control in integrated HIV and chronic disease clinics in Uganda in the SEARCH study. *BMC Public Health* 2019;19(1):511. doi: 10.1186/s12889-019-6838-6 [published Online First: 2019/05/08]
14. Li Q, Li L, Fan XL, et al. The values of evidence-based comprehensive care for patients with type 2 diabetes mellitus and cardiovascular diseases to improve the quality of life. *Heart* 2013;99(SUPPL. 3):A282-A83. doi: <http://dx.doi.org/10.1136/heartjnl-2013-304613.797>
15. Mahomed OH, Asmall S, Freeman M. An integrated chronic disease management model: a diagonal approach to health system strengthening in South Africa. *Journal of health care for the poor and underserved* 2014;25(4):1723-29. doi: <http://dx.doi.org/10.1353/hpu.2014.0176>
16. Narayanan G, Prabhakaran D. Integrating mental health into cardiovascular disease research in India. *National Medical Journal of India* 2012;25(5):274-80.
17. Nigatu T. Integration of HIV and noncommunicable diseases in health care delivery in low- and middle-income countries. *Preventing chronic disease* 2012;9:E93.
18. Nyabera RA, Yonga G, Mwangemi F, et al. Evaluation of a project integrating cardiovascular care into HIV programmes. *Cardiovascular Journal of Africa* 2011;22(3 SUPPL. 1):S17.
19. Patel P, Speight C, Maida A, et al. Integrating HIV and hypertension management in low-resource settings: Lessons from Malawi. *PLoS medicine* 2018;15(3):e1002523. doi: 10.1371/journal.pmed.1002523
20. Patel V, Chatterji S. Integrating Mental Health In Care For Noncommunicable Diseases: An Imperative For Person-Centered Care. *Health affairs (Project Hope)* 2015;34(9):1498-505. doi: 10.1377/hlthaff.2015.0791
21. Rabkin M, Palma A, McNairy ML, et al. Integrating cardiovascular disease risk factor screening into HIV services in Swaziland: lessons from an implementation science study. *Aids* 2018;32:S43-S46. doi: 10.1097/qad.0000000000001889
22. Samb B, Desai N, Nishtar S, et al. Chronic Diseases: Chronic Diseases and Development 4 Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries. *Lancet* 2010;376(9754):1785-97. doi: 10.1016/s0140-6736(10)61353-0
23. Sarraf-Zadegan N, Sadri G, Malek Afzali H, et al. Isfahan Healthy Heart Programme: a comprehensive integrated community-based programme for cardiovascular disease prevention and control. Design, methods and initial experience. *Acta cardiologica* 2003;58(4):309-20. doi: 10.2143/ac.58.4.2005288
24. Sushilkumar PL, Mahendrakumar BJ, Suman B, et al. Implementation and evaluation of health screening services to diabetic and hypertensive patients in a selected community pharmacy at belgaum city. *Asian Journal of Pharmaceutical and Clinical Research* 2015;8(3):305-15.
25. Tedjokusumo R. Introducing the integrated cardiovascular services at Dr. Hasan Sadikini Hospital. *Heart Lung and Circulation* 2003;12(SUPPL. 2):S82-384. doi: <http://dx.doi.org/10.1046/j.1443-9506.2003.t01-4-x>

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26. Tiam A, Oyebanji O, Nkonyana J, et al. Family health days: An innovative approach to providing integrated health services for HIV and non-communicable diseases among adults and children in hard-to-reach areas of Lesotho. *Journal of the International AIDS Society* 2012;15(SUPPL. 3):236. doi: <http://dx.doi.org/org/10.7448/IAS.15.5.18438>
27. Wasay M, Jabbar A. Fight against chronic diseases (high blood pressure, stroke, diabetes and cancer) in Pakistan; cost-effective interventions. *JPMA The Journal of the Pakistan Medical Association* 2009;59(4):196-7.
28. Bachmann MO, Bateman ED, Stelmach R, et al. Integrating primary care of chronic respiratory disease, cardiovascular disease and diabetes in Brazil: Practical Approach to Care Kit (PACK Brazil): study protocol for randomised controlled trials. *Journal of Thoracic Disease* 2018;10(7):4667-77.
29. Hong T. Web-Based Collaborative Care for Patients With Diabetes and Depression. <https://clinicaltrials.gov/show/nct01985711> 2013
30. Kowalski AJ, Poongothai S, Chwastiak L, et al. The INtegrating DEPrEssioN and Diabetes treatMENt (INDEPENDENT) study: Design and methods to address mental healthcare gaps in India. *Contemporary clinical trials* 2017;60:113-24. doi: 10.1016/j.cct.2017.06.013
31. McKee MD, Fletcher J, Sigal I, et al. A collaborative approach to control hypertension in diabetes: outcomes of a pilot intervention. *Journal of primary care & community health* 2011;2(3):148-52. doi: 10.1177/2150131911401028
32. Mendis S, Johnston SC, Fan W, et al. Cardiovascular risk management and its impact on hypertension control in primary care in low-resource settings: a cluster-randomized trial. *Bulletin of the World Health Organization* 2010;88(6):412-9. doi: 10.2471/blt.08.062364
33. Pibernik-Okanovic M, Hermanns N, Ajdukovic D, et al. Does treatment of subsyndromal depression improve depression-related and diabetes-related outcomes? A randomised controlled comparison of psychoeducation, physical exercise and enhanced treatment as usual. *Trials* 2015;16:305. doi: 10.1186/s13063-015-0833-8
34. Saleh S, Farah A, Dimassi H, et al. Using Mobile Health to Enhance Outcomes of Noncommunicable Diseases Care in Rural Settings and Refugee Camps: Randomized Controlled Trial. *JMIR mHealth and uHealth* 2018;6(7):e137. doi: 10.2196/mhealth.8146
35. Sarrafzadegan N, Kelishadi R, Esmailzadeh A, et al. Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran. *Bull World Health Organ* 2009;87(1):39-50. doi: 10.2471/blt.07.049841
36. Tourkmani AM, Abdelhay O, Alkhashan HI, et al. Impact of an integrated care program on glycemic control and cardiovascular risk factors in patients with type 2 diabetes in Saudi Arabia: an interventional parallel-group controlled study. *BMC Fam Pract* 2018;19:10. doi: 10.1186/s12875-017-0677-2
37. Wenxi T, Yan Z, Liang Z. Effects of provider incentives in integrated healthcare delivery system reform: a quasiexperiment on patients with chronic diseases in rural China. *International Journal of Integrated Care (IJIC)* 2017;17(3):171-72. doi: 10.5334/ijic.3207

Supplementary file 3: Summary of interventions according to the TIDiER checklist: Integrated models of care

Study ID	Ameh 2017		Rawat 2018*	Havlir 2019	
Intervention groups	Intervention	Control	Intervention	Intervention	Control
Name of intervention	Integrated chronic disease management (ICDM) model	Standard care in clinics where ICDM model was not piloted	Implementation of national policy to integrate HIV care into all PHC facilities	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and patient-centered care	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care
Aim of the intervention	To improve management of patients with HIV, TB, hypertension, diabetes, COPD, asthma, epilepsy and mental health conditions at PHCs	Not reported	To provide comprehensive HIV care (prevention, diagnosis, treatment initiation and follow-up) at PHC facilities	To remove patient-level barriers and maximise the efficiency of the health system To overcome barriers of universal access to HIV treatment and to be able to reach UNAIDS goals	Not reported
Physical and informational materials used	Not reported	Not reported	Not reported	Treatment guidelines ART tablets SMS reminders	National treatment guidelines
Procedures, activities and processes used in the intervention	Facility reorganisation: designated chronic care area; supply of critical	Not reported	Policy to integrate HIV care into PHC clinics	Community health campaigns (CHCs): Multi-disease testing for HIV, diabetes and	Community health campaigns: Multi-disease testing for HIV, diabetes and hypertension;

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	<p>medicines; pre-packaging of medication</p> <p>Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral</p> <p>Ward-based outreach teams to ensure individual responsibility and “assisted” self-management</p> <p>Health promotion and population screening</p>		<p>Training of nurses in comprehensive management of HIV: Nurse initiated Management of ART (NIMART)</p> <p>Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)</p> <p>Additional staff to strengthen drug delivery systems</p>	<p>hypertension; counselling and clinic appointments for participants with positive tests; HIV positive participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>Home-based testing for participants that did not attend CHCs</p> <p>Linkage to ART: HIV positive participants not on ART received appointments to initiate ART within a maximum of 7 days; clinic staff introduced themselves in person or by mobile phone; participants could contact hotline via phone or text message for questions or support; phone/SMS reminders about clinic visits</p> <p>Patient-centered care for HIV, diabetes, hypertension: 3-month</p>	<p>counselling and clinic appointments for participants with positive tests; HIV positive participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>ART, diabetes and hypertension treatment: provided in accordance with national guidelines</p>
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				visit intervals; flexible clinic hours; reduced waiting time at clinics; welcoming staff; ART to all HIV positive participants; if not eligible for ART according to national guidelines, trial provided Tuvada; hypertension and diabetes treated according to standard algorithms	
Who provided the intervention	Nurses	Nurses	Nurses	CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya Patient-centered care: government clinics augmented by trial staff	CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya Care in clinics: Clinic staff, augmented by additional staff funded by trial to mitigate staff shortages
Modes of delivery	Not reported	Not reported	Practical implementation of policy varied across clinics: Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for	Face-to-face, via telephone or text message	Face-to-face

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			all diseases in single consultation room		
Location of the intervention	Primary healthcare facilities	Primary healthcare facilities	Primary healthcare clinics: 37 urban clinics 65 rural clinics 30 clinics from former homeland	CHCs: Under large tents in all communities, or home-based Patient-centered care: At clinics	CHC: Under large tents in all communities, or home-based ART, diabetes, hypertension care: At clinics
When and how much the intervention was delivered	Unstable HIV and hypertension patients: follow-up every month Stable HIV and hypertension patients: follow-up every 2-3 months Routine referral of all patients to doctor: Every 6 months	Not reported	Not reported	CHCs: lasted 2 weeks at baseline, annually and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: 3-month intervals	CHCs: lasted 2 weeks at baseline and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: not reported
Tailoring of the intervention	Not reported	Not reported	Modular structures and pharmacy renovations to address space concerns in some clinics	Not reported	Not reported
Modifications of the intervention	Not reported	Not reported	Not reported	The end point of the trial was reduced from 5 years to 3 years	Control clinics implemented ART guidelines that were specific to Uganda and Kenya; during the trial, the threshold for eligibility for ART in these

					countries expanded from a specific CD4+ T-cell count (ranging from <350 to <500) to universal treatment (regardless of CD4+ T-cell count)
Assessment of intervention adherence/fidelity	Not reported	Not reported	Not reported	Not reported	Not reported
Intervention delivered as planned	Not reported	Not reported	Not reported	Not reported	Not reported

*No control intervention described

HIV human immunodeficiency virus, TB tuberculosis, COPD chronic obstructive pulmonary disease, PHC primary healthcare clinics

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Supplementary file 4: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated management of care

Study ID	Fairall 2016		Prabhakaran 2018	
Intervention groups	Intervention	Control	Intervention	Control
Name of intervention	Primary Care (PC) 101	Usual care in for non-communicable and communicable diseases: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS)	mWellcare	Enhanced usual care
Aim of the intervention	To provide comprehensive care for all symptoms, including NCDs, HIV, TB, mental health conditions, women's health	To provide a user-friendly management tool that integrates and harmonises disease-specific guidelines and presents them in a simple format, aligned with patient presentation in primary health care settings, expanded nurses' scope of practice and prescribing (not covering all NCDs)	To facilitate integrated management of hypertension, diabetes, comorbid depression, and alcohol and tobacco use	Not reported
Physical and informational materials used	PC 101 guideline: a 101-page clinical management tool in form of a ring-bound, colour illustrated booklet	Latest version (2011/2012) of PALSA PLUS: clinical management tool	mWellcare system: m-Health-based electronic decision-support system that generates recommendations based on patient profile and risk level used on Android tablet	Nurses received a tablet to collect baseline data (without the mWellcare system) Visible charts on the management of the conditions

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	Desk pads with key messages for priority conditions to facilitate booking of follow-up appointments		Visible charts on the management of the conditions Pamphlets containing lifestyle advice	Pamphlets containing lifestyle advice
Procedures, activities and processes used in the intervention	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Expanded prescribing provisions for nurses</p> <p>Letters and SMS reminders of follow-up visits</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of physicians on current clinical management guidelines and orientation to mWellcare system</p> <p>Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use</p> <p>Onsite supervision and support</p> <p>SMS reminders of follow-up visits and medication adherence</p>	<p>Training of physicians on clinical management guidelines for hypertension and diabetes</p> <p>Training of NCD nurses in management of hypertension and diabetes mellitus</p>
Who provided the intervention	<p>Training of facility trainers: Experienced adult education practitioner with a background in nursing, family physician who lead the expansion of the clinical management tool</p> <p>Educational outreach sessions: Nurse trainers</p>	<p>Training of facility trainers: not reported</p> <p>Educational outreach sessions: Nurse trainers</p> <p>Care: Nurses</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>

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	Care: Nurses			
Modes of delivery	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PC 101 to guide management, details not reported</p>	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PALS PLUS to guide management, details not reported</p>	<p>All training: face-to-face</p> <p>Care: Patient baseline data entered into mWellcare system which generated a decision support recommendation, lifestyle advice and suggested date for follow-up (printout). The recommendation was reviewed by the physician. Any changes to the recommended plan we captured in the mWellcare system. The nurse provided lifestyle advice and pamphlets</p>	<p>All training: face-to-face</p> <p>Care: According to clinical judgement of physician. Nurses provided and explained pamphlets on lifestyle advice</p>
Location of the intervention	In primary healthcare clinics	In primary healthcare clinics	Community Health Centres	Community Health Centres
When and how much the intervention was delivered	<p>Training of facility trainers: 5-days, in May 2011 and quarterly 1-day workshops</p> <p>Educational outreach sessions: Total of 155 educational outreach sessions, 8 sessions lasting 90 minutes at each of the 19 intervention clinics</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Educational outreach sessions: 90 minute sessions</p> <p>Follow-up sessions every year</p> <p>Distribution of updated tool every year</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Training for nurses using the mWellcare system: 3 days</p> <p>Onsite supervision: 2 days</p> <p>Care: follow-up visits according to the recommendation provided by the mWellcare system</p>	<p>Not reported</p> <p>Care: follow-up visits according to the discretion of the physician</p>

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Tailoring of the intervention	Not reported	Not reported	Not reported	Not reported
Modifications of the intervention	<p>Unexpected co-intervention by the district department of health: “Chronic Disease Season” (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p> <p>Facilitated group session to resolve tensions between nurses, doctors and pharmacists related to expanded prescribing provisions</p>	<p>Unexpected co-intervention by the district department of health: “Chronic Disease Season” (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p>	None reported	None reported
Assessment of intervention adherence/fidelity	<p>Nurse trainers were observed during 5-day workshop and quarterly 1-day workshops</p> <p>Two nurse trainers were interviewed and focus group discussions were held in four</p>	Not reported	Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source documents examination, protocol	Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source documents examination, protocol

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	intervention clinics in December 2011		adherence and recording of adverse events Site visits by investigators: to monitor enrolment process, intervention delivery and protocol adherence	adherence and recording of adverse events Site visits by investigators: to monitor enrolment process, intervention delivery and protocol adherence
Intervention delivered as planned	<p>Good uptake of nurse trainers, who completed all outreach sessions, and repeated some sessions to ensure that most staff could attend</p> <p>Due to absenteeism and shifts, not all nurses attended all the outreach sessions. In total, 18 nurses attended a median of six training sessions, five pharmacists and four doctors were trained</p> <p>Some variations in the uptake of the PC 101 tool were observed</p>	By 2011, 70% of nurses working in the relevant districts had received training in PALS PLUS.	Not reported	Not reported

Supplementary file 5: Risk of bias assessments for included studies

Prabhakaran 2018

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	“An independent biostatistician performed central computer-based randomization of CHCs stratified by states (Haryana and Karnataka) and within each state by the availability of NCD nurses recruited under NPCDCS.” “using block randomisation (with a block size of 2)”
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study.
Baseline outcome measurements similar	Low risk	Measurement of outcomes was conducted in a standardised way. Outcomes were pre-defined and subjective
Baseline characteristics similar	Low risk	The EUC arm had a higher proportion of participants with peripheral vascular disease (4.4% versus 0.3%), self-reported tobacco use (17.5% versus 10.0%) and alcohol use (12.3% versus 7.8%), and higher mean SBP (157.0 mm Hg versus 152.5 mm Hg). Outcome measures adjusted for relevant baseline characteristics.
Incomplete outcome data	Low risk	No incomplete outcome data suspected. Number of participants in whom the outcomes were assessed were mentioned in a general manner.
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All/ “Given the nature of the cluster-randomized trial design, neither personnel nor participants were blinded to the intervention.”
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All/ “Assessments at study end were carried out by independent outcome assessors” “It was difficult to blind independent assessors who carried out the end-of-study evaluations”
Protection against contamination	Low risk	Outcome group: All/ low possibility of contamination across clusters
Selective Outcome reporting	Low risk	Data on cost-effectiveness mentioned in protocol but not reported in full report of the study, because primary outcome do not differ substantially, otherwise all primary and secondary outcomes reported
Recruitment bias (<i>e.g. individuals are recruited to the trial after the clusters have been randomized</i>)	Unclear	Patients were recruited after randomisation. Of eligible participants, n=165 in the intervention group and n=193 in the control group were not enrolled in the trial.
Baseline differences clusters	Unclear	Characteristics of cluster not described
Loss of clusters	Low risk	No loss of clusters reported
Incorrect analysis	Low risk	Adjusted for clustering
Comparability (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search.

Fairall 2016

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention.”
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study. “Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention”
Baseline outcome measurements similar	Low risk	No differences between groups reported: Baseline BP and HbA1C similar
Baseline characteristics similar	Unclear	Baseline characteristics seem similar, but no statistical tests reported
Incomplete outcome data	Low risk	Loss to follow-up similar across groups and less than 20%
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All “Blinding of the intervention was not possible at the clinic level due to the nature of the intervention”
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All No blinding of outcome assessors reported Outcome assessors not blinded. This might have influenced BP readings, but not HbA1C (blood test)
Protection against contamination	Unclear	Outcome group: All Contamination of study arms unlikely. Control clinics might have had access to the guidelines although cluster randomisation took place
Selective Outcome reporting	Low risk	No selective outcome reporting suspected, all outcomes listed in the methods section are also reported in the results section – All pre-specified outcomes listed in the trial registration record reported on
Recruitment bias	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention” All patients were enrolled after the clusters were randomised. However, all eligible patients were included in the study.
Baseline differences (clusters)	Low risk	Control clinics had more nurses per clinic and more pharmacies on site compared to the intervention group, but patient load was also higher in the control clinics. Ratio of nurses to patients was similar in both groups
Loss of clusters	Low risk	All clinics completed the trial
Incorrect analysis	Low risk	Analysis conducted on individual level, but results adjusted for cluster effects. “The cluster randomisation design was accounted for using robust cluster variance-covariance estimates.”
Compatibility (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search
Other bias	Unclear	“Midway through the trial, the district health department launched a 3-mo campaign called Chronic Disease Season in all clinics to improve NCD recognition and care. Chronic Disease Season focused on hypertension and diabetes and involved both community and clinic health workers. The community-level interventions included several “health screening days” in which free blood pressure and finger-prick glucose measurements were offered at venues such as shopping centres and town halls” (Page 7, end)

Havliir 2019

Domain	Risk of bias	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate method – mix of methods used, including computer generated, coin tossing and drawing of lots See description in protocol (p45 version 2.0 (Nov 2012))
Allocation concealment (selection bias)	Low risk	Communities were matched and randomised within each pair. Method adequate to not be able to predict allocation
Baseline outcome measurements similar	Unclear	No baseline outcome measurements for HIV and hypertension control Page 25, online supplement to article
Baseline characteristics similar	Low risk	No obvious difference observed
Incomplete outcome data	Unclear	Unclear for HIV and Hypertension cohort, not clear how many at baseline.
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants and personnel due to the nature of the intervention. Can influence behaviour of both participants and personnel
Blinding of outcome assessment (detection bias)	Unclear	Not reported
Protection against contamination	Unclear	Distance from other potential trial communities taken into consideration as part of the eligibility criteria. Migration in and out of communities
Selective Outcome reporting	Unclear	Not clear whether dual control of HIV and Hypertension/NCDS was pre-specified
Recruitment bias	Low risk	Communities were recruited (selected) before randomisation. Participants were recruited after randomisation, but a household census and Community health campaigns to reach most people in community
Baseline differences (clusters)	Unclear	No description of clusters, but cluster pairs were matched for randomisation
Loss of clusters	Low risk	No loss of clusters
Incorrect analysis	Unclear	Not clear whether adequately adjusted for clustering
Compatibility (with RCTs randomised by individuals)	Low risk	No similar studies using individual randomisation found in our search
Other bias	Unclear	Primary endpoint should have been 5-year cumulative HIV incidence, but this was shortened to 3 years as the WHO recommendation on ART therapy changed

Rawat 2018

Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other intervention identified. Also, clinics were excluded if they were identified as 'priority sites' that were specifically designed to deliver ART.
The shape of the intervention effect was pre-specified	High risk	The shape of the intervention effect was not pre-specified.
The intervention was unlikely to affect data collections	Low risk	Data was collected from TIER.net (3 interlinked electronic registers) and the District Health Information System (DHIS) for data collected before and after the intervention.
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Low risk	Outcomes were based on indicators monitored by the Free State Department of Health. Methods of data collection were similar before and after the intervention, therefore the intervention did not affect data collection.
Incomplete outcome data was likely to bias results	Unclear	Post-intervention data for diabetes outcomes only available for 18 months post intervention. For other outcomes there is data for 30 months.
Outcomes were reported selectively	Low risk	All outcomes reported in the methods section were reported in the results section
Other risks of bias	Low risk	No other risks of bias identified. As integration took place at various intervals, seasonality assumed not to have an effect.

