Beyond Value-Based Health Care

How to use outcomes to improve quality of care in heart care?

Nina Zipfel

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Promotor:	Prof. dr. G.P. Westert
Copromotoren:	Dr. P.B. van der Nat (St. Antonius Ziekenhuis, Nieuwegein)
	Dr. A.S. Groenewoud
	Dr. B.W.J.M. Rensing (St. Antonius Ziekenhuis, Nieuwegein)
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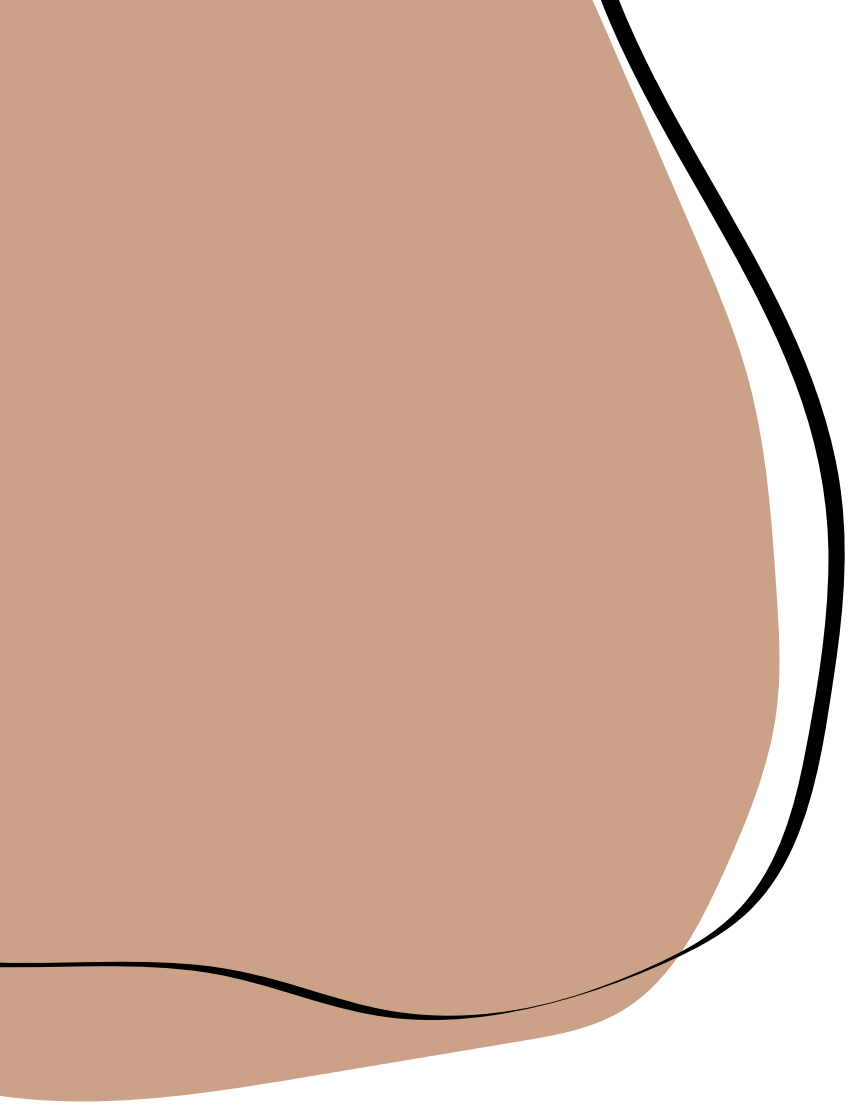
Für Papa

Contents



1

General introduction

Delivering and receiving care with the best possible result for each patient is the ultimate goal for patients and health care providers. This goal encompasses the delivery of appropriate care suiting the needs of each individual patient. To determine appropriate care, patients and providers need to gain insights into the outcomes that are relevant for the patient. Insights into and use of patient-relevant outcomes are said to enhance quality improvement, which in turn can lead to better patient satisfaction and generate cost savings [1,2].

Measurement of patient-relevant outcomes can also enhance improvement of quality of healthcare. Berwick et al. (2003) explained two pathways to quality improvement: through selection and through changes in care. The first, selection, entails the possibility of choosing among health care providers who deliver the best outcomes [3]. In the Netherlands, steps have been set in the past years towards quality improvement through selection by, for example, the creation of websites informing patients, such as "KiesBeter" (Choose better) and "Zorgkaart" (Care map), to choose a suitable health care provider [4]. This pathway does not directly lead to a hospital delivering better outcomes, but it can lead to patients choosing a certain provider and thus shifting business. The second pathway describes improvement through changes [3]. This route requires understanding of measurements related to aims and the underlying processes in order to change them. *Change*, in the terms of Berwick et al. (2003), thus, requires measurement of, for instance, standard sets of patient-relevant outcomes or processes in order to enable quality improvement.

Despite the early efforts of Berwick et al. (2003) to stress the necessity of measurement and insights into outcomes, it is unknown *how* outcome measurement contributes to improved quality of healthcare. A method supporting measurement of outcomes is value-based health care (VBHC) [5]. VBHC focusses on the measurement of patient-relevant outcomes relative to costs of care. However, studies on the use of outcome measures leading to quality improvement are scarce.

The purpose of this thesis is to evaluate *how* outcome measures lead to quality improvement and which steps are needed to contribute to improvement of outcomes. The main research question is: *how can patient-relevant outcomes contribute to quality of care improvement?* For this thesis we have applied the concept of VBHC as a framework for quality of care improvement.

In order to answer the main research question, this study addresses the following sub-questions:

1. *To what extent are outcome measures from clinical registries used to implement and monitor quality improvement initiatives? (Chapter 2)*
2. *How can improvement interventions be selected based on insights into outcomes for surgical treatment of aortic valve disease (AVD)? (Chapter 3)*
3. *How can improvement interventions that were selected based on insights into outcomes be implemented? (Chapter 4)*
4. *What are the effects of a carefully selected improvement intervention in the context of VBHC on patient-relevant outcomes for surgical treatment of aortic valve disease (AVD)? (Chapter 5-6)*
5. *Can process measures be of additional value in an outcome-oriented VBHC approach and how can process measures – in addition to outcome measures - be selected with impact on patient-relevant outcomes, and which process measures are most relevant for surgical treatment of aortic valve disease (AVD)? (Chapter 7-8)*

Sub-questions 2, 4 and 5 are investigated specifically in the context of the surgical treatment of AVD.

In the following paragraphs, the focus on AVD patients will be explained. In addition, the concepts used in this thesis will be introduced: VBHC, AVD and outcome measurement, outcome measurement and clinical registries, from outcome data to improvement and process measurement makes the difference, followed by the outline of this thesis.

Value-based health care

In order to respond to the increasing demand for health care and rising health care costs, many approaches were developed to reduce health care spending [6,7] among which value-based health care (VBHC) [5]. VBHC, is a concept aiming to contribute to better quality of healthcare by creating higher value for patients [5]. Value within VBHC is defined as follows:

$$VALUE = \frac{\text{THE SET OF OUTCOMES THAT MATTER FOR THE CONDITION}}{\text{THE TOTAL COSTS OF DELIVERING THESE OUTCOMES OVER THE FULL CARE CYCLE}}$$

The aim of VBHC is to combine several goals of stakeholders in healthcare into one overarching objective: achieving higher value for patients [8]. Outcomes, in this concept, are the actual results of care achieved. According to the World Health Organization (WHO) health outcomes are defined as "a change in health status of an individual, group or population which is attributable to a planned intervention or series of interventions" [9]. Within VBHC the outcome set should be specific to a medical condition. A medical

condition is a set of medical circumstances as for example AVD, diabetes or lung cancer. The medical condition includes circumstances for the full cycle of care and not only an intervention or specialist care. Value is proposed not to be created just for a single intervention, but it can include multiple interventions or specialisms, which contributes to shared accountability for value among all involved providers. Costs, the denominator of the equation, refer to the total costs required for the full cycle of care of a medical condition [10]. This includes the costs of devices, medication, inpatient and outpatient care and any other associated services. The value equation is not per se supposed to lead to a single number, but illustrates the relationship between outcomes and costs.

Data on results would challenge health care providers to learn and improve [10]. Within the concept of VBHC a three-tier outcome hierarchy is proposed to define patient-relevant outcomes. The three levels are: health status achieved or retained, process of recovery and sustainability of health [10]. The levels are proposed to cover short-term and long-term consequences of treatment for a medical condition. Until recently, the focus in healthcare has mainly been on process measurement in the sense of guideline adherence or patient satisfaction. Process measures could contribute to improved outcomes, but some disadvantages have been described as well [11]. First, they do not depict the true result of a treatment of a medical condition. Second, the measurement of many process measures can lead to a burden for health care providers and are often imposed externally [12]. Therefore, the outcomes hierarchy was proposed to capture a limited set of patient-relevant measures. Experts consider that measuring a standard set of outcomes is key to drive improvement and increase value for patients [12].

Aortic valve disease and outcome measurement

In order to evaluate how outcomes can be used for improvement, this study focusses on one medical condition: aortic valve disease (AVD).

AVD is a highly prevalent disease in the western countries. The prevalence of all AVD in the elderly accounts for 12.4% and the prevalence of severe AVD demanding aortic valve replacement is 3.4% [13]. AVD is a heart disease caused by valve stenosis or obstruction to flow or a backward leakage, referred to as valve regurgitation, or a combination of both [14]. The latter is a leakage of the valve into the left ventricle during filling of the heart (diastole). Leakage of the valve can either be acute or chronic and demands direct treatment. Valve stenosis is the narrowing of the aortic valve opening during contraction of the heart mostly caused by calcified valve cusps that emerge with ageing. Treatment options for aortic stenosis and valve regurgitation include open-heart surgery, hereafter referred to as surgical aortic valve replacement (SAVR) , minimally invasive aortic valve

replacement, also called transcatheter aortic valve replacement (TAVR) or medical treatment (conservative treatment) [14].

In the Netherlands and specifically the St. Antonius Hospital, the concept of VBHC is supported and most advanced in heart care. Due to its high prevalence and the application of VBHC, AVD was chosen as a focus for this thesis. In this thesis, when referred to AVD, it concerns the two interventional treatments of SAVR and TAVR.

The Dutch foundation "Meetbaar Beter" (Measurably Better) developed several outcome measure sets for heart diseases based on the VBHC concept, which are used at the St. Antonius Hospital [15]. For the development of the outcome measures the concept of value-based health care (VBHC) was used [16]. This thesis uses outcome measures sets from the Netherlands Heart Registry (NHR) (**Appendix 1** and **Appendix 2**). These outcome measures were used for analysis purposes of this thesis in chapter 3, chapter 5 and chapter 6.

Outcome measurement and clinical registries

In order to use outcome measurements for quality improvement clinical registries are crucial. A clinical registry is defined as "an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcome measures for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical or policy purposes" [17]. Several clinical registries have been implemented internationally presenting potential for improving health outcomes and increasing healthcare value [18]. Clinical registries have a long precedence of use in cancer care. Reportedly, the first registries were attempted in Hamburg in 1927, New York in 1940 and Denmark 1942 [19]. The development of clinical registries in heart care date back to 1989 with the New York state cardiac surgery registry [20]. In Sweden, for example, the national registry Swedeheart presented improvement in adherence to guidelines for treating acute myocardial infarction [21].

In the Netherlands, a clinical registry for heart diseases was developed by "Meetbaar Beter" (Measurably Better) with the goal of contributing to improved quality of healthcare by measuring a minimal set of outcome measures per medical condition. In 2017, the foundation merged with existing Dutch registries for cardiology (NCDR) and thoracic surgery (BHN) to form one (multidisciplinary) registry for heart care: the Netherlands Heart Registry (NHR). The NHR aims to improve quality of healthcare by transparently reporting reliable data from 21 Dutch heart centers [16]. The NHR reports outcome measures from the participating hospitals in an annual report. For the annual report, outcome measures are adjusted for case-mix factors to facilitate benchmarking. However, the question whether

clinical registries lead to better quality, and *how* to use these outcome measures and insights to improve quality of healthcare is still unknown. This thesis, therefore starts with a review of the literature on the effects of clinical registries and the use of quality improvement methods on outcome measures (RQ1, Ch2). The remainder of this thesis, focusses on the outcome measures from the NHR and uses data provided by the NHR.

From outcome data to improvement

Experts suggest that measuring outcomes is crucial for improving results and reducing costs [10]. Measurement of outcomes through the application of VBHC is presented to trigger the initiation of improvements [22]. Outcome measures are also applied in classical medical research as in randomized-controlled trials, however the concept of VBHC uses outcome measures for benchmarking and monitoring purposes with the goal of improving quality of care. Current studies use VBHC, and in particular outcome measurement, as a sole solution to drive improvement [22]. The VBHC movement established the International Consortium for Health Outcome Measurement (ICHOM), which developed several standardized outcome measure sets [12]. The goal for ICHOM is to facilitate standardized sets of outcome measures to facilitate national and international benchmarking of patient-relevant outcome measures. However, the methods on how to get from measurement to possible improvement initiatives remains unclear. This thesis will focus on the development of an approach on how to use outcome measurement to identify and select improvement initiatives (RQ2, Ch3).

Quality improvement, hereafter referred to as QI, has gained increasing attention not only for authorities due to rising healthcare costs [23], but also managers, physicians and patients [24]. QI has been introduced as an improvement methodology for the identification of improvement and implementation, which is closely linked to implementation science. Implementation science focusses on methods to improve systematic uptake of research findings and evidence-based practices into routine care, and thus, improve quality of healthcare [25]. In this thesis, we will also study the implementation of improvement initiatives in the context of VBHC (RQ3, Ch4).

Following successful implementation of an improvement initiative, the effect on outcome measures needs to be evaluated. One method for the evaluation of QIs is the comparison of outcome measures before introduction of the intervention with after the intervention: the so-called before-and-after design [26]. This thesis evaluates the effect of an improvement initiative in the context of VBHC in the form of a before-and-after evaluation (RQ4, Ch5-6).

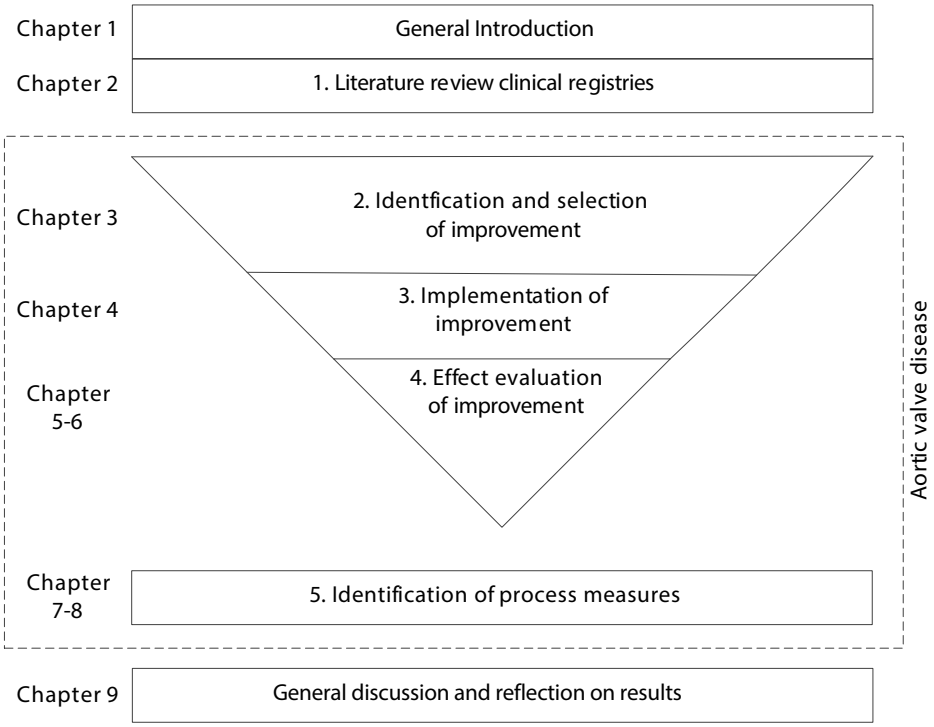
Process measurement makes the difference

Process measures describe the steps or actions of care patients receive [27]. An advantage of process measures compared to outcome measures is that they are relatively easy to interpret and are more sensitive to differences in quality of care [11]. A mortality rate of myocardial infarction is an interesting measure and makes outcome measures of intrinsic interest. Process measures on its own can be of little interest if they cannot be linked to an outcome measures [11]. Previous research in surgical care has found strong associations between process measures and improved patient outcomes [27]. Studies have identified that it is difficult to identify one isolated factor that improved outcome measures [28]. Whereas, process measures can be linked to a specific action of a clinician to allow monitoring of what went well or whether the action has been applied by a clinician [28]. Therefore, this thesis also looked at process measures for AVD impacting outcome measures and in a wider VBHC context (RQ5, Ch7-8).

OUTLINE OF THIS THESIS

The purpose of this thesis is to investigate how VBHC can contribute to improvement of quality of healthcare. This thesis specifically focusses on quality improvement for AVD (RQ 3,4 and 5). To achieve this purpose a number of steps were followed that are described in the following chapters of this thesis. The thesis is structured in seven chapters with five empirical studies. The outline of this thesis is displayed in Figure 1.

Figure 1. Outline of this thesis.



Chapter 1 includes this general introduction. **Chapter 2** presents a systematic review to identify evidence that clinical registries lead to improved outcome measures and to identify what drivers were key to those improvements. Clinical registries are important for benchmarking and improving quality of healthcare [29]. Through benchmarking outcome measures, and by identifying variation in patient-relevant outcomes competition is stimulated by achieving best practices [29]. However, evidence whether clinical registries actually lead to improved outcome measures, is still scarce.

Chapter 3-6 comprise studies on the application of VBHC. The use of outcome measurement for QI is studied in detail with the goal of actual improvement of the quality of healthcare with an improvement intervention. Measurement of patient-relevant outcomes is believed to improve outcome measures, but how can potential for improvement be identified using these outcome measures? St. Antonius Hospital (Nieuwegein, the Netherlands), one of the participating hospitals of the NHR, started discussing the results for AVD in 2015 according to the VBHC concept. However, VBHC does not offer a framework

on how to identify and select improvement based on outcome measures. Moving from outcome measurement to quality improvement was identified one of the main challenges for successful application of VBHC [15]. A method to fill this gap is reported in **Chapter 3**. Second, an implementation method was studied for the implementation of improvement interventions in the context of VBHC. Not only the identification and selection of improvement interventions is important to contribute to better quality of healthcare, but also successful *implementation* of improvements into clinical practice. The concept of VBHC pretends to "fix" healthcare, but the concept does not offer a systematic method on the implementation of improvement initiatives. Grol et al. offer a model to systematically implement change; the so-called Implementation of Change model (ICM) [30]. **Chapter 4** presents a case study of the implementation processes of two quality improvement interventions. One followed a systematic approach for implementation with the help of the ICM. The other did not apply a systematic implementation method. The success factors for implementation while monitoring value are reported. Third, we examined whether the implementation of an improvement intervention chosen and implemented based on the presented methods leads to improvement in outcome measures. The improvement intervention that was selected is preoperative protein-enriched diet. The aim was to optimally prepare older patients with AVD by offering protein-enriched familiar foods. **Chapter 5** evaluates the effect of the improvement intervention. Next to the evaluation of the effect of protein-enriched diet on protein-intake as an intermediate outcome, the impact on outcome measures (NHR outcome measures) is evaluated in **Chapter 6**.

Chapter 7 consists of a study as part of the standard QI work at place at the St. Antonius Hospital. Outcome measures defined according to the concept of VBHC are also standardly discussed in the St Antonius Hospital since 2015. Bimonthly meetings were organized in a multidisciplinary team to discuss the outcome measure sets of MB. But only using outcome measures for improvement of quality of healthcare also has its limitations. This chapter describes a method for the identification of process measures with impact on patient-relevant outcome measures and a set of process measures for AVD. This study was conducted in the context of the standard QI team of the St. Antonius Hospital in order to complement to the outcome measure set for monitoring improvement. In **Chapter 8**, we reflect on the evolution and combination of process, structure and outcome measures in the light of Donabedian.

In **Chapter 9**, the general discussion, the results of the studies from previous chapters are discussed as well as recommendations presented. This chapters reflects on the case of AVD and working with VBHC, as well as the general application of VBHC for quality of healthcare improvement.

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APPENDICES

Appendix 1. Outcome measures of SAVR. Adapted from the Netherlands Heart Registry [16]**.**

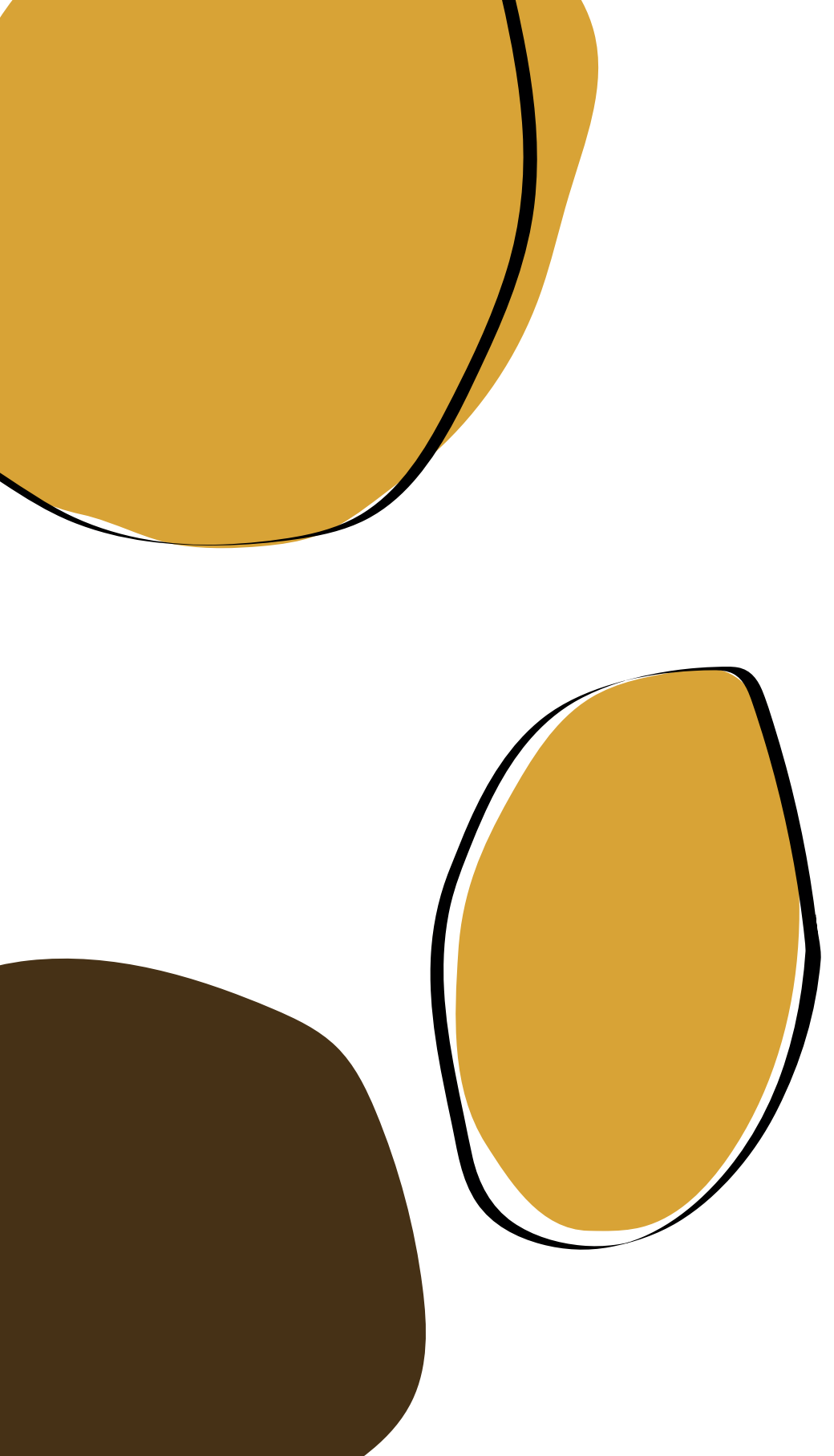
Tier	Level	Outcome measure	Definition
Health status achieved or retained	Survival	120-day mortality	Patients who die regardless of cause of death within 120 days (≤ 120 days) after intervention.
		Long-term survival	Patients who survive as a result of the number of days elapsed after the intervention with a maximum follow-up of 5 years.
	Degree of health or recovery	Quality of Life	Quality of life of the patients measured before and after intervention. Measurement before intervention=measured no longer than a maximum of 2 months before intervention. Measurement after intervention=measured between 10-14 months after intervention. Measured with the Short Form (36) Health Survey.
Process of recovery	Time to recovery and time to return to normal activities	Not applicable	Not applicable
	Disutility of care or treatment process	Cerebrovascular accident (CVA)	Patients for which a neurological determination of a postoperative stroke has occurred within 72 hours (≤ 72 hours) after intervention (excluding Transient Ischemic Attack).
		Implantation of a new permanent pacemaker	Post-operative implantation of a new (no replacement) permanent pacemaker within 30 days (≤ 30 days) after intervention.
		Deep sternal wound infection	Deep sternal wound infection developing within 30 days (≤ 30 days) after intervention. It is assumed that the patient returns to the treatment hospital.
Sustainability of health	Sustainability of health or recovery and nature of recurrences	Freedom of valve-re-intervention	Patients who are free from aortic valve re-intervention (aortic valve replacement, aortic valve repair or percutaneous paravalvular leakage (PVL) closure) on the same aortic valve as a function of the number of days elapsed after intervention.
	Long-term consequences	Not applicable	Not applicable

Appendix 2. Outcome measures of TAVR. Adapted from the Netherlands Heart Registry [16].

Tier	Level	Outcome measure	Definition
Health status achieved or retained	Survival	120-day mortality	Patients who die regardless of cause of death within 120 days (≤ 120 days) after intervention.
		Long-term survival	Patients who survive as a result of the number of days elapsed after the intervention with a maximum follow-up of 5 years.
		30- day mortality	Patients who die regardless of cause of death within 30 days (≤ 30 days) after intervention. Excluding mortality during the procedure (procedural mortality) (≤ 0 days).
		Procedural mortality	Patients who die during the procedure regardless of cause of death (≤ 0 days).
	Degree of health or recovery	Quality of Life	Quality of life of the patients measured before and after intervention. Measurement before intervention=measured no longer than a maximum of 2 months before intervention. Measurement after intervention=measured between 10-14 months after intervention. Measured with the Short Form (36) Health Survey.
Process of recovery	Time to recovery and time to return to normal activities	Not applicable	Not applicable
	Disutility of care or treatment process	Cerebrovascular accident (CVA)	Patients for which a neurological determination of a postoperative stroke has occurred within 72 hours (≤ 72 hours) after intervention (excluding Transient Ischemic Attack).
		Implantation of a new permanent pacemaker	Post-operative implantation of a new (no replacement) permanent pacemaker within 30 days (≤ 30 days) after intervention.
		Vascular complications	Patients who develop a vascular complication within 30 days (≤ 30 days) (diagnosis according to the VARC-2 definition) from the start of the intervention (including pre-operative vascular complications).

Appendix 2. Continued.

Tier	Level	Outcome measure	Definition
Sustainability of health	Sustainability of health or recovery and nature of recurrences	Freedom of valve-re-intervention	Patients who are free from aortic valve re-intervention (aortic valve replacement, aortic valve repair or percutaneous paravalvular leakage (PVL) closure) on the same aortic valve as a function of the number of days elapsed after intervention.
	Long-term consequences	Not applicable	Not applicable



2

Health outcomes measurement and organizational readiness support quality improvement: a systematic review

Nynke Kampstra*
Nina Zipfel*
Paul van der Nat
Gert Westert
Philip van der Wees
Stef Groenewoud

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*Alphabetic order, first shared authorship.

ABSTRACT

Background: Using outcome measures to advance healthcare continues to be of widespread interest. The goal is to summarize the results of studies which use outcome measures from clinical registries to implement and monitor QI initiatives. The second objective is to identify a) facilitators and/or barriers that contribute to the realization of QI efforts, and b) how outcomes are being used as a catalyst to change outcomes over time.

Methods: We searched the PubMed, EMBASE and Cochrane databases for relevant articles published between January 1995 and March 2017. We used a standardized data abstraction form. Studies were included when the following three criteria were fulfilled: 1) they relied on structural data collection, 2) when a structural and comprehensive QI intervention had been implemented and evaluated, and 3) impact on improving clinical and/or patient-reported outcomes was described. Data on QI strategies, QI initiatives and the impact on outcomes was extracted using standardized assessment tools.

Results: We included 21 articles, of which eight showed statistically significant improvements on outcomes using data from clinical registries. Out of these eight studies, the Chronic Care Model, IT application as feedback, benchmarking and the Collaborative Care Model were used as QI methods. Encouraging trends in realizing improved outcomes through QI initiatives were observed, ranging from improving teamwork, implementation of clinical guidelines, implementation of physician alerts and development of a decision support system. Facilitators for implementing QI initiatives included a high quality database, audits, frequent reporting and feedback, patient involvement, communication, standardization, engagement, and leadership.

Conclusion: This review suggests that outcomes collected in clinical registries are supportive to realize QI initiatives. Organizational readiness and an active approach are key in achieving improved outcomes.

BACKGROUND

The use of clinical registries is considered crucial to systematically measure clinical outcomes in achieving better value for patients [1]. A clinical or patient registry is defined as "an organized system that uses observational study methods to collect uniform data (clinical data as structure, process and outcome measures) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure" [2]. Registries that are used for evaluating patient outcomes are used for the purpose of this review. The importance of clinical registries has been widely recognized as a tool to realize quality improvement (QI) and public accountability [1,3–8]. Medical associations use clinical registries for collecting data using pre-defined measures in patients undergoing a certain procedure or for a specific disease [9]. In particular, feedback based on clinical registry data is used to identify and monitor improvement initiatives [10]. Therefore, registries are seen as a promising tool to achieve improvements in value for the patient by measuring outcomes [1]. A previous review on the structure, use and limitations of current clinical registries showed that registries and their respective measures are used for monitoring providers, discussion platforms for QI, improving risk adjustment modelling and for improving preoperative risk profiling [11]. However, the current body of literature lacks insights into the extent to which the use of outcome measures from clinical registries, either when identifying, selecting or monitoring QI initiatives, can impact health outcomes.

With rising healthcare costs, service restrictions, differences in quality and costs, there is an increasing need for reform to improve value of healthcare [12]. Value in healthcare is defined as outcomes relative to costs [13]. Value-based health care aims at achieving higher value for patients while ensuring sustainability of the healthcare system by an efficient and effective delivery of care [14]. This goal is assumed to be achieved by measuring and using outcomes per medical condition for the identification of improvement potential across the full cycle of care [12]. Higher value for patients by measuring outcomes is one of the potential methods for improving quality of healthcare relative to the costs spent. For the purposes of this review, we only focused on outcome measures and not on the respective costs.

Quality of healthcare is generally assessed by using structure, process or outcome measures [15]. The latter provide insights into outcomes of a certain disease or several diseases, for instance on survival, functional status, and quality of life [16]. The aim of measuring outcomes is diverse; guiding clinical decision-making, initiating improvement interventions, benchmarking, monitoring, scientific research and public accountability. Measuring outcomes structurally and using them to identify possible improvements contributes to the aim of achieving higher value for patients [17].

The goal is to summarize the results of studies which use outcome measures from clinical registries to implement and monitor QI initiatives. For the purposes of this study, QI was defined as the application of a defined improvement process to achieve measurable improvement by implementing an improvement intervention. Registry data itself is not sufficient as they need QI methods in order to achieve actual improvement. The second objective is to identify a) facilitators and/or barriers that contribute to the realization of QI efforts, and b) how outcomes are being used as a catalyst to change outcomes over time.

METHODS

A systematic review was conducted of studies published between January 1995 and March 2017. The search strategy was designed for PubMed, EMBASE and Cochrane databases. To identify evidence for the use of clinical registries to improve or contribute to patient health outcomes, the following PubMed Mesh terms were used to identify studies: *mortality*, *patient outcome assessment* and *treatment outcome*. These terms were combined with a variety of search terms related to QI and diverse disease specific registry studies. No specific patient group or study design was defined. Details of the complete search strategy are provided in the online supplementary content (**Appendix 1**). Additional hand-searching has been conducted for systematic reviews on the subject during the review process. The hand-search was conducted in Google Scholar.

Inclusion and exclusion criteria

Studies were included when they met each of the following criteria: 1) published in peer-reviewed journals, 2) published in English, French or German, 3) the study actively implemented a strategy using outcome data to realize QI, 4) the study relied on structural data collection, and 5) the study evaluated the QI interventions realized. Whether a study made use of a QI effort, falling under criteria 3 and 5, was evaluated after reviewing the full text papers and was therefore not part of the search string. After title screening, included studies were evaluated on criteria 3 and 5. Studies were excluded when they analyzed the effect of new intervention(s) on outcomes (testing drugs, new techniques or the effect of an intervention) or when the data had solely been collected to evaluate an intervention in a clinical trial.

Data extraction and quality assessment

For the initial selection each reviewer reviewed a random set on first title, second abstract, and finally full text to determine eligibility. The full text articles were critically reviewed and judged by all reviewers. Any disagreement between reviewers was discussed by the

full review team until consensus was achieved. The selected articles were evaluated using a standardized predesigned form listing whether the inclusion criteria were met.

A thorough review process was carried out for the data quality assessment, which consisted of the following three steps.

Step 1: Data abstraction
The Cochrane data abstraction form for intervention reviews (RCTs and non-RCTs) was used as a tool to extract data on study design and methodological quality (online supplementary content **Appendix 2**) [18]. Furthermore, data on the target group, main results, main outcome measures, data source, geographical setting and funding sources was abstracted.

Step 2: Rigor of QI intervention
The included studies were evaluated using the Quality Improvement Minimum Quality Criteria Set (QI-MQCS) as a critical appraisal instrument, developed by the RAND Corporation (online supplementary content **Appendix 3**) [19]. The QI-MQCS contains 16 domains to evaluate the QI intervention, resulting in a scoring system to evaluate whether this domain was met or not. The QI-MQSC did not introduce a threshold concerning acceptability of the quality of the papers. Therefore, we agreed on the following criteria in order to adequately interpret the QI-MQSC score. The study was considered to be of perfect quality (>15 items ranked *yes*), good quality (>12 items ranked *yes*), moderate quality (>9 items ranked *yes*) and insufficient quality (≤9 items ranked *yes*).

Step 3: Rigor of data collection and analysis
In addition to the QI-MQCS, 13 items were added for further evaluation. Two questions (item 2 and 18) from the Downs & Black (1998) criteria were used to reflect on whether the main outcomes to be measured had been clearly described in the introduction or methods section and whether the statistical tests used to assess the main outcomes were appropriate [20]. In addition, three questions (item 10c, 11a and 11b) from the SQUIRE guidelines were used: 1) whether a method was employed for assessing completeness and accuracy of data, 2) whether quantitative methods were used to draw inferences from the data and 3) whether methods were applied for understanding variation within the data, including the effects of time as a variable [21]. Furthermore, it was evaluated how the included studies dealt with missing values, whether they performed audits, reported on secular trends, performed case-mix adjustments, whether clear inclusion and exclusion criteria had been defined for the patient population and when possible whether a power analysis was conducted.

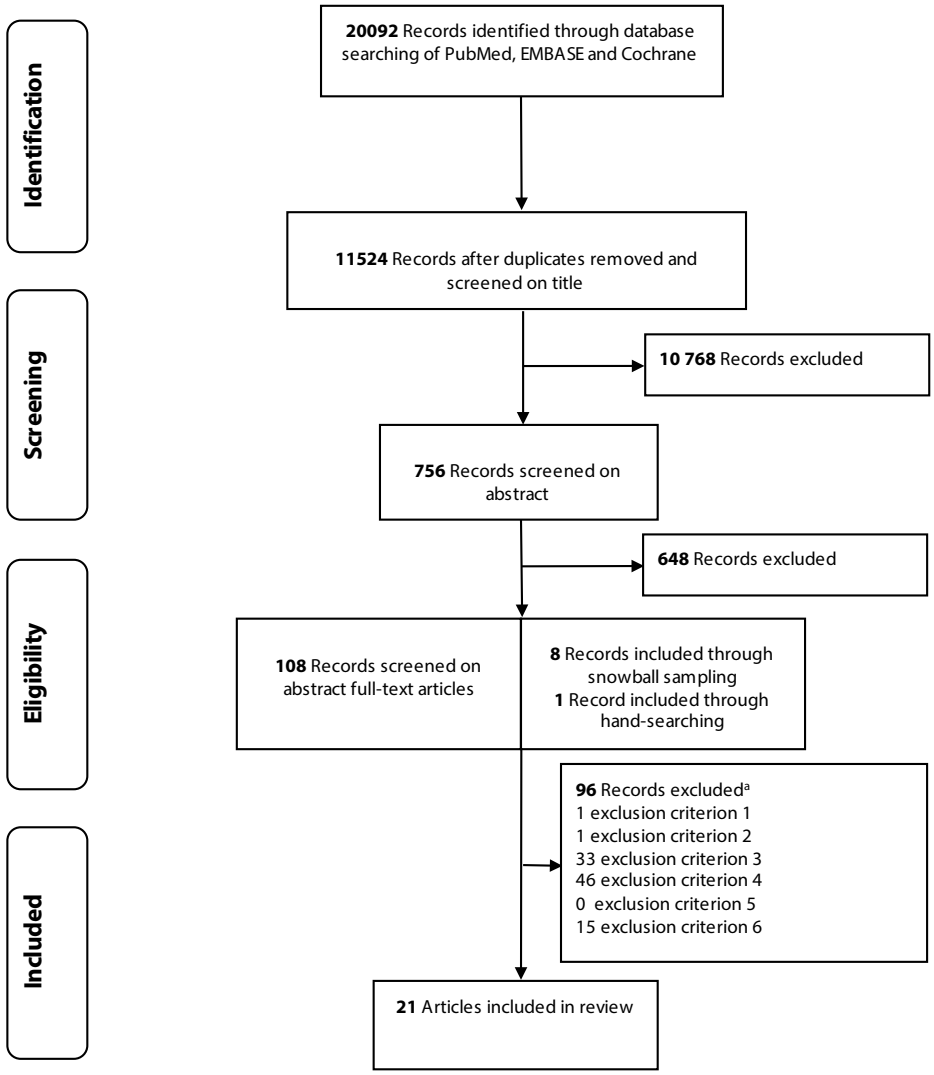
In conclusion, the Cochrane data abstraction form was used to abstract data from the selected articles in order to identify changes in outcomes and facilitators. Data synthesis was guided by 1) the QI-MQCS results, 2) the merged and modified version of the Downs & Black (1998), SQUIRE guidelines, and self-developed questions. Due to the diversity of outcomes, a pooled effect of the results was not conducted.

RESULTS

Search Results and Included Studies

The final systematic search resulted in 11524 records for initial screening; 117 articles were included to review the full text version of which 96 studies were excluded because they did not meet the inclusion criteria (Figure 1) [22]. One additional article was included from a relevant systematic review, which emerged from hand-searching [23,24]. Table 1 presents the characteristics of the 21 included studies. The studies focused on registries for the following patient groups; patients with diabetes [24–31], children with chronic conditions [32], patients with lung cancer [33,34], patients with cystic fibrosis [35–37], patients with cardiac anomalies [38], patients undergoing cardiac surgery [39–41], patients with acute myocardial infarction [42], and patients referred for home health services [43]. The majority of the registries presented voluntary participation [25,26,41–43,27,29–31,35,36,38,40]. Three registries required mandatory participation [28,33,34]. Most of the presented registries had the purpose of achieving QI [24,25,39,41–43,28–34,37]. The remaining studies have introduced their clinical registry for research and educational purposes [26,27,35,36,38,40,44].

Figure 1. Flow diagram



Source: Authors' analysis, format source from PRISMA [22]

Notes: [a] Exclusion criteria: 1. Studies published in peer-reviewed journals; 2. Studies published in English; 3. Did not actively implement a strategy making use of outcome data to realize quality improvement; 3. Did not relay on structural data collection; 5. Did not evaluate quality improvement interventions using data from outcome registries.

Table 1. Characteristics of Included Studies (*n*=21).

Characteristics	No. (%)
Geographical setting	
United States [24,25,39–41,43,44,27–29,31,32,35,37,38]	15 (71%)
Sweden [26,42]	2 (9.5%)
Denmark [33,34]	2 (9.5%)
Germany [36]	1 (4.8%)
Singapore [30]	1 (4.8%)
Target group	
Diabetes [24–31]	8 (38.1%)
Depression [44]	1 (4.8%)
Children with chronic conditions [32]	1 (4.8%)
Lung Cancer [33,34]	2 (9.5%)
Cystic fibrosis [35–37]	3 (14.3%)
Congenital heart disease [38]	1 (4.8%)
Myocardial infarction [42]	1 (4.8%)
Patients undergoing cardiac or cardiothoracic surgery [39–41]	3 (14.3%)
Patients referred for home health services [43]	1 (4.8%)
Study design	
Observational study [29–31,33–37,39,41]	10 (47.6%)
Randomized-Controlled Trial [24,25,27]	3 (14.3%)
Case study [26,28]	2 (9.5%)
Cohort study [38]	1 (4.8%)
Before and after study [32,40,42]	3 (14.3%)
Quasi-experimental study [44]	1 (4.8%)
Prospective evaluation study [43]	1 (4.8%)
Funding sources	
National funding [25,27,28,31,32,36,42,43]	8 (38.1%)
Private funding [24,29,35,37,44]	5 (23.8%)
Unknown [26,30,33,34,38–41]	8 (38.1%)
Registry participation type	
Voluntary [25,26,41–43,27,29–31,35,36,38,40]	13 (62%)
Mandatory [28,33,34]	3 (14.3%)
Unknown [24,32,37,39,44]	5 (23.8%)
Registry purpose	
Quality improvement [24,25,39,41–43,28–34,37]	14 (66.7%)
Research and education [26,27,35,36,38,40,44]	7 (33.3%)
Quality improvement efforts	
Benchmarking [33,34,38–40]	6 (28.6%)
Plan-do-check-act (PDCA) [36]	2 (9.5%)
Collaborative Care Model [26,28,42,44]	4 (19%)
The Chronic Care Model [25,32]	2 (9.5%)
Learning and Leadership Collaborative [35]	1 (4.8%)
Plan-do-check-act (PDCA) and the Chronic Care Model [37]	1 (4.8%)
IT application as feedback tool [24,27,30,41]	4 (19%)
No clear QI method [29,31,43]	3 (14.3%)

Source: Authors' analysis.

Impact of quality improvement

Eight studies showed statistically significant improvement in outcomes resulting from the implementation of QI initiatives [25,27,29,31,33,34,42,44]. Statistically significant improvements were achieved in long-term survival [33,34], mortality [42], readmission rate [42], bleeding complications [42], systolic blood pressure [27], HbA1C [27,29], LDL [27,29], exercise habits [25], depression improved in the acute phase (PHQ-9 score) [44], and hospitalization with ambulatory care-sensitive conditions [31]. The remaining studies did not show statistically significant improvements. All included studies presented outcome measures for their respective improvement work, five of which also measured additional process measures [27,28,45,29–33,35,41,44]. Table 2 presents outcomes measures used, QI methods applied and whether statistically significant improvement of outcome measures was achieved. A detailed overview of the significance of outcome measures can be found in the online supplementary content (**Appendix 4**). None of the studies identified an impact on patient value or evaluated the impact on costs of care.

Quality of the studies

Rigor of quality improvement interventions

The overall quality of included articles was moderate (see Table 3). On the 16 domains of the QI-MQCS four articles achieved a score of 13, which is the highest score among included studies [24,26,32,37]. These articles are therefore considered to be of good quality. Four articles were ranked as moderate quality with a score of 12 [35,39,42,44]. Five articles scored poorly on the QI-MQCS with a score ≤7, which is ranked as low quality [31,33,34,38,41].

Rigor of data collection and analysis

The overall results of the quality assessment on data collection and analyses are displayed in the online supplementary content (**Appendix 5**). Four studies have applied generalized linear mixed models for the analysis of change in outcomes [25,27,36,42]. One study used as generalized estimating equations model with repeated measurements [24]. Inferential statistics have also been used in the form of survival analyses, logistic regression and chi-square analyses [29,31,33,39,44]. The remaining studies made use of descriptive statistical analyses only [26,30,32,38,43]. In order to monitor change run charts have been applied in five studies [28,35,37,40,41].

On the additional item criteria, two studies have applied methods to account for missing values in their data, while also conducting a power analysis [25,27].

Table 2. Improvement in outcomes and/or processes.

Author/year	Outcome measures	Significant improvement +[1]/0[2]/0[a 3]	RAND QI-MQCS score	QI methods	QI focus
Dziuban et al., (1994) [39]	Risk adjusted mortality	0[a]	12	Benchmarking	Hospital-specific and physician-specific results published annually in cardiac surgery.
Adams et al., (1998) [43]	Ambulation/locomotion	0	10	No clear QI method	Implementation of and outcome-based quality improvement concept including two outcome reports.
	Bathing	0			
	Management of oral medications	0			
	Pain	0			
	Dyspnoea	0			
Halpin et al., (2004) [40]	Postoperative Atrial fibrillation	0[a]	11	Benchmarking	Implementation of a new guideline based on insights into outcomes, literature and roundtable discussion. An Outcome Center was formed and a multidisciplinary Performance Improvement Committee.
	Operative mortality	0			
	Cardiac arrest	0			
	Reoperation for bleeding	0			
	Pneumonia	0			
	Deep sternal infection	0			
	Permanent stroke	0			
	Transient stroke	0			
	Prolonged ventilation	0			
	Length of stay	0			
Moller et al., (2005) [38]	Overall operative Mortality	0[a]	7	Benchmarking	Developed a centralized data acquisition and analysis method (through the creation of the network paediatric Cardiac Care Consortium). A uniform diagnostic and procedure classification system was created. Differences in patient populations cared for at the cardiac centres were compared.

Table 2. Continued.

Author/year	Outcome measures	Significant improvement +[1]/0[2]/0[a 3]	RAND QI-MQCS score	QI methods	QI focus
Thomas et al., (2007) [24]	HgbA1c	0	13	IT application as feedback tool	Registry-generated audit, feedback and patient reminder targeted at residents.
	LDL cholesterol	0			
	Blood pressure	0			
Peterson et al., (2008) [27]	Mean systolic blood pressure	+	10	IT application as feedback tool	Multicomponent intervention: implementation of an electronic diabetes registry, visit reminders, and patient-specific physician alerts.
	HbA1c	+			
	Mean LDL	+			
Carlhed et al., (2009) [42]	Mortality	+	12	Collaborative Care Model	Multidisciplinary teams consisted of critical care unit nurses and cardiologists were assigned at each of the 19 volunteering hospitals. 19 teams of 4 to 5 persons met at 4 (group A) or 2 (group B) training sessions during which education by QI experts was provided, using the Breakthrough Series curricula.
	Readmission rate	+			
	Bleeding complication	+			
Jakobsen et al., (2009) [33]	1-year survival	+	5	Benchmarking	Indicators (staging, surgical procedures, complications and survival) have been registered in 5007 patients who underwent surgery. Each year the results have been audited locally, regionally and nationally and improvements have been proposed, implemented, monitored and evaluated by the audit-plenary.
	2-year survival	+			
	5-year survival	0			
	30-day mortality	0[a]			
Kraynack et al., (2009) [35]	FEV1	0[a]	12	Learning and Leadership Collaborative	A QI process is described from the initial team-building phase, through the assessment of care processes, standardization of care, and developing a culture of continuous improvement aiming to improve pulmonary function of the paediatric patients.

Table 2. Continued.

Author/year	Outcome measures	Significant improvement +[1]/0[2]/0[a 3]	RAND QI-MQCS score	QI methods	QI focus
MacLean et al., (2009) [25]	Blood pressure	0	10	The Chronic Care Model	Providing decision support and patient decision support in diabetes care delivery.
	BMI	0			
	SF-12 Physical	0[a]			
	SF-12 Mental	0			
	Quality of life				
	Exercise habit	+			
Toh et al., (2009) [30]	Poor HbA1c (9% and above)	0[a]	11	IT application as feedback tool	Chronic disease management system with patient reminders based on registry data.
	Good LDL-control below 2.6 mmol/L	0[a]			
Baty et al., (2010) [29]	% with HbA1c <7%	+	10	No clear QI method	Implementing a comprehensive system-based disease management process including a diabetes registry and quality reports.
	% with HbA1c <9%	+			
	%with LDL <100	+			
Beaulieau et al., (2010) [41]	Mortality	0[a]	7	Benchmarking IT application as feedback tool	Implementing a method for linking administrative and registry data to track quality improvement initiatives through dashboards.
	Infusion rate	0[a]			
Bricker et al., (2010) [28]	A1C	0[a]	9	Collaborative Care Model	Implementing the Chronic Care Model through regional care learning collaborative with focus on team-based care, patient-centred care coordination, delivery of evidence-based care, patient self-management, use of a patient registry system and culturally and linguistically competent care.
	Blood pressure	0[a]			
	LDL Cholesterol levels	0[a]			

Table 2. Continued.

Author/year	Outcome measures	Significant improvement +[1]/0[2]/0[a 3]	RAND QI-MQCS score	QI methods	QI focus
Bauer et al. (2011) [44]	Depression improved in acute phase (PHQ-9 score)	+	12	Collaborative Care Model	Implementing a collaborative care model including a web-based disease registry, care management to support treatment and organized psychiatric consultation.
Stern et al., (2011) [36]	A1C testing	0	10	Plan-do-check-act (PDCA)	Realizing continuous quality improvement through benchmarking in cystic fibrosis care.
	FEV1 > 80 < 18	0[a]			
	FEV1 >80 >18	0[a]			
	BMI>19	0[a]			
	WH>90	0[a]			
Jakobsen et al., (2013) [34]	1-year survival	+	5	Benchmarking	Indicators were established, validated, and monitored. 40,000 patients have been included in the database. Results were reported periodically and submitted to realize auditing on an annual basis.
	2-year survival	+			
	5-year survival	+			
Siracusa et al., (2014) [37]	Median FEV1	0[a]	13	Plan-do-check-act (PDCA) The Chronic Care Model	Several improvement interventions implemented between 2001 and 2007 with focus on patient and family engagement in CF care, improve access and use of data, individualized scheduling, improving vaccination rates, infection control aiway clearance, standardization of care processes, and forming and QI team.
	Median body mass index (BMI)	0[a]			
Peterson et al., (2015) [26]	Systolic blood pressure	0[a]	13	Plan-do-check-act (PDCA) Collaborative Care Model	The effect of 23 diabetes teams joining a quality collaborative on patient outcomes.
	HbA1c	0[a]			
	LDL	0[a]			

Table 2. Continued.

Author/year	Outcome measures	Significant improvement +[1]/0[2]/0[a 3]	RAND QI-MQCS score	QI methods	QI focus
Han et al. (2016) [31]	Hospitalization with ambulatory care-sensitive conditions	+	7	No clear QI method	Using clinical registry data to identify patients who should receive reminders for preventive/follow-up care and send reminders to those patients. Generate a list of patients by condition to use for quality improvement.
	ED visits	+			
Lail et al., (2017) [32]	Disease remission	0[a]	13	The Chronic Care Model	Eighteen condition teams implemented interventions varying from: establishing pre-visit planning (PVP), identifying the target populations, selecting and measuring outcomes and supporting processes, building and implementing care coordination, and assessing and addressing self-management support. The teams were free to choose the interventions that they thought would work best.
	Disease control	0[a]			
	Quality of life	0[a]			
	Symptom management	0[a]			

[1] + means that the result was statistically significant at a p-value of 0.05.

[2] 0 means that there was no significant improvement in outcomes.

[3] 0[a] means that there was improvement, but significance was not tested or reported.

Table 3-A. Scoring of the RAND QI-MQCS.

