Improving patient safety for the critically ill

The challenges of implementation

Borgert, M.

Publication date
2017
Document Version
Other version
License
Other

04

A FLOWCHART FOR BUILDING EVIDENCE-BASED CARE BUNDLES IN INTENSIVE CARE: BASED ON A SYSTEMATIC REVIEW

Marjon Borgert, Jan Binnekade, Frederique Paulus,Astrid Goossens and Dave Dongelmans

Int J Qual Health Care 2017;1;29:163-175.

ABSTRACT

Purpose. The Institute for Healthcare Improvement is the founder of the care bundled approach and described the methods used on how to develop care bundles. However, other useful methods are published as well. In this systematic review, we identified what different methods were used to design evidence-based care bundles in intensive care units. The results were used to build a comprehensive flowchart to guide through the care bundle design process.

Data sources. Electronic databases were searched for eligible studies in PubMed, EMBASE and CINAHL from January 2001 to August 2014.

Study selection. There were no restrictions on the types of study design eligible for inclusion. Methodological quality was assessed by using the Downs and Black checklist or Appraisal of Guidelines, REsearch and Evaluation II.

Data extraction. Data extraction were independently performed by two reviewers.

Results of data synthesis. A total of 4665 records were screened and 18 studies were finally included. The complete process of designing bundles was reported in 33% (6/18). In 50% (9/18) one of the process steps was described. A narrative report was written about care bundles in general in 17% (3/18). We built a comprehensive flowchart to visualize and structure the process of designing care bundles.

Conclusions. We identified useful methods for designing evidence-based care bundles. We built a comprehensive flowchart to provide an overview of the methods used to design care bundles so that others could choose their own applicable method. It guides through all necessary steps in the process of designing care bundles.

INTRODUCTION

Guidelines are developed in order to standardize care processes to improve the quality of care. However, it is known that guidelines are often not followed completely and therefore patients do not receive the care they need.[1] In 2001, the Institute for Healthcare Improvement (IHI) developed the concept of care bundles.[2] Care bundles aim to enhance the reliability of care and to improve clinical outcomes by bundling a small set of interventions together.[2]

The IHI defined criteria for evidence-based care bundles. For example, care bundles consist of three to a maximum of five evidence-based interventions, or so called 'elements', for a clinical process or patient population. The elements should be applied together in every eligible patient. The completion of an element could only be answered with 'yes' or 'no'. Compliance should be measured by using the all-or-none approach. This means that the bundle should be counted as completed only in case all included bundle elements are performed. The strength of bundling a small set of elements is to ensure that evidence-based care will be uniformly applied together in every eligible patient so that patients receive reliable care.[2-4]

Care bundles are widely applied tools in intensive care units (ICUs). They are frequently introduced as components of quality improvement initiatives.[5,6] The earliest developed care bundles, i.e. the central line bundle and ventilator bundle, are nowadays generally accepted in ICUs.[5] The effectiveness of these bundles has led to the development of more care bundles for other care processes or patient populations, such as the sepsis care bundle[7] or the urinary tract infection bundle (UTI).[8]

The IHI described the process on how they developed the central line bundle and ventilator bundle.[3,4] Their reports were descriptive in nature. They described the main steps of the bundle design process as well as the particular methods they have used within each process step. For instance, the first step they described was to identify certain processes at risk for ICU patients or that contributed to great harm.[2-4] This was done by systematically reviewing the literature.[9] Throughout the bundle development process other methods were used by the IHI. However, the methods used by the IHI may not always be applicable to all ICUs and in every situation. For example, use of systemic reviews is not for all ICUs a useful method to identify risks when the results are not valid due to the heterogeneity of data or due to the low quality of the included studies. In the literature, other useful methods to design care bundles have been published as well, such as a Root Cause Analysis (RCA) to identify risks or the use of a weighing and scoring technique for selecting bundle elements.[10,11] We wanted to identify what methods were

available that could also support the development of new bundles for the ICU besides the IHI approach. Therefore, we conducted a systematic review. The primary objective was to identify what different methodologies were used in the literature to design new evidence-based ICU care bundles. Based on the results, we built a comprehensive flowchart to provide an overview of the methods used so that others could choose their own desired method and to guide through the necessary steps of the development of new evidence-based care bundles for the ICU.

MATERIALS & METHODS

Design

A systematic review was conducted to identify methods for designing new care bundles for adult ICUs. The protocol for this study was not registered.

Selection criteria

We included studies that described the different methods within the whole care bundle design process in adult ICUs or the methods described in just certain parts of the design process. Studies were also included in case one or more IHI methods were used. Studies of any design were included and published in the English language.

Search strategy

A systematic search was performed in the electronic databases PubMed, EMBASE and CINAHL from the year care bundles were designed in January 2001 to August 2014. Furthermore, the reference lists of the full-text articles were screened. The search was designed for maximal retrieval, with no limitation of language or types of study design to be identified. The complete list of search terms and strategy of PubMed can be found in Supplementary File 1.

Study selection

The screening of the titles and abstract was conducted in two parts. At first, one author (M.B.) roughly screened all titles and abstracts. Studies were excluded when: (i) the language was not in English; (ii) the bundle was designed for pediatric departments or non-ICU departments or (iii) care bundles were not the subject of the study. Secondly, the titles and abstracts of the remaining articles were again screened. Two authors independently screened the titles and abstracts (M.B.,D.D.). In case of discrepancies, we reached consensus through discussion. A third reviewer was involved in case of disagreement. Full-text studies were reviewed and selected by two authors

independently. Studies were included in the analyses in case a description was given of the methodologies used on how to develop care bundles on ICUs for adult patients. Consensus was reached by discussion and a third author was involved in case of disagreement.

