BMJ Open

Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review

Deepti Shanbhag,[1] Ian D Graham,[2] Karen Harlos,[3] R. Brian Haynes,[4] Itzhak Gabizon,[5] Stuart J Connolly,[5] Harriette Gillian Christine Van Spall[4,5]

To cite: Shanbhag D, Graham ID, Harlos K, *et al*. Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review. *BMJ Open* 2018;**8**:e017765. doi:10.1136/bmjopen-2017-017765

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2017-017765).

Received 16 May 2017
Revised 5 December 2017
Accepted 11 January 2018

[1]Bachelor of Health Sciences Program, McMaster University, Hamilton, Ontario, Canada
[2]School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada
[3]Department of Business and Administration, University of Winnipeg, Winnipeg, Manitoba, Canada
[4]Department of Medicine and Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada
[5]Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada

Correspondence to
Dr. Harriette Gillian Christine Van Spall;
Harriette.VanSpall@phri.ca

ABSTRACT

Background The uptake of guideline recommendations that improve heart failure (HF) outcomes remains suboptimal. We reviewed implementation interventions that improve physician adherence to these recommendations, and identified contextual factors associated with implementation success.

Methods We searched databases from January 1990 to November 2017 for studies testing interventions to improve uptake of class I HF guidelines. We used the Cochrane Effective Practice and Organisation of Care and Process Redesign frameworks for data extraction. Primary outcomes included: proportion of eligible patients offered guideline-recommended pharmacotherapy, self-care education, left ventricular function assessment and/or intracardiac devices. We reported clinical outcomes when available.

Results We included 38 studies. Provider-level interventions (n=13 studies) included audit and feedback, reminders and education. Organisation-level interventions (n=18) included medical records system changes, multidisciplinary teams, clinical pathways and continuity of care. System-level interventions (n=3) included provider/institutional incentives. Four studies assessed multi-level interventions. We could not perform meta-analyses due to statistical/conceptual heterogeneity. Thirty-two studies reported significant improvements in at least one primary outcome. Clinical pathways, multidisciplinary teams and multifaceted interventions were most consistently successful in increasing physician uptake of guidelines. Among randomised controlled trials (RCT) (n=10), pharmacist and nurse-led interventions improved target dose prescriptions. Eleven studies reported clinical outcomes; significant improvements were reported in three, including a clinical pathway, a multidisciplinary team and a multifaceted intervention. Baseline assessment of barriers, staff training, iterative intervention development, leadership commitment and policy/financial incentives were associated with intervention effectiveness. Most studies (n=20) had medium risk of bias; nine RCTs had low risk of bias.

Conclusion Our study is limited by the quality and heterogeneity of the primary studies. Clinical pathways, multidisciplinary teams and multifaceted interventions appear to be most consistent in increasing guideline uptake. However, improvements in process outcomes were rarely accompanied by improvements in clinical outcomes. Our work highlights the need for improved research methodology to reliably assess the effectiveness of implementation interventions.

Strengths and limitations of this study

- ► While previous reviews have evaluated implementation interventions, to our knowledge, this review is the first to examine interventions to improve heart failure care, and to identify contextual factors associated with implementation success.
- ► We conducted an extensive search of nine databases and include 38 studies spanning nine implementation intervention categories.
- ► A limitation of our review is that moststudies (n=28) used observational or quasi-experimental designs, which are subject to bias and confounding. Only 10 studies were randomised controlled trials.

INTRODUCTION

Heart failure (HF) has a prevalence of approximately 10% in the elderly, and is a common cause of hospitalisation and death in older adults.[1] Patients diagnosed with HF have a 30% risk of mortality at 3 years, and those hospitalised for HF face a substantially higher risk.[1] Patients with HF are classified as having reduced ejection fraction (ie, ≤40%) or preserved ejection fraction (ie, >50%).[2] Evidence-informed treatments can improve clinical outcomes in HF, and recommendations surrounding their use are published in clinical practice guidelines.[2–5] Class I/level A recommendations are supported by strong evidence, and are associated with reduced hospitalisation and mortality. Class I recommendations include the assessment of heart function and provision of self-care education for all patients with HF; for patients with reduced ejection fraction, class I recommendations also include specific pharmacological

and device therapies.[2] However, studies show that the uptake of these guidelines by physicians into routine clinical practice remains slow and inconsistent.[6–8]

Implementation interventions are designed to bridge the gap between evidence and practice, and are broadly classified at the provider, organisational or health system levels. Interventions may be single or multifaceted.[9] Implementation success also depends on the intervention development process and organisational context. While previous reviews have evaluated implementation interventions,[10–12] none, to our knowledge, have evaluated interventions within HF care or identified contextual factors associated with implementation success.

Accordingly, the primary objective of our review was to examine the effectiveness of implementation interventions in increasing physician adherence to the specified HF guideline recommendations. Our secondary objectives were to assess the effect of implementation interventions on clinical outcomes, and to identify process and contextual factors that influence implementation success.

METHODS AND ANALYSIS

The systematic review protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42015017155), and published in a peer-reviewed journal.[13] The only deviation from the protocol was the inclusion of uncontrolled before-after studies.

Eligibility criteria

We included trials evaluating one or more interventions aimed at improving physician adherence to class I HF guidelines, relative to usual care. Interventions were categorised by level (ie, provider, organisation or system level) and type (ie, education, decision support, financial incentives) according to the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy.[9]

Outcomes

While implementation interventions were targeted towards healthcare providers, outcomes were measured at the level of the patient (eg, number of patients receiving guideline-appropriate care). Primary outcomes were process indicators, defined as measures that assess guideline-consistent activities undertaken by a provider.[14] The primary outcomes included the proportion of eligible patients with HF who: were prescribed a guideline-recommended pharmacological treatment such as β-blockers, ACE inhibitors (ACEI), angiotensin II receptor blockers (ARB) or mineralocorticoid receptor antagonists (MRA); were referred for implantable cardioverter defibrillator (ICD) and/or cardiac resynchronisation therapy (CRT) consideration; were provided self-care education at discharge; and/or had their left ventricular ejection fraction (LVEF) quantified. Secondary outcomes were clinical outcomes such as HF-related hospitalisations, readmissions and mortality. In the absence of HF-specific clinical outcomes, we extracted and reported all-cause clinical outcomes.

Study design

We included randomised controlled trials (RCT), cohort studies (with comparisons), controlled and uncontrolled before and after studies, and interrupted time series studies.

Study selection

We searched for all English language articles published since 1990 in MEDLINE, EMBASE, HEALTHSTAR, CINAHL, The Cochrane Library, The Campbell Collaboration, The Joanna Briggs Institute Evidence-based Practice Database, The Agency for Healthcare Research and Quality Evidence-based Practice Centers' Research Reports, and the University of York Centre for Reviews and Dissemination Database. Our primary search strategy used the following terms: heart failure, guideline adherence, practice guideline, evidence-based medicine, implement (online supplementary appendix 1). Our secondary search included terms for each of the different EPOC intervention types and heart failure (online supplementary appendix 2). Two authors independently screened titles and abstracts, and then assessed select full-text articles according to the eligibility criteria.

Data extraction and management

Two authors independently extracted details about study design, statistical analysis, intervention, patient and provider characteristics, follow-up and outcomes using the EPOC Data Collection Checklist.[9] In addition, the Process Redesign framework was used to extract and synthesise details on the intervention development process, and relevant contextual factors.[15]

Assessment of risk of bias

In addition to identifying the limitations inherent within specific study designs, two authors independently applied design-specific criteria to assess the internal validity of studies retained for analysis. We used the criteria outlined in the EPOC Data Collection Checklist to evaluate RCTs, cluster RCTs, controlled before-after studies and interrupted time series studies.[9] For cluster RCTs, we used the additional criteria of recruitment bias, loss of cluster and incorrect analysis according to the Cochrane Handbook for Systematic Reviews of Interventions.[16] For cohort studies, we used the Cochrane Collaboration's tool to assess risk of bias in cohort studies.[17] For uncontrolled before-after studies, we used the National Institute of Health's quality assessment tool for before-after studies with no control group.[18] Because our goal was to assess internal validity, we did not use tool criteria pertaining to applicability or external validity, precision and quality of reporting. We categorised studies as low risk of bias if one criterion was not satisfied, medium risk if two to three criteria were not satisfied and high risk if more than three criteria were not satisfied.

Table 1 Cochrane Effective Practice and Organisation of Care taxonomy

Intervention	Description
Provider level	
Education	Distribution of educational materials, education sessions, or education outreach visits to providers
Audit and feedback	Summary of clinical performance over a specified period, with or without recommendations for clinical action.
Reminders	Patient or encounter-specific information provided verbally, on paper, or on a computer screen to prompt health professionals to perform or avoid certain action
Organisation level	
Changes in medical records systems	Modification of existing medical records systems (eg, changing from paper to computerised records)
Clinical multidisciplinary teams	A team of health professionals of different disciplines who work collaboratively to care for patients
Clinical pathways	Evidence-based care management tool for a specific group of patients with a predictable clinical course
Continuity of care	Formal arrangements for community-based assessment and treatment after hospital discharge
System level	
Provider financial incentives/penalties	Financial reward or penalty for specific action by an individual provider
Institutional financial incentives/penalties	Financial reward or penalty for specific action by an institution or group of providers

Data synthesis

We classified the implementation interventions according to the level targeted (provider, organisation and system) and the type of intervention (eg, education, decision support, audit and feedback, financial) using the EPOC taxonomy.[9] An abbreviated version of the EPOC taxonomy is presented in table 1. We explored the suitability of a meta-analysis of the results within each intervention category by first assessing clinical heterogeneity at face value on the basis of included patient populations, settings (inpatient/outpatient), intervention types and outcome measures. We then assessed statistical heterogeneity using the I^2 statistic, defining substantial heterogeneity as I^2>75%. For studies not suitable for meta-analysis, we narratively synthesised results.[19 20] We performed vote counting for each outcome measure in each EPOC intervention category, by noting the number of studies reporting significant improvements compared with those with no significant improvements.

