


# BMJ Open Effects of integrated models of care for diabetes and hypertension in low-income and middle-income countries: a systematic review and meta-analysis

Anke Rohwer <sup>1</sup>, Jeannine Uwimana Nicol <sup>1,2</sup>, Ingrid Toews,<sup>3</sup> Taryn Young,<sup>1</sup> Charlotte M Bavuma,<sup>4</sup> Joerg Meerpohl<sup>3,5</sup>

**To cite:** Rohwer A, Uwimana Nicol J, Toews I, *et al.* Effects of integrated models of care for diabetes and hypertension in low-income and middle-income countries: a systematic review and meta-analysis. *BMJ Open* 2021;**11**:e043705. doi:10.1136/bmjopen-2020-043705

► Prepublication history and additional online supplemental material for this paper are available online. To view these files, please visit the journal online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-043705>).

AR and JUN are joint first authors.

Received 12 August 2020  
Accepted 15 June 2021



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Anke Rohwer;  
[arohwer@sun.ac.za](mailto:arohwer@sun.ac.za)

## ABSTRACT

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

**Design** Systematic review.

**Data sources** We searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, 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-and-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 Grading of Recommendations Assessment, Development and Evaluation.

**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 with 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 with 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 glycated haemoglobin (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 number** 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 Grading of Recommendations Assessment, Development and Evaluation 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

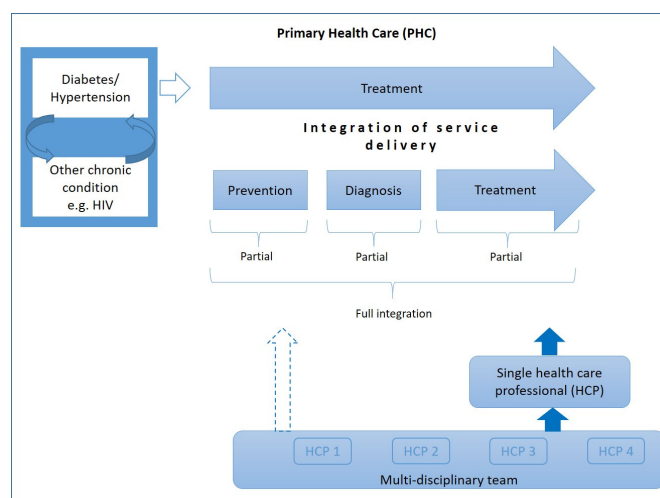
Low-income and middle-income countries (LMICs) are facing an increasing burden of non-communicable diseases (NCDs).<sup>1</sup> A recent report of the WHO on NCDs indicates that 41 million people succumb to NCDs globally which is the equivalent of 71% of total global deaths. Fifteen million people (between the ages of 30 and 69 years) die prematurely due to NCDs every year and 85% of these premature deaths occur in LMICs.<sup>1 2</sup> Furthermore, NCDs are projected to exceed communicable, maternal, perinatal and nutritional diseases as the most common causes of death by 2030.<sup>3</sup> In LMICs, the vast majority of NCD deaths are caused by cardiovascular diseases (CVDs), mainly due to coronary artery diseases and stroke,<sup>4</sup> diabetes, cancer and chronic respiratory diseases; and they account for 54% of NCD disability-adjusted life-years.<sup>1 5</sup> Diabetes and hypertension are

the major cardiovascular risk factors for target organ damage of brain, heart and kidney.<sup>1</sup>

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.<sup>6</sup> 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.<sup>7</sup> 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 multimorbidity. Because of the progress made with scaling up of antiretroviral 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 effects.<sup>8–11</sup> According to a recent systematic review examining the prevalence of NCDs among PLHIV in LMICs,<sup>12</sup> 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.<sup>13</sup> The chronic nature of NCDs puts strain on the already scarce resources of healthcare systems and affected individuals in LMICs.<sup>14</sup> Hence there is a need to design effective interventions to address the increasing burden of NCDs such as 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.<sup>15–17</sup> Recent studies from LMICs have assessed integration of HIV/AIDS and tuberculosis (TB) services at primary healthcare (PHC) level,<sup>18–20</sup> 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.<sup>21</sup> 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 healthcare 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 care.<sup>21</sup>

Although integrated models of care have been widely advocated, and various models and programmes have



**Figure 1** Logic model of integrated care.

been implemented and described, there is a lack of evidence on the effectiveness of integrated care compared with other models of care in LMICs. We previously conducted a scoping review to assess existing systematic reviews on the effectiveness of integrated models of care in people with diabetes or hypertension and any other comorbid disease.<sup>22</sup> We found five reviews<sup>23–27</sup> that met our inclusion criteria, but only one of these included studies conducted in LMICs. Furthermore, none of the included studies assessed integrated care for diabetes or hypertension and communicable diseases (eg, HIV). A subsequent systematic review by Haldane *et al* examined existing programmes of integrated healthcare delivery for diabetes, hypertension or CVDs with HIV/AIDS.<sup>28</sup> However, included studies mostly described existing programmes with no thorough evaluation of the effectiveness of these programmes. A descriptive study from Cambodia looked at the management of HIV/AIDS, diabetes and hypertension and found that integration of services for these conditions was highly acceptable and led to good health outcomes with improved CD4 count, glycated haemoglobin (HbA1c) and blood pressure (BP) levels.<sup>29</sup> Dudley and Garner<sup>30</sup> assessed the effectiveness of strategies to integrate PHC services in LMICs. They included studies that integrated family planning into existing services; nutrition and infectious disease interventions; and sexually transmitted infections, HIV/AIDS and TB treatment. None of the included studies reported on NCDs.