Ameh 2017

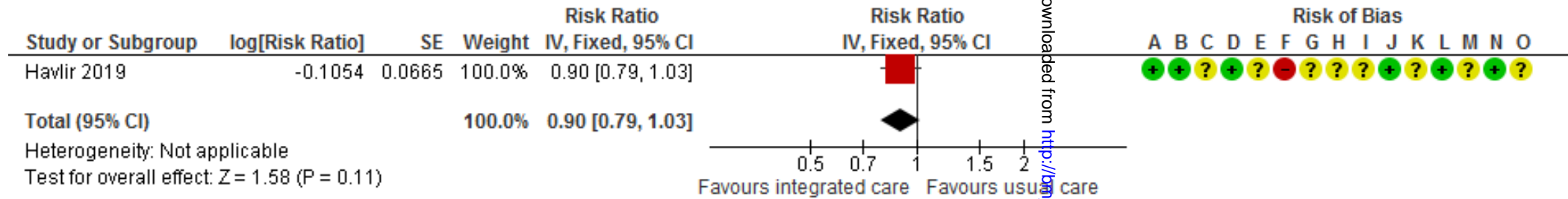
Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other changes reported.
The shape of the intervention effect was pre-specified	Low risk	Point of analysis is the point of intervention
The intervention was unlikely to affect data collections	Unclear	It can be assumed that the re-organisation of care delivery also affected data collection in the intervention facilities
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Low risk	Data was collected retrospectively from patient records. Patients were recruited in June 2013, and data collected from Jan 2011 to June 2013. Methods of data collection were similar before and after the intervention and the intervention did not affect data collection.
Incomplete outcome data was likely to bias results	Low risk	No incomplete outcome data suspected. No attrition or missing cases reported, only data for diabetes patients was not reported because there were too few cases (n=4)
Outcomes were reported selectively	Low risk	No selective outcome reporting suspected. All outcomes reported in the methods section are reported in the results section
Other risk of bias	Low risk	No other sources of bias identified

Supplementary file 6: Forest plots

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Comparison 1: Integrated models of care vs. usual care

Outcome: Mortality



Risk of bias legend

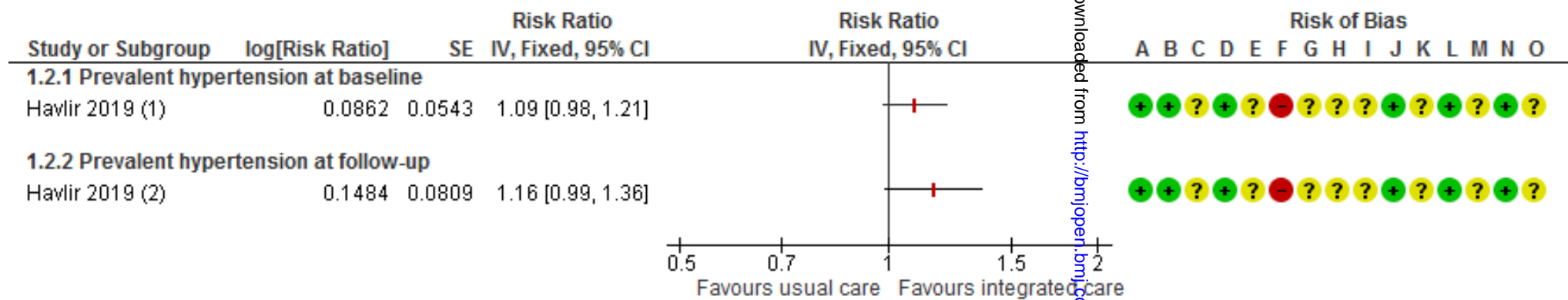
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 1: Integrated models of care vs. usual care

Outcome: BP control



Footnotes

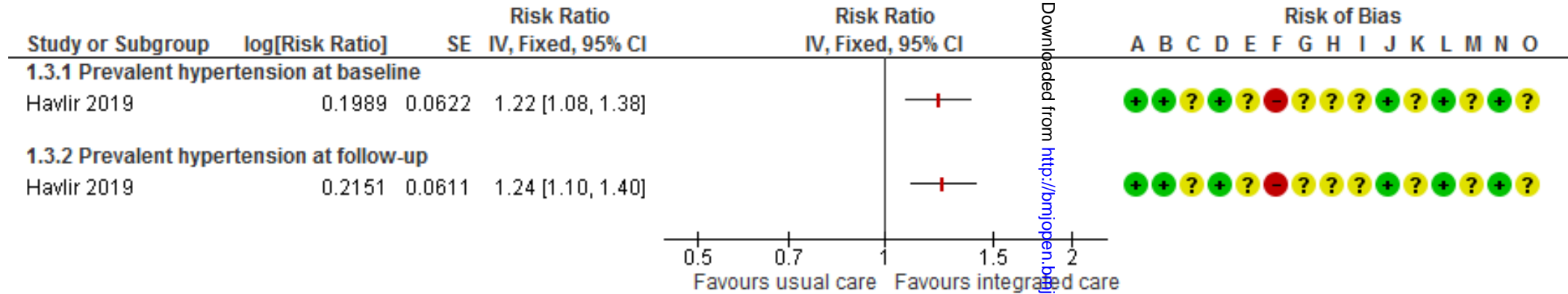
- (1) Among people living with HIV (PLHIV)
- (2) Among people living with HIV (PLHIV)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care

Outcome: BP and HIV control



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

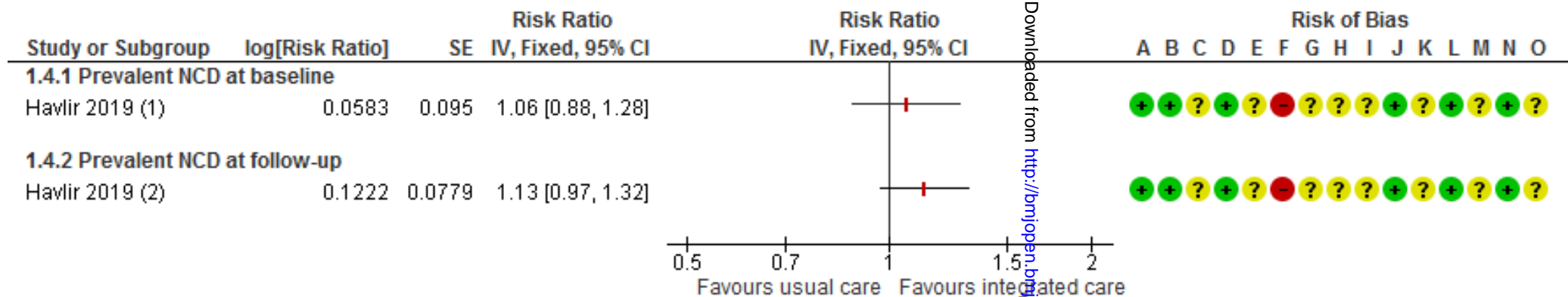
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Comparison 1: Integrated models of care vs. usual care

Outcome: NCD control



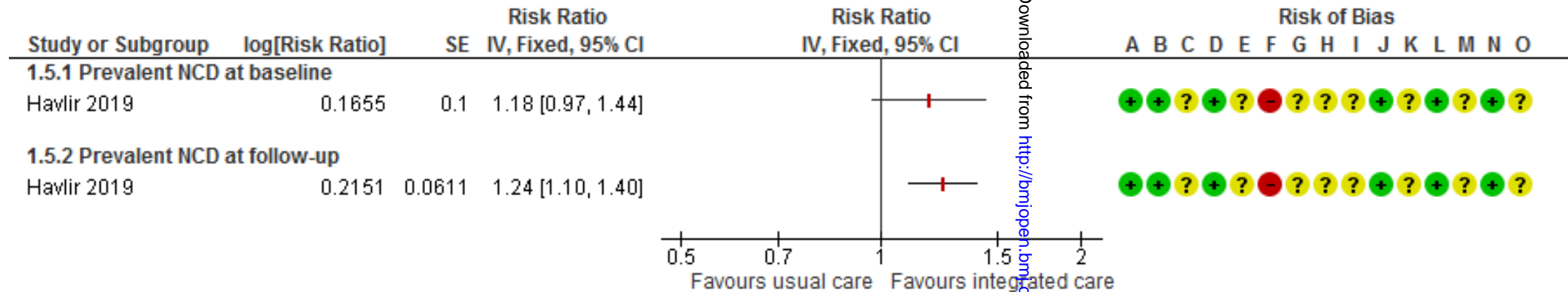
Footnotes

- (1) Among PLHIV
- (2) Among PLHIV

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care
 Outcome: NCD and HIV control



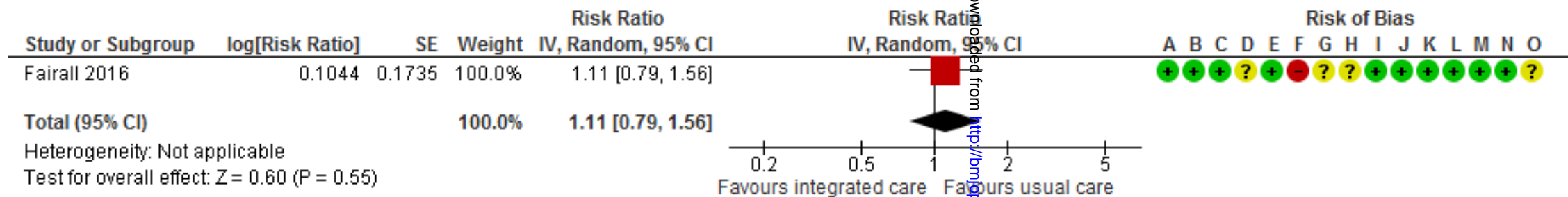
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Mortality

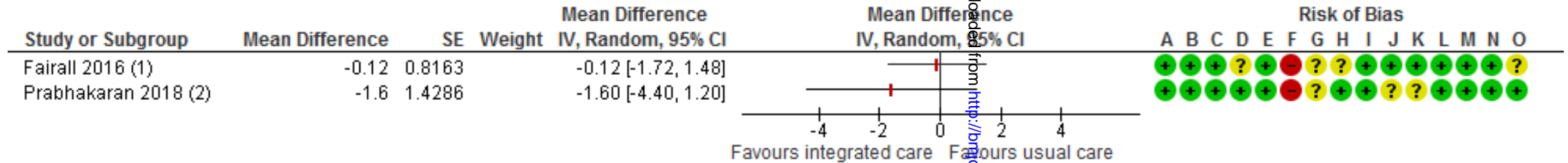


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Depression



Footnotes

- (1) Change from baseline to follow-up; 10-item Center for Epidemiologic Studies...
- (2) Value at follow-up; Patient Health Questionnaire-9

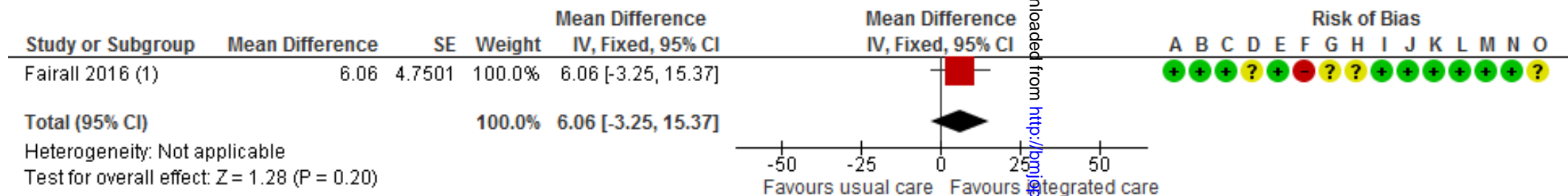
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristic similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCT randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Quality of life



Footnotes

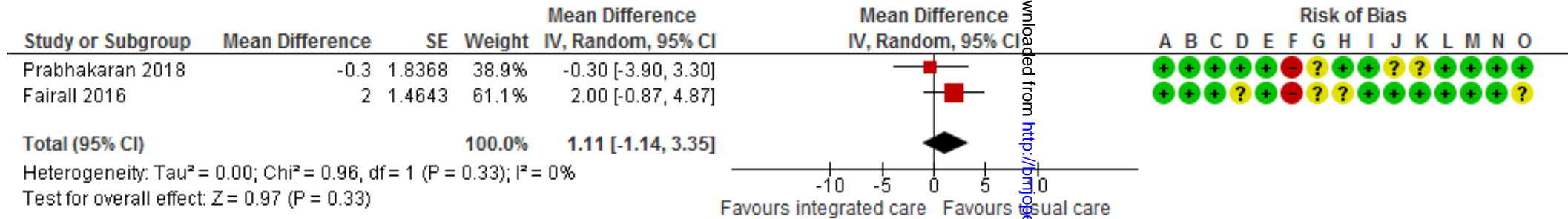
(1) Euro-Qol-5D visual analogue scale: 0=worst imaginable state of health,...

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
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- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Change in systolic BP



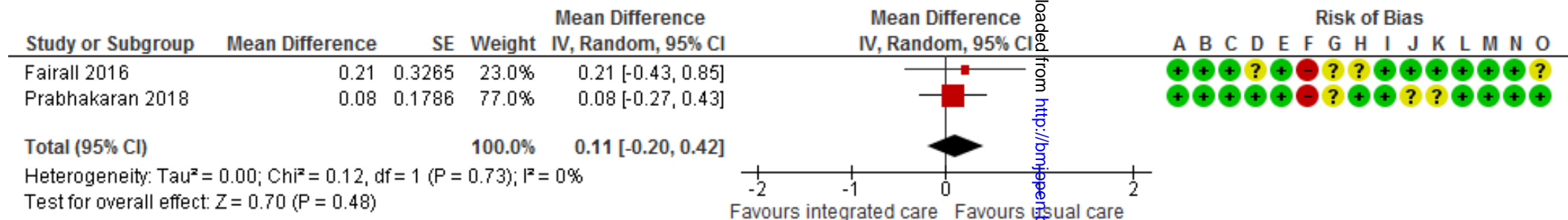
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Change in HbA1c

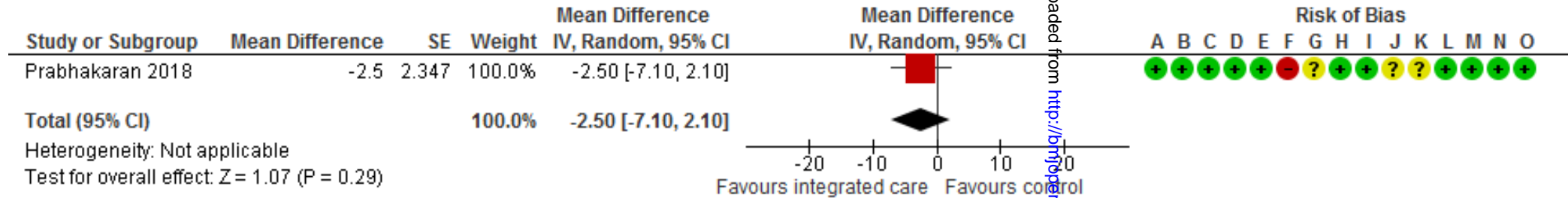


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Change in total cholesterol



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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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
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4-5
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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary 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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
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.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
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.	6



PRISMA 2009 Checklist

Page 1 of 2

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).	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7, Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO, follow-up period) and provide the citations.	8-12, Supplementary files 3 and 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).	13, Figure 3, 4 and supplementary file 5
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.	Supplementary file 6
Synthesis of results	21	13-20	11-18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 3 and 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
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).	20
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).	21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22
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.	22



PRISMA 2009 Checklist

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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

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Page 2 of 2

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Effects of integrated models of care for diabetes and hypertension in low-and middle-income countries. A systematic review and meta-analysis

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Effects of integrated models of care for diabetes and hypertension in low-and middle-income countries. A systematic review and meta-analysis

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Integrated care, diabetes, hypertension, low-and middle-income countries

Abstract

Objectives

To assess the effects of integrated models of care for people with multi-morbidity including at least diabetes or hypertension in low-and middle-income countries on health and process outcomes.

Design

Systematic review

Data sources

We searched MEDLINE, EMBASE, CENTRAL, LILACS, Africa-Wide, CINAHL, and Web of Science up to 12 December 2019.

Eligibility criteria

We included randomised controlled trials (RCTs), non-RCTs, controlled before-after studies and interrupted time series (ITS) studies of people with diabetes and/or hypertension plus any other disease, in LMICs; assessing the effects of integrated care.

Data extraction and synthesis

Two authors independently screened retrieved records; extracted data and assessed risk of bias. We conducted meta-analysis where possible and assessed certainty of evidence using GRADE.

Results

Of 7568 records, we included five studies - two ITS studies and three cluster RCTs. Studies were conducted in South Africa (n=3), Uganda/Kenya (n=1), and India (n=1). Integrated models of care compared to usual care may make little or no difference to mortality (very low certainty), the number of people achieving blood pressure (BP) or diabetes control (very low certainty), and access to care (very low certainty); may increase the number of people who achieve both HIV and BP/diabetes control (very low certainty); and may have a very small effect on achieving HIV control (very low certainty). Interventions to promote integrated delivery of care compared to usual care may make little or no difference to mortality (very low certainty), depression (very low certainty) and quality of life (very low certainty); and may have little or no effect on HbA1c (low certainty), systolic BP (low certainty), and total cholesterol levels (low certainty).

Conclusions

Current evidence on the effects of integrated care on health outcomes is very uncertain. Programmes and policies on integrated care must consider context-specific factors related to health systems and populations.

PROSPERO registration: CRD42018099314

Strengths and limitations of this study

- We included study designs that are able to provide reliable evidence on the effects of integrated models of care on health and process outcomes
- We performed a comprehensive search for published and unpublished studies up to 12 December 2019, with no language restrictions.

- We assessed the certainty of evidence using the GRADE approach taking into consideration study limitations, inconsistency, imprecision, publication bias and indirectness when downgrading the certainty of evidence.
- Our review did not aim to answer questions on aspects linked to implementation of integrated models of care and barriers and facilitators to integrated models of care at individual and health-system level

Introduction

Low- and middle-income countries (LMICs) are facing an increasing burden of non-communicable diseases (NCDs).¹ A recent report of the World Health Organization (WHO) on NCDs indicates that 41 million people succumb to NCDs globally which is the equivalent of 71% of total global deaths. Fifteen million people die prematurely due NCDs every year (between the ages of 30 and 69 years) and 85% of these premature deaths occur in LMICs.^{1 2} Furthermore, NCDs are projected to exceed communicable, maternal, perinatal, and nutritional diseases as the most common causes of death by 2030.³ In LMICs, the vast majority of NCD deaths are caused by cardiovascular diseases (CVDs), mainly due to coronary artery diseases and stroke,⁴ diabetes, cancer and chronic respiratory diseases; and they account for 54% of NCD disability adjusted life years.^{1 5} Diabetes and hypertension are the major cardiovascular risk factors for target organ damage of brain, heart and kidney.¹

Currently, it is estimated that 425 million people in LMICs live with diabetes. This number is expected to increase up to 629 million in 2045.⁶ According to the International Society of hypertension, around 40% of people over age of 25 years have hypertension worldwide and two thirds of them live in LMICs.⁷ Due to the existing high burden of communicable diseases, especially HIV infection, in sub-Saharan Africa and other LMICs, a lot of people are living with multi-morbidity. Because of the progress made with scaling up of anti-retroviral therapy (ART), the life expectancy of people living with HIV (PLHIV) has increased substantially, putting them at risk of NCDs that are common in older people. In addition to the traditional risk factors for NCDs, such as smoking, poor diet and a sedentary lifestyle, PLHIV have an increased risk of NCDs (especially CVD, cervical cancer, depression and diabetes), related to HIV itself and to ART related side effects⁸⁻¹¹ According to a recent systematic review examining the prevalence of NCDs among PLHIV in LMICs,¹² the pooled prevalence estimate of hypertension was 21.2% (95%CI 16.3 to 27.1); while that of depression was 24.4% (95%CI 12.5 to 42.1%). The prevalence of diabetes among PLHIV was reported to be between 1.2 and 18% and authors ascribed the variation in the findings to actual differences in populations, as well as the lack of standardised diagnostic criteria for diabetes.

In LMICs, people with NCDs such as diabetes and hypertension are generally characterised by very poor outcomes due to various other factors such as limited access to reliable healthcare services.¹³ The chronic nature of NCDs puts strain on the already scarce resources of healthcare systems and affected individuals in LMICs.¹⁴ Hence there is a need to design effective interventions to address the increasing burden of NCDs such diabetes and hypertension, in particular in complex patients with co-morbidities such as HIV infection and other CVDs. Provision of integrated care has been advocated by researchers and many international bodies such as the WHO as a way of tackling the rising burden of NCDs and strengthening the health systems particularly in LMICs.¹⁵⁻¹⁷ Recent studies from LMICs have assessed integration of HIV/AIDS and tuberculosis (TB) services at primary healthcare (PHC) level,¹⁸⁻²⁰ which is usually the first point of contact with health services for people living in LMICs. Based on these integrated models of care, we conceptualised integrated care either as partial integration or full integration as illustrated in Figure 1.²¹ Fully integrated care is seen as a “one-stop-shop” model whereby a patient receives all necessary care or services under one roof by one or more health-care professionals. In a partially integrated model of care, patients receiving treatment for one disease such

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2 as diabetes receive additional care related to either prevention, diagnosis or treatment of another
3 disease, but do not receive the full package of care ²¹.

4
5 Although integrated models of care have been widely advocated, and various models and
6 programmes have been implemented and described, there is a lack of evidence on the effectiveness
7 of integrated care compared to other models of care in LMICs. We previously conducted a scoping
8 review to assess existing systematic reviews on the effectiveness of integrated models of care in people
9 with diabetes or hypertension and any other comorbid disease. ²² We found five reviews²³⁻²⁷ that met
10 our inclusion criteria, but only one of these included studies conducted in LMICs. Furthermore, none
11 of the included studies assessed integrated care for diabetes or hypertension and communicable
12 diseases (e.g. HIV). A subsequent systematic review by Haldane and colleagues examined existing
13 programmes of integrated healthcare delivery for diabetes, hypertension or CVDs with HIV/AIDS.²⁸
14 However, included studies mostly described existing programmes with no thorough evaluation of the
15 effectiveness of these programmes. A descriptive study from Cambodia looked at the management of
16 HIV/AIDS, diabetes, and hypertension and found that integration of services for these conditions was
17 highly acceptable and led to good health outcomes with improved CD4 count, glycated haemoglobin
18 (HbA1c) and blood pressure levels.²⁹ Dudley and Garner³⁰ assessed the effectiveness of strategies to
19 integrate PHC services in LMICs. They included studies that integrated family planning into existing
20 services; nutrition and infectious disease interventions; and sexually transmitted infections (STIs),
21 HIV/AIDS and TB treatment. None of the included studies reported on NCDs.

22
23 In light of limited information in existing reviews, we conducted this review to assess the effects of
24 integrated models of care at PHC level for people living in LMICs, with multi-morbidity, of which
25 diabetes or hypertension is one, compared to no integrated care on health and process outcomes.

31 Methods

32
33 Our systematic review followed the methods pre-specified in a published protocol.²¹ We followed the
34 PRISMA reporting guideline to report on the findings of our systematic review.

35 Criteria for considering studies for inclusion

36 *Types of study designs*

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38 Randomised controlled trials (RCTs), including cluster RCTs, controlled (non-randomised) clinical trials
39 (CCTs) or cluster non-randomised trials, interrupted time series (ITS) studies with at least three data
40 points before and after the intervention, and controlled before-and-after (CBA) studies were eligible
41 for inclusion. Cluster randomised, cluster non-randomised or CBA studies were only included if there
42 were at least two intervention sites and two control sites.

43 *Types of participants*

44
45 We included studies with adults and children attending PHC clinics, presenting with diabetes or
46 hypertension, and patients may potentially have had additional chronic diseases (multi-morbidity) in
47 LMICs. We defined LMICs according to the 2016 classification of the World Bank,³¹ that defined low-
48 income economies as those with a gross national income (GNI) per capita of \$1035 or less, lower
49 middle income economies as those with a GNI per capita of \$1006 to \$3995, and upper middle
50 economies as those with a GNI per capita of \$3956 to \$12235.

51 *Types of interventions*

52
53 Eligible interventions were models of full or partial integration of services at PHC and community
54 level. Full integration of service delivery was defined as models where patients (primarily treated for
55 diabetes, hypertension or any other disease) received the full package of care (prevention, diagnosis
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2 and treatment) for diabetes or hypertension and any other chronic disease at the same point of care
3 by one or more healthcare professionals. Partial integration of services was defined as models where
4 patients treated for diabetes, hypertension, or any other chronic disease received part of the package
5 of care (either prevention, diagnosis, or treatment) for another disease (see Figure 1). Partially
6 integrated models of care therefore refer to a lower level of integration compared to fully integrated
7 models of care. For example, with partially integrated care, patients receiving treatment for
8 hypertension would be tested for HIV and referred for treatment; whereas with fully integrated care,
9 patients receiving treatment for hypertension would be tested and treated for HIV during the same
10 clinic visit.
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13 Included studies did not provide adequate information for us to categorise interventions as fully
14 integrated models of care or partially integrated models of care and we thus categorised interventions
15 as either 1) integrated models of care or 2) interventions that promoted integrated delivery of care.
16 Integrated models of care assessed the effect of integration of service delivery i.e. integration of two
17 previously separate models of delivery of care into one model of delivery of care, for example
18 integrating HIV services into general PHC services. We distinguished these interventions from
19 interventions that promoted an integrated approach to providing care in PHC facilities. In these cases,
20 services as such were not integrated, but healthcare workers were encouraged to provide holistic
21 patient care, for example through the provision and use of clinical management tools that supported
22 an integrated approach to care.
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26 *Types of comparisons*

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28 We aimed to compare fully integrated models of care to stand-alone care; partially integrated models
29 of care to stand-alone care; and fully integrated models of care to partially integrated models of care.
30 However, for all included studies, comparisons were reported as standard or usual care and authors
31 did not provide an adequate description of what that entailed. Although these seemed to refer to less
32 integrated care, we unable to categorise them as partially integrated models of care or stand-alone
33 care. We therefore compared integrated models of care to usual care, and interventions to promote
34 integrated delivery of care to usual care.
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37 *Types of outcomes*

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39 We included studies that reported on either primary or secondary outcomes, as defined by primary
40 study authors. Primary outcomes were all-cause mortality, disease specific morbidity as reported in
41 included studies (e.g. disease control metrics), quality of life, glycated haemoglobin (HbA1c), systolic
42 Blood pressure (SBP) and cholesterol levels. Secondary outcomes were access to care, retention in
43 care, adherence, continuity of care, quality of care and cost of care.
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45

46 *Search strategy*

47
48 We searched MEDLINE (PubMed), EMBASE (Ovid), the Cochrane Central Register of Controlled Trials
49 (CENTRAL), LILACS, Africa-Wide Information (via EBSCO host), CINAHL, and Web of Science (Core
50 collection) (Date of last search: 12 December 2019). We searched the WHO International Clinical Trials
51 Registry Platform (ICTRP) and Clinicaltrials.gov for ongoing studies, as well as conference abstracts
52 from the International AIDS Society Online Resource Library, the HIV/AIDS Implementers' Meetings
53 and the NCDs Alliance meetings. Search terms included 'diabetes', 'hypertension', 'comorbidities',
54 'integrated health care delivery', 'low-and middle-income countries', and their synonyms. The full
55 search strategies for all databases are provided in Supplementary file 1. To supplement the search of
56 electronic databases, we screened reference lists of included studies and reference lists of relevant
57 systematic reviews, and contacted experts in the field and relevant organisations (e.g. NCD Alliance)
58 for unpublished studies. We did not have any restrictions related to language, date of publication or
59 publication status.
60

Selection of studies

Two authors (JUN and AR or a research assistant) independently screened titles and abstracts of studies identified by the search, using Covidence software.³² We retrieved full texts of potentially eligible studies. Two authors (JUN and AR/TY/CMB) independently screened full texts for eligibility. Discrepancies were resolved through discussion with a third author (JJM/IT). We classified studies as included, excluded or ongoing and provided reasons for excluding studies.