Contextual factors

Context generally refers to the physical, social, political and economic influences on healthcare practices.[21] We used the Process Redesign framework to systematically evaluate contextual factors that may influence the effectiveness of implementation interventions.[15] The Process Redesign framework classifies context into categories: outer setting, inner setting and characteristics of individuals and teams. The inner context refers to the structural characteristics of the clinical setting (eg, inpatient, outpatient, community-based care, academic status), networks and communications, culture and climate. The characteristics of individuals and teams more specifically refer to professional roles, responsibilities and authority within the organisation. The outer context refers to factors related to the broader social, political and economic environment in which the intervention is applied. We considered processes that introduced and adapted the intervention to the organisation as part of the intervention, rather than the context. An abbreviated and modified version of the framework is presented in table 2.

RESULTS

Identification, screening and selection of studies

Our systematic search produced 3742 unique articles, of which 3590 were excluded on the basis of title and/or abstract review. We assessed 152 full-text articles, of which 38 studies met eligibility criteria. We excluded articles that: were abstracts, protocols or letters (n=17); did not test implementation interventions (n=26); did not focus on patients with HF (n=4); had no comparator group (n=6); or had no outcomes of interest (n=61) (see figure 1).

Characteristics of included studies

Setting

A majority of the studies were conducted in the USA (n=26), and the remainder in Europe (n=10) and Australia (n=2). Sixteen studies were conducted in inpatient settings, twenty-one in outpatient settings and one involved care in both settings (table 3).

Table 2 Adapted Process Redesign framework

Construct	Description
Process of implementation (applied here as an intervention factor)	
Planning	Degree to which intervention steps are developed in advance of implementation and with consideration of various possible scenarios
Assessing	Formal assessment of the problem or condition to be changed, including needs of users, and barriers and facilitators of change
Staging and iteration	Whether the implementation is carried out in incremental steps, refined iteratively or implemented in its entirety within a specified period
Access to information, training and education	Staff access to information or education about the intervention
Inner setting (contextual factor)	
Team and network characteristics	Influence, breadth, depth and role diversity of teams and networks engaged in the Process Redesign
Teams, networks and communications	Quality of teams and social networks; formal/informal communication and information exchange within an organisation or between organisations
Culture	Norms, values and beliefs within a team, unit or practice that affect views of Process Redesign and its implementation
Mandate	Whether adherence to the intervention is expected or mandated
Leadership commitment	Degree of commitment, involvement and accountability of leaders and managers to quality improvement and to the specific intervention
Human factors	Whether features of the physical and technical environment are designed to optimise human use, accessibility and uptake in patient care
Outer setting (contextual factor)	
External networks	Degree to which an organisation is networked with other organisations engaged in similar Process Redesign activities
External pressure	Pressure emanating from outside the organisation to introduce an intervention
External policy and incentives/ disincentives	Laws, regulations, governmental recommendations and/or payment schemes that affect the decision to adopt or abandon the Process Redesign efforts
Characteristics of individuals and teams (contextual factor)	
Role	Individual's or team's role and responsibilities, and the extent of multiple or shared roles
Authority	Perceived and actual authority to make decisions and act autonomously

Types of implementation interventions

Thirteen studies offered interventions directed at the level of healthcare providers, 18 at the organisation level, three at the health system level and four across multiple levels. Provider-level interventions included: audit and feedback (n=4 studies),[22–25] reminders (n=5),[26–30] education (n=2)[31 32] and a combination of these (n=2).[33 34] Organisation-level interventions included: changes in medical records systems (ie, adaptations to existing systems on the basis of organisational need) (n=4),[35–38] clinical multidisciplinary teams (n=8),[26 39–45] clinical pathways (n=5)[46–50] and continuity of care (n=1).[51] System-level interventions included: financial incentives for providers (n=1)[52] and financial incentives for institutions (n=2).[53 54] Four studies offered interventions across multiple levels. A common feature across all six multifaceted interventions was the use of audit and feedback (table 3).

Study design

Among the 38 studies included, 10 were RCTs. Five were randomised at the level of patients,[26 39 40 44 46] and five were cluster randomised by practice or hospital.[22 23 31 33 41] Twenty-three studies used quasi-experimental designs: three were controlled before-after studies,[32 41 53] two were interrupted time series studies[34 35] and 18 were uncontrolled before-after studies.[24 25 27–30 34–38 42 43 47 48 55 56] Four studies used a retrospective cohort design,[45 49 50 52] while one used a combination of retrospective and prospective cohort designs[51] (see table 3).

Risk of bias

Most studies had a medium risk of bias according to design-specific criteria (online supplementary appendix 3). Five patient-level RCTs,[26 39 40 44 46] and four of the five cluster RCTs had a low risk of bias.[23 31 33 46]

Quality of reporting

We evaluated the quality of reporting in RCTs using the Consolidated Standards of Reporting Trials statement, including the extension for cluster RCTs. Among the five RCTs, four did not provide information on the methods of

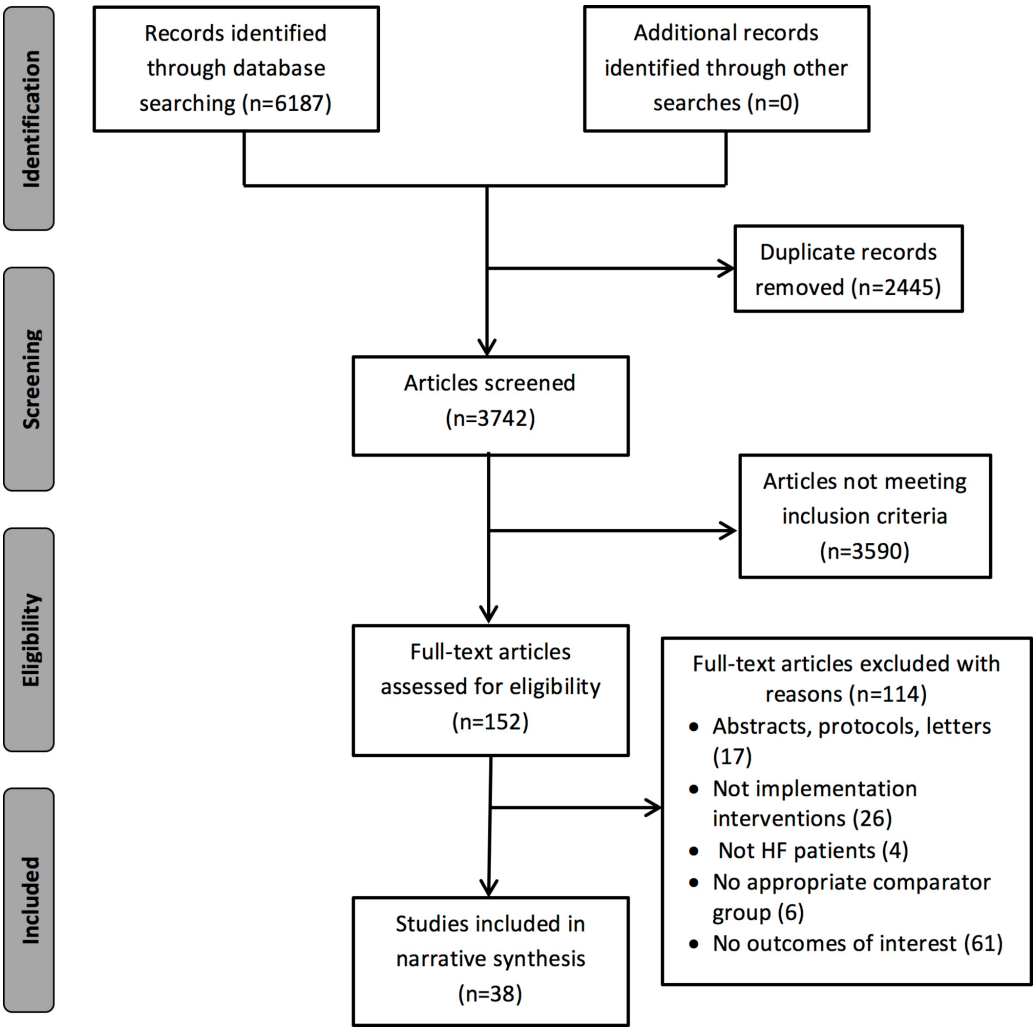

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of study selection. HF, heart failure.

randomisation or allocation concealment.[26 39 44 46] None of the five studies reported the precision of effect size estimates or provided relative effect sizes in addition to absolute risk differences.[26 39 40 44 46] Among the five cluster RCTs, four did not provide information on the methods of randomisation or allocation concealment,[22 31 33 41] three did not describe eligibility criteria,[20 21 29] three did not provide sample size calculations[22 33 41] and four did not provide intra-cluster correlation values.[22 23 31 41]

Outcomes reported

Thirty-seven studies reported the proportion of patients prescribed recommended medications (ie, ACEI/ARBs, β-blockers, MRAs); 30 studies reported prescription of indicated medications at any dose,[22 24–26 28 29 33–40 42 44–50 52–54 57–59] and 12 reported prescriptions of medications at target doses.[26 31 33 39 41 43–45 47 48 51 56] Other studies reported: patient self-care education prior to discharge (n=9)[23 27 38 42 46 54 55 57 59]; referrals for ICD/CRT (n=2)[30 55]; and LVEF assessments (n=11).[27 33 34 38 46 47 49 53 54 57 58] In addition to these primary outcomes, 11 studies reported clinical outcomes such as mortality, hospitalisation and readmission rates.[26 32 39 40 42 44–46 49 51 55] I^2 calculations produced a value greater than 80% for most categories of interventions, precluding the possibility of a meta-analysis. Therefore, the studies were synthesised narratively.