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

## METHODS

Our systematic review followed the methods prespecified in a published protocol.<sup>21</sup> We followed the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline to report on the findings of our systematic review.

### Criteria for considering studies for inclusion

#### Types of study designs

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

#### Types of participants

We included studies with adults and children attending PHC clinics in LMICs, presenting with diabetes or hypertension. Patients potentially had additional chronic diseases (multimorbidity). We defined LMICs according to the 2016 classification of the World Bank,<sup>31</sup> that defined low-income economies as those with a gross national income (GNI) per capita of \$1035 or less, lower middle income economies as those with a GNI per capita of US\$1006–US\$3995, and upper middle economies as those with a GNI per capita of US\$3956–US\$12 235.

#### Types of interventions

Eligible interventions were models of full or partial integration of services at PHC and community level. Full integration of service delivery was defined as models where patients (primarily treated for diabetes, hypertension or any other disease) received the full package of care (prevention, diagnosis and treatment) for diabetes or hypertension and any other chronic disease at the same point of care by one or more healthcare professionals. Partial integration of services was defined as models where patients treated for diabetes, hypertension or any other chronic disease received part of the package of care (either prevention, diagnosis or treatment) for another disease (see figure 1). Partially integrated models of care, therefore, refer to a lower level of integration compared with fully integrated models of care. For example, with partially integrated care, patients receiving treatment for hypertension would be tested for HIV and referred for treatment; whereas with fully integrated care, patients receiving treatment for hypertension would be tested and treated for HIV during the same clinic visit.

Included studies did not provide adequate information for us to categorise interventions as fully integrated models of care or partially integrated models of care and we thus categorised interventions as either (1) integrated models of care or (2) interventions that promoted integrated delivery of care. Integrated models of care assessed the effect of integration of service delivery that is, integration of two previously separate models of delivery of care into one model of delivery of care, for example,

integrating HIV services into general PHC services. We distinguished these interventions from interventions that promoted an integrated approach to providing care in PHC facilities. In these cases, services as such were not integrated, but healthcare workers were encouraged to provide holistic patient care, for example through the provision and use of clinical management tools that supported an integrated approach to care.

#### Types of comparisons

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

#### Types of outcomes

We included studies that reported on either primary or secondary outcomes, as defined by primary study authors. Primary outcomes were all-cause mortality, disease-specific morbidity as reported in included studies (eg, disease control metrics), quality of life, HbA1c, systolic BP (SBP) and cholesterol levels. Secondary outcomes were access to care, retention in care, adherence, continuity of care, quality of care and cost of care.

#### Search strategy

We searched MEDLINE (PubMed), EMBASE (Ovid), the Cochrane Central Register of Controlled Trials, LILACS, Africa-Wide Information (via EBSCO host), CINAHL and Web of Science (Core collection) (Date of last search: 12 December 2019). We searched the WHO International Clinical Trials Registry Platform and ClinicalTrials.gov for ongoing studies, as well as conference abstracts from the International AIDS Society Online Resource Library, the HIV/AIDS Implementers' Meetings and the NCDs Alliance meetings. Search terms included 'diabetes', 'hypertension', 'comorbidities', 'integrated healthcare delivery', 'LMICs' and their synonyms. The full search strategies for all databases are provided in online supplemental file 1. To supplement the search of electronic databases, we screened reference lists of included studies and reference lists of relevant systematic reviews, and contacted experts in the field and relevant organisations (eg, NCD Alliance) for unpublished studies. We did not have any restrictions related to language, date of publication or publication status.

#### 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.<sup>32</sup> 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 (JM/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 prespecified, piloted data extraction form and assessed risk of bias. Discrepancies were resolved through discussion or by consulting a third author (TY/JM). 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)<sup>33</sup> and the PRISMA-Complex Interventions extension checklist<sup>34</sup> 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 studies.<sup>35</sup> 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.<sup>36</sup> For ITS studies, we assessed whether (1) the intervention was independent of other changes, (2) the shape of the intervention effect was prespecified, (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% CI. For continuous outcomes, we reported mean differences (MD) with 95% CI if outcomes were measured in the same way across studies, or standardised MD with 95% CI where outcomes were measured differently across studies and where standard deviations (SDs) were reported. For ITS studies, we reported beta coefficients ( $\beta$ ) 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 V.5.<sup>37</sup> We did not include studies with more than one treatment arm in our review.