Data extraction

Two authors (JUN, AR and IT) independently extracted data for included studies using a pre-specified, piloted data extraction form and assessed risk of bias. Discrepancies were resolved through discussion or by consulting a third author (TY/JJM). We extracted data related to the study design, participants, intervention, comparison, outcomes, setting, context and funding sources. We used the template for intervention description and replication (TIDieR)³³ and the PRISMA-Complex Interventions extension checklist³⁴ to guide data extraction and reporting related to the interventions.

Risk of bias assessment

We used guidance from Cochrane Effective Practice and Organisation of Care (EPOC) to assess risk of bias for included studies³⁵. Risk of bias was assessed as low, high, or unclear for each domain. For RCTs, non-randomised trials and CBA studies, we assessed the following nine domains: 1) random sequence generation, 2) allocation concealment, 3) baseline outcome measurements, 4) baseline characteristics, 5) incomplete outcome data, 6) knowledge of allocated intervention (blinding), 7) protection against contamination, 8) selective outcome reporting and 9) other risks of bias. For cluster RCTs, we assessed additional risk of bias linked to recruitment, cluster baseline differences, loss of clusters, incorrect analysis and compatibility with RCTs randomised by individuals, as per the Cochrane handbook.³⁶ For ITS studies, we assessed whether 1) the intervention was independent of other changes, 2) the shape of the intervention effect was pre-specified, 3) the intervention was unlikely to affect data collections, 4) knowledge of the allocated intervention was adequately prevented during the study, 5) incomplete outcome data was likely to bias results, 6) outcomes were reported selectively and 7) there were any other risks of bias.

Data analysis

We extracted relevant data for each outcome per included study. For dichotomous outcomes, we reported risk ratios (RR) and 95% confidence intervals (CI). For continuous outcomes, we reported mean differences (MD) with 95% CI if outcomes were measured in the same way across studies, or standardised mean differences (SMD) with 95% CI where outcomes were measured differently across studies and where standard deviations (SD) were reported. For ITS studies, we reported beta coefficients (β) with 95% CI or standard error (SE). We contacted study authors to request information on missing data. We did not impute any data.

All included cluster RCTs appropriately adjusted for the effects of clustering in their analysis, we thus used these adjusted effect estimates and standard errors in our meta-analysis using the generic inverse-variance method in Review Manager 5.³⁷ We did not include studies with more than one treatment arm in our review.

We explored clinical heterogeneity by clearly documenting study characteristics related to the population, intervention, outcomes and context in table format. We assessed statistical heterogeneity in each meta-analysis by inspecting forest plots and calculating Chi² test values and I² statistics. We considered heterogeneity to be important if the p-value of the Chi² test was < 0.10, and the I² statistic was above 30%, as per the recommendations in the Cochrane handbook.³⁶

1
2 We pooled data from individual studies if we judged them to be sufficiently homogeneous in terms of
3 design, population, intervention and comparator. As we anticipated some degree of heterogeneity,
4 we performed random-effects meta-analysis. We did not pool data from RCTs and non-randomised
5 studies in a single meta-analysis. Where we judged included studies to be too heterogeneous to pool,
6 we used narrative synthesis and presented data in tabular format. We did not perform subgroup or
7 sensitivity analysis, as only two studies contributed to the meta-analysis. We were unable to examine
8 reporting biases by means of funnel plots, as we only included two studies in the meta-analysis.
9

10 11 Certainty of evidence

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13 We wrote statements about the evidence (e.g., "little or no effect" vs. "very small effect") according
14 to guidance of GRADE³⁸ for the following outcomes: mortality, disease specific morbidity, quality of
15 life, HbA1c, systolic BP, cholesterol levels and access to care. We created a 'Summary of findings' table
16 using GRADEpro software.³⁹ Our judgements to downgrade the certainty of evidence were based on
17 assessment of the following five domains: 1) study limitations, 2) inconsistency, 3) imprecision, 4)
18 indirectness and 5) publication bias. According to GRADE guidance, non-randomised studies (such as
19 CBAs and ITS studies) start at low certainty evidence. We considered upgrading the certainty of
20 evidence for non-randomised studies if there was a large effect, a dose-response and cases where all
21 plausible residual confounding would reduce a demonstrated effect or would suggest a spurious effect
22 if no effect was observed.
23

24
25 For each outcome, we described the certainty of evidence as high, moderate, low or very low.⁴⁰ For
26 outcomes reported by both RCTs and non-randomised studies, we made separate GRADE judgements
27 for both types of studies. Where we arrived at the same level of certainty of evidence, we summarised
28 this in a single judgement per outcome. We interpreted the certainty of evidence according to
29 guidance provided by the GRADE working group, which takes into consideration the size of the effect
30 and the certainty of evidence.⁴¹
31

32 Patient and public involvement

33 No patients were involved in the development of this systematic review.
34
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36 Results

37
38 The results of the search are depicted in the PRISMA flow diagram (Figure 2). We screened titles and
39 abstracts of 7568 records. We obtained and screened full texts of 49 potentially relevant studies. We
40 included five studies,⁴²⁻⁴⁶ (Table 1) reported in six articles and excluded 37 articles and reported
41 reasons for exclusion (Supplementary file 2). For one study⁴⁷ that met eligibility criteria, we were only
42 able to access the conference abstract. We classified this study as 'awaiting assessment', as we are
43 unable to definitively decide on inclusion or exclusion until we have access to the full report. We
44 identified five ongoing RCTs,⁴⁸⁻⁵¹ investigating integrated care for depression and hypertension in
45 China;⁴⁸ integrated care for depression and hypertension⁴⁹ or depression and diabetes/HIV⁵⁰ in South
46 Africa; integrated care for common mental disorders and hypertension, diabetes or ischemic heart
47 disease in India;⁵¹ and diabetes and TB in India.⁵²
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Table 1: Summary of characteristics of included studies

Study ID	Study design	Country and Setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes ¹
<i>Integrated models of care</i>							
Ameh 2017 ⁴²	Controlled ITS study	South Africa: Primary health care (PHC) facilities, Ehlanzeni health district, Mpumalanga Province	Patients with chronic disease (HIV, diabetes or hypertension) n=878	Integrated chronic disease management (ICDM) model Clinics: n=7 Participants: n=435 (Hypertension: n=210; Diabetes: n=2; HIV: n=141; Comorbidities: n=82)	Usual care in PHC facilities Clinics: n=5 Participants: n=443 (Hypertension: n=91; Diabetes: n=2; HIV: n=282; Comorbidities: n=68)	30 months Pre-intervention: 6 months Post-intervention: 24 months	<ul style="list-style-type: none"> - Blood pressure (BP) control² - CD4 count control³ - Number of healthcare visits
Havlir 2019 ⁴⁶	Cluster RCT	Kenya and Uganda: Rural regions in south-western and eastern Uganda, and western Kenya	Clusters: Communities of 9000 to 11 000 people Participants: People residing in community n=150 395 (baseline)	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and streamlined, patient-centered care Clusters: n=16 Participants: n=79 818 (baseline) (Hypertension in adults over 30 years: n=5953)	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care (not integrated) Clusters: n=16 Participants: n=70 577 (baseline)	36 months	<ul style="list-style-type: none"> - Cumulative HIV incidence - Time to initiation of ART - Viral suppression - Death - Incident tuberculosis or death due to illness - Control of hypertension⁴ among HIV-infected persons - Control of diabetes⁵ or hypertension (NCD) among HIV infected persons - Control of HIV⁶ and hypertension - Control of HIV and NCDs⁷

¹ Outcomes relevant to this review are in bold

² Defined as: BP <140/90mmHg

³ Defined as: CD4 count >350 cells/mm³

⁴ Defined as: At least one systolic BP measurement <140mmHg, and at least one diastolic measurement of <90mmHg

⁵ Defined as: Finger prick blood glucose ≤11 mmol/L

⁶ Defined as: Suppressed viral replication (<500 copies/ml)

⁷ Defined as: Control of all prevalent NCDs (hypertension or diabetes)

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					(Hypertension in adults over 30 years: n=5911)		<ul style="list-style-type: none"> - Control of hypertension in the overall population - Control of diabetes in the overall population
Rawat 2018 ⁴⁵	ITS study	South Africa: PHC clinics in the Free state Province	Patients attending PHC clinics (focus on diabetes and hypertension) n=not reported	Integration of HIV care into HC facilities n=131 clinics	No control group	48 months Pre-intervention: 12 months Post-intervention: 36 months	<ul style="list-style-type: none"> - Population level new diabetics on treatment - Clinic level new diabetics on treatment - Population-level new hypertensive on treatment - Clinic level new hypertensive on treatment - Total ART patients - New patients initiated on ART
<i>Interventions to promote integrated delivery of care</i>							
Fairall 2016 ⁴³	Cluster RCT	South Africa: Mostly rural PHC clinics in Eden and Overberg districts, Western Cape Province	Patients with one or more of the following: hypertension, diabetes, chronic respiratory disease, depression n=4393	Primary Care (PC) 101 management tool Clinics: n=19 Participants: n=2166 (Hypertension: n=1555; diabetes: n=851)	Usual care: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool Clinics: n=19 Participants: n=2227 (Hypertension: n=1672; diabetes: n=991)	14 months	<ul style="list-style-type: none"> - Treatment intensification for hypertension, diabetes and chronic respiratory disease - Depression - CVD risk - Systolic BP - HbA1C - Body Mass Index (BMI) - Smoking status - Health-related quality of life - Mortality - Healthcare utilisation
Prabhakaran 2019 ⁴⁴	Cluster RCT	India: Community Health Centres (CHC) from 4 districts in Haryana and 2 districts in Karnataka	Patients with confirmed diagnosis of diabetes or hypertension n=3698	mWellcare system CHCs: n=20 Participants: n=1842	Enhanced usual care CHCs: n=20 Participants: n=1856	12 months	<ul style="list-style-type: none"> - Mean change in systolic BP - Mean change in HbA1C - Mean change in fasting plasma glucose - Mean change in total cholesterol - Mean change in CVD risk - Mean change in Tobacco use - Mean change in BMI - Alcohol use

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								<ul style="list-style-type: none"> - Depression score - Adherence - Perceived quality of care
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Characteristics of included studies

We included three cluster RCTs and two ITS studies. One cluster RCT was conducted in South Africa,⁴³ one in India,⁴⁴ and the Sustainable East Africa Research in Community Health (SEARCH) trial was conducted in Uganda and Kenya.⁴⁶ The two ITS studies were both conducted in South Africa^{42 45} (Table 1). All studies were conducted in PHC facilities in mostly rural settings. All five studies assessed the effect of strategies for full integration of care compared to partial integration of care.

The two ITS studies^{42 45} and the SEARCH trial⁴⁶ assessed the effects of integrated models of care for chronic diseases (Table 2). Ameh and colleagues⁴² conducted a controlled ITS study, comparing the integrated chronic disease management (ICDM) model to usual care over a period of 30 months. Rawat and colleagues⁴⁵ examined the effect of integrating HIV care into PHC clinics over a 48 months period. The SEARCH trial⁴⁶ assessed the effects of universal ART and streamlined, patient-centered care (integrated care) compared to usual care as per national guidelines. Interventions are described in more detail according to the TIDieR checklist in supplementary file 3.

The other two cluster RCTs^{43 44} assessed the effectiveness of interventions to promote integration of care (Table 2). Fairall and colleagues⁴³ introduced the Primary Care (PC) 101 clinical management tool to promote provision of comprehensive care for all symptoms including NCDs, HIV, TB, mental health and women's health, in PHC clinics randomised to the intervention, while the control clinics continued using the Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool, which did not cover all NCDs and was the standard of care at the time of the trial. Prabhakaran and colleagues⁴⁴ introduced the mWellcare system, a m-health based electronic decision support system, to promote integrated management of hypertension, diabetes, depression, and alcohol and tobacco use in PHC centres randomised to the intervention. Control centres continued with usual care. Interventions are described in more detail according to the TIDieR checklist in supplementary file 4.

Table 2: Key components of included interventions

Name and Study ID	Components related to provision of care in the clinic	Components related to provision of care in the community/at home	Training	Appointment reminders
Integrated chronic disease management (ICDM) model Ameh 2017	Facility reorganisation: designated chronic care area; supply of critical medicines; pre-packaging of medication Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral	Ward-based outreach teams to ensure individual responsibility and "assisted" self-management Health promotion and population screening	-	-

<p>National policy to integrate HIV care into all PHC facilities Rawat 2018</p>	<p>Policy to integrate HIV care into PHC clinics</p> <p>Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for all diseases in single consultation room</p> <p>Additional staff to strengthen drug delivery systems</p>	<p>-</p>	<p>Training of nurses in comprehensive management of HIV: Nurse initiated Management of ART (NIMART)</p> <p>Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)</p>	<p>-</p>
<p>SEARCH intervention Havlr 2019</p>	<p>Patient-centered, integrated care for HIV, diabetes, hypertension: 3-month visit intervals; ART to all HIV positive participants; hypertension and diabetes treated according to standard algorithms</p>	<p>Community health campaigns (CHCs): Testing for HIV, diabetes and hypertension; counselling and clinic appointments; blood tests for HIV positive participants; transportation voucher for first clinic visit</p> <p>Home-based testing for participants that did not attend CHCs</p> <p>Appointments to initiate ART within 7 days for HIV positive participants not on ART; introductory phone call from clinic staff; support hotline available via phone or text message</p>	<p>-</p>	<p>Phone/SMS reminders about clinic visits</p>
<p>Primary Care (PC) 101 Fairall 2016</p>	<p>PC 101 guideline: Ring-bound, colour illustrated booklet</p> <p>Expanded prescribing provisions for nurses</p> <p>Desk pads with key messages</p>	<p>-</p>	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p>	<p>Letters and SMS reminders of follow-up visits</p>

<p>mWellcare Prabhakaran 2018</p>	<p>mWellcare system: m-Health-based electronic decision-support system</p> <p>Visible charts on the management of the conditions</p> <p>Onsite supervision and support</p>	<p>Pamphlets containing lifestyle advice</p>	<p>Training of physicians on current clinical management guidelines and orientation to mWellcare</p> <p>Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use</p>	<p>SMS reminders of follow-up visits and medication adherence</p>
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Risk of bias in included studies

For the two ITS studies, we judged risk of bias to be low or unclear in all domains (Figure 3). For the three cluster RCTs, we judged risk of selection bias to be low, risk of performance bias to be high, as blinding of participants and personnel was not possible due to the nature of the interventions, and risk of detection bias to be unclear for all three studies. We judged attrition bias to be low for two cluster RCTs^{43 44} and unclear for the SEARCH trial⁴⁶ (Figure 4). Detailed judgements for each included study are reported in supplementary file 5.

Integrated models of care compared to usual care

We included three studies as part of this comparison.^{42 45 46} Results are summarised in the summary of findings table (Table 3) and forest plots are available in supplementary file 6.

Table 3: Summary of findings for integrated models of care compared to usual care for diabetes and hypertension in LMICs

Patient or population: Patients with multi-morbidity (diabetes and/or hypertension and other chronic conditions e.g. HIV) Setting: Low- and middle-income countries Intervention: Integrated care for hypertension, diabetes and HIV Comparison: Usual care				
Outcome	Effect (95%CI)	No of participants (studies)	Certainty of evidence (GRADE)	Comments
Mortality	RR 0.90 (0.79 to 1.02) Risk with usual care: 0.56 per 100 person-years Risk with integrated care: 0.51 per 100 person-years	171 431 (1 RCT)	⊕○○○ VERY LOW a,b,c	Integrated care compared to usual care may make little or no difference to the rate of death, but the evidence is very uncertain
BP control (number of PLHIV achieving BP control)	RCT: Prevalent hypertension at baseline: RR 1.09 (0.98 to 1.21)	2319 (2 studies: 1 RCT, 1 ITS study)	⊕○○○ VERY LOW a,c,d,e,f	Integrated care compared to usual care may make little or no difference to achieving BP control but the evidence is very uncertain
	RCT: Prevalent hypertension at follow-up: RR 1.16 (0.99 to 1.36)			
	ITS study: $\beta=0.010$ (0.003 to 0.016)			
BP or diabetes (NCD) control (number of PLHIV achieving NCD control)	Prevalent NCD at baseline: RR 1.06 (0.88 to 1.27)	1 RCT*	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may make little or no difference to achieving NCD control but the evidence is very uncertain
	Prevalent NCD at follow-up: RR 1.13 (0.97 to 1.32)			
HIV control (CD4 count control)	The probability of CD4 count control was 6% greater in intervention clinics compared to control clinics	878 (1 ITS study)	⊕○○○ VERY LOW e,f	Integrated care may have a very small effect on achieving CD4 count control, but the evidence is very uncertain
BP and HIV control (number of people achieving both HIV viral suppression and BP control)	Prevalent hypertension at baseline: RR 1.22 (1.08 to 1.37)	1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both BP and HIV control but the evidence is very uncertain
	Prevalent hypertension at follow-up: RR 1.24 (1.10 to 1.40)			
BP or diabetes (NCD) and HIV control (number of people achieving both HIV viral suppression and NCD control)	Prevalent NCD at baseline: RR 1.18 (0.97 to 1.44)	1441 (1 RCT)	⊕○○○ VERY LOW a,c,d	Integrated care compared to usual care may result in a slight increase in the number of people achieving both NCD and HIV control but the evidence is very uncertain
	Prevalent NCD at follow-up: RR 1.24 (1.10 to 1.40)			
Quality of life	-	-	-	Not reported
Systolic BP	-	-	-	Not reported
HbA1c	-	-	-	Not reported
Cholesterol levels	-	-	-	Not reported

<p>Access to care</p>	<p>There was no change in trend from pre- to post-intervention for population level new diabetics on treatment, clinic level new diabetics on treatment and clinic-level new hypertensive patients on treatment. There was a slight decrease in new hypertensive patients on treatment at population level at 36 months</p>	<p>1 ITS*</p>	<p>⊕○○○ VERY LOW e.g</p>	<p>Integrated care may make little or no difference to short term access to care and may result in a slight decrease in long-term access to hypertensive care, but the evidence is very uncertain.</p>
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CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **BP:** Blood pressure; **HIV:** Human Immunodeficiency Virus; **HbA1c:** Glycated Haemoglobin; **NCD:** Non-communicable disease; **RCT:** Randomised controlled Trial; **ITS:** Interrupted time series

*Sample size not reported

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Footnotes: Explanation of GRADE certainty of evidence

Randomised controlled trials:

- a) Downgraded by 1 due to study limitations: high risk of performance bias and unclear risk of bias for other domains
- b) Downgraded by 1 due to indirectness: Results are based on number of participants at baseline, however authors did not report how many participants had HIV plus hypertension/diabetes at baseline. At 3-year follow-up, less than 1% of participants at follow-up had hypertension/diabetes and HIV infection (0.7% (694/103 777) in the control group and 0.6% (747/121 347) in the intervention group)
- c) Downgraded by 1 due to indirectness: Usual care comprised care according to national guidelines in Kenya and Uganda. Authors did not report what this entails. It is not clear to what extent care was integrated or not
- d) Downgraded by 1 due to imprecision: Small sub-sample with hypertension and HIV in the RCT with wide 95% confidence intervals

Interrupted time series studies:

- e) Observational study, starting at low certainty evidence
- f) Downgraded by 1 due to indirectness: Intervention clinics experienced stock-outs of anti-hypertensive drugs and malfunctioning of BP machines. We are therefore not confident that the intervention was delivered as intended
- g) Downgraded by 1 due to indirectness: Study reported on population level new diabetics on treatment, clinic level new diabetics on treatment, population level new hypertensive patients on treatment and clinic level new hypertensive patients on treatment. This is an indirect measure of access to care

All-cause mortality: The SEARCH trial⁴⁶ reported the rate of all-cause mortality among baseline residents in included communities. Results suggest that integrated compared to usual care may make little or no difference to the mortality rate when compared to usual care but the evidence is very uncertain (RR 0.90 95%CI 0.79 to 1.02, n=171 431, 1 RCT, very low-certainty evidence).

Disease-specific morbidity (BP control): Integrated care compared to usual care may make little or no difference to achieving BP control, but the evidence is very uncertain. Results from the SEARCH trial⁴⁶ suggest that integrated care compared to usual care may make little or no difference to the number of PLHIV who achieve BP control with prevalent hypertension at baseline (RR 1.09, 95%CI 0.98 to 1.21, 1 RCT, very low-certainty evidence) and PLHIV with prevalent hypertension at follow-up (RR 1.16, 95%CI 0.99 to 1.36, n=1441, 1 RCT, very low- certainty evidence). Results of the controlled ITS study⁴² suggest that integrated care compared to usual care may increase the probability of achieving BP

control by 1%, but the evidence is very uncertain ($\beta=0.010$, 95%CI 0.003 to 0.016, n=878, 1 ITS study, very low-certainty evidence).

Disease-specific morbidity (NCD control): Results from the SEARCH trial⁴⁶ suggest that integrated care compared to usual care may make little or no difference to the number of PLHV who achieve NCD (diabetes and/or hypertension) control with prevalent NCD at baseline (RR 1.06, 95%CI 0.88 to 1.27, 1 RCT, very low-certainty evidence) and prevalent NCD at follow-up but the evidence is very uncertain (RR 1.13, 95%CI 0.97 to 1.32, 1 RCT, very low-certainty evidence).

Disease-specific morbidity (HIV control): One ITS study⁴² reported on HIV control in terms of CD4 count control. Results suggest that integrated care compared to usual care may increase the probability of achieving CD4 count control by 6%, but the evidence is very uncertain ($\beta=0.057$, 95%CI 0.056 to 0.058, n=878, 1 ITS study, very low-certainty evidence).

Disease-specific morbidity (HIV and BP control): Results from the SEARCH trial⁴⁶ suggest that integrated care compared to usual care may increase the number of PLHIV who achieve both HIV viral suppression (HIV control) and BP control with prevalent hypertension at baseline (RR 1.22, 95%CI 1.08 to 1.37, 1 RCT, very low-certainty evidence) and with prevalent hypertension at follow-up (RR 1.24, 95%CI 1.10 to 1.40, n=1441, 1 RCT, very low-certainty evidence).

Disease-specific morbidity (HIV and NCD control): Integrated care compared to usual care may make little or no difference to the number of PLHIV who achieve both HIV viral suppression (HIV control) and NCD control with prevalent NCD at baseline (RR 1.18, 95%CI 0.97 to 1.44, 1 RCT, very low certainty), but may result in a slight increase in the number of PLHIV who achieve both HIV viral suppression (HIV control) and NCD control with prevalent NCD at follow-up (RR 1.24, 95%CI 1.10 to 1.40, 1 RCT very low-certainty evidence). However, the evidence is very uncertain for these outcomes.

Access to care: One ITS study reported on access to care⁴⁵ in terms of the change in post-integration trend compared to pre-integration trend for population level new diabetics on treatment, clinic level new diabetics on treatment, population-level new hypertensive patients on treatment, and clinic level new hypertensive patients on treatment. Integrated care may make little or no difference to population level new diabetics on treatment at 18 (1/100 000, Standard Error (SE)=2, p=0.50, very low certainty) and 36 months (1/100 000, SE=3, p=0.61, very low-certainty evidence) post-integration; clinic level new diabetics on treatment at 18 (0/100 000, SE=1; p=0.96, very low-certainty evidence) and 36 months post-integration; clinic level new hypertensive patients on treatment at 18 (0/100 000, SE=1; p=0.78, very low-certainty evidence) and 36 months (0/100 000, SE=0; p-value=0.57, very low-certainty evidence) post-integration, and population level new hypertensive patients on treatment at 18 months post-integration (-7/100 000, SE=4; p=0.08, very low-certainty evidence). Results suggest that there was a slight decrease in population level new hypertensive patients on treatment at 36 months post-integration (-6/100 000; SE=3; p=0.02, very low-certainty evidence). However, the evidence is very uncertain for these outcomes.

Authors also reported on the total number of patients on anti-retroviral treatment (ART) and the number of new patients initiated on ART. Overall, the number of patients for both outcomes increased during each year of follow-up. No effect size was reported. No other secondary outcomes were reported for this comparison.

Interventions to promote integrated delivery of care compared to usual care

We included two studies in this comparison.^{43 44} Results are summarised in the summary of findings table (Table 4) and forest plots are available in supplementary file 6.