Effectiveness of implementation interventions

A summary of study outcomes is presented in table 3. A majority of studies (n=32, 84%) reported significant improvements in at least one primary outcome.

Prescription of indicated medications

Reminders, clinical pathways, changes in medical records systems and multifaceted interventions were commonly associated with an increase in guideline-recommended prescriptions. In four studies that reported prescriptions of more than one indicated medication, significant improvements were observed in the prescription of β-blockers and MRAs, but not in the prescription of ACEIs. In these studies, the prescription rates at baseline for ACEIs were substantially higher than those of β-blockers or MRAs, ranging from 78.0% to 86.3%.[28 34 36 48]

Table 3 Summary of studies evaluating strategies for the implementation of heart failure (HF) clinical guidelines

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Professional interventions						
Education						
Thilly *et al*[31] (2003) France	Tertiary care; inpatient	Cluster RCT	Hospitals (20)/ patients (370)	**Intervention:** Cardiologists presented guidelines and discussed cases with colleagues. Educational aids and guideline booklets were supplied to physicians. **Control:** Usual care; no implementation intervention **Process:** *Planning/assessment*— prior to developing the educational intervention, a preliminary survey was conducted to identify specific guideline deviations in practice. Guidelines determined to be of particular concern were made the focus of the intervention.	**Target ACEI +27%†, P=0.003**	
Asch *et al*[32] (2005) USA	Tertiary care; inpatient	Controlled before-after	Patients (489)	**Intervention:** Provider teams attended three training sessions where national Quality Improvement and HF experts guided them in studying, testing and implementing systematic improvements in HF care processes. **Control:** Usual care; no implementation intervention	**ACEI +18%‡, P<0.0001**; β-blockers –2%‡, P=0.49; LVEF +3%‡, P=0.49	
Audit and feedback						
Kasje *et al*[22] (2006) Netherlands	Primary care	Cluster RCT	Providers (57)/ patients (508)	**Intervention:** Providers received patient-specific feedback on a sample of patients, and attended structured meetings to discuss guidelines and current management, identify problems and propose solutions for improving HF patient care. **Control:** Providers received education on management of type II diabetes. **Process:** *Planning/assessment*—Optimal intervention design was determined through literature review. Specific barriers to guideline adherence were identified by physicians during peer-review meetings as part of the intervention.	ACEI +5%†, P>0.05	
Frijling *et al*[23] (2003) Netherlands	Primary care	Cluster RCT	Practices (124)/ patients (236)	**Intervention:** Physician assistants provided physicians with a practice-specific feedback report, identified areas needing improvement and provided guidance and resources for improvement. **Control:** Usual care; no implementation intervention	Education OR 0.85, P=0.636	
Cancian *et al*[24] (2013) Italy	Primary care	Before-after	Patients (1905)	**Intervention:** Performance data were aggregated across 21 health units. Project leaders reviewed data and identified barriers to unit leaders, who conveyed the data to all physicians involved. **Control:** Usual care; no implementation intervention **Process:** *Access to information, training, education*—Intervention was explained to participating physicians through two health unit training meetings	**ACEI +3.6%†, P=0.008**; **β-blockers +10.8%†, P<0.0001**	
Matthews *et al*[25] (2007) USA	Tertiary care; outpatient	Before-after	Patients (265)	**Intervention:** Following discharge of patients from the hospital, outpatient physicians were provided quality of care reports outlining services received in hospital and areas for HF care improvement. This included instructions for medication titration and detailed HF education. **Control:** Usual discharge information	**ACEI +6.4%, P=0.042†**; β-blockers –1.1%†, P=0.73; MRA +11.1%†, P=0.26	
Reminders						
Ansari *et al*[26] (2003) USA	Primary care	RCT	Patients (115)	**Intervention:** In addition to education on β-blocker use, physicians received a list of their patients with HF eligible for β-blockers as well as electronic alerts when accessing patients' EMRs for the first two visits after randomisation. **Control:** Education on the use of β-blockers via grand rounds presentations and guideline dissemination **Process:** *Planning/assessment*—The intervention was designed to address a barrier identified at baseline.	β-blockers –17%†, P>0.05; target β-blockers –8%†, P>0.05	HF-related hospitalisations +4%†, P>0.05; 1-year all-cause mortality –12%†, P=0.05
Braun *et al*[28] (2011) Germany	Primary care	Before-after	Patients (190)	**Intervention:** Computer-based system displayed a pop-up window of a condensed version of the HF guidelines during clinical consultations. **Control:** Usual care; no implementation intervention	ACEI –4.4%†, P=0.3; **β-blockers +12.3%†, P=0.03**; **MRA +9.2%†, P=0.04**	

Continued

Table 3 Continued

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Butler *et al*[27] (2006) USA	Tertiary care university hospital; inpatient	Before-after	Patients (1275)	**Intervention:** Computerised physician order entry system provided point-of-care reminders for select quality measures and included a prescription writer function. **Control:** Usual order entry form without disease-specific prompts **Process:** *Planning/assessment*—The intervention was developed iteratively prior to the intervention phase of the study. The programme was modified based on institutional requirements, developer-initiated improvements and user feedback.	ACEI +13%†, P=0.10; **education +53%†, P<0.001**; LVEF +5%†, P=0.86	
Qian *et al*[29] (2011) USA	Tertiary care university hospital; inpatient	Before-after	Patients (5000)	**Intervention:** Computer program flagged eligible patients not receiving ACEI/ARB. Pharmacists verified the flags and notified the medical team via EMR. Patients were reflagged if no action was taken within 24 hours. **Control:** Usual care; no implementation intervention **Process:** *Planning*— Comprehensive plan-do-study-act cycle occurred over a period of 1 year prior to the intervention phase. Problems were identified in the system's operating process and adjusted to increase work flow efficiency.	**ACEI +9.2%†, P<0.002**	
Gravelin *et al*[30] (2011) USA	Cardiology clinics; outpatient	Before-after	Patients (6632)	**Intervention:** EMR screening tool identified patients with left ventricular ejection fraction <35% and prompted cardiologists to refer to electrophysiologist for consideration of ICD and/or CRT. **Control:** Usual care; no implementation intervention	**ICD/CRT referral: site 1 +47%†, P<0.02; site 2 +40%†, P<0.001**	
Organisational interventions						
Changes in medical records systems						
Reingold and Kulstad[37] (2007) USA	Tertiary care university hospital; inpatient	Before-after	Patients (171)	**Intervention:** Existing HF order sets were modified to be more succinct and visually organised, with the addition of narrative information to encourage utilisation. **Control:** Routine order sets **Process:** *Planning/assessment*—The improvement process was initiated 5 years in advance of intervention phase, and the intervention was developed based on staff feedback.	**ACEI +58%†, P=0.008**	
Oujiri *et al*[38] (2011) USA	Tertiary care university hospital	Before-after	Patients (153)	**Intervention:** A discharge face sheet embedded into the EMR reminded physicians of evidence-based measures and required physicians to indicate reasons for unmet measures. **Control:** Computerised order entry form included reminders to address each diagnosis, but no prompts to follow treatment guidelines. Discharge orders were not easily accessible within the EMR, making it difficult to assess adherence to HF quality measures. **Process:** *Planning/assessment*—The institution's admission and discharge processes were reviewed extensively to identify barriers to guideline adherence at baseline, and these were addressed in the intervention design.	**ACEI +18%†, P<0.01**; education +5%†, P>0.05; LVEF +12%†, P>0.05	
Baker *et al*[36] (2011) USA	Primary care	ITS	Patients (276)	**Intervention:** Pre-visit paper reminders of outstanding quality deficits were printed and placed outside the patient's examination room to supplement existing electronic reminders within the EMR. **Control:** Electronic system offered point-of-care reminders, captured contraindications and patient refusals, and generated lists of patients not receiving essential medications. **Process:** *Planning/assessment*—Following earlier introduction of an electronic reminder system, physician adherence to guideline recommendations was evaluated. Reasons for gaps were identified among a subset of physicians and addressed in the design of the paper intervention.	ACEI +0% per year§, P=0.95; **β-blockers +2.9% per year§, P=0.004**	
Persell *et al*[35] (2011) USA	Primary care	ITS	Patients (not clear)	**Intervention:** An existing reminder system was updated to be minimally intrusive and include standardised means to capture contraindications. **Control:** EMR generated interruptive 'pop-up' reminders at point of care, and did not possess a mechanism to record contraindications. **Process:** *Planning/assessment*—Limitations in the EMR system were identified at baseline and addressed in the system redesign.	**ACEI +5.3% per year§, P<0.001**; **β-blockers +5.7% per year§, P<0.001**	