Data extraction

We extracted the following data from the identified studies: author, publication year, research design, setting, type of care bundle, methods used to develop the care bundle. Data extraction was independently performed by two authors (M.B.,D.D.). In case of discrepancies, consensus was reached by discussion. A third author was involved in case of disagreement.

Quality assessment

Given the diversity in study designs of the selected articles, we used two different tools for assessing the quality of the studies. For studies that primarily described the development of a care bundle, we used the Appraisal of Guidelines, REsearch and Evaluation II (AGREE II) instrument.[12,13] This instrument is designed for assessing the process of guideline development and how well this process is described.[13] To categorize the study quality we used the following cut-off points: excellent: (90-100); good (70-89); fair (50-69; poor (≤49).[13]

The checklist of Downs and Black was used for studies that primarily assessed clinical outcomes by using non-randomized study designs.[14] Checklist item number 27 about sample size calculation was simplified to a score of 0 (no sample size calculation) or 1 (sample size calculation reported). The following cut-off points have been reported to categorize studies by quality: excellent (26–28); good (20–25); fair (15–19) and poor (≤ 14).[15,16] Quality assessments were conducted by two reviewers independently. Disagreement between the reviewers was resolved through discussion. A third reviewer was involved in case of disagreement.

Flowchart

Based on the IHI methods as well as on the results of the systematic review we built a comprehensive flowchart for designing new care bundles. The flowchart contains the main process steps that should be followed. Each step contains methods that can be used for that particular part of the bundle design process. The development of the flowchart will be explained in the next paragraphs.

Expert team

For the development of the flowchart, a multidisciplinary expert team was created. The team consisted of two senior researchers (J.B.,F.P.), an intensivist/senior researcher (D.D.) and a junior researcher (M.B.). The junior researcher provided all the information for the consensus meetings. Two senior researchers (J.B.,F.P.) were former ICU nurses who are now involved in quality and patient safety initiatives on the ICU. The intensivist/senior researcher (D.D.) is experienced and trained in quality and safety in healthcare. This multidisciplinary team has a wide experience in the ICU care processes and was familiar with the conditions or requirements of care bundles.

Development process

The IHI was the founder of the care bundled approach. They described the methods they used to develop the central line bundle and ventilator bundle.[2-5] Their reports were more descriptive in nature.[2-5] These IHI reports formed the basis to structure the flowchart. We analyzed the IHI methods on how they have developed the central line bundle and ventilator bundle.[2,5] We analyzed their process in two ways. At first, we converted their descriptive reports into main process steps. For example, the IHI started the bundle development process by identifying problems by using the results of a systematic review. Therefore, this first main process step was labelled as: 'identify problems/risks'. Subsequently, the main steps were identified for the whole bundle development process. All steps were structured in a flowchart. Secondly, we selected the specific methods the IHI used for designing the central line bundle or ventilator bundle. For example, the IHI started the bundle development process by identifying problems by using the results of a systematic review. We incorporated the method of a systematic review in process step one: 'identify problems/risks'. Additionally, the methods identified by the literature search were incorporated in one of the main process steps of the flowchart.

Consensus meetings

We used consensus meetings with the expert team to analyze the IHI reports. At first, we identified the main process steps. Secondly, we built the flowchart and thirdly, we selected the methods and placed it in one of the process steps. Two meetings were arranged for defining the main process steps and to build the flowchart and two for filling in the specific methodologies per process step of the flowchart. Differences between the members were discussed until 100% consensus was reached. The meetings were highly structured by using the nominal group technique.[18] This is a structured meeting with experts about a certain issue and consists of two rounds in which the experts rate, discuss and rerate topics or issues.[17]

RESULTS

In total, 4665 articles were identified for possible inclusion through the initial search (Fig. 1). After screening titles and abstract, 107 full-text articles were reviewed. A final set of 18 articles met the inclusion criteria and were included in this study.