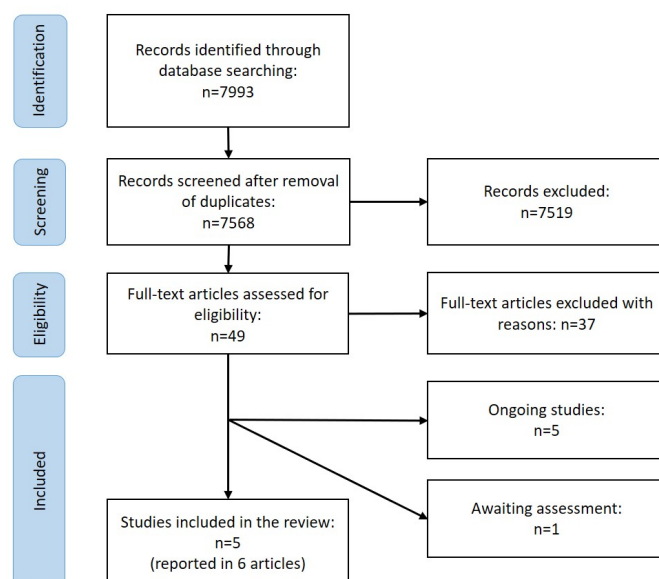
We explored clinical heterogeneity by clearly documenting study characteristics related to the population, intervention, outcomes and context in table format. We assessed statistical heterogeneity in each meta-analysis by inspecting forest plots and calculating  $\chi^2$  test values and  $I^2$  statistics. We considered heterogeneity to be important if the p value of the  $\chi^2$  test was  $<0.10$ , and the  $I^2$  statistic was above 30%, as per the recommendations in the Cochrane handbook.<sup>36</sup>

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

### Certainty of evidence

We wrote statements about the evidence (eg, 'little or no effect' vs 'very small effect') according to guidance of Grading of Recommendations Assessment, Development and Evaluation (GRADE)<sup>38</sup> for the following outcomes: mortality, disease specific morbidity, quality of life, HbA1c, SBP, cholesterol levels and access to care. We created a 'Summary of findings' table using GRADEpro software.<sup>39</sup> Our judgements to downgrade the certainty of evidence were based on assessment of the following five domains: (1) study limitations, (2) inconsistency, (3) imprecision, (4) indirectness and (5) publication bias. According to GRADE guidance, non-randomised studies (such as CBAs and ITS studies) start at low certainty evidence. We considered upgrading the certainty of evidence for non-randomised studies if there was a large effect, a dose-response and cases where all plausible residual confounding would reduce a demonstrated effect or would suggest a spurious effect if no effect was observed.

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



**Figure 2** PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

## Patient and public involvement

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

## RESULTS

The results of the search are depicted in the PRISMA flow diagram (figure 2). We screened titles and abstracts of 7568 records. We obtained and screened full texts of 49 potentially relevant studies. We included five studies, <sup>42–46</sup> (table 1) reported in six articles and excluded 37 articles and reported reasons for exclusion (online supplemental file 2). For one study <sup>47</sup> that met eligibility criteria, we were only able to access the conference abstract. We classified this study as ‘awaiting assessment’, as we are unable to definitively decide on inclusion or exclusion until we have access to the full report. We identified five ongoing RCTs, <sup>48–51</sup> investigating integrated care for depression and hypertension in China; <sup>48</sup> integrated care for depression and hypertension <sup>49</sup> or depression and diabetes/HIV <sup>50</sup> in South Africa; integrated care for common mental disorders and hypertension, diabetes or ischaemic heart disease in India <sup>51</sup>; and diabetes and TB in India. <sup>52</sup>

## Characteristics of included studies

We included three cluster RCTs and two ITS studies. One cluster RCT was conducted in South Africa, <sup>43</sup> one in India, <sup>44</sup> and the Sustainable East Africa Research in Community Health (SEARCH) trial was conducted in Uganda and Kenya. <sup>46</sup> The two ITS studies were both conducted in South Africa <sup>42 45</sup> (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 with partial integration of care.

The two ITS studies <sup>42 45</sup> and the SEARCH trial <sup>46</sup> assessed the effects of integrated models of care for chronic diseases (table 2). Ameh *et al* <sup>42</sup> conducted a controlled ITS study, comparing the integrated chronic disease management (ICDM) model to usual care over a period of 30 months. Rawat *et al* <sup>45</sup> examined the effect of integrating HIV care into PHC clinics over a 48-month period. The SEARCH trial <sup>46</sup> assessed the effects of universal ART and streamlined, patient-centred care (integrated care) compared with usual care as per national guidelines. Interventions are described in more detail according to the TIDieR checklist in online supplemental file 3.

The other two cluster RCTs <sup>43 44</sup> assessed the effectiveness of interventions to promote integration of care (table 2). Fairall *et al* <sup>43</sup> introduced the primary care 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 management tool, which did not cover all NCDs and was the standard of care at the time of the trial. Prabhakaran *et al* <sup>44</sup> 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 online supplemental file 4.

## 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 <sup>43 44</sup> and unclear for the SEARCH trial <sup>46</sup> (figure 4). Detailed judgements for each included study are reported in online supplemental file 5.