Continued

Table 3 Continued

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Clinical multidisciplinary team						
McCarren *et al*[41] (2013) USA	Tertiary care; outpatient	Cluster RCT	Hospitals (12)/ patients (220)	**Intervention:** Pharmacists were asked to invent methods to improve prescribing practices. Pharmacists received data on facility guideline adherence, along with a list of patients with suboptimal HF therapy. **Control:** Pharmacists were asked to invent methods to improve prescribing practices. Pharmacists received data on facility guideline adherence. **Process:** *Planning*—Intervention methods were designed to be pragmatic (ie, data collection and presentation required by each pharmacist was minimal to promote participation).	Target β-blockers +1%†, P>0.05	
Mejhert *et al*[39] (2004) Sweden	Tertiary university hospital; outpatient	RCT	Patients (208)	**Intervention:** A nurse monitored patients after discharge and adjusted their medications under the supervision of a senior cardiologist. **Control:** Conventional follow-up in primary care	**Target ACEI +14%†, P<0.05**; ACEI –5%†, P>0.05; β-blockers –6%, P>0.05	4-year all-cause mortality +7%†, P>0.05; 4-year all-cause readmissions +0%†, P>0.05
Kasper *et al*[40] (2002) USA	Tertiary university hospital; outpatient	RCT	Patients (200)	**Intervention:** In the intervention group, HF nurses closely followed up with patients after discharge and implemented the cardiologist-developed treatment algorithm. The control group received care from the primary physician alone. **Control:** Conventional follow-up in primary care	ACEI +12.3%†, P=0.07; β-blockers +8.1%†, P=0.27	
Ansari *et al*[26] (2003) USA	Primary care at a university hospital; outpatient	RCT	Patients (105)	**Intervention:** In addition to receiving education on β-blocker use, NPs, under physician supervision, were responsible for initiating, titrating and maintaining eligible patients with HF on β-blockers. **Control:** All providers received education on the use of β-blockers via grand rounds presentations and guideline dissemination. **Process:** *Planning/assessment*— The intervention was designed to address a barrier identified at baseline.	**β-blockers +32%†, P<0.001**; **target β-blockers +33%†, P<0.001**	HF-related hospitalisations –1%†, P=0.66 1-year all-cause mortality –5%†, P=0.05
Güder *et al*[44] (2015) Germany	Tertiary university hospital; outpatient	RCT	Patients (390)	**Intervention:** HF specialist nurses closely followed up with patients after discharge and uptitrated medications under cardiologist supervision. **Control:** Conventional follow-up in primary care	**ACEI +4.9%†, P<0.05**; **target ACEI +25.1%†, P<0.001**; **β-blockers +7.4%†, P<0.05**; **target β-blockers +23.9%†, P<0.001**; MRA +5.7%†, P>0.05; target MRA +0.3%, P>0.05	
Warden *et al*[42] (2014) USA	Tertiary care; inpatient	Before-after	Patients (150)	**Intervention:** Pharmacists reviewed patients' records, addressed prescription concerns to the primary care team and made suggestions for medication treatment and monitoring. **Control:** Usual care; medication reconciliation and patient management by physicians and nurses	**ACEI +13%†, P=0.02**; **education +17%†, P=0.007**	30-day HF-related readmissions –12%†, P=0.11 **30-day all-cause readmissions –21%†, P=0.02**
Martinez *et al*[43] (2013) USA	HF clinic; outpatient	Before-after	Patients (144)	**Intervention:** Pharmacists managed a clinic in which they initiated and adjusted medication dosages based on clinical characteristics. **Control:** Usual care; medication titration conducted by cardiologists **Process:** *Planning/assessment*—The intervention was introduced to address previously identified gaps in HF care.	**Target ACEI +21.9%†, P=0.007**; **target β-blockers +24.3%†, P=0.012**	
Crissinger *et al*[45] (2015) USA	HF clinic; outpatient	Cohort	Patients (899)	**Intervention:** Nurse practitioners and pharmacists adjusted medication dosages based on clinical characteristics under HF physician supervision. **Control:** Patients were managed by general cardiologists.	ACEI +6%†, P>0.05; **>50% target ACEI +10%†, P<0.0167**; **β-blockers +44%†, P<0.0167**; **>50% target β-blockers +43%†, P<0.0167**	

Continued

Table 3 Continued

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Clinical pathways						
Panella *et al*[46] (2005) Italy	Tertiary care; inpatient	RCT	Patients (68)	**Intervention:** An integrated care pathway displayed patient care goals and provided the sequence and timing of actions necessary to achieve goals. **Control:** Usual care; no implementation intervention **Process:** *Information, training and education*—The intervention group received training to use the pathway. *Planning/assessment* - There was a 6-month planning period prior to the intervention phase to build work teams, review practices, develop the pathway and perform ongoing evaluation and improvement.	ACEI +8.28%†, P>0.05; **education +27.7%†, P<0.01**; **LVEF +35.4%†, P<0.01**	30-day all-cause readmissions –4.36%†, P>0.05 **30-day all-cause mortality –7.33%†, P<0.05**
Garin *et al*[47] (2012) Switzerland	Tertiary care; inpatient	Before-after	Patients (363)	**Intervention:** A computerised clinical pathway included order sets for each stage of the hospital stay and required specific evaluation, treatment and education criteria to be met prior to the next stage. **Control:** Usual care; no implementation intervention	Target ACEI +0.2%†, P=0.97; **β-blockers +14.3%†, P=0.006**; **LVEF +16%†, P=0.002**	30-day all-cause mortality –0.4%†, P=0.8; 90-day all-cause mortality –0.8%†, P=0.11; 30-day all-cause readmissions –6.6%†, P=0.11; 90-day all-cause readmissions –8.2%†, P=0.11
Whellan *et al*[48] (2001) USA	HF clinic; outpatient	Before-after	Patients (117)	**Intervention:** Based on predefined protocols and severity of the patient's illness, a follow-up schedule for clinic visits and telephone calls was initiated at the time of enrolment. **Control:** Usual care; no implementation intervention **Process:** *Access to information, training and education*—Pre-enrolment, internal medicine house staff and primary care physicians in the network were presented an outline of the programme; pocket cards with inclusion criteria and referral phone numbers were also provided for all nursing stations at the hospital. *Planning/assessment*—The programme was designed by adapting practices from other disease management programmes to the needs of the local health system.	**β-blockers +24%†, P<0.01**; **target β-blockers +7%†, P<0.01**; ACEI +1%†, P=0.75	**1.5 (control) vs 0 (intervention) all-cause hospitalisations per patient-year, P<0.01**
McCue *et al*[49] (2009) USA	Tertiary care; inpatient	Cohort	Patients (6013)	**Intervention:** A clinical pathway comprised an order sheet, clinical outcomes monitoring checklist, explanations for nursing and disease-specific patient education forms. **Control:** Usual care; no implementation intervention **Process of implementation:** *Planning/assessment*—Design of the clinical pathway was dynamic; practitioner feedback was continuously sought and incorporated into pathway design throughout the intervention period.	**ACEI +17.2%†, P<0.001**; **LVEF +10.6%†, P<0.001**	
Ranjan *et al*[50] (2003) USA	Tertiary care; inpatient	Cohort	Patients (371)	**Intervention:** A clinical pathway for HF care was implemented. **Control:** Usual care; no implementation intervention	**ACEI +33%†, P<0.001**	
Continuity of care						
Hickey *et al*[51] (2016) Australia	HF clinic; outpatient	Cohort	Patients (335)	**Intervention:** HF disease management clinic facilitates communication between hospital and primary care by means of a comprehensive medication titration form outlining recommended target dose of medications, the order of titration and primary clinician responsible for managing titration. **Control:** Discharge titration form was available, but rarely used to facilitate patient transition from hospital to community. **Process:** *Planning/assessment*—A steering committee comprising cardiologists, general practitioners, pharmacists and nurses met quarterly to refine the implementation intervention in an iterative PDSA cycle. Barriers and solutions were developed by interviewing physicians and practice managers.	Target ACEI +11%† (2010), +18%† (2011), P=0.051; **target β-blockers –5%† (2010), +13%† (2011), P=0.045**	
Financial interventions						