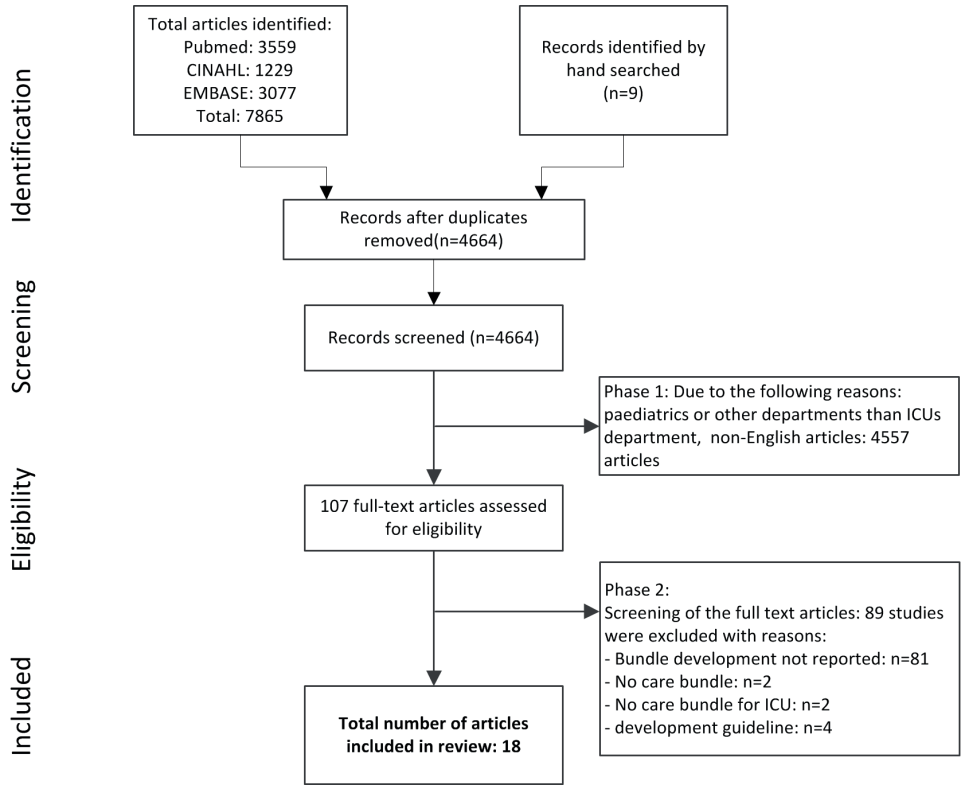

Figure 1. Flowchart of the study selection procedure

Study characteristics

The development of the ventilator bundle was reported in 17% (3/18) and for central line placement as well as for prescribing antibiotics in 11% (2/18). The remaining studies reported the methods used for the following bundles: sepsis; cerebral ventricular drainage; ventriculostomy placement; palliative care; thirst intensity and thirst distress (Table 1). In 33% (6/18), the whole bundle design process was reported. In 50% (9/18),

only one method for one process step was reported, i.e. conducting a literature review to identify risks in step 1.[31] In 89% (16/18), a literature review was used as a method to design bundles. In 75% (12/16) of these studies, a review was only used for identifying problems. In 12,5% (2/16), a review was used to underpin elements with evidence. In 12,5% (2/16), a bundle development process was described in general and that systematic reviews could be used to find evidence for the bundle elements. In 17% (3/18), a narrative report was written about bundles in general. Quality improvements were described in 39% (7/18), methodological studies in 17% (3/18), before and after designs in 11% (2/18). The remaining designs were one randomized trial, one case series and one observational study.

Table 1. Study characteristics

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
Hocking[17], 2013, New Zealand	Before and After study	Oct 2007-Apr 2011	Central line associated bacteraemia rate	General	Central line High risk patient bundle	Reduce infections In the high risk population	1) Analysis of the implementation data of the CLABSI insertion bundle and maintenance bundle: the data highlighted a group of patients who were continuing to get a CLABSI despite good compliance in both the insertion and maintenance bundle. 2) Search for literature for adding elements in the high risk bundle.
Berenholtz[19], 2007, USA	Description of bundle methodology	NR	Develop a preliminary set of quality measures for ICU patients with sepsis	ICU in general	Sepsis care bundle	Improve outcomes for patients with sepsis	1) Identify evidence based elements that improves outcomes: establish goals of the initiative and discuss potential quality measures 2) Review of the literature 3) Review the literature synthesis: the panel had to list their own recommendations for domains of sepsis care that should be evaluated as a potential quality measure. All measures were discussed in the panel until complete agreement was achieved. 4) Using the GRADE approach to evaluate the quality of the evidence and to balance the potential benefits and harms for each potential measure. 5) Writing the design specification for each measure or explicit definitions. Consensus in the panel was achieved through an iterative process.
Berenholtz[20], 2004, USA	Quality improve-ment	Mar 4-Apr 29, 2002	Percentage of ventilator days per week when patients received the bundle elements	Surgical	Ventilator bundle	Reduce infections	1) Qualitative review of the ICU quality indicators: a) Systematic review: identify interventions that improves patient outcomes in the ICU. b) Potential measures were evaluated based on the impact, feasibility, variability and the strength of the evidence to support each measure and to categorize each measure as outcome, process, access or complication measures 2) Four measures retrieved from the search were selected that were associated with improved outcomes in patients receiving mechanical ventilation. 3) These four core measures were grouped into a bundle: the ventilator bundle

Table 1. (continued)

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
Chatzi[21], 2014, Greece	Clinical prospective case series	2007-2012	Prevalence and outcome of external cerebral ventricular drainage-associated ventriculitis	General	Bundle of external cerebral ventricular drainage associated ventriculitis	Reduce infections	1) Assess clinical and microbiological patient data 2) Study the risk factors which are associated with ventriculitis 3) Literature review: the bundle was based on published data, adjusted on local protocols and setting.
Cooke[22], 2007, UK	Narrative report	NR	Propose of an antibiotic care bundle for prescribing antibiotics	NR	Antibiotic bundle	To select antibiotics to cure the patient, reducing risks of side effects and the risk of resistance and C. difficile.	1) Review of the literature 2) Selected elements were based on the IHI criteria (elements are evidence based)
Fulbrook[23] ,2003, UK	Narrative report/review	NR	Explain what contributes a care bundle and describe how it can be implemented	NR	Care bundle in general	General: improve clinical effectiveness	1) identify a critical care theme 2) identify a cluster of interventions/practices within the same theme 3) Undertake literature searches, related to each of the interventions/ practices, to identify all relevant research 4) extract the research literature 5) Categorize the available research according to its quality 6) Delete any intervention/practice from your list that do not have an adequate evidence base to refer to 7) On the basis of analyze research evidence, develop evidence based interventions/practices.