All-cause mortality: Results from one cluster RCT⁴³ suggest that interventions to promote integrated care compared to usual care may make little or no difference in mortality (RR 1.11; 95% CI 0.79 to 1.56;

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2 n=3393; 1 RCT, very low-certainty evidence) when compared to usual care, but the evidence is very
3 uncertain.
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5 **Disease-specific morbidity (depression):** Results from two RCTs^{43 44} suggest that interventions to
6 promote integrated care compared to usual care may have little or no effect on change in HbA1c from
7 baseline to follow-up (MD 0.11%; 95%CI -0.20 to 0.42; n=1687; 2 RCTs, low-certainty evidence). This
8 means that the change in HbA1c was similar in both groups. Fairall 2016 reported the change in
9 depression scores from baseline to follow up using the 10-item Center for Epidemiologic Studies
10 Depression Scale and reported no difference between groups (MD -0.12; 95%CI -1.72 to 1.48; n=3976,
11 very low-certainty evidence). Prabhakaran 2019 measured depression scores at follow-up using the
12 Patient Health Questionnaire-9 and reported no difference between groups (MD -1.6; 95%CI -4.4 to
13 1.2; n=3324, very low-certainty evidence).
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16 **Quality of life:** Results from one RCT⁴³ suggest that interventions to promote integrated care compared
17 to usual care may make little or no difference to quality of life, but the evidence is very uncertain. The
18 RCT reported on the change in health-related quality of life from baseline to follow-up using the
19 EuroQol-5D visual analogue scale and the EuroQol-5D index score. There was no difference between
20 groups, neither for the Euro-Qol-5D visual analogue scale (MD 6.06; 95%CI -3.25 to 15.36; n=3969, very
21 low- certainty evidence) nor for the EuroQol-5D index score (MD 0.00; 95%CI -0.05 to 0.06; n=3969,
22 very low-certainty evidence).
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26 Table 4: Summary of findings for interventions to promote integrated delivery of care compared to
27 usual care for diabetes and hypertension in LMICs
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Patient or population: Patients with diabetes, hypertension and other chronic diseases Setting: Low- and middle-income countries Intervention: Strategies to promote integrated care Comparison: Usual care						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with Strategies to promote integrated care				
Mortality	29 per 1,000	32 per 1,000 (23 to 45)	RR 1.11 (0.79 to 1.56)	4393 (1 RCT)	⊕ ○ ○ ○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to the risk of death, but the evidence is very uncertain
Depression	10-item Center for Epidemiologic Studies Depression Scale: MD -0.12 (-1.72 to 1.48)		-	7293 (2 RCTs)	⊕ ○ ○ ○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference to depression scores, but the evidence is very uncertain
	Patient Health Questionnaire-9: MD -1.6 (-4.4 to 1.2)					
Change in quality of life (Euro-Qol-5D visual analogue scale)	Quality of life scores with usual care improved by a mean of 6.4 points	The mean change in quality of life with integrated care was 6.06 points higher (3.25 points lower to 15.36 points higher)	-	3969 (1 RCT)	⊕ ○ ○ ○ VERY LOW ^{a,b,c}	Integrated care compared to usual care may make little or no difference in quality of life, but the evidence is very uncertain
Change in HbA1c	The mean change in HbA1c with usual care ranged from -0.58 to -0.2%	The mean change in HbA1c with integrated care was 0.11 % higher (0.2 lower to 0.42 higher)	-	1687 (2 RCTs)	⊕⊕ ○ ○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on HbA1c
Change in systolic BP	The mean change in systolic BP with usual care ranged from -13.7 to -1.1 mmHg	The mean change in BP with integrated care was 1.11 mmHg higher (1.14 lower to 3.35 higher)	-	4807 (2 RCTs)	⊕⊕ ○ ○ LOW ^{a,c}	Integrated care compared to usual care may have little or no effect on systolic BP

<p>Change in total cholesterol</p>	<p>The mean change in total cholesterol with usual care was 2.0 mg/dl</p>	<p>The mean change in total cholesterol with integrated care was 2.5 mg/dl lower (7.1 lower to 2.1 higher)</p>	<p>-</p>	<p>3324 (1 RCT)</p>	<p>⊕⊕ ○ ○ LOW^{a,c}</p>	<p>Integrated care compared to usual care may have little or no effect on total cholesterol levels</p>
<p>*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; RR: Risk ratio; MD: Mean difference; BP: Blood pressure; HbA1c: Glycated haemoglobin; RCT: Randomised controlled trial High certainty: We are very confident that the true effect lies close to that of the estimate of the effect Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect <i>Footnotes: Explanation of GRADE certainty of evidence</i> a. Downgraded by 1 due to study limitations: high risk of performance bias and unclear risk of bias in some other domains b. Downgraded by 1 due to imprecision: study not adequately powered for this outcome, small sample size and wide 95% CI c. Downgraded by 1 due to indirectness: The interventions comprised strategies to promote integrated care at clinic level, and not integrated models of healthcare delivery at health system level</p>						

HbA1c: Results from two cluster RCTs^{43 44} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in HbA1c from baseline to follow-up (MD 0.11%; 95%CI -0.20 to 0.42; n=1687; 2 RCTs, low-certainty evidence).

Systolic BP: Results from two cluster RCTs^{43 44} suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in systolic BP from baseline to follow-up (MD 1.11mmHg; 95%CI -1.41 to 3.35; n=4807; 2 RCTs, low-certainty evidence).

Total cholesterol: Results from one cluster RCT⁴⁴ suggest that interventions to promote integrated care compared to usual care may have little or no effect on change in total cholesterol from baseline to follow-up (MD -2.50mg/dl; 95%CI -7.10 to 2.10; n=3324; low-certainty evidence). The mean change in total cholesterol with usual care was 2.0 mg/dl higher.

Retention in care: Fairall 2016 reported the number of clinic visits three months before the follow-up interview and found no difference between groups (incidence rate ratio 1.02; 95%CI 0.93 to 1.13; n=3121).

Adherence: One cluster RCT reported absolute numbers for drug adherence during the past seven days.⁴⁴ Patients in the intervention group reported greater adherence for both hypertensive drugs (833/1027; 81.1% vs. 648/1119; 57.9%) and anti-hyperglycemic drugs (683/829; 82.4% vs. 570/827; 68.9%) compared to patients receiving usual care.

Quality of care: One cluster RCT⁴⁴ reported on perceived change in quality of care as a composite perception on availability of drugs, guidance from physicians, quality of care, frequency of blood pressure measurement, and care provided by NCD nurses. Perceived quality of care improved in both groups. Patients receiving integrated care (n=1637), reported that quality of care was slightly/much better (96.6%), about the same (3.3%) and somewhat/much worse (0.2%).

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2 Patients receiving usual care (n=1687) reported that quality of care was slightly/much better (95%),
3 about the same (4.4%) and somewhat/much worse (0.5%).
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5 Neither of the two cluster RCTs included in this comparison reported on access to care, continuity of
6 care or cost of care.
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8 9 Discussion

10 11 Summary of main results

12 We included five studies and two comparisons in this review. Three studies were conducted in South
13 Africa, one in India and one in Kenya and Uganda. Two ITS studies and one cluster RCT provided data
14 for the first comparison, integrated models of care compared to usual care. Results suggest that
15 integrated models of care compared to usual care may make little or no difference to mortality, the
16 number of people achieving BP or diabetes control, and access to care; may increase the number of
17 people who achieve both HIV and BP/diabetes control; and may have a very small effect on achieving
18 HIV control. However, the evidence for all outcomes is very uncertain. Two cluster RCTs provided data
19 for the second comparison, interventions to promote integrated delivery of care compared to usual
20 care. Results suggest that interventions to promote integrated delivery of care compared to usual care
21 may make little or no difference to mortality, depression and quality of life, but the evidence is very
22 uncertain. Interventions to promote integrated delivery of care compared to usual care may have little
23 or no effect on HbA1c, systolic BP, and total cholesterol levels. Process outcomes were poorly reported
24 across included studies, with none of the studies reporting on continuity of care or cost of care.
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30 31 Agreements and disagreements with other reviews

32 Other systematic reviews that assessed the effects of integrated models of care on health outcomes
33 in LMICs had similar findings. Dudley and Garner³⁰ assessed strategies to integrate PHC services on
34 healthcare delivery and health status in LMICs. They found no evidence that integrated services
35 improved healthcare delivery or health status. However, none of the included studies assessed
36 integrated care for NCDs. Haldane and colleagues²⁸ described existing integrated models of care for
37 HIV and NCDs and assessed health outcomes, barriers and facilitators. However, most of the included
38 studies were descriptive or observational and health outcomes were poorly reported. Indeed, they
39 highlighted the need for rigorous research that includes long-term follow-up and the role of incentives.
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42 43 Overall completeness and applicability of evidence

44 Although we considered multi-morbidity in terms of diabetes and/or hypertension plus any other
45 disease, four out of five studies were conducted in sub-Saharan Africa and included people with
46 diabetes and/or hypertension (and other NCDs) and HIV. All studies were conducted in rural settings.
47 Due to successful transformation of the health systems to deliver HIV programmes, sub-Saharan Africa
48 is presented with a unique opportunity to leverage the investments made in order to scale-up NCD
49 services. This can be achieved in various ways, such as integrating NCD services into facilities originally
50 providing HIV care only, integrating HIV care into PHC facilities that offer NCD care, or concurrent
51 introduction of HIV and NCD services.⁸ However, even though this is recognised, there are still
52 questions linked to the implementation of integrated models of care. In South Africa, the ICDM model,
53 the intervention evaluated in the ITS study by Ameh and colleagues,⁴² is one example where the
54 vertical HIV programme was integrated into general PHC facilities. As part of the pilot programme,
55 Ameh and colleagues not only evaluated the impact on health outcomes, but also conducted a
56 qualitative study to explore the perspectives of healthcare providers and patients on the quality of
57 care in the ICDM model.⁵³ They found that PHC facilities experienced BP drug stock-outs, lack of
58 functioning BP machines and staff shortages, among others, which impacted on the delivery of care
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2 and indirectly therefore on the health outcomes. Integrated NCD and HIV care is implemented to a
3 varying degree in other sub-Saharan African countries. A study examining policies and programmes for
4 integrated HIV and NCD care in Malawi, Kenya, South Africa and Swaziland found that these countries
5 still experience challenges in implementing integrated care. Some of these are related to inadequate
6 data to determine the burden of NCDs among PLHIV at a local level, lack of evidence to support the
7 implementation of integrated care models, inadequate stakeholder engagement, lack of NCD care
8 capacity and other health system challenges.⁵⁴
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11 Our definition of integrated care was based on a “one-stop-shop” model whereby a patient receives
12 all necessary care or services under one roof by one or more health-care professional (Figure 1), which
13 is just one way of describing integrated care. Indeed, a narrative review by Njuguna, et al.⁵⁵ aimed to
14 describe various models of integrated care for HIV and NCDs in sub-Saharan Africa. Based on the
15 definition by WHO, the authors defined integrated care as the “coordination, co-location, or
16 simultaneous delivery of HIV and NCD services to patients who need it, when they need it” and
17 identified five models. These include community-based integrated HIV and NCD screening in the
18 general population; screening for NCD risk factors among PLHIV; integrated care for HIV and NCDs in
19 healthcare facilities through leveraging the HIV infrastructure to manage NCDs; differential care for
20 people well-controlled HIV or NCDs, which includes longer follow-up periods for stable patients; and
21 population health for all patients with any need.⁵⁵
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24 25 Strengths and limitations

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27 We followed a rigorous and systematic process according to standard systematic review methods. We
28 performed a comprehensive search of published and unpublished studies up to 12 December 2019,
29 with no language restrictions. We purposefully included study designs that are able to provide reliable
30 evidence on the effects of integrated care on health and process outcomes, and followed guidance
31 provided by Cochrane EPOC. We assessed the certainty of evidence using the GRADE approach across
32 outcomes, taking into consideration study limitations, inconsistency, imprecision, publication bias and
33 indirectness when downgrading the certainty of evidence.
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37 Integration of care for NCDs and HIV or other diseases is complex, partly due to the complex nature of
38 health systems.⁵⁶ We aimed to compare fully integrated models of care to partially integrated models
39 of care or stand-alone care. However, it was difficult to classify interventions according to our pre-
40 specified definitions and we thus lumped interventions that integrated service delivery as ‘integrated
41 models of care’. We included two cluster RCTs that aimed to promote integrated delivery of care
42 through clinical management tools, which is different from integrated care at facility level. We
43 discussed this within our team and concluded that the aim of these interventions was to provide care
44 in a holistic way and to address all the needs of an individual when s/he presents to a healthcare
45 facility, and thus met our eligibility criteria. Furthermore, included studies did not provide adequate
46 information on the level of integration in comparisons, but rather referred to these as standard or
47 usual care. While these referred to a lesser degree of integration compared to the interventions, we
48 were not able to categorise these as either partially integrated care or stand-alone care.
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52 Our review focused on the effectiveness of integrating care for people with diabetes, hypertension
53 and other co-morbidities in terms of health outcomes, which is just one question that needs to be
54 answered. In other words, the question of our review focused on one building block of health systems
55 as described by the WHO.⁵⁶ Although we aimed to examine process outcomes, these were limited to
56 access to care, retention in care, adherence, continuity of care, quality of care and cost of care; and
57 were poorly reported across included studies. The scope of our review did not include outcomes
58 related to implementation or perspectives from health providers and patients, which are important
59 aspects to consider. Although the literature predominantly highlights the need to integrate NCD and
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2 HIV care, integrating mental health services into existing NCD and or HIV services is just as important.
3 Four⁴⁸⁻⁵¹ of the five ongoing studies that we identified examine integration of mental health with NCDs.
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6 Conclusion

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8 The evidence on the effectiveness of integrated models of care for people with diabetes, hypertension
9 and other co-morbidities, on health outcomes is very uncertain. We therefore do not know whether
10 integrated models of care lead to better or worse outcomes, or may make no difference at all among
11 people with diabetes, hypertension and other chronic conditions. There is a need to scale-up NCD
12 services, particularly in LMICs. In the context of an increasing burden of NCDs against a backdrop of
13 other chronic diseases, and scarce health system resources, such as human capacity and funding,
14 policies and programmes need to promote integrated models of care and holistic, patient-centred
15 services. However, these need to take into consideration context-specific factors related to the health
16 system and the targeted population.
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19 Further rigorous studies assessing the effects of integrated models of care on health outcomes are
20 needed. These studies should include an adequate description of the integrated model of care, assess
21 long term health effects as well as patient important outcomes, and cost of care. Furthermore, there
22 is a need to conduct implementation research, economic evaluations as well as qualitative research on
23 the barriers and facilitators to integrated models of care at patient and health-system level in order to
24 guide policy makers in planning and allocation of resources in order to maximise the potential benefits
25 of integrated care as well strengthening the health systems in achieving universal health coverage in
26 LMICs.
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30 Authors' contributions

31 All authors contributed to development of the review protocol. JUN and AR screened titles and
32 abstracts; JUN, AR, TY and CMB participated in full text screening; TY, JJM and IT helped to resolve
33 discrepancies. AR, JUN and IT extracted data and assessed risk of bias. AR and IT assessed certainty of
34 evidence with input from TY and JJM. TY and JJM provided overall methodological guidance. JUN
35 drafted the background and discussion sections, AR drafted the rest of the manuscript. JUN, IT, TY, and
36 CMB critically read and revised the manuscript. All authors have approved the final version of the
37 manuscript.
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42 Acknowledgements

43 We would like to thank Anel Schoonees for conducting the search of electronic databases, Birhanu
44 Ayele for statistical input, and Selvan Naidoo for assistance with screening titles and abstracts.
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48 Data availability statement

49 All data relevant to the study are included in the article or uploaded as supplementary information.
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52 Ethics Approval

53 This systematic review does not involve human participants. All data included are in the public
54 domain and ethics approval was thus not sought.
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Competing interests statement

All authors have no known conflict of interest.

Protocol

Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension in low- and middle-income countries (LMICs): Protocol for a systematic review. *Syst Rev* 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]

Figures

Figure 1: Logic model of integrated care

Figure 2: PRISMA flow diagram

Figure 3: Risk of bias in ITS studies

Figure 4: Risk of bias for cluster RCTs

Supplementary files

Supplementary file 1: Search strategies for all databases

Supplementary file 2: Table of excluded studies

Supplementary file 3: Summary of interventions according to the TIDiER checklist: Integrated models of care

Supplementary file 4: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated delivery of care

Supplementary file 5: Risk of bias assessments for included studies

Supplementary file 6: Forest plots

- Please ensure to provide ethics approval statement in main document file with a heading 'Ethics Approval'. It should be the same as stated in the ScholarOne system including the approval number (if any), if there's none, please provide an explanation.

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References

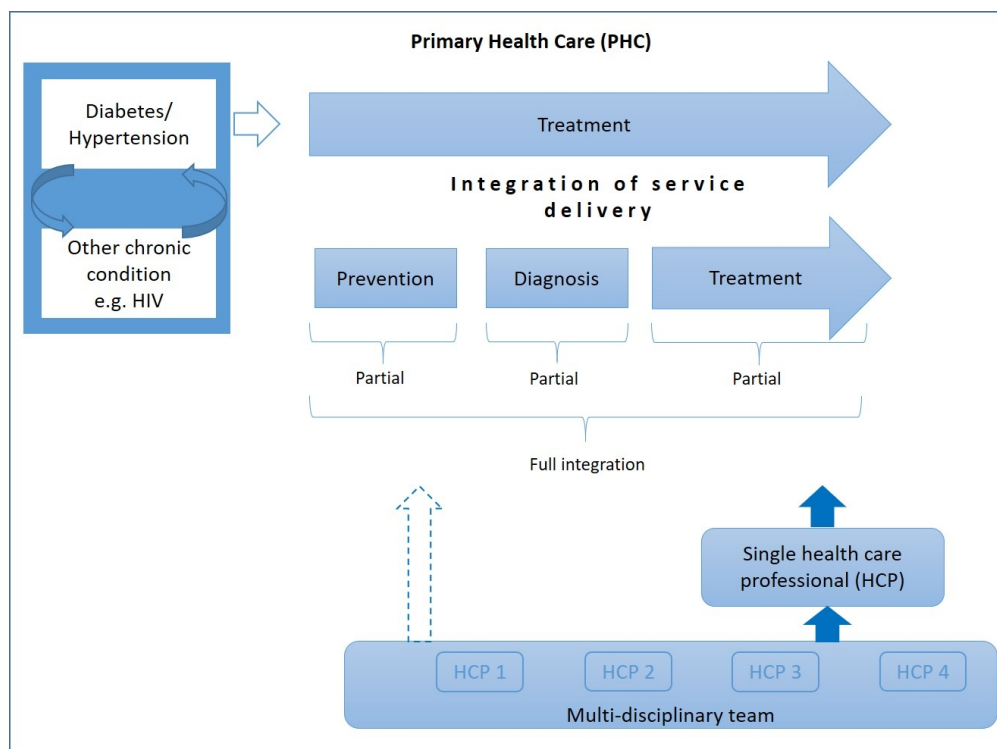
1. WHO. Noncommunicable diseases, 2018.
2. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390(10100):1211-59. doi: 10.1016/S0140-6736(17)32154-2 [published Online First: 2017/09/19]
3. Alliance N. Tackling non-communicable diseases in workplace settings in low- and middle-income countries. A CALL TO ACTION AND PRACTICAL GUIDANCE. Non- Communicable diseases (NCD) Alliance, 2017.
4. WHO. Cardiovascular diseases (CVDs) 2017 [Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))].
5. WHO. Global status report on non-communicable diseases 2010. Description of the global burden of NCDs, their risk factors and determinants, 2010.
6. Federation ID. IDF diabetes Atlas 8th Edition. 8 ed2017. Available from: <https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/134-idf-diabetes-atlas-8th-edition.html>.
7. Campbell NRC, Lackland DT, Niebylski ML. High Blood Pressure: Why Prevention and Control Are Urgent and Important-A 2014 Fact Sheet From the World Hypertension League and the International Society of Hypertension. *Journal of Clinical Hypertension* 2014;16(8):551-53. doi: 10.1111/jch.12372
8. Duffy M, Ojikutu B, Andrian S, et al. Non-communicable diseases and HIV care and treatment: models of integrated service delivery. *Tropical Medicine and International Health* 2017;22(8):926-37. doi: 10.1111/tmi.12901
9. Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African primary healthcare. *South African Medical Journal* 2015;105(2):134-38. doi: 10.7196/SAMJ.8696
10. Remais JV, Zeng G, Li G, et al. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *International Journal of Epidemiology* 2013;42(1):221-27. doi: 10.1093/ije/dys135
11. Rabkin M, Kruk ME, El-Sadr WM. HIV, aging and continuity care: strengthening health systems to support services for noncommunicable diseases in low-income countries. *AIDS* 2012;26
12. Patel P, Rose CE, Collins PY, et al. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis. *AIDS* 2018;32 Suppl 1:S5-S20. doi: 10.1097/QAD.0000000000001888 [published Online First: 2018/06/29]
13. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012 doi: 10.1016/S0140-6736(12)61728-0
14. Mbanya JCN, Motala AA, Sobngwi E, et al. Diabetes in sub-Saharan Africa, 2010.
15. Atun R, De Jongh T, Secci F, et al. A systematic review of the evidence on integration of targeted health interventions into health systems. *Health Policy and Planning* 2010;25(1):1-14. doi: 10.1093/heapol/czp053
16. Shigayeva A, Atun R, McKee M, et al. Health systems, communicable diseases and integration. *Health Policy and Planning* 2010;25(Suppl. 1):i4-i20. doi: 10.1093/heapol/czq060
17. WHO. Package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings.
18. Legido-Quigley H, Montgomery CM, Khan P, et al. Integrating tuberculosis and HIV services in low- and middle-income countries: A systematic review. *Tropical Medicine and International Health* 2013;18(2):199-211. doi: 10.1111/tmi.12029
19. Naidoo K, Gengiah S, Yende-Zuma N, et al. Addressing challenges in scaling up TB and HIV treatment integration in rural primary healthcare clinics in South Africa (SUTHI): A cluster randomized controlled trial protocol. *Implementation Science* 2017;12(1):1-12. doi: 10.1186/s13012-017-0661-1

20. Uyei J, Coetzee D, Macinko J, et al. Integrated delivery of HIV and tuberculosis services in sub-Saharan Africa: A systematic review. *The Lancet Infectious Diseases* 2011;11(11):855-67. doi: 10.1016/S1473-3099(11)70145-1
21. Uwimana Nicol J, Rohwer A, Young T, et al. Integrated models of care for diabetes and hypertension in low- and middle-income countries (LMICs) : Protocol for a systematic review. *Syst Rev* 2018;7(1):203. doi: 10.1186/s13643-018-0865-8 [published Online First: 2018/11/22]
22. Yiu KC, Rohwer A, Young T. Integration of care for hypertension and diabetes: a scoping review assessing the evidence from systematic reviews and evaluating reporting. *BMC Health Serv Res* 2018;18(1):481. doi: 10.1186/s12913-018-3290-8 [published Online First: 2018/06/22]
23. Atlantis E, Fahey P, Foster J. Collaborative care for comorbid depression and diabetes: a systematic review and meta-analysis. *BMJ Open* 2014;4(4):e004706. doi: 10.1136/bmjopen-2013-004706 [published Online First: 2014/04/15]
24. Huang Y, Wei X, Wu T, et al. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. *BMC Psychiatry* 2013;13:260. doi: 10.1186/1471-244X-13-260 [published Online First: 2013/10/16]
25. Joshi R, Alim M, Kengne AP, et al. Task shifting for non-communicable disease management in low and middle income countries--a systematic review. *PLoS One* 2014;9(8):e103754. doi: 10.1371/journal.pone.0103754 [published Online First: 2014/08/15]
26. Smith SM, Wallace E, O'Dowd T, et al. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database Syst Rev* 2016;3:CD006560. doi: 10.1002/14651858.CD006560.pub3 [published Online First: 2016/03/16]
27. Watson LC, Amick HR, Gaynes BN, et al. Practice-based interventions addressing concomitant depression and chronic medical conditions in the primary care setting: a systematic review and meta-analysis. *J Prim Care Community Health* 2013;4(4):294-306. doi: 10.1177/2150131913484040 [published Online First: 2013/06/27]
28. Haldane V, Legido-Quigley H, Chuah FLH, et al. Integrating cardiovascular diseases, hypertension, and diabetes with HIV services: a systematic review. *AIDS Care* 2018;30(1):103-15. doi: 10.1080/09540121.2017.1344350 [published Online First: 2017/07/07]
29. Janssens B, Van Damme W, Raleigh B, et al. BulleJohnson, W., Onuma, O., Owolabi, M., & Sachdev, A. S. (207AD). Bulletin of the World Health Organization Stroke: a global response is needed. Bulletin of the World Health Organization, 85(February), 660–667. <https://doi.org/10.2471/BLTtin> of the Worl. *Bulletin of the World Health Organization* 2007;85:880-85. doi: 10.2471/BLT
30. Dudley L, Garner P. Strategies for integrating primary health services in low- and middle-income countries at the point of delivery. *Cochrane Database of Systematic Review* 2011(7) doi: doi: 10.1002/14651858.CD003318.pub3.
31. Bank W. World Bank list of economies 2016 [Available from: Siteresources.worldbank.org/DATASTATISTICS/Resources/CLASS.XLS]
32. Covidence systematic review software [program]. Melbourne, Australia: Veritas Health Innovation
33. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687. doi: 10.1136/bmj.g1687 [published Online First: 2014/03/13]
34. Guise JM, Butler ME, Chang C, et al. AHRQ series on complex intervention systematic reviews-paper 6: PRISMA-CI extension statement and checklist. *J Clin Epidemiol* 2017;90:43-50. doi: 10.1016/j.jclinepi.2017.06.016 [published Online First: 2017/07/20]
35. (EPOC) CEPaOoC. Suggested risk of bias criteria for EPOC reviews. . EPOC Resources fo r review authors, 2017.
36. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019): Cochrane 2019. Available from: www.training.cochrane.org/handbook
37. Review Manager (RevMan) [program]. 5.3 version. Copenhagen: The Cochrane Collaboration, 2014.