Continued

Table 3 Continued

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Provider incentives						
Esse *et al*[52] (2013) USA	Tertiary care; inpatient	Cohort	Patients (4304)	**Intervention:** Primary physicians responsible for patients in the Medicare Advantage Prescription Drug Plan were financially compensated for utilisation of evidence-based HF therapy. **Control:** Usual care; no implementation intervention	ACEI –1.85%†, P=0.244; β-blockers –0.06%†, P=0.972	All-cause hospitalisations: acute visits +2.58%†, P=0.100; ER visits +0.62%†, P=0.675
Institutional incentives						
Lindenauer *et al*[53] (2007) USA	Tertiary care; inpatient	Controlled before-after	Patients (50678)	**Intervention:** Hospitals submitted data on 33 HF quality measures. Those performing in the top decile for a given year received a 2% bonus payment in addition to usual Medicare reimbursement. **Control:** Usual care; no implementation intervention	ACEI +2%‡, P=0.34; **LVEF +5.1%‡, P<0.001**	
Sutton *et al*[54] (2012) England	Tertiary care; inpatient	Controlled before-after	Patients (not clear)	**Intervention:** Hospitals submitted data on 28 HF quality measures. At the end of the first year, hospitals that reported quality scores in the top quartile received a 4% bonus. **Control:** Usual care; no implementation intervention	ACEI +1.4%‡; LVEF +8.1%‡, no P values reported; education +15.2%‡	30-day all-cause mortality –0.6%†, P=0.3
Combined interventions						
Peters-Klimm *et al*[33] (2008) Germany	Primary care	Cluster RCT	Providers (37)/ patients (168)	**Intervention:** Physicians engaged in four didactic, interdisciplinary educational meetings with primary care physicians, cardiologists and psychosomatic specialists; and received pharmacotherapy feedback (% target dose) on individual patients. **Control:** Physicians received a standard lecture on guideline-recommended treatment of HF. **Process:** *Information, training and education*—Physicians received initiation visit, which included an introduction to the intervention and a handout of the trial investigator file. *Opinion leaders*—Education component of the intervention was provided by a senior cardiologist with didactic expertise.	ACEI +8.7%†, P=0.15; **target ACEI +12.3%†, P=0.04**; β-blockers –4.8%†, P=0.67; target β-blockers +1.7%†, P=0.26	
Fonarow *et al*/ Gheorghiade *et al*[55 56] (2010/2012) USA	Cardiology clinic; outpatient	Before-after	Patients (15 177)	**Intervention:** The intervention consisted of a guideline-based clinical decision support tool kit, educational materials, practice-specific data reports, benchmarked quality of care reports and structured educational opportunities. **Control:** Usual care; no implementation intervention **Process:** *Information, training and education*—A 1-day workshop for practice personnel provided overview of study goals and tool kit. *Planning/assessment*—A steering committee was appointed to follow a structured, rigorous, guideline-driven process to develop the pathways and tools prior to the intervention phase. *Opinion leaders*—The educational component of the intervention included expert opinions regarding best practices in HF care.	**ACEI +6.7%†, P<0.001**; target ACEI +1.8%, P=0.053†; **β-blockers +7.4%†, P<0.001**; target β-blockers +9.8%, P≤0.001; **MRA +27.4%†, P<0.001**; target MRA +4.1%, P=0.107; **education +9.1%†, P<0.001**; **ICD referral +30.3%†, P<0.001**	
Goff *et al*[34] (2005) USA	Primary care	Before-after	Patients (3141)	**Intervention:** Physicians received performance audit and feedback, aggregated across a multicounty health service area; and patient-specific chart reminders regarding medications and education. **Control:** Usual care; no implementation intervention **Process:** *Planning*—The intervention planning team identified and addressed barriers at provider and patient levels. *Patients*—The intervention planning team developed an educational brochure based on results of focus groups with patients with HF.	ACEI –2.7%†, P=0.26; **β-blockers +15.2%†, P<0.0001**; **LVEF +4.3%†, P<0.0001**	

Continued

Table 3 Continued

Author (year) Country	Setting	Study design	Unit of recruitment/ analysis (n)	Intervention and process of implementation (when described)	Process outcomes*	Clinical outcomes*
Riggio *et al*[57] (2009) USA	Tertiary care; inpatient	Before-after	Patients (4728)	**Intervention:** The intervention consisted of a computerised discharge checklist with electronic prompts on medication use, LVEF assessment and discharge instructions; personalised resident performance reports; financial bonus for residents achieving a threshold of quality compliance; lectures on hospital/state/nation quality performance. **Control:** Usual care; no implementation intervention **Process:***Planning*—The intervention planning team received and incorporated ongoing feedback from residents and physicians in developing the reminder system prior to the intervention phase.	**ACEI +15.7%†, P<0.001**; **education +55.8%†, P<0.001**; LVEF –0.2%†, P=0.78	
Scott *et al*[58] (2004) Australia	Mixed; tertiary and primary care practices	Before-after	Patients (904)	**Intervention:** The in-hospital component consisted of: reminders on patient charts; clinical pathways for emergency chest pain assessment and management; educational presentations as grand rounds, seminars, workshops and case-based meetings; briefing of hospital and primary care physicians by clinical pharmacists. The discharge planning component consisted of standardised discharge referral summaries with personal treatment targets; medication lists forwarded to community pharmacists; pharmacist counselling of patients about lifestyle changes, drug therapy and risk factor modification; postdischarge telephone follow-up by clinical pharmacists of high-risk patients. **Control:** Usual care; no implementation intervention **Process:** *Planning/assessment*— Intervention was designed to address several implementation barriers that were identified through literature review.	**ACEI +15%†, P=0.04**; **β-blockers +21%†, P=0.01**; LVEF +9%†, P=0.06	30-day HF-related readmissions +0.8%†, P>0.05 **All-cause mortality: 30 days –2.9%†, P<0.04; 6 months –7.6%†, P<0.001; 1 year +10.4%†, P=0.005**
Dykes *et al*[59] (2005) USA	Tertiary care; inpatient	Before-after	Patients (314)	**Intervention:** This involved a clinical pathway in EMR; an HF self-management education tool; and ongoing performance feedback. **Control:** Usual care; no implementation intervention	Medication prescription +6.4%†, P=0.389; **education +64.9%†, P=0.000**	

*Statistically significant results are shown in bold letters.
†Absolute risk difference reported as (intervention group – control group).
‡Difference in difference (controlled before/after studies) reported as [intervention group (Time 2 – Time 1) – control group (Time 2 – Time 1)].
§Difference in rate of change (ITS studies) reported as (intervention group rate of change – control group rate of change).
ACEI, ACE inhibitor; ARB, angiotensin II receptor blocker; CRT, cardiac resynchronisation therapy; EMR, electronic medical records; ER, emergency room; HF, heart failure; ICD, internal cardioverter defibrillator; ITS, interrupted time series; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NP, nurse practitioner; PDSA, plan-do-study-act cycle; RCT, randomised controlled trial.

Reminders

Two of four studies on reminders within electronic medical records (EMR) reported a significant increase in the per cent of patients prescribed an indicated medication.[28 29] One study in which reminders were unsuccessful had suboptimal intervention fidelity; stratification by actual use of the reminder system revealed a significant improvement in prescription rates.[27]

Clinical pathways

Four of five studies on clinical pathways reported a significant increase in the per cent of patients prescribed an indicated medication.[47–50] The single study that reported no significant change was an RCT in a remote community hospital, in contrast with the urban and/or teaching hospital settings of other clinical pathway studies.

Medical records systems

All four studies evaluating changes to EMRs reported significant increases in the per cent of patients prescribed an indicated medication.[35–38] In each of these interventions, existing EMRs were enhanced by addressing identified limitations (table 3).

Combination interventions

Two studies evaluated combinations of provider-level interventions. A combination of education with audit and feedback did not significantly increase the per cent of patients prescribed an indicated medication,[33] while a combination of education, reminders, and audit and feedback did.[34]

Four studies combined implementation interventions across different levels of the EPOC taxonomy.[55–59] Two studies combined clinical pathways with audit and feedback; one reported a significant increase in the per cent of patients prescribed an indicated medication.[55] Another study that combined a computerised order set, reminders, audit and feedback, financial incentives and provider educational meetings also reported a significant increase in the per cent prescribed an indicated medication.[57] Finally, an intervention that fostered hospital-community integration using a combination of reminders, education for providers, audit and feedback, discharge summaries and patient follow-up by pharmacists[58] reported a significant increase in β-blocker prescriptions in-hospital, and in all medications 6 months after discharge.

Prescription of target dose medications

Clinical multidisciplinary team interventions were consistently successful in increasing prescription of target dose medications, with five of six studies reporting significant improvements for this outcome.[26 39 43–45] The five successful clinical multidisciplinary team interventions—including three RCTs[26 39 44]—involved nurses or pharmacists initiating or titrating medications according to a protocol. Among these studies, the absolute increase in proportion of patients prescribed target dose ACEIs ranged from 10% to 25.1%.[39 43–45] The absolute increase in proportion of patients prescribed target dose β-blockers ranged from 23.9% to 43%.[26 44 45] In contrast, an unsuccessful intervention tasked pharmacists with improving prescribing practices, without clearly defining the mechanism to do so.[41]

One of two studies[47 48] evaluating clinical pathways reported a significant increase (from 6% to 13%) in prescription of target dose β-blockers.[48] Of the two studies evaluating multifaceted interventions, an intervention combining education with audit and feedback reported a significant improvement (from 44% to 72%) in the prescription of target dose ACEIs,[33] while a comprehensive intervention combining education, reminders, audit and feedback and clinical pathways did not report significant improvements.[56] In the successful multifaceted intervention, feedback was focused strictly on medication dosing for individual patients.[33]

A study evaluating a continuity of care intervention, including the provision of instructions for medication titration to the outpatient general practitioner, reported a significant improvement (from 38% to 51%) in the prescription of target dose β-blockers within 6 months of discharge.[51]

Provision of patient self-care education

Only nine studies reported on the provision of self-care education to patients. Three multifaceted intervention studies reported this outcome measure, with a significant improvement in each case.[55 57 59] Provision of patient education also increased with a reminder system,[27] a clinical multidisciplinary team[42] and a clinical pathway.[46] In contrast, interventions that did not produce significant improvements included audit and feedback[23] and changes to medical records systems.[38] One study, on financial incentives, did not report statistical significance.