Table 1. (continued)

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
Pulcini[24], 2008, UK	Quality improvement	NR	Develop and test a set of process measures	NR	'Day 3 bundle'	Assess and improve the reassessment of inpatient empirical antibiotic prescriptions around day 3.	1) Literature search: selection of key process measures by one reviewer 2) selection of 3 to 5 measures thought to be valid and easy to collect.
Khalid[11], 2013, Saudi Arabia	Quality improvement	2009-2012	CLABSI rates	Medical-surgical ICU	Central line bundle	CLABSI reduction in developing countries	1) identify problems with a RCA 2) a flowchart was developed to identify the steps in the process and discover the potential weak links in the process. 3) all aspects of central line insertion and maintenance were analyzed and depicted in a flowchart 4) by using the flowchart: improvement plans and strategic interventions were developed.
Kollef[25], 2011, USA	Narrative report/review	NR	Prevention of nosocomial pneumonia	ICU in general	VAP prevention bundle	Prevention of VAP	1) Using the SMART approach: - **S**pecific interventions: a) identify bundle elements likely to be successful b) review evidence in support of proposed bundle elements c) consult with experts d) do not become sold on any single bundle element without evidence that it actually works - **M**easurable outcomes: a) use clinically relevant criteria to define outcome (e.g. VAP) b) demonstrated ability to accurately measure outcome of interest c) be aware of reporting biases, especially when using b/a or time series methods - **A**chievable program a) develop prevention strategy according to availability of local resources b) Target one problem or outcome at a time c) Start with a smaller problem to refine the local approach then apply to larger problems

Table 1. (continued)

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
							- **R**elevant a) Target problems that have direct clinical significance and consequences to patient care b) ensure that updated information is employed in the development of the prevention program c) update prevention program over time - **T**ime-Bound a) use discrete time periods for the implementation of the various phases b) have a cut-off time at which to determine the success or failure of the prevention program c) have specific time periods over which the prevention program will be re-evaluated to determine whether it needs updating or efforts to re-establish compliance with its components.
Kubilay[26], 2013, USA	Quality improvement	Q4 2006-Q1 2012	Infection rates	Neuro ICU	Ventricu-lostomy placement bundle	Decrease the ventricular catheter associated in-fection rate	1) Define the problem 2) FMEA was used to identify failure modes and solutions and to implement change and track results. 3) Broad literature review to outline evidence-based best practices.
Nelson[27], 2006, USA	Quality improvement	2003-2004	Create a palliative care bundle	ICUs in general	Palliative care bundle	Improving comfort and communi-cation in palliative care	1) Describe the problem 2) Review of the literature 3) Identify processes that were associated with desirable outcomes 4) Consensus about the candidate list of indicators 5) Specify and define the quality measures 6) Pilot test the quality measures

Table 1. (continued)

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
Puntillo[28], 2014, USA	RCT	NR	Thirst intensity thirst distress	Medical-Surgical, neurologic cardio-vascular ICU	Intervention bundle for thirst intensity thirst distress and dry mouth	Reduce thirst intensity and thirst distress.	1) Identify problem, 2) Evaluating prior research to find interventions to relieve thirst or dry mouth 3) Combining the single interventions into a bundle 4) Test the new care bundle
Rello[27], 2010	Description of bundle methodology	NR	Developing a comprehensive care bundle	ICUs in general	Ventilator-Associated Pneumonia care bundle	Reduce the incidence of VAP	1) Findings of a previous review of hospital acquired pneumonia and VAP guidelines across Europe were used to produce a comprehensive list of interventions. 2) The MCDA (Multi-criteria decision analysis) method was used to develop the bundle. MCDA is a weighting and scoring technique that supports decision making when numerous and conflicting evaluations are being assessed.
Rello[29], 2011	Description of bundle methodology	NR	Developing a comprehensive care bundle	ICUs in general	VAP care bundle: VAP diagnoses bundle and VAP treatment bundle	Promote guideline compliance	1) Findings of a previous review of hospital acquired pneumonia and VAP guidelines across Europe were used to produce a comprehensive list of interventions. 2) The MCDA (Multi-criteria decision analysis) method was used to develop the bundle. MCDA is a weighting and scoring technique that supports decision making when numerous and conflicting evaluations are being assessed.
Romero[30], 2013, Chile	Before and After study	Mar'09-Jul'11	Medication errors	Medical-Surgical ICU	Preventive Interventions Program bundle (PIP-bundle): interventions on medication errors	Reduce medication errors	1) Each bundle intervention was selected based on the types and causes of medication errors during the baseline period. 2) A multidisciplinary team systematically evaluated every stage of medication use to identify the causes of medication errors.

Table 1. (continued)

Author/ year of publication/ country	Design	Study period	Study outcomes	ICU	Type of bundle	Aim of the bundle	Methods used in the care bundle design process
Titsworth [31], 2012, USA	Observational study	Aug'08 – Dec'10	Catheter-associated urinary tract infections	Neuro ICU	Urinary Tract Infections (UTI) prevention bundle	Reduce the incidence of catheter-associated UTI	1) Review of the literature
Álvarez[32], 2014, Spain	Quality improvement	NR	Description of the methods applied to identify the recommendations to be included in the zero-VAP bundle and to accomplish implementation	ICUs in general	"zero-VAP" bundle	Reduction of the national VAP incidence rate by 25% and to less than 9 episodes per 1000 days of mechanical ventilation	1) Define the objectives of the bundle 2) Selection of VAP prevention measures derived from the literature 3) Classification of the interventions as "functional", "mechanical" or ""pharmacological". 4) Evaluation of the measures by teams with at least 2 members of the national Task Force team by using GRADE 5) Quantitative assessment by 11 members of the panel considering: 1) quality of the evidence, 2) its safety, 3) its feasibility in Spanish ICUs. 6) Finally, feasibility and cost criteria were applied based on which groups of 7 basic mandatory and 3 highly recommended measures were generated.
Harnage[33], 2007, USA	Quality improvement	Jan'06-Mar'07	Infection rates	Medical, surgical, Trauma, Neurologic ICU	Central line bundle	Reduce Catheter Related Blood Stream Infections	1) Reviewing and updating the current practices and procedures. 2) Review of the literature 3) Compare the current policies and procedures with the literature. 4) Determine if the policies and procedures matched the evolution of available products 5) meetings with product representatives for the multitude of products used in the placement and care of central venous catheters. 6) Bundle selection was based on available research, CDC recommendations, new product technology, changes required by the nurse and ease of use by the end user.