	Dziuban et al., (1994) [39]	Adams et al., (1998) [43]	Halpin et al., (2004) [40]	Moller et al., (2005) [38]	Thomas et al., (2007) [24]	Carlhed et al., (2008) [42]	Peterson et al., (2008) [27]	Jakobsen et al., (2009) [33]	MacLean et al., (2009) [25]	Kraynack et al., (2009) [35]
1. Organizational motivation	Y	Y	Y	N	Y	Y	N	N	N	N
2. Intervention rationale	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
3 Intervention description	Y	N	Y	Y	Y	Y	Y	N	Y	Y
4. Organizational characteristics	Y	Y	Y	N	N	Y	N	N	Y	Y
5. Implementation	Y	N	Y	Y	Y	Y	Y	N	Y	Y
6. Study design	Y	Y	N	N	Y	Y	Y	Y	Y	Y
7. Comparator	Y	N	Y	N	Y	Y	Y	N	Y	Y
8. Data source	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Timing	Y	Y	Y	N	Y	Y	Y	N	Y	Y
10. Adherence and fidelity	N	N	Y	N	N	N	N	N	N	Y
11. Health outcomes	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. Organizational readiness	Y	N	Y	N	Y	N	N	N	N	Y
13. Penetration and reach	N	N	N	N	N	Y	Y	Y	Y	N
14. Sustainability	N	Y	N	Y	Y	N	N	N	N	N
15. Spread	N	Y	N	Y	Y	N	N	N	N	Y
16. Limitations	Y	Y	N	N	Y	Y	Y	Y	N	N
Total score (Y)	***12***	***10***	***11***	***7***	***13***	***12***	***10***	***5***	***10***	***12***

Table 3-B. Scoring of the RAND QI-MQCS.

	Bricker et al., (2010) [28]	Beaulieau et al., (2010) [41]	Bauer et al. (2011) [44]	Stern et al., (2011) [36]	Jakobsen et al., (2013) [34]	Siracusa et al., (2014) [37]	Peterson et al., (2015) [26]	Han et al., (2016) [31]	Lail et al., (2017) [32]	Toh et al., (2009) [30]	Baty et al., (2010) [29]
1. Organizational motivation	N	Y	Y	N	N	Y	N	N	Y	Y	Y
2. Intervention rationale	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3 Intervention description	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4. Organizational characteristics	N	N	Y	Y	N	Y	Y	N	N	N	Y
5. Implementation	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y
6. Study design	Y	N	Y	N	N	N	Y	N	N	N	N
7. Comparator	Y	N	Y	Y	N	Y	Y	Y	N	Y	Y
8. Data source	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Timing	Y	N	Y	Y	N	Y	Y	Y	Y	Y	N
10. Adherence and fidelity	N	N	N	N	N	Y	Y	N	Y	N	N
11. Health outcomes	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. Organizational readiness	N	Y	Y	N	N	Y	N	N	Y	Y	Y
13. Penetration and reach	Y	Y	N	N	Y	Y	N	N	Y	N	N
14. Sustainability	Y	N	N	Y	N	Y	Y	N	Y	N	N
15. Spread	N	N	N	Y	N	N	Y	N	Y	Y	N
16. Limitations	N	N	Y	N	N	N	Y	Y	Y	Y	Y
Total score (Y)	***9***	***7***	***12***	***10***	***5***	***13***	***13***	***7***	***13***	***11***	***10***

Notes: Based on the Quality Improvement Minimum Quality Criteria Set (QI-MQCS) developed by the RAND Corporation [19].

Methods used to achieve improvements

We identified six methods to achieve QI: benchmarking [33,34,38–41], a collaborative care model [26,42,44], Plan-Do-Check-Act [36], the Chronic Care Model [25,28,32,37], Learning and Leadership Collaborative [35] and IT driven interventions [24,27,29–31]. There were some studies where no clear QI method was used [29,31,43]. We will discuss these methods in the following paragraphs.

Benchmarking

Benchmarking has been applied in several of the included studies [33,34,38,39,41]. Data was mostly compared among different hospitals [33,34,38]. Annual publication of data in the form of reports has most commonly been applied to report on results [33,34,41]. One study complemented their national report with an additional disease specific report with supplementary measures [33]. Another method of benchmarking used was a discussion of the results at a (monthly or annual) meeting [28,38,40,41]. During the annual meeting, results from reports were discussed and further evaluated [38]. Also, short-term feedback cycles with monthly publication of reports were applied [39]. The use of a strong data-driven system in combination with audits was characteristic of initiatives that applied benchmarking in order to improve outcomes as well as a model to change practice [33,34,39,40].

Collaborative Care Model

Three studies applied the Breakthrough Collaborative Model (BCM) to structure the goal of improving outcomes [26,28,42]. One study applied a Web-based disease registry to track patients with symptoms of depression to support treatment management in primary care [44]. In addition, evidence-based depression management training was provided to primary care providers. Moreover, in all sites, most patients experienced meaningful improvement in depression.

The BCM was used to design a cycle of structured discussion sessions during which outcomes were analyzed, presented and variation in work processes were discussed [26,28]. The model was furthermore used as a guide to facilitate improvement efforts and insights into data [26,42].

Plan-Do-Check-Act

In two studies Plan-Do-Check-Act (PDCA) cycles were used to improve outcomes and/or processes [26,36,37]. Yet, the cycle was presented as a supporting tool to other methods, either for the application of the BCM [26] or for benchmarking [36]. For the latter it was applied as a method to prepare for national benchmarking by organizing three PDCA

cycles before data was shared [36]. The method was applied by organizing multidisciplinary meetings, where outcomes were discussed and improvement initiatives were identified [36]. Three cycles were organized in order to prepare public benchmarking after the third cycle [36].

The other study, which primarily used the methods outlined for the BCM, used the PDCA to structure and evaluate the learning sessions [26]. However, it was not the primary method for improving outcomes. In another study PDCA was used to continually evaluate local cystic fibrosis care practices, and they were able to improve pulmonary function and nutritional outcomes [37].

The Chronic Care Model

Three studies applied the Chronic Care Model (CCM) [25,28,32,37]. One study that applied the CCM used supporting techniques such as: audit and feedback, electronic registry, clinician reminders, patient reminders, and abbreviated patient education. It is, thus, rather a framework offering practical tools [25]. They did not find expected improvements in outcomes. Here, authors suggested that another, more collaborative approach would be needed to improve outcomes of chronic diseases [25]. The second study applied the CCM in children with various chronic conditions, in combination with PDCA cycles, failure mode and effect analysis and Pareto charts of failures [32]. This study resulted in improvement of respective outcomes [32]. The third study applied the CCM to ensure that all aspects of cystic fibrosis management were covered, and combined this with the PDCA to continually evaluate the processes of best practices in cystic fibrosis care. They did not evaluate the effectiveness of applying the CCM.

Learning and Leadership Collaborative

The Learning and Leadership Collaborative (LLC) was applied in one study [35]. Commitment of a team to participate in a QI program, developing a sense of common responsibility as an organization for the improvement, measuring outcomes and processes and patient involvement were defined as key ingredients for QI. LLC has been used for training staff towards structured discussions on outcomes and/or processes and the introduction of a patient registry [35]. Data was registered and analyzed at one particular hospital, but presented to all participating hospitals. Participation in the LLC has led to the initiation of an improvement initiative at the hospital where the data were registered and analyzed.

IT application as feedback tool

Five studies made used of (self-developed) IT applications, to empower patients and/or physicians to manage patients with greater care. The studies aimed at linking administrative

and key clinical data and made use of reminder functions [24,27,30]. One study concluded their patients received better overall coordination of care [30]. Another two studies reported significant improvements in the percentage of type 2 diabetic patients and at-risk populations utilizing diabetes registries achieving recommended values for SBP, LDL, and HbA1C [27]. In one study, data were in addition displayed in operating room theatre, surgical office suites and nursing units [41]. Another study reported improved adherence to diabetes care processes in a continuity clinic due to the registry-generated audit, feedback, and patient reminders [24].

Facilitators for quality improvements

A noticeable facilitator leading to QI was frequent reporting and feedback either annually or even monthly [28,33,34,38–41]. The use of a database with high quality data, audits and reports as well as a strong stakeholder involvement were also found to be important factors contributing to successful QI [33,34]. Structured registry data and an improvement intervention that can be linked to outcomes led to improvement in respective outcome measures [42]. In addition, other factors mentioned that would be needed for successful QI in one or more of the included studies are (1) patient involvement, communication, and standardization; (2) attitude and enthusiastic commitment from physician leadership, clinical managers and central administration and (3) appreciation concerning the importance of measurements [28,35,40,41]. Moreover, improvement in outcomes appeared to be successful if supported by a proven QI approach [42]. Inconsistencies were found regarding the importance of involving an expert in the field of QI. On the one hand, involvement of a QI expert was considered positive for the start of an improvement agenda as it contributed to a more rapid implementation of improvement initiatives [42]. On the other hand, involving no additional expert or formal team was not experienced as a contributing factor to the success of outcome improvement [26]. This was only possible because a structured data registry was already present [26].

Catalyst to improve outcomes over time

Outcomes can be improved over time through systematic use of outcome registries and facilitators. Outcome data and its interpretation helps to achieve improvements in outcomes over time even faster compared to studies that did not use outcome data [34]. It was stated that outcomes were not only used to identify possible improvement interventions but also to monitor and secure improvements in the long run [34].

A computerized system was presented as a success factor to accelerate data from clinical registries to change outcomes and/or processes [24,26,36,42,27–29,31–35]. Such a computerized system ensured valid and timely results [33]. Moreover, it allows for real-time feedback, which, in turn, leads to faster identification of improvement areas [28,29,31,42].

Further use of outcome data for outcome improvement included the development of checklists, improved use of diagnostic standards, creation of data transparency, guidelines, improved patient recall and empowerment and discussions and leadership towards improvement [28,29,31,36].

DISCUSSION

Eight out of the 21 included studies reported statistically significant improvements in outcomes including long-term survival, mortality, readmission rate, bleeding complications, systolic blood pressure, HbA1C, LDL, exercise habits (FEV1), depression improved in the acute phase (PHQ-9 score) and hospitalization with ambulatory care-sensitive conditions resulting from the implementation of QI initiatives. Out of these eight studies, the Chronic Care Model, IT application as feedback, benchmarking and the Collaborative Care Model were used as QI methods. A diverse set of clinical outcomes were collected and no patient-reported outcome measures (PROMs) were applied in any of the studies. Yet, only one study that reported statistically significant improvements in outcomes was of good quality. The improvement interventions were diverse, ranging from the implementation of guidelines, development of physician/patient alerts, improved teamwork, patient engagement methods through IT applications and the development of a supportive decision system. Many improvement interventions were combined in order to build a multifaceted approach to QI [24,27,28,32,37,42,44]. Facilitators for realizing QI include a high quality database, the use of pre-defined outcome measures, audits, frequent reporting and feedback, patient involvement, improved communication and standardization. Systematic approaches were used for structuring the improvement cycle. In order to use data from clinical registries as a catalyst to change outcomes, this review suggests that having a strong computerized system is supportive in aiding frontline clinical process management and improvement work.

A facilitator identified in this review was the organization of discussions for mapping and selecting best practices. It was further shown that a sound data management has a catalyzing effect. This data can be aggregated in annual reports, while it can also be used to compare with peers and/or perform nationwide comparisons. Also, a registry can facilitate access to real-time outcome and process data which can engage the team in realizing active improvements. Other registry programs such as the Get With The Guidelines-Stroke study, a large registry and performance improvement program for hospitalized patients with stroke and transient ischemic attack, also use annual reports for benchmark and feedback purposes [46].

Other systematic reviews concluded that audit and feedback can lead to small but important improvements in professional practice and healthcare outcomes [47]. They furthermore concluded that the effectiveness of audit and feedback depends on how the feedback was provided as well as on baseline performance. In addition, comparing this review to ours, there was one paper we have both included [24]. However, the objectives are very different, which can explain there was not more overlap in included studies.

In addition, barriers and success factors to the effectiveness of feedback have been identified [48]. However, the authors were not able to draw sound conclusions on the effect of feedback on the quality of care and its potential to improve outcomes. Another review concerning renal registry data reflected on the potential of registry data and help advancing the nephrology care delivery [49].

None of the reviews studied the effect of QI efforts, besides from audit and feedback, on the quality of care and outcomes. This is the first study for which the literature was searched in detail in order to identify barriers and facilitators supporting QI interventions based on information from clinical registries.

The use of clinical registries can be seen as an important tool in order to systematically measure clinical outcomes and to achieve the goals of value-based health care. This is not only in line with our conclusions, but also acknowledged by others [1,50,51]. Other data sources can also be valuable for QI efforts, such as data from randomized controlled trials. However, this review aimed at including studies where structural data was collected through the use of a clinical registry.

In order to improve value, measuring both one or more outcomes and costs is essential [50]. Working with international registries makes it possible to make global comparisons, for example identifying practice variations and therefore improving quality of care for the whole patient group [52].

Implications

We did not observe many efforts to incorporate patient reported outcome measure (PROMs). It is, however, generally considered important to measure the impact on health related quality of life (HRQoL) in the evaluation of the effect of QI initiatives [53]. The studies included for this review did not reflect on why they did not use PROMs and what would be the added value if they did. Even so, one study does report however the start of measuring quality of life in patients with cystic fibrosis [36]. The authors report this will lead to more insights into the complexity of QI efforts and personal patient gains in the

experienced quality of life. It will also enable reporting on to what extent value was created from the patient's perspective. Future QI efforts very likely combine QI with benchmarking incorporating quality of life outcomes.

None of the included studies reported costs, causing our study to be unable to evaluate the true impact on value. Incorporating costs will enable to identify cost drivers and comparing improvement interventions as proposed by the value-based healthcare principles [50]. A recent study showed that surgery for the oldest patients with colorectal cancer did not lead to increased hospital costs [51]. However, this study did identify variation in cost driver distribution. Patients under 85 years old had lower costs looking at the ward, operation and intensive care unit. Therefore, identifying costs and its main drivers will enable to develop improvement programs for specific sub-groups. This might be a powerful tool to reduce e.g. complications and thus hospital costs. Value-based health care could be the overarching concept guiding improvement initiatives, combined with the well-defined methods. However, the field lacks a clear guide on implementation examples. Studies reflecting on impact, outcomes and costs are needed. Finally, the standardization of outcome measures is key, although they should be defined for a specific patient population. Transparent measurement of outcomes and costs has the potential to improving the value of care for all patients. Both providers, patients and payers can benefit from this collective common goal of transparency.

Limitations

This review has some inherent limitations. Firstly, due to the very heterogeneous types of QI programs and their respective patient groups, it is difficult to generalize the results achieved in the included studies. Moreover, our inclusion criteria for QI programs may be to some extent arbitrary, which could possibly lead to a bias in inclusion or exclusion of studies.

Also, the context in which the clinical registry is organized can impact outcomes. Moreover, important differences were observed in e.g. whether the registry was linked to reimbursement or public reporting versus primarily initiated for scientific or QI purposes or whether it was a voluntary or mandatory registry.

Secondly, the studies included in this review mainly focused on experiences in non-communicable diseases and thus often chronic patient groups. However, our aim was not to exclude communicable diseases from the study but we did not identify any studies in our literature search. This could indicate that chronic patient groups benefitted most from the realization of registries and respective QI interventions. As a result, improvement

projects concerning other (non-chronic) patient groups have not been included in this review. Thirdly, due to publication bias, studies reporting no effect will be very likely not published and therefore missed out. Finally, two studies randomized practices [25,27]. One study randomly allocated 19 volunteering hospitals to 1 of 2 intervention groups, where the intervention differed both in design and intensity [42]. In the other studies it should be noted that complete randomization was not possible, since the intervention hospitals involved were e.g. volunteering. Therefore, these hospitals might differ in their willingness to improve, causing potential selection bias.

CONCLUSION

The results from this evaluation of studies which use outcome measures from clinical registry data to implement and monitor QI initiatives may help policy makers, managers and clinicians to understand the effectiveness, practicality and challenges of implementing QI interventions. An active and systematic approach is needed to improve outcomes. Continuous feedback from the data linked to clinical practice is crucial. Our review indicates that successful QI and consequently improved outcomes, is dependent on an active approach and organizational readiness.

There are many QI methods, and the majority of improvement interventions contain a combination of several methods. Clinical registries can be seen as supportive instruments in the process of improving quality of care. However, a clinical registry can only be successful in realizing QI efforts when there is commitment and leadership at both the physician and manager level, as well as a benchmarking facility, a well-integrated computerized system, and a collective aim to identify best practices.

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APPENDICES

Appendix 1. Search string PubMed, Embase and Cochrane.

PubMed

("Mortality"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR "Treatment Outcome"[Mesh] OR mortality[tiab] OR patient outcome*[tiab] OR patient reported outcome*[tiab] OR patient relevant outcome*[tiab] OR treatment outcome*[tiab] OR clinical outcome*[tiab] OR "outcome of care"[tiab] OR "outcomes of care"[tiab]) AND ("quality improvement registry" [tiab] OR "quality improvement registries" [tiab] OR "quality improvement register" [tiab] OR "quality registry" [tiab] OR "quality registries" [tiab] OR "quality register" [tiab] OR "device registry" [tiab] OR "device registries"[tiab] OR "device register" [tiab] OR "pregnancy registry" [tiab] OR "pregnancy registries" [tiab] OR "pregnancy register" [tiab] OR "disease registry"[tiab] OR "disease registries"[tiab] OR "disease register"[tiab] OR "medical registry"[tiab] OR "medical registries"[tiab] OR "medical register"[tiab] OR "patient registry"[tiab] OR "patient registries" [tiab] OR "patient register" [tiab] OR "clinical registry"[tiab] OR "clinical registries"[tiab] OR "clinical register"[tiab] OR "clinical data registry"[tiab] OR "clinical data registries"[tiab] OR "clinical data register"[tiab] OR "outcome registry"[tiab] OR "outcome registries"[tiab] OR "outcome register"[tiab] OR "outcomes registry"[tiab] OR "outcomes registries"[tiab] OR "outcomes register"[tiab] OR "cardiac registry"[tiab] OR "cardiac registries"[tiab] OR "cardiac register"[tiab] OR "cardiovascular registry"[tiab] OR "cardiovascular registries"[tiab] OR "cardiovascular register"[tiab] OR "stroke registry"[tiab] OR "stroke registries"[tiab] OR "stroke register"[tiab] OR "cancer registry"[tiab] OR "cancer registries"[tiab] OR "cancer register"[tiab] OR "diabetes registry"[tiab] OR "diabetes registries"[tiab] OR "diabetes register"[tiab] OR "chronic disease registry" [tiab] OR "chronic disease registries"[tiab] OR "chronic disease register"[tiab] OR "rare disease registry"[tiab] OR "rare disease registries"[tiab] OR "rare disease register" [tiab] OR "paediatric registry"[tiab] OR "pediactric registries"[tiab] OR "paediatric register"[tiab] OR "psychiatric registry"[tiab] OR "psychiatric registries"[tiab] OR "psychiatric register"[tiab] OR "respiratory tract registry"[tiab] OR "respiratory tract registries"[tiab] OR "respiratory tract register"[tiab] OR "anesthesia registry"[tiab] OR "anesthesia registries"[tiab] OR "anesthesia register"[tiab] OR "intensive care registry"[tiab] OR "intensive care registries"[tiab] OR "intensive care register"[tiab] OR "circulation registry"[tiab] OR "circulation registries"[tiab] OR "circulation register"[tiab] OR "musculoskeletal registry"[tiab] OR "musculoskeletal registries"[tiab] OR "musculoskeletal register"[tiab] OR "orthopaedic registry"[tiab] OR "orthopaedic registries"[tiab] OR "orthopaedic register"[tiab] OR "rehabilitation registry"[tiab] OR "rehabilitation registries"[tiab] OR "rehabilitation register"[tiab] OR "rheumatology registry"[tiab] OR "rheumatology registries"[tiab] OR "rheumatology

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Embase

('mortality'/exp OR 'treatment outcome'/de OR mortality:ab,ti OR ((patient OR 'patient reported' OR 'patient relevant' OR 'clinical' OR 'treatment') NEXT/1 outcome*):ab,ti) OR 'outcome of care'/de AND ('quality improvement registry' OR 'quality improvement registries' OR 'quality improvement register' OR 'device registry' OR 'device registries' OR 'device register' OR 'pregnancy registry' OR 'pregnancy registries' OR 'pregnancy register' OR 'disease registry' OR 'disease registries' OR 'disease register' OR 'patient registry' OR 'patient registries' OR 'patient register' OR 'medical registry' OR 'medical registries' OR 'medical register' OR 'clinical registry' OR 'clinical registries' OR 'clinical register' OR 'clinical data registry' OR 'clinical data registries' OR 'clinical data register' OR 'outcome registry' OR 'outcome registries' OR 'outcome register' OR 'outcomes registry' OR 'outcomes registries' OR 'outcomes register' OR 'cardiac registry' OR 'cardiac registries' OR 'cardiac register' OR 'cardiovascular registry' OR 'cardiovascular registries' OR 'cardiovascular register' OR 'stroke registry' OR 'stroke registries' OR 'stroke register' OR 'cancer registry' OR 'cancer registries' OR 'cancer register' OR 'diabetes registry' OR 'diabetes registries' OR 'diabetes register' OR 'chronic disease registry' OR 'chronic disease registries' OR 'chronic disease register' OR 'rare disease registry' OR 'rare disease registries' OR 'rare disease register' OR 'paediatric registry' OR 'pediactric registries' OR 'paediatric register' OR 'psychiatric registry' OR 'psychiatric registries' OR 'psychiatric register' OR 'respiratory tract registry' OR 'respiratory tract registries' OR 'respiratory tract register' OR 'anesthesia registry' OR 'anesthesia registries' OR 'anesthesia register' OR 'intensive care registry' OR 'intensive care registries' OR

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Cochrane Library

(mortality OR patient outcome* OR patient reported outcome* OR patient relevant outcome* OR treatment outcome*):ab,ti AND ("quality improvement registry" OR "quality improvement registries" OR "quality improvement register" OR "device registry" OR "device registries" OR "device register" OR "pregnancy registry" OR "pregnancy registries" OR "pregnancy register" OR "disease registry" OR "disease registries" OR "disease register" OR "patient registry" OR "patient registries" OR "patient register" OR "clinical registry" OR "clinical registries" OR "clinical register" OR "clinical data registry" OR "clinical data registries" OR "clinical data register" OR "outcome registry" OR "outcome registries" OR "outcome register" OR "outcomes registry" OR "outcomes registries" OR "outcomes register" OR "cardiac registry" OR "cardiac registries" OR "cardiac register" OR "cardiovascular registry" OR "cardiovascular registries" OR "cardiovascular register" OR "stroke registry" OR "stroke registries" OR "stroke register" OR "cancer registry" OR "cancer registries" OR "cancer register" OR "diabetes registry" OR "diabetes registries" OR "diabetes register" OR "chronic disease registry" OR "chronic disease registries" OR "chronic disease register" OR "rare disease registry" OR "rare disease registries" OR "rare disease register" OR "paediatric registry" OR "pediactric registries" OR "paediatric register" OR "psychiatric registry" OR "psychiatric registries" OR "psychiatric register" OR "respiratory tract registry" OR "respiratory tract registries" OR "respiratory tract register"

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Appendix 2. Eligibility Form Data collection form for intervention reviews: RCTs and non-RCTs.

Data collection form for intervention reviews: RCTs and non-RCTs
Version 1, may 2016

This form can be used as a guide for developing your own data extraction form. Sections can be expanded and added, and irrelevant sections can be removed. It is difficult to design a single form that meets the needs of all reviews, so it is important to consider carefully the information you need to collect, and design your form accordingly. Information included on this form should be comprehensive, and may be used in the text of your review, 'Characteristics of included studies' table, risk of bias assessment, and statistical analysis. Using this form, or an adaptation of it, will help you to meet MECIR standards for collecting and reporting information about studies for your review, and analysing their results (see MECIR standards C43 to C55; R41 to R45).

Notes on using data extraction form:

- Be consistent in the order and style you use to describe the information for each report.
- Record any missing information as unclear or not described, to make it clear that the information was not found in the study report(s), not that you forgot to extract it.
- Include any instructions and decision rules on the data collection form, or in an accompanying document. It is important to practice using the form and give training to any other authors using the form.

Title of the article/article/report	
Study ID *(surname of first author and year first full report of study was published e.g. Smith 2001)*	
Report ID of other reports of this study including errata or retractions	
Notes	

1. General Information

1.1 Date form completed *(dd/mm/yyyy)*	
1.2 Name/ID of person extracting data	
1.3 Reference citation	
1.4 Study author contact details	
1.5 Publication type and Journal *(e.g. full report, abstract, letter)*	
Notes:	

2. Characteristics of included studies

2.1 Methods

	Descriptions as stated in report/ paper	**Location in text or source** *(pg & ¶/fig/table/other)*
2.1.1 Aim of study *(e.g. efficacy, equivalence, pragmatic)*		
2.1.2 Design *(e.g. parallel, crossover, non-RCT)*		
2.1.3 Allocation of comparison *(by individuals, cluster/ groups or body parts)*		
2.1.4 Start date		
2.1.5 End date		
2.1.6 Duration of participation *(from recruitment to last follow-up)*		
2.1.7 Ethical approval needed/ obtained for study	☐ Yes ☐ No ☐ Unclear	
Notes:		

3.2 Participants

	Description *Include comparative information for each intervention or comparison group if available*	**Location in text or source** *(pg & ¶/fig/table/other)*
3.2.1 Population description *(from which study participants are drawn)*		
3.2.2 Setting *(including location and social context)*		
3.2.3 Inclusion criteria		
3.2.4 Exclusion criteria		
3.2.5 Method of recruitment of participants *(e.g. phone, mail, clinic patients)*		
3.2.6 Informed consent obtained	☐ Yes ☐ No ☐ Unclear	

3.2 Continued

	Description *Include comparative information for each intervention or comparison group if available*	**Location in text or source** *(pg & ¶/fig/table/other)*
3.2.7 Total no. of pop. at start of study for NRCTs		
3.2.8 Clusters *(if applicable, no., type, no. people per cluster)*		
3.2.9 Baseline imbalances		
3.2.10 Age		
3.2.11 Sex		
3.2.12 Race/Ethnicity		
3.2.13 Severity of illness		
3.2.14 Co-morbidities		
3.2.15 Other relevant sociodemographics		
3.2.16 Subgroups measure		
3.2.17 Subgroups reported		
Notes:		

3.3 Intervention groups

Copy and paste table for each intervention and comparison group

Intervention Group 1

	Description as stated in report/ paper	**Location in text or source** *(pg & ¶/fig/table/other)*
3.3.1 Group name		
3.3.2 No. randomised to group *(specify whether no. people or clusters)*		
3.3.3 Theoretical basis *(include key references)*		
3.3.4 Description *(include sufficient detail for replication, e.g. content, dose, components)*		

3.3 Continued

	Description as stated in report/ paper	**Location in text or source** *(pg & ¶/fig/table/other)*
3.3.5 Duration of treatment period		
3.3.6 Timing *(e.g. frequency, duration of each episode)*		
3.3.7 Delivery *(e.g. mechanism, medium, intensity, fidelity)*		
3.3.8 Providers *(e.g. no., profession, training, ethnicity etc. if relevant)*		
3.3.9 Co-interventions		
3.3.10 Economic information *(i.e. intervention cost, changes in other costs as result of intervention)*		
3.3.11 Resource requirements *(e.g. staff numbers, cold chain, equipment)*		
3.3.12 Integrity of delivery		
Compliance		
Notes:		

3.4 Outcomes

Copy and paste table for each outcome.

Outcome 1

	Description as stated in report/ paper	**Location in text or source** *(pg & ¶/fig/table/other)*
3.4.1 Outcome name		
3.4.2 Time points measured *(specify whether from start or end of intervention)*		
3.4.3 Time points reported		
3.4.4 Outcome definition *(with diagnostic criteria if relevant)*		

3.4 Continued

	Description as stated in report/ paper	**Location in text or source** *(pg & ¶/fig/table/other)*
3.4.5 Person measuring/ reporting		
3.4.6 Unit of measurement *(if relevant)*		
3.4.7 Scales: upper and lower limits *(indicate whether high or low score is good)*		
Notes:		

3.5 Other

3.5.1 Study funding sources *(including role of funders)*		
3.5.2 Possible conflicts of interest *(for study authors)*		
Notes:		

5. Data and analysis

Copy and paste the appropriate table for each outcome, including additional tables for each time point and subgroup as required.

a. For RCT/CCT

Dichotomous outcome

	Description as stated in report/paper				**Location in text or source** *(pg & ¶/ fig/table/other)*
5.1a Comparison					
5.2a Outcome					
5.3a Subgroup					
5.4a Time point *(specify from start or end of intervention)*					
5.5a Results	Intervention		Comparison		
	No. with event	Total in group	No. with event	Total in group	

a. Continued

	Description as stated in report/paper		**Location in text or source** *(pg & ¶/ fig/table/other)*
5.6a Any other results reported *(e.g. odds ratio, risk difference, CI or P value)*			
5.7a No. missing participants			
5.8a Reasons missing			
5.9a No. participants moved from other group			
5.10a Reasons moved			
5.11a Unit of analysis *(by individuals, cluster/ groups or body parts)*			
5.12a Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*			
5.13a Reanalysis required? *(specify, e.g. correlation adjustment)*	☐ Yes ☐ No ☐ Unclear		
5.14a Reanalysis possible?	☐ Yes ☐ No ☐ Unclear		
5.15a Reanalysed results			
Notes:			

b. For RCT/CCT

Continuous outcome

	Description as stated in report/paper	**Location in text or source** *(pg & ¶/fig/table/other)*
5.1b Comparison		
5.2b Outcome		
5.3b Subgroup		
5.4b Time point *(specify from start or end of intervention)*		

b. Continued

		Description as stated in report/paper					Location in text or source *(pg & ¶/fig/table/other)*
5.5b Post-intervention or change from baseline?							
5.6b Results	Intervention			Comparison			
	Mean	SD *(or other variance, specify)*	No. participants	Mean	SD *(or other variance, specify)*	No. participants	
5.7b Any other results reported *(e.g. mean difference, CI, P value)*							
5.8b No. missing participants							
5.9b Reasons missing							
5.10b No. participants moved from other group							
5.11b Reasons moved							
5.12b Unit of analysis *(individuals, cluster/ groups or body parts)*							
5.13b Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*							
5.14b Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear						
5.15b Reanalysis possible?	☐ Yes ☐ No ☐ Unclear						
5.16b Reanalysed results							
Notes:							

c. For RCT/CCT

Other outcome

	Description as stated in report/paper				**Location in text or source** *(pg & ¶/fig/ table/other)*
5.1c Comparison					
5.2c Outcome					
5.3c Subgroup					
5.3c Time point *(specify from start or end of intervention)*					
5.4c No. participant	Intervention		Control		
5.5c Results	Intervention result	SE (or other variance)	Control result	SE (or other variance)	
	Overall results		SE (or other variance)		
5.6c Any other results reported					
5.7c No. missing participants					
5.8c Reasons missing					
5.9c No. participants moved from other group					
5.10c Reasons moved					
5.11c Unit of analysis *(by individuals, cluster/ groups or body parts)*					
5.12c Statistical methods used and appropriateness of these					
5.13c Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear				
5.14c Reanalysis possible?	☐ Yes ☐ No ☐ Unclear				
5.15c Reanalysed results					
Notes:					

d. For Controlled Before-and-After study (CBA)

	Description as stated in report/paper				**Location in text or source** *(pg & ¶/fig/table/other)*
5.1d Comparison					
5.2d Outcome					
5.3d Subgroup					
5.4d Time point *(specify from start or end of intervention)*					
5.5d Post-intervention or change from baseline?					
5.6d No. participants	Intervention		Control		
5.7d Results	Intervention result	SE *(or other variance, specify)*	Control result	SE *(or other variance, specify)*	
	Overall results		SE *(or other variance, specify)*		
5.8d Any other results reported					
5.9d No. missing participants					
5.10d Reasons missing					
5.11d No. participants moved from other group					
5.12d Reasons moved					
5.13d Unit of analysis *(individuals, cluster/groups or body parts)*					
5.14d Statistical methods used and appropriateness of these					
5.15d Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear				
5.16d Reanalysis possible?	☐ Yes ☐ No ☐ Unclear				
5.17d Reanalysed results					
Notes:					

e. For Interrupted Time Series study (ITS)

	Description as stated in report/paper				**Location in text or source** *(pg & ¶/fig/table/other)*
5.1e Comparison					
5.2e Outcome					
5.3e Subgroup					
5.4e Length of time points measured *(e.g. days, months)*					
5.5e Total period measured					
5.6e No. participants measured					
5.7e No. missing participants					
5.8e Reasons missing					
	Pre-intervention		Post-intervention		
5.9e No. time points measured					
5.10e Mean value *(with variance measure)*					
5.11e Any other results reported					
5.12e Unit of analysis *(individuals or cluster/ groups)*					
5.13e Statistical methods used and appropriateness of these					
5.14e Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear				
5.15e Reanalysis possible?	☐ Yes ☐ No ☐ Unclear				
Individual time point results					
5.16e Read from figure?	☐ Yes ☐ No				
5.17e Reanalysed results	Change in level	SE	Change in slope	SE	
Notes:					

6. Other information

	Description as stated in report/paper	**Location in text or source** *(pg & ¶/fig/table/ other)*
6.1 Key conclusions of study authors		
6.2 References to other relevant studies		
6.3 Correspondence required for further study information *(from whom, what and when)*		
Notes:		

7. Definitions

Assumed risk estimate	An estimate of the risk of an event or average score without the intervention, used in Cochrane 'Summary of findings tables'. If a study provides useful estimates of the risk or average score of different subgroups of the population, or an estimate based on a representative observational study, you may wish to collect this information.
Bias	A systematic error or deviation in results or inferences from the truth. In studies of the effects of health care, the main types of bias arise from systematic differences in the groups that are compared (selection bias), the care that is provided, exposure to other factors apart from the intervention of interest (performance bias), withdrawals or exclusions of people entered into a study (attrition bias) or how outcomes are assessed (detection bias). Reviews of studies may also be particularly affected by reporting bias, where a biased subset of all the relevant data is available.
Change from baseline	A measure for a continuous outcome calculated as the difference between the baseline score and the post-intervention score.
Clusters	A group of participants who have been allocated to the same intervention arm together, as in a cluster-randomised trial, e.g. a whole family, town, school or patients in a clinic may be allocated to the same intervention rather than separately allocating each individual to different arms.
Co-morbidities	The presence of one or more diseases or conditions other than those of primary interest. In a study looking at treatment for one disease or condition, some of the individuals may have other diseases or conditions that could affect their outcomes.

7. Continued

Assumed risk estimate	An estimate of the risk of an event or average score without the intervention, used in Cochrane 'Summary of findings tables'. If a study provides useful estimates of the risk or average score of different subgroups of the population, or an estimate based on a representative observational study, you may wish to collect this information.
Compliance	Participant behaviour that abides by the recommendations of a doctor, other health care provider or study investigator (also called adherence or concordance).
Contemporaneous data collection	When data are collected at the same point(s) in time or covering the same time period for each intervention arm in a study (that is, historical data are not used as a comparison).
Controlled Before and After Study (CBA)	A non-randomised study design where a control population of similar characteristics and performance as the intervention group is identified. Data are collected before and after the intervention in both the control and intervention groups
Exclusions	Participants who were excluded from the study or the analysis by the investigators.
Imputation	Assuming a value for a measure where the true value is not available (e.g. assuming last observation carried forward for missing participants).
Integrity of delivery	The degree to which the specified procedures or components of an intervention are delivered as originally planned.
Interrupted Time Series (ITS)	A research design that collects observations at multiple time points before and after an intervention (interruption). The design attempts to detect whether the intervention has had an effect significantly greater than the underlying trend.
Post-intervention	The value of an outcome measured at some time point following the beginning of the intervention (may be during or after the intervention period).
Power	In clinical trials, power is the probability that a trial will obtain a statistically significant result when the true intervention effect is a specified size. For a given size of effect, studies with more participants have greater power. Note that power should not be considered in the risk of bias assessment.
Providers	The person or people responsible for delivering an intervention and related care, who may or may not require specific qualifications (e.g. doctors, physiotherapists) or training.

7. Continued

Assumed risk estimate	An estimate of the risk of an event or average score without the intervention, used in Cochrane 'Summary of findings tables'. If a study provides useful estimates of the risk or average score of different subgroups of the population, or an estimate based on a representative observational study, you may wish to collect this information.
Quasi-randomised controlled trial	A study in which the method of allocating people to intervention arms was not random, but was intended to produce similar groups when used to allocate participants. Quasi-random methods include: allocation by the person's date of birth, by the day of the week or month of the year, by a person's medical record number, or just allocating every alternate person.
Reanalysis	Additional analysis of a study's results by a review author (e.g. to introduce adjustment for correlation that was not done by the study authors).
Report ID	A unique ID code given to a publication or other report of a study by the review author (e.g. first author's name and year of publication). If a study has more than one report (e.g. multiple publications or additional unpublished data) a separate Report ID can be allocated to each to help review authors keep track of the source of extracted data.
Sociodemographics	Social and demographic information about a study or its participants, including economic and cultural information, location, age, gender, ethnicity, etc.
Study ID	A unique ID code given to an included or excluded study by the review author (e.g. first author's name and year of publication from the main report of the study). Although a study may have multiple reports or references, it should have one single Study ID to help review authors keep track of all the different sources of information for a study.
Theoretical basis	The use of a particular theory (such as theories of human behaviour change) to design the components and implementation of an intervention
Unit of allocation	The unit allocated to an intervention arm. In most studies individual participants will be allocated, but in others it may be individual body parts (e.g. different teeth or joints may be allocated separately) or clusters of multiple people.
Unit of analysis	The unit used to calculate N in an analysis, and for which the result is reported. This may be the number of individual people, or the number of body parts or clusters of people in the study.

7. Continued

Assumed risk estimate	An estimate of the risk of an event or average score without the intervention, used in Cochrane 'Summary of findings tables'. If a study provides useful estimates of the risk or average score of different subgroups of the population, or an estimate based on a representative observational study, you may wish to collect this information.
Unit of measurement	The unit in which an outcome is measured, e.g. height may be measured in cm or inches; depression may be measured using points on a particular scale.
Validation	A process to test and establish that a particular measurement tool or scale is a good measure of that outcome.
Withdrawals	Participants who voluntarily withdrew from participation in a study before the completion of outcome measurement.

Sources:

Cochrane Collaboration Glossary, 2010. Available from www.cochrane.org/glossary.

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Last JM (editor), A Dictionary of Epidemiology, 4th Ed. New York: Oxford University Press, 2001.

Schünemann H, Brożek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendation. Version 3.2 [updated March 2009]. The GRADE Working Group, 2009.

Appendix 3. Quality Improvement Minimum Quality Criteria Set (QI-MQCS) items.

Items	Yes/No
1 Organisational motivation assesses whether the motivational context of the organisation in which the intervention was introduced was described; for example to convey whether a given quality problem—such as shortcomings in quality of care indicators—was being addressed.	
2 Intervention rationale assesses whether a rationale was given that suggests why the intervention may produce improvements in the outcome (empirical evidence, theories or logic models). **NOTE:** - Quality improvement processes can be the intervention	
3 Intervention description (change in organizational or provider behaviour) requires a detailed description of the change in the structure or organisation of healthcare, including personnel involved. QI interventions are diverse and may address changes in care processes (eg, use of care managers) or strategies aiming to change provider behaviour (eg, electronicreminders), and the content (eg, avoiding catheterrelated blood stream infections), and the means to achieve the goal (eg, audit and feedback) are often intertwined. We restricted the definition to permanent structural or organisational changes, not temporary activities aiming to develop or introduce the change.	
4 Organisational characteristics assesses whether key demographics of the setting are described to provide information that enables readers to assess the generalizability to their organisation. **NOTE:** - describing e.g. the number of patients out of XX county wide or number of clinics out of the XX clinics nationwide. - Factors which are key/central for that particular population are described.	
5 Implementation addresses temporary activities used to introduce the permanent change, for example, staff education to introduce a new care protocol. The QI-MQCS focuses here on the introduction of the intervention into clinical practice, not its development.	
6 Study design assesses whether the evaluation design to determine whether the intervention was successful was identified. Acknowledging that different questions require different study designs, the quality emphasis is on outlining the evaluation approach, not on specific designs or features (eg, randomisation).	
7 Comparator assesses the control condition to which the intervention is compared, for example, routine care before the intervention was introduced. We added this item, most prominently described in the Workgroup for Intervention Development and Evaluation Research (WIDER) criteria, in response to TEP discussions and empirical evidence. Given that healthcare contexts are continually evolving, it is important to know whether the comparison group comprised current 'state-of-the-art' or poor quality care	

Appendix 3. Continued.

Items	Yes/No
8 Data source considers how data were obtained for the evaluation and whether the primary outcome was defined; conveying what exactly was measured should avoid a 'false implicit understanding' of terms and definitions and is independent from the study design selected for the evaluation.	
9 Timing addresses the clarity of the timeline in relation to the evaluation of the intervention, for example, when a complex change was fully implemented and when evaluated, in order to determine the follow-up period.	
10 Adherence/fidelity addresses compliance with the intervention. QI interventions can be introduced with enthusiasm, but whether personnel actually adhere to them (eg, a new assessment tool) in busy routine clinical practice is another matter. Readers need to be able to judge whether any intervention failure was attributable to the intervention itself, suboptimal translation in clinical practice, or a combination of both. Any information on adherence (including the lack thereof) is acknowledged in assessing this domain.	
11 Health outcomes considers whether patient health outcomes are part of the evaluation. Although an intervention may result in changes in healthcare processes (eg, tests ordered), they may not necessarily improve patient outcomes. The QI-MQCS acknowledges studies that assess this crucial patient-centered question.	
12 Organisational readiness refers to the QI culture and resources present in the organisation, which helps to assess the transferability of results.	
13 penetration/reach assesses what proportion of eligible units participated. This domain requires a denominator; stating the number of participating sites without also reporting how many sites were initially approached or were eligible is not sufficient.	
14 sustainability addresses whether information on the sustainability of the intervention is available; including positive evidence (eg, an extended intervention period) or acknowledgment that the intervention may be maintained only with additional resources.	
15 spread addresses the ability of the intervention to be spread to or replicated in other settings. The minimum quality standard is met if the potential or unsuccessful attempts at spread or positive evidence of spread (eg, large-scale rollouts) are presented.	
16 limitations refers to disclosed limitations of the evaluation of the intervention.	

From: Hempel, Susanne, Paul G. Shekelle, Jodi L. Liu, Margie Sherwood Danz, Robbie Foy, Yee-Wei Lim, Aneesa Motala, and Lisa V. Rubenstein. Development of the Quality Improvement Minimum Quality Criteria Set (QI-MQCS): a tool for critical appraisal of quality improvement intervention publications. *BMJ quality & safety* (2015): bmjqs-2014.

Appendix 4. Detailed Summary of Included Studies.

Source	Design	Aim	Target group	Main results	Data source
Peterson et al., (2015) [26]	Case study design	To study how quality improvement collaboration (QIC) can impact clinical practice and outcomes for patients with diabetes mellitus.	Diabetes care delivery/ patients	QIC helped teams to improve patient outcomes compared to national average for systolic blood pressure, and low density lipoprotein levels.	National Diabetes Register (NDR)
Jakobsen et al., (2009) [33]	Observational study	To study how to improve the quality of care through quality measures.	Lung cancer patients	Overall 1- and 2-year survival improved: 69% and 50% in year 2000 to 77% and 60% in 2005, respectively (p = 0.001 and 0.004, respectively). 30-day mortality after surgery decreased from 5.2% (2000) to 3.6% (2007). Patients having surgery within 14 days from referral increased from 69% (2000) to 83% (2007).	Danish lung cancer registry
Peterson et al., (2008) [27]	Group-RCT	To determine if the implementation of a multicomponent organizational intervention can impact diabetes care and outcomes in community primary care practices.	Diabetes	Diabetes process measures increased significantly more in intervention than in control practices: foot examinations 35.0% (p < 0.0.001); annual eye examinations 25.9% (p < 0.001); renal testing 28.5% (p < 0.001); A1C testing 8.1%(p < 0.001); blood pressure monitoring 3.5% (P = 0.05); and LDL testing 8.6% (p < 0.001). Mean A1C (adjusted for sex, age and comorbidity) decreased significantly in intervention practices (p < 0.02). At 12 months, intervention practices had significantly greater improvements in achieving recommended values for SBP, A1C, and LDL than control clinics (p = 0.002).	-

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
MacLean et al., (2009) [25]	RCT	To evaluate the impact of a registry and decision support system on physiologic results & control and process of care.	Diabetes care delivery/ patients	Intervention subjects were significantly more likely to receive guideline-appropriate testing for cholesterol (OR = 1.39; [95%CI 1.07, 1.80] p = 0.012), creatinine (OR = 1.40; [95%CI 1.06, 1.84] p = 0.018), and proteinuria (OR = 1.74; [95%CI 1.13, 1.69] p = 0.012), but not A1C (OR = 1.17; [95% CI 0.80, 1.72] p = 0.43). Rates of control of A1C and LDL cholesterol were similar in the two groups. No differences in blood pressure, body mass index, or functional status were observed.	Vermont Diabetes Information System (VCIS)
Beaulieau et al., (2010) [41]	Observational study	To develop a registry database linking administrative data to provide information of institution's performance.	Patients undergoing cardiothoracic surgery (CABG and/or valve repair or replacement)	Through continuous feedback reduced transfusion rate by more than three standard deviations in the operative setting.	Clinical registry entered by a senior cardiovascular perfusionist linking with administrative data
Bricker et al., (2010) [28]	Case study	To implement the Chronic Care Model and provide coaching, monthly measurement and patient registry support in order to improve performance.	Diabetes	Outcome measures as hemoglobin A1C, blood pressure and LDL cholesterol improved slowly over the years. Process improvements took place at a greater rate.	Electronic medical record system or an electronic patient registry
Bauer et al., (2011) [44]	Quasi-experimental study	To analyze the role of site on specific process measures of depression treatment and on clinical outcomes by implementing a model of collaborative care	Patients having symptoms of depression between 2006 and 2009	Among patients with who had valid PHQ-9 scores between six and 12 weeks the probability of discontinuing treatment differed significantly across clinics, as did the probability of improvement (range 0.36-0.84). Patients with early follow-up were more likely to improve (OR=1.64, p<0.01).	Web-based disease registry

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
Stern et al., (2011) [36]	Observational study	To study how to realize continuous quality improvement through benchmarking.	Cystic fibrosis	A statistically significant correlation was found between the presence of Pseudomonas aeruginosa and reduced FEV1 (mean FEV1 98.9 vs. 87.3% in children and adolescents, 72.2 vs. 56.4% in adults, $p = 0.001$).	German Cystic Fibrosis Quality Assurance (CFQA)
Jakobsen et al., (2013) [34]	observational study	To describe the methods used by DLCG and DLCR and the results obtained through this work. Also, to discuss possibilities how to improve the quality of lung cancer care through monitoring quality indicators.	All patients diagnosed in Denmark with primary lung cancer included in DLCR since Jan 1, 2000 through Dec 31, 2012	One-year survival increased from 36.6% to 42.7%, 2-year survival has increased from 19.8% to 24.3%, 5-year survival from 9.8% to 12.1%.	Danish Lung Cancer Registry (DLCR)
Halpin et al., (2004) [40]	Before-after study design	To describe how an interdisciplinary committee of health professionals led to a 50% reduction in the incidence of postoperative AF from 2000 to 2002.	All patients having CABG and valve replacement/ repair from January 1, 2000 to June 30, 2002	The incidence of postoperative atrial fibrillation for a CABG or valve replacement procedure decreased from 19% to 13.5%. Clinical pathway variances in length of stay secondary to atrial fibrillation decreased from 8.5% to 5.6%, which translates into a 1-2-day reduction in expected length of stay.	The STS National Adult Cardiac Surgery Database
Møller et al., (2005) [38]	Registry-based cohort study	To develop and create methods for analysis and comparisons of pediatric-aged patients undergoing cardiac catherization and cardiac operation.	Pediatric-aged patients undergoing cardiac catherization and cardiac operation.	Annual meetings of the participating hospitals were held. Mortality for the centers has decreased from 12% (1982) to 6% (2001). Center volume did not affect survival. The data has been used to develop a consensus based method for risk adjustment.	The registry developed by the PCCC

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
Adams et al., (1998) [43]	Prospective evaluation study	To determine if the outcome-based quality improvement model enhanced outcomes for health maintenance organization patients who receive care under contracted home health agencies.	Health maintenance organization patients referred for home health services who receive care from contracted home health agencies between April 29, 1996 and September 14, 1997.	The percentage of patients who improved between baseline and quarter four was not statistically significant. The percentages of stabilized patients on oral medications and on dyspnea were statistically significant greater at quarter four compared to baseline.	The Outcome Assessment and Information Set (OASIS)
Dziuban et al., (1994) [39]	Report	To describe experiences of a New York State (NYS) cardiac surgery program. Methods by which staff used outcome data to discover meaningful information and program changes were studied	Cardiac surgery patients from in New York State the Department of Health (DOH) and specifically patients undergoing a CABG procedure	Improvements resulted from a process of debating and searching and resulted in increased collaboration and sense of shared staff responsibility Number deaths were reported in 1993 compared to 1992 and 1991 in patients undergoing emergency CABG procedure. Risk-adjusted mortality decreased compared to the public DOH data (3.7% in 1990, 6.6% in 1992, and 5.8% in 1992) 1.8% in 1993. Thus, internal results for 1993 indicate that overall actual mortality was about half of the 1992 data.	DOH data from New York State

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
Kraynack et al., (2009) [35]	Observational study	To describe the process of gradual application of quality improvement methodology over 5 years by pediatric providers, at the Lewis Walker Cystic Fibrosis Center at Akron Children's Hospital in Akron, Ohio.	Patient visiting CF clinic between the age of 6 to 18 years (for trial and later for all patients over the age of 6)	A 5.9% relative increase in median FEV1 in the pilot of the pulmonary exacerbation score (PES). Since standardization of PES median FEV1 has continued to improve in the 6-18 year old population.	The cystic fibrosis (CF) registry through the cystic fibrosis foundation (CFF)
Carlhed et al., (2009) [42]	Before-after study design	To study a combination of a real-time, interactive feedback generating national quality registry and a systematic quality improvement collaborative on realizing clinical improvements.	Clinical Outcome After Acute Myocardial Infarction	In the QUICC hospitals 2.8 lives per 100 patient years (14.2 to 11.4) and 9.3 readmissions for cardiac diagnoses per 100 patient years (49.5 to 40.2) were saved after comparing to before the QI intervention, corresponding to a 20% and 19% relative decrease in incidence.	RIKS-HIA
Thomas et al., (2007) [24]	Randomized controlled trial	To implement registry-generated audit, feedback and patient reminders into an Internal Medicine (IM) resident continuity clinic and to assess the effect on process and intermediate outcomes	Diabetes	Clinical outcomes including HgbA1c, LDL cholesterol and blood pressure did not improve in the intervention group compared to the control group.	Clinical information systems, automatically queried clinical databases and reported summaries without manual effort

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
Lail et al., (2017) [32]	Before-after study design	To help disease-based teams use the principles of improvement science and implement components of the CCM. To improve care for children with chronic and complex conditions.	Children with chronic conditions.	50% of included patients had the desired or an improved outcome. 25% had improvement in disease remission higher than expected, 3% improvement higher than expected in disease control, 21% improvement higher than expected in quality of life, 20% improvement higher than expected in symptom management. Eleven of the 18 participating teams achieved the goal of 20% improvement in their chosen outcome.	Electronic health record of the Cincinnati Children's Hospital Medical
Baty et al., (2010) [29]	Observational study	To study whether the application of a successful system-based approach making use of a computerized patient registry could reduce disparity in care for cultural, ethnic and socioeconomic minorities	Diabetes	Every tracked indicator improved except HbA1c control > 9%. Mean outcomes in diabetes quality measures ranged from +22% improvement in the percent of patients with HbA1c below 7% to +400% mean improvement in the percent of patients who had a retinopathy screen in the past year.	Expanded patient registry used at Advantage Health physician offices (CDEMS)
Toh et al., (2009) [30]	Report	To facilitate continuity of care for patients with chronic diseases and for greater efficiency in outcome management.	Diabetes	There was a gradual reduction of patients with poor HbA1c (9% and above) in primary care clinic patients from 12% to 9% and an increase in the proportion of patients with good LDL-c control from 35.5% to 52.0%. At the hospitals a similar trend in LDL-c control was observed, but the proportion of patients with poor HbA1c remained the same.	Chronic disease management registry

Appendix 4. Continued.