LVEF assessment

Eleven studies reported the per cent of patients who received an LVEF assessment. All three clinical pathway studies, including an RCT, reported significant improvements in this outcome.[46 47 49] Of the two studies evaluating institutional financial incentives,[53 54] only one reported significant improvements.[53] Only one of three studies[34 57 58] evaluating multifaceted interventions that included audit and feedback as well as reminders reported significant increases in LVEF assessment.[34] Education,[32] reminders[27] and changes in medical records systems[38] did not significantly increase LVEF assessment

ICD/CRT referral

Only two studies measured the per cent of indicated patients who received an ICD/CRT referral. These studies evaluated a reminder intervention,[30] and a multifaceted intervention combining reminders, clinical pathways, education, and audit and feedback,[55] respectively, with significant improvements reported in each case.

Evidence from RCTs

Very few RCTs were available for most intervention types; none were available for medical records system changes or financial incentives. Five RCTs evaluated the effect

of clinical multidisciplinary teams on overall prescription rates[26 39 40 44] and target dose prescriptions.[26 39 41 44] Among these, two of four reported significant improvement in overall prescription rates,[26 44] and three of four reported significant improvements in target dose prescriptions.[26 39 44] Two RCTs evaluated audit and feedback interventions,[22 23] with no significant improvements in the reported outcomes. An RCT evaluating education[31] reported significant improvements for all outcomes measured, while an RCT assessing reminders[26] reported no significant improvements. The RCT evaluating a clinical pathway[46] significantly increased patient self-care education,[46] and the RCT assessing a multifaceted intervention significantly increased the prescription of some target dose medications.[33]

Clinical outcomes

While five of the six studies reporting all-cause mortality successfully improved process outcomes, only two reported a significant decrease in mortality: an RCT evaluating a clinical pathway[46] and a before-after study assessing a multifaceted transitional care intervention.[58]

While all six studies reporting all-cause hospitalisation or readmission rates improved process outcomes,[32 39 42 46–48] significant improvements in the clinical outcomes were only reported in two: a multidisciplinary team study[42] and a clinical pathway study.[48] Both studies used a before-after design with medium risk of bias. There was no improvement in two studies assessing clinical pathways,[46 47] one assessing multidisciplinary interventions,[39] and one assessing an educational intervention.[32]

While three of four studies reporting HF-related hospitalisations or readmissions[14 34] improved process outcomes, none reported significant improvements in the HF-related clinical outcomes.

Process of implementation

Six studies reported provision of preliminary training, education and resources to introduce clinicians to the implementation intervention and encourage utilisation; in each case, interventions were effective in improving at least one process outcome (table 3).[23 27 40 47 48] Nine studies assessed barriers to guideline implementation at baseline and adapted the interventions accordingly.[18 30 33 37 42 46 51 57] This was associated with implementation success for all interventions, with the exception of audit and feedback.[46] Seven studies used an iterative process, where the programme was regularly updated on the basis of institutional requirements and user feedback.[28 34 36 40 51 56 59] An iterative intervention development process was associated with implementation success across the range of interventions in which it was reported.

Contextual factors

Online supplementary appendix 4 presents the contextual factors influencing implementation interventions among the included studies.

Inner setting

Five interventions that improved at least one process outcome reported leadership support from either the department or hospital level.[28 34 41 56 57]

Outer setting

In nine US studies,[28–30 36–38 42 56 59] there were pre-existing initiatives by the Centers for Medicare and Medicaid Services or The Joint Commission, including financial reimbursements or accreditation on the basis of HF readmission rates, and public reporting of quality of care data. These contextual factors encouraged organisations to implement interventions to improve guideline adherence. This is in contrast to the lack of success observed when financial interventions were used as the implementation intervention itself.

DISCUSSION

In this systematic review, we assessed the effectiveness of implementation interventions aimed at improving physician adherence to class I HF guideline recommendations. We synthesised our findings narratively as the variation in study design, intervention and outcomes across studies precluded meta-analysis.

We found that a majority (84%) of the 38 studies reported significant improvements in at least one process outcome. A process outcome commonly reported across studies and interventions was the proportion of patients prescribed an indicated medication: 12 studies reported on the prescription of ACEIs,[22 27 29 37 38 42 46 49 50 53 54 57] two on the prescription of β-blockers,[26 47] 12 on the prescription of ACEIs and β-blockers,[24 32–35 39 40 45 48 52 58] and four on the prescription of ACEIs, β-blockers and MRAs.[25 28 44 55] Electronic medical system interventions were associated with significant improvements in the prescription of at least one medication in 100% of studies (4/4 studies),[35 37 38 60] followed by clinical pathways (80%, 4/5 studies),[47–50] multifaceted interventions (66%, 4/6 studies)[34 55 57 58] and reminders (50%, 2/4 studies).[28 29] Very few studies on education or audit and feedback reported this outcome, making direct comparisons with other interventions challenging. However, on the whole, the results across a number of studies suggest that educational seminars[30] and audit and feedback[20 21] are minimally effective in isolation. Audit and feedback appears to be an important component of multifaceted interventions, however,[34 55 57 58] and it is possible that factors such as the type of feedback and cointerventions to address gaps in care can influence its effectiveness.[61]

Results from RCTs reinforced overall findings that clinical multidisciplinary teams, with clear predefined responsibilities, seem to be especially effective in titrating patients to their target dose.[26 39–41 44] These findings are important; despite evidence of dose-related improvements in hospitalisation and mortality, only a small proportion of patients with HF receive an appropriate dose of evidence-informed medications.[62–64] A study

using registry data from 21 European and Mediterranean countries from 2011 to 2013 found that while ACEIs, β-blockers and MRAs were used in 92.2%, 92.7% and 67.0% of patients, respectively, only 30% of these patients received medications at the target dosage.[65]

In general, improvements in process outcomes as a result of implementation interventions were rarely accompanied by improvements in clinical outcomes. In some studies, the gap between process and clinical outcomes may be attributed to insufficient statistical power to detect improvements in clinical outcomes.[13 25 33] The gap may also be explained by study designs that did not account for background trends or adjust for confounding variables. Finally, HF clinical outcomes are multifactorial, and depend on the prescription of appropriate medications, the patient's adherence to these medications, and follow-up care.[32] The studies that showed a trend towards reduction in HF-related readmissions, although not significant, are those that addressed more than one of these factors.[40 42]

The context in which an implementation intervention is applied can influence its success.[61 66] The limited contextual details available in the included studies made it difficult to identify facilitators of implementation efforts. In general, support of organisation leaders, and external policies and incentives for guideline adherence seemed to be associated with guideline uptake. These findings are consistent with results from a 2011 study that used iterative, formal discussions with leaders in patient safety and healthcare systems to identify leadership involvement and external factors (eg, financial or performance incentives or patient safety regulations) as context domains important to quality improvement initiatives.[67]

Consistent with existing literature,[61 68] our results did not demonstrate a clear relationship between the number of intervention components and intervention success. An extensive review by Grimshaw *et al* concluded that while multifaceted interventions are not inherently more effective than single interventions, they may be more effective when built on a comprehensive assessment of barriers.[60 69 70] Among the studies on multifaceted interventions in our review, the four studies that reported significant improvements in medication prescription rates carefully considered barriers at baseline and sought user feedback throughout the intervention development process.[34 55–58]

Our results are concordant with recently published findings from the American Heart Association's comprehensive Get With The Guidelines-HF programme, which used a combination of educational approaches, multidisciplinary teams and public hospital performance reporting to improve care.[71] The intervention was carefully adapted and introduced at each hospital site through collaborative discussions of barriers and solutions, and iterative plan-do-study-act cycles prior to the intervention phase.[72]

There were a number of limitations to our review. First, the variation in interventions, settings, study designs and outcome measures precluded meta-analyses, and in turn, our ability to draw substantive conclusions regarding specific implementation strategies and their comparative effectiveness. We chose to use a 'vote counting' approach to synthesis. While this method is useful in presenting an initial description of the trends found across studies, it is limited by the fact that it assigns equal weight to studies of varying sample sizes, effect sizes and significance levels.[73]

Another limitation was the methodological quality of the primary studies. Most studies used observational and quasi-experimental study designs. Quasi-experimental and observational designs possess some inherent risks of bias. In uncontrolled before-after studies, which formed the majority of studies in this review, temporal trends or sudden changes make it difficult to attribute the observed effects to the intervention alone. A time series design increases confidence with which the observed effect can be attributed to the intervention; however, it does not protect against simultaneous events that may influence the intervention effect. Controlled before-after studies can protect against these effects, but cannot match groups on the basis of unknown confounders. We found that most quasi-experimental and observational studies possessed at least a medium risk of bias. Though almost all included RCTs demonstrated low risk of bias, they were largely applied in the evaluation of multidisciplinary team interventions, and less so to the evaluation of other implementation interventions.