## Integrated models of care compared with usual care

We included three studies as part of this comparison. <sup>42 45 46</sup> Results are summarised in the summary of findings table (table 3) and forest plots are available in online supplemental file 6.

## All-cause mortality

The SEARCH trial <sup>46</sup> reported the rate of all-cause mortality among baseline residents in included communities. Results suggest that integrated compared with usual care may make little or no difference to the mortality rate when compared with usual care but the evidence is very

**Table 1** Summary of characteristics of included studies

Study ID	Study design	Country and setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes*
<b>Integrated models of care</b>							
Ameh <i>et al</i> <sup>42</sup>	Controlled ITS study	South Africa: Primary healthcare (PHC) facilities, Ehlanzeni health district, Mpumalanga Province	Patients with chronic disease (HIV, diabetes or hypertension) n=878	Integrated chronic disease management 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 Preintervention: 6 months Postintervention: 24 months	<ul style="list-style-type: none"> <li>▲ <b>Blood pressure (BP) control</b><sup>†</sup></li> <li>▲ <b>CD4 count control</b><sup>‡</sup></li> <li>▲ <b>Number of healthcare visits</b></li> </ul>
Havilir <i>et al</i> <sup>46</sup>	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 and national plus annual testing, universal ART and streamlined, patient-centred 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) (Hypertension in adults over 30 years: n=5911)	36 months	<ul style="list-style-type: none"> <li>▲ Cumulative HIV incidence</li> <li>▲ Time to initiation of ART</li> <li>▲ Viral suppression</li> <li>▲ <b>Death</b></li> <li>▲ Incident tuberculosis or death due to illness</li> <li>▲ <b>Control of hypertension§ among HIV-infected persons</b></li> <li>▲ <b>Control of diabetes¶ or hypertension (NCD) among HIV infected persons</b></li> <li>▲ <b>Control of HIV** and hypertension</b></li> <li>▲ <b>Control of HIV and NCDs††</b></li> <li>▲ Control of hypertension in the overall population</li> <li>▲ Control of diabetes in the overall population</li> </ul>

Continued

Table 1 Continued

Study ID	Study design	Country and setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes*
Rawat <i>et al</i> <sup>45</sup>	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 Preintervention: 12 months Postintervention: 36 months	<ul style="list-style-type: none"> <li>▲ Population level new diabetics on treatment</li> <li>▲ Clinic level new diabetics on treatment</li> <li>▲ Population-level new hypertensive on treatment</li> <li>▲ Clinic level new hypertensive on treatment</li> <li>▲ Total ART patients</li> <li>▲ New patients initiated on ART</li> </ul>
Interventions to promote integrated delivery of care							
Fairall <i>et al</i> <sup>43</sup>	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 101 management tool Clinics: n=19 Participants: n=2166 in South Africa (PALSA) (Hypertension: n=1555; diabetes: n=851)	Usual care: Practical Approach to Lung Health and HIV/AIDS PLUS) management tool Clinics: n=19 Participants: n=2227 (Hypertension: n=1672; diabetes: n=991)	14 months	<ul style="list-style-type: none"> <li>▲ Treatment intensification for hypertension, diabetes and chronic respiratory disease</li> <li>▲ Depression</li> <li>▲ CVD risk</li> <li>▲ Systolic BP</li> <li>▲ HbA1C</li> <li>▲ BMI</li> <li>▲ Smoking status</li> <li>▲ Health-related quality of life</li> <li>▲ Mortality</li> <li>▲ Healthcare utilisation</li> </ul>

Continued

**Table 1** Continued

Study ID	Study design	Country and setting	Participants	Intervention	Control	Study duration (follow-up)	Outcomes*
Prabhakaran <i>et al</i> <sup>44</sup>	Cluster RCT	India: Community Health Centres (CHC) from four districts in Haryana and two 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	▲ 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

\*Outcomes relevant to this review are in bold.

†Defined as: BP <140/90 mm Hg,

‡Defined as: CD4 count >350 cells/mm<sup>3</sup>.

§Defined as: At least one systolic BP measurement <140 mm Hg, and at least one diastolic measurement of <90 mm Hg,

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

\*\*Defined as: Suppressed viral replication (<500 copies/mL).

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

ART, antiretroviral therapy; BMI, body mass index; CVD, cardiovascular disease; HbA1c, glycated haemoglobin; ITS, interrupted time series; NCDs, non-communicable diseases; RCTs, randomised controlled trials.



**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 model Amei 2017	Facility reorganisation: designated chronic care area; supply of critical medicines; prepackaging 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 Training of nurses through the Practical Approach to Lung Health in South Africa	-
SEARCH intervention Havir 2019	Patient-centred, 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 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	-	Phone/SMS reminders about clinic visits
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-u-w-u 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

ART, antiretroviral therapy; CVD, cardiovascular disease; PHC, primary healthcare.