NR: None Reported; ICUs: Intensive cares; CLABSI: Central Line Associated Bloodstream Infection; VAP: Ventilator Associated Pneumonia; UTI: Urinary Tract Infections; MCDA: Multi-criteria decision analysis; FMEA: Failure Mode Evaluation and Analysis; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; RCT: Randomized Clinical Trial; CDC Centers for Disease Control and Prevention.

Quality assessment

For nine studies the checklist of Downs and Black was used. In 56% (5/9), studies scored between 15-19 points and were classified as 'fair'. One study scored 24 points and was classified as 'good'.[28] Studies were classified as 'poor' quality in 33% (3/9) (Supplementary File 2, Table 1). In six studies the AGREE II was used. Quality scores were calculated per domain[13] (Supplementary File 2, Table 2). For Domain 1, all six studies were classified as 'good', which means that the scope and purpose of the bundle were clearly explained. Six studies were classified as 'fair' for Domain 2, i.e. stakeholder involvement and for Domain 4, i.e. clarity of presentation. For three studies it was not possible to assess their quality, because narrative reports were written about care bundles in general and no assessment tools were available.

Flowchart for bundle design

The expert team created a flowchart containing all process steps to design new care bundles. The outline of the flowchart is shown in Figure 2. Three evaluations were added to the flowchart. These moments can be used to assess if the bundle conditions are met or to identify risks or problems prospectively.[2]

Reported methods for bundle design

The methods identified by the review were placed in either one of the main process steps. Table 2 shows all methods per process step. The table is complementary to Figure 2. In four process steps no other methods than the IHI methods were found.

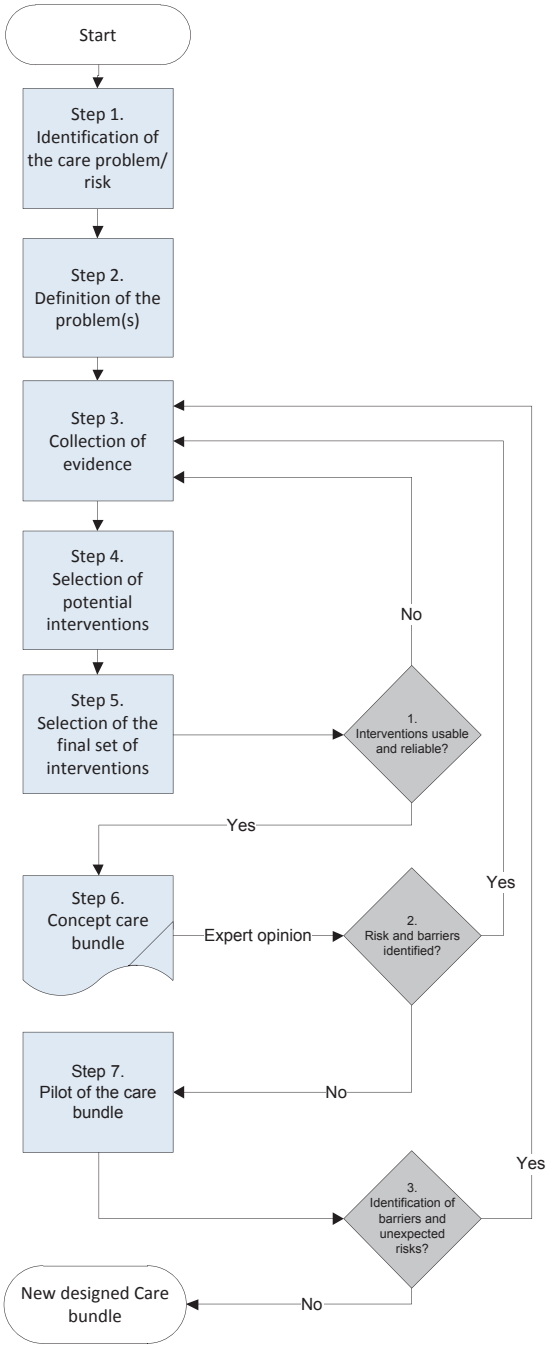

Figure 2. Outline of the comprehensive flowchart for designing new care bundles

Table 2. Process steps to design evidence-based care bundles

Process steps		Reported methods of the IHI	Additional reported methods
Step 1.	Identify problems or risks in a specific patient population or intervention that contributes to great harm and/or high costs.	Systematic reviews[2,10,19,20,23,29,33] Adverse Event Trigger Tool.[2]	Analysing own clinical patient data[18,21,30]; Root Cause Analyses[11]; Failure Mode Evaluation and Analysis (FMEA)[26]
Step 2.	The identified care problems or risks should be clearly defined.	Comprehensive literature search strategy[2]	No additional methods reported
Step 3.	Conduct a literature search to collect relevant evidence for the problems or risks and to find related elements.	Collect evidence from the international electronic databases and from the distillation from (inter)national clinical guidelines[2,19,20,23,26-28,32,33]	No additional methods reported
Step 4.	Select potential relevant and feasible elements from the literature search.	Select those elements that were described in the literature and were associated with the identified problem[2,10,18,19-33] or from local or (inter)national clinical guidelines[10,21,29]	Selected elements by analysing the medication errors[30]
Step 5.	Select a final set of maximally five elements	Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to evaluate the quality of the evidence of the elements.[19,24,32]	Weighing and scoring technique to select the most suitable, reliable or most appropriate key elements[10,29,32]; Root Cause Analyses[11]; FMEA[26]; Through discussion sessions or consensus meetings with experts or hospital staff.[19,23,25,27]
Step 6.	Create the care bundle in draft form.	Create the bundle in draft form and check if the IHI bundle requirements are met.[2,22,24]	No additional methods reported
Step 7.	Pilot test the care bundle in order to assess the reliability.	The pilot should be performed in a small sample of patients to identify (potential) risks or barriers for implementation. It is important to monitor the performance of all bundle elements to identify potential problems or risks and to evaluate if the care bundle is feasible, comprehensive, effective and easy to use[2,25,27,28]	No additional methods reported