Source	Design	Aim	Target group	Main results	Data source
Siracusa et al., (2014) [37]	Report	To improve clinical outcomes (FEV1 and BMI) for patients with CF through quality improvement aimed at increasing patient centeredness and improving healthcare delivery	Patients with cystic fibrosis age 0-21	Median FEV1 increased from 81.7% to 100.1% with an absolute improvement of 18.4% predicted. BMI improved from the 35th centile to the 55th centile, which was a 1.7-fold improvement.	The Cystic Fibrosis Foundation National Patient Registry
Han et al., (2016) [40]	Observational study	To examine the impact of using a registry for patient reminders is associated with differences in quality of care and hospital utilization rates	Diabetes	Patients with type 2 diabetes trated in practices using registries for patient reminders were more likely to have completed the recommended laboratory testing (OR=1.26, p<0.01) and dilated retinal examinations (OR=1.14, p<0.01). Patients in practices with registries for quality improvement were less likely to have avoidable hospitalization (OR=9.83, p<0.01) and emergency room visits (OR=0.76, p<0.01). There was no effect of the use of a diabetes registry on quality of care for patients with type 1 diabetes	Data obtained from electronic health record system and claims data

Appendix 5a. Scoring of the Downs & Black criteria, SQUIRE guidelines and additional self-developed tool.

	Stern et al., (2011) [36]	**Peterson et al., (2015) [26]**	**Peterson et al., (2008) [27]**	**Adams et al., (1998) [43]**	**Halpin et al., (2004) [40]**	**Moller et al., (2005) [38]**	**Thomas et al., (2007) [24]**	**MacLean et al., (2009) [25]**	**Kraynack & MacBride, (2009) [35]**	**Beaulieau et al., (2010) [41]**
Downs & Black criteria [a]										
Have the main outcomes to be measured been clearly described in the introduction or methods section? (2)	N	Y	Y	N	Y	Y	Y	Y	Y	N
Were the statistical tests used to assess the main outcomes appropriate? (18)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Total score (Y)	**0**	**2**	**2**	**1**	**2**	**2**	**2**	**2**	**2**	**1**
Squire Guideline [b]										
Was a method employed for assessing completeness and accuracy of data? (10c)	Y	N	N	N	N	N	N	N	N	Y
Were quantitative methods used to draw inferences from the data?* (11a)	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Were methods applied for understanding variation within the data, including the effects of time as a variable? (11b)	N	N	N	N	N	N	N	N	N	N
Total score (Y)	**2**	**1**	**0**	**1**	1	**1**	1	**1**	1	**2**
Self-developed Checklist										
Has a method been applied for handling missing values?*Remarks: What is the threshold that was applied?	N	N	Y	N	N	N	N	Y	N	N
Has an audit / data check been performed? *Remarks: Sanity checks on logical correlations between variables? Outliers? Etc.	N	N	N	N	N	N	N	N	N	Y

Appendix 5a. Continued.

	Stern et al., (2011) [36]	Peterson et al., (2015) [26]	Peterson et al., (2008) [27]	Adams et al., (1998) [43]	Halpin et al., (2004) [40]	Moller et al., (2005) [38]	Thomas et al., (2007) [24]	MacLean et al., (2009) [25]	Kraynack & MacBride, (2009) [35]	Beaulieau et al., (2010) [41]
	Self-developed Checklist									
Do the researchers discuss secular trends (trends in data due to improvements in health care over time independent to the study)?	N	Y	N	N	N	N	N	N	N	N
Do the researchers discuss the impact of other changes/QI processes within the hospital potentially interfering with outcomes?	N	Y	N	N	N	N	N	N	N	N
Have outcomes in the analysis been adjusted for case mix? Remarks: If not, is it discussed why? Etc.	N	N	Y	Y	N	Y	N	Y	N	N
Are definitions given for the main outcomes (or references to those definitions)?	Y	Y	Y	N	Y	Y	Y	N	Y	N
Is the patient group/ target group of the registry described?*Remarks: Are clear definitions given including inclusions and exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Has a power analysis been conducted?	N	N	Y	N	N	N	Y	Y	N	N
Total score (Y)	**2**	**4**	**5**	**2**	***2***	**3**	**3**	**4**	**2**	**2**

[a] From the Downs & Black questionnaire, question 2 and 18 have been used [20].
[b] From the SQUIRE guidelines, question 10c,11a and 11b have been used [21].

Appendix 5b. Scoring of the Downs & Black criteria, SQUIRE guidelines and additional self-developed tool.

	Bricker et al., (2010) [28]	**Jakobsen et al., (2013) [34]**	**Jakobsen et al., (2009) [33]**	**Dziuban et al., (1994) [39]**	**Carlhed et al., (2008) [42]**	**Han et al., (2016) [31]**	**Baty et al., (2010) [29]**	**Bauer et al., (2011) [44]**	**Siracusa et al., (2014) [37]**	**Lail et al., (2017) [32]**	**Toh et al., (2009) [30]**
						Downs & Black criteria [a]					
Have the main outcomes to be measured been clearly described in the introduction or methods section? (2)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the statistical tests used to assess the main outcomes appropriate? (18)	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N
Total score (Y)	**1**	1	**2**	**2**	**2**	**2**	**2**	**2**	1	**2**	1
						Squire Guideline [b]					
Was a method employed for assessing completeness and accuracy of data? (10c)	N	Y	N	Y	Y	N	N	N	N	N	N
Were quantitative methods used to draw inferences from the data?* (11a)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Were methods applied for understanding variation within the data, including the effects of time as a variable? (11b)	N	N	N	Y	Y	N	N	Y	N	N	N
Total score (Y)	**1**	**2**	**1**	**3**	**3**	1	**1**	3	2	**1**	**0**

Appendix 5b. Continued.

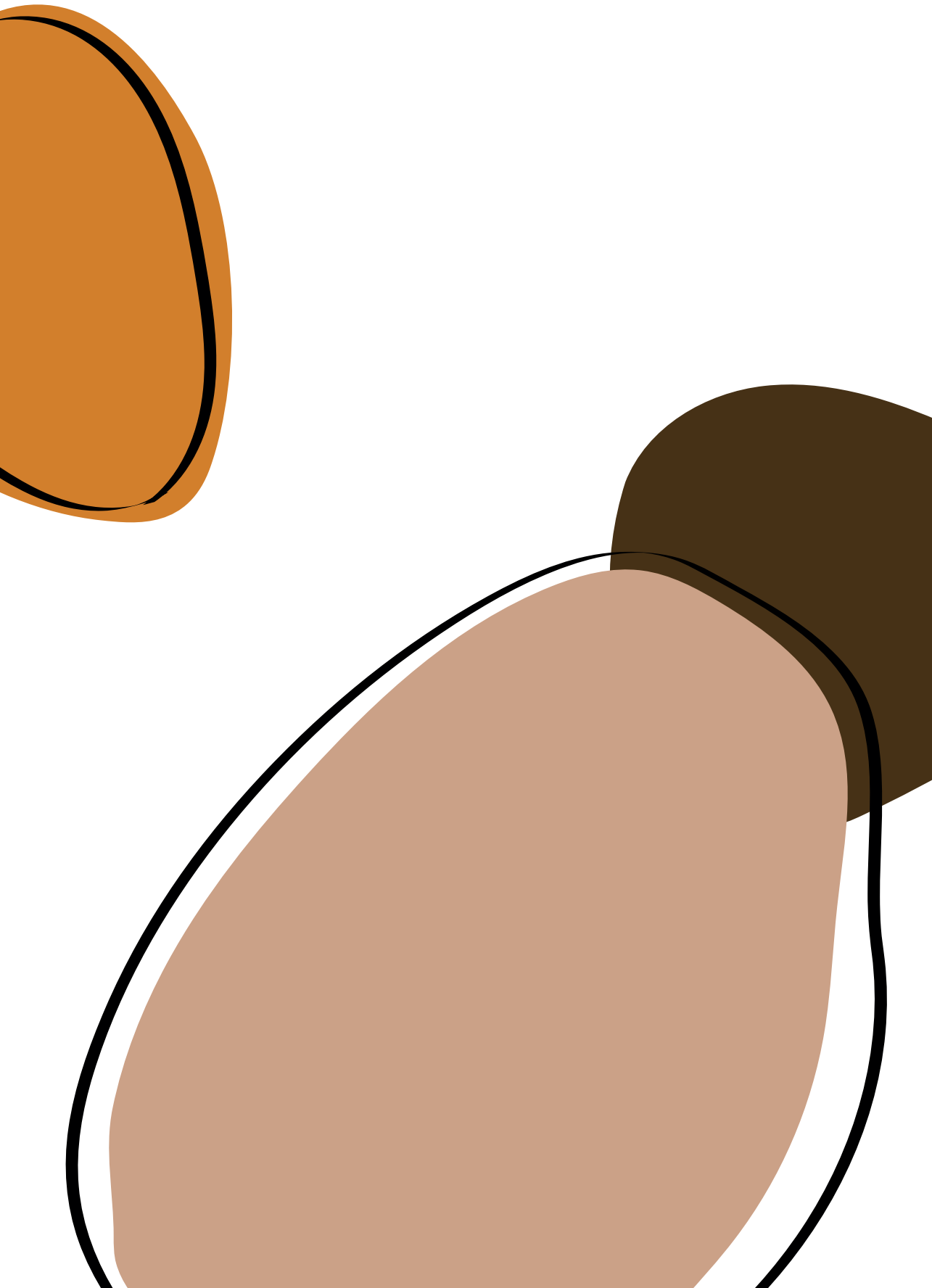
	Bricker et al., (2010) [28]	Jakobsen et al., (2013) [34]	Jakobsen et al., (2009) [33]	Dziuban et al., (1994) [39]	Carlhed et al., (2008) [42]	Han et al., (2016) [31]	Baty et al., (2010) [29]	Bauer et al., (2011) [44]	Siracusa et al., (2014) [37]	Lail et al., (2017) [32]	Toh et al., (2009) [30]
	Self-developed Checklist										
Has a method been applied for handling missing values?*Remarks: What is the threshold that was applied?	N	N	N	N	N	N	N	N	N	N	N
Has an audit / data check been performed? *Remarks: Sanity checks on logical correlations between variables? Outliers? Etc.	N	Y	N	N	Y	N	N	N	N	N	N
Do the researchers discuss secular trends (trends in data due to improvements in health care over time independent to the study)?	N	N	Y	N	Y	N	N	N	N	N	N
Do the researchers discuss the impact of other changes/QI processes within the hospital potentially interfering with outcomes?	N	N	N	N	Y	N	N	N	N	N	Y
Have outcomes in the analysis been adjusted for case mix? Remarks: If not, is it discussed why? Etc.	N	N	N	N	Y	Y	N	Y	N	N	N

Appendix 5b. Continued.

	Bricker et al., (2010) [28]	**Jakobsen et al., (2013) [34]**	**Jakobsen et al., (2009) [33]**	**Dziuban et al., (1994) [39]**	**Carlhed et al., (2008) [42]**	**Han et al., (2016) [31]**	**Baty et al., (2010) [29]**	**Bauer et al., (2011) [44]**	**Siracusa et al., (2014) [37]**	**Lail et al., (2017) [32]**	**Toh et al., (2009) [30]**
						Self-developed Checklist					
Are definitions given for the main outcomes (or references to those definitions)?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Is the patient group/target group of the registry described?*Remarks: Are clear definitions given including inclusions and exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Has a power analysis been conducted?	N	N	N	N	N	N	N	N	N	N	N
Total score (Y)	**1**	3	**3**	**3**	**6**	**3**	**2**	**3**	2	2	3

[a] From the Downs & Black questionnaire, question 2 and 18 have been used [20].

[b] From the SQUIRE guidelines, question 10c,11a and 11b have been used [21]



3

Selecting interventions to improve patient-relevant outcomes in health care for aortic valve disease – The intervention selection toolbox

Nina Zipfel
Stef Groenewoud
Benno Rensing
Edgar Daeter
Lea Dijksman
Jan-Henk Dambrink
Philip van der Wees
Gert Westert
Paul van der Nat

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ABSTRACT

Background: Measuring and improving outcomes is a central element of value-based health care. However, selecting improvement interventions based on outcome measures is complex and tools to support the selection process are lacking. The goal was to present strategies for the systematic identification and selection of improvement interventions applied to the case of aortic valve disease and to combine various methods of process and outcome assessment into one integrated approach for quality improvement.

Methods: For this case study a concept-driven mixed-method approach was applied for the identification of improvement intervention clusters including: (1) benchmarking outcomes, (2) data exploration, (3) care delivery process analysis, and (4) monitoring of ongoing improvements. The main outcome measures were long-term survival and 30-day mortality. For the selection of an improvement intervention, the causal relations between the potential improvement interventions and outcome measures were quantified followed by a team selection based on consensus from a multidisciplinary team of professionals.

Results: The study resulted in a toolbox: the Intervention Selection Toolbox (IST). The toolbox comprises two phases: (a) identifying potential for improvement, and (b) selecting an effective intervention from the four clusters expected to lead to the desired improvement in outcomes. The improvements identified for the case of aortic valve disease with impact on long-term survival in the context of the studied hospital in 2015 include: anticoagulation policy, increased attention to nutritional status of patients and determining frailty of patients before the treatment decision.

Conclusions: Identifying potential for improvement and carefully selecting improvement interventions based on (clinical) outcome data demands a multifaceted approach. Our toolbox integrates both care delivery process analyses and outcome analyses. The toolbox is recommended for use in hospital care for the selection of high-impact improvement interventions.

BACKGROUND

The importance of improving outcomes in health care has widely been recognized [1–5], while the improvement of quality in health care is a science in itself [6]. Closely linked is the science of outcome research, which has been accepted in research as a "foundation of knowledge about what constitutes ideal care and what gaps exist between ideal and actual care" [7]. Measuring and improving outcomes is a central element of value-based health care (VBHC) [8]. However, selecting improvement interventions based on outcome measures is complex and tools to support the selection process are lacking. Improvement interventions are interventions or tools that change processes leading to improved quality of care [9,10]. For the purpose of this study, improvement interventions may concern any deliberate action aimed at achieving positive change in outcomes through structure and/or process interventions.

Value-based health care aims at achieving higher value for patients relative to the costs [11]. In order to achieve a value-based system, care delivery should be organized around health conditions. The care delivery value chain (CDVC) describes activities that add value for patients and can be used to analyze processes to maximize this value for patients. In the CDVC, value of a single activity can only be understood by considering the full cycle of care and thus the relation to other care delivery activities [12].

In the literature several quality improvement models are presented [13–16]. For example, the "Implementation of Change Model" for achieving change in a systematic manner [13]. They identified a seven-step plan to successfully implement change for improving the quality of health care delivery [17]. However, this model lacks a focus on outcome measures as a basis for the identification of improvement initiatives. Furthermore, the literature suggests "a clinical value compass" as a method to select an improvement intervention, which measures on the following four domains: (1) functional status, risk status, and well-being, (2) costs, (3) satisfaction with health care and perceived benefit, and (4) clinical outcomes [14]. This method lacks a step for identifying improvement potential. Another possible method for the identification of an improvement intervention could be the plan-do-study-act (PDSA) model [15]. The PDSA model focuses on processes of care delivery in order to achieve improvement and change. However, it does not offer clear tools on how to identify and select a focus for improvement. A different approach for improving quality of care is benchmarking. Benchmarking is the process of identifying so-called "best practices", which are the highest excellence standards [18]. Benchmarking means identifying good practices as a result of comparisons with other organizations that lead to better patient-relevant outcomes [19]. Benchmarking can take place on different levels,

for example as performance comparisons, process comparisons, or strategic comparisons [18]. Another method described to change processes of care in order to improve the quality of care is "Lean thinking", which puts process evaluation central, and focuses on reducing waste and synchronizing work flows to combat and manage variability in work flow [16]. Six Sigma has been introduced along with Lean in order to improve the organizational structure through improvement projects while making use of the several steps [16]. It lacks outcome measures and focuses merely on structure indicators. All these models use different approaches or cycles for continuous quality improvement. However, all of them lack an explicit focus on patient-relevant outcome measures when designing an improvement intervention.

This paper integrates the identification and selection of improvement interventions, the focus on patient-relevant outcomes, and underlying care delivery processes into a single coherent approach. The primary aim is to develop a toolbox for selecting improvement interventions that positively influence health outcomes in the right direction. The secondary aim is to apply this toolbox to aortic valve disease. For this aim we used outcome data from the clinical outcome registry of the Dutch national initiative Measurably Better (MB). MB is an initiative in the Netherlands that aims to improve quality and transparency of care for patients with heart diseases using patient-relevant outcome measures [20]. In 2017, MB merged with the national registries for cardiology and thoracic surgery forming the Netherlands Heart Registry [21]. MB offers the infrastructure to construct a case for the development and application of a toolbox.

The overall goal is to provide health care professionals with a tool that fills the existing gap between measuring and improving patient-relevant health outcomes.

METHODS

Case study setting

We chose a single case-study design. We then purposefully selected a nested single case in order to understand strategies on how to identify and select improvement initiatives based on the VBHC concept [22]. MB was selected, because it offered the needed infrastructure. The setting of the case study was a Dutch non-academic teaching hospital with a high volume cardiac intervention center. The focus of the case is aortic valve disease with a specific focus on two treatment modalities: Surgical Aortic Valve Replacement (SAVR) and Transcatheter Aortic Valve Replacement (TAVR). The analysis was conducted by means of chronological description. A non-medical scientific research declaration was obtained from

the Medical Research Ethics Committees United (MEC-U) of the St. Antonius Hospital with the following reference number: W15.006.

Methodological approach: Concept-driven mixed-method approach

This paper describes a strategy including four steps for (A) the identification of improvement potential, and two steps for (B) the selection of improvement interventions. Figure 1 presents a flow chart of all methodological steps and their goals. A multidisciplinary team, led by a project team consisting of researchers (N=2), was involved to collect expert opinions from all stakeholders in the care delivery process for aortic valve disease. The multidisciplinary team was formed in June 2015 and consisted of cardiologists (N=2), cardiothoracic surgeons (N=2), nurses (N=2), anaesthesiologists (N=2), a data manager (N=1) and researchers (N=2) of the St. Antonius Hospital in the Netherlands. Verbal consent to participate in the multidisciplinary team was obtained before participation.

A: Identification of improvement potential

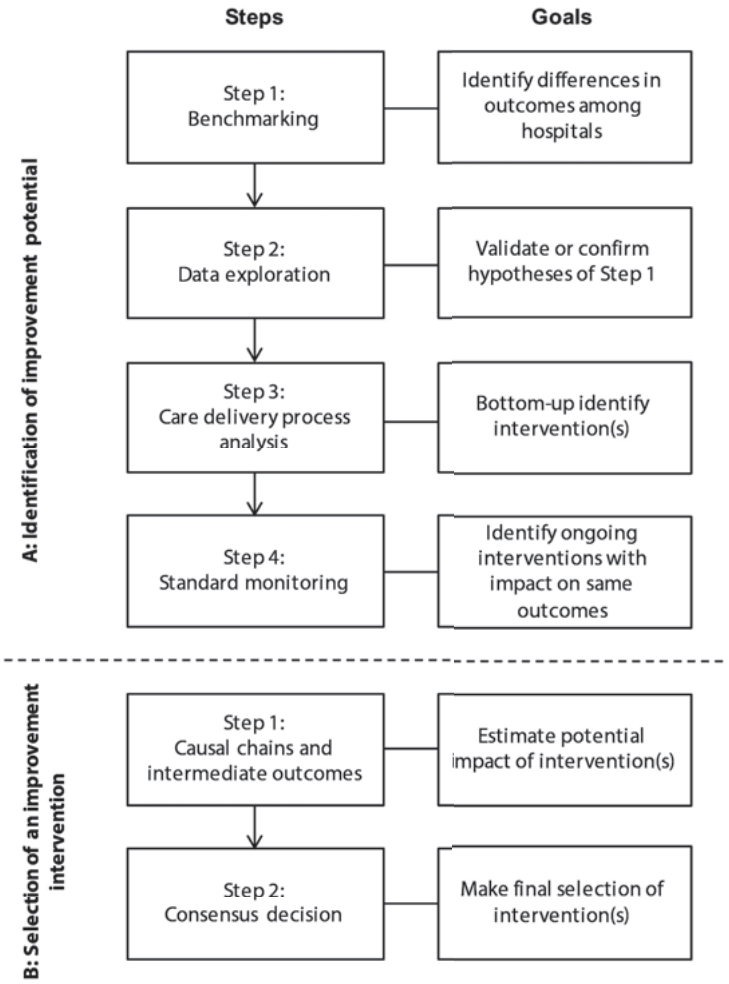
The identification of potential for improvement consisted of four steps: benchmarking, data exploration, care delivery process analysis and monitoring. The four steps are described chronologically.

Step 1: Benchmarking

In the first step, called "benchmarking", we conducted a systematic analysis to identify meaningful differences in patient-relevant outcomes among hospitals. In general, benchmarking includes the following steps: identification of outcomes to be benchmarked, establish organization to benchmark with, collect data, analyse for differences, determine future trends and reveal results. For our analyses we used the annual report of MB, including outcome data of 19 Dutch heart centers [23]. The outcome measures that were used are long-term survival, 120-day mortality, 30-day mortality (only TAVR), Quality of Life, cerebrovascular accident (CVA), deep sternal wound infection (only SAVR), implantation of a new permanent pacemaker, vascular complications (only TAVR) and freedom of valve re-intervention [21,23,24]. For detailed definitions see **Appendix 1**.

The multidisciplinary team discussed the outcome measures indicated by the measurements to have a below average performance or a negative (absolute or relative) trend over time of the primary hospital. The team decided whether differences observed in outcomes were clinically relevant and subsequently formulated hypotheses for the probable causes of these differences.

Figure 1. Flowchart of methodological mixed-method approach.



Flowchart of methodological mixed-method approach for (A) the identification of improvement potential and (B) selection of an improvement intervention describing the goals of each step.

Step 2: Data exploration

Data exploration is a method to understand data and their characteristics. For this step, we performed data analyses to validate or confirm the hypotheses of Step 1. In addition, further analyses were performed to identify subgroups of the total patient population with higher risks of negative outcomes. To be able to perform these analyses, five hospitals from MB provided patient-level data over the period from 2010 to 2014 [21]. We tested these hypotheses with univariable and multivariable logistic regression and applied these methods to identify significant predictors of 30-day mortality. The goal was to

explain possible causes of differences in long-term mortality by giving more insights into differences between the 30-day mortality of the primary hospital and other MB hospitals. We conducted an additional Cox-regression analysis for insights into the 30-day survival. All analyses were conducted with IBM SPSS statistics 22 [25]. We further complemented this step with literature research in order to find possible improvement interventions fitting the risk groups identified. Literature was searched based on search terms resulting from the data analyses including risks, patient-relevant outcomes, processes and mortality.

Step 3: Care delivery process analysis
In the third step we conducted a CDVC analysis for aortic valve disease (Appendix 2). In this analysis, the care process was laid out describing all processes for the full cycle of care of a disease. Following, the care processes were prioritized by the multidisciplinary team. The aim of this step was two-fold: to identify specific interventions that could possibly improve the patient-relevant outcomes and to gather additional bottom-up identification of improvement interventions. The multidisciplinary team used a scoring tool based on the CDVC framework to score each process component per treatment based on the following criteria: (1) impact on patient-relevant outcomes, (2) room for improvement, and (3) feasibility to improve. For every potential improvement intervention the multidisciplinary team members were asked to link it to one of the outcome measures used by MB (**Appendix 3**). After a compilation and evaluation of the ranking, we organized a second expert session to discuss and present results, with the aim to identify possible improvement interventions. The result was a list of interventions.

Step 4: Standard monitoring
A fourth step was used to monitor and integrate ongoing improvements that could impact patient-relevant outcomes. Monitoring ongoing improvement could include a list of improvement interventions with their associated processes and/or outcomes. This monitoring step is needed to identify potential ongoing improvement interventions with impact on the same outcome measures as identified in Step 1 and 2. What is also needed is an overview of ongoing improvement interventions to be able to judge the added value of the improvement interventions resulting from Step 1-3. We regularly updated the standard monitoring whenever new improvement interventions were started up at the primary hospital. A list of ongoing improvement interventions linked to outcome measures resulted from this step.

B: Selection of an improvement intervention
After the identification, we needed to select an improvement intervention, which required two steps.

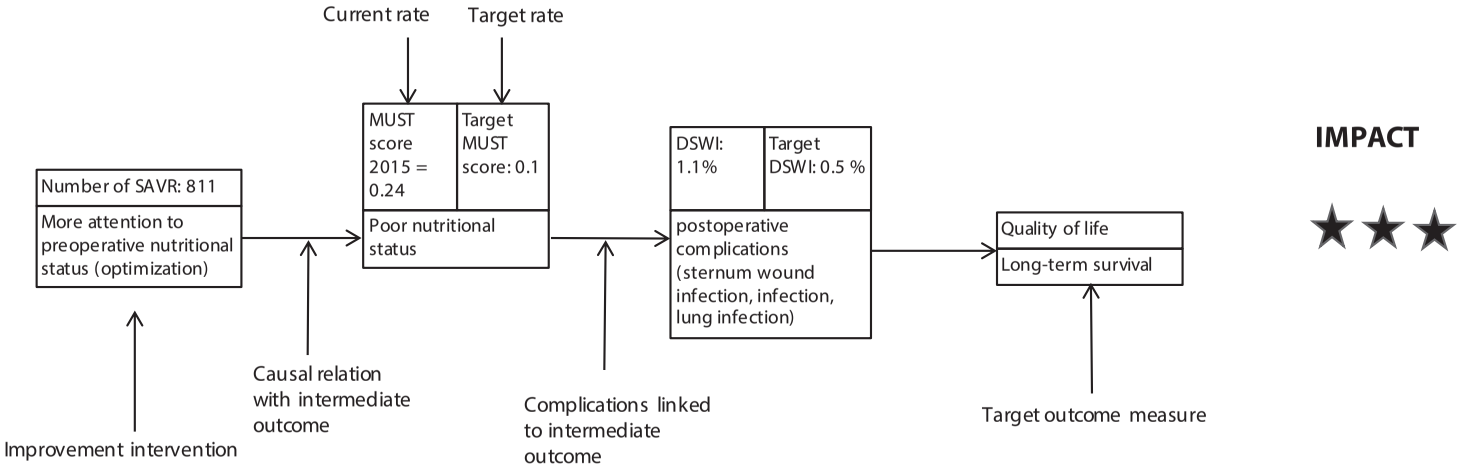
Step 1: Causal chains and intermediate outcomes

The goal of the first step was to analyze the impact of potential improvement interventions on patient-relevant outcomes. To estimate the potential impact of the improvement interventions on the outcome measures, we developed and performed a causal chain analysis (Figure 2). A causal chain is the path from improvement intervention to outcome measure. In between the intervention and a patient-relevant outcome are intermediate outcomes, which are outcomes that are impacted more directly by the intervention. Intermediate outcomes were relevant for monitoring the impact of an improvement intervention. They also allow for proving an effect when the impact on the outcome measures would be too small to measure statistically significant impact. The results of A formed the basis for this step. Two researchers and a cardiologist ranked the results according to relevance. Relevance was scored on a three-star scale from limited to high impact with the following criteria which were added to an overall score: (a) impact on the outcome measure, (b) technical and practical feasibility, and (c) feasibility in terms of costs. The aim of this ranking was to narrow down a pre-selection to offer a sharper scope of the possible improvement interventions.

Step 2: Consensus decision

In the second step we used an adjusted Delphi method to make the final selection of the improvement intervention(s). The multidisciplinary team was asked to score the improvement interventions once with the information on the causal chains according to the impact on patient-relevant outcomes during a team meeting. The multidisciplinary team was given the chance to revise their choice at the end of the first round of prioritization. The final decision was made at the end of the meeting and follow-up meetings were organized to further design implementation of the intervention.

Figure 2. Example of a causal chain.



MUST is the Malnutrition Universal Screening Tool. DSWI is deep sternum wound infection. One star indicates a small impact on outcome measures. Two stars indicate a slightly bigger (intermediate) impact on outcome measures. Three starts represent a large impact on outcome measures.

RESULTS

A: Identification of improvement potential

Step 1: Benchmarking

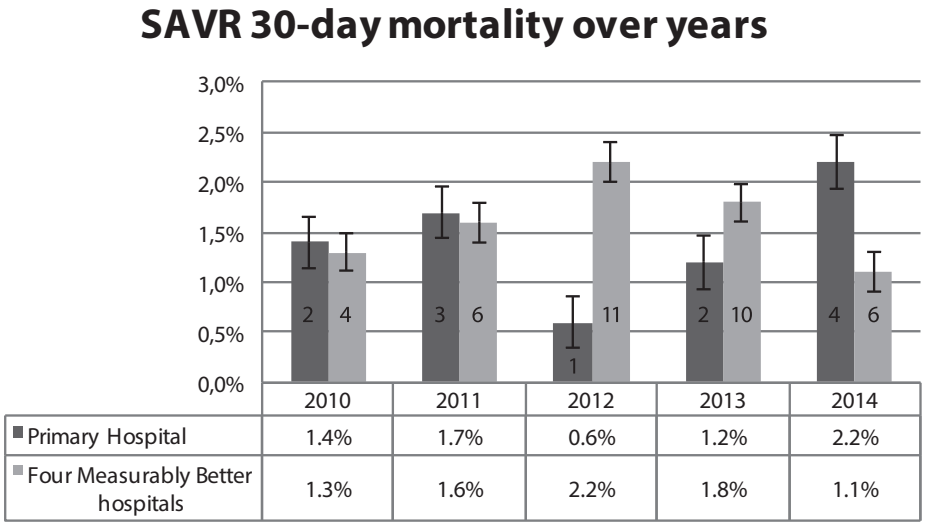
Benchmarking resulted in one outcome measure for both SAVR and TAVR: long-term survival. We observed a difference in long-term survival between the primary hospital and the other hospitals in the benchmark [23]. This result led to formulating the following hypotheses for follow-up data analyses with the goal of explaining the differences:

1. There are no differences in survival within 30 days for SAVR.
2. Differences in long-term survival for TAVR can be attributed to a number of explanatory variables and do not persist in 30-day mortality.

Step 2: Data exploration

We tested the hypotheses, to explore whether unfavorable results in long-term survival occurred due to factors that can be attributed to the operation and operating technique (**Appendix 1**). We conducted the SAVR analysis for the primary hospital and compared it to available data from four MB hospitals; we did not correct it for other explanatory variables. The analysis of the 30-day mortality of the SAVR treatment is shown in Figure 3.

Figure 3. SAVR 30-day mortality for the primary hospital and four MB hospitals over time.

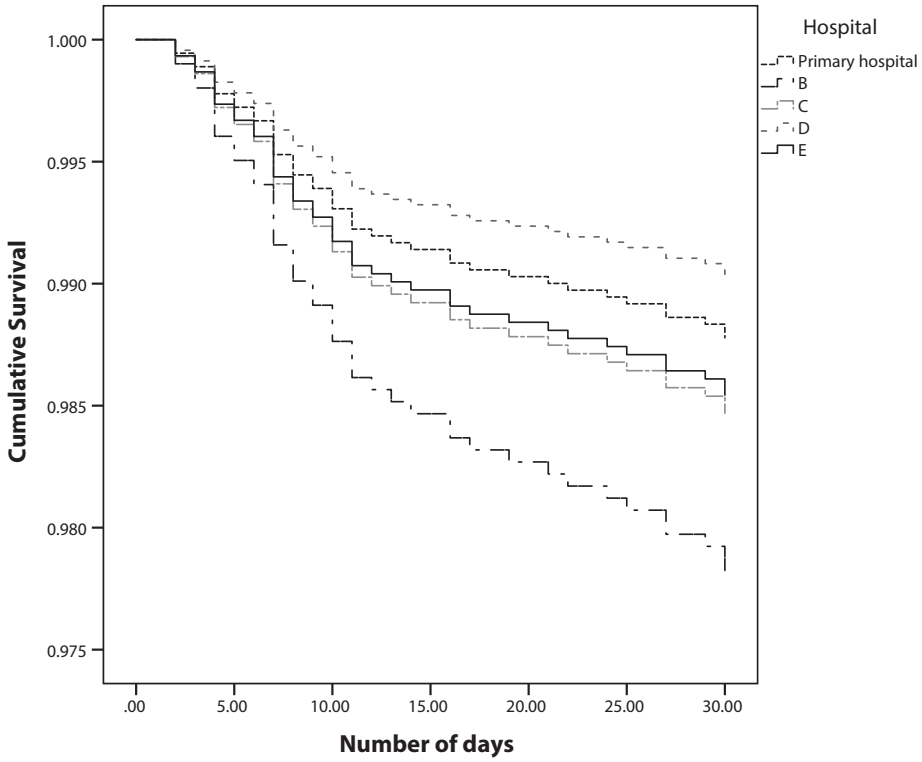


	2010	2011	2012	2013	2014
Primary Hospital	1.4%	1.7%	0.6%	1.2%	2.2%
Four Measurably Better hospitals	1.3%	1.6%	2.2%	1.8%	1.1%

Measurably Better data report 2015. Including the number of cases occurred per year for the primary hospital and four Measurably Better hospitals.

The insights into the 30-day mortality for SAVR was not considered sufficient to identify whether differences in long-term survival can be attributed to factors linked to the operation. Therefore, we conducted an additional Cox-regression to identify differences in survival within 30 days after the procedure. These insights would help identify a focus for improvement; improvement around the procedure or improvement with impact on long-term survival. We excluded procedural mortality for this analysis, because the focus was not on mortality during the operation, but post-surgery. Moreover, 23 cases had missing values and were for that reason excluded from the analysis. The primary hospital did not differ significantly in survival within 30 days after the procedure from the other participating hospital (hospital B: HR 1.79, 95% CI 0.7-4.57, p=0.224; hospital C: HR 1.26, 95% CI 0.46-3.46, p=0.661; hospital D: HR 0.79, 95% CI 0.33-1.9, p=0.592; hospital E: HR 1.19, 95% CI 0.5-2.88, p=0.694) (Figure 4).

Figure 4. Cox-regression survival curves within 30 days after procedure.



Primary hospital compared to four hospitals corrected for EuroSCORE. Procedural mortality was excluded for this analysis. Analysis starts at one day post-procedure. Hospital B (N=318) (HR 1.79, 95% CI 0.7-4.57, p=0.224), hospital C (N=359) (HR 1.26, 95% CI 0.46-3.46, p=0.661), hospital D (N=947) (HR 0.79, 95% CI 0.33-1.9, p=0.592), hospital E (N=618) (HR 1.2, 95% CI 0.5-2.88, p=0.694) did not differ significantly from the primary hospital (N=822) in survival within 30 days after procedure.

Both the crude analysis and the Cox-regression gave valuable insights into crude differences in hospitals and showed that potential to improve could possibly be achieved by QI targeting long-term survival instead of 30-day mortality and procedural improvements. Furthermore, the hypothesis was tested whether 30-day mortality can be explained by valve type at the primary hospital. The result of the logistic regression model for SAVR was not statistically significant (Table 1).

For TAVR we conducted univariable logistic regression analysis (Table 1). Due to the small amount of cases for the subclavian access route we added cases to the transapical category, and transaxillary cases to the direct aortic category. For this analysis we also excluded emergency and rescue cases due to the small amount of cases (N=3). For the 30-day mortality four missing values were identified and excluded from the analysis. The only variables found to be independent predictors for 30-day mortality were transfemoral access route (OR 0.5, 95% CI 0.28-0.80, p=0.006), vascular complication (OR 2.5, 95% CI 1.66-3.70, p<0.001), previous mitral valve stenosis (OR 0.6, 96% CI 0.4-.096, p=0.033), hospital B (OR 0.7, 95% CI 0.43-0.98, p=0.041), hospital D (OR 0.4, 95% CI 0.21-0.76, p=0.005) and renal dysfunction (OR 1.6, 95% CI 1.13-2.27, p=0.008) (Table 1). There was no difference in outcome between a logistic regression model that included variables with a p value <0.1 in the univariable analysis and a model that included variables with a p value <0.05. The Hosmer-Lemeshow test showed a goodness of fit (χ^2=13.28, p=0.066). The results provided us with valuable insights into predictors and hospitals associated with 30-day mortality, which led to contact with hospitals. The identification of significant predictors also helped to set the focus for higher risk groups of patients.

Step 3: Care delivery process analysis

Step 3 resulted in total in 40 potential improvement initiatives (Table 2). Those potential improvements were the result of the focus set on higher risk groups of patients in step 2 and the contact with other hospitals. We identified eighteen improvement interventions for SAVR. The care delivery process analysis resulted in several interventions that aim to improve awareness toward care for older patients. In the TAVR care delivery process analysis we identified 22 improvement initiatives.

Step 4: Standard monitoring

Step 4 resulted in an overview of five local initiatives that were implemented in the period of the first research step (Table 3). We ordered the improvement interventions according to treatment group (SAVR or TAVR). The identified intervention, with an impact on both long-term survival and 30-day mortality, measured a frailty score before hospitalization for TAVR. Frailty is part of the MB measures as an initial condition.

Table 1. Univariable and multivariable logistic regression results predicting 30-day mortality.

Treatment	Predictor	Category	Univariable			Multivariable		
			OR	(95% CI)	*p* value	OR	(95% CI)	*p* value
SAVR (N=3760)	Valve type	Bio prosthetic valve	1.0					
		Mechanical valve	1.5	(0.32-6.88)	.607			
TAVR (N=1929)	Access route	Direct aortic	1.0			1.0		
		Transfemoral	0.5	(0.28-0.80)	0.006	0.4	(0.19-0.75)	0.005
		Transapical	1.4	(0.83-2.47)	0.196	1.4	(0.65-2.87)	0.417
	Vascular complication		2.5	(1.66-3.70)	<0.001	2.9	(1.92-4.63)	<0.001
	Valve re-intervention		0.8	(0.19-3.66)	0.819			
	Previous heart operation		0.9	(0.67-1.45)	0.932			
	Previous CVA[a]		1.4	(0.85-2.14)	0.203			
	Previous mitral valve stenosis		0.6	(0.4-0.96)	0.033	1.4	(0.84-2.22)	0.213
	Hospital[b]	Primary hospital	1.0			1.0		
		A	0.7	(0.46-1.19)	0.214	1.0	(0.56-1.80)	0.993
		B	0.7	(0.43-0.98)	0.041	0.9	(0.54-1.47)	0.658
		C	1.1	(0.7-1.71)	0.691	0.2	(0.09-0.57)	0.002
		D	0.4	(0.21-0.76)	0.005	0.2	(0.06-0.68)	0.010
		E	0.4	(0.16-1.05)	0.063	0.09	(0.01-0.70)	0.021
	Urgency[c]	Elective	1					
		Urgent	0.8	(0.48-1.33)	0.390			
	Severe left ventricular dysfunction	>50%	0.6	(0.21-1.77)	0.363			
		<50%	1.0	(0.33-2.77)	0.935			
	Age		1.0	(0.98-1.06)	0.427			
	Renal dysfunction		1.6	(1.13-2.27)	0.008	1.9	(1.27-2.82)	0.002

[a] CVA cerebrovascular accident

[b] Analysis for Hospital was conducted relative to the primary hospital. Measurably Better data 2015.

[c] Urgency: for urgent operations, no emergency and rescue operations.

Table 2. Results care delivery process analysis.

Treatment	Process Phase	Potential improvement intervention	Impact on outcome
SAVR	Monitoring and preventing	Identify high-risk patients by measuring a Frailty Score	Mortality, Quality of Life
		Organize a specific pre-operative screening for older patients	None*
	Diagnosing	Introduce a frailty protocol	Quality of Life, mortality
		Discuss older patients in a multidisciplinary team	Quality of Life, Mortality
		Introduce a checklist for uniform imaging	Quality of Life, Mortality
		Screen abdominal vascular disease	Mortality
		Screen for long-vein narrowing	Mortality
	Preparing	Adjust the anticoagulation protocol	Mortality
	Intervening	Standardize with a protocol for the blood or crystalloid cardioplegia	Mortality
		Use of MECC[a] and improve experience of the operation team	Mortality
		Implant the long-term pacemaker as fast as possible after operation	Mortality
	Recovery/Rehab	Conduct an echocardiography only with indication	Quality of Life
		Improve nightly supervision at the ICU[b] (cultural change)	Mortality, valve re-intervention
		Offer every patient heart rehabilitation program	Quality of Life
		Raise more attention to diet of the patient, practice spirometry	Quality of Life
		Introduce a checklist for the exit consult	Re-intervention
	Monitoring/ Managing	Adjust the medication protocol	Quality of Life

Table 2. Continued.

Treatment	Process Phase	Potential improvement intervention	Impact on outcome
TAVR	Monitoring and preventing	Optimize Frailty identification	None*
		Introduce home monitoring system for measuring blood pressure (E-Health)	Quality of Life
	Diagnosis	Introduce more frequent TAVR team meetings to discuss patients	Mortality, Quality of Life
		Improve hospital logistics (with the support of the Lean method)	Mortality, Quality of Life
		Assure that an echo is always available before diagnosis	Complications
		More frequent TAVR Team meetings to discuss patients	Mortality
		Digitalize the treatment plan	Mortality
		Involve an anesthetist in the TAVR Team meetings	Mortality
		Introduce a diagnosis checklist for treatment choices	None*
	Preparing	Conduct pre-operative check-up and CT-scan on the same day	Waiting-times
		Introduce a checklist for the check-up	Mortality
		Involve an anesthetist much more this phase	Complications
		More local anesthesia	Mortality
		More procedures in one day or another day for TAVI procedure to shorten the waiting times	None*
	Intervening	Introduce the presence of a surgeon, cardiologist and anesthetist during the procedure	Complications
		Use ACIST Pump[c] (control of injection rate)	None*
		Only use the new generation of valves (replaceable valves)	Mortality
		Use of a debris catch device	Stroke
	Recovery/Rehab	Introduce clinical pathway	Quality of Life
		Ensure removal of the pacemaker the following day and directly implant the long-term pacemaker if needed	Infections
		Apply telemetry monitoring for full period until dismissal	None*
	Monitoring/Managing	Define targets for medication	Re-intervention

*The proposed potential improvement intervention is not expected to have considerable impact on one of the patient-relevant outcome measures, but process or structure measures.

[a] MECC is minimal extracorporeal circulation.

[b] ICU is intensive care unit.

[c] ACIST Pump simplifies contract injection for procedures.

Table 3. Monitoring overview.

MONITORING IMPROVEMENT								
Treatment	**Indicator**	**Initiative**	**Based on outcome measures yes/no**	**How did it take place?**	**Implementation date**	**Intended impact on which outcome**	**Implementation completion (%)**	**How is it measured?**
TAVR	30-day mortality	1) Pre-TAVR/frailty outpatient clinic started in 2014, 2) TAVR complication discussion started in 4th quarter 2014 with the following issues discussed: A) Choice of valve selection, B) Creation of a specialization team, C) Add additional CT images in report to the TAVI Team.	yes		1st quarter 2015	30-day mortality	100%	Valve choice: registry measured
	1-year mortality	Pre-TAVR/frailty outpatient clinic started in 2014	yes		4th quarter 2014	1-year mortality	100%	Not
	long-term survival	Proposal change training plan - development of online course small private online course for residents with focus on frailty, functional decline and shared decision making	no	specific project team for elderly care	4th quarter 2015	none	0%	Not
	Vascular complications	1) Routine CT scan required pre-TAVR, 2) Start study new closing device in 2015, 3) Start complication discussions in 4th quarter 2014, where it was discussed to lower the threshold for a surgical cut down	yes		4th quarter 2014	Vascular complications	100%	Not
SAVR	Re-sternotomy	Coagulation policy: Optimization of the transfusion policy based on for example the TEG[a] at the operation room, or no coagulation correction. In addition, the aim is to reduce the number of blood transfusions. The number of re-sternotomies could decrease at a targeted corrected clotting status of the patient.	no	Initiative from Anesthesiologists who conducted research	1st quarter 2015	Bleeding complications	50%	As part of a study

[a] TEG thromboelastography for testing the efficiency of blood coagulation

B: Selection of an improvement intervention

Step 1: Causal chains and intermediate outcomes

Causal chains were constructed for each improvement intervention resulting in eighteen causal chains for SAVR and twenty-two for TAVR.

For SAVR we ranked three causal chains with three stars for the impact on outcome measures, specifically long-term survival. These initiatives were: implementing an anticoagulation policy, offering a cardiac rehabilitation program to all patients, improving preoperative nutritional status of patients and paying more attention to the frail and elderly. For TAVR, we ranked four causal chains with three out of three stars for impact on patient-relevant outcome measures: improve speed of treatment decision, determine a frailty score in the prevention phase, introduce a checklist for the preoperative check-up and improve logistics with the Lean methodology. Two interventions presented no impact on patient-relevant outcome measures, but rather on cost savings. These were, firstly, develop a clinical pathway for the recovery phase, and, secondly, carry out echocardiography only on indication.

Step 2: Consensus decision

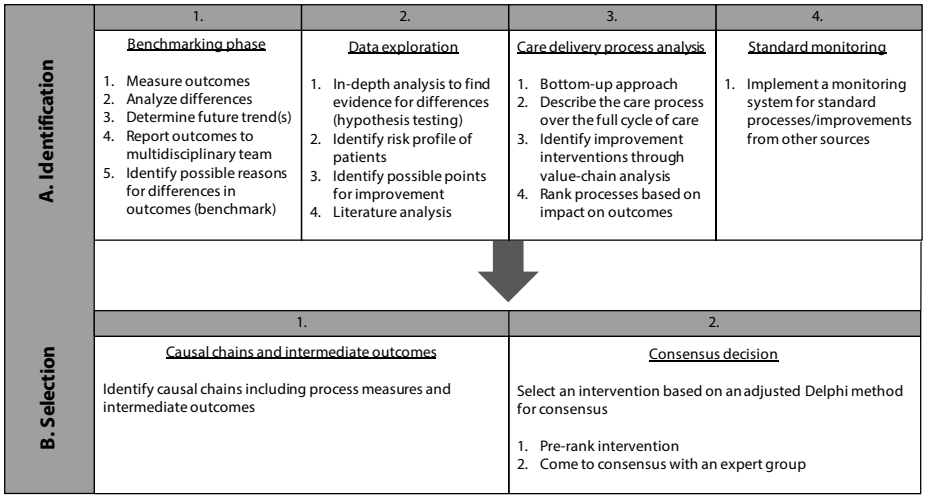
We presented the results to the multidisciplinary team, who, through discussion, took a consensus decision on potential improvement interventions with the highest impact on outcome measures from phase A. The adjusted Delphi method resulted in a top four improvement intervention overview for both treatments, which was further discussed in the multidisciplinary team. The multidisciplinary team was specifically interested in an initiative that would change the treatment plan and the process of both treatments, because of the expected highest impact on outcomes. Also, as the aim was to select only one final improvement initiative, the impact on patient-relevant outcomes would be bigger with an initiative that suited both the SAVR and TAVR treatment. Since interventions targeting the frail elderly were mentioned most frequently in the multidisciplinary team and the older age category was associated with 30-day mortality, we decided to focus on more attention to the diet of our patients. The decision was taken with a specific intervention plan to improve the nutritional status and condition of older patients through a protein-enriched diet before the operation. We opted for this initiative because of its potential impact on long-term survival, 30-day mortality and also a cost measure, namely length of stay.

A toolbox for the identification and selection of an improvement intervention

On the basis of existing quality improvement (QI) programs and our experiences from the process we developed an integrated and combined approach from both patient-relevant

outcomes and processes to identify and select improvement interventions aiming at improving quality of care: the Intervention Selection Toolbox (IST) (Figure 5). The IST was tested and applied to improve the quality of care for aortic valve disease. IST consists of two phases to identify improvement interventions with an expected high impact on outcome measures. In phase A: Identification, the following steps were identified: 1. Benchmarking, 2. Data exploration, 3. Care delivery process analysis and 4. Standard monitoring. In phase B: Selection, two steps were identified: 1. Causal chains and intermediate outcomes and 2. Consensus decision. The steps of the IST are generically described in Additional file 4.

Figure 5. The Intervention Selection Toolbox (IST).



The IST presents steps for two phases for identifying and selection improvement interventions based on patient-relevant outcome measures.

DISCUSSION

Meaning of findings

This paper delivered a toolbox for identifying and selecting improvement interventions, the IST, as well as the selection of an improvement intervention for the treatment of aortic valve disease in the primary hospital of investigation.

We developed the identification and selection toolbox based on existing methods from the literature [11,13,15,16]. The challenges with designing complex interventions have earlier been described [26]. The IST is unique, as its focus is on the design of an improvement intervention with the highest expected impact on outcomes for patients instead of

processes, but it does not neglect processes. For the IST, outcomes and processes are combined into one toolbox. Earlier frameworks focus on the optimization of interventions [26]. Whereas, the IST focusses on the identification of improvement potential for outcomes by identifying and selecting an improvement intervention. As Donabedian stressed, only by connecting structure, process and outcome quality improvement can be achieved [27]. This is often forgotten in other improvement models. VBHC was introduced with the promise to solve the cost crisis [28]. But, how outcome measures should be used for improving quality of care and reducing costs, was not described. Measurements forms the basis for improvements in health care. With the help of these measurements, a feedback loop on what is the current state of health care can be implemented. As suggested by the VBHC concept, outcome measures are needed to introduce competition to tempt professionals to improve care for patients [29]. In order to find adequate QI interventions it is not sufficient to merely measure and benchmark outcome measures. Additional data analysis and process analysis will lead to new ideas that will have the potential to improve beyond best practices from benchmarking. The IST combines the strength of both strategies: 1) to analyze and compare health outcomes and 2) to analyze and study the care delivery process and find clues for improvement. Most approaches so far focus on one of both strategies.

The overall goal is to achieve statistically significant and clinically relevant improvements in patient-relevant outcomes. To determine these statistically significant improvements in patient-relevant outcomes, we often need long follow-up periods and big samples. In order to achieve this goal we could use the intermediate outcomes that give insights into improvements on a smaller scale to predict an effect on patient-relevant outcomes.

To ensure a successful identification and selection of improvement interventions certain barriers and facilitators have to be considered. Barriers and facilitators could be relevant on the following levels: (1) the readiness to change of individual care providers, (2) social context, (3) organizational context, and (4) economic and legal context [13]. Skills, attitude, resources, and regulations could hinder a successful improvement toolbox implementation [13]. In order to facilitate a successful implementation, a preliminary context and resource analysis could strengthen the success of the toolbox. If the multidisciplinary team was not ready for improvement, the results and overall success of this investigation would certainly have been different. Moreover, the selection of an intervention is influenced by its feasibility. An improvement intervention that was not feasible for implementation was more easily disregarded by the multidisciplinary team. It is, thus, important that the above-mentioned barriers are firstly identified to prevent unsuccessful processes.

Improvement interventions that were identified, but not selected need to remain under the attention of the multidisciplinary team. We presented the interventions identified in our study to the multidisciplinary team for further decision making. Further implementation could follow from the pool of identified interventions if required.

Limitations

Our study has some limitations that need to be mentioned. The hospital of investigation had a general aim of improving patient-relevant outcomes in the strategic plan. Hence, the ambition of the multidisciplinary team might be driven by the overall movement toward improvement. In order to fully evaluate this approach, it would need to be tested in several different settings and for different medical conditions for transferability. The proof of principle of the IST will come from analyzing the impact of the resulting improvement initiatives in practice. The protein-enriched diet for preoperative optimization will be implemented and evaluated within the primary hospital.

The starting point for identifying and selecting improvement interventions is the availability of outcome data. In the current situation, the IST was applied by using available local outcome data which was part of a Dutch clinical outcome registry [21]. The use of local data might have affected the results of the current study. In order to apply the IST an outcome registry accelerates the identification and selection process.