	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	+	+	+	?	+	+	?	?	+	+	+	+	+	+	?
Havilr 2019	+	+	+	?	+	+	?	?	?	+	+	?	+	+	?
Prabhakaran 2018	+	+	+	+	+	+	?	+	+	?	+	+	+	+	+

**Figure 4** Risk of bias for cluster RCTs. RCTs, randomised controlled trials.

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 with usual care may make little or no difference to achieving BP control, but the evidence is very uncertain. Results from the SEARCH trial<sup>46</sup> suggest that integrated care compared with 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 study<sup>42</sup> suggest that integrated care compared with 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 trial<sup>46</sup> suggest that integrated care compared with usual care may make little or no difference to the number of PHLV 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 study<sup>42</sup> reported on HIV control in terms of CD4 count control. Results suggest that integrated care compared with 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 trial<sup>46</sup> suggest that integrated care compared with 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 with 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.

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

**Patient or population:** Patients with multimorbidity (diabetes and/or hypertension and other chronic conditions eg, HIV) setting: LMICs

**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 <sup>a,b,c</sup>	Integrated care compared with usual care may make little or no difference to the rate of death, but the evidence is very uncertain
BP control (no of PLHIV achieving BP control)	RCT: Prevalent hypertension at baseline: RR 1.09 (0.98 to 1.21) RCT: Prevalent hypertension at follow-up: RR 1.16 (0.99 to 1.36) ITS study: $\beta=0.010$ (0.003 to 0.016)	2319 (two studies: 1 RCT, 1 ITS study)	⊕○○○ VERY LOW <sup>a,c,d,e,f</sup>	Integrated care compared with usual care may make little or no difference to achieving BP control but the evidence is very uncertain
BP or diabetes (NCD) control (no of PLHIV achieving NCD control)	Prevalent NCD at baseline: RR 1.06 (0.88 to 1.27) Prevalent NCD at follow-up: RR 1.13 (0.97 to 1.32)	1 RCT*	⊕○○○ VERY LOW <sup>a,c,d</sup>	Integrated care compared with 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 (1 ITS study) compared with control clinics	878	⊕○○○ VERY LOW <sup>e,f</sup>	Integrated care may have a very small effect on achieving CD4 count control, but the evidence is very uncertain
BP and HIV control (no of people achieving both HIV viral suppression and BP control)	Prevalent hypertension at baseline: RR 1.22 (1.08 to 1.37) Prevalent hypertension at follow-up: RR 1.24 (1.10 to 1.40)	1441 (1 RCT)	⊕○○○ VERY LOW <sup>a,c,d</sup>	Integrated care compared with 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 (no of people achieving both HIV viral suppression and NCD control)	Prevalent NCD at baseline: RR 1.18 (0.97 to 1.44) Prevalent NCD at follow-up: RR 1.24 (1.01 to 1.40)	1441 (1 RCT)	⊕○○○ VERY LOW <sup>a,c,d</sup>	Integrated care compared with 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

Continued

Table 3 Continued

Patient or population: Patients with multimorbidity (diabetes and/or hypertension and other chronic conditions eg, HIV)

setting: LMICs

Intervention: integrated care for hypertension, diabetes and HIV

Comparison: usual care

Outcome	Effect (95% CI)	No of participants (studies)	Certainty of evidence (GRADE)	Comments
Access to care	There was no change in trend from preintervention to postintervention 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	1 ITS*	⊕○○○ VERY LOW <sup>e,g</sup>	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.

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.

Randomised controlled trials: (a) Downgraded by one due to study limitations: high risk of performance bias and unclear risk of bias for other domains (b) Downgraded by one 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 years

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 one 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

extend care was integrated or not (d) Downgraded by one due to imprecision: Small sub-sample with hypertension and HIV in the RCT with wide 95% CI.

Interrupted time series studies: (e) Observational study, starting at low certainty evidence (f) Downgraded by one due to indirectness: intervention clinics experienced stock-outs of

antihypertensive drugs and malfunctioning of BP machines. We are therefore not confident that the intervention was delivered as intended (g) Downgraded by one 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.

\*Sample size not reported

BP, blood pressure; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HbA1c, glycosylated haemoglobin; ITS, interrupted time series; LMICs, low-income and

middle-income countries; MD, mean difference; NCD, non-communicable disease; PLHIV, people living with HIV; RCT, randomised controlled trial; RR, risk ratio.



### Access to care

One ITS study reported on access to care<sup>45</sup> in terms of the change in postintegration trend compared with preintegration 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, SE=2,  $p=0.50$ , very low certainty) and 36 months (1/100 000, SE=3,  $p=0.61$ , very low certainty evidence) postintegration; clinic level new diabetics on treatment at 18 (0/100 000, SE=1;  $p=0.96$ , very low certainty evidence) and 36 months postintegration; 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) postintegration, and population level new hypertensive patients on treatment at 18 months postintegration (-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 postintegration (-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 with usual care

We included two studies in this comparison.<sup>43 44</sup> Results are summarised in the summary of findings table (table 4) and forest plots are available in online supplemental file 6.

#### All-Cause mortality

Results from one cluster RCT<sup>43</sup> suggest that interventions to promote integrated care compared with usual care may make little or no difference in mortality (RR 1.11; 95% CI 0.79 to 1.56;  $n=3393$ ; 1 RCT, very low certainty evidence) when compared with usual care, but the evidence is very uncertain.