DISCUSSION

The results of our systematic review show that besides the IHI approach various additional methods exist to design care bundles. Most included studies reported only one part of the design process (67%, 12/18), while in 33% (6/18) the whole process was described. Given the diversity in the methods used for designing care bundles, it might be suggested that the original IHI methods may not always be applicable to all ICUs and in every situation. For example, Romero *et al.* selected a set of elements by using the results of their analysis on medication errors. The potential elements were based on the types and causes of medication errors that were reported during their baseline period.[30] To prevent these errors, a care bundle was created based on these types and causes of medication errors. In this case, the IHI method for identifying risks might not have given the best results for this ICU. Moreover, Khalid *et al.* used a RCA for identifying risks.[11] They show that this is an effective tool to clearly identify the local risks and discover the potential weak links in the process. They show that the results of a RCA could form a perfect basis to design new care bundles. Furthermore, we identified studies in which different types of bundles were developed. Besides the well-known central line bundle and ventilator bundle, other care bundles were described in the literature such as the bundle for prescribing antibiotics[22], ventriculostomy placement[26] or for the bundle in palliative care.[27]

The first step in the bundle design process is to identify (potential) problems or risks.[2] The IHI used the adverse event trigger tool for this step.[34] Besides this tool, we identified additional risks assessment tools, such as a RCA[11] or FMEA.[26] These can be highly effective in the bundle design process due to their focus on local problems or risks.[11,26] This is important for designing care bundles because the included bundle elements should be a generally accepted practice in order to deliver reliable care.[2-4] Rello *et al.* used the Multi-Criteria Decision Analysis (MCDA) to design the ventilator bundle. They showed that this method is highly structured and efficient to use in the bundle design process.[10,29] Another example is the use of a systematic review. The IHI used this method for designing the ventilator bundle.[4] Systematic reviews were also reported in the literature to underpin evidence for the bundle elements in step 3 of the development process.

It is important that care bundles meet the IHI criteria. One of the criteria is that bundle elements must be supported by level 1 evidence.[2-4] However, robust evidence of care processes in relation to patient outcomes is often not available.[35,36] Therefore, evidence could also consist of clinical practice guidelines or other peer-reviewed synthesis of the evidence or studies published in a peer-reviewed journal.[35,36] Even though care bundles

aim to improve quality of care, the possibility exists that bundled elements have unexpected negative effects on other care processes. This issue is not well described in the literature but should not be neglected. Therefore, moments for evaluations were incorporated in the bundle design process intended to identify unexpected risks (Fig. 2).

Strengths and weaknesses

To our knowledge, this is the first study that reported about the different methodologies used in literature to develop new evidence-based care bundles. Our systematic review has several limitations. A description of the bundle development process is not often reported in detail nor described in abstracts. Therefore, we might have missed some relevant articles. We searched for bundles that were developed for ICUs, while methods used in other hospital areas might be relevant and valid as well. However, the first developed bundles of the IHI were also designed for adult ICUs. Furthermore, the complexity in ICU care is not comparable with other hospital wards. We screened the titles and abstracts of the articles in two steps. During the first, step one author screened all titles and abstracts. However, predetermined unambiguously clear exclusion criteria were applied. In case there was any uncertainty, the study was included for the second step in this screening process. In the second step the titles and abstract were screened by two authors independently as recommended in the PRISMA-statement.[37] The quality assessment of the articles were conducted by two persons independently. However, the interrater reliability was not calculated. Although the outline of the flowchart is based on the IHI approach, the order of the process phases and incorporating the methodologies in each process phase was conducted by opinions of the expert group. However, we have used a validated consensus method to overcome this issue. By combining both IHI and additional methods, we created a flowchart on how to develop new evidence-based ICU care bundles. We only searched for studies that described the methods used for bundle development and we incorporated these methods into the flowchart (Fig. 2). However, other methods might also be applicable that were not identified in our literature search. For instance, in step 1 (Fig. 2) other risk assessment tools might be effective instead, such as a BowTie analyses[38] or using the analysis from incident reporting systems[39,40] or 'lean management'.[41]

CONCLUSIONS

In this systematic review, we identified useful methods to design new evidence-based care bundles for ICUs, besides the original IHI methods. The results were used to build a generic comprehensive flowchart for designing new evidence-based care bundles. The flowchart provides a detailed view of all process steps of the bundle development process. The flowchart can be used as a useful tool to guide through all necessary steps in the process of designing care bundles. Further research is needed to validate the process steps of the flowchart.

Competing interest

The authors declare that they have no competing interests.