Following the steps of the IST offered valuable insights into improvement of care processes based on outcomes. However, in our case it was relatively time-consuming to follow all the steps for care professionals, considering the amount of multidisciplinary team meetings and analyses to be conducted. In further research it should also be tested whether the phases and steps could be followed quicker. For this study, we did not evaluate how experts have experienced this process. On the other hand, it has not yet been evaluated what the results would have been if another approach was chosen. When a different sequence of the steps was opted for, the results could possibly have been different. Also, if certain steps would not have been taken or additional steps had been added to the toolbox, the results might have changed. To minimize these possibilities of different results, an evaluation should be conducted in future studies. Furthermore, in our approach one improvement intervention was selected to suit two treatments of aortic valve disease. This made the decision for one suitable intervention more complex. Further research applying the toolbox could test whether choosing one improvement per treatment would lead to better results. The toolbox development is based on a case study and not an evidence-based improvement or clinical trial. Moreover, further validation in another case is required in order to test transferability.

CONCLUSION

The IST combines care delivery process analyses and outcome analyses and offers a practical guide on how to identify and select improvement interventions based on VBHC. The approach identified within this study could guide other hospitals in the selection of high-impact improvement interventions.

ABBREVIATIONS

VBHC = Value-based health care; MB = Measurably Better; SAVR = Surgical Aortic valve replacement; TAVR = Transcatheter aortic valve replacement; QI = Quality Improvement

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APPENDICES

Appendix 1. Definitions of variables and coding.

Name variable	Definition	Coding
Outcome measures SAVR		
Long-term survival	Patients who survive as a result of the number of days elapsed after the intervention with a maximum follow-up of 5 years.	Not applicable
120-day mortality	Patients who die regardless of cause of death within 120 days (≤ 120 days) after intervention.	3 categories: 0=no mortality, 1=mortality, 9=unknown
30- day mortality	Patients who die regardless of cause of death within 30 days (≤ 30 days) after intervention. Excluding mortality during the procedure (procedural mortality) (≤ 0 days).	3 categories: 0=no mortality, 1=mortality, 9=unknown
Quality of Life	Quality of life of the patients measured before and after intervention. Measurement before intervention=measured no longer than a maximum of 2 months before intervention. Measurement after intervention=measured between 10-14 months after intervention. Measured with the Short Form (36) Health Survey.	Not applicable
Cerebrovascular accident (CVA)	Patients for which a neurological determination of a postoperative stroke has occurred within 72 hours (≤ 72 hours) after intervention (excluding Transient Ischemic Attack).	3 categories: 0=no CVA, 1= CVA, 9=unknown
Deep sternal wound infection	Deep sternal wound infection developing within 30 days (≤ 30 days) after intervention. It is assumed that the patient returns to the treatment hospital.	3 categories: 0=no deep sternal wound infection, 1=deep sternal wound infection, 9=unknown
Implantation of a new permanent pacemaker	Post-operative implantation of a new (no replacement) permanent pacemaker within 30 days (≤ 30 days) after intervention.	3 categories: 0=no implantation new permanent pacemaker, 1= implantation new permanent pacemaker, 9=unknown
Freedom of valve-re-intervention	Patients who are free from aortic valve re-intervention (aortic valve replacement, aortic valve repair or percutaneous paravalvular leakage (PVL) closure) on the same aortic valve as a function of the number of days elapsed after intervention.	3 categories: 0=no valve re-intervention, 1=valve re-intervention, 9=unknown

Appendix 1. Continued.

Name variable	Definition	Coding
Initial conditions SAVR		
EuroSCORE	Last determined logistic EuroSCORE II measured before the intervention (measured continuously in % with 2 decimals).	3 categories: 1=low < 10%, 3=high > 10%, 9=unknown
Outcome measures TAVR		
Long-term survival	Patients who survive as a result of the number of days elapsed after the intervention with a maximum follow-up of 5 years	Not applicable
30-day mortality	Patients who die regardless of cause of death within 30 days (≤ 30 days) after intervention.	3 categories: 0=no mortality, 1=mortality, 9=unknown
Quality of Life	Quality of life of the patients measured before and after intervention. Measurement before intervention=measured no longer than a maximum of 2 months before intervention. Measurement after intervention=measured between 10-14 months after intervention. Measured with the Short Form (36) Health Survey.	Not applicable
Cerebrovascular Accident (CVA)	Patients for which a neurological determination of a postoperative stroke has occurred within 72 hours (≤ 72 hours) after intervention (excluding Transient Ischemic Attack).	3 categories: 0=no CVA, 1= CVA, 9=unknown
Implantation of a new permanent pacemaker	Post-operative implantation of a new (no replacement) permanent pacemaker within 30 days (≤ 30 days) after intervention.	3 categories: 0=no implantation new permanent pacemaker, 1= implantation new permanent pacemaker, 9=unknown
Vascular complications	Patients who develop a vascular complication within 30 days (≤ 30 days) (diagnosis according to the VARC-2 definition) from the start of the intervention (including pre-operative vascular complications).	3 categories: 0=no vascular complications, 1=vascular complications, 9=unknown
Freedom of valve re-intervention	Patients who are free from aortic valve re-intervention (aortic valve replacement, aortic valve repair or percutaneous paravalvular leakage (PVL) closure) on the same aortic valve as a function of the number of days elapsed after intervention.	3 categories: 0=no valve re-intervention, 1=valve re-intervention, 9=unknown

Appendix 1. Continued.

Name variable	Definition	Coding
Explanatory variables TAVR		
Access route	Applied access route for TAVR.	4 categories: 1=transfemoral , 2=transapical and subclavian , 4=direct aortic and transaxillary, 9=unknown
Previous heart operation	Patients who have undergone previous cardiac surgery, with opening of the pericardium, prior to the intervention throughout life.	3 categories: 0=no previous heart operation, 1=previous heart operation, 9=unknown
Previous stroke	Patients who have undergone a CVA prior to the intervention throughout life (excluding TIA).	3 categories: 0=no previous CVA, 1=previous CVA, 9=unknown
Previous mitral valve stenosis	Patients with mitral valve stenosis that has been diagnosed prior to the intervention. Measured with the last echocardiogram up to 1 year before intervention.	3 categories: 0=no or mild mitral valve stenosis, 1=moderate/serious mitral valve stenosis, 9=unknown
Hospital	Measurably Better hospitals participating in the study that offered data from 2010-2014.	100=Primary hospital, 3=B, 4=C, 6=D, 8=E
Urgency of the procedure	Urgency of the procedure. Elective means that patients have a routine intake for the intervention. Urgent means patients who are not elective for the operation but need an intervention within the current admission for medical reasons. These patients cannot be sent home without a definitive procedure. Emergency and rescue cases were excluded.	3 categories: 1=elective, 2=urgent, 9=unknown
Severe left ventricular dysfunction	Left ventricular dysfunction is expressed as an ejection fraction (EF, in %). The registered EF may not have been established for more than 6 months prior to intervention. The last measured EF before intervention is used.	4 categories: 1=EF>50%, 2=EF 30-50%, 3=EF<30%, 9=unknown
Age	Age in years at start of the intervention.	Not applicable
Renal dysfunction	Renal dysfunction is calculated based on the creatinine level and is defined as a reduced glomerular filtration rate (GFR) of <60 ml/min/1.73 m2. The GFR is calculated according to the MDRD formula.	3 categories: 0=no renal dysfunction, 1=renal dysfunction, 9=unknown

Appendix 2. CDVC ranking list example.

	1. IMPACT on outcomes	2. ROOM for improvement	3. FEASIBILITY to improve	Comment
Monitoring and preventing				
preventive measures within hospital				
Diagnosing				
Waiting times				
Assessment results of imaging				
Anamnesis				
Defining treatment plan				
Preparing				
pre-operative policlinic				
Pre-operative check-up				
Intervening				
Access route				
Access route closure				
Volume (number of procedures)				
Recovering/Rehab				
In hospital recovering				
Regular checkups				
Support				
Counselling/education on prevention				
Monitoring/Managing				

Appendix 3. Example evaluation tool from CDVC.

Improvement possible?			Yes		No
No.	**Potential improvement intervention**	**Influences which outcome**	**Follow-up action**	**Comment**	**Who**
1	...	...	...	...	...
2	…	...	…	...	...
3	…	...	…	...	...

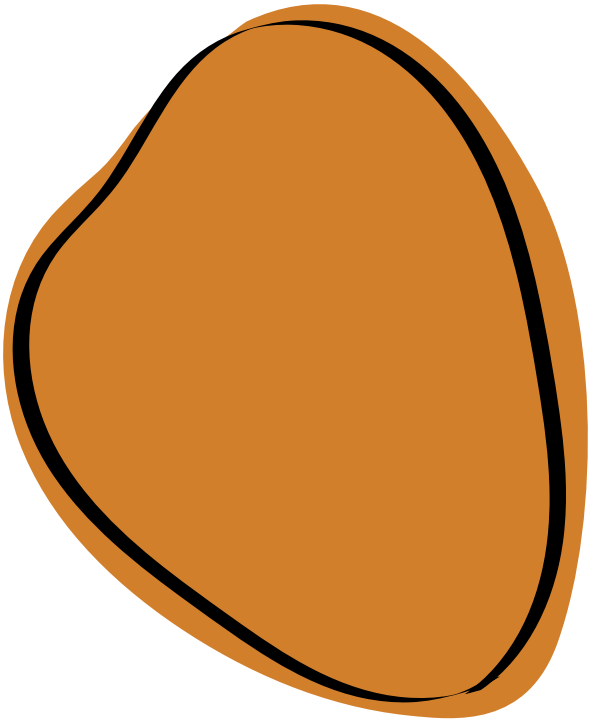
Appendix 4. Generic description of the steps the IST.

A. Identification

1. Benchmarking: Benchmarking includes: the identification of outcomes to be benchmarked, organizations to benchmark with, data collection, analysis of differences, determination of future trend and sharing results with a multidisciplinary team of experts. The multidisciplinary team may comment and formulate hypotheses for the explanation of identified differences.
2. Data exploration: Data exploration aims at understanding data and their characteristics. In this step, the formulated hypotheses of the previous steps are tested with the help of statistical hypothesis testing. Possible risk groups or risk factors may be identified. Next to statistical analyses, literature study may support hypothesis testing.
3. Care delivery process analysis: The care process(es) need to be described in detail. The care delivery value chain developed by Porter et al (2008) may support this process. Important is to consider the processes of the full cycle of care. After description, a prioritization by a multidisciplinary team follows, who rank the processes based on its potential impact on outcomes and feasibility to change.
4. Standard monitoring: In order to identify interventions with highest expected impact on outcomes, a list describing all improvement interventions with impact on outcomes needs to be established. The aim of the list is not to eliminate ongoing improvement interventions, but rather to get an overview of improvement interventions that are aimed to improve the same outcomes under investigation. The standard monitoring can be a dashboard or simply a list of improvement interventions.

B. Selection

1. Causal chains and intermediate outcomes: Establishment of the causal relation between a potential improvement intervention and the outcome measures, helps to identify possible intermediate outcomes that may be useful for the evaluation of the effectiveness of the improvement intervention.
2. Consensus decision: Based on expert opinions of a multidisciplinary team, consensus on one (or more) intervention(s) needs to be taken. By ranking the interventions, a multidisciplinary team of experts can choose the intervention(s) with highest expected impact on outcomes.



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The implementation of change model adds value to value-based health care: a qualitative study

Nina Zipfel
Paul van der Nat
Benno Rensing
Edgar Daeter
Gert Westert
Stef Groenewoud

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ABSTRACT

Background: Value-based healthcare (VBHC) is a concept that focuses on outcome measurement to contribute to quality improvement. However, VBHC does not offer a systematic approach for implementing improvement as implementation science does. The aim is to, firstly, investigate the implementation of improvement initiatives in the context of VBHC and secondly, to explore how implementation science could be of added value for VBHC and vice versa.

Methods: A case study with two cases in heart care was conducted; one without the explicit use of a systematic implementation method and the other one with the use of the Implementation of Change Model (ICM). Triangulation of data from document research, semi-structured interviews and a focus group was applied to evaluate the degree of method uptake. Interviews were held with experts involved in the implementation of Case 1 (N=4) and Case 2 (N=7). The focus group was held with experts also involved in the interviews (N=4). A theory-driven qualitative analysis was conducted using the ICM as a framework.

Results: In both cases, outcome measures were seen as an important starting point for the implementation and for monitoring change. Several themes were identified as most important: support, personal importance, involvement, leadership, climate and continuous monitoring. Success factors included intrinsic motivation for the change, speed of implementation, complexity and continuous evaluation.

Conclusion: Application of the ICM facilitates successful implementation of quality-improvement initiatives within VBHC. However, the practical use of the ICM shows an emphasis on processes. We recommend that monitoring of outcomes be added as an essential part of the ICM. In the discussion, we propose an implementation model that integrates ICM within VBHC.

BACKGROUND

Improving the quality of care while reducing costs is a major goal on many hospital agendas [1,2]. The goal of value-based healthcare (VBHC) is to reorganize health care in order to increase value for patients [3]. 'Value' in VBHC is defined as patient-relevant health outcomes relative to costs [3]. Porter suggests that this goal can be achieved by measuring outcomes and costs per medical condition, which will allow for the identification of variation in outcomes across the full cycle of care [4]. Experts suggest that, based on this insight into outcomes, improvement potential can be identified and quality of care improved [5]. In current practice, VBHC is used as a concept leading to improvement by measuring outcomes in registries and supporting more efficient coordination of care through benchmarking and reporting [6]. However, the current application of VBHC lacks a systematic approach for the implementation of improvements. The concept is sometimes presented as the sole solution for improving outcomes and reducing costs, but *how* improvements should be implemented remains unclear. In the literature, a lack of a systematic approach for using VBHC and specifically a method for the implementation of improvement initiatives was identified [1]. Measurement of outcomes and costs has been shown to provide valuable insights into practice variation and waste, which can lead to process improvement [7,8]. Literature on the implementation of improvement initiatives in the context of VBHC is scarce. One example was identified in the context of a project for orthopaedics, in which the identification of variation in hospital stay led to improvement [7]. Another example, which involved prostate cancer care, showed that improvement based on outcomes led to a relevant decrease in incontinence rates [9]. Moreover, within heart care several improvement initiatives were implemented based on identified variation in outcomes [1]. How the improvements were implemented was, however, not described. Therefore, we aimed to investigate the implementation of improvement initiatives in the context of VBHC and whether a systematic implementation method has added-value for VBHC. The resulting insight could enrich the concept of VBHC [10].

In order to investigate whether systematic implementation could add value to VBHC, a suitable framework needed to be identified. A previous review identified implementation frameworks, models and theories for the process of implementation [11]. The most commonly cited frameworks include the PARIHS [12], Conceptual Model [13], the Implementation of Change Model [14], Ecological Framework [15] and the CFIR [16]. Based on the results of this review, the Implementation of Change Model (ICM) seemed to be the most suitable for the purpose of offering a systematic approach for the implementation of improvements since it specifies practical steps for the process of implementation [14]. Several quality improvement projects have applied the Implementation of Change Model or parts of it [17–19].

This paper describes how improvement initiatives which were selected based on insights into outcomes were implemented. To show the added-value of a systematic implementation approach for VBHC, we selected two cases. The goal was to use VBHC as a guideline for both projects in the identification and selection of an improvement intervention. Both interventions emerged from a VBHC improvement cycle. In an earlier systematic literature review only very few improvement interventions based on insights into outcomes were identified [20]. Therefore, the aim was to compare two improvement interventions that used the same starting point to compare the implementation process. The first case was implemented *without* the explicit use of a systematic implementation approach, while the second case was implemented *with* the explicit use of a systematic implementation approach, i.e. the ICM. By analysing and comparing the two cases, the goal of this paper was to learn what went well and what could be improved in order to give recommendations on how to implement improvement initiatives in the context of VBHC. The analysis was not intended to evaluate the improvement on outcomes, but to explore the implementation process of two improvement initiatives.

Theoretical framework

ICM

The ICM was developed based on examples from the practice of implementing change in health care and examples from the literature [14]. The ICM consists of seven steps for guiding the implementation of improvement (Table 1). The first step of the model is development of a proposal and target for change, which includes a detailed analysis of the characteristics of the possible innovation and/or change. Secondly, actual performance or outcome variation at baseline has to be assessed in order to gain insights into the current situation and indications for change [21]. The following step of the ICM is the problem analysis, which is seen as a crucial step to the implementation of an improvement initiative [14]. The analysis of barriers and facilitators should include a structured analysis of relevant stakeholders, determinants of change, and subgroups in the target population [22]. Based on the analysis of possible barriers, implementation strategies can be identified [21]. This step is followed by a pilot implementation and the integration into routine care [21]. The last step of the model is the evaluation of the change, which could lead to modifications and a return to earlier steps of the model [21].

Table 1. Seven steps of the ICM.

Step	Principles of the ICM[1]
1.	Development of a proposal for change
2.	Analysis of actual performance, targets for change
3.	Problem analysis of target group and setting
4.	Development and selection of strategies and measures to change practice
5.	Development, testing and execution of implementation plan
6.	Integration of changes into routine care
7.	(Continuous) evaluation and (where necessary) adapting plan

1. Adapted from Grol et al. (2013) [14].

METHODS

Design: Case study

A collective case study design was chosen to test the ICM for two cases. Cases in collective case studies are similar, yet can have a different context [23]. The goal of a collective case study is to compare two or more cases [24]. For this analysis, a within-site collective case study was conducted. According to Creswell (1998), theory can be employed in different ways in a case study design: before or after data collection [23]. For the purposes of exploring the application of the ICM, theory was employed both for supporting the interview guide before the interview and for comparing both cases for interpretation after the interview. For this study the Consolidated criteria for reporting qualitative studies (COREQ) were applied.

Case selection and setting

The two cases were selected according to the principles of purposive sampling [23]. Purposive sampling can be used to identify cases that show different perspectives on the same problem [23]. To provide a clear comparison of the implementation approaches used in the two cases, deviant case sampling was applied. In deviant case sampling, cases are selected that are contrasting in some way [25]. For our purposes, one case was chosen that implemented an improvement initiative without the explicit application of a systematic implementation method, while in the other case there was explicit use of the ICM. Both cases emerged based on insights into outcomes according to the VBHC concept. The starting point for the development of both improvement initiatives was the same set of outcome measures and both initiatives share the goal of improving outcomes. Therefore, both cases are comparable due to their context, yet they can also be contrasted. Creswell (1998) suggests that the more cases are studied, the less depth the cases have [23]. Only

two cases were chosen to ensure that they were "information rich"; it was not the purpose of the study to achieve statistical generalization [26]. The research was carried out at a Dutch hospital from June 2017 until January 2018. The first selected case concerns a pre-incision checklist for cardiac surgery to improve cultural behaviour in the operating theatre and reduce 120-day mortality rate (Table 2). The second case is about a protein-enriched diet given to patients two weeks before the operation in order to improve their fitness before cardiac surgery and prevent postoperative complications (Table 2).

Table 2. Description of the cases.

Case 1: A pre-incision checklist for cardiac surgery	**Case 2: Preoperative protein-enriched diet**
The pre-incision checklist for cardiac surgery is an addition to the surgical safety checklist that was previously developed by the World Health Organization [27]. Items specific to cardiac surgery are added to the checklist and patients are divided into three risk categories: low, intermediate and high risk. Peri- or postoperative complications are identified with a focus on six main organ-specific topics: cardiac, pulmonary, renal, neurologic, inflammation and coagulation. The checklist is part of a greater project from an external hospital that identified this "best practice" based on insights into outcomes [28]. The checklist was identified based on differences in 120-day mortality rate among benchmarking hospitals [1]. This external project is expected to contribute positively to communication between various members of the operation team. This is expected to contribute to more risk awareness, structured consultation and a better culture [28]. Evidence has shown that the checklist contributes to significantly lower 120-day mortality rate compared to a group of patients who did not receive the checklist [29]. At the current research setting only questions from the pre-incision checklist were implemented. The goal of the intervention was to improve outcomes (120-day mortality rate).	Elderly patients undergoing Surgical Aortic Valve Replacement (SAVR) or Transcatheter Aortic Valve Replacement (TAVR) receive a protein-enriched diet during a two-week period prior to the scheduled surgery. Offering a preoperative protein-enriched diet had a positive effect on health outcomes in cancer patients, patients with hip fracture undergoing surgery and patients with end-stage liver disease who needed to undergo transplantation [30–33]. In a study of non-cancer patients, malnutrition was most frequently identified in patients undergoing major vascular surgery [34]. The initiative was selected based on insights into outcomes and in-depth data and process analyses with the goal of optimizing preoperative preparation of older patients. The diet consists of familiar foods enriched with protein in order to reach the recommended protein intake for elderly people with an illness of 1.2-1.5 g/kg/d during and after hospitalization [35]. The goal is to increase protein intake by 45 grams per day spread over meals during the day. Protein intake is measured with validated 24-hour recall questionnaires. The protein-enriched diet is expected to contribute to higher protein intake, fewer postoperative complications and faster recovery. The effect of a preoperative protein-enriched diet for elderly patients undergoing aortic valve replacement is currently being evaluated.

Data collection methods

Triangulation of data sources was applied. Using multiple sources for data collection is advised for case studies [23]. First, a document analysis of minutes, presentations and memos was conducted. The documents were made available by a member involved during each of the implementation processes per case. Second, interviews were conducted with professionals involved in the implementation process of the two selected cases. Interviews were semi-structured with a length of approximately 20 minutes. An interview guide based on the theoretical framework including the ICM was used (see **Appendix 1**). All interviews were audio-recorded and transcribed verbatim. Third, a focus group interview was conducted in order to recapitulate the results from the interviews. The focus group was intended for feedback purposes and gathering perceptions, and it allowed participants to make additional comments on each other's opinions [36]. The focus group was audio-recorded and transcribed. The interviews and focus group were conducted by a researcher. The language of the interviews and focus group was Dutch and transcripts were translated into English.

Sampling of participants

Participants for the interviews were selected through a mix of criterion sampling and snowball sampling. Criterion sampling is a method of choosing all participants that meet a predefined criterion [36]. The criterion for selection was that participants must have had an active role in the implementation of the case. Additional snowball sampling [36] was applied by asking participants whether other participants were involved in the implementation process who could provide more information. Participants were asked to participate via e-mail. For the first case, four professionals were chosen (N=4) including a cardio-thoracic surgeon, a perfusionist, an anaesthesiologist and a data manager. This was the maximum number fulfilling the criterion, including participants suggested through snowball sampling, because no other participants were involved in the implementation of the intervention. For the second case, seven interviews were conducted (N=7) with two cardiologists, a cardio-thoracic surgeon, a nurse, a researcher and two secretaries. Also for this case the maximum number of participants was chosen through both sampling strategies. This sample size was chosen because it was not the purpose of the cases to draw externally generalizable conclusions, but instead to collect all possible viewpoints, opinions and thoughts of relevant stakeholders about the case [36]. Informed consent was obtained from all participants before the start of the interviews.

The same participants from both cases were also invited to participate in the focus group in order to comprise a multidisciplinary group of experts from both cases. Convenience sampling was applied. This setup was chosen because participants could relate to comments made by colleagues since they shared experiences during the implementation

process [37]. Four experts agreed to participate in the focus group (N=4). Two experts were involved in the implementation of Case 1 and two of Case 2.

Data analysis

We analysed the results in three steps: 1) Chronological case description with a within-case analysis from the documents and interviews, 2) Cross-case analysis from the interviews, and 3) Focus group analysis.

As recommended by Creswell (1998), the detailed case description is done chronologically [23]. The advantage of this approach is that each case can be described separately in order to understand each case as a holistic entity [25]. For this analysis both the documents as well as the interviews were used. The interviews were coded by one researcher. Subsequently, a within-case analysis was conducted with a detailed description of each case and themes within the case [23]. Each case can be seen separately as holistic and context sensitive [25]. A holistic perspective, according to Patton (2002), is one in which the whole context is seen as a complex system [25]. Thus, only when all interviews and sources from the document analysis are combined is the whole case formed. Context sensitivity refers to comparative case analysis and identifying patterns for transferability to a different setting [25]. Data for this analysis were gathered through document analysis and interviews.

A thematic analysis across cases was then carried out, which is known as a cross-case analysis [23]. The data were analysed using deductive analysis techniques based on the theoretical framework of ICM [25]. In order to contrast and compare the cases, constant comparative analysis was applied [25]. Qualitative comparative analysis seeks to compare cases in order to generate explanations. For the analysis, a so-called truth table was developed in order to test the absence or presence of each step of the ICM [25]. The goal of this analysis approach was not to force the data into predetermined categories, but to show that the ICM enhances the knowledge of the implementation process of both cases. For this analysis the interviews were used. Subsequently, the focus group was analysed by comparing discussions of similar themes [37]. Both cases were interpreted in terms of success factors. Successful implementation was defined as a positive experience by participants.

Analyses were performed in atlas.ti 7.0.

The results of the case analysis are presented in three steps: 1) a chronological case description with a within-case analysis, 2) a cross-case analysis, and 3) the focus group analysis resulting in success factors for the implementation.

RESULTS

The interviews and focus group were held by a researcher (the primary researcher of the study).

1) Case descriptions

A reconstruction of both cases was made.

Chronological steps of Case 1 with a within-case analysis (introduction of a pre-incision checklist for cardiac surgery in a hospital) (Figure 1):

a. The *proposal for change* was derived from results of another partnering hospital. At the partnering hospital a larger project was initiated, which included a pre-incision checklist. That hospital presented favourable outcomes in a benchmarking analysis with other Dutch heart centres, which was underpinned by the results of the document analysis. Insights into explanations for the differences in patient-relevant outcome measures showed that a pre-incision checklist could contribute to a reduction of 120-day mortality rate.
b. The initial start of Case 1 took place with a pilot phase without the requirement to comply with the intervention. No clear *implementation team* was in place to inform potential participants about the use of the intervention, which left users unaware of its existence and added-value.
c. It was reported that an intervention was started, but it was not carried out as a standard part of the care process. An analysis through questionnaires was carried out in the beginning to investigate whether the initiative was considered important and whether the *culture and context* would be open to it. The questionnaire included questions on the importance of the checklist to the users and the climate for implementing the checklist which resulted from the document analysis. Questions focused on how long employees have been working at the hospital, whether they thought that colleagues in the ward were treated with respect, whether they felt that they can tell when something is not going well in the operation room, whether they agreed with the introduction of the pre-incision checklist and whether the timing of the check just before incision of the patient was right. These questions were comparable to the validated Team Climate Inventory (TCI), which is an instrument used to measure organizational climate and team building and development [38].
d. It was reported that the implementation took place very fast and time was needed to carry out more analyses and develop appropriate implementation strategies. A brief *implementation plan* was offered from an external partnership that had previously developed and implemented the initiative.

e. Next, the checklist was announced during a *team meeting* of cardio-thoracic surgeons and disseminated via e-mail to operation assistants. The dissemination was supposed to happen from within. Thus doctors and an anaesthesiologist were the primary contact persons in order to facilitate a low-threshold for asking questions and to prevent resistance from the people applying the checklist.
f. A period of *voluntary participation* with regard to applying the checklist for cardiac surgery was established for about one to two months.
g. In the subsequent step, the checklist was implemented in *routine care*. The implementation took place with a simple start and communication among involved colleagues.
h. An *evaluation* followed, which led to the conclusion of cardio-thoracic surgeons in the hospital that the initiative did not add value to their work. An e-mail was sent to all involved parties and the checklist was stopped. However, some questions that are part of the checklist were integrated into the standard time-out form of the hospital.

The implementation process of Case 1 took place between December 2015 and February 2016.

Chronological steps of Case 2 with a within-case analysis (preoperative protein-enriched diet) (Figure 2):

a. The implementation process started with an *outcome analysis as a basis* for the target. The analysis was based on an outcome registry. Results of the analysis of outcome measures of the hospital made participants feel an urge to change with the development of an improvement intervention. The analysis resulted in a clear target. The target was considered feasible, but difficult to combine with the aims and wishes of the patients to receive an operation as fast as possible.
b. The protein-enriched diet and the number of patients with undernutrition were analyzed and discussed in a multidisciplinary *implementation team*. The team consisted of a researcher, cardiologist, cardio-thoracic surgeon, anaesthesiologist, dietician, head of the hospital kitchen, nurse and researcher.
c. The target was refined and a *context analysis* conducted. The context analysis included an analysis of the current preoperative process for older patients. This analysis could lead to a delay in implementation. The context analysis was conducted and discussed in the implementation team, but not further disseminated to all participants involved with the initiative in order to increase support for the implementation. The context analysis was done in several steps to gain as much insight as possible into the current

process of care. This analysis formed the basis for the *problem analysis* to identify possible barriers and develop an implementation plan.

d. The *implementation plan* was drafted. The implementation plan included a financial plan. It also led to the development of implementation strategies. The implementation plan was adjusted based on feedback from the implementation team. After adjustments, each team member disseminated the implementation plan to the broader involved team in the hospital. Individuals were offered training on their future tasks concerning the implementation.
e. Subsequently, the protein-enriched diet was implemented in the form of a *pilot* aimed at including five patients.
f. After these inclusions, an *evaluation meeting* was organized with the implementation team. The implementation plan and inclusion criteria were adjusted and long-term goals were formulated.
g. In the subsequent step, *continuous feedback* was given via e-mail followed by another evaluation meeting with the implementation team where first results and outcomes were monitored. Following this meeting, adjustments to the plan were made and *implementation in routine care* was prepared.

The implementation of Case 2 took place between April 2016 and February 2017.

Figure 1. Flowchart of the implementation process of Case 1. Describes the process of the implementation of Case 1.

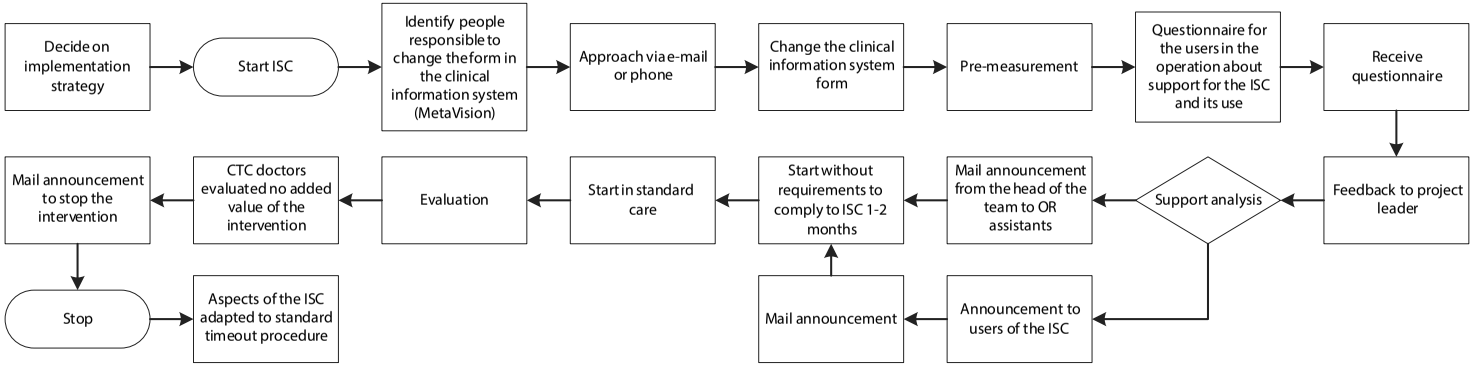
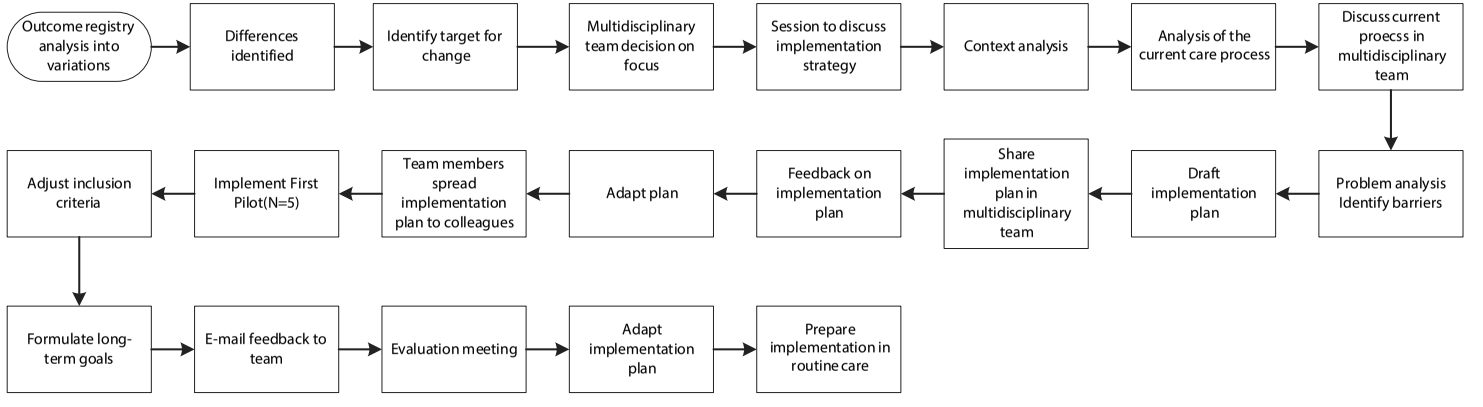


Figure 2. Flowchart of the implementation process of Case 2. Describes the process of the implementation of Case 2.



2) Cross-case analysis

Each case was tested against the ICM. Table 3 summarizes to what extent both cases were implemented according to the steps of the ICM.

Table 3. Checklist whether the steps of ICM have been applied per case.

		Case 1	Case 2
ICM	Development of a proposal for change	X	✓
	Analysis of actual performance	✓	✓
	Problem analysis of target group and setting	✓	✓
	Development and selection of strategies and measures to change practice	✓	✓
	Development, testing and execution of the implementation plan	X	✓
	Integration of changes into routine care	✓	X
	Continuous evaluation and adapting plan	X	✓

The first case was implemented without the application of a specific implementation approach, unlike the second case which used the ICM. Differences in the processes of both cases, as described in the case descriptions, included the development of a proposal for change, elaboration of an implementation plan, development of implementation strategies, testing and execution of the implementation plan and implementation into routine care. For the first case, the proposal for change was imposed by an external hospital through a network of hospitals [1]. Whereas, for the second case a detailed outcome analysis was conducted together with health care professionals who proposed to implement change based on the results of the analysis. The implementation of Case 1 started directly with a pilot phase followed by a culture and context analysis. An implementation plan was used from the external hospital, which was transferred to the current setting without adjustments. In Case 2, after formation of an implementation team, a detailed context analysis was conducted followed by drafting of an implementation plan suitable to the context. Concerning the implementation strategies, in Case 1 an announcement of the intervention during a team meeting and dissemination via e-mail was considered sufficient. In Case 2, the implementation plan was offered to individuals that would be affected by the intervention. The individuals were given the chance to comment and receive training on their tasks for the execution of the intervention. Furthermore, Case 1 was implemented into routine care after a short period of voluntary participation. The second case was not, yet, implemented into routine care, since evidence on the effect on outcomes was desired for the intervention to be implemented into routine care. In Case 1, no further interim evaluations took place. Only an end evaluation determining the stop of the intervention was organized. In comparison, for Case 2 continuous feedback was given followed by an evaluation meeting.

In the case comparison, a number of themes have been identified as most important for the implementation of improvement interventions with a focus on monitoring value (Table 4). These themes showed that the steps of the ICM enhance the implementation process of both cases.

- Support: Support is important in the beginning of the implementation and includes support for the proposal for change, but also for execution of the implementation plan. Support can also be linked to other steps of the ICM later on in the process, such as involvement and leadership.
- Personal importance of the target: Respondents mentioned that when an initiative feels important to them, the implementation process is improved.
- Involvement: For the problem analysis, involvement has been identified as a theme. For the first case, involvement was lacking and neither outcomes nor progress were shared with all participants involved in the initiative. That led to frustration and less uptake of the initiative.
- Leadership: Participants mentioned that there was no clarity on how to use the intervention in Case 1. This should have been resolved by having one leader in the operation room. That leader was not clearly defined and did not clearly perform his tasks. Therefore, the initiative lacked uptake.
- Climate: Development and maintenance of a positive climate were mentioned as being important for successful implementation. Room for critique and adjustment should be present.
- Monitoring: Monitoring, as part of the last step of the ICM, has been identified as important. Monitoring in the first case would have supported uptake as well. As mentioned by R2, if it had been monitored how often the checklist was used, it would have been possible to intervene faster.

These themes are linked to steps of the ICM in order to see whether the ICM has added-value for the implementation of improvement initiatives in the context of VBHC. However, for one step of the ICM, namely step 6. Integration of changes into routine, no important theme across cases was identified.

Table 4. Results of the cross-case analysis.

Steps of the ICM	Theme that emerged from cross-case analysis	Representative quotations
1. Development of a proposal for change	Support	R6: "The people who perform it are often not involved in such a thing." R2: "So you are asking for extra commitment from people; if you ask, you also have to return something. If that does not happen, and there is not much support in advance, then it will break down."
2. Analysis of actual performance	Personal importance of the target	R7:"We have all looked at whether this is a feasible goal and how can we do it all based on the analysis we had." R5: "Certainly, the goal is that every patient who is undergoing an aortic valve replacement receives a protein-enriched diet (…). That it becomes a standard of care is actually the goal; it must be a standard concern."
3. Problem analysis of target group and setting	Involvement	R2: "So that you're involved, that you should receive the result, so that's important." R6: "I was always kept up to date, so that was nice". R2: "Yes, I think it's important that everyone is involved. In particular, because if it does not happen, or someone forgets or does not feel like it, or quickly wants to do it, that someone in that operation room, even if it's the operation nurse, can say: 'Hey, those questions should also be asked.' If the whole team knows that the question has to come up, they will do it, but if only the surgeon knows and he forgets, you think: yes, it happened again." R2: "I think in advance, everyone's role should be clearer, not just the one who does it, the surgeon and the anaesthesiologist, but also the others."
4. Development and selection of strategies and measures to change practice	Leadership	R2: "So in the group, that is certainly decisive in the operation room, there was a difference in opinion that did not really help. If all surgeons would say: 'No, we should definitely do that', that is important."
5. Development, testing and execution of the implementation plan	Climate	R1: "I think that the climate is good and that people feel free to indicate that. That is also one of the prerequisites for successfully implementing something like this, that every player on the team is free and feels free to simply say what he or she thinks."

Table 4. Continued.

Steps of the ICM	Theme that emerged from cross-case analysis	Representative quotations
6. Integration of changes into routine care	No theme across cases identified	Not applicable
7. Continuous evaluation and adapting plan	Monitoring	R2: "If you see after two weeks that only half of the patients have been done, you should say: It was only 50%; it should improve. And then you have to go back two weeks later to make sure that you get 60%. Otherwise, you have to talk to people about: How did this happen?" R3: "We have been sitting extensively on those Thursdays, what should change to improve the success of the implementation and whether there are additional patient groups that can be included." R8: "Yes, sometimes sending a mail like: guys, remember it."

3) Focus group analysis: Success factors for the implementation of improvement interventions

A focus group interview was conducted with four professionals who were also involved in the earlier interviews to critically reflect on the results of the interviews. Several success factors were identified: intrinsic versus extrinsic motivation, a multi-centre intervention compared to a single-centre intervention, the name of the intervention, speed of the implementation process, complexity, continuous feedback and output.

Firstly, the aspect participants reflected on was the fact that the motivation for successful implementation differs when the *motivation is extrinsic*, i.e. an intervention that is adapted from another hospital versus an intervention that the hospital developed itself. Adapting an external improvement intervention could potentially lead to social pressure for implementation, which could impact success.

> "That of course makes a difference whether you invented something yourself and have time to roll it out or if you adapt something from outside. If you really want to participate, then you have to start before a certain date. Otherwise we are too late. That is missing here." (R4)

Secondly, the *name of the intervention* which includes the name of another hospital has an impact on the success of the implementation, as elaborated by R7:

> "Yes, or what you call it. I hear you call it differently. What is the difference from the original name? So then it is just what you call the intervention, because maybe you do it the right way, but you just call it a number of things under a different name. If it would have been called a different name, maybe we would have been more willing to apply it."

Thirdly, the *speed* of an implementation is dependent on whether the intervention involves a multidisciplinary team or a smaller team. Participants mentioned that a systematic implementation model would be applicable for straightforward interventions, but decisions have to be made for interventions that require more extensive research in order to follow.

> "The first case is something you have to implement with a whole team; it's multidisciplinary. You have to get the anaesthesiologist, all participants of the time-out, the perfusion, the nurse, everyone has to support it. So many people need to say yes; I don't see this happening." (R4)

Fourthly, the *complexity* of an intervention influences the success and speed of the implementation. An intervention that is less complex would not need to follow all the steps of the model.

> "I think if you do something with some kind of work agreement – so this is a work agreement that, for example, you only let members of the medical staff operate – then you need to follow fewer of those steps. I mean, it's something you do that you agreed on with the whole team. But if you do something like Case 2 where you also have to measure things, then you have to start with the measurement. You have to organize something for recording the outcome (…) and have good data, and then yes, develop a proposal for an improvement. Yes, that sometimes starts before step 1." (R4)

Fifthly, *continuous evaluation* of outcome measures can be time-consuming, but are also crucial for successful implementation and support. Participants also discussed continuous feedback.

> "But shouldn't you let the proposal for change come back continuously because that is at step 3, then data analysis, problem analysis. If you are going to implement strategies, then you actually want to see what effect it has. (…) Because if you have implemented your number of things, then you actually want to know what is the effect of that. And maybe it has no effect. So I would repeat the proposal for change more frequently." (R4)

The participants noted that it could also be necessary to return from one step to the beginning in a systematic implementation model.

Sixthly, *output* was also mentioned as being important for successful monitoring. Output, the goal of a successful implementation, should be defined before implementation and, next to outcome measures, be evaluated continuously.

> "This is not even outcome, it is output. In terms of input, throughput, output, outcome. I always make the comparison with a vaccination program. Output is how many people you vaccinate, and the outcome is the observed decrease in the prevalence of a condition in an area." (R7)

The focus group interview identified six success factors for the implementation of improvement initiatives in the context of VBHC.

DISCUSSION

The study had three objectives: to investigate the implementation of improvement initiatives in the context of VBHC, to explore how implementation science could be of added-value for VBHC and vice versa, and to investigate what we can learn from the implementation of two cases in the context of VBHC. To accomplish these objectives, we compared two cases, one that used the ICM and one that did not. In this study, we showed that the use of an implementation model such as the ICM contributed to a more positive experience of the implementation team and better uptake.

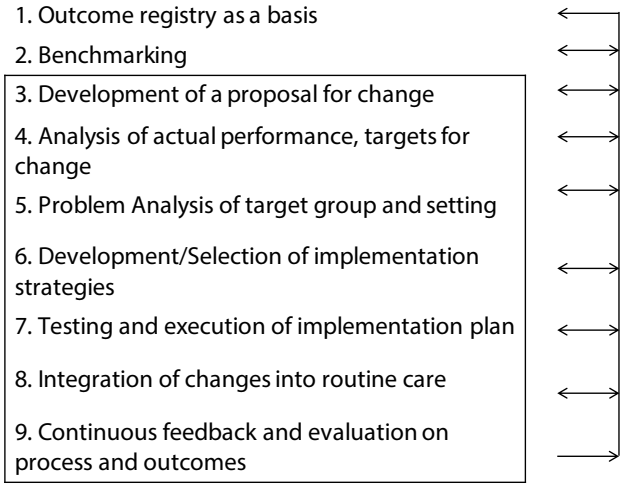
Our study identified important themes for the implementation of improvement initiatives in the cross-case analysis. The factors identified in this study are in line with previous research from implementation science. Grol et al. also identified incentives for uptake in relation to the ICM steps, which include conveying a positive attitude towards change and motivation [39]. The literature identified the practitioners' or users' support the change as a leading factor for guideline adherence [40]. In our study, personal and professional involvement in the design of the intervention played an important role in the success of the implementation. Previous research also identified involvement as a success factor for uptake of clinical practice guidelines [40,41]. Implementation of guidelines is comparable to implementation of improvement interventions. Furthermore, participants mentioned the importance of strong leadership and a climate in which users feel free to discuss issues. Incentives for change can be established at various levels, such as in the social context

[39]. In the literature, the social context includes culture, leadership and collaboration [39]. The absence of social norms can hinder uptake [42]. Moreover, the composition of an improvement team should be diverse and include all relevant healthcare professionals, as noted in a systematic review of factors influencing guideline implementation [43].

The implementations themselves were considered successful based on the results of the interviews. The implementation process was experienced more positively for Case 2, even though it was not yet implemented into routine care. Nevertheless, the implementation of Case 2 does not yet show an effect on relevant outcome measures. The themes that emerged from the cross-case analysis indicate that the implementation of Case 2 was experienced more positively when support for the implementation is created through involvement, the improvement initiative is of personal importance, leadership was present and a positive climate was created. The implementation itself was considered successful based the process of the implementation, even though it was not yet implemented into routine care during the exploration of the current study. After completion of the current study, the improvement initiative laid out in Case 2 led to continued work. The results of the effect of the improvement initiative showed a significant improvement in protein intake and an indication of an improvement in hospital length-of-stay (results to be published). Based on these results, we expect that preoperative protein-enriched diet will become part of a bundle of improvement initiatives targeting frail elderly people undergoing surgery. Case 2 showed that an improvement initiative targeting preoperative preparation could improve protein intake and potentially outcomes. In contrast, in Case 1 participants felt uninvolved and that their needs were ignored since no room for evaluation was created. Whether the implementation in terms of impact on patient-relevant outcomes was successful could not be determined with this exploration on how improvement initiatives focussing on monitoring value were implemented. The goal of this study was not to reach a certain goal in quantitative terms, but rather explore what went well and what could be improved in the implementation process of VBHC improvement initiatives based on two cases.

Based on the results of this study, we built a framework for the implementation of improvement interventions. From the analysis of the success factors for the implementation of improvement initiatives, it appears that the ICM can add value to VBHC and the implementation of value-based improvement initiatives. We, therefore, propose an implementation model that integrates new steps identified through the interviews that are unique to VBHC in order to add value to the ICM and vice versa (Figure 3). The Integrated Implementation Model (IIM) consists of two additional steps next to the steps of the ICM. These two steps include: outcome registry as a basis and benchmarking.

Figure 3. Integrated Implementation Model (IIM) for improvement projects.



The steps adapted from the ICM are framed in black. The other steps are new additional steps to the IIM. The arrows on the side indicate the possibility for repetition of steps.

Currently, in the ICM there is insufficient focus on the measurement and application of patient-relevant outcomes measures. The final step of the ICM is 'Continuous feedback and evaluation' which includes evaluation of performance [14]. Grol et al., however, do not further define performance. Therefore, a focus on outcome measurement is necessary when applying the ICM in the context of VBHC. It is important to consider the proposed implementation model as a roadmap for implementation where at every step of the process possible adaptations need to take place and earlier steps must be repeated. There is support in the literature for our proposal of continuous monitoring of outcomes and adaptation where needed [39].

In the context of VBHC an implementation approach was lacking to guide the implementation of improvement interventions. Whether the IIM adds value to VBHC and vice-versa is yet to be determined and future research should focus on validation of the IIM. However, in the literature, the benefit of new models compared to parallel approached is discussed [44]. The application of an existing, suitable implementation approach is favourable [45]. However, depending on the context and needs a combination of frameworks is necessary [45].

Despite our efforts to rigorously follow the steps of qualitative research, this study has limitations. Firstly, complexity was identified as a limitation. In the first case, doctors

needed to change behaviour by adding questions to their usual time-out procedure, which is less complex than targeting the patients as in the second case. Whether an improvement requires doctors or patients to change, can impact support and uptake. As for guideline adherence, guidelines that can be easily understood and are thus less complex have a greater chance of uptake [43]. In our study, strong support and involvement before implementation were identified as important for ensuring successful implementation of complex improvement interventions. Secondly, the first case was part of a larger improvement initiative initiated by another hospital. The initial project included various aspects next to a pre-incision checklist, e.g. the implementation of additional information from actual transoesophageal echocardiography images immediately after induction of anaesthesia [28]. At the current hospital, only a small part of the larger improvement project was implemented, which could have impacted results and motivation for this initiative. Thirdly, comparability of the cases could have influenced the cross-case analysis. The intention was to choose two cases that could be contrasted, yet were also comparable. The cases can be contrasted given the fact that in the first case no structural implementation method was used, whereas in the second case, the ICM was used for the implementation. The cases are comparable, because both initiatives emerged based on outcome measures. However, substantial differences concerning the nature of the cases including the involvement of the health care professionals, the impact on workload, the type of outcome measures and timing, could impact the results. Both cases were implemented as value-based improvement initiatives as an organizational intervention. Fourthly, the composition of the focus group could also potentially impact the results. The focus group consisted of doctors, nurses, data managers and secretaries. Hierarchy could have potentially affected the data [37], as participants may have felt inhibited by the presence of a doctor. Fifthly, the number of interviewed participants was relatively small. Including more participants could have enhanced the description of the cases. However, all possible participants were included in the study. Sixthly, to quantitatively determine the success of the implementation, ideally we would measure the number of safety-checks filled in Case 1 and the number of patients in Case 2 that received protein-enriched diet. However, we did not follow the implementations prospectively, but instead retrospectively analysed the implementation process based on document analysis and interviews. The goal of this study was not to measure success in quantitative terms, but in terms of experience of the implementation process by participants. Seventhly, the data coding was conducted by a single researcher (NZ), which could have posed a threat to the reliability of coding. However, the results of the codes were discussed with three researchers (SG, GW and PvdN) to increase reliability of results. The coding method may have impacted the results of the analysis. Lastly, contamination of both cases may have influenced the implementation process of Case 2 as both interventions were implemented in the same

setting. However, both the interventions were implemented at different times (Case 1 between December, 2015 and February 2016 and Case 2 between April 2016 and February, 2017). Since Case 1 preceded Case 2, possible lessons from Case 1 may have influenced the process of Case 2. However, the teams that were involved in both implementations were substantially different.

We aimed to illustrate how a systematic implementation method could support the implementation of improvement interventions based on outcomes. In order to determine the degree of successful implementation, we recommend further studies to evaluate the effect of each case on the health outcomes relevant to the case. We also recommend to test the suggested IIM in a different setting.

CONCLUSION

Applying an implementation method such as the ICM which offers guidance for the implementation was found to be valuable for successful implementation. The primary focus for implementation of improvement interventions should be outcome measures because insights into outcomes (that are relevant for patients) give an actual picture of the value added of the improvement. This focus is applicable in general for the ICM, not only in the context of VBHC. We, therefore, propose using the IIM for interventions with the aim of quality improvement. Further research needs to be conducted to evaluate the use of the integrated model.

ABBREVIATIONS

VBHC = Value-based health care; ICM = Implementation of Change Model; TEE = Transoesophageal echocardiography; SAVR = Surgical Aortic Valve Replacement; TAVR = Transcatheter Aortic Valve Replacement

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APPENDIX

Appendix 1. Interview guide based on the ICM and VBHC concept.

Topic list ISC case
Start questions:

1. What was your role in the implementation?

2. Are there parts of the implementation process that you cannot say anything about due to lack of knowledge about the process?

Elements of the theoretical framework

1. Development of a proposal for change

- Was there a "target" / target for improvement identified at the beginning of the implementation?
- What was the target / goal for improvement?
- How was the target / target identified?
- What was the target based on?
- Was there sufficient support for the goal?
- Was the goal "attractive" enough for a change?
- Was the scope / impact of the goal feasible?
- Has the change proposal met your needs? (personal needs)

2. Analysis of actual performance, targets for change

- Was there a review of the actual performance? This assessment contains questions such as: what kind of care is given? What are the most important deviations from the proposed method?
- Did this analysis lead to a feeling of urgency / interest in the implementation?
- Has this analysis led to a sense of responsibility? Did you yourself feel responsible for the necessary improvement?
- Have concrete targets for improvement been discussed on the basis of this analysis?
- Was this analysis fed back to you?

3. Problem analysis of target group and setting

- Has an analysis been made of the context in which the change should be applied?
- Has an analysis been made about the facilitating or impeding factors for a successful implementation?
- Was the change proposal well communicated?
- Have you felt involved in the implementation of the goal?