#### Disease-specific morbidity (depression)

Results from two RCTs<sup>43 44</sup> suggest that interventions to promote integrated care compared with 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). This means that the change in HbA1c was similar in both groups. Fairall *et al* reported the change in depression scores from baseline to follow-up using the 10-item Centre for Epidemiologic Studies Depression Scale and reported no difference between groups (MD -0.12; 95% CI -1.72 to 1.48;  $n=3976$ ,

very low certainty evidence). Prabhakaran *et al* measured depression scores at follow-up using the Patient Health Questionnaire-9 and reported no difference between groups (MD -1.6; 95% CI -4.4 to 1.2;  $n=3324$ , very low certainty evidence).

#### Quality of life

Results from one RCT<sup>43</sup> suggest that interventions to promote integrated care compared with usual care may make little or no difference to quality of life, but the evidence is very uncertain. The RCT reported on the change in health-related quality of life from baseline to follow-up using the EuroQol-5 Dimension Visual Analogue Scale and the EuroQol-5D index score. There was no difference between groups, neither for the EuroQol-5D visual analogue scale (MD 6.06; 95% CI -3.25 to 15.36;  $n=3969$ , very low certainty evidence) nor for the EuroQol-5D index score (MD 0.00; 95% CI -0.05 to 0.06;  $n=3969$ , very low certainty evidence).

#### HbA1C

Results from two cluster RCTs<sup>43 44</sup> suggest that interventions to promote integrated care compared with 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<sup>43 44</sup> suggest that interventions to promote integrated care compared with usual care may have little or no effect on change in SBP from baseline to follow-up (MD 1.11 mm Hg; 95% CI -1.41 to 3.35;  $n=4807$ ; 2 RCTs, low certainty evidence).

#### Total cholesterol

Results from one cluster RCT<sup>44</sup> suggest that interventions to promote integrated care compared with usual care may have little or no effect on change in total cholesterol from baseline to follow-up (MD -2.50 mg/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 *et al* reported the number of clinic visits 3 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 7 days.<sup>44</sup> Patients in the intervention group reported greater adherence for both hypertensive drugs (833/1027; 81.1% vs 648/1119; 57.9%) and antihyperglycaemic drugs (683/829; 82.4% vs 570/827; 68.9%) compared with patients receiving usual care.

#### Quality of care

One cluster RCT<sup>44</sup> reported on perceived change in quality of care as a composite perception on availability

**Table 4** Summary of findings for interventions to promote integrated delivery of care compared with usual care for diabetes and hypertension in LMICs

Patient or population: Patients with diabetes, hypertension and other chronic diseases

Setting: LMICs

Intervention: Strategies to promote integrated care

Comparison: Usual care

Anticipated absolute effects* (95% CI)		Risk with Strategies to promote integrated care	Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
Outcomes	Risk with usual care					
Mortality	29 per 1000	32 per 1000 (23 to 45)	RR 1.11 (0.79 to 1.56)	4393 (1 RCT)	⊕○○○ VERY LOW <sup>a,b,c</sup>	Integrated care compared with usual care may make little or no difference to the risk of death, but the evidence is very uncertain
Depression	10-item Centre for Epidemiologic Studies Depression Scale: MD -0.12 (-1.72 to 1.48) Patient Health Questionnaire-9: MD -1.6 (-4.4 to 1.2)			7293 (2 RCTs)	⊕○○○ VERY LOW <sup>a,b,c</sup>	Integrated care compared with usual care may make little or no difference to depression scores, but the evidence is very uncertain
Change in quality of life (Euro-QoL-5 Dimension 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 <sup>a,b,c</sup>	Integrated care compared with 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 <sup>a,c</sup>	Integrated care compared with 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 mm Hg	The mean change in BP with integrated care was 1.11 mm Hg higher (1.14 lower to 3.35 higher)	-	4807 (2 RCTs)	⊕⊕○○ LOW <sup>a,c</sup>	Integrated care compared with 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 <sup>a,c</sup>	Integrated care compared with usual care may have little or no effect on total cholesterol levels

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: (a) Downgraded by one due to study limitations: high risk of performance bias and unclear risk of bias in some other domains, (b) Downgraded by one due to imprecision: study not adequately powered for this outcome, small sample size and wide 95% CI, (c) Downgraded by one 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.

\*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). BP, blood pressure; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HbA1c, glycated haemoglobin; LMICs, low-income and middle-income countries; MD, mean difference; RCT, randomised controlled trial; RR, risk ratio.

of drugs, guidance from physicians, quality of care, frequency of BP 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%).

Neither of the two cluster RCTs included in this comparison reported on access to care, continuity of care or cost of care.