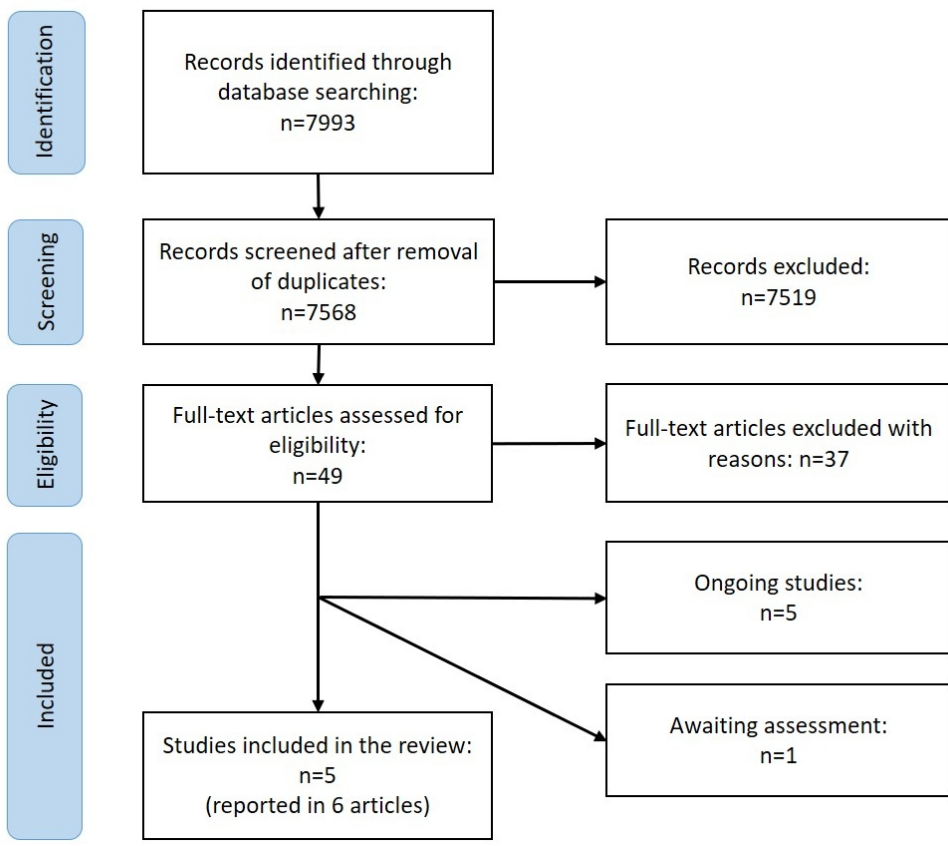
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38. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026 [published Online First: 2011/01/05]
39. GRADEpro GDT: GRADEpro Guideline Development Tool [Software] [program]: McMaster University, 2015.
40. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64(4):401-6. doi: 10.1016/j.jclinepi.2010.07.015 [published Online First: 2011/01/07]
41. Santesso N, Glenton C, Dahm P, et al. GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol* 2020;119:126-35. doi: 10.1016/j.jclinepi.2019.10.014 [published Online First: 2019/11/13]
42. Ameh S, Klipstein-Grobusch K, Musenge E, et al. Effectiveness of an Integrated Approach to HIV and Hypertension Care in Rural South Africa: Controlled Interrupted Time-Series Analysis. *Journal of acquired immune deficiency syndromes (1999)* 2017;75(4):472-79. doi: 10.1097/qai.0000000000001437
43. Fairall LR, Folb N, Timmerman V, et al. Educational Outreach with an Integrated Clinical Tool for Nurse-Led Non-communicable Chronic Disease Management in Primary Care in South Africa: A Pragmatic Cluster Randomised Controlled Trial. *PLoS medicine* 2016;13(11):e1002178. doi: 10.1371/journal.pmed.1002178
44. Prabhakaran D, Jha D, Prieto-Merino D, et al. Effectiveness of an mHealth-Based Electronic Decision Support System for Integrated Management of Chronic Conditions in Primary Care: The mWellcare Cluster-Randomized Controlled Trial. *Circulation* 2018 doi: 10.1161/CIRCULATIONAHA.118.038192
45. Rawat A, Uebel K, Moore D, et al. Integrated HIV-Care into Primary Health Care Clinics and the Influence on Diabetes and Hypertension Care: An Interrupted Time Series Analysis in Free State, South Africa over 4 Years. *Journal of Acquired Immune Deficiency Syndromes* 2018;77(5):476-83. doi: <http://dx.doi.org/10.1097/QAI.0000000000001633>
46. Havlir DV, Balzer LB, Charlebois ED, et al. HIV Testing and Treatment with the Use of a Community Health Approach in Rural Africa. *N Engl J Med* 2019;381(3):219-29. doi: 10.1056/NEJMoa1809866 [published Online First: 2019/07/18]
47. Integrated versus referred management of cardiovascular disease (CVD) risk factors for HIV-positive patients on antiretroviral therapy in Swaziland 20th International Workshop on Comorbidities and Adverse Drug Reactions in HIV; 2018; New York, USA.
48. Chen S, Conwell Y, Xue J, et al. Protocol of an ongoing randomized controlled trial of care management for comorbid depression and hypertension: the Chinese Older Adult Collaborations in Health (COACH) study. *BMC geriatrics* 2018;18(1):124. doi: 10.1186/s12877-018-0808-1
49. Petersen I, Bhana A, Folb N, et al. Collaborative care for the detection and management of depression among adults with hypertension in South Africa: study protocol for the PRIME-SA randomised controlled trial. *Trials* 2018;19(1):192. doi: 10.1186/s13063-018-2518-6
50. Myers B, Lund C, Lombard C, et al. Comparing dedicated and designated models of integrating mental health into chronic disease care: study protocol for a cluster randomized controlled trial. *Trials* 2018;19(1) (no pagination) doi: 10.1186/s13063-018-2568-9
51. Srinivasan K, Mazur A, Mony PK, et al. Improving mental health through integration with primary care in rural Karnataka: study protocol of a cluster randomized control trial. *BMC Fam Pract* 2018;19(1):158. doi: 10.1186/s12875-018-0845-z [published Online First: 2018/09/13]
52. Devarsetty P. Diabetes and Tuberculosis - Integrated management using the primary healthcare infrastructure in India 2017 [Available from: <http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=15771>]
53. Ameh S, Klipstein-Grobusch K, D'Ambruoso L, et al. Quality of integrated chronic disease care in rural South Africa: user and provider perspectives. *Health Policy Plan* 2017;32(2):257-66. doi: 10.1093/heapol/czw118 [published Online First: 2017/02/17]
54. Matanje Mwagomba BL, Ameh S, Bongomin P, et al. Opportunities and challenges for evidence-informed HIV-noncommunicable disease integrated care policies and programs: lessons from

- 1
2 Malawi, South Africa, Swaziland and Kenya. *AIDS* 2018;32 Suppl 1:S21-S32. doi:
3 10.1097/QAD.0000000000001885 [published Online First: 2018/06/29]
4 55. Njuguna B, Vorkoper S, Patel P, et al. Models of integration of HIV and noncommunicable disease
5 care in sub-Saharan Africa: lessons learned and evidence gaps. *AIDS* 2018;32 Suppl 1:S33-S42.
6 doi: 10.1097/QAD.0000000000001887 [published Online First: 2018/06/29]
7 56. WHO. Everybody's business: Strengthening Health Systems to improve Health Outcomes. WHO's
8 Framework for Action. , 2007.
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	Intervention was independent of other changes	The shape of the intervention was pre-specified	The intervention was unlikely to affect data collection	Knowledge of the allocated intervention adequately prevented during the study	Incomplete outcome data was likely to bias results	Outcomes were reported selectively	Other bias
Ameh 2017	+	+	?	+	+	+	+
Rawat 2018	+	?	+	+	?	+	+

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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data (attrition bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Protection against contamination	Selective reporting (reporting bias)	Recruitment bias	Baseline differences (clusters)	Loss of clusters	Incorrect analysis	Compatibility with RCTs randomised by individuals	Other bias
Fairall 2016	+	+	+	?	+	-	?	?	+	+	+	+	+	+	?
Havilir 2019	+	+	?	+	?	-	?	?	?	+	?	+	?	+	?
Prabhakaran 2018	+	+	+	+	+	-	?	+	+	?	?	+	+	+	+

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Supplementary file 1: Search strategies for electronic databases

1. Medline (PubMed) search strategy

#1 "Hypertension"[Mesh] OR (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)[title/abstract]

#2 diabetes OR "diabetes mellitus"[title/abstract] OR "Diabetes Mellitus"[Mesh]

#3 #1 OR #2

#4 (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein)[title/abstract] OR "Dyslipidemias"[Mesh]

#5 (((HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR hiv infect* OR human immunodeficiency virus OR human immune deficiency virus OR human immuno-deficiency virus OR human immune-deficiency virus OR ((human immun*) AND (deficiency virus)) OR acquired immunodeficiency syndromes OR acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immune-deficiency syndrome OR ((acquired immun*) AND (deficiency syndrome)) OR HIV/AIDS))) OR ((HIV infections [MeSH] OR HIV [MeSH]))

#6 (tuberculosis OR tuberculoses OR tb)[Title/Abstract] OR "tuberculosis"[Mesh]

#7 "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR NCD OR NCDs OR "Noncommunicable Diseases"[Mesh]

#8 (comorbid* OR co-morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity")[title/abstract] OR "Multimorbidity"[Mesh] OR "Comorbidity"[Mesh]

#9 multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring condition* OR cooccurring condition*

#10 chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle" OR "Multiple Chronic Conditions"[Mesh] OR "Chronic Disease"[Mesh]

#11 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

#12 "Delivery of Health Care, Integrated"[Mesh] OR "delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "Comprehensive Health Care"[Mesh] OR "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "Continuity of Patient Care"[Mesh] OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "Patient-Centered Care"[Mesh] OR "patient centered care" OR "patient centred care"

#13 "Referral and Consultation"[Mesh] OR (referral AND consultation)

#14 integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of

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2 programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR
3 "integration of services" OR integrat* delivery OR integrat* management OR "integration of
4 management"

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6 **#15** coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of services"
7 OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR
8 "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR
9 coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat*
10 management OR "coordination of management"

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13 **#16** co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of
14 services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes"
15 OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service
16 delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-
17 ordinat* management OR "co-ordination of management"

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20 **#17** horizontal care OR vertical care OR horizontal services OR vertical services OR horizontal
21 programmes OR horizontal programs OR vertical programmes OR vertical programs OR horizontal
22 service delivery OR vertical service delivery OR horizontal services OR vertical services OR horizontal
23 delivery OR vertical management OR vertical management

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25 **#18** "multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR "multi
26 service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR "multi
27 delivery" OR multidelivery OR "multi management"

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29 **#19** #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18

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31 **#20** #3 AND #11 AND #19

32
33 **#21** Developing Countries[Mesh:noexp] OR Africa[Mesh:noexp] OR Africa, Northern[Mesh:noexp] OR
34 Africa South of the Sahara[Mesh:noexp] OR Africa, Central[Mesh:noexp] OR Africa,
35 Eastern[Mesh:noexp] OR Africa, Southern[Mesh:noexp] OR Africa, Western[Mesh:noexp] OR
36 Asia[Mesh:noexp] OR Asia, Central[Mesh:noexp] OR Asia, Southeastern[Mesh:noexp] OR Asia,
37 Western[Mesh:noexp] OR Caribbean Region[Mesh:noexp] OR West Indies[Mesh:noexp] OR South
38 America[Mesh:noexp] OR Latin America[Mesh:noexp] OR Central America[Mesh:noexp] OR
39 Afghanistan[Mesh:noexp] OR Albania[Mesh:noexp] OR Algeria[Mesh:noexp] OR American
40 Samoa[Mesh:noexp] OR Angola[Mesh:noexp] OR "Antigua and Barbuda"[Mesh:noexp] OR
41 Argentina[Mesh:noexp] OR Armenia[Mesh:noexp] OR Azerbaijan[Mesh:noexp] OR
42 Bahrain[Mesh:noexp] OR Bangladesh[Mesh:noexp] OR Barbados[Mesh:noexp] OR
43 Benin[Mesh:noexp] OR Byelarus[Mesh:noexp] OR Belize[Mesh:noexp] OR Bhutan[Mesh:noexp] OR
44 Bolivia[Mesh:noexp] OR Bosnia-Herzegovina[Mesh:noexp] OR Botswana[Mesh:noexp] OR
45 Brazil[Mesh:noexp] OR Bulgaria[Mesh:noexp] OR Burkina Faso[Mesh:noexp] OR
46 Burundi[Mesh:noexp] OR Cambodia[Mesh:noexp] OR Cameroon[Mesh:noexp] OR Cape
47 Verde[Mesh:noexp] OR Central African Republic[Mesh:noexp] OR Chad[Mesh:noexp] OR
48 Chile[Mesh:noexp] OR China[Mesh:noexp] OR Colombia[Mesh:noexp] OR Comoros[Mesh:noexp] OR
49 Congo[Mesh:noexp] OR Costa Rica[Mesh:noexp] OR Cote d'Ivoire[Mesh:noexp] OR
50 Croatia[Mesh:noexp] OR Cuba[Mesh:noexp] OR Cyprus[Mesh:noexp] OR
51 Czechoslovakia[Mesh:noexp] OR Czech Republic[Mesh:noexp] OR Slovakia[Mesh:noexp] OR
52 Djibouti[Mesh:noexp] OR "Democratic Republic of the Congo"[Mesh:noexp] OR
53 Dominica[Mesh:noexp] OR Dominican Republic[Mesh:noexp] OR East Timor[Mesh:noexp] OR
54 Ecuador[Mesh:noexp] OR Egypt[Mesh:noexp] OR El Salvador[Mesh:noexp] OR Eritrea[Mesh:noexp]
55 OR Estonia[Mesh:noexp] OR Ethiopia[Mesh:noexp] OR Fiji[Mesh:noexp] OR Gabon[Mesh:noexp] OR
56 Gambia[Mesh:noexp] OR "Georgia (Republic)"[Mesh:noexp] OR Ghana[Mesh:noexp] OR
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1
2 Greece[Mesh:noexp] OR Grenada[Mesh:noexp] OR Guatemala[Mesh:noexp] OR
3 Guinea[Mesh:noexp] OR Guinea-Bissau[Mesh:noexp] OR Guam[Mesh:noexp] OR
4 Guyana[Mesh:noexp] OR Haiti[Mesh:noexp] OR Honduras[Mesh:noexp] OR Hungary[Mesh:noexp]
5 OR India[Mesh:noexp] OR Indonesia[Mesh:noexp] OR Iran[Mesh:noexp] OR Iraq[Mesh:noexp] OR
6 Jamaica[Mesh:noexp] OR Jordan[Mesh:noexp] OR Kazakhstan[Mesh:noexp] OR Kenya[Mesh:noexp]
7 OR Korea[Mesh:noexp] OR Kosovo[Mesh:noexp] OR Kyrgyzstan[Mesh:noexp] OR Laos[Mesh:noexp]
8 OR Latvia[Mesh:noexp] OR Lebanon[Mesh:noexp] OR Lesotho[Mesh:noexp] OR Liberia[Mesh:noexp]
9 OR Libya[Mesh:noexp] OR Lithuania[Mesh:noexp] OR Macedonia[Mesh:noexp] OR
10 Madagascar[Mesh:noexp] OR Malaysia[Mesh:noexp] OR Malawi[Mesh:noexp] OR Mali[Mesh:noexp]
11 OR Malta[Mesh:noexp] OR Mauritania[Mesh:noexp] OR Mauritius[Mesh:noexp] OR
12 Mexico[Mesh:noexp] OR Micronesia[Mesh:noexp] OR Middle East[Mesh:noexp] OR
13 Moldova[Mesh:noexp] OR Mongolia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR
14 Morocco[Mesh:noexp] OR Mozambique[Mesh:noexp] OR Myanmar[Mesh:noexp] OR
15 Namibia[Mesh:noexp] OR Nepal[Mesh:noexp] OR Netherlands Antilles[Mesh:noexp] OR New
16 Caledonia[Mesh:noexp] OR Nicaragua[Mesh:noexp] OR Niger[Mesh:noexp] OR Nigeria[Mesh:noexp]
17 OR Oman[Mesh:noexp] OR Pakistan[Mesh:noexp] OR Palau[Mesh:noexp] OR Panama[Mesh:noexp]
18 OR Papua New Guinea[Mesh:noexp] OR Paraguay[Mesh:noexp] OR Peru[Mesh:noexp] OR
19 Philippines[Mesh:noexp] OR Poland[Mesh:noexp] OR Portugal[Mesh:noexp] OR Puerto
20 Rico[Mesh:noexp] OR Romania[Mesh:noexp] OR Russia[Mesh:noexp] OR "Russia (Pre-
21 1917)"[Mesh:noexp] OR Rwanda[Mesh:noexp] OR "Saint Kitts and Nevis"[Mesh:noexp] OR Saint
22 Lucia[Mesh:noexp] OR "Saint Vincent and the Grenadines"[Mesh:noexp] OR Samoa[Mesh:noexp] OR
23 Saudi Arabia[Mesh:noexp] OR Senegal[Mesh:noexp] OR Serbia[Mesh:noexp] OR
24 Montenegro[Mesh:noexp] OR Seychelles[Mesh:noexp] OR Sierra Leone[Mesh:noexp] OR
25 Slovenia[Mesh:noexp] OR Sri Lanka[Mesh:noexp] OR Somalia[Mesh:noexp] OR South
26 Africa[Mesh:noexp] OR Sudan[Mesh:noexp] OR Suriname[Mesh:noexp] OR Swaziland[Mesh:noexp]
27 OR Syria[Mesh:noexp] OR Tajikistan[Mesh:noexp] OR Tanzania[Mesh:noexp] OR
28 Thailand[Mesh:noexp] OR Togo[Mesh:noexp] OR Tonga[Mesh:noexp] OR "Trinidad and
29 Tobago"[Mesh:noexp] OR Tunisia[Mesh:noexp] OR Turkey[Mesh:noexp] OR
30 Turkmenistan[Mesh:noexp] OR Uganda[Mesh:noexp] OR Ukraine[Mesh:noexp] OR
31 Uruguay[Mesh:noexp] OR USSR[Mesh:noexp] OR Uzbekistan[Mesh:noexp] OR Vanuatu[Mesh:noexp]
32 OR Venezuela[Mesh:noexp] OR Vietnam[Mesh:noexp] OR Yemen[Mesh:noexp] OR
33 Yugoslavia[Mesh:noexp] OR Zambia[Mesh:noexp] OR Zimbabwe[Mesh:noexp]

41 **#22** Macedonia[tw] OR Madagascar[tw] OR Malagasy Republic[tw] OR Malaysia[tw] OR Malaya[tw]
42 OR Malay[tw] OR Sabah[tw] OR Sarawak[tw] OR Malawi[tw] OR Nyasaland[tw] OR Mali[tw] OR
43 Malta[tw] OR Marshall Islands[tw] OR Mauritania[tw] OR Mauritius[tw] OR Agalega Islands[tw] OR
44 Mexico[tw] OR Micronesia[tw] OR Middle East[tw] OR Moldova[tw] OR Moldavia[tw] OR
45 Moldovan[tw] OR Mongolia[tw] OR Montenegro[tw] OR Morocco[tw] OR Ifni[tw] OR
46 Mozambique[tw] OR Myanmar[tw] OR Myanma[tw] OR Burma[tw] OR Namibia[tw] OR Nepal[tw] OR
47 Netherlands Antilles[tw] OR New Caledonia[tw] OR Nicaragua[tw] OR Niger[tw] OR Nigeria[tw] OR
48 Northern Mariana Islands[tw] OR Oman[tw] OR Muscat[tw] OR Pakistan[tw] OR Palau[tw] OR
49 Palestine[tw] OR Panama[tw] OR Paraguay[tw] OR Peru[tw] OR Philippines[tw] OR Philipines[tw] OR
50 Phillipines[tw] OR Phillippines[tw] OR Poland[tw] OR Portugal[tw] OR Puerto Rico[tw] OR
51 Romania[tw] OR Rumania[tw] OR Roumania[tw] OR Russia[tw] OR Russian[tw] OR Rwanda[tw] OR
52 Ruanda[tw] OR Saint Kitts[tw] OR St Kitts[tw] OR Nevis[tw] OR Saint Lucia[tw] OR St Lucia[tw] OR
53 Saint Vincent[tw] OR St Vincent[tw] OR Grenadines[tw] OR Samoa[tw] OR Samoan Islands[tw] OR
54 Navigator Island[tw] OR Navigator Islands[tw] OR Sao Tome[tw] OR Saudi Arabia[tw] OR Senegal[tw]
55 OR Serbia[tw] OR Montenegro[tw] OR Seychelles[tw] OR Sierra Leone[tw] OR Slovenia[tw] OR Sri
56 Lanka[tw] OR Ceylon[tw] OR Solomon Islands[tw] OR Somalia[tw] OR Sudan[tw] OR Suriname[tw] OR
57 Surinam[tw] OR Swaziland[tw] OR Syria[tw] OR Tajikistan[tw] OR Tadzhikistan[tw] OR Tadjikistan[tw]

1
2 OR Tadjik[tw] OR Tanzania[tw] OR Thailand[tw] OR Togo[tw] OR Togolese Republic[tw] OR
3 Tonga[tw] OR Trinidad[tw] OR Tobago[tw] OR Tunisia[tw] OR Turkey[tw] OR Turkmenistan[tw] OR
4 Turkmen[tw] OR Uganda[tw] OR Ukraine[tw] OR Uruguay[tw] OR USSR[tw] OR Soviet Union[tw] OR
5 Union of Soviet Socialist Republics[tw] OR Uzbekistan[tw] OR Uzbek OR Vanuatu[tw] OR New
6 Hebrides[tw] OR Venezuela[tw] OR Vietnam[tw] OR Viet Nam[tw] OR West Bank[tw] OR Yemen[tw]
7 OR Yugoslavia[tw] OR Zambia[tw] OR Zimbabwe[tw] OR Rhodesia[tw]
8
9

10 **#23** Africa[tw] OR Asia[tw] OR Caribbean[tw] OR West Indies[tw] OR South America[tw] OR Latin
11 America[tw] OR Central America[tw] OR Afghanistan[tw] OR Albania[tw] OR Algeria[tw] OR
12 Angola[tw] OR Antigua[tw] OR Barbuda[tw] OR Argentina[tw] OR Armenia[tw] OR Armenian[tw] OR
13 Aruba[tw] OR Azerbaijan[tw] OR Bahrain[tw] OR Bangladesh[tw] OR Barbados[tw] OR Benin[tw] OR
14 Byelarus[tw] OR Byelorussian[tw] OR Belarus[tw] OR Belorussian[tw] OR Belorussia[tw] OR Belize[tw]
15 OR Bhutan[tw] OR Bolivia[tw] OR Bosnia[tw] OR Herzegovina[tw] OR Hercegovina[tw] OR
16 Botswana[tw] OR Brasil[tw] OR Brazil[tw] OR Bulgaria[tw] OR Burkina Faso[tw] OR Burkina Fasso[tw]
17 OR Upper Volta[tw] OR Burundi[tw] OR Urundi[tw] OR Cambodia[tw] OR Khmer Republic[tw] OR
18 Kampuchea[tw] OR Cameroon[tw] OR Cameroons[tw] OR Cameron[tw] OR Camerons[tw] OR Cape
19 Verde[tw] OR Central African Republic[tw] OR Chad[tw] OR Chile[tw] OR China[tw] OR Colombia[tw]
20 OR Comoros[tw] OR Comoro Islands[tw] OR Comores[tw] OR Mayotte[tw] OR Congo[tw] OR
21 Zaire[tw] OR Costa Rica[tw] OR Cote d'Ivoire[tw] OR Ivory Coast[tw] OR Croatia[tw] OR Cuba[tw] OR
22 Cyprus[tw] OR Czechoslovakia[tw] OR Czech Republic[tw] OR Slovakia[tw] OR Slovak Republic[tw] OR
23 Djibouti[tw] OR French Somaliland[tw] OR Dominica[tw] OR Dominican Republic[tw] OR East
24 Timor[tw] OR East Timur[tw] OR Timor Leste[tw] OR Ecuador[tw] OR Egypt[tw] OR United Arab
25 Republic[tw] OR El Salvador[tw] OR Eritrea[tw] OR Estonia[tw] OR Ethiopia[tw] OR Fiji[tw] OR
26 Gabon[tw] OR Gabonese Republic[tw] OR Gambia[tw] OR Gaza[tw] OR Georgia Republic[tw] OR
27 Georgian Republic[tw] OR Ghana[tw] OR Gold Coast[tw] OR Greece[tw] OR Grenada[tw] OR
28 Guatemala[tw] OR Guinea[tw] OR Guam[tw] OR Guiana[tw] OR Guyana[tw] OR Haiti[tw] OR
29 Honduras[tw] OR Hungary[tw] OR India[tw] OR Maldives[tw] OR Indonesia[tw] OR Iran[tw] OR
30 Iraq[tw] OR Isle of Man[tw] OR Jamaica[tw] OR Jordan[tw] OR Kazakhstan[tw] OR Kazakh[tw] OR
31 Kenya[tw] OR Kiribati[tw] OR Korea[tw] OR Kosovo[tw] OR Kyrgyzstan[tw] OR Kirghizia[tw] OR Kyrgyz
32 Republic[tw] OR Kirghiz[tw] OR Kirgizstan[tw] OR "Lao PDR"[tw] OR Laos[tw] OR Latvia[tw] OR
33 Lebanon[tw] OR Lesotho[tw] OR Basutoland[tw] OR Liberia[tw] OR Libya[tw] OR Lithuania[tw]
34
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39