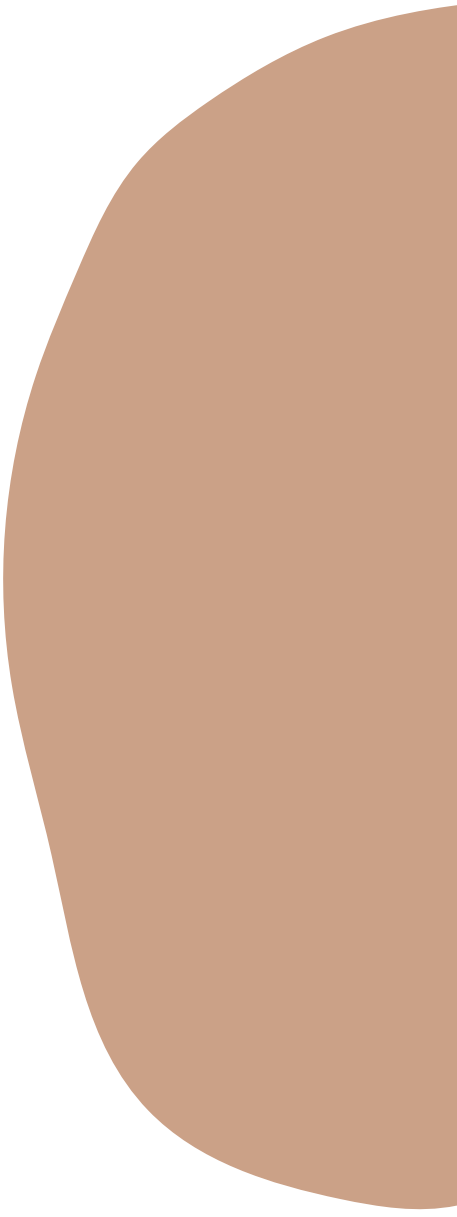
4. Development and selection of strategies and measures to change practice / Development or selection of improvement strategies
- Have implementation strategies been developed for successful implementation of the goal / change such as protocols, audit, feedback, computer-aided decision making, patient education, redevelopment of care processes?
- Have strategies been defined for dissemination of the goal / change?
- Was there a protocol / implementation plan shared with you?
- Was a plan for finances worked out? Was this plan shared with you?

5. Development, testing, and execution of an implementation plan
- Was the implementation plan tested in a smaller group?
- Was a pilot carried out?
- Was feedback requested on the implementation plan?
- Was the implementation plan adjusted with feedback?
- Was a proposal made as to how the project could be rolled out further?
- Are you involved in the evaluation of the pilot?
- Was your feedback on the pilot included in adjustments?

6. Integration of changes in routine care
- Have long-term goals been formulated?
- There was clear leadership
- Was there good cooperation?
- Are more people involved in the project if it was needed to spread it further?

7. Continuous evaluation and (possible) adaptions to the plan
- Was feedback regularly requested on the change?
- Has the change / purpose been monitored?
- Was feedback regularly requested on performance?
- Was the project adapted if it was necessary to guarantee sustainability?
- Have short-term, intermediate, and long-term goals been formulated?

Note: Respondents only need to answer questions that apply.

5

Offering protein-enriched familiar foods increases preoperative protein intake in older cardiac patients

Nina Zipfel
Stef Groenewoud
Jeanne de Vries
Benno Rensing
Eline de Heus
Edgar Daeter
Gert Westert
Paul van der Nat

Submitted.

ABSTRACT

Background: Older people with disease have a higher need for dietary protein to support good health and promote recovery after hospitalization than older people without disease. To achieve the recommended protein intake for older people with disease, protein consumption spread throughout all mealtimes of the day is suggested. The aim of this study was to increase protein intake by offering protein-enriched foods before hospitalization with a goal of 25 g protein per meal to contribute to optimal synthesis in the body.

Methods: For this intervention study with one treatment group, elective Surgical Aortic Valve Replacement (SAVR) patients aged ≥ 65 years and elective Transcatheter Aortic Valve Replacement (TAVR) patients ≥ 70 years were eligible (n=63). Two weeks prior to hospital admission, participants received protein-enriched foods and drinks at home to consume 45 g extra protein per day. Protein intake was assessed by online or paper-based food questionnaires on two days before and during the two-week intervention period. Protein and energy intakes were calculated with the 2010 Dutch food composition database. A paired-sample t-test was used to evaluate the within-subject change in protein intake, comparing intake before to intake during the intervention.

Results: Of the 96 patients enrolled in the study, 63 were included in the analysis. Protein intake increased on average by 54 g (SD ± 60) per day; from 84 (SD ± 32) to 138 (SD ± 66) g (p<0.001). Optimal protein intake of 25 g protein per meal was reached more often during the intervention for breakfast, lunch and dinner than before the intervention.

Conclusion: Offering familiar protein-enriched foods and drinks to older patients before cardiac surgery significantly increased protein intake.

INTRODUCTION

The prevalence of undernutrition among hospitalized patients is a frequent and serious problem [1,2]. Prevalence rates range between 25 and 30% in hospitalized patients in Europe [1–4]. In the Netherlands, 10 to 15% of hospitalized patients have a risk of undernutrition [5]. Among older hospitalized patients in the Netherlands, around 7.7% experience undernutrition assessed with the Malnutrition Universal Screening Tool (MUST) [6]. For the purpose of this study, undernutrition is defined as deficiency of a nutrient, such as protein [7]. An adequate intake of dietary protein is important for maintaining muscle and lean body mass [8]. The Dutch Health Council and EFSA recommend a protein intake of 0.8 grams per kg body weight per day (g/kg/d) as being adequate for healthy older individuals [9]. The recently published ESPEN guideline on nutrition and hydration in geriatrics recommends a protein intake of at least 1 g/kg/d protein [10]. For people with disease, there is a discussion as to whether this recommendation needs to be increased to 1.2-1.5 g/kg/d during and after hospitalization to contribute to improved recovery [11]. The recommendation of 1.2-1.5 g/kg/d is rarely met by elderly patients during or after hospitalization [12–14]. There are indications that a protein distribution over the day with 25-30 g protein per mealtime may contribute to optimal synthesis of protein [15]. Consumption of protein during all mealtimes is, therefore, even more important. In the Netherlands, however, protein is mainly consumed during lunch and dinner accounting for 30% and 40% of daily protein intake, respectively.

Consequences related to undernutrition in elderly people include impaired muscle function, decreased bone mass, impaired immune function, delayed wound healing, delayed recovery from surgery, prolonged hospitalization, increased mortality and extra healthcare costs [16–20]. Extra healthcare costs may be caused by prolonged hospitalization, hospital-acquired infections or costs for the treatment of undernutrition [21,22]. Previous studies on the effect of preoperative nutritional support have been conducted in patients undergoing surgery, but these studies mainly included cancer patients regardless of age, patients with hip fracture, and patients with end-stage liver disease [23–26]. Studies suggest the added-value of nutritional support for patients without proven undernutrition [27,28]. Early studies identified that undernutrition in hospitalized patients was most frequent in patients undergoing major vascular surgery [29]. Therefore, for older patients with disease it is even more important to prevent undernutrition during hospitalization by improved protein intake before hospital admission. A previous study found that 22.6% of older cardiac patients had inadequate protein or energy intake preoperatively [30].

Measuring and improving patient-relevant outcomes for patients in heart care has been a focus in the Netherlands since 2011 [31]. The current study was conducted as part of a larger project to improve outcomes of older patients undergoing aortic valve replacement with a preoperative protein-enriched diet. These patients are at relatively high risk for prolonged length of stay, higher mortality and postoperative complications [32–34].

The primary aim is to investigate whether consumption of familiar protein-enriched foods before hospital admission for Surgical Aortic Valve Replacement (SAVR) or Transcatheter Aortic Valve Replacement (TAVR) leads to higher protein intake and to investigate the protein intake per meal.

METHODS

Participants

Two relevant treatments were chosen as a focus for the current study due to their relevance as part of an improvement project at a Dutch teaching hospital, the St. Antonius Hospital. SAVR is an invasive open-heart surgery that requires extensive rehabilitation. Patients are eligible for TAVR, a minimally invasive aortic valve replacement procedure if they are older than 70 years of age and have a decreased condition compared to a patient eligible for SAVR [35].

Participants were selected if they were elective SAVR patients aged 65 years or older or elective TAVR patients aged 70 years or older. TAVR surgery is a procedure that is suitable for frail older patients from the age of 70 and older which led to the divergent inclusion threshold for these two treatment groups. SAVR patients classified as vital in the heart team center, where treatment decisions are made, can also be eligible to receive open-heart surgery above the age of 70 years. Patients were eligible if their aortic valve operation took place between January 2017 and February 2019. Additional protein intake may be harmful for older cardiac patients with kidney dysfunction and hyperkalaemia [36,37]. Potential participants were not eligible if they suffered from [36] kidney dysfunction (estimated Glomerular Filtration Rate Modification of Diet in Renal Disease (eGFR MDRD)<60), hyperkalaemia (potassium >5.0 millimoles per liter (mmol/L)) or cognitive impairment, which was assessed after patients presented at their first outpatient clinic visit [30]. High protein intake may lead to or aggravate kidney disease [38]. It is, therefore, recommended to consume a low protein and low potassium diet. Patients with cognitive impairment were excluded to prevent recall bias on the questionnaires. In order to inform potential participants for this study, the electronic patient records were consulted to examine

the inclusion criteria. Study participants were recruited in three ways: by regular mail consisting of information letters and brochures on the intervention and protein-enriched foods, by personal contact with the doctor during the visit to the outpatient clinic (for SAVR patients) or to the elderly outpatient clinic (for TAVR patients), and by phone by the researchers. The physicians received information on the study through a presentation and written information. For the contact by phone, a detailed script was developed. Patients received an informed consent form by post and gave written consent. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Medical Research Ethics Committees United of the St. Antonius Hospital (Reference number: W16.170). Written informed consent was obtained from all patients.

Design

This prospective intervention study consisted of one intervention group of older patients undergoing SAVR or TAVR receiving protein-enriched familiar foods (Figure 1). A quasi-experimental study with a one-group pretest-posttest design without a control group is commonly used to test the effectiveness of an intervention and is superior to observational studies [39]. This study design was chosen due to the fact that this intervention was part of a larger improvement project targeted to include all eligible patients. The study was performed in the participants' home environment for two weeks before cardiac surgery.

Dietary intervention

Participants were offered two boxes containing various protein-enriched familiar foods during a two-week intervention period prior to scheduled aortic valve replacement. Familiar foods included bread products, juices, soups and pastry (Table 1).

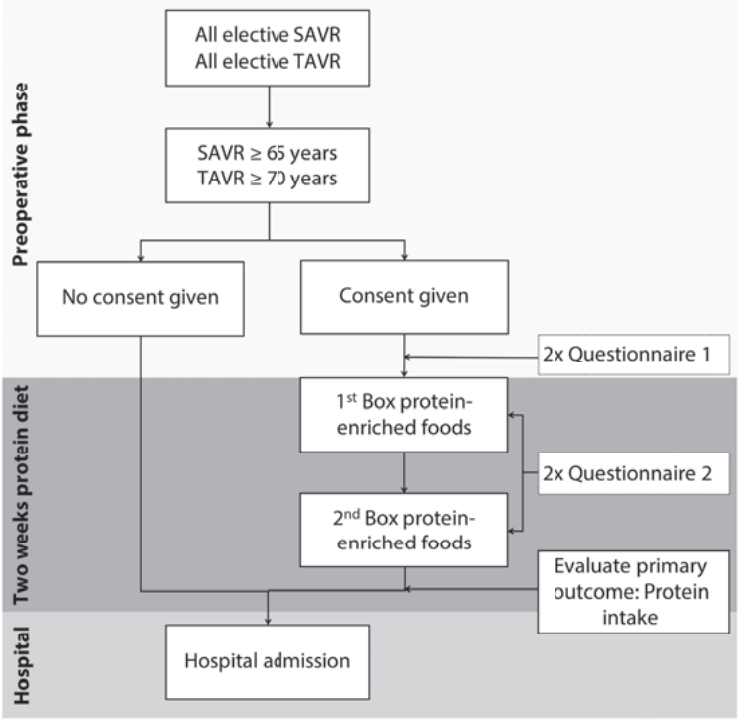
Table 1. Provided type of foods and protein content per serving size.

Food group	Food options	Serving size	Protein (g) per serving size intervention products	Protein (g) per serving size regular products [40]
Bread	White	35 g	6.0/9.5[A]	3.4
	Whole meal	35 g	6.1/8.5[A]	3.9
	Whole meal bun	40 g	6.3	3.4
	Raisin bun	65 g	7.6	3.4
Dairy drinks[B]	Forest fruits	150 ml	10.4	4.9
	Tropical fruits	150 ml	10.4	4.9
	Red fruits	150 ml	10.7	4.9
Juice	Apple-strawberry	150 ml	10.7	0.15
	Apple-blue berry	150 ml	10.5	0.3
	Orange	150 ml	11.0	0.9
Soup	Mushroom	150 ml	11.0	1.8
	Broccoli-cauliflower	150 ml	11.6	1.8
	Tomato	150 ml	10.5	1.8
Pastry	Apple cake	65 g	9.7	2.3
	Plain cake	50 g	10.1	3.6
	Muffin	50 g	10.1	3.5

A. Change in protein content of foods since 26.02.2018.
B. Dairy drinks not offered after 26.02.2018.

Participants received the foods in their home- environment to incorporate them into their regular diet. The foods were intended as a substitute to the regular foods consumed during breakfast, morning snack, lunch, afternoon snack and evening snack, which was stated in the patient information letter. The foods were not intended for dinner since previous studies have indicated that elderly people consume sufficient protein during their hot meal which is dinner in the Netherlands [24,41]. Each box contained foods and drinks for seven days for the two-week intervention period. The boxes contained products to achieve the desirable goal of 25 g of protein per mealtime from both animal- and plant sources. All participants received the same amount of foods in the box to achieve 25 g of protein per mealtime regardless of age, gender and bodyweight. In the first week, all patients received a standard box including the entire assortment of protein-enriched products (Figure 1). In the second week, participants could choose between three standard boxes with different products to reach the desired goals. Participants did not receive information with consumption targets or instructions. They were free to consume the products throughout the day suitable for their own diet.

Figure 1. Process scheme of the study group.



Describes the points in time of questionnaires and evaluation of results for patients who consented to participate compared to patients who did not consent to participate.

Assessment of patient characteristics and dietary intake

At baseline, the participant's descriptive measures were retrieved from the electronic medical record, including birth date, gender, medical procedure type, self-reported preoperative weight and height, and risk of undernutrition assessed with the Malnutrition Universal Screening Tool (MUST) [42]. The MUST measures the risk of undernutrition in three score categories; low risk (MUST=0), medium risk (MUST =1) or high risk (MUST ≥2). In addition, the mean body mass index (BMI) of each patient was calculated as body weight divided by height squared (kg/m^2). Protein intake was calculated per kg of body weight and considered adequate at an amount of ≥1.2 g protein/kg of body weight [10]. Unadjusted body weight was used for this study since this complies with an earlier similar study [43]. For the analysis of protein distribution over the day, the goal was to achieve the aim of 25 g for the three main meals of the day (breakfast, lunch and dinner) in order to contribute to optimal protein synthesis in the body [21]. Protein distribution over the day was calculated as protein intake for the following meals: breakfast, morning snack, lunch, afternoon snack, dinner and evening snack.

Dietary intake was assessed on four occasions: on two different days a week apart before the start of the intervention period; and on two days during the intervention; once in week one of the intervention and once in week two (Figure 1). The double measurements for both periods were used to account for within-person variability. In order to receive representation of all days of the week, a mix of weekend days and weekdays was attempted. At both time points before and during intervention, the average of the two days was calculated. Data was included in the study if participants responded to at least one questionnaire before and one during intervention. Validated 24-hour food questionnaires (24hr) were used for this [44–47], and completed by the participants online or on paper according to the preference of the participant. The questionnaire is based on the web-based 24hr module Compl-eat™ [47]. The 24 hr. recall questionnaire was deemed a valid method for protein intake assessment [48]. The questions concerned what participants ate on the day before, irrespective of the day of the week. The questionnaire was structured according to meals during the day and included both drinks and foods. Questions were asked about the amount consumed for a specific food item. For example: "How many table spoons of breakfast cereals (e.g. muesli, cornflakes, crispy rice cereal, etc.) did you eat at breakfast yesterday". Answer categories ranged from 0 to 10 table spoons. In case of different food types, follow-up questions were asked on the amount per type For example, after the question: "How much cheese did you eat for breakfast on your sandwich yesterday?", the follow-up question was: "How much cheese per type (hard cheese, soft cheese, cream cheese) did you eat at that time?". Intake was assessed with common household measures such as serving spoons. Protein and energy intake were calculated with the 2010 Dutch food composition database [40]. In order to identify underreporting of energy intake, the physical activity level (PAL) was calculated with the ratio of the total energy intake to basal metabolic rate (EI:BMR). This method is used to identify under-estimation of food intake from self-reported dietary assessment. A cut-off value of 1.35 indicates possible underreporting. An indication for compliance to the intervention was measured based on responses on the 24hr recall questionnaires, but it was not structurally measured.

Sample size calculation

Sample size was calculated to detect a 15 gram increase of protein intake per day as statistically significant. With a standard deviation of 25 g protein per day, a minimum of 22 participants was required (power = 0.80, $\alpha = 0.05$). This standard deviation was also applied in an earlier study with older Dutch people [49]. In order to account for a 10% dropout rate, a sample of 25 patients was considered sufficient. However, since the study was part of a larger improvement study, more patients were desirable.

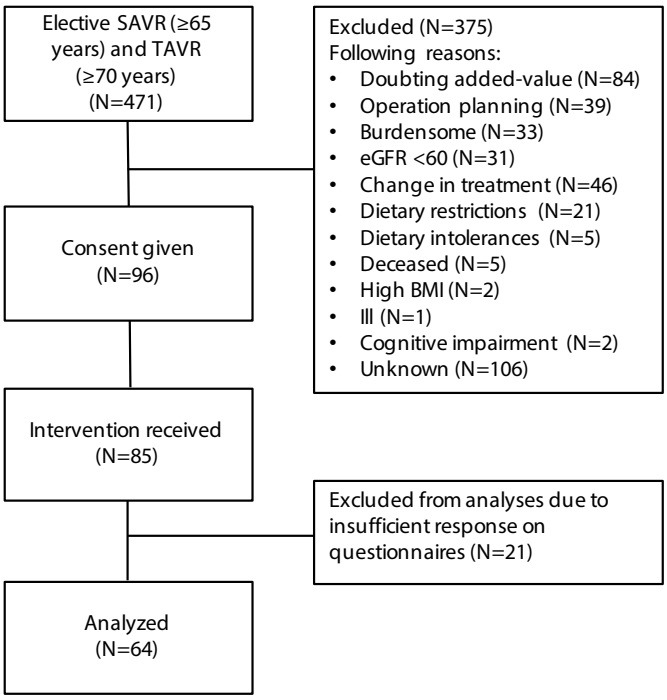
Statistical analysis

Descriptive statistics were used to describe baseline characteristics. Continuous data are presented as means and their standard deviations (SD), while categorical data are presented as numbers and percentages. The change in protein intake was analyzed by using a paired-sample t-test comparing means of protein intake of two days before and during the intervention. Subgroup analysis on protein intake was conducted for SAVR and TAVR patient groups. P-values of < 0.05 were considered statistically significant.

RESULTS

During the two-year study period (January 17th, 2017 until January 31st, 2019), 471 elective SAVR and TAVR patients of at least 65 years of age were screened for eligibility. After screening according to the pre-defined exclusion criteria, 300 patients were eligible of whom 96 signed consent for participation. Besides the defined exclusion criteria, the reasons for not participating varied from logistical issues with the operation planning to patients not wanting to participate because they did not see an added-value of taking protein-enriched foods. From the 96 participants, 89 participants had received the intervention at the time of the analysis. The remaining seven patients were still awaiting the operation date. The waiting list for a TAVR could be up to 12 weeks. Finally, 63 participants were included for analysis after excluding 26 participants due to insufficient response on the 24hr food questionnaire (Figure 2).

Figure 2. Flow chart of inclusion of participants and exclusion reasons.



At baseline, the participants had a mean age of 75.6 ± 5.6 years (Table 2). The majority of participants had a low risk of undernutrition according to the MUST score (76.2%). Before intervention, approximately 49% of participants had an inadequate protein intake according to the previously mentioned recommendation for older patients with disease (protein intake <1.2 g/kg/d). Of the participants at risk of undernutrition (MUST≥1), 50% had inadequate protein intake (protein intake <1.2 g/kg/d). Baseline characteristics did not differ for the remaining seven patients who also consented to participate.

Table 2. Baseline characteristics of study participants.

Baseline Characteristics	(n=63)	Range
Gender	31 (49.2)	
· Male, n (%)	32 (50.8)	
· Female, n (%)		
Age (y), mean ± SD	75.6 ± 5.6	65-87
Body weight (kg), mean ± SD	81.6 ± 20.3	51-155
Height (cm), mean ± SD	169.6 ± 8.9	149-192
BMI (kg/m^2), mean ± SD	28.3 ± 6.4	18-51
Procedure type	41 (65.1)	
· SAVR, n (%)	22 (34.9)	
· TAVR, n (%)		
Duration hospital admission (days), mean ± SD	7.6 ± 4.3	3-24
Risk of malnutrition (MUST score)[A], n (%)	48 (76.2)	
· MUST 0	4 (6.3)	
· MUST 1	2 (3.2)	
· MUST ≥ 2	9 (14.3)	
· Unknown[o]		
In-/Adequate protein intake[B], n (%)	31 (49.2)	
· Inadequate < 1.2 g/kg/d	15 (23.8)	
· 1.2 – 1.5 g/kg/d	8 (12.7)	
· ≥1.5 g/kg/d	9 (14.3)	
· Missing[C]		

BMI = Body Mass Index; MUST = Malnutrition Universal Screening Tool
A. Low risk: MUST = 0; medium risk: MUST=1; high risk: MUST ≥2
B. ≥1.2 g protein/kg BW per day is considered as an adequate protein intake according to the recommendations from the ESPEN Expert Group [11]. Unadjusted body weight was used.
C. MUST score not reported in the electronic medical record or not obtained

In the total group of participants eligible for analysis, the mean protein intake increased by 54 g (SD ± 60) per day from 84 (SD ± 32) to 138 g (SD ± 66) (p<0.001) during the intervention period. This corresponded to an increase of mean protein intake from 1.1 g/kg/d (SD ± 0.46) to 1.8 g/kg/d (SD ± 0.94) (p<0.001) for unadjusted body weight (Table 3). For SAVR patients, protein intake increased on average by 42 g (SD ± 53) per day (p<0.001) and for TAVR patients, which are the older patients unfit to undergo open-heart surgery, protein intake increased by 67 g (SD ± 64) per day (p<0.001). The energy intake increased significantly from 1783 (SD ± 691) to 2263 (SD ± 2263) kcal/d (p<0.01). The difference in total fat intake was borderline; intake increased from 60.7 (SD ± 31.8) g/d to 79.6 (SD ± 38.7) g/d (*p=0.054)*. For carbohydrates, the mean in gram per day increased from 187.0 (SD ± 71.4) to 230 g (SD ± 106) (p<0.01)

Table 3. Dietary intake before and during the intervention (n=63).

	Before	During	P-value[A]
Energy (kJ/d) ± SD	7020 ± 2776	9111 ± 4129	< 0.001
Energy (kcal/d) ± SD	1783 ± 691	2263 ± 1019	< 0.001
Protein (g/d) all patients ± SD	84 ± 32	138 ± 66	< 0.001
SAVR protein (g/d) (N=41)	88 ± 29	130 ± 65	< 0.001
TAVR protein (g/d) (N=22)	77 ± 37	144 ± 52	< 0.001
Protein (g/kg/d)[B] all patients ± SD	1.1 ± 0.46	1.8 ± 0.94	< 0.001
SAVR protein (g/kg/d) (N=41)	1.1 ± 0.45	1.7 ± 0.95	< 0.001
TAVR protein (g/kg/d) (N=22)	1.0 ± 0.49	2.1 ± 0.91	< 0.001
Fat (g/d) ± SD	60.7 ± 31.8	79.6 ± 38.7	0.054
Carbohydrates (g/d) ± SD	187.0 ± 71.4	230 ± 106.0	0.001

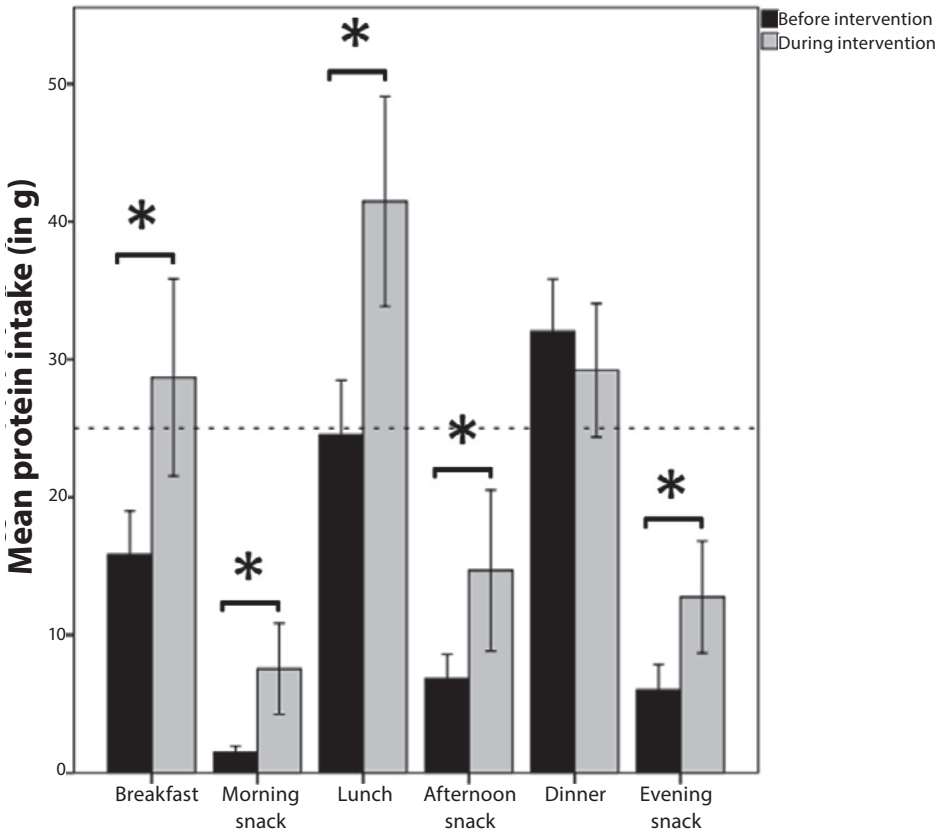
A. $p < 0.05$ indicates statistical significance
B. Unadjusted body weight was used

Protein intake per meal for the meals breakfast, morning snack, lunch, afternoon snack and evening snack increased in the intervention period compared to before the intervention (Figure 3). Only protein intake during dinner did not increase significantly. The recommendation to reach 25 g protein intake per meal during the three main meals of the day in order to contribute to optimal protein synthesis was reached for the three main meals (breakfast, lunch and dinner) during the intervention period compared to only one meal (dinner) before the intervention.

In order to evaluate possible underreporting, the ratio of the average energy intake to basal metabolic rate was calculated. The average energy intake (EI) to basal metabolic rate (BMR) ratio was on 1.2 before the intervention and 1.53 after the intervention. The ratio before intervention is below the cut-off value of 1.35 indicating possible underreporting. After intervention the mean food intake level is substantially above the estimated cut-off value of 1.35 [50].

Additionally, protein intake per food group was calculated according to the 2010 Dutch food composition database (**Appendix 1**). Protein in grams per day increased significantly during the intervention period for the following two food groups: alcohol or non-alcoholic drinks (p=0.027) and eggs (p<0.001).

Figure 3. Protein intake per meal before and during the intervention.



The figure describes the mean protein intake in gram for the six meal times (n = 63) before intervention and during intervention. The * indicates that there was a significant difference between before and during the intervention. The horizontal reference line was set at 25 g per mealtime.

DISCUSSION

To the best of our knowledge, this is the first study investigating the effect of preoperative consumption of protein-enriched familiar foods on protein intake in older patients in the preoperative phase for patients undergoing cardiac surgery. The use of the protein-enriched foods resulted in a significantly higher protein intake of 54 g per day, an increase from 84 to 138 g during the two-week intervention period. Almost all participants reached or exceeded the dietary protein intake recommendation for elderly people with disease of 1.2 g/kg/d during the intervention. The optimal protein intake of 25 g protein was reached for breakfast, lunch and dinner and the highest increase in protein intake was seen for breakfast and lunch.

Our findings are in line with previous intervention studies with protein-enriched foods performed in the Netherlands with an intervention period ranging from 3 days to 12 weeks, which demonstrated an increase in protein intake in elderly people [13,43,51–53]. A randomized controlled trial (RCT) with elderly participants showed an increase of 14.6 g for mean total daily protein intake in the intervention group when compared to the control group after an intervention of two weeks in the home environment (p=0.004) [53]. Comparable to our study, this study was performed in the participants' home environment, but the intervention products included readymade dinner meals besides protein-enriched bread. Our intervention foods were not intended for dinner, since research has shown that Dutch elderly people consume their protein intake mainly during dinner [41]. Another recent study used comparable protein-enriched products targeting hospitalized patients aged 65 years and older. The protein intake in the intervention group was 17.5 g/d higher compared to the control group (105.7 ± 34.2 vs. 88.2 ± 24.4 g/d (p<0.001), respectively) corresponding with a higher protein intake in g/kg/d (1.51 vs. 1.22 g/kg/d (p<0.001), respectively) [43]. Another recent pilot study in the clinical setting also found improvement in protein intake in patients without a risk of undernutrition [54]. However, like most other studies [13,52,55], this study was performed in a clinical setting instead of in the home environment. Morilla et al. (2016) analyzed studies concerning enriched and fortified foods in frail elderly patients and also found an increase in protein intake (a difference in protein of 7.0 g/day), even though substantially lower than the protein intake of the current study [56]. A remarkable difference between previous clinical studies and the current study lies in the food distribution and freedom of choice. Instead of provision of the protein-enriched intervention products per day, the foods in the current study were delivered at the patients' home per week. Participants were free to consume any of the provided intervention foods without provision of specific guidance on which products should be consumed per day. This freedom, however, might have led to the unwanted consumption of additional energy. The additional increase in energy intake indicates the need for consumption guidance in future studies. Considering both the use of familiar foods and performance in the home setting might have contributed to a desirable compliance to the intervention which was, however, not structurally measured in this study. Due to the study setting, it was not possible to observe food consumption. The self-reported questionnaires were designed to ask questions about specific consumption of the intervention foods, which gave an indication as to whether foods were consumed. In addition, the participants received a standard box with a large variety of food types and flavors in the first week and in the second week they could choose the foods they preferred. This might also have contributed to the compliance and might support the use of the protein-enriched foods in the long-term. However, we observed an undesired increase of energy intake. An earlier systematic review found similar results of increased energy intake [56]. The goal of this study was to keep energy intake at a similar level while increasing protein intake. Therefore, substitution

of foods from the regular diet of participants was only partially successful. Furthermore, protein is believed to decrease appetite [57]. In our study, this did not influence the intake as participants seemed to consume more energy during intervention. In our study, protein intake even exceeded the recommended intake of 1.5 g/kg/d. However, previous studies did not find a maximum anabolic response to protein intake and anabolic response declines with age, which would support our findings that older patients need to consume more protein to allow for optimal protein synthesis [58,59]. Another recent study in older cardiac patients also used the recommendation of 1.5 g/kg/d and concluded that older patients require a higher protein intake post-surgery [60]. Compensation behaviour can occur when participants consume specific other foods due to increased awareness towards this food group. No unwanted compensation behavior was observed since protein intake from the participants' regular diet (e.g. from meat, fish and cheese) remained the same (**Appendix 1**). However, participants consumed significantly more eggs, indicating an increased awareness about consuming more protein and a borderline increase in fat intake was observed. In order to determine the impact on plasma glucose, additional blood tests would have been necessary. However, since the goal of this study was not to implement an invasive intervention, additional blood and physical strength tests were not conducted. It is recommended that future studies include consumption guidance for protein-enriched products to prevent excess energy intake. Another strength of this study is the use of protein-enriched foods that are familiar to older patients. However, it is arguable whether the intervention should be recommended to all older patients. The majority of patients did not have a risk of undernutrition, but still had protein intake below 1.2-1.5 g/kg/d, which is what is recommended in the literature for older patients with disease [10]. Future research should focus on in-depth analysis of patients who had an adequate protein intake compared to patients with an inadequate protein intake in relation to patient-relevant outcomes. Those outcomes may include muscle strength, hospital length of stay, postoperative infections or even mortality. If a relationship between protein intake and postoperative and functional outcomes can be established, preoperative protein intake should be recommended to all older patients irrespective of their nutritional status. Next to improving the nutritional status of patients, functional capacity can have a significant impact on postoperative outcomes. Therefore, a study improving physical activity along with nutritional status could lead to the desired effect. The combination of three different recruitment methods (regular mail, personal contact during preoperative screening and potential phone contact) is considered an additional strength, as patients were actively approached. We recommend that future studies also use a combination of these three recruitment methods. However, we experienced that some patients remained unwilling to participate after personal or phone contact. Engaging patients preoperatively in a study was challenging. If health care providers would emphasize the importance of nutrition, it would be easier for future studies to involve patients. In the context of the

study, participants received the products free of charge, which might have improved their willingness to participate. In order to implement the protein-enriched foods into standard care, a payment support system, such as reimbursement, should be considered, as the higher costs associated with possible complications and longer hospital stays could be prevented. If long-term outcomes can be improved, investment in providing protein-enriched products preoperatively is relatively effortless and reasonable. This aspect will be further studied in the context of the larger improvement project.

This study faced potential limitations. First, a different study design, e.g. a randomized controlled trial, would have improved conclusions regarding the effect of a preoperative protein-enriched diet of familiar foods on protein intake. For the purpose of this study, a pretest-posttest study design was chosen without a control group. Addition of a control group and randomization would result in a stronger design, but was not possible due to feasibility and ethical considerations of an improvement project to be offered to all patients. Second, the use of 24hr recall questionnaires might have affected the results of the study. The dietary intake assessment method depends on the participants' short-term memory and cognitive abilities that are often affected in the older population. However, participants with cognitive impairment were not included in our study. The use of 24hr recall questionnaires on two occasions before and two during the intervention might not have been sufficient to account for day-to-day variation. Other studies used 3-day food records to monitor dietary intake [30]. Besides, the dietary intake was self-reported, which may have led to under- or over reporting. However, validity of two non-consecutive 24hr recall questionnaires was deemed sufficiently valid in earlier studies to assess protein intake on the population level [48]. Moreover, results on the consumption of the intervention products relied on the self-reported questionnaire. Since the setting of this intervention was the home environment, it was not possible to observe whether patients truly consumed the intervention products. Research has shown that underreporting of food intake is especially present in elderly people and people with a high BMI [61]. Moreover, we attempted to include all patients who participated in the analysis. The minimum criterion to be included in the analysis was that at least one preoperative and one postoperative questionnaire was filled in. In order to account for day-to-day variation, two questionnaires per time point would be preferred. Therefore, the results might be impacted by the limited possibility to account for day-to-day food consumption variation and might depict the most ideal scenario of the participants consumption. We also conducted the analysis with only including participants who filled in all four questionnaires (N=32). The results did not differ. Third, with the current study design and recruitment methods, selection bias could potentially have impacted the results. The exclusion criteria were formulated based on recommendations from the literature [36,37]. Patients also refused to participate due to the following reasons: the operation planning

gave too little time for the two-week intervention period, patients doubted the added-value of consuming protein-enriched foods, and patients found the study burdensome. This group would potentially also be less compliant with the intervention. The patients who were included were, therefore, potentially the most motivated ones and were thus compliant with the intervention products. In order to implement the study as standard care practice, it has to be acknowledged that for a hospital, logistics need to be in place for the operation planning and preoperative screening to collaborate for planning elective patients. Communication was seen as an important factor, as the operation planning needed to arrange a minimum of two weeks between first preoperative screening and hospital admission. For this study, an intervention period of two weeks was chosen based on earlier studies using preoperative ONS and feasibility [62]. Future research should focus on the effect of longer periods preoperatively in order to impact long-term outcomes, as a duration of ONS for patients with undernutrition or at risk of undernutrition of at least one month is recommended [10]. However, earlier studies on oral nutritional supplements consumption presented poor long-term compliance [63,64]. In the current study, facilitation of the research team was important. To implement the intervention in the standard care practice, a system needs to be in place for planning elective surgery of patients ahead. In the Netherlands, undernutrition occurs in 7.7% of hospital patients and in non-cancer groups undernutrition is most serious in patients undergoing major vascular surgery [20,29]. However, screening for undernutrition is not always a standard care practice. To make patients more willing to participate in nutrition interventions, it is recommended that health care professionals mention the added-value of a protein-enriched diet before undergoing cardiac surgery.

In other patient groups, a protein-enriched diet resulted in better health outcomes compared to groups that did not receive protein-enriched foods, even in groups without an indication for undernutrition [17–20]. Further research should investigate the effect of preoperative protein-enriched diet with familiar foods on health outcomes, i.e. mortality, postoperative infections and length of stay. A future study investigating the effect on outcomes (hospital length of stay, mortality and stroke) is currently underway and will follow-up on this present study. Furthermore, it is suggested that researchers implement the preoperative protein-enriched diet before undergoing cardiac surgery in additional hospitals, to be able to investigate the impact on health outcomes.

CONCLUSION

This study has shown that offering preoperative protein-enriched familiar foods to motivated older patients before undergoing cardiac surgery significantly increases protein intake.

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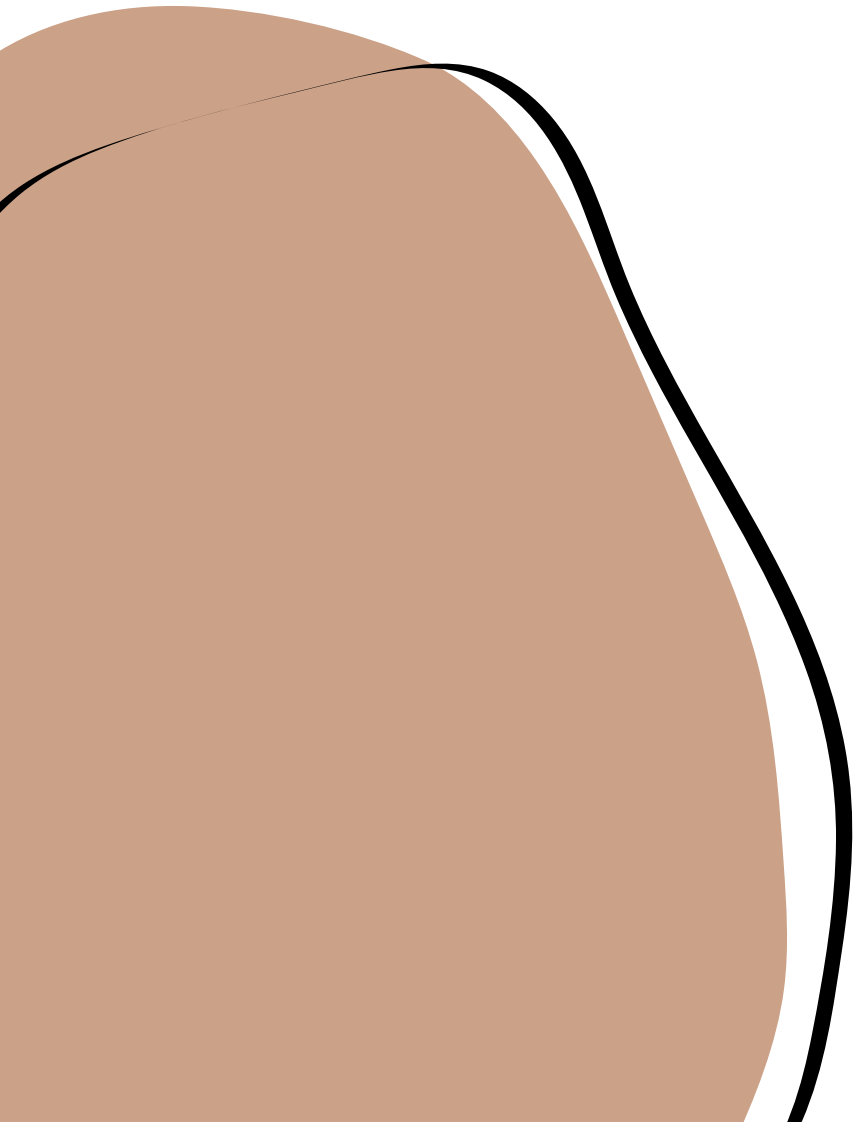
APPENDIX

Appendix 1. Protein intake before and during intervention per food group (N=63).

Food group[A]	Protein (g/d) before, mean ± SD	Protein (g/d) during, mean ± SD	P-value[B]
Soup	1.0 ± 1.7	1.5 ± 2.3	0.054
Alcoholic or non-alcoholic drinks	0.8 ± 1.1	1.1 ± 1.8	0.027
Bread	12.7 ± 7.9	13.2 ± 7.3	0.520
Nuts, seeds and snacks	6.9 ± 9.1	7.6 ± 11.4	0.638
Eggs	2.1 ± 3.6	4.8 ± 5.5	<0.001
Potatoes	1.3 ± 1.3	1.4 ± 1.2	0.788
Vegetables	1.9 ± 1.7	1.6 ± 1.7	0.274
Pastry and cake	3.2 ± 2.9	3.4 ± 3.6	0.438
Milk and milk products	11.9 ± 9.3	13.4 ± 10.8	0.164
Cheese	7.2 ± 8.6	7.4 ± 6.6	0.791
Grain products	1.5 ± 2.9	0.9 ± 1.7	0.120
Legumes	2.2 ± 4.4	2.2 ± 4.8	0.918
Savory bread spread	1.3 ± 2.6	1.4 ± 2.8	0.855
Soy products and vegetarian products	1.5 ± 6.4	0.9 ± 3.7	0.395
Fish	4.7 ± 12.7	4.1 ± 8.8	0.650
Meat	18.1 ± 15.5	18.1 ± 13.2	0.991



6

Value-based health care: improving outcomes with preoperative protein intake

Nina Zipfel
Stef Groenewoud
Benno Rensing
Edgar Daeter
Tom Oirbans
Gert Westert
Paul van der Nat

Submitted.

ABSTRACT

Background: Older patients have an increased risk of postoperative complication and prolonged length of stay (LOS) after aortic valve replacement (AVR). Preoperative preparation of older patients may contribute to higher satisfaction, prevent adverse events and lead to shorter LOS. The aim was to reduce LOS, mortality and stroke by offering preoperative protein enriched diet with familiar foods. The study was conducted in the context of a larger research program on Value-Based Health Care (VBHC) investigating how VBHC can be used to drive quality improvement (QI).

Methods: VBHC improvement cycles were used for this project. A multidisciplinary team was involved to select and implement the QI project and outcomes were monitored.

Intervention: Preoperative preparation included a two-week preoperative protein enriched diet. The intervention products were offered to all patients older than 65 and sent to patients' home. The surgery planning ensured a minimum of two weeks for the intervention period. LOS, 30-day mortality and stroke were evaluated

Results: After the two-year QI period, 47 patients who underwent surgical aortic valve replacement (SAVR) and 52 patients who underwent transcatheter aortic valve replacement (TAVR) participated. For all participating patients an intervention period of two weeks preoperative protein-enriched diet was ensured. LOS did not reduce with statistical significance in the total QI group compared to the group without intervention (p=0.756). For the separate treatment groups, the QI group had a slightly shorter median LOS of one day (SAVR: LOS=9 days compared to LOS= 10 days, p=0.338; TAVR LOS= 5 days compared to LOS= 6 days, p=0.079). Secondary outcomes for 30-day mortality and stroke did not differ significantly. The time effect analysis showed no trend.

Conclusion: The results showed a slightly shorter LOS, but due to power, the results were not statistically significant. VBHC can help to quickly generate an impact, but where an initiative has not been proven effective yet, an RCT would be preferred. Future studies should include a larger patient group to draw inferences.

PROBLEM

Value-Based Health Care (VBHC) was developed to redesign health care delivery to improve value for patients where value is defined as patient-relevant outcomes divided by costs over the full cycle of care [1]. However, it is yet unknown whether and how VBHC helps to actually improve outcomes or value. Using insights into outcomes based on the concept of VBHC to implement quality improvement (QI) initiatives can be experienced as more successful by involved staff [2]. But the way improvement interventions that were developed in the context of VBHC based on insights into outcome can be evaluated is not yet described.

In the context of a broader VBHC research program in heart care at a large Dutch teaching hospital in which the focus was on the use of outcome measures (the numerator of the VBHC value equation), improvement of preoperative preparation through protein-enriched diet was implemented. Older patients who need to undergo aortic valve replacement have a higher risk of postoperative complications as myocardial infarction, bleeding, vascular complications and long-term complications as neurological events including strokes, paravalvular regurgitation and endocarditis [5]. Postoperative complications can increase hospital length of stay (LOS) by up to an additional 14 days for TAVR and up to seven additional days for SAVR [6-8].

BACKGROUND

Aortic valve disease (AVD) most commonly occurs with age [3]. The prevalence of AVD in older patients accounts for 12.4% [4]. 3.4% of patients suffering from severe symptomatic AVD require aortic valve replacement [4]. Without surgery, the 5-year mortality is estimated to range between 50% to 80% [5]. For symptomatic AVD two treatments are recommended: Surgical Aortic Valve Replacement (SAVR) and Transcatheter Aortic Valve Replacement (TAVR), where TAVR is mostly chosen for older and frail patients that cannot undergo open heart surgery [6]. TAVR and SAVR patients can suffer from postoperative complications as myocardial infarction, bleeding, vascular complications and long-term complications as neurological events including strokes, paravalvular regurgitation and endocarditis [7]. Postoperative complications can increase hospital length of stay (LOS) by up to an additional 14 days for TAVR and up to seven additional days for SAVR [8–10].

The preoperative identification and management of morbidities and potential risk are crucial for reducing the risk of postoperative complications, prolonged LOS and mortality

[11]. Morbidities and higher risk for adverse outcomes are even more important in older patients [12]. Therefore, careful preoperative assessment of older patients can improve care of patients as well as contribute to higher satisfaction of surgeons due to efficiently planned surgeries and cost savings [11]. Currently, preoperative preparation of patients focusses on the history of patients including present illness, allergies, current medication and physical examination with vital signs [11,13].

Malnutrition among older patients occurs frequently [14,15]. Standard preoperative assessment should include screening for severe malnutrition [16], but nutritional support is most commonly only offered to the severely malnourished. It has been reported that nutritional support of several days preoperatively may reduce complications in severely malnourished patients [17]. In addition, studies suggest that nutritional support for older patients without proven malnutrition may also be beneficial in terms of improved outcomes [18,19]. Specifically, adequate intake of dietary protein can support recovery from surgery and maintenance of muscle and lean body mass [20,21].

Previous sub-studies in the broader VBHC program described the method of selecting and implementing improvement initiatives within VBHC [21,22]. The aim of the current study is not only to investigate whether a QI project aiming at improving preoperative preparation of older patients with protein-enriched diet, but at the same time to also investigate how improvement initiatives within VBHC can best be evaluated. A previous study suggests a framework for the evaluation of complex interventions. The framework, however, focusses on the effect evaluation of interventions in trial settings only. As reported, insights into outcomes enable quality improvement [31]. So it remains questionable whether trials are the holy grail for the evaluation of improvement interventions that emerged from VBHC.

To investigate evaluation possibilities of QI interventions from VBHC, the effect of preoperative protein-enriched diet on LOS, 30-day mortality and stroke was evaluated.

METHODS

Context

The St. Antonius hospital is one of the largest Dutch teaching hospitals in the Netherlands with a renowned heart center performing around 2000 heart operations yearly. The nursing ward of the cardiology department, where TAVR patients are treated postoperatively, has 32 beds. For patients undergoing SAVR, the cardiothoracic surgery nursing ward offers a

total of 80 beds. Approximately 65% of the SAVR patients are older than 65 years of age and 100% of TAVR patients are older than 65 years of age.

The hospital made use of the VBHC concept to continuously monitor and report outcomes since 2013 alongside several other Dutch heart centers [22]. The goal of the St. Antonius hospital was to apply VBHC to implement QI cycles and QI projects in order to improve outcomes. The outcome-based improvement cycle included the following elements: 1) monitoring outcomes, 2) identification of improvement potential, 3) selection of improvement initiatives, 4) implementation of improvement initiatives [22]. These steps were followed by the St. Antonius hospital and preoperative protein-enriched diet was identified, selected and implemented as the QI intervention with highest expected impact on outcomes.

Currently, preoperative preparation of older patients includes assessment of the history of patients including earlier surgery and earlier Transient Ischemic Attack, present illness including chronic lung diseases, diabetes and other chronic conditions with current medication, but also examination of the current illness and physical examination including vital signs and blood testing. Furthermore, patients are screened for malnutrition with the Malnutrition Universal Screening Tool (MUST). Patients with a risk of malnutrition (a score higher than 2 according to the Malnutrition Universal Screening Tool (MUST) [23] at preoperative screening are referred to a specialized dietician for further assessment for dietary intervention. Patients without a prevalent risk of malnutrition according to the global MUST score do not receive further dietary guidance or intervention.

Design of the improvement intervention

The intervention used for this QI project was preoperative protein-enriched foods and drinks. The details of the outcome-based improvement cycle are described elsewhere [22]. The intervention was selected in a multidisciplinary team of experts, including cardiologists (N=2), cardio-thoracic surgeons (N=2), anaesthesiologists (N=2), nurses (N=2), a data manager (N=1) and researchers (N=2) as part of a VBHC research program.

After the selection of the QI project, it was systematically implemented [2]. Eligibility criteria were formulated and the surgery planning informed to ensure the two-week intervention period.

All older patients regardless of their nutritional status receiving TAVR or SAVR were eligible to participate. Patients were free to decide whether they wanted to participate. Exclusion criteria were kidney dysfunction (eGFR MDRD < 60) and hyperkalaemia (potassium > 5.0

mmol/L) as additional protein intake may be harmful for patients [24,25]. The inclusion procedure is described in detail elsewhere [26]. Participants were offered two boxes of protein-enriched foods familiar to their regular diet including bread, juice, soup and pastry intended for all meals of the day except the warm meal, which is usually dinner in the Netherlands. Participants received two boxes, one for each week, of the two-week intervention period prior to hospital admission for TAVR or SAVR. The specific intervention products and their effect on protein intake have been described earlier [26]. All eligible patients were informed about the study through regular mail and received an additional phone call to offer more information on the QI project. Next to the primary researcher, a cardiologist and cardio-thoracic surgeon were involved and informed their colleagues on the improvement intervention. The administrative employees of the hospital operation planning were briefed about the intervention. Throughout the process of the QI project, the primary researcher kept the hospital operation planning informed about all patients participating in the study so that operation planning could act accordingly to ensure the interventions period of two weeks prior to surgery. The intervention products led to an average increase of protein intake by 54 g (SD ± 60) per day and recommended protein intake of 25 g protein per meal was reached during three meals after intervention compared to one before intervention which is in line with earlier studies on protein enrichment of familiar foods [26,27]. Eligible patients that did not want to receive the intervention products were still monitored on their outcomes.

The dismissal policy was not modified as the hypothesis was that offering preoperative protein enriched foods and drinks would enhance fitness of patients before undergoing surgery with the aim of enhanced or equal fitness postoperatively with the consequence of shorter LOS. The reason for not modifying the hospital's dismissal policy was to keep the evaluation of the effect of the QI as clean as possible.