## DISCUSSION

### Summary of main results

We included five studies and two comparisons in this review. Three studies were conducted in South Africa, one in India and one in Kenya and Uganda. Two ITS studies and one cluster RCT provided data for the first comparison, integrated models of care compared with usual care. Results suggest that integrated models of care compared with usual care may make little or no difference to mortality, the number of people achieving 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. However, the evidence for all outcomes is very uncertain. Two cluster RCTs provided data for the second comparison, interventions to promote integrated delivery of care compared with usual care. Results suggest that interventions to promote integrated delivery of care compared with usual care may make little or no difference to mortality, depression and quality of life, but the evidence is very uncertain. Interventions to promote integrated delivery of care compared with usual care may have little or no effect on HbA1c, SBP and total cholesterol levels. Process outcomes were poorly reported across included studies, with none of the studies reporting on continuity of care or cost of care.

### Agreements and disagreements with other reviews

Other systematic reviews that assessed the effects of integrated models of care on health outcomes in LMICs had similar findings. Dudley and Garner<sup>30</sup> assessed strategies to integrate PHC services on healthcare delivery and health status in LMICs. They found no evidence that integrated services improved healthcare delivery or health status. However, none of the included studies assessed integrated care for NCDs. Haldane *et al*<sup>28</sup> described existing integrated models of care for HIV and NCDs and assessed health outcomes, barriers and facilitators. However, most of the included studies were descriptive or observational and health outcomes were poorly reported. Indeed, they highlighted the need for rigorous research that includes long-term follow-up and the role of incentives.

### Overall completeness and applicability of evidence

Although we considered multimorbidity in terms of diabetes and/or hypertension plus any other disease, four

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

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



## Strengths and limitations

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

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

Our review focused on the effectiveness of integrating care for people with diabetes, hypertension and other comorbidities in terms of health outcomes, which is just one question that needs to be answered. In other words, the question of our review focused on one building block of health systems as described by the WHO.<sup>56</sup> Although we aimed to examine process outcomes, these were limited to access to care, retention in care, adherence, continuity of care, quality of care and cost of care; and were poorly reported across included studies. The scope of our review did not include outcomes related to implementation or perspectives from health providers and patients, which are important aspects to consider. Although the literature predominantly highlights the need to integrate NCD and HIV care, integrating mental health services into existing NCD and or HIV services is just as important. Four<sup>48–51</sup> of the five ongoing studies that we identified examine integration of mental health with NCDs.

## CONCLUSION

The evidence on the effectiveness of integrated models of care for people with diabetes, hypertension and other

comorbidities, on health outcomes is very uncertain. We therefore do not know whether integrated models of care lead to better or worse outcomes, or may make no difference at all among people with diabetes, hypertension and other chronic conditions. There is a need to scale up NCD services, particularly in LMICs. In the context of an increasing burden of NCDs against a backdrop of other chronic diseases and scarce health system resources, such as human capacity and funding, policies and programmes need to promote integrated models of care and holistic, patient-centred services. However, these need to take into consideration context-specific factors related to the health system and the targeted population.

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

## Author affiliations

<sup>1</sup>Centre for Evidence-based Health Care, Division of Epidemiology and Biostatistics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

<sup>2</sup>School of Public Health, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda

<sup>3</sup>Institute for Evidence in Medicine (for Cochrane Germany Foundation), Medical Center & Faculty of Medicine, University of Freiburg, Freiburg, Germany

<sup>4</sup>Kigali University Teaching Hospital, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda

<sup>5</sup>Cochrane Germany, Cochrane Germany Foundation, Freiburg, Germany

**Twitter** Jeannine Uwimana Nicol @jeannine nicol and Taryn Young @TarynYoung3

**Acknowledgements** We would like to thank Anel Schoonees for conducting the search of electronic databases, Birhanu Ayele for statistical input, and Selvan Naidoo for assistance with screening titles and abstracts.

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

**Funding** This systematic review was supported by the funding from the Collaboration for Evidence-based Healthcare and Public Health in Africa (CEBHA+) project which is funded by the German Federal Ministry of Education and Research (BMBF) as part of the Research Networks for Health Innovation in Sub-Saharan Africa Funding Initiative. Award/Grant number is not applicable.

**Disclaimer** The funder did not have any role in the review process.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** This systematic review does not involve human participants. All data included are in the public domain and ethics approval was thus not sought.



**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as online supplemental information.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iDs