Funding

There is no funding to report for this publication

REFERENCES

1. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA.* 1999;282:1458-65.
2. Resar R, Griffin FA, Haraden C, Nolan TW. Using Care Bundles to Improve Health Care Quality. IHI Innovation Series white paper. Cambridge, Massachusetts: Institute for Healthcare Improvement; 2012. Available at: www.ihi.org/resources/Pages/IHIWhitePapers/UsingCareBundles.aspx. Accessed 23 June, 2015.
3. How-to Guide: Prevent Central Line-Associated Bloodstream Infections. Cambridge, MA: Institute for Healthcare Improvement; 2012. Available at: www.ihi.org/resources/Pages/Tools/HowtoGuidePreventCentralLineAssociatedBloodstreamInfection.aspx. Accessed 23 June, 2015.
4. How-to Guide: Prevent Ventilator-Associated Pneumonia. Cambridge, MA: Institute for Healthcare Improvement; 2012. Available at: http://www.ihi.org/resources/Pages/Tools/HowtoGuidePreventVAP.aspx. Accessed 23 June, 2015.
5. Pronovost PJ, Berenholtz SM, Goeschel C, et al. Improving patient safety in intensive care units in Michigan. *J Crit Care.* 2008;23:207-21.
6. Longmate AG, Ellis KS, Boyle L, et al. Elimination of central-venous-catheter-related bloodstream infections from the intensive care unit. *BMJ Qual Saf.* 2011;20:174-180.
7. Dellinger P, Mitchell M, Levy, et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. *Crit Care Med.* 2013;41:580-637.
8. Saint S, Olmsted RN, Fakih MG, et al. Translating health care-associated urinary tract infection prevention research into practice via the bladder bundle. *Jt Comm J Qual Patient Saf.* 2009;35:449-55.
9. Berenholtz SM, Dorman T, Ngo K, Pronovost PJ. Qualitative review of intensive care unit quality indicators. *J Crit Care.* 2002;17:1-12.
10. Rello J, Lode H, Cornaglia G, Masterton R, VAP Care Bundle Contributors. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med.* 2010;36:773-80.
11. Khalid I, Al Salmi H, Qushmaq I, Al Hroub M, Kadri M, Qabajah MR. Itemizing the bundle: Achieving and maintaining "zero" central line-associated bloodstream infection for over a year in a tertiary care hospital in Saudi Arabia. *Am J Infect Control.* 2013;41:1209-13.
12. Vlayen J, Aertgeerts B, Hannes K, Sermeus W, Ramaekers D. A systematic review of appraisal tools for clinical practice guidelines: multiple similarities and one common deficit. *Int J Qual Health Care.* 2005;17:235-42.
13. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Can Med Assoc J.* 2010;182: E839-842.

14. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52:377-84.

15. Hooper P, Jutai JW, Strong G, Russell-Minda E. Age-related macular degeneration and low-vision rehabilitation: a systematic review. *Can J Ophthalmol.* 2008;43:180-7.

16. Chudyk AM, Jutai JW, Petrella RJ, Speechley M. Systematic review of hip fracture rehabilitation practices in the elderly. *Arch Phys Med Rehabil.* 2009;90:246-62.

17. Hocking C, Pirret AM. Using a combined nursing and medical approach to reduce the incidence of central line associated bacteraemia in a new Zealand critical care unit: a clinical audit. *Intensive Crit Care Nurs.* 2013;29:137-46.

18. Jones J. Qualitative Research: Consensus methods for medical and health services research. *BMJ.* 1995;311:376.

19. Berenholtz SM, Pronovost PJ, Ngo K, et al. Developing quality measures for sepsis care in the ICU. *Jt Comm J Qual Patient Saf.* 2007;33:559-68.

20. Berenholtz SM, Milanovich S, Faircloth A, et al. Improving care for the ventilated patient. *Jt Comm J Qual Saf.* 2004;30:195-204.

21. Chatzi M, Karvouniaris M, Makris D, et al. Bundle of measures for external cerebral ventricular drainage-associated ventriculitis. *Crit Care Med.* 2014;42:66-73.

22. Cooke FJ, Holmes AH. The missing care bundle: antibiotic prescribing in hospitals. *Int J Antimicrob Agents. 2007*;30:25-9.

23. Fulbrook P, Mooney S. Care bundles in critical care: a practical approach to evidence-based practice. *Nurs Crit Care.* 2003;8:249-255.

24. Pulcini C, Defres S, Aggarwal I, Nathwani D, Davey P. Design of a 'day 3 bundle' to improve the reassessment of inpatient empirical antibiotic prescriptions. *J Antimicrob Chemother.* 2008;61:1384-8.

25. Kollef MH. Prevention of nosocomial pneumonia in the Intensive Care Unit: beyond the use of bundles. *Surg Infect (Larchmt).* 2011;12:211-20.

26. Kubilay Z, Amini S, Fauerbach LL, Archibald L, Friedman WA, Layon AJ. Decreasing ventricular infections through the use of a ventriculostomy placement bundle: experience at a single institution. *J Neurosurg.* 2013;118:514-520.

27. Nelson JE, Mulkerin CM, Adams LL, Pronovost PJ. Improving comfort and communication in the ICU: a practical new tool for palliative care performance measurement and feedback. *Qual Saf Health Care.* 2006;15:264-71.

28. Puntillo K, Arai SR, Cooper BA, Stotts NA, Nelson JE. A randomized clinical trial of an intervention to relieve thirst and dry mouth in intensive care unit patients. *Intensive Care Med.* 2014;40:1295-302.

29. Rello J, Chastre J, Cornaglia G, Masterton R. A European care bundle for management of ventilator-associated pneumonia. *J Crit Care.* 2011;26:3-10.

30. Romero CM, Salazar N, Rojas L, et al. Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients. *J Crit Care*. 2013;28:451-60.