Study of the intervention and measures

Currently, randomized-controlled trials (RCTs) are considered the golden standard to investigate the effect of interventions. But RCTs have major disadvantages. Namely, the population under investigation may not be representative of the real-world population, they are timely and costly and it can, therefore, take a long time before patients can benefit from the intervention. Only a small part of health care is based on evidence-based medicine, but rather practice-guided [28]. It is, therefore, important to investigate how these improvements can be evaluated [29]. With this study, a new form of evaluation of improvements was investigated, in which an intervention is implemented directly for all eligible patients and the impact on outcomes in a real-world setting is continuously evaluated.

The outcomes were chosen based on earlier analyses of the selection of an improvement intervention as they were expected to be improved by the QI project [30]. 30-day mortality and stroke were selected outcome measures from the Netherlands Heart Registry [31]. LOS was chosen as an intermediate outcome with impact on 30-day mortality in the earlier selection assessment.

The primary outcome LOS was measured in days from hospital admission prior TAVR or SAVR until discharge. Since the St. Antonius is a specialized hospital receiving patients from many different hospitals in the Netherlands, for the historic cohort and non-participating group only non-referral patients were included in the evaluation on the impact on LOS due to feasibility to extract data. In the patient group that participated in the QI, all patients who were discharged home after surgery, even if they were referred from other hospitals, were included in the study. Only patients that were not admitted in the primary hospital before surgery were included.

The secondary outcome was 30-day mortality, which was defined as death of any cause occurring within 30-days after TAVR or SAVR. All data was retrieved automatically from the electronic patient records. To ensure accuracy of the data, a random sample was selected and checked with information from the electronic patient records.

The goal of the evaluation of the QI project was not to evaluate its effectiveness in a trial setting, but to use historic data that were collected for the VBHC improvement cycle.

Analyses

To assess improvement in outcomes, prospective data of the patients participating in the QI project (February 2017-March 2019) was compared to data of a group of patients in the same period who did not participate. Normally distributed variables were expressed as a mean with standard deviation, and compared using Student's t-test. Categorical variables were presented as numbers and percentages and compared using the Chi-square test. Non-normally distributed variables were expressed as a median with standard deviation and compared using the Mann-Whitney U test (two-tailed). In order to assess the development in outcome measures over the years a global trend analysis was conducted including additional historical data from the period 2015-2016 to get optimal insight into the effect of the intervention. For the trend analysis crude data was analyzed with a positive trend defined as seven consecutive points below or above the overall median. All analyses were conducted using IBM SPSS Statistics using version 24 with a set p value at $p \leq 0.05$ as the criterion for significance.

RESULTS

Evolution of the intervention

Over the course of the two-year QI project 163 patients, including 58 SAVR patients, were included. The process of the QI project can be found in Figure 1. The mean patient age in the group without improvement intervention was 78.3 ± 6.1 and 74.4 ± 11.1 in the group with the improvement intervention (Table 1). Notably, the creatinine level was lowest in the prospective cohort with intervention, 89.9 ± 34.2, respectively. In terms of QI efforts, 47 SAVR patients received the improvement intervention and 52 TAVR patients received the improvement intervention as shown in Table 1.

Table 1. Baseline Characteristics for historic and prospective cohort and study participation.

Characteristic[A]	Prospective cohort without intervention (N=163)	Prospective cohort with intervention (N=99)	P Value[B]
Age	78.3 ± 6.1	77.1 ± 6	0.114
Male	89 (54.6)	52 (52.5)	0.744
Height	169.6 ± 9.5	169.5 ± 9.1	0.937
Weight	77 ± 13.4	80.3 ± 15.8	0.076
Diabetes mellitus	38 (22.3)	27 (27.3)	0.443
Creatinine (mg/dL)	99.8 ± 35.4	89.9 ± 34.2	<0.001
LVEF	49 ± 13.4	51.4 ± 12.1	0.132
Chronic lung disease	29 (17.8)	18 (18.2)	0.936
Previous cardiac surgery	43 (26.4)	13 (13.1)	0.011
Previous cerebrovascular accident (CVA)	18 (11)	7 (7.1)	0.289
SAVR	58 (35.6)	47 (47.5)	0.060

A. Characteristics are presented in mean ± SD, or n (%).
B. P Values were calculated with Student t test or the Chi-square test, as appropriate, for the difference between the prospective cohort without intervention and prospective cohort with intervention. P Value was found significant at $p \leq 0.05$.

Relevant outcomes

Table 2 shows the primary outcome LOS and Table 3 the secondary outcome 30-day mortality. The results show that LOS did not differ significantly between the prospective cohort without intervention (median=7) and the prospective cohort with intervention (median=7) (U=7726.5 , z=-0.578 , p=0.563). In terms of median LOS when considering both treatment groups separately, LOS was one day shorter in the group that participated in the QI project even though not statistically significant (SAVR: 10 days compared to 9 days, U=1255.5, z=-0.699, p=0.485); TAVR: 6 days compared to 5 days, U=2256.5, z=-1.784, p=0.074).

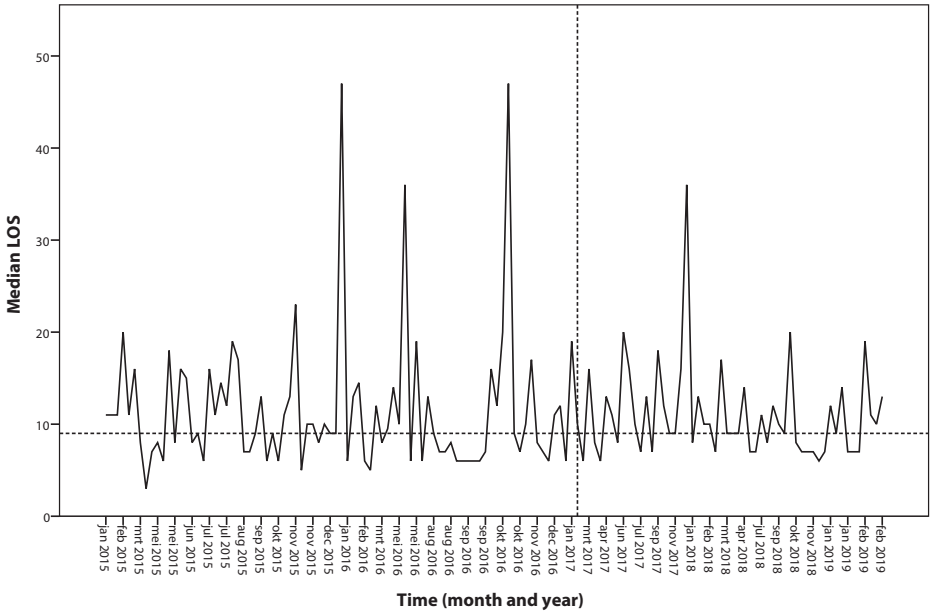
Table 2. Results length of stay (LOS).

	Prospective cohort w/t intervention (N=163)	Prospective cohort w/ intervention (N=99)	P Value[B]
LOS[A] total	7 ± 6.8	7 ± 8.5	0.563
LOS SAVR	10 ± 5.2	9 ± 11.3	0.485
LOS TAVR	6 ± 7.4	5 ± 3.4	0.074

A. LOS is presented in median days ± SD.
B. P Values were calculated with Mann-Whitney U test for the difference between the prospective cohort without intervention and prospective cohort with intervention (two-tailed).

When looking at the trend of LOS per month over the years of non-participants (2015-2019) in order to identify whether time is a factor contributing to reductions in LOS, no clear trend can be observed for SAVR (Figure 1).

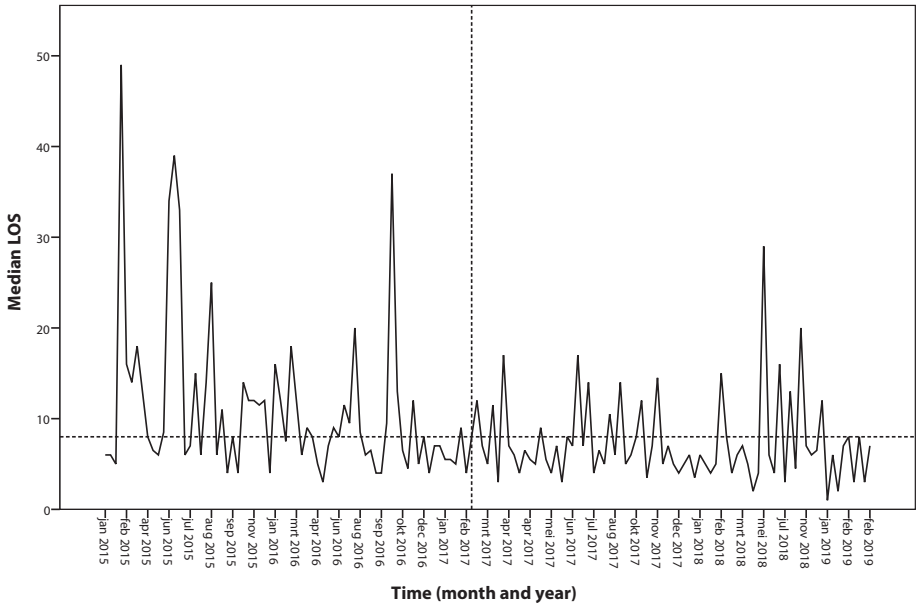
Figure 1. Length of stay (LOS) for SAVR per month for the period 2015-2019.



The horizontal reference line indicates the median (9 ± 7.5). The vertical reference line indicates the start of the improvement intervention (February 2017). Includes only and non-participants (N=151).

For TAVR an indication for a reduction in LOS per month was observed over the years (2015-2019) in non-participants with more points below the median of the historic cohort (Figure 2).

Figure 2. Length of stay (LOS) for TAVR per month for the period 2015-2019.



The horizontal reference line indicates the median of the historic cohort (2015-2016) (8 ± 9.3). The vertical reference line indicates the start of the improvement intervention (February 2017). Includes only non-participants (N=188).

For the secondary outcomes stroke and 30-day mortality, the QI group did not differ significantly (p=0.688 and p=0.53) (Table 3).

Table 3. Stroke and 30-day mortality.

	Prospective cohort w/t intervention (N=163)	Prospective cohort w/ intervention (N=99)	P Value[B]
Stroke[A]	9 (5.5)	2 (2)	0.688
Stroke SAVR	3 (5.2)	1 (2.1)	0.418
Stroke TAVR	6 (5.7)	1 (1.9)	0.279
30-day mortality	5 (4.8)	2 (2)	0.530
30-day mortality SAVR,	0 (0)	0 (0)	0.360
30-day mortality TAVR	3 (3.2)	1 (1.9)	0.383

A. Outcomes are presented in n (%).
B. P Values were calculated with Median test or Chi-square test, as appropriate, for the difference between the prospective cohort without intervention and prospective cohort with intervention.

EVALUATION OF QI INTERVENTIONS WITHIN VBHC

This QI project aimed to evaluate the whether preoperative protein-enriched diet in the context of a larger VBHC research program can lead to improvements and how improvement interventions can be evaluated.

The design of the study was believed to be the most suitable as outcomes were monitored for all patients in order to detect possible improvements. This was a large study with an extensive inclusion period. As the goal of the VBHC research program was to improve all outcomes for all eligible patients and all health care professionals knew of the QI project in order to inform patients, contamination might have contributed to the results in the group who did not participate. We believe, that the choice for direct implementation for all eligible patients versus an RCT approach should depend on the burden of proof and existing body of evidence. If an improvement initiative is expected to be effective and non-harmful based on existing evidence, an implementation for all eligible patients should be considered. It is important to distinguish this QI project from an RCT where evaluation of effectiveness would be the primary goal [31]. Whereas, the goal of this study was not only to generate new knowledge but to create positive change [31]. VBHC can help to quickly generate an impact, but where an initiative might pose possible harm and has not been proven effective yet, an RCT would be the preferred research design. In addition, it is important to realize that current research shows that outcomes of RCTs can show different results then outcomes of studies based on real-world data [43]. This would mean that if an RCT approach has been performed, a real-world validation would automatically need to follow.

Follow-up research is needed to provide better guidelines to support the decision on which research design or evaluation method is needed for specific situations. Independent of this decision, the current approach with detailed monitoring of the outcomes of a QI project is an improvement compared to the current situation in healthcare, since many improvement initiatives are now being implemented without evaluation [22,32].

DISCUSSION

In our two-year QI project of offering preoperative protein enriched diet to older patients, older patients who received the diet did not differ statistically significant from patients who did not receive protein enriched diet in terms of LOS, mortality and stroke. Although the slightly shorter LOS in the group who received protein enriched diet prior to hospital

admission was not statistically significant due to the power of the study, a possible indicative reduction was observed.

Our results are in agreement with earlier studies reporting that nutritional interventions have a positive effect on protein intake but weak effects on postoperative complications and LOS [33,34]. The study of Potter et al. reported a substantial reduction in LOS in an adequately nourished group, which supports our hypothesis that patients regardless of nutritional status can benefit from this QI [33]. Concerning mortality, earlier studies found significant associations between serum albumin as a marker for protein level and mortality [35]. A recent trial also found a statistically significant decline in mortality in older patients at nutritional risk and 37 patients with a need to treat to prevent one death [36]. Another randomized controlled trial investigated the effect of a high protein oral nutritional supplement and found 20.3 patients as the number to treat to prevent one death and also significantly lower 90-day mortality in the intervention group [37]. Our study could not find a significant improvement in 30-day mortality in the QI group. But since earlier trials suggest a positive effect on mortality and adverse outcomes, enhancing our study with a larger study group or a longer follow-up time might lead to statistically significant improvements. With regard to the secondary outcome stroke, stroke was found to positively contribute to lowering blood pressure which can decrease the risk of strokes [38]. Since hypertension is a strong risk factor for stroke, our hypothesis was that the number of strokes can be reduced by offering protein enriched diet. The results of our study, however, did not show improvement in stroke rates, which is in agreement with an earlier study conducted with a male Japanese population [39]. This is also confirmed by a study conducted in a female western population presenting inconsistent results on the association of protein and a lower risk of stroke [40].

Preoperative protein enriched foods and drinks could enhance preoperative preparation of older patients by maintaining muscle mass. It is suggested, however, that especially when combining nutritional interventions with exercise training, smoking cessation, reduction in alcohol intake, anaemia management and psychosocial support preoperative interventions have a chance of significantly improving postoperative outcomes and enhance rapid recovery [41,42]. An increase in protein intake may support improvement in walking capacity before surgery [43]. In order to improve postoperative outcomes, a bundle of preoperative interventions may be beneficial. In our study, physical exercise was not taken into account. Future studies should focus on the determination of combining protein intake and physical exercise for improving preoperative fitness of older patients.

This QI project required the involvement of various professionals involved in the care delivery process of older patients with aortic valve disease. Next to involvement, dedication from an executive team to guide the provision of information, arrange the delivery of protein enriched products to the patient's home and ensure accurate operation planning in order to allow a two-week intervention period are crucial to successful implementation of the QI project. The current QI project was implemented in a cultural context with eagerness to monitor outcomes based on the concept of VBHC. An open culture that embeds standard monitoring of outcomes for all patients might have contributed to the results. Replication of this QI project could be hindered by a lack of motivation of health care professionals, lack of financial support and lack of personnel to distribute protein enriched products and monitoring outcomes. Additionally, it is uncertain and context-dependent whether LOS can be reduced since discharge policies differ between healthcare providers. This may limit generalizability to other settings. Furthermore, this QI project was bound to a defined time frame which might have influenced the achievement of the desired number of patients for this study in order to discriminate an effect on 30-day mortality. Furthermore, in order to evaluate the effect of preoperative protein enriched diet a different outcome measure as for example re-hospitalization would be interesting to consider next to LOS and mortality. For this analysis re-hospitalization was not feasible as in the intervention group patients that were also referred from other hospitals were included. Data transfer about re-hospitalization was not possible. Future studies should focus on other endpoints to evaluate whether preoperative protein enriched diet contributes to faster recovery.

CONCLUSION

Improving preoperative preparation of older patients through increased protein intake did not lead to statistically significant improvement in outcome measures. However, preoperative protein-enriched diet is a relatively noninvasive QI intervention to improve outcomes which supports management of care beyond the hospital admission. The sustainability of a QI related to the provision of preoperative protein may ultimately depend on the involvement of the patient and health care professional. Future studies should include a larger patient group to draw inferences of the effect of preoperative protein enriched diet and improved outcomes.

Continuous monitoring and evaluations of outcomes as advocated by VBHC can help faster adoption of improvement initiative. However, as a result of the shift towards continuous monitoring of outcomes in healthcare, the distinction between scientific studies and quality improvement initiatives becomes less clear and needs better guidelines.

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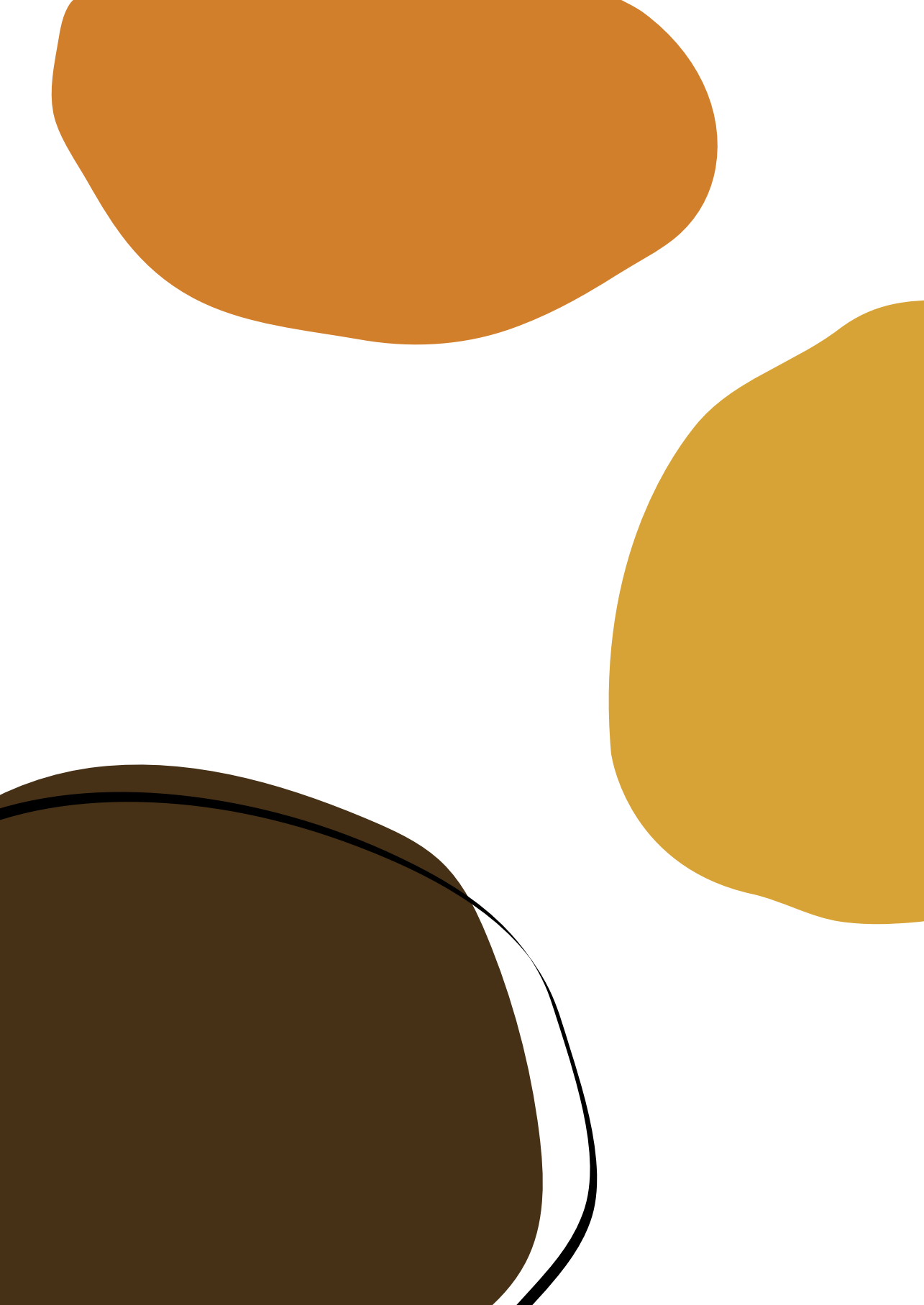

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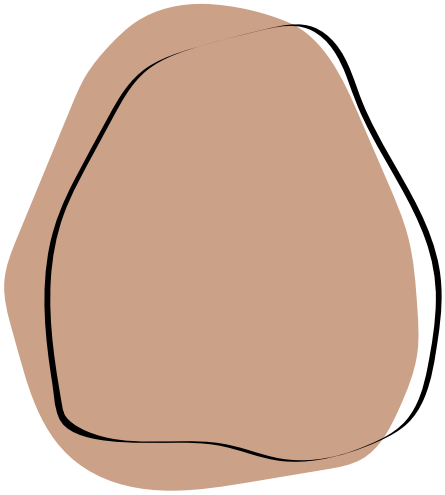
Developing process measures in value-based health care – the case of aortic valve disease



Berdel Akmaz
Nina Zipfel
Roland Bal
Benno Rensing
Edgar Daeter
Paul van der Nat

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ABSTRACT

Background: As process measures can be means to change practices, this article presents process measures that impact on outcome measures for surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) within value-based healthcare.

Methods: Desk research and observations of patient trajectories were performed to map the processes involved in TAVR and SAVR. Semistructured interviews were conducted with healthcare professionals (N=8) and patients (N=2) to explore which processes were most important in relation to a standard set of outcome measures that was already monitored. Additionally, open interviews (N=2) were held to prioritise results. A focus group was performed for validation of the formulated process measures. Numerical data for these measures was not collected.

Results: Process maps of the full cycle of care of TAVR and SAVR treatments in theory and in practice were developed. 28 processes were found important by interview participants due to their expected impact on patient-relevant outcomes. Seven processes were prioritised to be most important and were formulated into 12 process measures for both TAVR and SAVR: 'Number of times that deficient information provision to SAVR patients causes negative outcomes', 'Type of TAVR/SAVR prosthesis', 'Brand of TAVR prosthesis', 'Number of times frailty score of TAVR/SAVR patient > 75 years is measured', 'Time between TAVR/SAVR surgery indication and surgery', 'Number of times that anticoagulants stopped within 3 days before surgery', 'Time in hours between TAVR/SAVR surgery and permanent pacemaker implantation' and 'Percentage of standardised pain measurements'.

Conclusion: This study proposes addition of select process measures to standard sets of outcome measures to improve healthcare quality. It illustrates a clear method for identifying process measures with impact on health outcomes in the future.

INTRODUCTION

Recently, there has been a shift towards patient-relevant outcome measures in the Netherlands, notably value-based healthcare (VBHC), which defines outcomes as the actual results of delivered care [1,2]. The core goal of VBHC is to improve value for patients, defined as the health outcome achieved relative to costs [3]. To measure value, causality chains leading to patient-relevant outcome measures have been developed [1]. Moreover, the concept of care delivery value chains (CDVCs) in VBHC helps practitioners to understand, improve and integrate the activities related to a medical condition in the full cycle of care [4]. However, in practice, hospitals struggle to find ways to improve outcomes. Process measures could play a role in solving this problem because processes are partial predictors of outcomes [5,6]. Outcomes may be appropriate quality measures, but the link between processes and outcomes before quality measurement is performed should be regarded [5,7]. After quality measurement, redirecting resources towards the processes that have the greatest effect on outcomes could help to improve quality of care in the most efficient way [7]. Process measures comprise 'whether what is now known to be "good" medical care has been applied' [5]. They can be seen as handholds for practice change and are often based on work-as-imagined (WAI), which covers what managers, regulators and authorities believe happens in practice. When developing process measures it is important to consider work-as-done (WAD) as it reflects what practitioners found works best in practice [8].

In the Netherlands, VBHC is most advanced in cardiology and cardiovascular surgery. Processes are not commonly measured in surgery, but studies showed that differences in processes can be associated with improved surgical outcomes [9]. Previous studies identified infection-related and general process measures for all surgeries [9,10]. The Dutch Health and Youth Care Inspectorate defined a process measure for pain measurement [11]. The Dutch Association for Intensive Care has identified process measures specifically for the intensive care unit (ICU) [12]. Some studies identified process measures for cardiac surgery, that can be found through the National Quality Forum that included several process measures for all cardiac surgery in its database [13]. Process measures and their relationship with outcomes have been studied in depth for procedures such as coronary artery bypass grafting [7,9,14]. Some outcome measures have been identified for aortic valve disease (AVD), such as deep sternal wound infection [15,16]. However, little research has been done on processes and their relationship with outcomes for surgical aortic valve replacement (SAVR), transcatheter aortic valve replacement (TAVR) and conservative treatment, the three treatments for AVD [14–20]. There is no complete set of process measures regarding the full cycle of AVD care [21]. One study formulated quality measures for mechanical and biological aortic valves based on guidelines [19]. The Netherlands Heart Registry

(NHR), which measures heart disease outcomes to improve quality and transparency in participating cardiac centres, makes that distinction, too, for SAVR treatment. The NHR has also identified process measures for TAVR treatment [15,16,18–20]. Further, process measures have been identified concerning for example the proficiency of physicians performing TAVR [18–20].

Overall, most process measures in the literature are formulated for (cardiac) surgeries in general or do not consider the full cycle of care of AVD. This article illustrates how process measures can be embedded in the concept of VBHC due to their impact on outcomes. It focusses on a case of AVD and identifies patient-relevant process measures for SAVR and TAVR with potentially the highest impact on patient-relevant outcomes.

METHODS

Study design

For this qualitative explorative case study, data and theoretical triangulation were applied to increase internal validity, by carrying out desk research, observations, and semi-structured interviews. The results of the data collection were discussed in a focus group. All data collection was carried out by the primary researcher, that is, the first author (BA). The first author was a researcher that was not part of the treatment team of the hospital and therefore no relationship existed with the treatment team during the participatory observations, the interviews and the focus group.

Setting

The study was conducted in the cardiac centre of a Dutch teaching hospital. This single case was selected purposefully since the hospital monitored a standard set of TAVR and SAVR outcome measures from the NHR already, while it did not measure processes in the full cycle of care for AVD [15–17,22]. Therefore, this case illustrates the possibly beneficial relation between process measures and outcomes. Conservative treatment for AVD was not included in this study since a standard set of outcome measures was not yet developed at the time of the current study.

Interview and focus group participants

During the semi-structured interviews, healthcare professionals (N=8), a TAVR patient (N=1) and a SAVR patient (N=1) were interviewed individually. Purposive sampling was used to select interview participants in order to engage each profession involved in the full cycle of AVD care and to select patients of both TAVR and SAVR treatment [22]. The healthcare

professionals were a cardiothoracic surgeon (N=1), cardiologist (N=1), anaesthesiologist (N=1), perfusionist (N=1), data manager for cardiothoracic surgery (N=1), nurse on the post-operative wards for TAVR surgery (N=1), nurse specialist on the postoperative wards for SAVR surgery (N=1) and nursing head of the preoperative nursing ward for SAVR surgery (N=1). The sample size was considered sufficient since data saturation was reached after eight interviews. Subsequently, the same cardiologist and another cardiothoracic surgeon were interviewed in a second round of interviews (N=2) to prioritise the important processes that were identified in the first round.

The focus group (N=11) was also selected through purposive sampling and consisted of a cardiothoracic surgeon (N=1), perfusionist (N=1), cardiothoracic nursing department head (N=1), data manager (N=1), senior advisor board of directors (N=1), care manager (N=1), fellow cardiologist (N=1), neurologist (N=1) and anaesthesiologists (N=3). The sample size was deemed sufficient because all professions were represented. Notes taken during the focus group were transcribed and analysed.

Data collection and analysis

Desk research focused on WAI [8] and involved studying healthcare policies, protocols, and patient brochures. In addition, CDVCs were readily available at the hospital to identify large parts of the processes and to prepare 'theoretical' process maps. The theoretical process maps followed five phases of the CDVC: 'Diagnosing', 'Preparing', 'Intervening', 'Recovering and rehabbing' and 'Monitoring and managing'. 'Monitoring and preventing' was excluded from the process maps because this phase concerns a period before hospital treatment and takes longer time such as early age dietary habits. Moreover, this phase differs for each patient; some are referred by other hospitals and others present at the outpatient clinic with new heart problems.

Participatory observations of patient trajectories took place with patients preoperatively (N=2), during surgery (N=4) and postoperatively (N=2). During the observations, informal interviews addressing questions about WAD [8] took place, which added depth to the data. Field notes taken during the observations were transcribed and analysed. Subsequently, the theoretical process maps were completed and revised and 'practical' process maps were developed.

Following, semistructured interviews with healthcare professionals and patients were conducted by the primary researcher. The aim was to investigate which processes were considered most important regarding their impact on patient-relevant outcomes. Patient interviews were performed to also elicit patient's perspectives on that matter. Interview

questions (**Appendix 1**) were based on the CDVC and the WAD process maps. The standard set of outcome measures for TAVR and SAVR of the NHR that was already monitored in this hospital was used as a reference tool in the interviews to identify processes that could influence these outcomes (**Appendix 2**) [15–17]. The WAD process maps were an additional interview tool during interviews with professionals to show them the full cycle of care of AVD and help them point out the processes that influence outcomes. The interviews were audio-recorded with consent of the participants. One participant did not give permission to record the interview. Instead, the interviewer took extensive field notes that were checked by the participant. To increase internal validity, the transcripts of the remaining interviews were sent to the participants for a member check.

The interviews were initially transcribed and analysed by the primary researcher, using ATLAS.ti 8.0 software. Interview coding followed grounded theory, producing an overview of primary, secondary and tertiary codes [22]. First, inductive content analysis took place with open coding. Then, axial coding deductively led to categories from the various labels. With selective coding, the five phases of the care cycle defined in the CDVC were used as categories for the axial coding terms. Each category was further divided into 'Important processes', 'Improvements' and 'Improvements process map', separately for TAVR and SAVR. The final category concerned improvements regarding the process maps. In order to ensure internal reliability, co-authors were given insight into coding work and codes were discussed among co-authors. Issues were resolved until consent was reached. Moreover, co-authors evaluated the results that were presented by the primary researcher following the analyses, to increase trustworthiness of results.

After the results of the semi-structured interviews (N=8), a cardiologist and cardiothoracic surgeon were interviewed in a second round of interviews. These interviews aimed to prioritise the identified important processes from the first round of interviews and were used to define which processes were most important to translate into process measures. The interviews were open and began with the question: *Which processes in this list should be monitored as process measures in the future, considering their impact on outcomes?* Since the interviews were semistructured and open, the researcher was able to ask questions until depth was reached to increase internal validity.

Processes were defined important based on the number of times the measure was mentioned and the subsequent prioritisation by the cardiologist and the cardiothoracic surgeon. Subsequently, they were formulated into process measures by the primary researcher and were discussed in a focus group for validation. The primary researcher led the focus group, posing questions on how accurate the group members found the process measures and whether these could be improved. Numerical data for these measures was

not collected since the purpose of this study was to illustrate how process measures can be embedded in VBHC due to their impact on outcomes.

To reach external reliability during data analysis, an audit trail was created by keeping a logbook about inconsistencies in results, which were resolved based on consent among the authors. Moreover, potential inconsistencies in results also came to light during the prioritisation interviews with the cardiologist and cardiothoracic surgeon.

Patient and Public Involvement

Two semistructured patient interviews were performed and patients were included using purposive sampling. The outcome measures applied in this study are derived from the NHR [16]. Patients were involved as part of a selection team for the development of these outcome measures [23].

RESULTS

Theoretical process maps of how TAVR and SAVR treatments are 'imagined' were developed through desk research (**Appendix 3**). Looking at how work is done in practice provided varying or additional descriptions of the processes taking place in the full AVD cycle of care. The practical process maps are shown in **Appendix 4**.

Interview participants found in total 28 processes within the full cycle of care of TAVR and SAVR important due to their impact on patient-relevant outcomes. After prioritisation by the cardiologist and the cardiothoracic surgeon, seven processes regarding TAVR and/or SAVR were identified as most important out of the 28 processes:

1. Information provision to patients about SAVR treatment.
2. Valve choice for TAVR and SAVR treatment.
3. Frailty screening of patients undergoing TAVR and SAVR treatment.
4. Managing waiting lists for TAVR and SAVR treatment.
5. Stopping anticoagulants in SAVR treatment.
6. Pacemaker in TAVR and SAVR treatment.
7. Pain measurement in patients after SAVR treatment.

The seven prioritised processes are elicited in the next sections. As can be seen, not all processes are important or applicable for both TAVR and SAVR. Moreover, three measures were formulated for 'Valve choice'. Therefore, twelve process measures were formulated in total for both TAVR and SAVR as shown in Table 1.

Table 1. Process measures derived from the processes identified as most important.

Process	Process measure	Treatment	Outcome measure	N*
1. Information provision to patients about SAVR treatment	1. 'Number of times that deficient information provision to SAVR patients causes negative outcomes'	SAVR	Deep sternal wound infection	4
2. Valve choice for TAVR and SAVR treatment	2. 'Type of SAVR prosthesis: bioprosthesis type unknown; stentless bioprosthesis; stented bioprosthesis; mechanical; homograft; autograft; adhesion-free bioprosthesis and unknown' (NHR) [16]	SAVR	Valve re-intervention	2
	3. 'Type of TAVR prosthesis: balloon expandable; self-expandable and unknown' (NHR) [16]	TAVR	Permanent pacemaker implantation	3
	4. 'Brand of TAVR prosthesis'			
3. Frailty screening of patients undergoing TAVR and SAVR treatment	5. 'Number of times the frailty score of a TAVR patient >75 years is measured'	TAVR & SAVR	Mortality	3
	6. 'Number of times the frailty score of a SAVR patient >75 years is measured'			
4. Managing waiting lists for TAVR and SAVR treatment	7. 'Time between TAVR surgery indication and operation'	TAVR	Mortality	1
	8. 'Time between SAVR surgery indication and operation'	SAVR	Quality of life	2
5. Stopping anticoagulants in SAVR treatment	9. 'Number of times that anticoagulants are stopped within 3 days before surgery' (negative)	SAVR	Re-sternotomy → deep sternal wound infection	2
6. Permanent pacemaker placements in TAVR and SAVR treatment	10. 'Time in hours between SAVR surgery and permanent pacemaker implantation'	SAVR	Infection	2
	11. 'Time in hours between TAVR surgery and permanent pacemaker implantation'	TAVR	Mobilisation → quality of life Infection	1
7. Pain measurement of patients after SAVR treatment	12. 'Percentage of standardised pain measurements' [11]	SAVR	Lung infections Mobilisation → quality of life	2

* N = number of times the measure was mentioned by interview participants. N <3 signifies that the process measure was selected according to the prioritization by the cardiologist or cardiothoracic surgeon.

1. Information provision to patients about SAVR treatment
Information provision about SAVR treatment is part of the standard care process. One participant thought that uncertainty, because of deficient (incomplete or confusing) information could lead to patients not knowing when to mobilise postoperatively, which could lead to sternal dehiscence, making otherwise preventable infections more likely. Thus, 'information provision' was suggested as a process measure for the outcome 'deep sternal wound infection'.

2. Valve choice for TAVR and SAVR treatment
The valve choice for TAVR patients depends on the size and access route (transfemoral or transapical) of the stent. Different suppliers produce different types and brands of TAVR stents. Participants mentioned valve choice for both TAVR and SAVR as important due to heart rhythm disturbances that can lead to the placement of a permanent pacemaker:

> *'Heart arrhythmia has to do with the type of valve, because you have different types. One valve is placed a bit lower down and it can disturb the heart rhythm more than others do. This also applies to the TAVRs.' [cardiothoracic surgeon]*

However, SAVR valve choice cannot account for heart rhythm disturbances. The valve choice depends on the patients' age and need for anticoagulant therapy: older patients (>65 years) are offered biological valves because these last 15 years. Anticoagulant therapy is not necessary with biological valves which is an advantage for both older and younger patients. According to the participants, the SAVR valve choice influences the outcome 'valve re-intervention'. Valve re-intervention is also influenced by infections such as endocarditis. Moreover, valve choice is also influenced by gender: women who anticipate becoming pregnant receive biological valves to prevent bleeding during childbirth due to anticoagulation use after a mechanical valve.

To sum up, 'valve choice for TAVR and SAVR' could be a process measure for the outcome measure 'permanent pacemaker implantation' for TAVR and 'valve re-intervention' for SAVR. Correction for gender and age would be necessary when measuring SAVR valve choice in practice.

3. Frailty screening of patients undergoing TAVR and SAVR treatment
Participants argued that it is important to distinguish when patients are too frail to be treated, especially TAVR patients who constitute an older and therefore vulnerable patient population. Being too frail is a contraindication for TAVR. This decision could impact mortality because it can lead to a shift in mortality rates: if surgery is done there is a

probability that the patient might be deceased shortly after surgery due to frailty or live longer because of the treatment. If no intervention is carried out, 30-day mortality may be lower but, for example, more people could die in 1 year because they were not treated. Overall, a process measure for both TAVR and SAVR patients could be 'measuring the frailty score', which influences the outcome measure 'mortality'.

4. Managing waiting lists for TAVR and SAVR treatment

Both TAVR and SAVR treatments have waiting lists until intervention. After the decision for surgery, a long waiting list is unfavourable for TAVR patients because time-related complications can occur. The interviewed TAVR patient in this hospital had to wait longer than he/she had been led to expect. In turn, when a SAVR waiting list is too short, important tests could be missing. This can cause changes in surgery planning and lead to procedural delays, which could lower the quality of life. The interviewed SAVR patient pointed out that their waiting time was quite short. Thus, 'waiting time' was mentioned as a process measure for 'mortality' of TAVR patients and 'quality of life' of SAVR patients, where a balance in the length of the waiting list needs to be found.

5. Stopping anticoagulants in SAVR treatment

When the patient is admitted to the ward, medication policy is different for TAVR and SAVR patients. TAVR patients need to receive platelet inhibitors before surgery and SAVR patients taking anticoagulants need to stop three days before surgery. Stopping anticoagulants on time is considered important because it can prevent re-sternotomy, which can be related to infections:

> *'Also important is stopping anticoagulants before surgery. People often get various anticoagulant drugs which do not affect valve re-intervention, but for example, do affect re-sternotomy, which is not in the table. But re-sternotomy is indirectly related to deep wound infection, so if you can reduce that one...' [cardiothoracic surgeon]*

Moreover, stopping anticoagulants on time influences the risk of bleeding and blood transfusions. 'The number of times that anticoagulants were stopped within 3 days before surgery', was mentioned as a negative process for the outcome measure 'deep sternal wound infections'.

6. Permanent pacemaker placements in TAVR and SAVR treatment

All SAVR patients receive a temporary pacemaker. SAVR patients could risk having the temporary pacemaker leads in place for too long which can cause infections and bleeding:

'How often do you actually still need them [pacemaker leads] and does that weigh against the fact that they are still in there? Letting them stay in there can cause infection and bleeding.' [nursing head]

TAVR patients might receive a transvenous temporary pacemaker with which they are not allowed to move. If the temporary pacemaker can be removed or replaced by a permanent pacemaker quicker, there is a lower chance of infection and unnecessary bedridden time. Mobilisation can also start sooner and therefore quality of life improves:

> *'I think we need to remove everything faster. (…) That is certainly vital for old people. Out of bed quickly, everything out fast, all lines out, standing beside the bed quickly, yes. [Keep it in] as short [a time] as possible, the pacemaker.' [cardiologist]*

However, a temporary pacemaker should not be removed too quickly because a disturbed heart rhythm can also restore itself and prevent a permanent pacemaker:

> *'On the one hand I think it could be faster, if it is clear that someone needs it, then it should be done fast. But yes, that period until it is clear that it is necessary should not be too short either. So, say you wait two weeks to see if the rhythm gets better, then it is also fine to say after two weeks that a pacemaker is needed.' [nurse specialist]*

The TAVR and SAVR patients differed in this matter. The TAVR patient had to stay in bed for 5 days but wanted to mobilise quicker. However, the SAVR patient had already mobilised quickly in the ICU.

In sum, the 'time until a permanent pacemaker' was identified as a process measure for the outcome measures 'infection' (TAVR and SAVR) and 'quality of life' (TAVR). It remains a matter of discussion what would be an appropriate time for this measure.

7. Pain measurement of patients after SAVR treatment

Postoperative pain monitoring after SAVR and TAVR surgery is considered vital. Pain management together with physiotherapy helps SAVR patients to breathe properly, which prevents lung infections. Pain scores must continue to be measured consistently:

> *'Pain score is also important because if people are in pain and unconsciously inhale less deeply, then they risk getting atelectasis and then pneumonia. It is really important to measure the VAS score[1] so that they do not have any pain.' [cardiothoracic surgeon]*

1 Patients can score the pain they feel from zero to ten on the Visual Analogue Scale (VAS).

Pain medication is important for mobilising the patient and having a pain team at a hospital is favourable. Both TAVR and SAVR patients pointed out that their pain was continuously measured.

Overall, 'measuring pain scores' could be a process measure that influences the outcome 'lung infections'. In addition, 'administration of pain medication' may be a process measure for mobilisation, which could influence 'quality of life'.

DISCUSSION

Our study identified an extensive list of process measures with highest impact on outcomes, covering all the phases of the full cycle of (AVD) care except for 'Monitoring and preventing'. In this case study it appeared challenging in practice to achieve the ambition of VBHC of only measuring outcomes to improve quality of care. Our hypothesis is that solely focusing on outcome measures without taking their context into account, could lead to uncertainty about what is causing the unfavourable outcomes and where improvement is needed. Though, simply focusing on process measures without looking at the consequences for relevant outcomes could lead to improving the wrong aspects. Process measures are actionable and offer feedback about which quality improvement activities are needed to improve patient outcomes [9,24]. They can often be measured more easily and quickly than outcomes. For example, data collection can be fed back continuously and real time. In contrast, outcomes such as 'quality of life' may require extensive follow-up time [1,24]. Therefore, it is recommended to focus on both types of measures. Using process measures in combination with outcome measurement should not be about guideline adherence, but about how processes influence outcomes and in what way outcomes can be improved through process optimization [1]. Standard sets of outcome measures can be defined and used for benchmarking, but the process measures that impact outcomes can differ between organizations and should not be included in obligatory registries.

This study clearly illustrates how processes could influence outcomes in VBHC. Whether using the identified process measures will influence and improve outcomes in practice requires further research. Further research is also recommended to develop process measures for multiple settings, besides AVD. The process measures in our study are considered a valuable addition to the existing process measures in the literature. The definitions of The Dutch Health and Youth Care Inspectorate and the NHR have been used

for our pain management and TAVR and SAVR prosthesis type process measures [11,15,16]. A substantiation for our process measures in the literature can be found in **Appendix 5**.

Within the VBHC concept an outcome measure hierarchy to guide the development of outcome measures was proposed [6]. However, there is no practical tool for developing process measures with impact on outcomes. This study drafts a proposal for a method to identify process measures. First, it recommends identifying the full cycle of care for a disease using the CDVC concept. Second, it is important to take differences between WAI and WAD into account when identifying processes. If the understanding of WAD is incomplete or incorrect, then the idea of a particular intervention (process measure) with a particular consequence (outcome measure) could fail [8]. Our study supports this argument because new process maps after the observations (WAD) enhanced the reflection of the real-life situation. Third, interview results need to be validated by a focus group to confirm whether health care professionals agree with the definitions of measures to avoid ambiguity [5]. A group needs to work together to formulate and measure the process measures, and therefore process measurement fosters teamwork [1]. As in this study, it may take time or need further research to decide on definitions, such as how soon a permanent pacemaker implantation should take place. Finally, it is important to consider the feasibility of measuring the selected process measures. The processes should be discrete data that are recorded in for instance the electronic patient record, so that information can automatically be generated [24].

Limitations

While this case study was a good illustration of the possible relation between processes and outcome measures, performing this research at one single institution might limit the generalisability of the results. Though, process measures are also determined locally and are hospital-specific. Moreover, 'Monitoring and preventing' is important when considering the full cycle of care. However, the aim was to consider process measures that can be influenced within the hospital of this study and therefore this phase was beyond the scope of this study. Additionally, only two patients were interviewed. Yet, the goal was not to reach data saturation because after the interviews it became clear that patients have relatively little (technical) insight about which processes are important regarding their impact on expected outcomes. Furthermore, the same cardiologist from the first round of interviews was interviewed again in the second round to elicit his view on the priority of the processes, which might have influenced the results for prioritisation. Finally, unfortunately no cardiologist was available to participate in the focus group while this may have been an important additional view on the process measures.

CONCLUSION

This study proposes working with a selection of process measures in addition to a standard set of outcomes to improve quality of care. Our study illustrates how process measures might be used to improve outcomes in VBHC. Besides case-specific process measures, we were able to identify a clear method for the identification of process measures with impact on health outcomes in the future.

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APPENDICES

Appendix 1. Interview questions

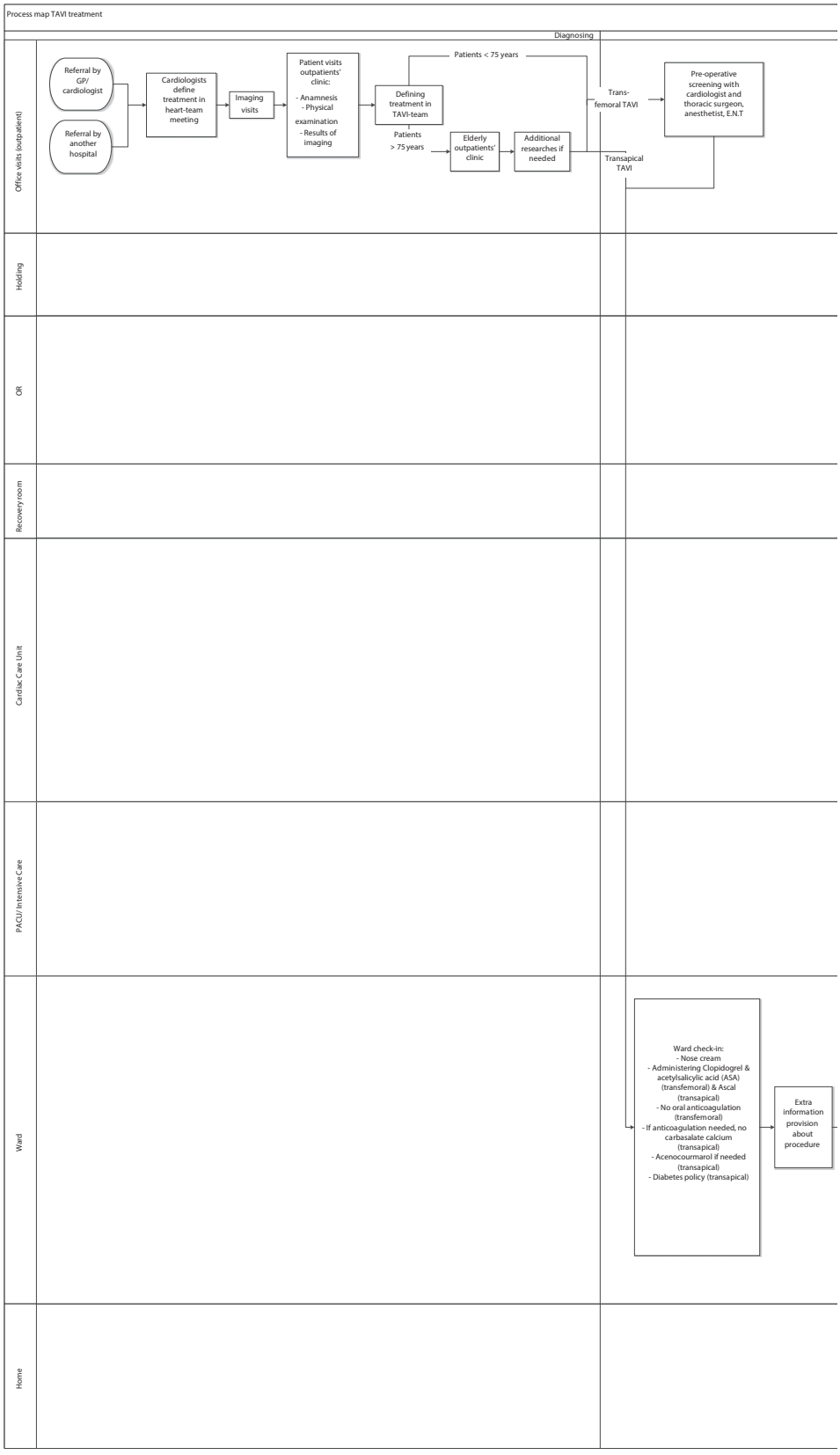
1. Which processes regarding Diagnosing/Preparing/Intervening/Recovering and rehabbing/Monitoring and managing do you think are the most important because they could influence outcomes? And why?
2. How would you prioritise them based on important to unimportant?
3. Are there any improvements possible within these processes? How could one handle these processes the best?
4. Are any other complications possible which may impact outcomes that severe, that you would want to measure and track them?