A minority of studies in this review (10 of 35 studies) were RCTs, considered the gold standard in establishing a causal link between an intervention and its outcome. Indeed, RCTs are an uncommonly used methodology in implementation studies. In a recent systematic review of implementation interventions for the management of intensive care unit delirium, only one of the 21 studies was an RCT, 16 were before-after studies and the remaining were cohort studies.[74] In another review on implementation interventions to improve the use of pain management assessments for hospitalised patients, only three of the 23 studies were controlled clinical trials, and the remaining 20 were uncontrolled before-after or time series studies.[75] While randomised trials are robust in methodology, they pose a number of logistical challenges that may make them suboptimal for implementation research; they are expensive and time consuming, often requiring years to complete.[76] Changes in healthcare delivery are often implemented under internal and external pressures that seek to resolve an institutional problem in the shortest time possible. Under such circumstances, quasi-experimental designs are often felt to be most feasible.[76 77] A solution may be found in pragmatic clinical trials—such as the stepped wedge cluster RCT—which can offer the methodological benefits of randomisation while being sensitive to the challenges of implementation research.[78]

Another limitation was that many studies failed to provide adequate details on the intervention, context, barriers, facilitators or fidelity to the intervention. A review by Proctor *et al* explores the reporting challenges in implementation research in significant detail. It offers

a theoretical discussion of principles for naming, defining and specifying implementation interventions.[79]

Suggestions for future studies

We identify a number of ways in which future research on the effectiveness of implementation interventions may be strengthened. First, there is a need for implementation interventions to be evaluated using more robust study designs that also account for the pragmatic challenges of implementation research. Furthermore, reporting of studies should adhere to standardised guidelines in order to better facilitate comparison between interventions. An example of reporting guidelines is the Quality Improvement Minimum Quality Criteria Set, which spans the spectrum of intervention characteristics and contextual factors.[80] Implementation research in HF may also benefit from more careful consideration of the contextual factors that influence implementation success. Finally, in addition to examining process outcomes, the direct impact of implementation interventions on clinical outcomes should be examined more consistently.

CONCLUSIONS

In this review, the heterogeneity of interventions, study designs and outcomes limited our ability to draw substantive conclusions regarding the comparative effectiveness of implementation interventions. Trends observed across the included studies suggest that effective implementation interventions include EMR systems, clinical multidisciplinary teams, clinical pathways and multifaceted interventions that include audit and feedback. There is a need for higher quality research to assess the effectiveness of implementation interventions on HF care processes and on clinical outcomes, and for the use of standardised reporting guidelines. Future work in the area should also include a closer examination of the organisational and external implementation context in order to better facilitate targeted application of implementation strategies.

Acknowledgements We thank Quazi Ibrahim for his help in assessing whether the study was amenable to meta-analysis.

Contributors HGCV and IDG conceived the study, and all authors contributed to the study design. DS informed the search strategy, extracted and synthesised study data, and drafted and edited the manuscript. IDG, KH, RBH and SJC contributed intellectual input and edited the manuscript for critical content. IG contributed to the search strategy and extracted study data. HGCV informed the search strategy, synthesised and analysed study data, drafted and edited the manuscript, obtained research funding, and supervised the conduct of the study.

Funding This study was funded by the Ontario's Ministry of Health and Long Term Care (MOHLTC) Health System Research Fund and the Canadian Institutes of Health Research (CIHR). IDG receives support from a CIHR Foundation Grant. HGCV receives salary support from the MOHLTC and Hamilton Health Sciences Early Career Research Award.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All relevant study data can be found in the online supplementary files.

Author note This work is dedicated to the memory of Aubrey Ignatius Van Spall, beloved father and friend.

REFERENCES

1. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. *Nat Rev Cardiol* 2011;8:30–41.
2. Yancy CW, Jessup M, Bozkurt B, *et al*. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013;128:1810–52.
3. Komajda M, Lapuerta P, Hermans N, *et al*. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *Eur Heart J* 2005;26:1653–9.
4. Fonarow GC, Yancy CW, Hernandez AF, *et al*. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. *Am Heart J* 2011;161:1024–30.
5. Van Spall HGC, Rahman T, Mytton O, *et al*. Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis. *Eur J Heart Fail* 2017;19:1427–43.
6. Fonarow GC, Yancy CW, Heywood JT. Adherence to heart failure quality-of-care indicators in US hospitals: analysis of the ADHERE Registry. *Arch Intern Med* 2005;165:1469–77.
7. Calvin JE, Shanbhag S, Avery E, *et al*. Adherence to evidence-based guidelines for heart failure in physicians and their patients: lessons from the Heart Failure Adherence Retention Trial (HART). *Congest Heart Fail* 2012;18:73–8.
8. Oertle M, Bal R. Understanding non-adherence in chronic heart failure: a mixed-method case study. *Qual Saf Health Care* 2010;19:e37–5.
9. Cochrane Effective Practice and Organisation of Care Review Group. *Data collection checklist*: Cochrane Effective Practice and Organisation of Care, 2002. https://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/datacollectionchecklist.pdf (cited 15 Oct 2014).
10. Grimshaw J, Eccles M, Thomas R, *et al*. Toward evidence-based quality improvement. Evidence (and its limitations) of the effectiveness of guideline dissemination and implementation strategies 1966-1998. *J Gen Intern Med* 2006;21(Suppl 2):14–20.
11. Unverzagt S, Oemler M, Braun K, *et al*. Strategies for guideline implementation in primary care focusing on patients with cardiovascular disease: a systematic review. *Fam Pract* 2014;31:247–66.
12. Brusamento S, Legido-Quigley H, Panteli D, *et al*. Assessing the effectiveness of strategies to implement clinical guidelines for the management of chronic diseases at primary care level in EU Member States: a systematic review. *Health Policy* 2012;107:168–83.
13. Van Spall HG, Shanbhag D, Gabizon I, *et al*. Effectiveness of implementation strategies in improving physician adherence to guideline recommendations in heart failure: a systematic review protocol. *BMJ Open* 2016;6:e009364.
14. Mainz J. Defining and classifying clinical indicators for quality improvement. *Int J Qual Health Care* 2003;15:523–30.
15. Smith LR, Ashok M, Sm D, *et al*. *Contextual frameworks for research on the implementation of complex system interventions*. Rockville, MD, US: Agency for Healthcare and Quality (US), 2014:8–26.
16. Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]*: The Cochrane Collaboration.
17. Cochrane. Cochrane tool to assess risk of bias in cohort studies [Internet]. 1st ed. 2016 http://methods.cochrane.org/bias/sites/methods.cochrane.org.bias/files/uploads/Tool%20to%20Assess%20Risk%20of%20Bias%20in%20Cohort%20Studies.pdf (cited 10 Sep 2015).
18. Nhlbi.nih.gov. Quality assessment tool for before-after (pre-post) studies with no control group. 2014 http://www.nhlbi.nih.gov/health-