40 **#24** "developing country"[tw] OR "developing countries"[tw] OR "developing nation"[tw] OR
41 "developing nations"[tw] OR "developing population"[tw] OR "developing populations"[tw] OR
42 "developing world"[tw] OR "less developed country"[tw] OR "less developed countries"[tw] OR "less
43 developed nation"[tw] OR "less developed nations"[tw] OR "less developed population"[tw] OR "less
44 developed populations"[tw] OR "less developed world"[tw] OR "lesser developed country"[tw] OR
45 "lesser developed countries"[tw] OR "lesser developed nation"[tw] OR "lesser developed
46 nations"[tw] OR "lesser developed population"[tw] OR "lesser developed populations"[tw] OR "lesser
47 developed world"[tw] OR "under developed country"[tw] OR "under developed countries"[tw] OR
48 "under developed nation"[tw] OR "under developed nations"[tw] OR "under developed
49 population"[tw] OR "under developed populations"[tw] OR "under developed world"[tw] OR
50 "underdeveloped country"[tw] OR "underdeveloped countries"[tw] OR "underdeveloped nation"[tw]
51 OR "underdeveloped nations"[tw] OR "underdeveloped population"[tw] OR "underdeveloped
52 populations"[tw] OR "underdeveloped world"[tw] OR "middle income country"[tw] OR "middle
53 income countries"[tw] OR "middle income nation"[tw] OR "middle income nations"[tw] OR "middle
54 income population"[tw] OR "middle income populations"[tw] OR "low income country"[tw] OR "low
55 income countries"[tw] OR "low income nation"[tw] OR "low income nations"[tw] OR "low income
56 population"[tw] OR "low income populations"[tw] OR "lower income country"[tw] OR "lower income
57 countries"[tw] OR "lower income nation"[tw] OR "lower income nations"[tw] OR "lower income
58 population"[tw] OR "lower income populations"[tw] OR "underserved country"[tw] OR "underserved
59 population"[tw] OR "underserved nations"[tw] OR "underserved populations"[tw] OR "underserved
60 world"[tw]

countries"[tw] OR "underserved nation"[tw] OR "underserved nations"[tw] OR "underserved population"[tw] OR "underserved populations"[tw] OR "underserved world"[tw] OR "under served country"[tw] OR "under served countries"[tw] OR "under served nation"[tw] OR "under served nations"[tw] OR "under served population"[tw] OR "under served populations"[tw] OR "under served world"[tw] OR "deprived country"[tw] OR "deprived countries"[tw] OR "deprived nation"[tw] OR "deprived nations"[tw] OR "deprived population"[tw] OR "deprived populations"[tw] OR "deprived world"[tw] OR "poor country"[tw] OR "poor countries"[tw] OR "poor nation"[tw] OR "poor nations"[tw] OR "poor population"[tw] OR "poor populations"[tw] OR "poor world"[tw] OR "poorer country"[tw] OR "poorer countries"[tw] OR "poorer nation"[tw] OR "poorer nations"[tw] OR "poorer population"[tw] OR "poorer populations"[tw] OR "poorer world"[tw] OR "developing economy"[tw] OR "developing economies"[tw] OR "less developed economy"[tw] OR "less developed economies"[tw] OR "lesser developed economy"[tw] OR "lesser developed economies"[tw] OR "under developed economy"[tw] OR "under developed economies"[tw] OR "underdeveloped economy"[tw] OR "underdeveloped economies"[tw] OR "middle income economy"[tw] OR "middle income economies"[tw] OR "low income economy"[tw] OR "low income economies"[tw] OR "lower income economy"[tw] OR "lower income economies"[tw] OR "low gdp"[tw] OR "low gnp"[tw] OR "low gross domestic"[tw] OR "low gross national"[tw] OR "lower gdp"[tw] OR "lower gnp"[tw] OR "lower gross domestic"[tw] OR "lower gross national"[tw] OR lmic[tw] OR lmics[tw] OR "third world"[tw] OR "lami country"[tw] OR "lami countries"[tw] OR "transitional country"[tw] OR "transitional countries"[tw]

#25 #21 OR #22 OR #23 OR #24

#26 #20 AND #25

2. CENTRAL

#1 MeSH descriptor: [Hypertension] explode all trees

#2 hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic

#3 diabetes OR "diabetes mellitus"

#4 MeSH descriptor: [Diabetes Mellitus] explode all trees

#5 #1 OR #2 OR #3 OR #4

#6 dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR "low density lipoprotein" OR "high density lipoprotein" OR "low-density lipoprotein" OR "high-density lipoprotein"

#7 MeSH descriptor: [Dyslipidemias] explode all trees

#8 HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR "hiv infection" OR "hiv infections" OR "human immunodeficiency virus" OR "human immune deficiency virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus"

#9 (human immun*) AND (deficiency virus)

#10 "acquired immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-deficiency syndrome" OR "acquired immune-deficiency syndrome"

#11 (acquired immun*) AND (deficiency syndrome)

#12 HIVAIDS

- 1
- 2 #13 MeSH descriptor: [HIV Infections] explode all trees
- 3
- 4 #14 MeSH descriptor: [HIV] explode all trees
- 5
- 6 #15 tuberculosis OR tuberculoses OR tb
- 7
- 8 #16 MeSH descriptor: [Tuberculosis] explode all trees
- 9
- 10 #17 "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable
- 11 disease" OR "non-communicable diseases" OR NCD OR NCDs
- 12
- 13 #18 MeSH descriptor: [Noncommunicable Diseases] explode all trees
- 14
- 15 #19 comorbidity OR comorbidities OR comorbid OR co-morbid OR co-morbidity OR co-
- 16 morbidity OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity"
- 17
- 18 #20 MeSH descriptor: [Multimorbidity] explode all trees
- 19
- 20 #21 MeSH descriptor: [Comorbidity] explode all trees
- 21
- 22 #22 multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-
- 23 condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple
- 24 syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent
- 25 illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing
- 26 illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing
- 27 condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR
- 28 cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-
- 29 occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring
- 30 condition* OR co occurring condition* OR cooccurring condition*
- 31
- 32
- 33 #23 chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle"
- 34
- 35 #24 MeSH descriptor: [Multiple Chronic Conditions] explode all trees
- 36
- 37 #25 MeSH descriptor: [Chronic Disease] explode all trees
- 38
- 39 #26 #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
- 40 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
- 41
- 42 #27 MeSH descriptor: [Delivery of Health Care, Integrated] explode all trees
- 43
- 44 #28 "delivery of care" OR "delivery of health" OR "delivery of healthcare"
- 45
- 46 #29 MeSH descriptor: [Comprehensive Health Care] explode all trees
- 47
- 48 #30 "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health"
- 49
- 50 #31 MeSH descriptor: [Continuity of Patient Care] explode all trees 23230
- 51
- 52 #32 "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity
- 53 of healthcare"
- 54
- 55 #33 MeSH descriptor: [Patient-Centered Care] explode all trees
- 56
- 57 #34 "patient centered care" OR "patient centred care"
- 58
- 59 #35 MeSH descriptor: [Referral and Consultation] explode all trees
- 60
- #36 referral AND consultation

1
2 #37 integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR
3 integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of
4 programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR
5 "integration of services" OR integrat* delivery OR integrat* management OR "integration of
6 management"

7
8 #38 coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of
9 services" OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR
10 "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR
11 coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat*
12 management OR "coordination of management"

13
14 #39 co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of
15 services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes"
16 OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service
17 delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-
18 ordinat* management OR "co-ordination of management"

19
20 #40 "horizontal care" OR "vertical care" OR "horizontal services" OR "vertical services" OR
21 "horizontal programmes" OR "horizontal programs" OR "vertical programmes" OR "vertical
22 programs" OR "horizontal service delivery" OR "vertical service delivery" OR "horizontal services" OR
23 "vertical services" OR "horizontal delivery" OR "vertical management" OR "vertical management"

24
25 #41 "multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR
26 "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR
27 "multi delivery" OR multidelivery OR "multi management"

28
29 #42 #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR
30 #39 OR #40 OR #41

31
32 #43 #5 AND #26 AND #42

33
34 #44 (Africa or Asia or Caribbean or "West Indies" or "South America" or "Latin America" or
35 "Central America")

36
37 #45 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia
38 or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
39 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
40 Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or "Burkina
41 Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or
42 Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or
43 Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or
44 Congo or "Republic of Congo" or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or
45 Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic")

46
47 #46 (Djibouti or "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or
48 "East Timur" or "Timor Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or
49 Eritrea or Estonia or Ethiopia or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia
50 or Georgian or Ghana or "Gold Coast" or Greece or Grenada or Guatemala or Guinea or Guam or
51 Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or
52 "Isle of Man" or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or
53 Kyrgyzstan or Kirghizia or "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or
54 Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania)

1
2 #47 (Macedonia or Madagascar or "Malagasy Republic" or Malaysia or Malaya or Malay or Sabah
3 or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius
4 or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldavia or Moldovan
5 or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or
6 Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or
7 "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or
8 Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or
9 "Puerto Rico")
10
11

12 #48 (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts"
13 or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or
14 Samoa or "Samoa Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi
15 Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka"
16 or Ceylon or "Solomon Islands" or Somalia or Sudan or South-sudan or Suriname or Surinam or
17 Swaziland or Syria or Tajikistan or Tadzjikistan or Tadjikistan or Tadjhik or Tanzania or Thailand or
18 Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or
19 Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist
20 Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet
21 Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia)
22
23
24

25 #49 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle
26 income" or low* NEXT income or underserved or "under served" or deprived or poor*) NEXT
27 (countr* or nation* or population* or world)
28

29 #50 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle
30 income" or low* NEXT income) NEXT (economy or economies)
31

32 #51 low* NEXT (gdp or gnp or "gross domestic" or "gross national")
33

34 #52 (low NEAR/3 middle NEAR/3 countr*)
35

36 #53 (Imic or Imics or "third world" or "lami country" or "lami countries")
37

38 #54 ("transitional country" or "transitional countries")
39

40 #55 #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54
41

42 #56 #43 AND #55
43

44 3. Embase

45
46 1 integrated health care system/ or integrated health care.mp.
47

48 2 *patient care/
49

50 3 ("comprehensive healthcare" or "comprehensive care" or "Continuity of Patient Care" or
51 "continuity of care" or "continuity of healthcare" or "Patient-Centered Care").ti.
52

53 4 ("comprehensive healthcare" or "comprehensive care" or "Continuity of Patient Care" or
54 "continuity of care" or "continuity of healthcare" or "Patient-Centered Care").ab.
55

56 5 (referral and consultation).mp.
57

58 6 ((integrated or integration) adj2 (care or services or program* or delivery or management)).ab.
59

60 7 ((integrated or integration) adj2 (care or services or program* or delivery or management)).ti.

- 1
2 8 ((coordination or coordinated) adj2 (care or services or program* or delivery or management)).ti.
3
4 9 ((coordination or coordinated) adj2 (care or services or program* or delivery or
5 management)).ab.
6
7 10 ((horizontal or vertical) adj2 (care or services or program* or delivery or management)).ab.
8
9 11 ((horizontal or vertical) adj2 (care or services or program* or delivery or management)).ti.
10
11 12 (Multiteam or multi-team or multi-care or multicare or multclinic or multiservice or multi-
12 program* or multidelivery or multi-management).ti. or (Multiteam or multi-team or multi-care or
13 multicare or multclinic or multiservice or multi-program* or multidelivery or multi-management).ab.
14
15 13 *health care delivery/
16
17 14 (delivery adj2 healthcare).mp.
18
19 15 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
20
21 16 hypertension.mp. or *hypertension/
22
23 17 (hypertension or hypertention or "blood pressure" or "arterial pressure" or systolic or
24 diastolic).ti. or (hypertension or hypertention or "blood pressure" or "arterial pressure" or systolic or
25 diastolic).ab.
26
27 18 diabetes.mp. or diabetes mellitus/
28
29 19 exp Neoplasms/
30
31 20 cardiovascular disease/
32
33 21 "heart disease".ti. or "heart disease*".ab.
34
35 22 *kidney disease/
36
37 23 ("kidney failure" or "renal failure" or "chronic kidney disease" or "renal disease").ti. or ("kidney
38 failure" or "renal failure" or "chronic kidney disease" or "renal disease").ab.
39
40 24 (dyslipidaemia or dyslipidemia or cholesterol or LDL or HDL or triglyceride or triglycerides or low
41 density lipoprotein or high density lipoprotein or low-density lipoprotein or high-density
42 lipoprotein).ti. or (dyslipidaemia or dyslipidemia or cholesterol or LDL or HDL or triglyceride or
43 triglycerides or low density lipoprotein or high density lipoprotein or low-density lipoprotein or high-
44 density lipoprotein).ab.
45
46 25 HIV infection.mp. or Human immunodeficiency virus infection/
47
48 26 tuberculosis/
49
50 27 non-communicable diseases.mp. or non communicable disease/
51
52 28 comorbidity.mp. or comorbidity/
53
54 29 multimorbidity.mp. or multiple chronic conditions/
55
56 30 (multi-disease* or multidisease* or multi disease* or multiple condition* or multi-condition* or
57 multi condition* or multiple illness* or multi-illness* or multi illness* or multiple syndrome* or
58 multi-syndrome* or multi syndrome* or concurrent condition* or concurrent illness* or concurrent
59 disease* or co-existing disease* or coexisting disease* or co-existing illness* or coexisting illness* or
60 co-existing syndrome* or coexisting syndrome* or co-existing condition* or coexisting condition* or
co-occurring disease* or co occurring disease* or cooccurring disease* or co-occurring illness* or co

1
2 occurring illness* or cooccurring illness* or co-occurring syndrome* or co occurring syndrome* or
3 cooccurring syndrome* or co-occurring condition* or co occurring condition* or cooccurring
4 condition*).ti.
5

6 31 (multi-disease* or multidisease* or multi disease* or multiple condition* or multi-condition* or
7 multi condition* or multiple illness* or multi-illness* or multi illness* or multiple syndrome* or
8 multi-syndrome* or multi syndrome* or concurrent condition* or concurrent illness* or concurrent
9 disease* or co-existing disease* or coexisting disease* or co-existing illness* or coexisting illness* or
10 co-existing syndrome* or coexisting syndrome* or co-existing condition* or coexisting condition* or
11 co-occurring disease* or co occurring disease* or cooccurring disease* or co-occurring illness* or co
12 occurring illness* or cooccurring illness* or co-occurring syndrome* or co occurring syndrome* or
13 cooccurring syndrome* or co-occurring condition* or co occurring condition* or cooccurring
14 condition*).ab.
15

16
17 32 (chronic disease* or lifestyle disease*).mp.
18

19 33 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
20

21 34 15 and 33
22

23 35 developing countries.mp. or developing country/
24

25 36 (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central
26 America).mp.
27

28 37 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or
29 Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
30 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
31 Herzegovina or Hercegovina or Botswana or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or
32 Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or
33 Camerons or Cameroon or Camerons or Cape Verde or Central African Republic or Chad or Chile or
34 China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa
35 Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Czechoslovakia or Czech Republic
36 or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or
37 East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or
38 Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia
39 Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea
40 or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or
41 Iran or Iraq or Isle of Man or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea
42 or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or
43 Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or
44 Madagascar or Malagasy Republic or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or
45 Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or
46 Mexico or Micronesia or Middle East or Moldova or Moldavia or Moldovan or Mongolia or
47 Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or
48 Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern
49 Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru
50 or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Puerto Rico or
51 Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts
52 or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan
53 Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia or
54 Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or
55 Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or
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Tadjikistan or TadzhiK or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia).mp.

38 ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ab.

39 ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ab. or ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti.

40 ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti.

41 (low* adj (gdp or gnp or gross domestic or gross national)).ti. or (low* adj (gdp or gnp or gross domestic or gross national)).ab.

42 (low adj3 middle adj3 countr*).ti. or (low adj3 middle adj3 countr*).ab.

43 (Imic or Imics or third world or lami countr*).ti. or (Imic or Imics or third world or lami countr*).ab.

44 transitional countr*.ti. or transitional countr*.ab.

45 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46 34 and 45

4. Web of Science (Core collection)

TOPIC: (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic OR diabetes OR "diabetes mellitus") AND TOPIC: (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein OR HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS OR tuberculosis OR tuberculoses OR tb OR "noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR NCD OR NCDs OR comorbid* OR co-morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity" OR multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring condition* OR cooccurring condition* OR chronic disease* OR lifestyle disease* OR "diseases of

1 lifestyle" OR "disease of lifestyle" OR "Multiple Chronic Conditions") AND TOPIC: ("delivery of care"
2 OR "delivery of health" OR "delivery of healthcare" OR "Comprehensive Health Care" OR
3 "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "Continuity of
4 Patient Care" OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR
5 "continuity of healthcare" OR "Patient-Centered Care" OR "patient centered care" OR "patient
6 centred care" OR "Referral and Consultation" OR integrat* care OR "integration of care" OR integrat*
7 services OR "integration of services" OR integrat* programmes OR integrat* programs OR
8 "integration of programmes" OR "integration of programs" OR integrat* service delivery OR
9 "integration of service delivery" OR integrat* services OR "integration of services" OR integrat*
10 delivery OR integrat* management OR "integration of management" OR coordinat* care OR
11 "coordination of care" OR coordinat* services OR "coordination of services" OR coordinat*
12 programmes OR coordinat* programs OR "coordination of programmes" OR "coordination of
13 programs" OR coordinat* service delivery OR "coordination of service delivery" OR coordinat*
14 services OR "coordination of services" OR coordinat* delivery OR coordinat* management OR
15 "coordination of management" OR co-ordinat* care OR "co-ordination of care" OR co-ordinat*
16 services OR "co-ordination of services" OR co-ordinat* programmes OR co-ordinat* programs OR
17 "co-ordination of programmes" OR "co-ordination of programs" OR co-ordinat* service delivery OR
18 "co-ordination of service delivery" OR co-ordinat* services OR "co-ordination of services" OR co-
19 ordinat* delivery OR co-ordinat* management OR "co-ordination of management" OR horizontal
20 care OR vertical care OR horizontal services OR vertical services OR horizontal programmes OR
21 horizontal programs OR vertical programmes OR vertical programs OR horizontal service delivery OR
22 vertical service delivery OR horizontal services OR vertical services OR horizontal delivery OR vertical
23 management OR vertical management OR "multi team" OR multiteam "multi care" OR multicare OR
24 "multi clinic" OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram
25 OR "multi programme" OR "multi delivery" OR multidelivery OR "multi management") AND TOPIC:
26 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or
27 Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or
28 Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or
29 Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or "Burkina
30 Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or
31 Cameroon or Camerouns or Cameron or Camerons or "Cape Verde" or "Central African Republic" or
32 Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or
33 Congo or "Republic of Congo" or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or
34 Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic" OR Djibouti or
35 "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or "East Timur" or "Timor
36 Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or Eritrea or Estonia or Ethiopia
37 or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia or Georgian or Ghana or "Gold
38 Coast" or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or
39 Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or "Isle of Man" or Jamaica or
40 Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or
41 "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or Lebanon or Lesotho or
42 Basutoland or Liberia or Libya or Lithuania OR Macedonia or Madagascar or "Malagasy Republic" or
43 Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or
44 "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or
45 "Middle East" or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni
46 or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or
47 "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat
48 or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or
49 Phillipines or Phillippines or Poland or Portugal or "Puerto Rico" OR Romania or Rumania or
50 Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint

Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoa Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands" or Somalia or Sudan or South-Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadjikistan or Tadjikistan or Tadjik or Tanzania or Thailand or Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia OR "developing country" OR "gross domestic" OR "gross national" OR "low income" OR "low-income" OR "middle income" OR "middle-income" OR LMIC OR LMICs OR "transitional country" OR "transitional countries" OR "third world" OR "lami country" OR "lami countries" OR "under developed" OR underdeveloped OR under-developed)

5. CINAHL

S1 MW hypertension OR ((hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)) OR ((diabetes OR "diabetes mellitus")) OR MW "Diabetes Mellitus" [320,859]

S2 ((dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein)) OR MW Dyslipidemias OR MW HIV OR MW HIV infections OR ((HIV OR hiv-1 OR hiv-2* OR hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS)) OR ((tuberculosis OR tuberculoses OR tb)) OR MW tuberculosis OR (("noncommunicable disease" OR "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR NCD OR NCDs)) OR MW "noncommunicable diseases" OR ((comorbid* OR co-morbid* OR "co morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity")) OR MW multimorbidity OR MW comorbidity [282,133]

S3 ((multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition* OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome* OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring condition* OR cooccurring condition*)) OR ((chronic disease* OR lifestyle disease* OR "diseases of lifestyle" OR "disease of lifestyle")) OR MW "Multiple Chronic Conditions" OR MW "Chronic Disease" [141,677]

S4 S2 OR S3 [399,117]

S5 MW "Delivery of Health Care, Integrated" OR MW "Comprehensive Health Care" OR MW "Continuity of Patient Care" OR MW "Patient-Centered Care" [38488]

S6 (("delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "comprehensive healthcare" OR "comprehensive care" OR "comprehensive health" OR "continuity of patient care" OR "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "patient centered

care" OR "patient centred care") OR ((referral AND consultation)) OR MW ("Referral and Consultation") OR ((integrat* care OR "integration of care" OR integrat* services OR "integration of services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR "integration of programs" OR integrat* service delivery OR "integration of service delivery" OR integrat* services OR "integration of services" OR integrat* delivery OR integrat* management OR "integration of management")) OR ((coordinat* care OR "coordination of care" OR coordinat* services OR "coordination of services" OR coordinat* programmes OR coordinat* programs OR "coordination of programmes" OR "coordination of programs" OR coordinat* service delivery OR "coordination of service delivery" OR coordinat* services OR "coordination of services" OR coordinat* delivery OR coordinat* management OR "coordination of management")) OR ((co-ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes" OR "co-ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service delivery" OR co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-ordinat* management OR "co-ordination of management")) OR ((horizontal care OR vertical care OR horizontal services OR vertical services OR horizontal programmes OR horizontal programs OR vertical programmes OR vertical programs OR horizontal service delivery OR vertical service delivery OR horizontal services OR vertical services OR horizontal delivery OR vertical management OR vertical management)) OR (("multi team" OR multiteam "multi care" OR multicare OR "multi clinic" OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi programme" OR "multi delivery" OR multidelivery OR "multi management")) [145,695]

S7 S5 OR S6 [145,695]

S8 "((developing country" OR "gross domestic" OR "gross national" OR "low income" OR "low-income" OR "middle income" OR "middle-income" OR LMIC OR LMICs OR "transitional country" OR "transitional countries" OR "third world" OR "lami country" OR "lami countries" OR "under developed" OR underdeveloped OR under-developed)) OR ("low- and middle-income") OR ("low and middle income")" [32,715]

S9 S1 AND S4 AND S7 AND S8 [71]

S10 PY 2019 [381,913]

S11 PY 2018 [419,274]

S12 S10 OR S11 [801,187]

S13 S9 AND S12 [17]

6. Africa-Wide Information (via EBSCO host)

S1 SM hypertension OR (hypertension OR hypertention OR "blood pressure" OR "arterial pressure" OR systolic OR diastolic)) OR ((diabetes OR "diabetes mellitus")) OR SM "Diabetes Mellitus"

S2 (dyslipidaemia OR dyslipidemia OR cholesterol OR LDL OR HDL OR triglyceride OR triglycerides OR low density lipoprotein OR high density lipoprotein OR low-density lipoprotein OR high-density lipoprotein) OR SM Dyslipidemias OR SM HIV OR SM HIV infections OR (HIV OR hiv-1 OR hiv-2* OR

1 hiv1 OR hiv2 OR hiv infect* OR "human immunodeficiency virus" OR "human immune deficiency
 2 virus" OR "human immuno-deficiency virus" OR "human immune-deficiency virus" OR "acquired
 3 immunodeficiency syndromes" OR "acquired immune deficiency syndrome" OR "acquired immuno-
 4 deficiency syndrome" OR "acquired immune-deficiency syndrome" OR HIV/AIDS) OR (tuberculosis
 5 OR tuberculoses OR tb) OR SM tuberculosis OR ("noncommunicable disease" OR
 6 "noncommunicable diseases" OR "non-communicable disease" OR "non-communicable diseases" OR
 7 NCD OR NCDs) OR SM "noncommunicable diseases" OR (comorbid* OR co-morbid* OR "co
 8 morbidity" OR multimorbidity OR multi-morbid OR "multi morbidity") OR SM multimorbidity OR SM
 9 comorbidity