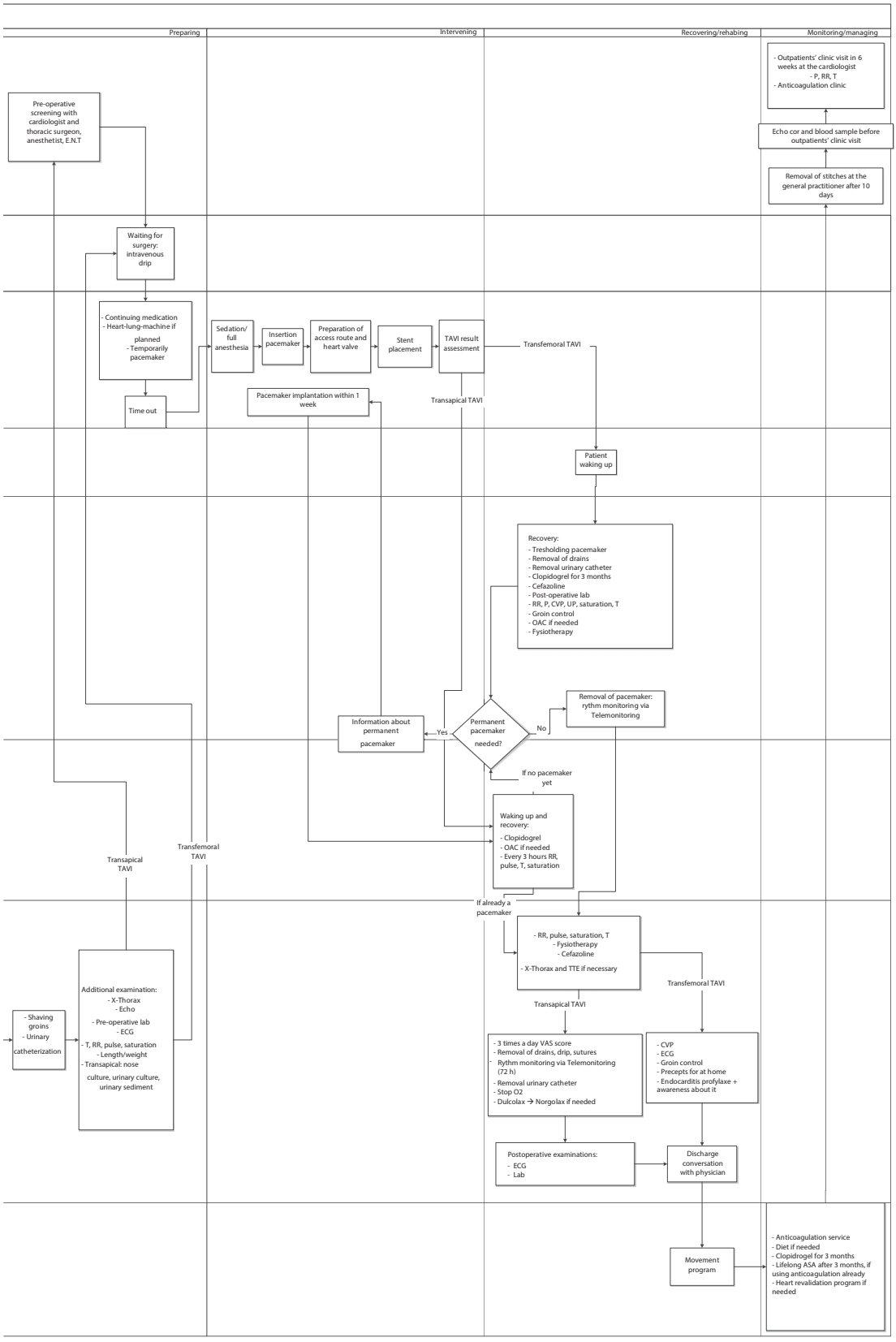
Appendix 2. Outcome measures set of the NHR

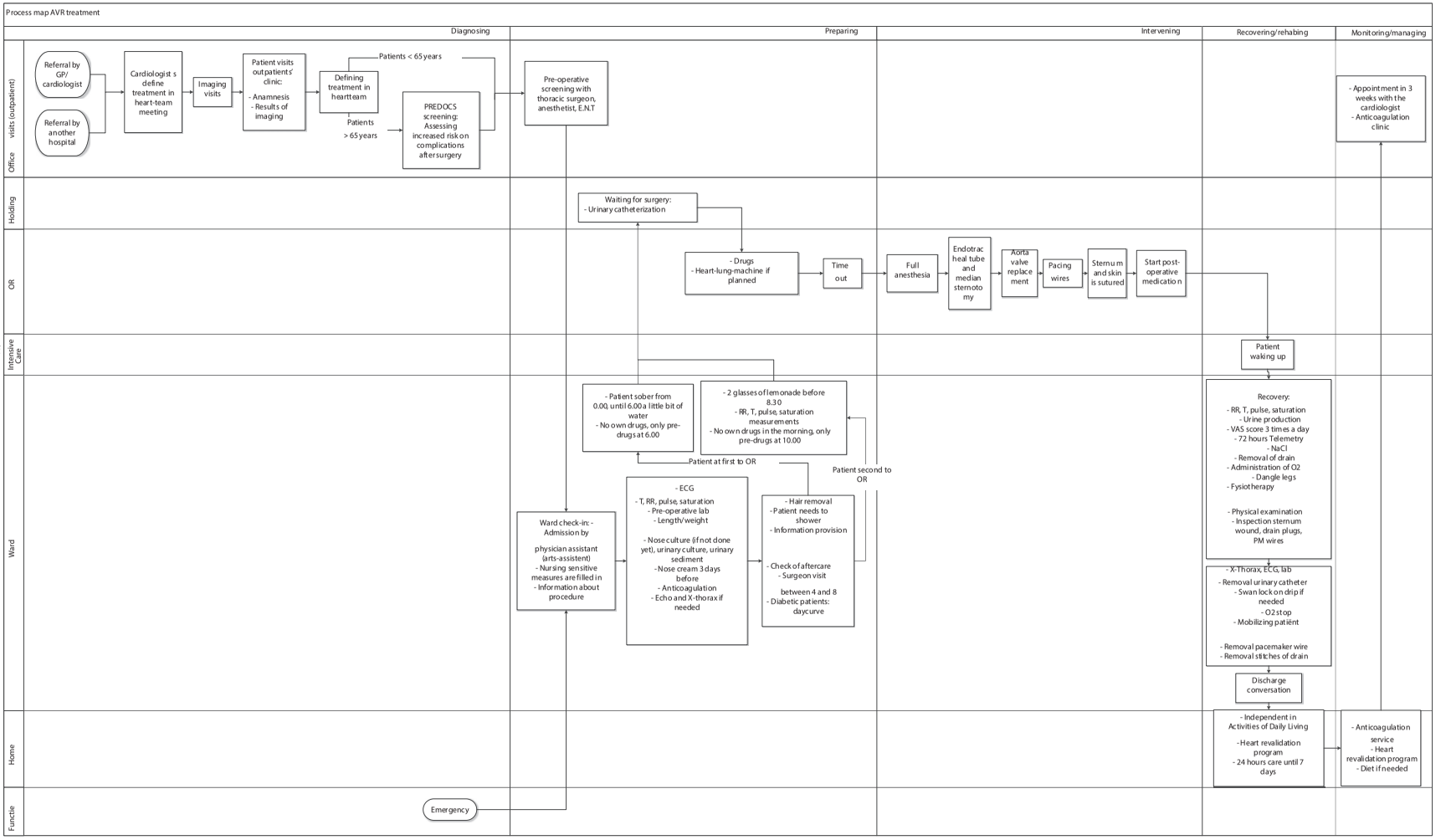
Hierarchy	Generic outcome measures	SAVR-specific outcome measures	TAVR-specific outcome measures
Survival	120-day mortality Long-term survival		Procedural mortality 30-day mortality
Degree of recovery/ health	Quality of life		NYHA classification
Damage of the treatment (side effects, complications or medical mistakes)		CVA Deep sternal wound infection Implantation new permanent pacemaker	CVA Implantation new permanent pacemaker Vascular complications
Durability of recovery or health		Freedom of valve re-intervention	Freedom of valve re-intervention

[1-3]

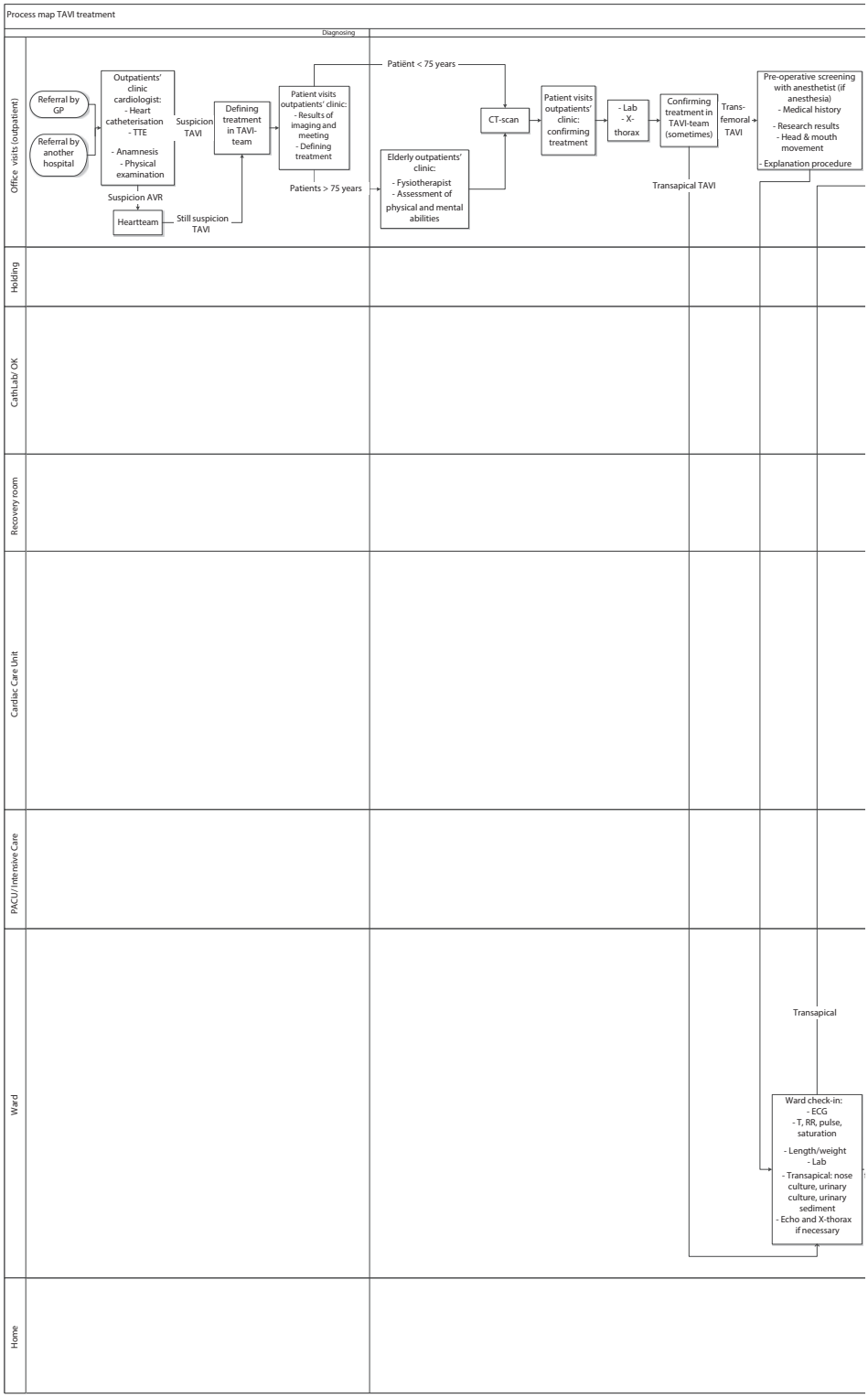
Appendix 3. Work-as-imagined TAVR and SAVR process maps

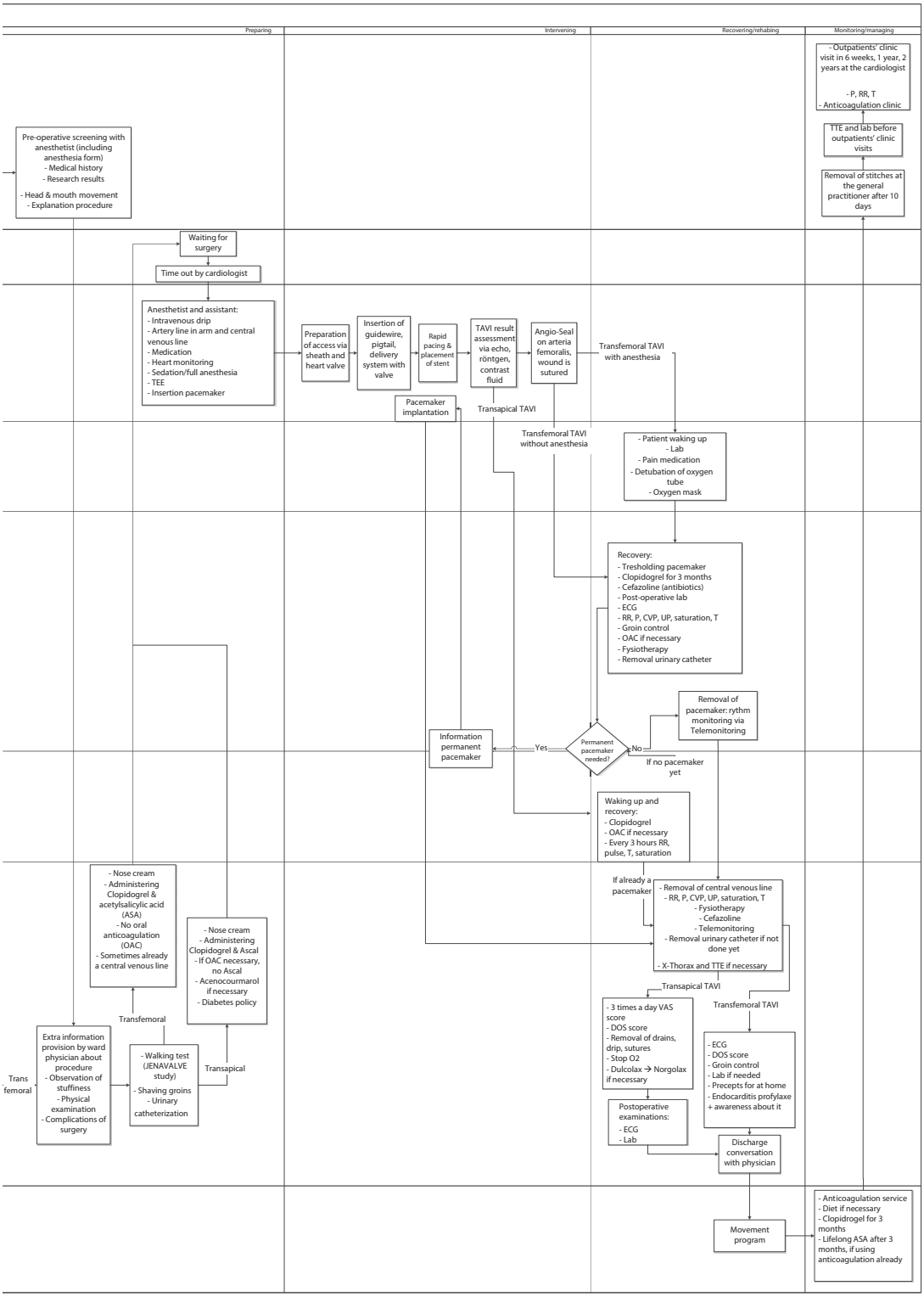


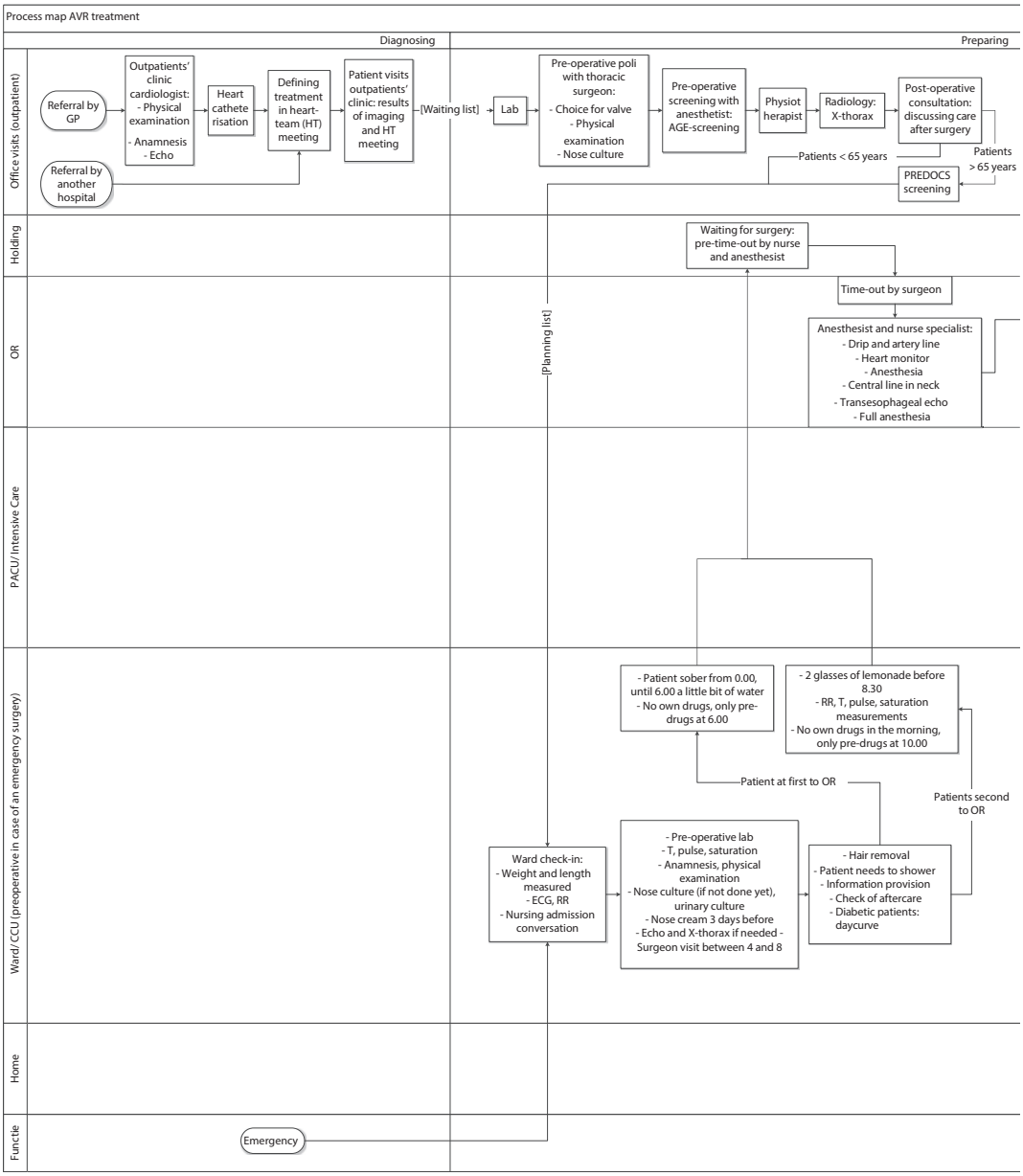

Preparing
Intervening
Recovering/rehabing
Monitoring/managing
Pre-operative screening with cardiologist and thoracic surgeon, anesthetist, E.N.T
Waiting for surgery: intravenous drip
- Continuing medication
- Heart-lung-machine if planned
- Temporarily pacemaker
Time out
Sedation/ full anesthesia
Insertion pacemaker
Preparation of access route and heart valve
Stent placement
TAVI result assessment
Transfemoral TAVI
Transapical TAVI
Pacemaker implantation within 1 week
Patient waking up
Recovery:
- Tresholding pacemaker
- Removal of drains
- Removal urinary catheter
- Clopidogrel for 3 months
- Cefazoline
- Post-operative lab
- RR, P, CVP, UP, saturation, T
- Groin control
- OAC if needed
- Fysiotherapy
Permanent pacemaker needed?
Yes
No
Information about permanent pacemaker
Removal of pacemaker: rythm monitoring via Telemonitoring
If no pacemaker yet
Waking up and recovery:
- Clopidogrel
- OAC if needed
- Every 3 hours RR, pulse, T, saturation
Transapical TAVI
Transfemoral TAVI
If already a pacemaker
- RR, pulse, saturation, T
- Fysiotherapy
- Cefazoline
- X-Thorax and TTE if necessary
Transfemoral TAVI
Transapical TAVI
- Shaving groins
- Urinary catheterization
Additional examination:
- X-Thorax
- Echo
- Pre-operative lab
- ECG
- T, RR, pulse, saturation
- Length/weight
- Transapical: nose culture, urinary culture, urinary sediment
- 3 times a day VAS score
- Removal of drains, drip, sutures
- Rythm monitoring via Telemonitoring (72 h)
- Removal urinary catheter
- Stop O2
- Dulcolax → Norgolax if needed
- CVP
- ECG
- Groin control
- Precepts for at home
- Endocarditis profylaxe + awareness about it
Postoperative examinations:
- ECG
- Lab
Discharge conversation with physician
Movement program
- Anticoagulation service
- Diet if needed
- Clopidrogel for 3 months
- Lifelong ASA after 3 months, if using anticoagulation already
- Heart revalidation program if needed
- Outpatients' clinic visit in 6 weeks at the cardiologist
- P, RR, T
- Anticoagulation clinic
Echo cor and blood sample before outpatients' clinic visit
Removal of stitches at the general practitioner after 10 days

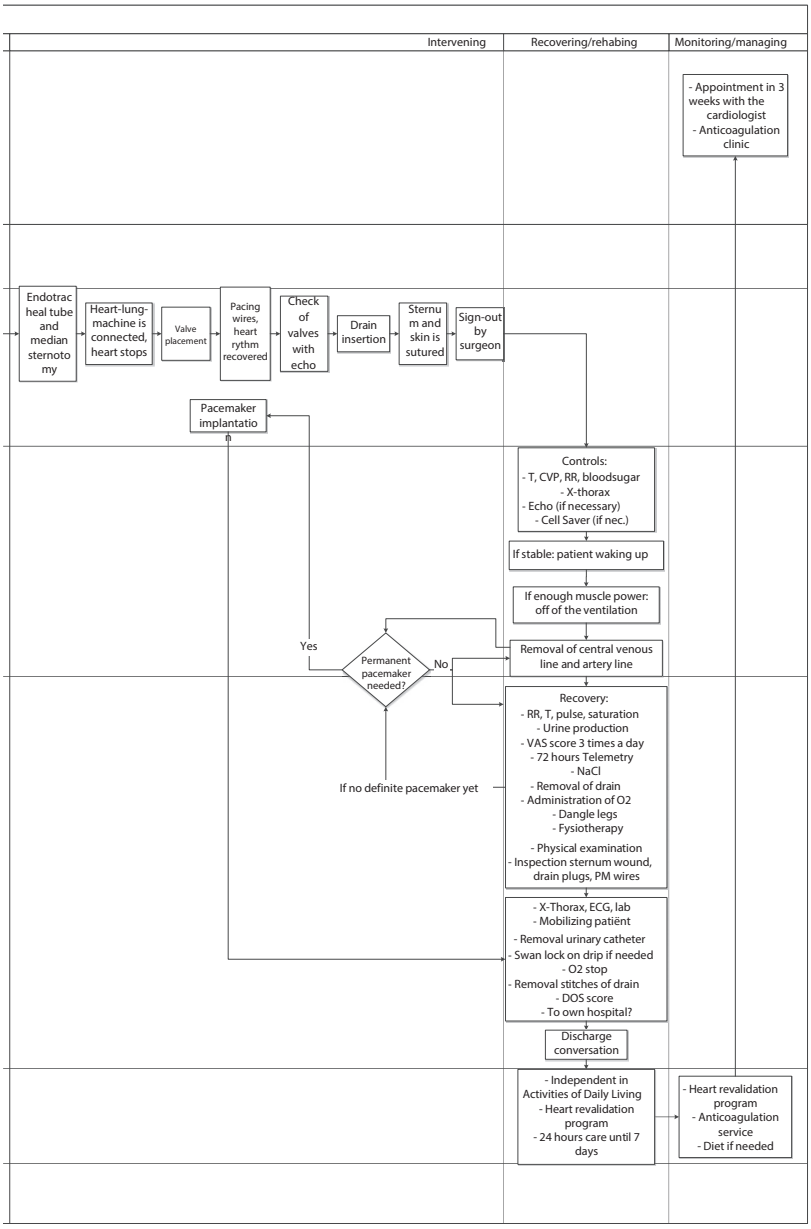

Process map AVR treatment
Diagnosing
Preparing
Intervening
Recovering/rehabing
Monitoring/managing
PACU/
visits (outpatient)
Office
Holding
OR
Intensive Care
Ward
Home
Functie
Referral by GP/ cardiologist
Referral by another hospital
Cardiologist s define treatment in heart-team meeting
Imaging visits
Patient visits outpatients' clinic:
- Anamnesis
- Results of imaging
Defining treatment in heartteam
Patients < 65 years
Patients > 65 years
PREDOCS screening: Assessing increased risk on complications after surgery
Pre-operative screening with thoracic surgeon, anesthetist, E.N.T
- Appointment in 3 weeks with the cardiologist
- Anticoagulation clinic
Waiting for surgery:
- Urinary catheterization
- Drugs
- Heart-lung-machine if planned
Time out
Full anesthesia
Endotrac heal tube and median sternoto my
Aorta valve replace ment
Pacing wires
Sternu m and skin is sutured
Start post-operative medicatio n
Patient waking up
- Patient sober from 0.00, until 6.00 a little bit of water
- No own drugs, only pre-drugs at 6.00
- 2 glasses of lemonade before 8.30
- RR, T, pulse, saturation measurements
- No own drugs in the morning, only pre-drugs at 10.00
Patient at first to OR
Patient second to OR
Recovery:
- RR, T, pulse, saturation
- Urine production
- VAS score 3 times a day
- 72 hours Telemetry
- NaCl
- Removal of drain
- Administration of O2
- Dangle legs
- Fysiotherapy
- Physical examination
- Inspection sternum wound, drain plugs, PM wires
Ward check-in: - Admission by physician assistant (arts-assistent)
- Nursing sensitive measures are filled in
- Information about procedure
- ECG
- T, RR, pulse, saturation
- Pre-operative lab
- Length/weight
- Nose culture (if not done yet), urinary culture, urinary sediment
- Nose cream 3 days before
- Anticoagulation
- Echo and X-thorax if needed
- Hair removal
- Patient needs to shower
- Information provision
- Check of aftercare
- Surgeon visit between 4 and 8
- Diabetic patients: daycurve
- X-Thorax, ECG, lab
- Removal urinary catheter
- Swan lock on drip if needed
- O2 stop
- Mobilizing patiënt
- Removal pacemaker wire
- Removal stitches of drain
Discharge conversation
- Independent in Activities of Daily Living
- Heart revalidation program
- 24 hours care until 7 days
- Anticoagulation service
- Heart revalidation program
- Diet if needed
Emergency

Appendix 4. Work-as-done TAVR and SAVR process maps




Preparing
Intervening
Recovering/rehabing
Monitoring/managing
- Outpatients' clinic visit in 6 weeks, 1 year, 2 years at the cardiologist
- P, RR, T
- Anticoagulation clinic
TTE and lab before outpatients' clinic visits
Removal of stitches at the general practitioner after 10 days
Pre-operative screening with anesthetist (including anesthesia form)
- Medical history
- Research results
- Head & mouth movement
- Explanation procedure
Waiting for surgery
Time out by cardiologist
Anesthetist and assistant:
- Intravenous drip
- Artery line in arm and central venous line
- Medication
- Heart monitoring
- Sedation/full anesthesia
- TEE
- Insertion pacemaker
Preparation of access via sheath and heart valve
Insertion of guidewire, pigtail, delivery system with valve
Rapid pacing & placement of stent
TAVI result assessment via echo, röntgen, contrast fluid
Angio-Seal on arteria femoralis, wound is sutured
Transfemoral TAVI with anesthesia
Pacemaker implantation
Transapical TAVI
Transfemoral TAVI without anesthesia
- Patient waking up
- Lab
- Pain medication
- Detubation of oxygen tube
- Oxygen mask
Recovery:
- Tresholding pacemaker
- Clopidogrel for 3 months
- Cefazoline (antibiotics)
- Post-operative lab
- ECG
- RR, P, CVP, UP, saturation, T
- Groin control
- OAC if necessary
- Fysiotherapy
- Removal urinary catheter
Removal of pacemaker: rythm monitoring via Telemonitoring
Information permanent pacemaker
Yes
Permanent pacemaker needed?
No
If no pacemaker yet
Waking up and recovery:
- Clopidogrel
- OAC if necessary
- Every 3 hours RR, pulse, T, saturation
If already a pacemaker
- Removal of central venous line
- RR, P, CVP, UP, saturation, T
- Fysiotherapy
- Cefazoline
- Telemonitoring
- Removal urinary catheter if not done yet
- X-Thorax and TTE if necessary
Transapical TAVI
Transfemoral TAVI
- 3 times a day VAS score
- DOS score
- Removal of drains, drip, sutures
- Stop O2
- Dulcolax → Norgolax if necessary
- ECG
- DOS score
- Groin control
- Lab if needed
- Precepts for at home
- Endocarditis profylaxe + awareness about it
Postoperative examinations:
- ECG
- Lab
Discharge conversation with physician
Movement program
- Anticoagulation service
- Diet if necessary
- Clopidrogel for 3 months
- Lifelong ASA after 3 months, if using anticoagulation already
- Nose cream
- Administering Clopidogrel & acetylsalicylic acid (ASA)
- No oral anticoagulation (OAC)
- Sometimes already a central venous line
- Nose cream
- Administering Clopidogrel & Ascal
- If OAC necessary, no Ascal
- Acenocourmarol if necessary
- Diabetes policy
Transfemoral
Transapical
Trans femoral
Extra information provision by ward physician about procedure
- Observation of stuffiness
- Physical examination
- Complications of surgery
- Walking test (JENAVALVE study)
- Shaving groins
- Urinary catheterization


Process map AVR treatment
Diagnosing
Preparing
Office visits (outpatient)
Holding
OR
PACU/ Intensive Care
Ward/ CCU (preoperative in case of an emergency surgery)
Home
Functie
Referral by GP
Referral by another hospital
Outpatients' clinic cardiologist:
- Physical examination
- Anamnesis
- Echo
Heart cathete risation
Defining treatment in heart-team (HT) meeting
Patient visits outpatients' clinic: results of imaging and HT meeting
[Waiting list]
Lab
Pre-operative poli with thoracic surgeon:
- Choice for valve
- Physical examination
- Nose culture
Pre-operative screening with anesthetist: AGE-screening
Physiot herapist
Radiology: X-thorax
Post-operative consultation: discussing care after surgery
Patients < 65 years
Patients > 65 years
PREDOCS screening
[Planning list]
Waiting for surgery: pre-time-out by nurse and anesthesist
Time-out by surgeon
Anesthesist and nurse specialist:
- Drip and artery line
- Heart monitor
- Anesthesia
- Central line in neck
- Transesophageal echo
- Full anesthesia
- Patient sober from 0.00, until 6.00 a little bit of water
- No own drugs, only pre-drugs at 6.00
- 2 glasses of lemonade before 8.30
- RR, T, pulse, saturation measurements
- No own drugs in the morning, only pre-drugs at 10.00
Patient at first to OR
Patients second to OR
Ward check-in:
- Weight and length measured
- ECG, RR
- Nursing admission conversation
- Pre-operative lab
- T, pulse, saturation
- Anamnesis, physical examination
- Nose culture (if not done yet), urinary culture
- Nose cream 3 days before
- Echo and X-thorax if needed -
Surgeon visit between 4 and 8
- Hair removal
- Patient needs to shower
- Information provision
- Check of aftercare
- Diabetic patients: daycurve
Emergency


Intervening
Recovering/rehabing
Monitoring/managing
- Appointment in 3 weeks with the cardiologist
- Anticoagulation clinic
Endotracheal tube and median sternotomy
Heart-lung-machine is connected, heart stops
Valve placement
Pacing wires, heart rythm recovered
Check of valves with echo
Drain insertion
Sternum and skin is sutured
Sign-out by surgeon
Pacemaker implantatio n
Controls:
- T, CVP, RR, bloodsugar
- X-thorax
- Echo (if necessary)
- Cell Saver (if nec.)
If stable: patient waking up
If enough muscle power: off of the ventilation
Yes
Permanent pacemaker needed?
No
Removal of central venous line and artery line
Recovery:
- RR, T, pulse, saturation
- Urine production
- VAS score 3 times a day
- 72 hours Telemetry
- NaCl
- Removal of drain
- Administration of O2
- Dangle legs
- Fysiotherapy
- Physical examination
- Inspection sternum wound, drain plugs, PM wires
If no definite pacemaker yet
- X-Thorax, ECG, lab
- Mobilizing patiënt
- Removal urinary catheter
- Swan lock on drip if needed
- O2 stop
- Removal stitches of drain
- DOS score
- To own hospital?
Discharge conversation
- Independent in Activities of Daily Living
- Heart revalidation program
- 24 hours care until 7 days
- Heart revalidation program
- Anticoagulation service
- Diet if needed

Appendix 5. Substantiation in literature

1. Information provision to patients about SAVR treatment

Our study proposes that a poor timing of mobilization might lead to sternal dehiscence. Important is that sternal dehiscence is not only caused by poor mobilization, but also other risk factors identified by earlier studies, such as obesity.[4] However, using the process measure about 'information provision' might lead to the first steps in the direction of quality improvement of the 'sternal wound infections' result.

2. Valve choice for TAVR and SAVR treatment

We used the process measures of the NHR for TAVR and SAVR prosthesis types in our definition for 'valve choice', which were '*Type of prosthesis of the SAVR*' and '*Type of prosthesis of the TAVR*'.[1] Previous studies concluded that the brand of the valve influences a permanent pacemaker implantation, because CoreValve prostheses showed a higher risk for pacemaker implantation than an Edwards Sapiens prosthesis after TAVR.[5 6] The 'valve choice' might not always be influenceable but measuring the amount of different types of prostheses would give insight in why specific treatment outcomes were found. It could illuminate whether other factors play a role in satisfying or disappointing treatment outcomes.

3. Frailty screening of patients undergoing TAVR and SAVR treatment

Despite the differences in frailty assessment tools between studies, frailty was found to be significantly associated with 1-year and 30-day mortality in multiple earlier studies.[7] No definition or criteria for a frailty score have been given in our study because different criteria are used in the literature.[8 9] Hospitals might want to choose a definition of frailty themselves to use during the elderly outpatients' clinic or the elderly screening but the goal should be the use of an universal frailty score.

It was also recommended in the literature to evaluate the procedural risk of TAVR patients in addition to the decision of the heart team, to prevent that too frail patients are subjected to an inappropriate treatment. In addition to our study, that study proposes to measure the quality of life of TAVR patients before and after the intervention. This is considered important because it indicates the clinical benefit and determines which patients benefit the most of TAVR.[10]

4. Managing waiting lists for TAVR and SAVR treatment

Our process measure 'time between the TAVR surgery indication and surgery' has also been supported in literature. A previous study found that a longer time on the waiting list is associated with higher mortality and morbidity. No threshold period was found below

which waiting times were safe because clinical events showed a constant relationship with waiting time.[11] Considering the results of our study, a long waiting list is unfavourable for vulnerable TAVR patients but a too short waiting list for SAVR patients can lead to changes in OR planning and procedural delays, which could lower the quality of life of the patient. The balance between a too short or too long waiting list is of importance here. However, this is subject for further research.

5. Stopping anticoagulants in SAVR treatment

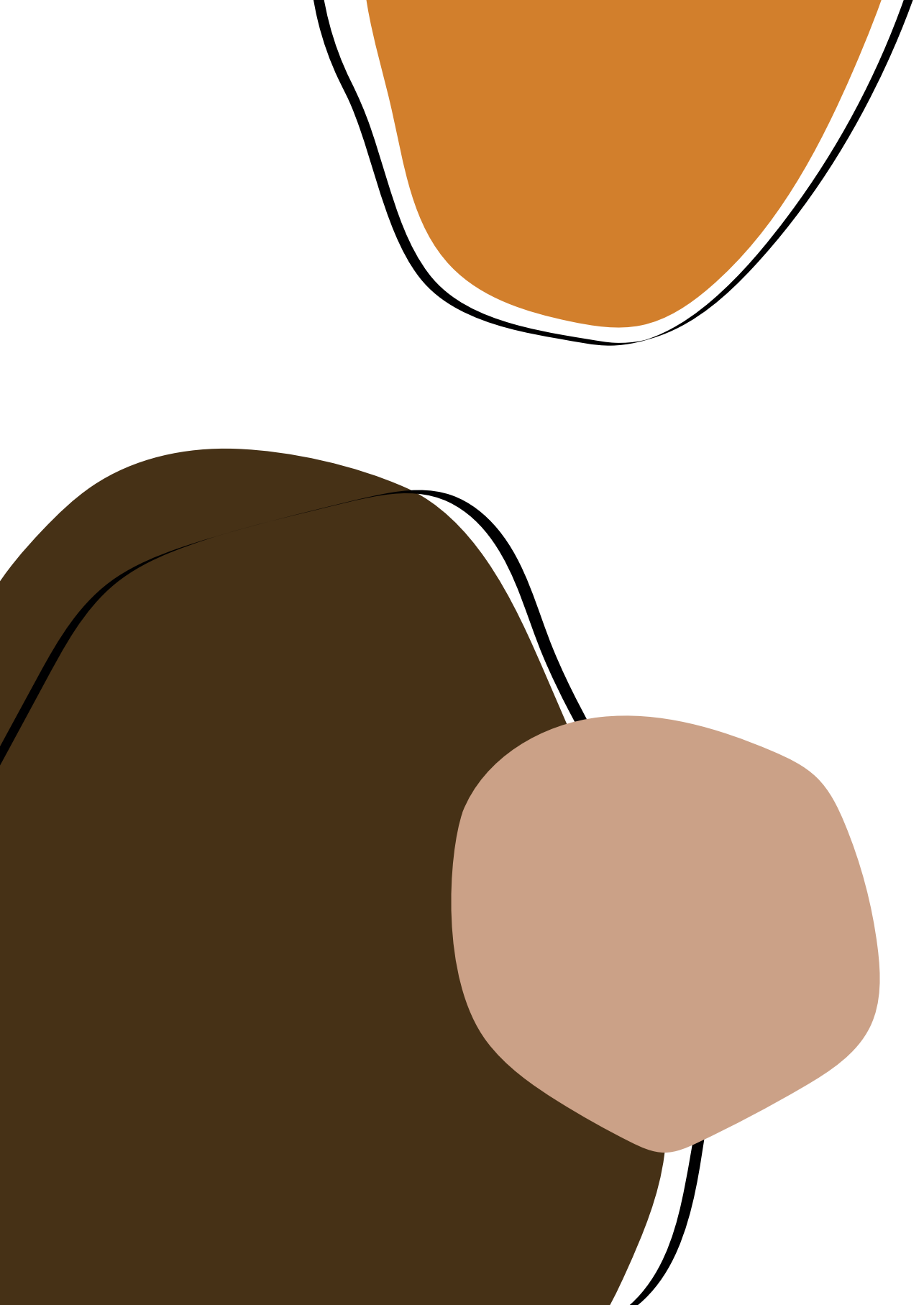
Regarding 'stopping anticoagulation on time', it was confirmed in previous studies that anticoagulation treatment before surgery increases the risk of resternotomy.[12]

6. Permanent pacemaker implantations in TAVR and SAVR treatment

It was found in previous studies that it is debatable whether 'permanent pacemaker implantations' take place fast enough. An association of early pacemaker implantation with death was found, but the permanent pacemaker implantation itself was not leading to lower survival.[13] Moreover, AV conduction disturbances were partially shown to recover over time.[6] Therefore, it is important for a hospital to decide on guidelines regarding the waiting time for heart rhythm to restore.

7. Pain measurement of patients after SAVR treatment

The importance of 'pain treatment' is also emphasized in previous studies because poor pain treatment may lead to for example negative cardiac, pulmonary and musculoskeletal effects. Regular measurement of pain is important in the treatment of pain.[14] We used the Dutch Health and Youth Care Inspectorate's measure to define our process measure for pain management, which was: *'The number of clinical surgical patients whose pain level is recorded digitally at least once a day during each day of admission'*.[15]



8

Quality improvement within value-based healthcare

Nina Zipfel
Stef Groenewoud
Gert Westert
Paul van der Nat

Submitted.

ABSTRACT

Over the course of decades the approach to improve quality changed and consecutively the three wagons of the Donabedian train passed by: structure, process and outcome. The early days of quality improvement focused on improvement of the conditions themselves. Later, the focus shifted towards process and structure improvement. In recent years, another shift occurred with the latest focus being on outcomes through, for example, Value-based health care. The attention towards outcomes is important. However, we have to reconnect with earlier attempts of quality improvement to integrate structure, process and outcome. Two main issues linking back to Donabedian's argument of the relation between structure, process and outcome were identified to be able to effectively apply Value-based health care.

PURPOSE

Over the course of decades the approach to improve quality changed and consecutively the three wagons of the Donabedian train passed by: structure, process and outcome [1]. It was stated that these three are different attributes of quality which are related to a probable extent in order to improve quality. "Inferences about quality are not possible unless there is a predetermined relationship among the three approaches." [1]. The early days of quality improvement were spent on improving the conditions under which care is provided (material and human resources) [2]. Later, much effort was given to improve processes by developing guidelines and protocols describing and often prescribing effective medical practice [3]. In many cases the association between structure and process versus the change in health of individuals (outcome) was not established. With the turn of the century, the shift from process to outcome increasingly gained broader attention [4]. For many decades, quality improvement work was improving processes of care and expecting gain in health automatically. However, the adherence to guidelines by professionals is modest and in many cases the association between process and outcome is not assessed [5–8].

CURRENT SITUATION

Nowadays, outcomes of care are paramount and value for patients is leading as described through the concept of Value-based health care [4]. Value-based health care (VBHC) is a concept that emerged as a response to the increasing demand for health care, variability in outcomes of care and rising health care costs [9,10].

The concept aims to create higher value for patients, where value is defined by a set of outcome measures that matter for the medical condition divided by the total costs of delivering these outcomes over the full cycle of care [4]. Experts consider that measuring a standard set of outcomes is key to drive improvement and increase value for patients [11]. A study published in 2017 stated that "VBHC worked as a trigger for initiating improvements related to processes, measurements and patients' health outcomes" [12]. However, so far the use of outcome measure in quality registries has led to few improvement initiatives [13]. Indeed, the focus on outcome measures is necessary, because we were slumped in processes and left results behind the horizon. Yet, we have to recall the earlier words of Donabedian. Only an integration of the three approaches: improve the conditions, improve the activities and monitor the results of healthcare, will produce high quality health care. This paper explores the importance of linking structure, process and outcome measures to truly improve quality of care.

We have identified two main issues linking back to Donabedian's argument of the relation between structure, process and outcome to be overcome before VBHC can truly be effective.

QUALITY IMPROVEMENT PROCESS

Within VBHC outcomes are disconnected from processes and structure of care
Within the concept of VBHC the emphasis is on outcome measures to be selected according to a three-tiered hierarchy: 1) health status achieved, 2) process of recovery, 3) sustainability of health [9]. However, in order to monitor improvements and give feedback on short cycled development of improvement, process and structure measures are needed as well [14,15]. Process and structure measures are more actionable and can directly be linked to improvement interventions [15].

VBHC introduces the concept of the care delivery value chain (CDVC) which helps to get a comprehensive overview of value creating activities during the care cycle of a patient for a specific medical condition [4]. With the CDVC, the relation between outcomes, processes and structures of care is described conceptually by Porter and Teisberg. However, VBHC does not describe (yet) how to link outcomes to processes and structures of care in practice. Linking structure, process and outcome can improve the determination of healthcare related aspects for improvement [16]. Porter recommends to start implementation by measuring outcomes [9]. However, measuring outcome helps to determine 'what' outcomes can be improved, but does not help with 'how' to improve these outcomes; what improvement activities have highest impact on outcomes?

CONTENT OF REFORM

Within VBHC a systematic approach to identify improvement initiatives is lacking
VBHC appears to trigger improvement [17–19]. VBHC currently does not offer a universal methodological approach to identify and select improvement interventions. Benchmarking of outcome measures is recommended by Porter and is used by several VBHC initiatives [11,19,20]. Benchmarking by comparing certain measures against norms or standards among healthcare providers is a well-known technique for the identification of best practices [21]. But merely benchmarking often does not suffice to identify improvement interventions [20]. First, if outcomes in a rudimentary benchmark do not differ between healthcare providers, this does not mean that there is no potential to improve. Significant differences can, for instance, still be present in patient subgroups. More importantly, if

there are no differences in outcomes in a benchmark, this, by no means, implies that there is no potential or urgency to improve. Second, if outcomes between hospitals differ, there is no straightforward approach to identify what is causing the better or worse performance. Benchmarking can lead to the conclusion that there is a difference in outcomes and potential to improve, but without finding a 'best practice' or without establishing proof for a causal relation between a potential 'best practice' and better outcomes.

Therefore, additional methods are needed to identify improvement initiatives based on outcomes. First of all, classic benchmarking needs to be extended with in-depth data analyses, using big data analytics and machine learning to identify trends or patterns relating (differences in) process and structures of care delivery to (differences in) patient-relevant outcomes. Application of big data analytics through, for example, predictive models for patient risk and resource use have the potential to improve quality of care and must be further developed [22]. But the application of in-depth data analyses is not sufficient to identify improvement interventions with highest impact on outcomes. We claim that it is essential to connect measuring and benchmarking of outcomes with existing quality improvement (QI) techniques on process improvement. Measuring and benchmarking of outcomes helps to identify improvement potential and subsequently process improvement can help to identify (hypotheses for) improvement initiatives that can improve these outcomes (see also the Intervention Selection Toolbox) [23].

CONCLUSION

With the analysis of processes, flaws or specific issues in the process with impact on outcomes can be identified as Donabedian emphasized. We need to revisit existing methodological approaches for QI and scrutinize the link between those, as for example the link of the Lean methodology, and VBHC.

Taking on a VBHC improvement project does not necessarily need to be the most lavish project. Even if no hard causal relationship has been proven, hypothesis-driven improvement based on the above mentioned in-depth data analyses and process analyses offer a novel way to improve quality of healthcare. Connecting these elements and reconnecting with earlier described concepts as by Donabedian, give VBHC the handholds needed to truly improve quality of health care. The literature offers sufficient QI methods that could enrich VBHC as for example from Lean, Implementation Science, or Process-Mapping.

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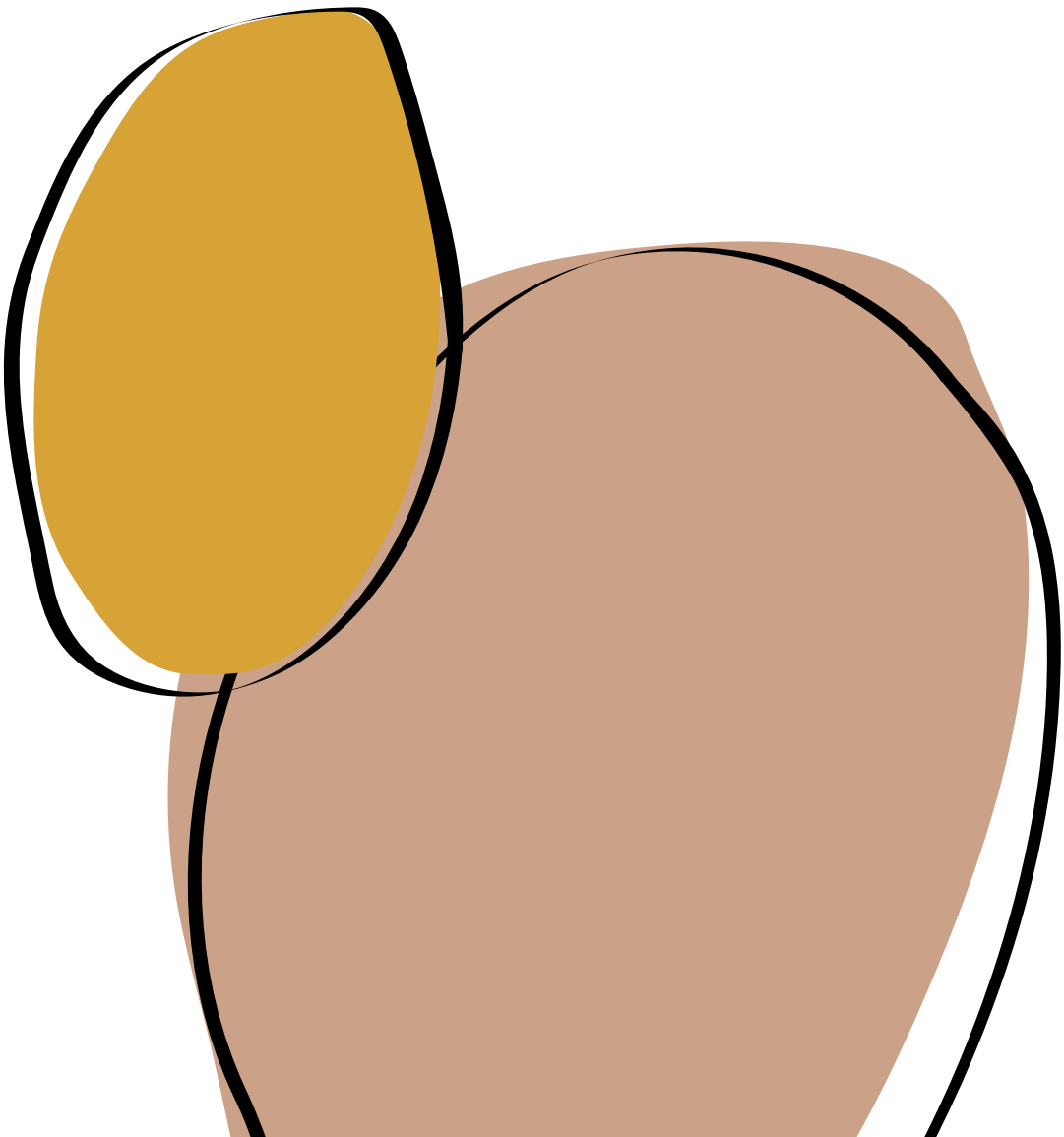

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General discussion

Value-based health care (VBHC) was introduced as a concept in order to improve quality of health care by using patient-relevant outcomes relative to costs. To date, in the literature, only little attentions has been paid to the question *how* the use of outcome measurement and application of VBHC contributes to quality improvement (QI). The aim of this thesis was to expand our knowledge on *how* outcome measurement through VBHC can contribute to improvement of quality of health care with focus on aortic valve disease.

The specific research questions were:

1. *To what extent are outcome measures from clinical registries used to implement and monitor quality improvement initiatives? (Chapter 2)*
2. *How can improvement interventions be selected based on insights into outcomes for surgical treatment of aortic valve disease (AVD)? (Chapter 3)*
3. *How can improvement interventions that were selected based on insights into outcomes be implemented? (Chapter 4)*
4. *What are the effects of a carefully selected improvement intervention offering preoperative protein-enriched diet in the context of VBHC on patient-relevant outcomes for surgical treatment of aortic valve disease (AVD)? (Chapter 5-6)*
5. *Can process measures be of additional value in an outcome-oriented VBHC approach, and how can process measures – in addition to outcome measures - be selected with impact on patient-relevant outcomes, and which process measures are most relevant for surgical treatment of aortic valve disease (AVD)? (Chapter 7-8)*

For **research question 1** we performed a literature review to study to what extent outcome measures from clinical registries were used to implement and monitor quality improvement initiatives. We found that only very few studies, 21 in total, used outcome measures for QI. The methods used for improving outcomes based on clinical registry outcome data varied profoundly, from the use of the Chronic Care Model, IT applications as feedback, benchmarking and the Collaborative Care Model. Our literature study showed that clinical registries can accelerate the implementation of QI initiatives through a high-quality database, audits, frequent reporting and feedback, patient involvement, communication, standardization, engagement and leadership. Important factors for achieving improved outcomes were found to be organizational readiness and an active QI approach (Chapter 2).

To answer research questions 2 to 5 we selected aortic valve disease as a medical condition of focus due to its high prevalence and long precedence of clinical registries in heart care. For **research question 2** we analyzed patient-level outcome data from 2010 to 2014 from five Dutch hospitals participating in the Dutch clinical outcome registry for heart diseases

and care delivery processes of the St. Antonius Hospital. Based on the applied methods, we developed a toolbox for identifying and selecting improvement interventions based on outcomes. Identifying and selecting improvement interventions based on clinical outcome data demands a multifaceted approach, which we integrated into our toolbox (Chapter 3). **Research question 3** was answered by conducting a qualitative study evaluating the implementation process of two improvement interventions that are based on clinical outcome data. VBHC focusses on outcome measurement to contribute to QI. However, the concept does not offer an implementation methodology for improvement interventions. Based on the well-known Implementation of Change Model, we proposed the Integrated Implementation Model (IIM) for the implementation of VBHC improvement interventions with focus on monitoring outcome measures (Chapter 4). To answer **research question 4** the evaluation of the improvement intervention was split into two studies: one evaluating the effect of protein-enriched diet with familiar foods on protein-intake, a pre-selected intermediate outcome (Chapter 5), and the other one evaluating the impact of the diet on hospital length of stay (LOS) (Chapter 6). For the first study, an intervention study with one treatment group was performed. Food record questionnaires before and during the intervention were evaluated. The results showed that protein-enriched diet with familiar foods increased protein intake by approximately 54 g, which even exceeded the initial goal of 45 g. Achieving a protein level of 25 g per meal was reached during breakfast, lunch and dinner compared to only dinner before the intervention. For the second study we evaluated the effect of the protein-enriched diet on LOS by analyzing patient-level data. The effect of LOS, even though not statistically significant, showed a clinically relevant reduction of one hospital admission day in the group of patients who received protein-enriched diet compared to those who did not receive this diet.

Research question 5 was addressed with a qualitative study making use of triangulation of study data. Starting with desk research and observations, process maps were constructed, followed by semi-structured interviews with healthcare professionals and patients to explore which processes were regarded to have the highest impact on outcomes. The qualitative data of the interviews and observations were validated through a focus group interview. In order to improve results of healthcare - outcomes that are relevant for patients - process measures were seen as valuable as they offer more insights into what specifically needs to be improved. Determining and selecting process measures that can be used to improve outcomes led to process measures that were not previously registered (Chapter 7). Approaching the identification of process measures from the perspective of the full cycle of care was deemed relevant in order to make the link between process measures and outcome measures for improving quality of care. To further discuss the link between

process, structure and outcome measures we discussed this issue by reflecting on the arguments by Donabedian in the form of a viewpoint paper (Chapter 8).

In this final chapter we first reflect on the main findings per research question. And then interpret our findings and present implications for clinical practice, science and policy.