Anke Rohwer <http://orcid.org/0000-0002-1092-5942>

Jeannine Uwimana Nicol <http://orcid.org/0000-0002-5983-3766>

#### REFERENCES

- WHO. Noncommunicable diseases 2018 <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>
- GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. 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;390:1211–59.
- NCD Alliance. 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 [www.ncdalliance.org](http://www.ncdalliance.org)
- WHO. Cardiovascular diseases (CVDs), 2017. Available: <https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-cvds>
- WHO. Global status report on non-communicable diseases 2010. description of the global burden of NCDs, their risk factors and determinants 2010 [https://www.who.int/nmh/publications/ncd\\_report\\_summary\\_en.pdf?ua=1](https://www.who.int/nmh/publications/ncd_report_summary_en.pdf?ua=1)
- International Diabetes Federation. *IDF diabetes atlas 8th edition*. 8 ED, 2017. <https://www.idf.org/e-library/epidemiology-research/diabetes-atlas>
- Campbell NRC, Lackland DT, Niebylski ML, et al. 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. *J Clin Hypertens* 2014;16:551–3.
- Duffy M, Ojikutu B, Andrian S, et al. Non-Communicable diseases and HIV care and treatment: models of integrated service delivery. *Trop Med Int Health* 2017;22:926–37.
- Lalkhen H, Mash R. Multimorbidity in non-communicable diseases in South African primary healthcare. *S Afr Med J* 2015;105:134–8.
- Remais JV, Zeng G, Li G, et al. Convergence of non-communicable and infectious diseases in low- and middle-income countries. *Int J Epidemiol* 2013;42:221–7.
- 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 Suppl 1:S77–83.
- 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:S5–20.
- 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. *Lancet* 2012;380:2095–128.
- Mbanya JCN, Motala AA, Sobngwi E, et al. Diabetes in sub-Saharan Africa. *The Lancet* 2010;375:2254–66.
- 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 Plan* 2010;25:1–14.
- Shigayeva A, Atun R, McKee M, et al. Health systems, communicable diseases and integration. *Health Policy Plan* 2010;25 Suppl 1:i4–20.
- WHO. Package of essential non-communicable (Pen) disease interventions for primary health care in low-resource settings 2010 [http://www.who.int/nmh/publications/essential\\_ncd\\_interventions\\_lr\\_settings.pdf](http://www.who.int/nmh/publications/essential_ncd_interventions_lr_settings.pdf)
- Legido-Quigley H, Montgomery CM, Khan P, et al. Integrating tuberculosis and HIV services in low- and middle-income countries: a systematic review. *Trop Med Int Health* 2013;18:199–211.
- Naidoo K, Gengiah S, Yende-Zuma N. 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;12:1–12.
- Uyei J, Coetzee D, Macinko J, et al. Integrated delivery of HIV and tuberculosis services in sub-Saharan Africa: a systematic review. *Lancet Infect Dis* 2011;11:855–67.
- 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;7:203.
- 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;18:481.
- Atlantis E, Fahey P, Foster J. Collaborative care for comorbid depression and diabetes: a systematic review and meta-analysis. *BMJ Open* 2014;4:e004706.
- 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.
- 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:e103754.
- 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.
- 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;4:294–306.
- Haldane V, Legido-Quigley H, Chuah FLH, et al. Integrating cardiovascular diseases, hypertension, and diabetes with HIV services: a systematic review. *AIDS Care* 2018;30:103–15.
- Jenssens B, Van Damme W, Raleigh B, et al. Bulletin of the world Health organization stroke: a global response is needed. *Bull World Health Organ* 2007;85:880–5.
- 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.
- World Bank. World bank list of economies 2016, 2016. Available: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>
- Veritas Health Innovation. *Covidence systematic review software*. Melbourne, Australia: Veritas Health Innovation, 2013.
- 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.
- Gaude J-M, 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.
- Cochrane Effective Practice and Organisation of Care. Suggested risk of bias criteria for EPOC reviews. EPOC resources for review authors 2017 <http://epoc.cochrane.org/resources/epoc-resources-review-authors>
- Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for systematic reviews of interventions version 6.0 (updated July 2019)*. London: Cochrane, 2019. [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook)
- The Cochrane Collaboration. *Review Manager (RevMan) [program]. 5.3 version*. Copenhagen: The Cochrane Collaboration, 2014.
- Guyatt G, Oxman AD, Akl EA, et al. Grade guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383–94.
- GRADEpro guideline development tool (GDT), 2015 McMaster University. Available: [www.gradepro.org](http://www.gradepro.org)
- Balshem H, Helfand M, Schünemann HJ, et al. Grade guidelines: 3. rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.
- 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.
- 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. *J Acquir Immune Defic Syndr* 2017;75:472–9.
- 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 Med* 2016;13:e1002178.
  - 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. [Epub ahead of print: 10 Nov 2018].
  - 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. *J Acquir Immune Defic Syndr* 2018;77:476–83.
  - 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;381:219–29.
  - 47 Bongomin P, Rabkin M, Palma AM, *et al.* Integrated versus referred management of cardiovascular disease (CVD) risk factors for HIV-positive patients on antiretroviral therapy in Swaziland. *20th International workshop on co-morbidities and adverse drug reactions in HIV; New York, USA* 2018:A9.
  - 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 Geriatr* 2018;18:124.
  - 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;19:192.
  - 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:no pagination.
  - 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;19:158.
  - 52 Devarsetty P. Diabetes and Tuberculosis - Integrated management using the primary healthcare infrastructure in India, 2017. Available: <http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=15771>
  - 53 Ameh S, Klipstein-Grobusch K, D'ambrosio L, *et al.* Quality of integrated chronic disease care in rural South Africa: user and provider perspectives. *Health Policy Plan* 2017;32:257–66.
  - 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 Malawi, South Africa, Swaziland and Kenya. *AIDS* 2018;32 Suppl 1:S21–32.
  - 55 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:S33–42.
  - 56 WHO. *Everybody's business: strengthening health systems to improve health outcomes. WHO's framework for action.* Geneva: WHO, 2007.