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 11
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 13 **S3** (multi-disease* OR multidisease* OR multi disease* OR multiple condition* OR multi-condition*
 14 OR multi condition* OR multiple illness* OR multi-illness* OR multi illness* OR multiple syndrome*
 15 OR multi-syndrome* OR multi syndrome* OR concurrent condition* OR concurrent illness* OR
 16 concurrent disease* OR co-existing disease* OR coexisting disease* OR co-existing illness* OR
 17 coexisting illness* OR co-existing syndrome* OR coexisting syndrome* OR co-existing condition* OR
 18 coexisting condition* OR co-occurring disease* OR co occurring disease* OR cooccurring disease* OR
 19 co-occurring illness* OR co occurring illness* OR cooccurring illness* OR co-occurring syndrome* OR
 20 co occurring syndrome* OR cooccurring syndrome* OR co-occurring condition* OR co occurring
 21 condition* OR cooccurring condition*) OR (chronic disease* OR lifestyle disease* OR "diseases of
 22 lifestyle" OR "disease of lifestyle") OR SM "Multiple Chronic Conditions" OR SM "Chronic Disease"

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 24
 25
 26 **S4** S2 OR S3

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 28 **S5** AB "Delivery of Health Care, Integrated" OR AB "Comprehensive Health Care" OR AB "Continuity
 29 of Patient Care" OR AB "Patient-Centered Care"

30
 31 **S6** ("delivery of care" OR "delivery of health" OR "delivery of healthcare" OR "comprehensive
 32 healthcare" OR "comprehensive care" OR "comprehensive health" OR "continuity of patient care" OR
 33 "continuity of care" OR "continuity of health" OR "continuity of healthcare" OR "patient centered
 34 care" OR "patient centred care") OR ((referral AND consultation)) OR SM ("Referral and
 35 Consultation") OR (integrat* care OR "integration of care" OR integrat* services OR "integration of
 36 services" OR integrat* programmes OR integrat* programs OR "integration of programmes" OR
 37 "integration of programs" OR integrat* service delivery OR "integration of service delivery" OR
 38 integrat* services OR "integration of services" OR integrat* delivery OR integrat* management OR
 39 "integration of management") OR (coordinat* care OR "coordination of care" OR coordinat*
 40 services OR "coordination of services" OR coordinat* programmes OR coordinat* programs OR
 41 "coordination of programmes" OR "coordination of programs" OR coordinat* service delivery OR
 42 "coordination of service delivery" OR coordinat* services OR "coordination of services" OR
 43 coordinat* delivery OR coordinat* management OR "coordination of management") OR (co-
 44 ordinat* care OR "co-ordination of care" OR co-ordinat* services OR "co-ordination of services" OR
 45 co-ordinat* programmes OR co-ordinat* programs OR "co-ordination of programmes" OR "co-
 46 ordination of programs" OR co-ordinat* service delivery OR "co-ordination of service delivery" OR
 47 co-ordinat* services OR "co-ordination of services" OR co-ordinat* delivery OR co-ordinat*
 48 management OR "co-ordination of management") OR (horizontal care OR vertical care OR
 49 horizontal services OR vertical services OR horizontal programmes OR horizontal programs OR
 50 vertical programmes OR vertical programs OR horizontal service delivery OR vertical service delivery
 51 OR horizontal services OR vertical services OR horizontal delivery OR vertical management OR
 52 vertical management) OR (("multi team" OR multiteam "multi care" OR multicare OR "multi clinic"
 53 OR multiclinic OR "multi service" OR multiservice OR "multi program" OR multiprogram OR "multi
 54 programme" OR "multi delivery" OR multidelivery OR "multi management")

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 60 **S7** S5 OR S6

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2 **S8** "(developing country" OR "gross domestic" OR "gross national" OR "low income" OR "low-
3 income" OR "middle income" OR "middle-income" OR LMIC OR LMICs OR "transitional country" OR
4 "transitional countries" OR "third world" OR "lami country" OR "lami countries" OR "under
5 developed" OR underdeveloped OR under-developed) OR ("low- and middle-income") OR ("low
6 and middle income")"

7
8 **S9** S1 AND S4 AND S7 AND S8
9

10 7. LILACS

11 (Words: hypertension OR "high blood pressure" OR systolic OR diastolic OR diabetes) AND

12 (Words: dyslipidemia OR cholesterol OR HIV OR tuberculosis OR multimorbidity OR comorbidity OR
13 non-communicable disease) AND

14 (Words: LMIC OR low income OR middle income OR low-income OR middle-income OR developing
15 country OR developing countries)
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Supplementary file 2: List of excluded studies and reasons for exclusion

Studies excluded for wrong population	Studies excluded for wrong study design	Studies excluded for wrong intervention
Abrahams-Gessel 2018 ¹ Adomaviciute 2014 ² Alharbi 2014 ³ Miao 2016 ⁴ Myers 2018 ⁵ Rakic 2011 ⁶ Sarrafzadegan 2006 ⁷ Spaak 2017 ⁸	Ajay 2016 ⁹ Al Asmary 2013 ¹⁰ Garrib 2018 ¹¹ Germe 2017 ¹² Kwarisiima 2019 ¹³ Li 2013 ¹⁴ Mahomed 2014 ¹⁵ Narayanan 2012 ¹⁶ Nigatu 2012 ¹⁷ Nyabera 2011 ¹⁸ Patel 2018 ¹⁹ Patel 2015 ²⁰ Rabkin 2018 ²¹ Samb 2010 ²² Sarraf-Zadegan 2003 ²³ Sushilkumar 2015 ²⁴ Tedjokusumo 2003 ²⁵ Tiam 2012 ²⁶ Wasay 2009 ²⁷	Bachmann 2018 ²⁸ Hong 2013 ²⁹ Kowalski 2017 ³⁰ McKee 2011 ³¹ Mendis 2010 ³² Pibernik-Okanovic 2015 ³³ Saleh 2018 ³⁴ Sarrafzadegan 2009 ³⁵ Tourkmani 2018 ³⁶ Wenxi 2017 ³⁷

1. Abrahams-Gessel S, Beratarrechea A, Irazola V, et al. Using mHealth tools to improve access, coverage and treatment of uninsured people with high cardiovascular disease risk in Argentina: a study protocol for a pragmatic cluster randomised trial. *BMJ innovations* 2018;4(3):135-41. doi: 10.1136/bmjinnov-2017-000255
2. Adomaviciute S, Watt H, Soljak M, et al. Impact of the Integrated Care Pilot on HbA1c, cholesterol and systolic blood pressure levels in patients with diabetes. *Diabetic Medicine* 2014;31(SUPPL. 1):175. doi: <http://dx.doi.org/10.1111/dme.12378> 2
3. Alharbi TJ, Tourkmani A, Alkhashan H, et al. Impact of integrated care program on glycemic control and cardiovascular risk in patients with type 2 diabetes; Interventional controlled study. *Diabetes Research and Clinical Practice* 2014;106(SUPPL. 1):S93-S94.
4. Miao Y, Zhang L, Sparring V, et al. Improving health related quality of life among rural hypertensive patients through the integrative strategy of health services delivery: A quasi-experimental trial from Chongqing, China. *International Journal for Equity in Health* 2016;15(1):132. doi: <http://dx.doi.org/10.1186/s12939-016-0421-x>
5. Myers B, Lund C, Lombard C, et al. Comparing dedicated and designated models of integrating mental health into chronic disease care: study protocol for a cluster randomized controlled trial. *Trials* 2018;19(1) (no pagination) doi: 10.1186/s13063-018-2568-9
6. Rakic D, Jakovljevic D. [Integrated approach to prevention and control of cardiovascular diseases]. *Srpski arhiv za celokupno lekarstvo* 2011;139(5-6):304-10.
7. Sarrafzadegan N, Baghaei A, Sadri G, et al. Isfahan healthy heart program: Evaluation of comprehensive, community-based interventions for non-communicable disease prevention. *Prevention and Control* 2006;2(2):73-84. doi: <http://dx.doi.org/10.1016/j.precon.2006.10.003>

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8. Spaak J, Brommels M, Kahan T, et al. Integrated, Multidisciplinary, Person-centered Care for Patients With Complex Comorbidities: Heart, Kidney and Diabetes, 2017.
9. Ajay VS, Jindal D, Roy A, et al. Development of a Smartphone-Enabled Hypertension and Diabetes Mellitus Management Package to Facilitate Evidence-Based Care Delivery in Primary Healthcare Facilities in India: The mPower Heart Project. *Journal of the American Heart Association* 2016;5(12) doi: 10.1161/jaha.116.004343
10. Al Asmary SM, Al-Harbi T, Tourkmani AM, et al. Impact of integrated care program on glycemic control and cardiovascular risk in adult patients with type 2 diabetes. *Journal of Clinical Outcomes Management* 2013;20(8):356-63.
11. Garrib A, Birungi J, Lesikari S, et al. Integrated care for human immunodeficiency virus, diabetes and hypertension in Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2018 doi: 10.1093/trstmh/try098
12. Germe M, Zingwari J, Matji R, et al. Baseline assessment of high volume facility capacity to provide integrated tuberculosis (TB) and diabetes (DM) services in South Africa. *Diabetes* 2017;66(Supplement 1):A460-A61.
13. Kwarisiima D, Atukunda M, Owaraganise A, et al. Hypertension control in integrated HIV and chronic disease clinics in Uganda in the SEARCH study. *BMC Public Health* 2019;19(1):511. doi: 10.1186/s12889-019-6838-6 [published Online First: 2019/05/08]
14. Li Q, Li L, Fan XL, et al. The values of evidence-based comprehensive care for patients with type 2 diabetes mellitus and cardiovascular diseases to improve the quality of life. *Heart* 2013;99(SUPPL. 3):A282-A83. doi: <http://dx.doi.org/10.1136/heartjnl-2013-304613.797>
15. Mahomed OH, Asmall S, Freeman M. An integrated chronic disease management model: a diagonal approach to health system strengthening in South Africa. *Journal of health care for the poor and underserved* 2014;25(4):1723-29. doi: <http://dx.doi.org/10.1353/hpu.2014.0176>
16. Narayanan G, Prabhakaran D. Integrating mental health into cardiovascular disease research in India. *National Medical Journal of India* 2012;25(5):274-80.
17. Nigatu T. Integration of HIV and noncommunicable diseases in health care delivery in low- and middle-income countries. *Preventing chronic disease* 2012;9:E93.
18. Nyabera RA, Yonga G, Mwangemi F, et al. Evaluation of a project integrating cardiovascular care into HIV programmes. *Cardiovascular Journal of Africa* 2011;22(3 SUPPL. 1):S17.
19. Patel P, Speight C, Maida A, et al. Integrating HIV and hypertension management in low-resource settings: Lessons from Malawi. *PLoS medicine* 2018;15(3):e1002523. doi: 10.1371/journal.pmed.1002523
20. Patel V, Chatterji S. Integrating Mental Health In Care For Noncommunicable Diseases: An Imperative For Person-Centered Care. *Health affairs (Project Hope)* 2015;34(9):1498-505. doi: 10.1377/hlthaff.2015.0791
21. Rabkin M, Palma A, McNairy ML, et al. Integrating cardiovascular disease risk factor screening into HIV services in Swaziland: lessons from an implementation science study. *Aids* 2018;32:S43-S46. doi: 10.1097/qad.0000000000001889
22. Samb B, Desai N, Nishtar S, et al. Chronic Diseases: Chronic Diseases and Development 4 Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries. *Lancet* 2010;376(9754):1785-97. doi: 10.1016/s0140-6736(10)61353-0
23. Sarraf-Zadegan N, Sadri G, Malek Afzali H, et al. Isfahan Healthy Heart Programme: a comprehensive integrated community-based programme for cardiovascular disease prevention and control. Design, methods and initial experience. *Acta cardiologica* 2003;58(4):309-20. doi: 10.2143/ac.58.4.2005288
24. Sushilkumar PL, Mahendrakumar BJ, Suman B, et al. Implementation and evaluation of health screening services to diabetic and hypertensive patients in a selected community pharmacy at belgaum city. *Asian Journal of Pharmaceutical and Clinical Research* 2015;8(3):305-15.
25. Tedjokusumo R. Introducing the integrated cardiovascular services at Dr. Hasan Sadikini Hospital. *Heart Lung and Circulation* 2003;12(SUPPL. 2):S82-384. doi: <http://dx.doi.org/10.1046/j.1443-9506.2003.t01-4-x>

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26. Tiam A, Oyebanji O, Nkonyana J, et al. Family health days: An innovative approach to providing integrated health services for HIV and non-communicable diseases among adults and children in hard-to-reach areas of Lesotho. *Journal of the International AIDS Society* 2012;15(SUPPL. 3):236. doi: <http://dx.doi.org/org/10.7448/IAS.15.5.18438>
 27. Wasay M, Jabbar A. Fight against chronic diseases (high blood pressure, stroke, diabetes and cancer) in Pakistan; cost-effective interventions. *JPMA The Journal of the Pakistan Medical Association* 2009;59(4):196-7.
 28. Bachmann MO, Bateman ED, Stelmach R, et al. Integrating primary care of chronic respiratory disease, cardiovascular disease and diabetes in Brazil: Practical Approach to Care Kit (PACK Brazil): study protocol for randomised controlled trials. *Journal of Thoracic Disease* 2018;10(7):4667-77.
 29. Hong T. Web-Based Collaborative Care for Patients With Diabetes and Depression. <https://clinicaltrials.gov/show/nct01985711> 2013
 30. Kowalski AJ, Poongothai S, Chwastiak L, et al. The INtegrating DEPrEssioN and Diabetes treatMENT (INDEPENDENT) study: Design and methods to address mental healthcare gaps in India. *Contemporary clinical trials* 2017;60:113-24. doi: 10.1016/j.cct.2017.06.013
 31. McKee MD, Fletcher J, Sigal I, et al. A collaborative approach to control hypertension in diabetes: outcomes of a pilot intervention. *Journal of primary care & community health* 2011;2(3):148-52. doi: 10.1177/2150131911401028
 32. Mendis S, Johnston SC, Fan W, et al. Cardiovascular risk management and its impact on hypertension control in primary care in low-resource settings: a cluster-randomized trial. *Bulletin of the World Health Organization* 2010;88(6):412-9. doi: 10.2471/blt.08.062364
 33. Pibernik-Okanovic M, Hermanns N, Ajdukovic D, et al. Does treatment of subsyndromal depression improve depression-related and diabetes-related outcomes? A randomised controlled comparison of psychoeducation, physical exercise and enhanced treatment as usual. *Trials* 2015;16:305. doi: 10.1186/s13063-015-0833-8
 34. Saleh S, Farah A, Dimassi H, et al. Using Mobile Health to Enhance Outcomes of Noncommunicable Diseases Care in Rural Settings and Refugee Camps: Randomized Controlled Trial. *JMIR mHealth and uHealth* 2018;6(7):e137. doi: 10.2196/mhealth.8146
 35. Sarrafzadegan N, Kelishadi R, Esmailzadeh A, et al. Do lifestyle interventions work in developing countries? Findings from the Isfahan Healthy Heart Program in the Islamic Republic of Iran. *Bull World Health Organ* 2009;87(1):39-50. doi: 10.2471/blt.07.049841
 36. Tourkmani AM, Abdelhay O, Alkhashan HI, et al. Impact of an integrated care program on glycemic control and cardiovascular risk factors in patients with type 2 diabetes in Saudi Arabia: an interventional parallel-group controlled study. *BMC Fam Pract* 2018;19:10. doi: 10.1186/s12875-017-0677-2
 37. Wenxi T, Yan Z, Liang Z. Effects of provider incentives in integrated healthcare delivery system reform: a quasiexperiment on patients with chronic diseases in rural China. *International Journal of Integrated Care (IJIC)* 2017;17(3):171-72. doi: 10.5334/ijic.3207

Supplementary file 3: Summary of interventions according to the TIDiER checklist: Integrated models of care

Study ID	Ameh 2017		Rawat 2018*	Havlir 2019	
Intervention groups	Intervention	Control	Intervention	Intervention	Control
Name of intervention	Integrated chronic disease management (ICDM) model	Standard care in clinics where ICDM model was not piloted	Implementation of national policy to integrate HIV care into all PHC facilities	Integrated care: Baseline HIV and multi-disease testing plus annual testing, universal ART and patient-centered care	Usual care: Baseline HIV and multi-disease testing and national guideline-restricted ART, hypertension and diabetes care as per country standard of care
Aim of the intervention	To improve management of patients with HIV, TB, hypertension, diabetes, COPD, asthma, epilepsy and mental health conditions at PHCs	Not reported	To provide comprehensive HIV care (prevention, diagnosis, treatment initiation and follow-up) at PHC facilities	To remove patient-level barriers and maximise the efficiency of the health system To overcome barriers of universal access to HIV treatment and to be able to reach UNAIDS goals	Not reported
Physical and informational materials used	Not reported	Not reported	Not reported	Treatment guidelines ART tablets SMS reminders	National treatment guidelines
Procedures, activities and processes used in the intervention	Facility reorganisation: designated chronic care area; supply of critical medicines; pre-packaging of medication	Not reported	Policy to integrate HIV care into PHC clinics Training of nurses in comprehensive management of HIV: Nurse initiated	Community health campaigns (CHCs): Multi-disease testing for HIV, diabetes and hypertension; counselling and clinic appointments for participants with	Community health campaigns: Multi-disease testing for HIV, diabetes and hypertension; counselling and clinic appointments for participants with positive

	<p>Clinical management support: use of guidelines to manage chronic diseases (PC101); human resources audit; capacity building; appropriate referral</p> <p>Ward-based outreach teams to ensure individual responsibility and “assisted” self-management</p> <p>Health promotion and population screening</p>		<p>Management of ART (NIMART)</p> <p>Training of nurses through the Practical Approach to Lung Health in South Africa (PALSA PLUS)</p> <p>Additional staff to strengthen drug delivery systems</p>	<p>positive tests; HIV positive participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>Home-based testing for participants that did not attend CHCs</p> <p>Linkage to ART: HIV positive participants not on ART received appointments to initiate ART within a maximum of 7 days; clinic staff introduced themselves in person or by mobile phone; participants could contact hotline via phone or text message for questions or support; phone/SMS reminders about clinic visits</p> <p>Patient-centered care for HIV, diabetes, hypertension: 3-month visit intervals; flexible clinic hours; reduced waiting time at clinics;</p>	<p>tests; HIV positive participants received blood tests (CD4, t-cell count, HIV/RNA levels) and one-time round trip transportation voucher for first clinic visit</p> <p>ART, diabetes and hypertension treatment: provided in accordance with national guidelines</p>
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				welcoming staff; ART to all HIV positive participants; if not eligible for ART according to national guidelines, trial provided Tuvada; hypertension and diabetes treated according to standard algorithms	
Who provided the intervention	Nurses	Nurses	Nurses	CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya Patient-centered care: government clinics augmented by trial staff	CHCs: Study team in collaboration with the local health units and the Ministry of Health in Uganda and Kenya Care in clinics: Clinic staff, augmented by additional staff funded by trial to mitigate staff shortages
Modes of delivery	Not reported	Not reported	Practical implementation of policy varied across clinics: Either disease-specific nurses in separate consulting rooms (co-location), or one nurse that provided comprehensive care for all diseases in single consultation room	Face-to-face, via telephone or text message	Face-to-face

<p>Location of the intervention</p>	<p>Primary healthcare facilities</p>	<p>Primary healthcare facilities</p>	<p>Primary healthcare clinics: 37 urban clinics 65 rural clinics 30 clinics from former homeland</p>	<p>CHCs: Under large tents in all communities, or home-based Patient-centered care: At clinics</p>	<p>CHC: Under large tents in all communities, or home-based ART, diabetes, hypertension care: At clinics</p>
<p>When and how much the intervention was delivered</p>	<p>Unstable HIV and hypertension patients: follow-up every month Stable HIV and hypertension patients: follow-up every 2-3 months Routine referral of all patients to doctor: Every 6 months</p>	<p>Not reported</p>	<p>Not reported</p>	<p>CHCs: lasted 2 weeks at baseline, annually and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: 3-month intervals</p>	<p>CHCs: lasted 2 weeks at baseline and at 3 year endpoint during weekdays, evenings and weekends Clinic visits: not reported</p>
<p>Tailoring of the intervention</p>	<p>Not reported</p>	<p>Not reported</p>	<p>Modular structures and pharmacy renovations to address space concerns in some clinics</p>	<p>Not reported</p>	<p>Not reported</p>
<p>Modifications of the intervention</p>	<p>Not reported</p>	<p>Not reported</p>	<p>Not reported</p>	<p>The end point of the trial was reduced from 5 years to 3 years</p>	<p>Control clinics implemented ART guidelines that were specific to Uganda and Kenya; during the trial, the threshold for eligibility for ART in these countries expanded from a specific CD4+ T-cell count (ranging from <350</p>

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					to <500) to universal treatment (regardless of CD4+ T-cell count)
Assessment of intervention adherence/fidelity	Not reported	Not reported	Not reported	Not reported	Not reported
Intervention delivered as planned	Not reported	Not reported	Not reported	Not reported	Not reported

*No control intervention described

HIV human immunodeficiency virus, TB tuberculosis, COPD chronic obstructive pulmonary disease, PHC primary healthcare clinics

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Supplementary file 4: Summary of interventions according to the TIDiER checklist: Interventions to promote integrated management of care

Study ID	Fairall 2016		Prabhakaran 2018	
Intervention groups	Intervention	Control	Intervention	Control
Name of intervention	Primary Care (PC) 101	Usual care in for non-communicable and communicable diseases: Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS)	mWellcare	Enhanced usual care
Aim of the intervention	To provide comprehensive care for all symptoms, including NCDs, HIV, TB, mental health conditions, women's health	To provide a user-friendly management tool that integrates and harmonises disease-specific guidelines and presents them in a simple format, aligned with patient presentation in primary health care settings, expanded nurses' scope of practice and prescribing (not covering all NCDs)	To facilitate integrated management of hypertension, diabetes, comorbid depression, and alcohol and tobacco use	Not reported
Physical and informational materials used	PC 101 guideline: a 101-page clinical management tool in form of a ring-bound, colour illustrated booklet Desk pads with key messages for priority conditions to facilitate	Latest version (2011/2012) of PALSA PLUS: clinical management tool	mWellcare system: m-Health-based electronic decision-support system that generates recommendations based on patient profile and risk level used on Android tablet	Nurses received a tablet to collect baseline data (without the mWellcare system) Visible charts on the management of the conditions

	booking of follow-up appointments		Visible charts on the management of the conditions Pamphlets containing lifestyle advice	Pamphlets containing lifestyle advice
Procedures, activities and processes used in the intervention	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Expanded prescribing provisions for nurses</p> <p>Letters and SMS reminders of follow-up visits</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of facility trainers</p> <p>Educational outreach sessions by facility trainers</p> <p>Financial compensation for patients (voucher for local grocery store) for travel costs and time</p>	<p>Training of physicians on current clinical management guidelines and orientation to mWellcare system</p> <p>Training of nurses in management of hypertension, diabetes, depression, and tobacco and alcohol use</p> <p>Onsite supervision and support</p> <p>SMS reminders of follow-up visits and medication adherence</p>	<p>Training of physicians on clinical management guidelines for hypertension and diabetes</p> <p>Training of NCD nurses in management of hypertension and diabetes mellitus</p>
Who provided the intervention	<p>Training of facility trainers: Experienced adult education practitioner with a background in nursing, family physician who lead the expansion of the clinical management tool</p> <p>Educational outreach sessions: Nurse trainers</p>	<p>Training of facility trainers: not reported</p> <p>Educational outreach sessions: Nurse trainers</p> <p>Care: Nurses</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>	<p>Training: Study authors</p> <p>Care: NCD nurses and physicians</p>

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	Care: Nurses			
Modes of delivery	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PC 101 to guide management, details not reported</p>	<p>Training and educational outreach sessions: face-to-face</p> <p>Care: Using PALSA PLUS to guide management, details not reported</p>	<p>All training: face-to-face</p> <p>Care: Patient baseline data entered into mWellcare system which generated a decision support recommendation, lifestyle advice and suggested date for follow-up (printout). The recommendation was reviewed by the physician. Any changes to the recommended plan we captured in the mWellcare system. The nurse provided lifestyle advice and pamphlets</p>	<p>All training: face-to-face</p> <p>Care: According to clinical judgement of physician. Nurses provided and explained pamphlets on lifestyle advice</p>
Location of the intervention	In primary healthcare clinics	In primary healthcare clinics	Community Health Centres	Community Health Centres
When and how much the intervention was delivered	<p>Training of facility trainers: 5-days, in May 2011 and quarterly 1-day workshops</p> <p>Educational outreach sessions: Total of 155 educational outreach sessions, 8 sessions lasting 90 minutes at each of the 19 intervention clinics</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Educational outreach sessions: 90 minute sessions</p> <p>Follow-up sessions every year</p> <p>Distribution of updated tool every year</p> <p>Care: Stable patients are seen by the nurse every 3-6 months</p>	<p>Training for nurses using the mWellcare system: 3 days</p> <p>Onsite supervision: 2 days</p> <p>Care: follow-up visits according to the recommendation provided by the mWellcare system</p>	<p>Not reported</p> <p>Care: follow-up visits according to the discretion of the physician</p>