pro/guidelines/in-develop/cardiovascular-risk-reduction/tools (cited 10 Sep 2015).
19. Arai L, Britten N, Popay J, *et al*. Testing methodological developments in the conduct of narrative synthesis: a demonstration review of research on the implementation of smoke alarm interventions. *Evidence & Policy: A Journal of Research, Debate and Practice* 2007;3:361–83.
20. Rodgers M, Sowden A, Petticrew M, *et al*. Testing methodological guidance on the conduct of narrative synthesis in systematic reviews. *Evaluation* 2009;15:49–73.
21. French B. Contextual factors influencing research use in nursing. *Worldviews Evid Based Nurs* 2005;2:172–83.
22. Kasje WN, Denig P, Stewart RE, *et al*. An educational programme for peer review groups to improve treatment of chronic heart failure and diabetes mellitus type 2 in general practice. *J Eval Clin Pract* 2006;12:613–21.
23. Frijling BD, Lobo CM, Hulscher ME, *et al*. Intensive support to improve clinical decision making in cardiovascular care: a randomised controlled trial in general practice. *Qual Saf Health Care* 2003;12:181–7.
24. Cancian M, Battaggia A, Celebrano M, *et al*. The care for chronic heart failure by general practitioners. Results from a clinical audit in Italy. *Eur J Gen Pract* 2013;19:3–10.
25. Matthews JC, Johnson ML, Koelling TM. The impact of patient-specific quality-of-care report cards on guideline adherence in heart failure. *Am Heart J* 2007;154:1174–83.
26. Ansari M, Shlipak MG, Heidenreich PA, *et al*. Improving guideline adherence: a randomized trial evaluating strategies to increase beta-blocker use in heart failure. *Circulation* 2003;107:2799–804.
27. Butler J, Speroff T, Arbogast PG, *et al*. Improved compliance with quality measures at hospital discharge with a computerized physician order entry system. *Am Heart J* 2006;151:643–53.
28. Braun V, Heintze C, Rufer V, *et al*. Innovative strategy for implementing chronic heart failure guidelines among family physicians in different healthcare settings in Berlin. *Eur J Heart Fail* 2011;13:93–9.
29. Qian Q, Manning DM, Ou N, *et al*. ACEi/ARB for systolic heart failure: closing the quality gap with a sustainable intervention at an academic medical center. *J Hosp Med* 2011;6:156–60.
30. Gravelin LM, Yuhas J, Remetz M, *et al*. Use of a screening tool improves appropriate referral to an electrophysiologist for implantable cardioverter-defibrillators for primary prevention of sudden cardiac death. *Circ Cardiovasc Qual Outcomes* 2011;4:152–6.
31. Thilly N, Briançon S, Juillière Y, *et al*. Improving ACE inhibitor use in patients hospitalized with systolic heart failure: a cluster randomized controlled trial of clinical practice guideline development and use. *J Eval Clin Pract* 2003;9:373–82.
32. Asch SM, Baker DW, Keesey JW, *et al*. Does the collaborative model improve care for chronic heart failure? *Med Care* 2005;43:667–75.
33. Peters-Klimm F, Müller-Tasch T, Remppis A, *et al*. Improved guideline adherence to pharmacotherapy of chronic systolic heart failure in general practice--results from a cluster-randomized controlled trial of implementation of a clinical practice guideline. *J Eval Clin Pract* 2008;14:823–9.
34. Goff DC, Massing MW, Bertoni AG, *et al*. Enhancing quality of heart failure care in managed Medicare and Medicaid in North Carolina: results of the North Carolina Achieving Cardiac Excellence (NC ACE) Project. *Am Heart J* 2005;150:717–24.
35. Persell SD, Kaiser D, Dolan NC, *et al*. Changes in performance after implementation of a multifaceted electronic-health-record-based quality improvement system. *Med Care* 2011;49:117–25.
36. Baker DW, Persell SD, Kho AN, *et al*. The marginal value of pre-visit paper reminders when added to a multifaceted electronic health record based quality improvement system. *J Am Med Inform Assoc* 2011;18:805–11.
37. Reingold S, Kulstad E. Impact of human factor design on the use of order sets in the treatment of congestive heart failure. *Acad Emerg Med* 2007;14:1097–105.
38. Oujiri J, Hakeem A, Pack Q, *et al*. Resident-initiated interventions to improve inpatient heart-failure management. *BMJ Qual Saf* 2011;20:181–6.
39. Mejhert M, Kahan T, Persson H, *et al*. Limited long term effects of a management programme for heart failure. *Heart* 2004;90:1010–5.
40. Kasper EK, Gerstenblith G, Hefter G, *et al*. A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission. *J Am Coll Cardiol* 2002;39:471–80.
41. McCarren M, Furmaga E, Jackevicius CA, *et al*. Improvement of guideline β-blocker prescribing in heart failure: a cluster-randomized pragmatic trial of a pharmacy intervention. *J Card Fail* 2013;19:525–32.
42. Warden BA, Freels JP, Furuno JP, *et al*. Pharmacy-managed program for providing education and discharge instructions for patients with heart failure. *Am J Health Syst Pharm* 2014;71:134–9.
43. Martinez AS, Saef J, Paszczuk A, *et al*. Implementation of a pharmacist-managed heart failure medication titration clinic. *Am J Health Syst Pharm* 2013;70:1070–6.
44. Güder G, Störk S, Gelbrich G, *et al*. Nurse-coordinated collaborative disease management improves the quality of guideline-recommended heart failure therapy, patient-reported outcomes, and left ventricular remodelling. *Eur J Heart Fail* 2015;17:442–52.
45. Crissinger ME, Marchionda KM, Dunlap ME. Adherence to clinical guidelines in heart failure (HF) outpatients: Impact of an interprofessional HF team on evidence-based medication use. *J Interprof Care* 2015;29:483–7.
46. Panella M, Marchisio S, Di Mario G, *et al*. The effectiveness of an integrated care pathway for inpatient heart failure treatment: results of a trial in a community hospital. *Journal of integrated Care Pathways* 2005;9:21–8.
47. Garin N, Carballo S, Gerstel E, *et al*. Inclusion into a heart failure critical pathway reduces the risk of death or readmission after hospital discharge. *Eur J Intern Med* 2012;23:760–4.
48. Whellan DJ, Gaulden L, Gattis WA, *et al*. The benefit of implementing a heart failure disease management program. *Arch Intern Med* 2001;161:2223–8.
49. McCue JD, Beck A, Smothers K. Quality toolbox: clinical pathways can improve core measure scores. *J Healthc Qual* 2009;31:43–50.
50. Ranjan A, Tarigopula L, Srivastava RK, *et al*. Effectiveness of the clinical pathway in the management of congestive heart failure. *South Med J* 2003;96:661–3.
51. Hickey A, Suna J, Marquart L, *et al*. Improving medication titration in heart failure by embedding a structured medication titration plan. *Int J Cardiol* 2016;224:99–106.
52. Esse T, Serna O, Chitnis A, *et al*. Quality compensation programs: are they worth all the hype? A comparison of outcomes within a Medicare advantage heart failure population. *J Manag Care Pharm* 2013;19:317–24.
53. Lindenauer PK, Remus D, Roman S, *et al*. Public reporting and pay for performance in hospital quality improvement. *N Engl J Med* 2007;356:486–96.
54. Sutton M, Nikolova S, Boaden R, *et al*. Reduced mortality with hospital pay for performance in England. *N Engl J Med* 2012;367:1821–8.
55. Fonarow GC, Albert NM, Curtis AB, *et al*. Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). *Circulation* 2010;122:585–96.
56. Gheorghiade M, Albert NM, Curtis AB, *et al*. Medication dosing in outpatients with heart failure after implementation of a practice-based performance improvement intervention: findings from IMPROVE HF. *Congest Heart Fail* 2012;18:9–17.
57. Riggio JM, Sorokin R, Moxey ED, *et al*. Effectiveness of a clinical-decision-support system in improving compliance with cardiac-care quality measures and supporting resident training. *Acad Med* 2009;84:1719–26.
58. Scott IA, Denaro CP, Bennett CJ, *et al*. Achieving better in-hospital and after-hospital care of patients with acute cardiac disease. *Med J Aust* 2004;180(10 Suppl):S83–8.
59. Dykes PC, Acevedo K, Boldrighini J, *et al*. Clinical practice guideline adherence before and after implementation of the HEARTFELT (HEART Failure Effectiveness & Leadership Team) intervention. *J Cardiovasc Nurs* 2005;20:306–14.
60. Baker R, Camosso-Stefinovic J, Gillies C, *et al*. Tailored interventions to address determinants of practice. *Cochrane Database Syst Rev* 2015;4:CD005470.
61. Ivers N, Jamtvedt G, Flottorp S, *et al*. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2012;6:CD000259.
62. Packer M, Poole-Wilson PA, Armstrong PW, *et al*. Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group. *Circulation* 1999;100:2312–8.
63. Konstam MA, Neaton JD, Dickstein K, *et al*. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. *Lancet* 2009;374:1840–8.
64. Bristow MR, Gilbert EM, Abraham WT, *et al*. Carvedilol produces dose-related improvements in left ventricular function and survival in subjects with chronic heart failure. MOCHA Investigators. *Circulation* 1996;94:2807–16.

65. Maggioni AP, Anker SD, Dahlström U, *et al*. Are hospitalized or ambulatory patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12,440 patients of the ESC Heart Failure Long-Term Registry. *Eur J Heart Fail* 2013;15:1173–84.
66. Squires JE, Graham ID, Hutchinson AM, *et al*. Identifying the domains of context important to implementation science: a study protocol. *Implement Sci* 2015;10:135.
67. Taylor SL, Dy S, Foy R, *et al*. What context features might be important determinants of the effectiveness of patient safety practice interventions? *BMJ Qual Saf* 2011;20:611–7.
68. Wensing M, Grol R. Single and combined strategies for implementing changes in primary care: a literature review. *Int J Qual Health Care* 1994;6:115–32.
69. Wensing M, van der Weijden T, Grol R. Implementing guidelines and innovations in general practice: which interventions are effective? *Br J Gen Pract* 1998;48:991–7.
70. Grimshaw JM, Thomas RE, MacLennan G, *et al*. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess* 2004;8:iii-iv, 1-72.
71. Patel DB, Shah RM, Bhatt DL, *et al*. Guideline-appropriate care and in-hospital outcomes in patients with heart failure in teaching and nonteaching hospitals: findings from get with the guidelines-heart failure. *Circ Cardiovasc Qual Outcomes* 2016;9:757–66.
72. Hong Y, LaBresh KA. Overview of the American Heart Association "Get with the Guidelines" programs: coronary heart disease, stroke, and heart failure. *Crit Pathw Cardiol* 2006;5:179–86.
73. Popay J, Roberts H, Sowden A, *et al*. *Guidance on the conduct of narrative synthesis in systematic reviews*: Economic and Social Research Council, 2006.
74. Trogrlić Z, van der Jagt M, Bakker J, *et al*. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. *Crit Care* 2015;19:157.
75. Ista E, van Dijk M, van Achterberg T. Do implementation strategies increase adherence to pain assessment in hospitals? A systematic review. *Int J Nurs Stud* 2013;50:552–68.
76. Eccles M, Grimshaw J, Campbell M, *et al*. Research designs for studies evaluating the effectiveness of change and improvement strategies. *Qual Saf Health Care* 2003;12:47–52.
77. Peters DH, Tran NT, Adam T. *Implementation research in health: a practical guide*. Geneva: World Health Organization, 2016:40. http://who.int/alliance-hpsr/alliancehpsr_irpguide.pdf
78. Portela MC, Pronovost PJ, Woodcock T, *et al*. How to study improvement interventions: a brief overview of possible study types. *BMJ Qual Saf* 2015;24:325–36.
79. Proctor EK, Powell BJ, McMillen JC. Implementation strategies: recommendations for specifying and reporting. *Implement Sci* 2013;8:139.
80. Hempel S, Shekelle PG, Liu JL, *et al*. Development of the quality improvement minimum quality criteria Set (QI-MQCS): a tool for critical appraisal of quality improvement intervention publications. *BMJ Qual Saf* 2015;24:796–804.