31. Titsworth WL, Hester J, Correia T, et al. Reduction of catheter-associated urinary tract infections among patients in a neurological intensive care unit: a single institution's success. *J Neurosurg*. 2012;116:911-20.

32. Álvarez Lerma F, Sánchez García M, Lorente L, et al. Guidelines for the prevention of ventilator-associated pneumonia and their implementation. The Spanish "Zero-VAP" bundle. *Med Intensiva*. 2014;38:226-36.

33. Harnage SA. Achieving zero catheter related blood stream infections: 15 months success in a community based medical center. *The Journal of the Association for Vascular Access*. 2007;12:218–224.

34. VHA/Institute for Healthcare Improvement. ICU Adverse Event Trigger Tool, January 2002 http://www.ihi.org/resources/Pages/Tools/ICUAdverseEventTriggerTool.aspx. Accessed 25 June, 2015.

35. Marwick C, Davey P. Care bundles: the holy grail of infectious risk management in hospitals? *Curr Opin Infect Dis*. 2009;22:364-369.

36. National Quality Measures Clearinghouse. http://www.qualitymeasures.ahrq.gov/tutorial/validity.aspx. Accessed 2 April, 2015.

37. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;21: e1000097.

38. Kerckhoffs MC, Van der Sluijs AF, Binnekade JM, Dongelmans DA. Improving patient safety in the ICU by prospective identification of missing safety barriers using the bow-tie prospective risk analysis model. *J Patient Saf*. 2013;9:154-9.

39. Pronovost PJ, Goeschel CA, Marsteller JA, Sexton JB, Pham JC, Berenholtz SM. Framework for patient safety research and improvement. *Circulation*. 2009;119:330-337.

40. Pronovost PJ, Cardo DM, Goeschel CA, Berenholtz SM, Saint S, Jernigan JA. A research framework for reducing preventable patient harm. *Clin Infect Dis*. 2011;52:507-513.

41. Faulkner B. Applying Lean Management Principles to the Creation of a Postpartum Hemorrhage Care Bundle. *Nursing for Women's Health*. 2013;17:400–411.

Supplementary File 1

Search strategy PubMed

((“Intensive Care Units”[Mesh] OR Intensive Care* OR ICU OR critical care OR “Critical Care”[Mesh]) AND (bundle* OR care bundle* OR evidence based*[tiab] OR “evidence-based practice”[MeSH] OR “Evidence-Based Medicine”[Mesh]) AND (development*[tiab] OR invent*[tiab] OR create*[tiab] OR method[tiab] OR methods[tiab] OR methodolog*[tiab] OR design*[tiab])) Filters: Publication date from 2002/01/01 to 2014/07/31

Supplementary File 2

Quality assessments

Table 1. Quality assessments by using the checklist of Downs and Black[15]

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total score
Harnage, 2007	1	1	0	1	0	0	0	0	1	0	1	0	1	0	0	0	1	0	0	0	1	1	0	0	0	1	0	10
Berenholtz, 2004	1	1	0	1	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	0	0	1	0	19
Khalid, 2013	1	1	0	1	0	1	1	0	1	1	1	0	1	0	0	0	1	1	1	1	0	1	0	0	0	1	0	15
Kubilay, 2013	1	1	1	1	0	1	0	0	1	0	1	0	1	0	0	0	1	1	1	1	0	1	0	0	0	1	0	14
Romero, 2013	1	1	1	1	0	1	1	0	1	1	1	0	1	0	0	0	1	1	1	1	0	1	0	0	0	1	0	16
Puntillo, 2014	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	24
Titsworth, 2012	1	1	1	1	0	0	0	0	1	1	1	0	1	0	0	0	1	1	1	1	0	1	0	0	0	1	0	14
Chatzi, 2014	1	1	1	1	0	1	1	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0	0	0	1	0	18
Hocking, 2012	1	1	1	1	0	0	1	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	0	0	0	1	0	17

Table 2. Quality assessments by using AGREE II[14]

	Domain 1 Scope and purpose				**Domain 2** Stakeholder involvement				**Domain 3** Rigour of development									**Domain 4** Clarity of presentation				**Domain 5** Applicability					**Domain 6** Editorial independence		
	1	2	3	DS	4	5	6	DS	7	8	9	10	11	12	13	14	DS	15	16	17	DS	18	19	20	21	DS	22	23	**DS**
Álvarez, 2014	5	6	6	**77**	3	2	5	**61**	4	2	1	1	1	4	1	1	**15**	4	4	6	**61**	2	6	4	5	**54**	6	6	**75**
Rello, 2010	6	6	6	**83**	6	4	2	**50**	7	5	5	6	6	4	1	1	**56**	5	4	6	**67**	2	4	4	5	**46**	5	6	**67**
Rello, 2011	6	6	6	**83**	6	4	2	**50**	7	5	5	6	6	4	1	1	**56**	5	4	6	**67**	2	4	4	5	**46**	5	6	**67**
Berenholtz, 2007	6	6	4	**72**	6	4	2	**50**	6	6	6	5	6	6	1	5	**69**	5	4	6	**67**	4	7	4	6	**60**	6	6	**75**
Nelson, 2006	6	6	4	**72**	6	4	2	**50**	6	5	4	4	6	5	6	1	**60**	5	4	6	**67**	2	6	4	6	**58**	5	6	**67**
Pulcini, 2008	6	6	4	**72**	6	4	2	**50**	3	3	2	2	4	2	2	2	**25**	5	4	6	**67**	2	5	4	6	**54**	5	6	**67**

DS = Domain score in percentages