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Tailoring of the intervention	Not reported	Not reported	Not reported	Not reported
Modifications of the intervention	<p>Unexpected co-intervention by the district department of health: "Chronic Disease Season" (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p> <p>Facilitated group session to resolve tensions between nurses, doctors and pharmacists related to expanded prescribing provisions</p>	<p>Unexpected co-intervention by the district department of health: "Chronic Disease Season" (3 month campaign), to improve NCD recognition and care, focusing on diabetes and hypertension, at clinic and community-level. In the community, free screening of blood pressure and glucose levels were offered in public spaces such as shopping centres. People with high values were referred to the clinic.</p> <p>Training of 33 community health workers to provide basic education on diet and lifestyle</p>	None reported	None reported
Assessment of intervention adherence/fidelity	<p>Nurse trainers were observed during 5-day workshop and quarterly 1-day workshops</p> <p>Two nurse trainers were interviewed and focus group discussions were held in four</p>	Not reported	Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source documents examination, protocol	Monthly visits to all sites by field coordinators who complete a checklist on: intervention delivery, source documents examination, protocol

	<p>intervention clinics in December 2011</p>		<p>adherence and recording of adverse events</p> <p>Site visits by investigators: to monitor enrolment process, intervention delivery and protocol adherence</p>	<p>adherence and recording of adverse events</p> <p>Site visits by investigators: to monitor enrolment process, intervention delivery and protocol adherence</p>
<p>Intervention delivered as planned</p>	<p>Good uptake of nurse trainers, who completed all outreach sessions, and repeated some sessions to ensure that most staff could attend</p> <p>Due to absenteeism and shifts, not all nurses attended all the outreach sessions. In total, 18 nurses attended a median of six training sessions, five pharmacists and four doctors were trained</p> <p>Some variations in the uptake of the PC 101 tool were observed</p>	<p>By 2011, 70% of nurses working in the relevant districts had received training in PALS PLUS.</p>	<p>Not reported</p>	<p>Not reported</p>

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Supplementary file 5: Risk of bias assessments for included studies

Prabhakaran 2018

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	"An independent biostatistician performed central computer-based randomization of CHCs stratified by states (Haryana and Karnataka) and within each state by the availability of NCD nurses recruited under NPCDCS." "using block randomisation (with a block size of 2)"
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study.
Baseline outcome measurements similar	Low risk	Measurement of outcomes was conducted in a standardised way. Outcomes were pre-defined and subjective
Baseline characteristics similar	Low risk	The EUC arm had a higher proportion of participants with peripheral vascular disease (4.4% versus 0.3%), self-reported tobacco use (17.5% versus 10.0%) and alcohol use (12.3% versus 7.8%), and higher mean SBP (157.0 mm Hg versus 152.5 mm Hg). Outcome measures adjusted for relevant baseline characteristics.
Incomplete outcome data	Low risk	No incomplete outcome data suspected. Number of participants in whom the outcomes were assessed were mentioned in a general manner.
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All/ "Given the nature of the cluster-randomized trial design, neither personnel nor participants were blinded to the intervention."
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All/ "Assessments at study end were carried out by independent outcome assessors" "It was difficult to blind independent assessors who carried out the end-of-study evaluations"
Protection against contamination	Low risk	Outcome group: All/ low possibility of contamination across clusters
Selective Outcome reporting	Low risk	Data on cost-effectiveness mentioned in protocol but not reported in full report of the study, because primary outcome do not differ substantially, otherwise all primary and secondary outcomes reported
Recruitment bias (<i>e.g. individuals are recruited to the trial after the clusters have been randomized</i>)	Unclear	Patients were recruited after randomisation. Of eligible participants, n=165 in the intervention group and n=193 in the control group were not enrolled in the trial.
Baseline differences clusters	Unclear	Characteristics of cluster not described
Loss of clusters	Low risk	No loss of clusters reported
Incorrect analysis	Low risk	Adjusted for clustering
Comparability (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search.

Fairall 2016

Domain	Risk of bias	Support for judgement
Random sequence generation (<i>selection bias</i>)	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention.”
Allocation concealment (<i>selection bias</i>)	Low risk	Unit of allocation was an institution. Allocation performed on all units at the start of the study. “Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention”
Baseline outcome measurements similar	Low risk	No differences between groups reported: Baseline BP and HbA1C similar
Baseline characteristics similar	Unclear	Baseline characteristics seem similar, but no statistical tests reported
Incomplete outcome data	Low risk	Loss to follow-up similar across groups and less than 20%
Blinding of participants and personnel (<i>performance bias</i>)	High risk	Outcome group: All “Blinding of the intervention was not possible at the clinic level due to the nature of the intervention”
Blinding of outcome assessment (<i>detection bias</i>)	Unclear	Outcome group: All No blinding of outcome assessors reported Outcome assessors not blinded. This might have influenced BP readings, but not HbA1C (blood test)
Protection against contamination	Unclear	Outcome group: All Contamination of study arms unlikely. Control clinics might have had access to the guidelines although cluster randomisation took place
Selective Outcome reporting	Low risk	No selective outcome reporting suspected, all outcomes listed in the methods section are also reported in the results section – All pre-specified outcomes listed in the trial registration record reported on
Recruitment bias	Low risk	“Randomisation was completed by the trial statistician using nQuery Advisor after recruitment of clinics, independently of the managers giving permission for the clinics to be included in the trial, and prior to patient recruitment and implementation of the intervention” All patients were enrolled after the clusters were randomised. However, all eligible patients were included in the study.
Baseline differences (clusters)	Low risk	Control clinics had more nurses per clinic and more pharmacies on site compared to the intervention group, but patient load was also higher in the control clinics. Ratio of nurses to patients was similar in both groups
Loss of clusters	Low risk	All clinics completed the trial
Incorrect analysis	Low risk	Analysis conducted on individual level, but results adjusted for cluster effects. “The cluster randomisation design was accounted for using robust cluster variance-covariance estimates.”
Compatibility (<i>with RCTs randomised by individuals</i>)	Low risk	No similar studies randomised by individuals found in our search
Other bias	Unclear	“Midway through the trial, the district health department launched a 3-mo campaign called Chronic Disease Season in all clinics to improve NCD recognition and care. Chronic Disease Season focused on hypertension and diabetes and involved both community and clinic health workers. The community-level interventions included several ^a health screening days ^o in which free blood pressure and finger-prick glucose measurements were offered at venues such as shopping centres and town halls” (Page 7, end)

Havlir 2019

Domain	Risk of bias	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate method – mix of methods used, including computer generated, coin tossing and drawing of lots See description in protocol (p45 version 2.0 (Nov 2012))
Allocation concealment (selection bias)	Low risk	Communities were matched and randomised within each pair. Method adequate to not be able to predict allocation
Baseline outcome measurements similar	Unclear	No baseline outcome measurements for HIV and hypertension control Page 25, online supplement to article
Baseline characteristics similar	Low risk	No obvious difference observed
Incomplete outcome data	Unclear	Unclear for HIV and Hypertension cohort, not clear how many at baseline.
Blinding of participants and personnel (performance bias)	High risk	No blinding of participants and personnel due to the nature of the intervention. Can influence behaviour of both participants and personnel
Blinding of outcome assessment (detection bias)	Unclear	Not reported
Protection against contamination	Unclear	Distance from other potential trial communities taken into consideration as part of the eligibility criteria. Migration in and out of communities
Selective Outcome reporting	Unclear	Not clear whether dual control of HIV and Hypertension/NCDS was pre-specified
Recruitment bias	Low risk	Communities were recruited (selected) before randomisation. Participants were recruited after randomisation, but a household census and Community health campaigns to reach most people in community
Baseline differences (clusters)	Unclear	No description of clusters, but cluster pairs were matched for randomisation
Loss of clusters	Low risk	No loss of clusters
Incorrect analysis	Unclear	Not clear whether adequately adjusted for clustering
Compatibility (with RCTs randomised by individuals)	Low risk	No similar studies using individual randomisation found in our search
Other bias	Unclear	Primary endpoint should have been 5-year cumulative HIV incidence, but this was shortened to 3 years as the WHO recommendation on ART therapy changed

Rawat 2018

Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other intervention identified. Also, clinics were excluded if they were identified as 'priority sites' that were specifically designed to deliver ART.
The shape of the intervention effect was pre-specified	High risk	The shape of the intervention effect was not pre-specified.
The intervention was unlikely to affect data collections	Low risk	Data was collected from TIER.net (3 interlinked electronic registers) and the District Health Information System (DHIS) for data collected before and after the intervention.
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Low risk	Outcomes were based on indicators monitored by the Free State Department of Health. Methods of data collection were similar before and after the intervention, therefore the intervention did not affect data collection.
Incomplete outcome data was likely to bias results	Unclear	Post-intervention data for diabetes outcomes only available for 18 months post intervention. For other outcomes there is data for 30 months.
Outcomes were reported selectively	Low risk	All outcomes reported in the methods section were reported in the results section
Other risks of bias	Low risk	No other risks of bias identified. As integration took place at various intervals, seasonality assumed not to have an effect.

Ameh 2017

Domain	Risk of bias	Support for judgement
Intervention was independent of other changes	Low risk	No other changes reported.
The shape of the intervention effect was pre-specified	Low risk	Point of analysis is the point of intervention
The intervention was unlikely to affect data collections	Unclear	It can be assumed that the re-organisation of care delivery also affected data collection in the intervention facilities
Knowledge of the allocated intervention (<i>adequately prevented during the study</i>)	Low risk	Data was collected retrospectively from patient records. Patients were recruited in June 2013, and data collected from Jan 2011 to June 2013. Methods of data collection were similar before and after the intervention and the intervention did not affect data collection.
Incomplete outcome data was likely to bias results	Low risk	No incomplete outcome data suspected. No attrition or missing cases reported, only data for diabetes patients was not reported because there were too few cases (n=4)
Outcomes were reported selectively	Low risk	No selective outcome reporting suspected. All outcomes reported in the methods section are reported in the results section
Other risk of bias	Low risk	No other sources of bias identified

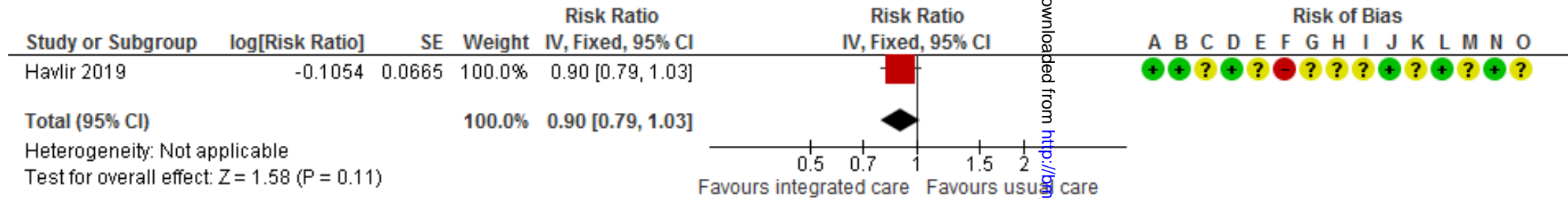
Supplementary file 6: Forest plots

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Comparison 1: Integrated models of care vs. usual care

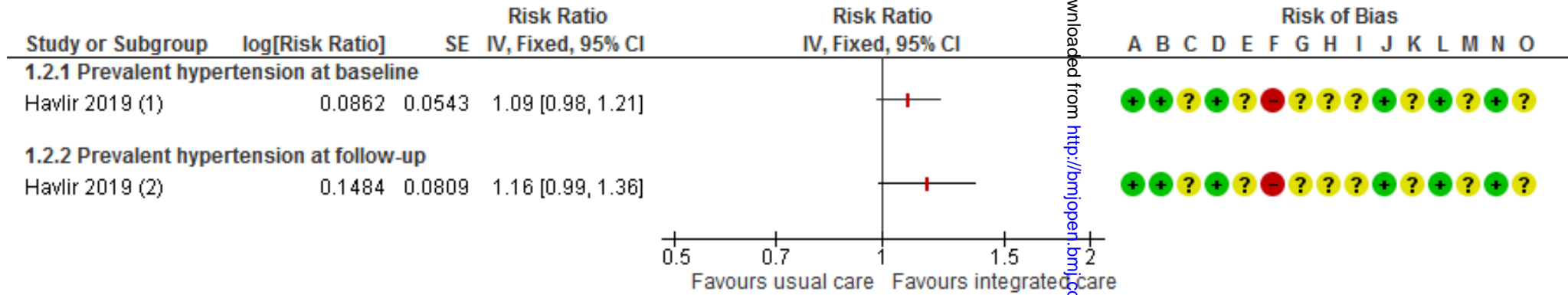
Outcome: Mortality



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care
 Outcome: BP control



Footnotes

- (1) Among people living with HIV (PLHIV)
- (2) Among people living with HIV (PLHIV)

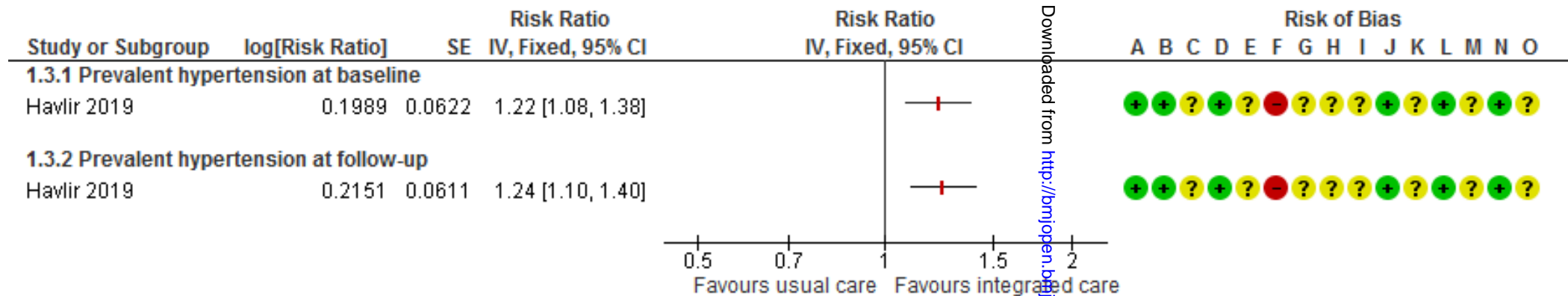
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 1: Integrated models of care vs. usual care

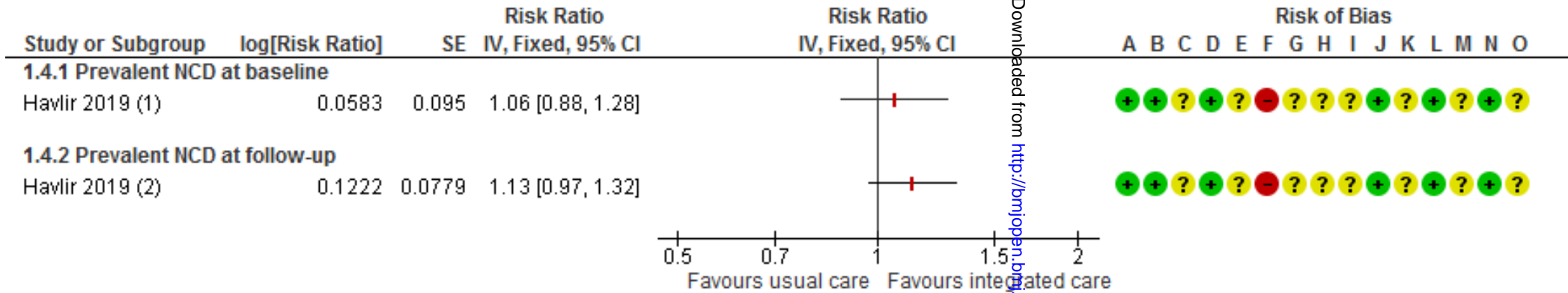
Outcome: BP and HIV control



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 1: Integrated models of care vs. usual care
 Outcome: NCD control



Footnotes

- (1) Among PLHIV
- (2) Among PLHIV

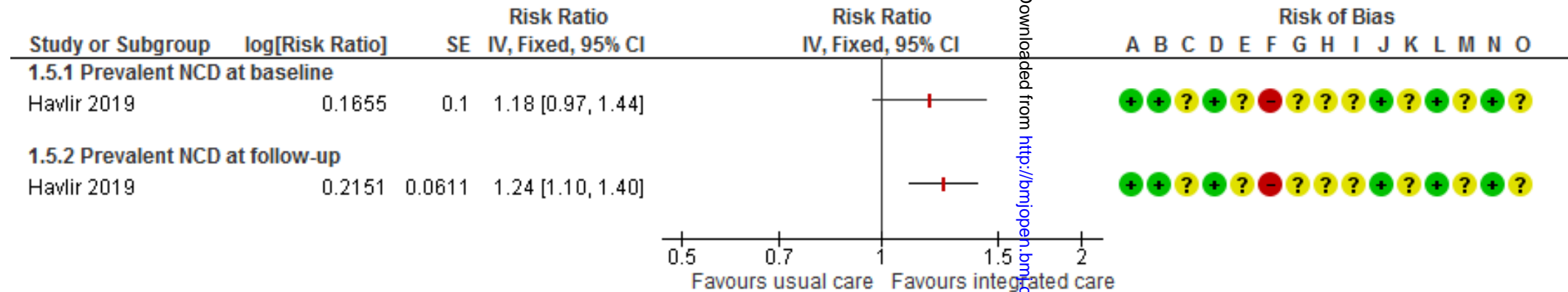
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 1: Integrated models of care vs. usual care

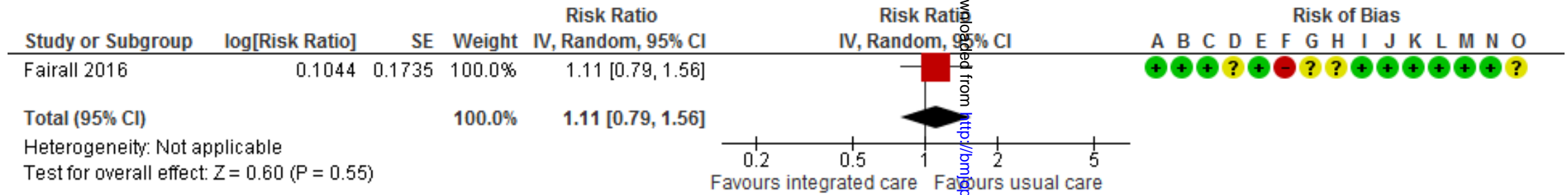
Outcome: NCD and HIV control



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Mortality



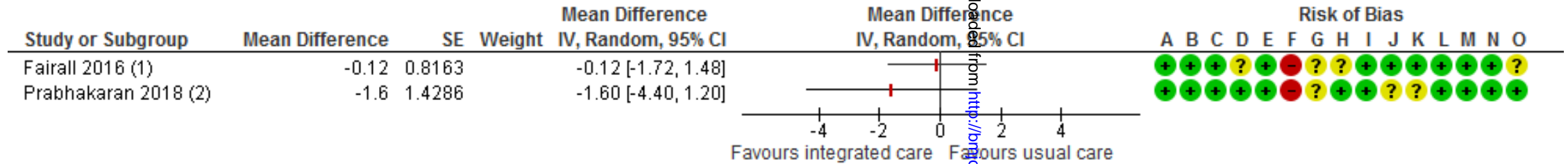
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Depression



Footnotes

- (1) Change from baseline to follow-up; 10-item Center for Epidemiologic Studies...
- (2) Value at follow-up; Patient Health Questionnaire-9

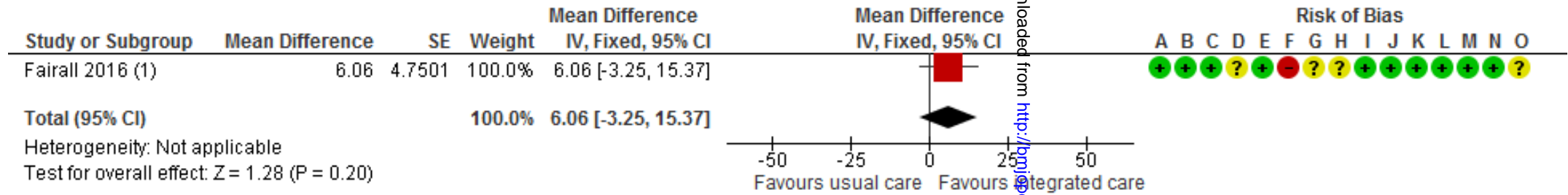
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristic similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCT randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Quality of life



Footnotes

(1) Euro-Qol-5D visual analogue scale: 0=worst imaginable state of health,...

Risk of bias legend

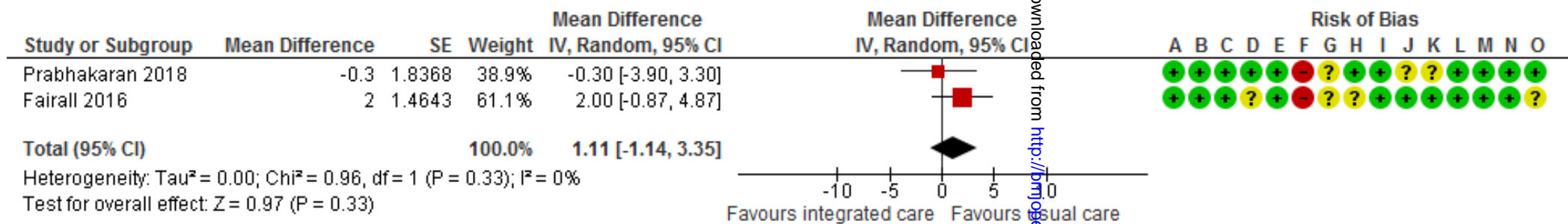
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
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- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

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Comparison 2: Strategies to promote integrated models of care vs. usual care

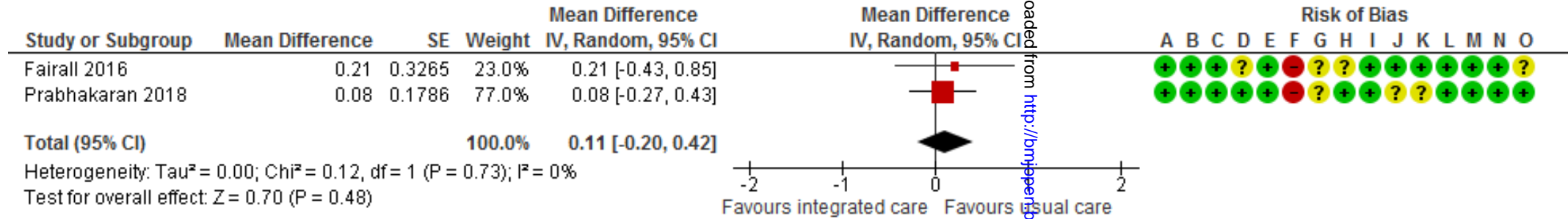
Outcome: Change in systolic BP



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 2: Strategies to promote integrated models of care vs. usual care Outcome: Change in HbA1c

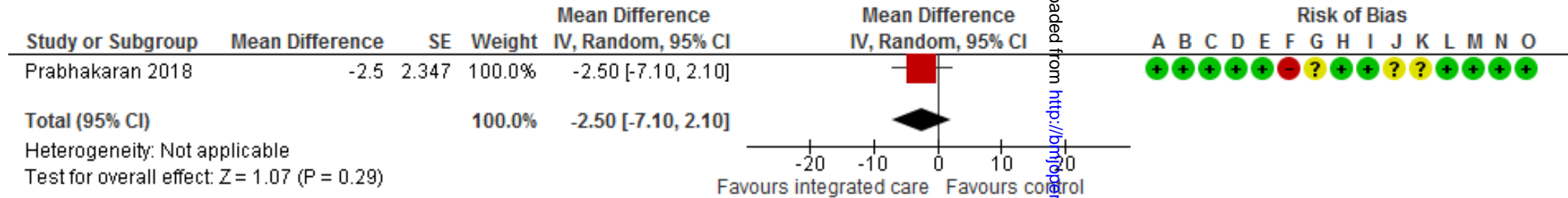


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias

Comparison 2: Strategies to promote integrated models of care vs. usual care

Outcome: Change in total cholesterol



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Baseline outcome measurements similar
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Blinding of participants and personnel (performance bias)
- (G) Blinding of outcome assessment (detection bias)
- (H) Protection against contamination
- (I) Selective reporting (reporting bias)
- (J) Recruitment bias
- (K) Baseline differences (clusters)
- (L) Loss of clusters
- (M) Incorrect analysis
- (N) Compatibility with RCTs randomised by individuals
- (O) Other bias



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
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
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.	4
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.	4-5
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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary 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).	5
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.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
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.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
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.	6



PRISMA 2009 Checklist

Page 1 of 2

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).	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7, Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO, follow-up period) and provide the citations.	8-12, Supplementary files 3 and 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).	13, Figure 3, 4 and supplementary file 5
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.	Supplementary file 6
Synthesis of results	21	13-20	11-18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 3 and 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
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).	20
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).	21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22
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.	22



PRISMA 2009 Checklist

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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.

Page 2 of 2

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