INTERPRETATIONS OF THE FINDINGS

Current use of outcome measures for quality improvement

From the analysis of relevant literature on the use of outcome measures from clinical registries 21 relevant studies were identified out of which eight showed statistically significant improvements in outcomes. The methods used to achieve improvements were highly diverse including benchmarking, collaborate care mode, Plan-Do-Check-Act, Chronic Care Model, Learning and Leadership Collaborative and IT driven interventions. The QI initiatives were heterogeneous in type, which made it difficult to generalize the results. The results of this study showed, that outcomes collected in clinical registries can lead to valuable QI initiatives. In the 21 studies the support of a high-quality database, audits, frequent reporting and feedback, patient involvement, communication, standardization, engagement and clear leadership were found relevant factors to the success of QI initiatives. Our results are in line with earlier studies. These report that research rarely informs on the impact of the use of clinical registries on health outcomes [1–3]. A similar systematic review focused on evaluating the effect of clinical registries on processes, health service use and clinical outcomes, whereas our review focused on the use of outcome measures and methods used based on clinical registries to improve outcomes [1]. Currently, only few registry outcome data are used to guide quality of healthcare improvement. The full potential of outcome measurement is not yet used. The added-value of outcome measurement was already recognized in the early 2000's where the use of outcome measurement was divided into two distinct, yet linked, pathways [4]. The first pathway described the use of outcome measurement for the selection of a suitable health care provider [4]. The second pathway illustrates outcome measurement as an opportunity for improvement through changes in care [4]. This explanation relates closely to the principles of VBHC where outcome measurement is considered to lead to improvement of value [5]. How clinical registries made use of outcome measures, as well as the methods used to improve outcomes, was very divergent, which led to our second research question: *How can improvement interventions be selected based on insights into outcomes for aortic valve disease (AVD)?*

A toolbox for the identification and selection of improvement interventions

Research question 2 addressed the ingredients needed to identify and select improvement interventions based on outcomes. VBHC pretends to be an integral solution to improve quality of healthcare, but it lacks a practical toolbox on how to use information from outcome measures to identify and select improvement interventions. Current literature focusses on the design of interventions from the perspective of results of randomized controlled trials [6,7]. Only randomized controlled trials would offer the desired evidence to implement improvement interventions to improve outcomes. With the emergence of VBHC, the need for aggressive, preventive or curative interventions involving high costs and normally extensive trial times, while being ineffective or inefficient, is questionable [8]. In an earlier attempt to create guidance for the development of improvement interventions, a systematic approach as developed [9]. However, that approach lacks clear description of *how* to use outcome measures to identify desired improvement interventions. The Intervention Selection Toolbox (IST), that we developed, looks at the practical ingredients and methods needed (Chapter 3). It describes the steps needed to both identify potential for improvement based on insights into outcomes (top-down) as well as an approach based on detailed insights into processes to identify potential for improvement (bottom-up). The IST moves away from the classic approaches of only hard evidence leading to possibilities for improvement. In contrast to evidence-based medicine, it takes into account innovative ways to explore the full spectrum of quality improvement potential from benchmarking, data exploration, care delivery process analysis and monitoring of ongoing improvements. Only the combination of these ingredients can offer the certainty of selecting the most appropriate improvement intervention in terms of highest expected impact on outcomes but also feasibility. Only interventions that are deemed feasible to implement should further be considered for implementation in order to achieve realistic goals. This would also keep health care professionals motivated for the improvement intervention. Since the success of the IST relies on involvement of professionals, feasibility is of great importance to the realization of an improvement intervention.

For the IST, both qualitative and quantitative methods were applied. As for the number of experts involved in the multidisciplinary team, we tried to involve at least one expert per professional field involved in providing care for AVD. It might have been interesting to interview also external experts in order to discuss reasons for modest differences observed during benchmarking. During the design process of Chapter 3, choices were made about the degree of details described for each step of the toolbox. Since our goal is that the toolbox can widely be applied, users can adjust and give substance to the steps as desired or needed. Concerning the composition of the multidisciplinary team,

the patient's perspective was not accounted for and future research should include the patient's view for the application of the IST. For the purpose of our analysis, the goal was to only involve health care professionals as they were chosen as the target group for developing a continuous improvement cycle in the health care organization's structure.

Implementation of improvement interventions

Implementation science focusses on the scientific study of methods to promote the systematic uptake of research findings into routine care and hence, to improve the quality of care [10]. Within VBHC the measurement of outcomes to improve quality of care has extensively been defined [11–14]. However, how improvements are implemented in the context of VBHC was not described. **Research question 3** attempted to bridge the gap between implementation science and VBHC. The application of a systematic implementation method as the commonly known Implementation of Change Model (ICM) facilitated successful implementation of a QI intervention in the context of VBHC. However, outcomes measures were not explicitly incorporated in the ICM. Integration of the ICM within VBHC with focus on monitoring outcomes can offer handholds for organizations to implement QI interventions. But not only a systematic approach is crucial for successful implementation besides the ICM, support, personal importance, involvement, leadership and climate were identified as important themes enhancing uptake.

For the interviews, we included all possible participants involved in both interventions, but failed to involve the patient's perspective as our goal was to evaluate the implementation process in the health care system by health care providers. The adjusted implementation model should be tested in a different setting and completeness should be evaluated, too. Furthermore, supporting the success of the implementation by quantifying the effect on outcomes would support the added-value of a systematic implementation approach.

Effect of a carefully selected improvement intervention on patient-relevant outcomes

The improvement intervention selected under **research question 2** was preoperative protein-enriched diet for older patients undergoing aortic valve replacement. The intervention products, namely protein-enriched familiar foods and drinks such as bread, pastry, juice, soups and dairy drinks, were evaluated by, firstly, determining protein intake of participating patients and, secondly, assessing the impact on hospital length of stay (LOS) and 30-day mortality.

This improvement intervention was chosen based on the IST and deemed most appropriate in terms of impact on outcomes and feasibility. Next to these arguments, the preoperative

protein-enriched diet was regarded an innovation, which might have contributed to motivation by health care professionals for this intervention. Preoperative protein-enriched diet was not earlier part of the preoperative preparation of older patients. It was chosen for its potential preventive effect of averting postoperative complications. At the time of the identification and selection of possible improvement initiatives, the incentive was to improve outcomes by implementing a novel initiative. The identification of possible wasteful acts or unnecessary processes was not examined as for example suggested by the principles of Lean [15]. Implementing improvement does not necessarily mean to implement novel initiatives. Change in healthcare can concern any problems observed in routine practice that demand a solution [16]. The drive to change in healthcare is, that current practice does not lead to intended or desired results, that mistakes occur, that patients are unsatisfied, or a process in inefficient or unsafe [16]. For this thesis, the analysis carried out with support of the IST did not show mistakes, unsafe or inefficient care. Therefore, the experience and preferences of the health care professionals constituted a great deal of influence to the choice of the improvement intervention and the desired impact on patient-relevant outcomes.

In order to assess the success of the improvement intervention, the goal was to evaluate its effect. Evaluation of health interventions, which includes QI interventions, consists of the collection of data with the purpose of valuing the intervention [17]. For the purpose of closely monitoring the effect of the QI, intermediate outcomes were measured, namely protein intake, next to postoperative outcomes, namely LOS, 30-day mortality and stroke. An intermediate outcome was selected because it could directly be linked to the consumption of the protein-enriched diet and could also have downstream consequences for LOS, 30-day mortality and stroke. The goal was to strengthen conclusions about the impact of the protein-enriched diet [18]. LOS, on the other hand, can also be considered a surrogate marker for the patient's well-being during hospital treatment and health care costs [19].

Whether the quality improvement intervention should be continued in standard care remains questionable. The goal of this VBHC improvement project was to implement an intervention that health care professionals believe to have highest impact on outcomes. Evidence for the effectiveness of the chosen protein-enriched diet existed in other cohorts or postoperatively. It remains arguable whether the IST including expert opinion offers sufficient evidence for implementing this QI project. Our results showed that offering preoperative protein-enriched familiar foods to patients increases protein intake and indicates improvement in LOS based on an intervention study design with one treatment group. Working with VBHC presented the possibility for improving quality of care without

waiting for trial data to support implementation. By continuously monitoring outcomes and intermediate outcomes as protein intake and LOS, the effect of the QI project was monitored and allowed for adjustment if needed. This way of improving quality of care opens the opportunity for fast and targeted improvement in health care. In our thesis, VBHC acted as the framework for measuring, monitoring and evaluating quality of care. Our thesis suggests a systematic approach on how to use VBHC as a framework in guiding improvement of quality of care. But only merely measuring outcomes does not automatically improve quality of care.

Value for heart patients

The protein-enriched diet was implemented in 2017 for a period of two years. Participant's protein intake increased on average by 54 g per day. The intervention was implemented for a two-week period prior to hospital admission for either surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR). The two-week period was thought to be sufficient for improving protein intake based on previous studies. Previous studies in different patient groups offered nutritional interventions for a minimum of two weeks but also longer periods with positive effects on protein intake and weak effects on postoperative complication and length of stay (LOS) [20–23]. Therefore, for the primary goal of improving protein intake the two-week intervention period was satisfactory. However, for achieving the second goal of improving LOS and 30-day mortality our results did not show significant improvements. For the analysis of LOS considering discharge policy is important. Therefore, only participants that were not referred from a different hospital could be included in the analysis on outcomes, which in turn limited the number of participants for the evaluation of LOS. The outcome measure LOS might also be too broad for evaluating the effect of protein-enriched diet. Subdividing LOS into LOS at the intensive or medium care and at the usual care ward could have given valuable insights into the effect of the protein. Other studies suggest the association between protein intake and lower readmission rates and protein intake and stimulation of wound healing [24–26]. In order to see a significant difference of one day in LOS 63 patients per group were needed for evaluation. When considering both treatment groups, the sample size of 63 patients was achieved. However, both treatments are substantially different in terms of postoperative recovery. Therefore, LOS should only be analyzed per treatment group (SAVR and TAVR). When splitting the groups, the study did not achieve the demanded power (SAVR: N=47 and TAVR: N=52). Concerning the effect on 30-day mortality and stroke, a significant difference could only be discriminated when including 4123 patients in the study for mortality and 820 patients per group for a difference in stroke. For this study, it was not feasible to include more patients within the given study-frame.

The goal of the intervention was to improve protein intake to reach the protein recommendation of 1.2-1.5 g/kg/d for older people with disease [27]. The recommendation was met by most patients in the current study and even exceeded by patients with an adequate protein intake prior to the intervention.

In the current study all patients were eligible regardless of nutritional status. The study was carried out in older patients undergoing aortic valve replacement. Earlier studies were conducted in different groups of patients including patients undergoing general surgery, with hip fracture and with liver disease [28–31]. However, no earlier studies focused on preoperative protein intake for patients with aortic valve disease. The link between nutritional status and LOS has earlier been evaluated [19,32–34]. These studies found that specifically malnutrition is a predictor of prolonged LOS [19]. Malnutrition in these studies was considered as weight changes, alterations in food intake, loss of subcutaneous fat and changes in functional capacity [19]. The specific goal of this intervention was to target all patients irrespective of their nutritional status.

Previous studies showed that a higher protein status has protective effects on elevated blood pressure and may contribute to improved cardiovascular health [23]. Therefore, evaluating other endpoints for this study might have supported robustness. Furthermore, the improvement intervention was evaluated without comparison to a control group, which would have added robustness to the study design itself. Drawing firm conclusions based on the results of the effect on outcomes is not possible, but concerning LOS the intervention has shown to lead to a clinically relevant improvement of 1 day in the intervention group compared to the non-intervention group. Certainly, in order to draw conclusions based on this result, upscaling of this study to include more patients would be necessary. Furthermore, improving protein intake of older patients before hospital admission could also become part of a bundle of interventions to optimize preoperative preparation of older patients. Next to improving the nutritional status of patients, functional capacity can have a significant impact on postoperative outcomes [35]. Therefore, improving physical activity along with stress prevention methods could, together with improvement of the nutritional status, lead to the desired effect of enhanced recovery in older patients.

Determination of the nutritional status of patients gives insights into the individual patient's needs. Currently at the St. Antonius Hospital, nutritional status is measured based on the Malnutrition Universal Screening Tool (MUST) [36]. For the MUST three independent criteria are used: 1) current weight using BMI, 2) unintentional weight loss, 3) acute disease effect leading to no nutritional intake [37]. It is, therefore, a rather global screening tool that

does not give indication on nutrient deficiencies. Choosing to measure nutritional status with a different tool might help to determine the patients in need for protein enriched diet. A screening tool that gives a more detailed overview the nutritional status which was specifically designed for elderly patients is the mini-nutritional assessment (MNA) [38]. Next to assessing a decline in food intake over 3 months, it also measures mobility, psychological stress and neuropsychological problems. This tool would give better insights into the status of older patients compared to the MUST. But in order to only identify patients with protein deficiency, blood measurement is inevitable. Patients receive a standard blood test at their first outpatient preoperative preparation appointment. The standard blood test, however, does not include measurement of the total serum protein. An alternative would be protein measurement in the urine. These alternatives, though, require additional testing which might be costly. If a bundle of preoperative optimization would be used, the MNA would give sufficient indications of high-risk patients. This option would be least invasive and relatively inexpensive.

Selection of process measures within VBHC

The significance of process measures and their added-value were addressed with **research question 5**. For this research question the full cycle of care was assessed. The so-called care-deliver value chain (CDVC) describes activities required to deliver care over the full cycle of care [39]. In order to achieve higher value, it would be important to link process measures to outcomes as has been described more than a decade ago and needs to be revitalized [40]. When developing process measures a sketch of all activities needs to be done through observations, interviews and real-world insights, otherwise the added-value of process measures that impact outcomes could fail [41]. Involving health care professionals in the development of process measures offers the opportunity to validate results, but also to foster collaboration which enhances quality improvement work (Chapter 7). Current literature on VBHC solely focusses on outcome measurement and improvement of these outcomes [12,42–44]. However, processes describe actions in order to identify *what* needs to be improved. Linking processes to their associated outcomes can work as a catalyst for quality improvement [45]. Early studies linked processes to outcomes and saw their relative advantage in contrast to outcome measures [46–48]. It was found, that processes of care are associated with a lower odds of an adverse outcomes [48]. However, in order to assess quality of care, a link must be assumed between structure, process and outcome [49]. When considering the link between structure, processes and outcomes, targeted improvement can be implemented [50]. In Chapter 7 we developed process measures for both a common but high risk procedure aortic valve replacement (SAVR and TAVR). For the purpose of short-term improvement cycles process measures deemed to be more relevant. Earlier studies for surgical care found a similar advantage for a common but high risk procedure [45].

The process measures for this study were chosen based on expert opinion. The focus group did not include a patient and was rather limited in the number of participants. Thus, pragmatic choices including ease of measurement, cost and availability could have influenced the results [51]. However, by linking process measures to outcomes the strength of the effect of a change in the process measures on a change in an outcome measures was leading in the choice of process measures. For this study, processes measures were suggested, but not measured yet in order to keep the choice as pure as possible without difficulties of measurement influencing the results. Certainly, in order to evaluate the relationship between process measures and outcomes, processes need to be measured first. The importance of the link between processes, structures and outcomes was further reflected on in the light of Donabedian in Chapter 8.

Reflection on the concept of VBHC to improve quality of healthcare

Originally, VBHC consists of 6 core elements [39]: 1. Organization of care into integrated practice units (IPUs), 2. Measurement of outcomes and costs for every patient, 3. Moving to bundled payments for care cycles, 4. Integration of care delivery across separate facilities, 5. Expansion of excellent services across geography and 6. Building an enabling information technology platform. This thesis focused on the measurement of outcomes (part of element 2.) and using these insights to improve quality of health care. The concept of VBHC mainly emerged from business strategies, which might be difficult to translate into health care [52]. But over almost the past decade, VBHC has been adopted in many western health care systems [12,53,54]. In the UK an assessment of the application of VBHC was published, explaining that VBHC was used in two ways: VBHC as part of the payment of health care providers with a purchaser-provider split or VBHC to distinguish high and low value services [54]. Both these applications neglect the improvement of health outcomes. For this thesis, VBHC was applied as a concept guiding continuous quality improvement by measuring outcomes, analyzing insights into outcomes, implementing an improvement intervention and evaluating that intervention. We believe that VBHC is not the only solution to the problem of increasing costs, but it offers valuable elements to start improving what is relevant. We reflected more on the pitfalls of VBHC in the viewpoint article Chapter 8 preceding this general discussion.

Costs within VBHC

Generally, measurement of costs constitute a difficult aspect, because they are difficult to ascertain since charges billed to the insurer do not give the true picture of the actual expense of patient care. Hospital charges are often inaccurate since identifying the true cost of care as itemized prices and labor costs are difficult to assess [55]. For this thesis, we chose to focus on outcome measurement to improve quality of care as it was stated, that

in order to achieve cost reduction outcomes need to be considered first [39]. Our main research question concerned improvement of quality of care and not costs.

Yet, a rough estimate can be given on the costs of the QI intervention. The total costs, only concerning the intervention products, were approximately €13,100 for all patients included in the study. Additional costs need to be considered, too, including administrative costs for the logistics and organization of the QI intervention.. In the Netherlands, a standard admission day at a nursing ward costs approximately €443 and a stay at the intensive care unit costs approximately €1,186 in 2014 [56]. Taking into account the inflation rate over the years, the costs of an admission day at a nursing ward are predicted to be €474 in 2020 [56]. Based on the results of our thesis only an indication for a possible cost reduction could be given. However, a change in length of stay could also influence structural changes in a hospital concerning number of beds. Therefore, shorter length of stay cannot directly be translated into cost savings. Since the total costs of care were not considered, no firm conclusions can be drawn on cost savings based on the QI intervention. This estimation only gives a crude overview on the cost savings through the implemented QI intervention.

Within VBHC time-driven activity-based (TDABC) costing is suggested as the most accurate method to measure the true costs of treating patients for a specific medical condition [57]. TDABC uses insights into the detailed care processes based on process maps to describe all clinical and administrative steps in a patient's care cycle including the resources used and time consumed. Additionally to process mapping, capacity costs are determined which include costs for each clinical resource involved as personnel, space, technology, supervision, training among others. And lastly, the capacity measured in hours is estimated [57]. These insights do not only facilitate cost reduction, but also process improvements. But using insights into costs as incentives for improvement is considered a delicate topic for health care professionals, currently. Focusing on cost reductions could lead to disinterest in continuous improvement as normally costs reductions are required from the management level of organizations and not the providers themselves. In this thesis, the goal was to maximally engage health care providers in the process of improvement to sustain QI work. It would not have been desirable to use VBHC as a management intervention to top-down reduce costs or even have an impact on personnel. Furthermore, the goal was not to change the reimbursement system in order to accommodate improvement based on TDABC.

GENERALIZABILITY OF FINDINGS

Our case studies were based on data from a national registry (Chapter 3) and data from the primary hospital (Chapter 4-7).
The IST was developed based on national data and applied in a single setting. The findings on the systematic approach can only be generalized with caution for other medical conditions in the Netherlands or other health care systems. Since the IST contains elements from existing improvement approaches as benchmarking, we believe that it can be transferred to other settings. Application in a different setting with other preconditions might affect speed and order of the steps.

In Chapter 4 we studied the implementation of improvement interventions in the context of VBHC by comparing two improvement interventions. To successfully implement improvements based on outcomes, a systematic implementation method can be advantageous. Implementation science, in turn, is mostly used for process-based implementation and lacks a focus on monitoring value. In this study, we evaluated two relatively comparable interventions who would both benefit from a systematic implementation method. However, improving in the context of VBHC does not necessarily mean implementation of complex interventions. We suggest that implementation science needs to be considered within VBHC but not necessarily in the form of the full proposed Integrated Implementation Model (IIM) in Chapter 4.

In this thesis, we studied the effect of a carefully selected improvement intervention on outcomes. Since the implementation (Chapter 4), evaluation of protein intake (Chapter 5) and the evaluation of LOS and 30-day mortality (Chapter 6) together offer a detailed description of the improvement intervention, our improvement intervention can be generalized to other health care settings of older patients with aortic valve disease.

We gave a detailed description of our care process (Chapter 7). When taking into account the setting, the process measures can be generalized to other locations in the Netherlands. Furthermore, we studied how outcome measures can be used to improve quality of healthcare. We used existing outcome data from a Dutch national registry as a starting point. Our findings can be generalized to other healthcare settings given outcome measurement, possibilities for benchmarking and the ambition of improving outcomes are already part of the organization. Our sub-studies were carried out in an organization that, beforehand, showed willingness and readiness to implement VBHC.

IMPLICATIONS FOR RESEARCH

In this thesis, we made a contribution to unravel *how* to use VBHC to improve quality of care. VBHC in heart care was used as starting point for implementing improvement cycles to continuously monitor and improve outcomes. The way VBHC was used in order to improve quality of care was mostly focused on improvement of outcome measures in contrast to cost improvement and redesigning of the heath care organization as suggested by Porter.

In our studies, we showed that a systematic methodology for the identification and selection of improvement interventions is essential in order to identify improvement interventions. The process was relatively time-consuming and it must be determined whether the process can be adapted to make it simpler to apply in practice outside of a research environment. Depending on availability of data and advancement of outcome measurement it needs to be determined whether all steps of the IST are compellingly necessary.

Monitoring outcomes during the implementation of improvement intervention was found to be important. Future research should focus on the use and applicability of the Integrated Implementation Model (IIM) for the implementation of improvement interventions with focus on monitoring outcomes. As the success of an implementation is determined by the feasibility of QI interventions, research should focus on minimizing the burden of implementing QI interventions. This may be done by investigating possibilities to simplify implementation approaches for the integration of implementation into a continuous QI cycle. The implementation approach and application of the IIM might also depend on the type of intervention. Certain interventions with proven effect might require a "softer" implementation approach following less steps of the IIM than interventions without proven effect. Future studies should investigate and adapt implementation approaches to fit situations of the improvement interventions.

Focusing on preoperative optimization is paramount to improve quality of care for patients suffering from aortic valve disease. As reported, the value focus for vascular surgery has shifted from improving perioperative and short-term outcomes to sustainability of health and long-term outcomes [58]. For this thesis, it was not feasible due to time constraints to consider sustainability of health through measurement of long-term outcomes, but it is recommended for future long-term research. Certainly, future studies including larger patient groups are needed to evaluate the effect of preoperative protein enriched diet on LOS, mortality and long-term outcomes, but the significant potential has been recognized [58,59].

In the context of VBHC several types of QI interventions have been observed: best practices or guidelines with proven evidence, improvement interventions with indications for evidence (e.g. in other patient groups) and those without evidence for a statistically significant impact on outcomes. Future research should investigate the difference between these types of QI interventions. Current research focusses on providing evidence for interventions before implementation into standard care. Firstly, these type of studies, including RCT studies, are time-consuming. Secondly, the implementation of interventions into standard care is slow. There might be an opportunity with VBHC to implement QI without proven evidence with the potential to improve quality of care. By measuring, monitoring and evaluating outcomes, VBHC offers guidance to improve quality of care in a systematic way when applying the suggested IST and implementation model in this thesis.

In summary, future research should focus on the following topics:

- The extent to which VBHC is implemented in health care organizations
- The evaluation of needed implementation approaches suited for different improvement interventions
- The way costs are used within VBHC to improve quality of care
- The integration of outcome measures, process measures and structure measure to improve quality of care
- The completeness, practicability and external evaluation of the IST
- Evaluation of the effect of preoperative protein enriched diet on postoperative outcomes
- Measurement and use of the suggested process measures for aortic valve disease in order to continuously improve quality of care
- Assess the patient's perspective for the selection of improvement interventions within VBHC
- Evaluate the patient's perspective for the QI with protein-enriched diet
- Appraise the difference between intervention with proven evidence for impact on outcomes vs. no proven evidence

IMPLICATIONS FOR POLICY

Outcome measurement has become paramount on the political agenda in the Netherlands as stated in the four-year plan of the Ministry of Health, Welfare and Sports [60]. The goal of the ministry is to improve quality of life for patients and improve job satisfaction as well as quality of the health care provision. This thesis shows that the term VBHC as it is currently applied will not solve the issues of increasing healthcare expenditure while

improving quality of care, but by completing the concept with practical tools and models, the application of VBHC can further be spread in the Netherlands. By involving the health care professionals throughout the entire process from the identification, selection and implementation of an improvement intervention, VBHC acted as a method for a continuous improvement cycle. The health care professionals felt engaged and therefore responsible to reflect and improve their outcomes. But only measuring the outcomes solves only part of the problem. We still need to use process measures to identify potential for improvement and monitor short-term developments. Without processes and improvement of activities, outcomes cannot be improved [50]. In the Netherlands, the ministry stimulates measurement of outcomes, but leaves processes measurement to the field. The added-value and importance of process measurement should not be undervalued by the health care professionals. In order to use insights into outcomes to achieve improved quality of care, support by the government for making best practices visible and increase knowledge on the implementation of VBHC is needed. By offering funding possibilities the concept of VBHC can further be explored in future research. Further research is needed to achieve the goal of the ministry to reach outcome-oriented care [60]. However, governments, but also insurers and other parties stimulating outcome measurement and VBHC, should not only pay attention to a good VBHC approach for improvement projects, but also consider good implementation of improvements to stimulate sustainability.

The results of this thesis fit seamlessly with the aims of the government to change healthcare systems in order to give insights into outcomes that are relevant for the patient. For realizing improvement of quality of care based on insights into outcomes practical tools, as developed in this thesis, need to be further spread and applied for a continuous improvement cycle based on insights into outcomes.

RECOMMENDATIONS

Based on this thesis some specific recommendations can be made for the application of outcome measures to improve quality of healthcare based on VBHC. Using outcome measures has given valuable insights into potential for improvement. The process for the identification, selection and implementation were relatively time-consuming and without an existing dedicated multidisciplinary team would have merely been impossible. We, therefore, recommend before attempting to improve health care outcomes, support in an organization needs to be created. Support for the concept of VBHC might act as a catalyst for achieving results in improvement work. Furthermore, choose realistic outcome measures for assessing improvement that can easily be derived from the organization's IT

system to prevent burden for health care professionals to register data. Sometimes long-term outcomes are most attractive to improve, but do not offer insights into the progress of the QI intervention and improvement in outcomes. In order to continuously evaluate the success of an improvement intervention, intermediate outcomes are recommended. These type of outcomes occur relatively frequently, as for example complications after surgery. They can offer indications and possibilities for improvement while adverse outcomes might occur too infrequent. Moreover, link process and structure measures to outcomes for reasons of actionability.

In order to implement QI based on insights into outcomes a continuous QI cycle needs to be developed. By continuously monitoring outcomes, processes and structures, possibilities for QI can easily be identified. For making a continuous QI cycle possible standard data bases are needed that ensure good quality control. VBHC, as it was used in this thesis, is a concept supporting continuous QI.

CONCLUDING REMARKS

We have evaluated *how* outcome measures lead quality improvement by making use of a systematic approach following steps from the identification of improvement to implementation and lastly evaluation. VBHC acted as a framework for improving quality of healthcare and we have successfully implemented an improvement intervention stemming from a systematic identification, selection and implementation process.

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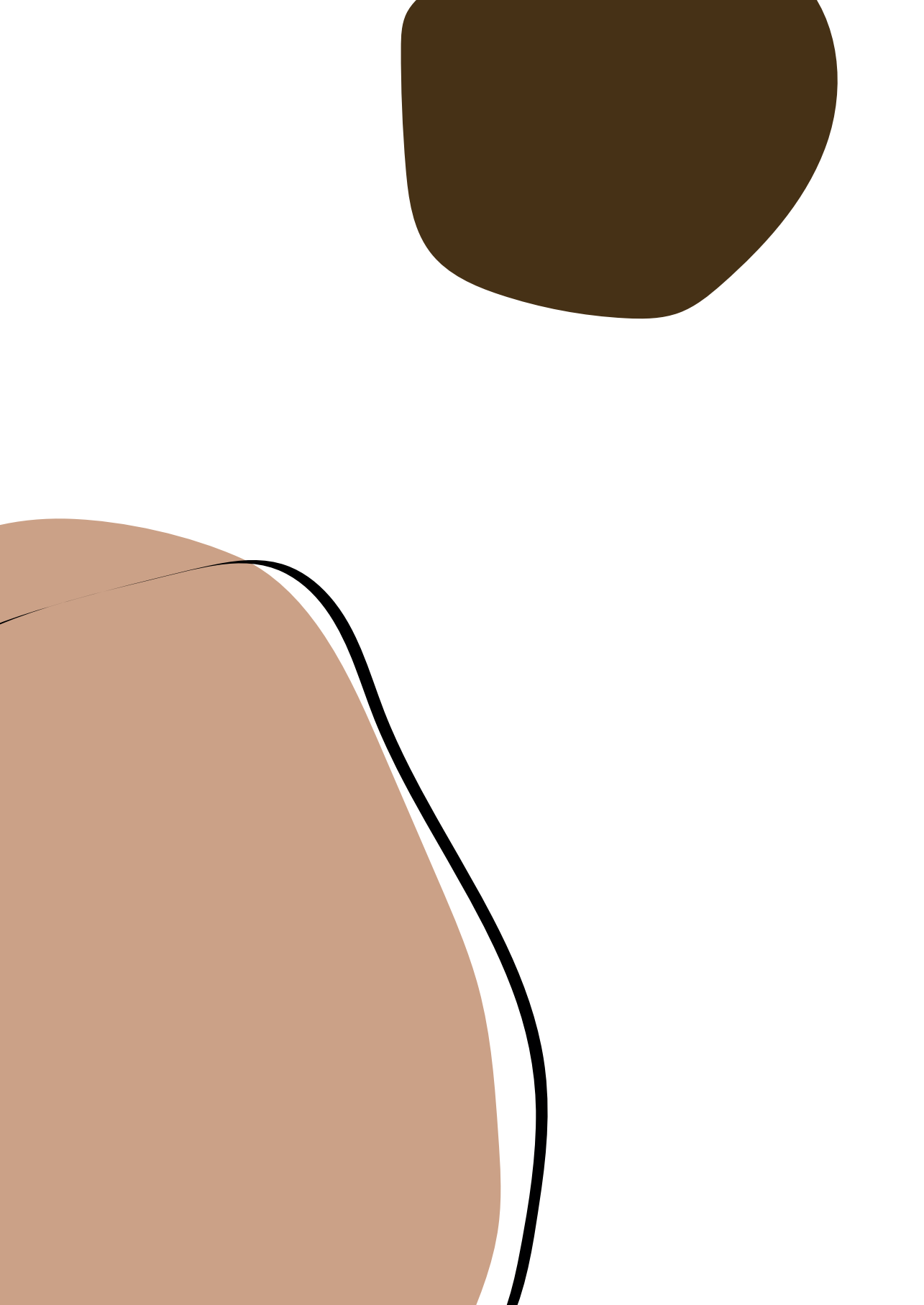

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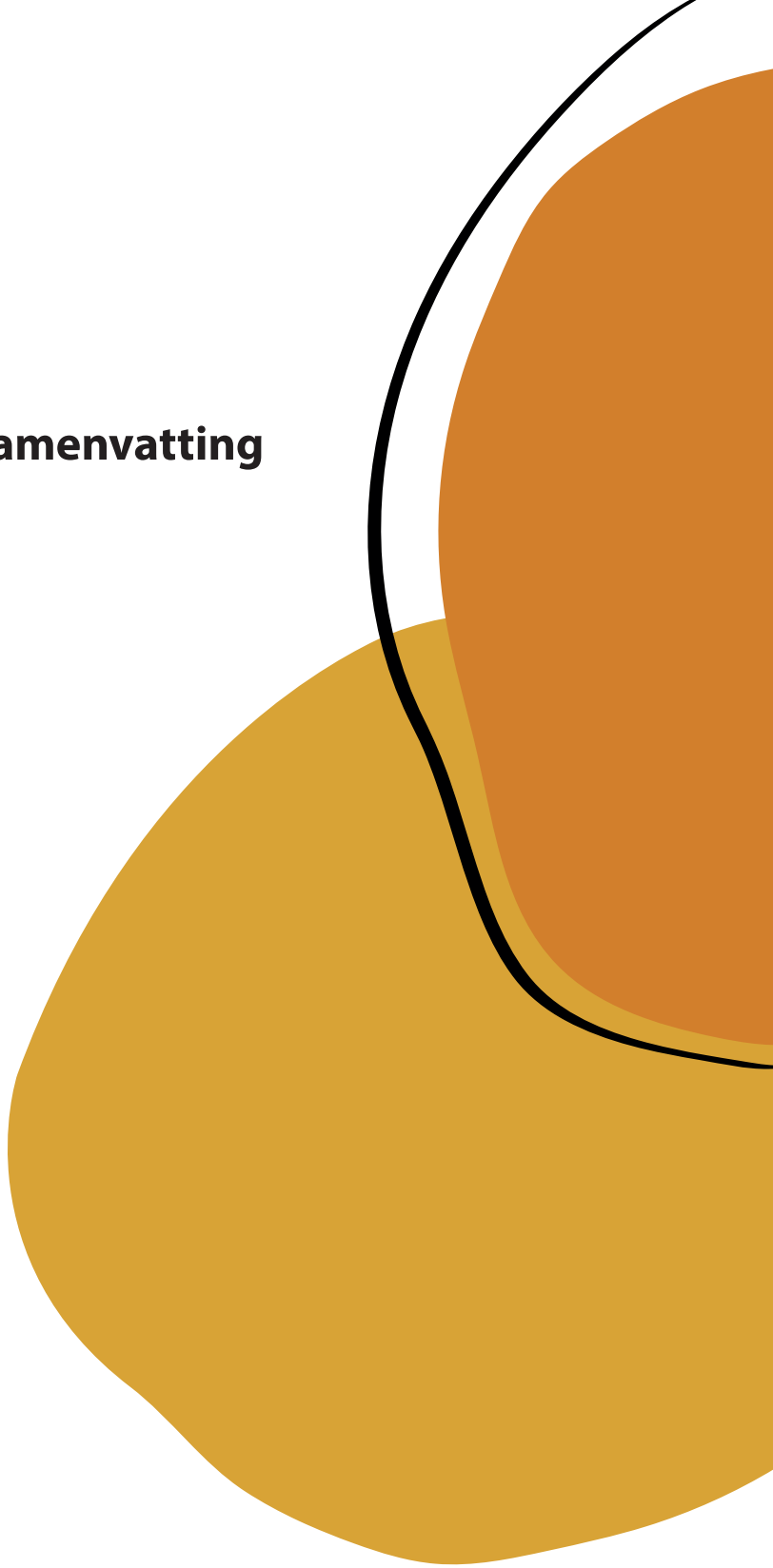

SUMMARY

The research in the context of this thesis aims at expanding our knowledge on *how* outcome measurement through Value-based health care (VBHC) can contribute to improvement of quality of health care applied to patients with aortic valve disease.

The importance of measuring and analyzing patient-relevant outcomes was already recognized by Berwick in 2003. VBHC is a concept of care that takes outcome measurement as its central starting point.
This thesis is divided into nine chapters.

The research starts with a systematic literature review to determine whether the use of clinical registries with outcome measures lead to better outcomes of care and to identify how possible improvements have been achieved. The systematic literature review is described in chapter 2. Out of a total of 11,524 unique publications, 21 studies were found that describe the use of outcome measures for quality improvement (QI). Eight of those studies demonstrated statistically significant improvements in outcomes based on data from clinical registries. The methods used for QI varied substantially, from the use of the Chronic Care Model, IT applications as feedback, benchmarking and the Collaborative Care Model. Improvement was observed in the following outcome measures: survival, hospitalization, depression, improvement in HbA1c and LDL, exercise habit, readmission rate, bleeding complication, and mortality rate. The type of QI initiatives is divers, ranging from improving teamwork, implementation of clinical guidelines, implementation of physician alters and development of a decision support system. Drivers for implementing QI initiatives include a high quality database, audits, frequent reporting and feedback, patient involvement, communication, standardization, engagement and leadership. Organizational readiness and an active approach are considered as most important for achieving improved outcomes in the systematic literature review.

Improvement based on insights into outcomes, therefore, appears to be possible, but how can improvement interventions be identified and selected? To answer this question, a case study with a concept-driven mixed-method approach was conducted. This is described in chapter 3. We analyzed patient-level outcome data from 2010-2014 from five Dutch hospitals participating in the Dutch clinical registry for heart disease (Netherlands Heart Registry). In addition, we mapped the processes of care of the St. Antonius Hospital for patients with aortic valve disease. The study resulted in a toolbox for the identification and selection of improvement interventions with an impact on outcomes: *the Intervention Selection Toolbox* (IST). With the toolbox one can: 1) measure and analyse outcomes, 2)

perform in-depth data exploration, 3) analyse the care process, 4) monitor ongoing improvement interventions, 5) describe the causal relationship between the improvement intervention and outcome measures and 6) arrive at a consensus decision. The identified improvements for the case of patients with aortic valve disease in the context of the St. Antonius Hospital include: anticoaugulation policy, increased attention to nutritional status of patients and determining frailty of patients before the treatment decision. The chosen improvement intervention with the highest expected impact on outcomes is preoperative protein enriched diet for elderly patients who have to undergo aortic valve replacement. Our toolbox integrates both care delivery process analyses with outcome analyses into an integrated approach to identify improvement interventions with the highest expected impact on patient-relevant outcomes. The IST is recommended for a wider application in VBHC projects.

Chapter 4 explored the implementation process of two improvement interventions that emerged from insights into outcomes. VBHC does not offer a systematic approach to implement improvement interventions like implementation science does. Using a qualitative comparison of two cases, the implementation process of a VBHC project *without* an explicit systematic approach (a safety checklist for heart surgery) was compared with the implementation of a VBHC improvement intervention (preoperative protein enriched diet for older patients) *with* the explicit use of a systematic approach. This qualitative study shows that outcome measures are important starting point for implementing improvement interventions and for monitoring change. Several themes were identified as most important: support, personal importance, involvement, leadership, climate and continuous monitoring. Success factors include: intrinsic motivation for the change, speed of implementation, complexity and continuous evaluation. We propose that the well-known Implementation of Change Model and VBHC strengthen each other and introduce the Integrated Implementation Model for the implementation of improvement intervention in the context of VBHC.

The effect of the chosen improvement intervention was evaluated on two levels: 1) the impact on the intermediate outcome: 'protein intake' (chapter 5) and 2) the impact on actual outcomes: hospital length-of-stay (LOS), 30-day mortality and stroke (chapter 6). To investigate the impact on protein intake, we conducted an intervention study with one treatment group requiring aortic valve replacement. The intervention consisted of protein enriched foods and drinks to be consumed before (and – which was optional- after) surgery. Participating patients completed food record questionnaires before the intervention period and also during consuming the protein enriched foods and drinks. Analysis of all questionnaires revealed the following: The study enrolled 96 patients, 63

of whom provided sufficient data to evaluate protein intake. Protein intake increased on average by 54 g (SD ± 60) per day; from 84 (SD ± 32) to 138 (SD ± 66) g per day (p<0.001). This result exceeded the initial goal to consume 45 g protein per day. Protein intake of 25 g per meal is recommended to allow for optimal protein synthesis in the body. This goal was reached more often during intervention for the meals breakfast, lunch and dinner than before the intervention only during dinner. Offering familiar protein enriched foods and drinks to older patients before cardiac surgery significantly increased protein intake.

Chapter 6 describes the evaluation of the effect of preoperative protein enriched diet on patient-relevant outcomes, namely length-of-stay (LOS), 30-day mortality rate and stroke. For this study 47 patients who underwent surgical aortic valve replacement (SAVR) and 52 patients who underwent transcatheter aortic valve replacement (TAVR) participated. The impact on LOS was not found statistically significant. Secondary outcomes, 30-day mortality rate and stroke, did not differ significantly between the intervention group and a group of patients who previously underwent the same surgery, but who did not receive any nutritional advice. Preoperative protein enriched diet is a relatively noninvasive QI intervention to improve postoperative outcomes of older patients with aortic valve disease. Based on our results, no conclusions can be drawn about a positive contribution of preoperative protein enriched diet on patient-relevant outcomes. In order to do so, larger studies including more patients need to be conducted to draw inferences.

Process measures are more actionable than outcome measures. Since process measures can be tools to change practice, chapter 7 presents process measures that influence outcomes for aortic valve disease. We studies a method to identify process measures that have an impact on outcomes. Processes were mapped during desk research and observations, followed by semi-structured interviews with health care providers and patients. Process measures were selected that were regarded to have highest impact on outcomes. In order to validate the results, a focus group was conducted. We conclude that – in addition to outcome measures – process measures are invaluable because they provide important indications for specific actions that can lead to quality improvement. 12 process measures were identified: 'Number of times that deficient information provision to SAVR patients causes negative outcomes', 'Type of SAVR/TAVR prosthesis', 'Brand of TAVR prosthesis', 'Number of times frailty score of SAVR/TAVR patients older than 75 years measured'. 'Time between SAVR/TAVR surgery indication and operation', 'Number of times that anticoagulation stopped within 3 days before surgery, 'Time in hours between TAVR/SAVR surgery and permanent pacemaker implantation' and 'Percentage of standardized pain measurements'. This study proposes to add process measures to the measurement of outcomes to improve quality of care.

In order to critically reflect on our findings of this thesis, we identified two main issues in the current application of VBHC with relevance to the relation between structure, process and outcome described in Chapter 8. With the increasing popularity of VBHC, outcome measures are often disconnected from process and structure indicators. However, in order to successfully apply VBHC, an integrated approach in which the outcome, process and structure indicators recur and strengthen each other is required. Currently, benchmarking of outcome measures is seen as the most important approach to identify improvement in the context of VBHC. However, benchmarking is not the last step, let alone an end in itself, but just the beginning; the first step in identifying improvement interventions. By expanding benchmarking with in-depth data analyses, trends and patterns can be identified. In this chapter, we claim that it is important to connect measuring and benchmarking of outcomes with existing QI techniques on process improvement. By revisiting existing methodological QI approaches would offer VBHC the handholds needed to truly improve quality of health care.

In Chapter 9, the main findings of this thesis, some methodological issues and an examination of the implications of the findings for research and policy are discussed. The results show how research into the outcomes of care can serve as a starting point for implementing improvement cycles to continuously monitor and improve outcomes. Outcome measurement has become paramount in the Netherlands as it promotes engagement and involvement of health care providers, challenges them to reflect on their (contribution to the) outcomes and stimulates improvement. However, the added-value of process measurement should not be undervalued: without insight into the relationship between process and outcome, no improves outcomes of care!

SAMENVATTING

Het onderzoek in het kader van dit proefschrift heeft als doel het vergroten van kennis over hoe uitkomstmeting kan bijdragen aan het verbeteren van de kwaliteit van de zorg, toegepast op patiënten met aortakleplijden. Het belang van het meten en analyseren van patiëntrelevante uitkomsten werd al in 2003 erkend door Berwick. Value-based health care is een visie op de zorg die uitkomstmeting als centraal uitgangspunt neemt. De laatste jaren is VBHC in Nederland een veelgebruikte visie om kwaliteit van zorg te verbeteren. Dit proefschrift is gestructureerd in negen hoofdstukken.

Het onderzoek is gestart met een systematische literatuurstudie om te bepalen of het gebruik van klinische registraties met uitkomstmetingen leidt tot een beter resultaat van zorg en te onderzoeken hoe eventuele verbeteringen tot stand zijn gekomen. Deze literatuurstudie wordt beschreven in hoofdstuk 2. Uit een totaal van 11524 unieke publicaties werden 21 artikelen gevonden, die het gebruik van uitkomstindicatoren voor kwaliteitsverbetering beschreven. Acht van de studies tonen statistisch significante verbeteringen aan in uitkomsten van zorg op basis van data uit klinische registraties. De studies gebruikten uiteenlopende methoden voor kwaliteitsverbetering, zoals het Chronic Care Model, IT-toepassingen als feedback, benchmarking en het Collaborative Care-model. Verbetering is waargenomen bij de volgende uitkomstindicatoren: overleving, ziekenhuisopname, depressie, verbetering van HbA1c en LDL waarden, lichaamsinspanning, heropnames, complicaties met bloedingen en sterfte. Het type verbeterinitiatieven is divers, variërend van verbetering van teamwerk, implementatie van klinische richtlijnen, verandering in werkwijze van artsen en ontwikkeling van een beslissingsondersteunend systeem. Bevorderende factoren voor de implementatie van kwaliteitsverbeteringsinitiatieven betreffen: een database van hoge kwaliteit, audits, frequente rapportage en feedback, patiëntbetrokkenheid, communicatie, standaardisatie, betrokkenheid en leiderschap. Bereidheid van de organisatie en een actieve aanpak wordt in de systematische literatuurstudie als het belangrijkste gezien voor het bereiken van verbeterde uitkomsten.

Verbetering op basis van inzichten in uitkomsten blijkt dus mogelijk, maar hoe kunnen verbeterinterventies het beste worden geïdentificeerd en geselecteerd? Om deze vraag te beantwoorden, werd een case studie met een combinatie van kwantitatieve en kwalitatieve methodes uitgevoerd. Deze is in hoofdstuk 3 beschreven. We analyseerden uitkomstgegevens uit de jaren 2010 tot en met 2014 op patiëntniveau van vijf Nederlandse ziekenhuizen. Daarnaast brachten we het proces in kaart van de zorg van het St. Antonius Ziekenhuis voor patiënten met aortakleplijden. De studie resulteerde in een *toolbox* voor de

identificatie en selectie van verbeterinterventies met impact op uitkomsten: de *Intervention Selection Toolbox* (IST). Met de toolbox kun je achtereenvolgens: 1) uitkomsten meten en analyseren, 2) diepgaande data analyse verrichten, 3) het zorgproces analyseren, 4) lopende verbeteracties monitoren, 5) het causale verband tussen de verbeterinterventie en uitkomstmaten beschrijven en 6) komen tot een consensusbeslissing. De geïdentificeerde verbeteringen voor de casus "patiënten met aortakleplijden" bij het St. Antonius Ziekenhuis zijn: anticoagulantia beleid, meer aandacht voor de voedingsstatus van patiënten en het bepalen van de kwetsbaarheid van patiënten vóór de behandelbeslissing. De gekozen verbeterinterventie met hoogste verwachte impact op uitkomsten is preoperatieve eiwit verrijkte voeding voor oudere patiënten die een aortaklepvervanging moeten ondergaan. De toolbox integreert procesanalyse met de analyse van uitkomstdata tot een integrale aanpak om verbeteracties te vinden met de grootste potentiele impact op patiënt-relevante uitkomsten. De IST wordt aanbevolen voor bredere toepassing in het kader van Value-based health care projecten.

Hoofdstuk 4 onderzoekt het implementatieproces van twee verbeterinterventies. VBHC biedt geen systematische aanpak voor het implementeren van verbetering zoals implementation science dat doet. Aan de hand van kwalitatieve vergelijking van twee casussen is het implementatieproces van een VBHC project *zonder* een systematische aanpak (een veiligheidschecklist voor hartchirurgie) vergeleken met de implementatie van een VBHC verbetering (preoperatieve eiwit verrijkte voeding voor ouderen) *met* een systematische aanpak. Deze kwalitatieve studie toont aan dat inzicht in uitkomsten een belangrijk uitgangspunt vormt voor het implementeren van verbeterinterventies en voor het monitoren van verandering. Verschillende aspecten blijken belangrijk: ondersteuning door alle betrokkenen, persoonlijk belang van betrokkenen, leiderschap, (werk)klimaat en continue monitoring. Succesfactoren zijn: intrinsieke motivatie voor de verandering, snelheid van implementatie, complexiteit van een interventie en continue evaluatie. Wij stellen voor dat het bekende *Implementation of Change Model* en VBHC elkaar versterken en introduceren het *Integrated Implementation Model* voor de implementatie van verbeterinterventies in het kader van VBHC.

Het effect van de gekozen verbeterinterventie is op twee niveaus geëvalueerd: 1) de impact op de intermediaire uitkomst: 'eiwitinname'(Hoofdstuk 5) en uiteindelijk de impact op daadwerkelijke uitkomsten: ligdagen in het ziekenhuis (LOS), 30-daagse mortaliteit en beroerte (CVA) (Hoofdstuk 6). Om de impact te onderzoeken van eiwitintake, voerde we een interventiestudie uit met één groep patiënten, die geopereerd moesten worden wegen een aortaklepaandoening. De interventie bestond uit het eten en drinken van eiwit verrijkte producten voorafgaand (en – dat was optioneel – na) de operatie. Deelnemende

patiënten vulden vragenlijsten in *voor* de periode van inname van eiwit verrijkt eten en drinken en ook *tijdens* die periode. Analyse van alle vragenlijsten wees het volgende uit: Aan het onderzoek namen 96 patiënten deel, van wie 63 voldoende gegevens boden voor de evaluatie op de eiwitinname. De eiwitinname steeg gemiddeld met 54 g (SD ± 60) per dag; van 84 (SD ± 32) tot 138 (SD ± 66) g per dag (p <0,001). Dit resultaat overtrof het oorspronkelijke doel om 45 g eiwit per dag te consumeren. Eiwitinname van 25 gram per maaltijd wordt aanbevolen om een optimale eiwitsynthese in het lichaam mogelijk te maken. De interventie resulteerde voor de maaltijdmomenten ontbijt, lunch en diner in significant meer eiwitinname. Het aanbieden van eiwit verrijkt eten en drinken aan oudere patiënten *vóór* hartchirurgie verhoogde de eiwitinname aanzienlijk.

Hoofdstuk 6 beschrijft de evaluatie van het effect van het preoperatief eiwit verrijkt dieet op patiëntrelevante uitkomsten, namelijk ligdagen (LOS), 30-daagse sterfte en beroerte (CVA). Voor deze studie zijn 47 patiënten bevraagd, die een chirurgische aortaklepvervanging (SAVR) ondergingen en 52 patiënten die een minimaal invasieve aortaklepvervanging (TAVR) ondergingen. De impact op LOS bleek niet statistisch significant. Secundaire uitkomsten, '30-daagse mortaliteit' en 'CVA', verschillen niet statistisch significant tussen de interventiegroep en een groep van patiënten die eerder vergelijkbare operaties ondergingen, maar die de voeding niet ontvingen. Preoperatief eiwit verrijkt dieet is een relatief niet-invasieve verbeterinterventie om de postoperatieve uitkomsten te verbeteren van oudere patiënten met aortaklepaandoeningen. Op basis van onze resultaten kunnen we geen conclusies trekken over een over een positieve bijdrage van een preoperatief eiwit verrijkt dieet aan patiëntrelevante uitkomsten. Om dit te wel te kunnen doen, dient een grotere studie met meer patiënten te worden uitgevoerd.

Aangezien procesindicatoren middelen kunnen zijn om de praktijk te veranderen, presenteert Hoofdstuk 7 procesindicatoren die van invloed zijn op uitkomsten voor aortakleplijden. Daartoe hebben we een methode bestudeerd om procesindicatoren te identificeren die impact hebben op uitkomsten. Met bureauonderzoek en observaties werden processen in kaart gebracht en vervolgens zijn er semigestructureerde interviews gehouden met zorgverleners en patiënten. We selecteerden *die* procesindicatoren, waarvan we verwachtten dat zij het grootste effect zouden hebben op uitkomsten. Om de resultaten te valideren werd een focusgroep bijeenkomst gehouden. We concluderen dat -naast uitkomstmaten - procesindicatoren van onschatbare waarde zijn omdat ze belangrijke aanwijzingen geven welke specifieke acties wel en welke niet leiden tot kwaliteitsverbetering. Er zijn 12 procesindicatoren geïdentificeerd: 'Aantal keren dat gebrekkige informatievoorziening aan SAVR-patiënten negatieve uitkomsten veroorzaakt', 'Type SAVR / TAVR-prothese', 'Merk van TAVR-prothese', 'Aantal

keer dat kwetsbaarheidsscore van oudere SAVR / TAVR-patiënten ouder dan 75 jaar is gemeten ', 'Tijd tussen indicatie voor operatie van SAVR / TAVR en de operatie', 'Aantal keren dat antistolling binnen drie dagen voor de operatie stopte', 'Tijd in uren tussen voorbereiding TAVR / SAVR-operatie en het plaatsen van een pacemaker', en 'Percentage gestandaardiseerde pijnmetingen'. Deze deelstudie stelt voor om procesindicatoren toe te voegen aan het meten van uitkomstindicatoren om de kwaliteit van zorg te verbeteren.

Hoofstuk 8 geeft een reflectie op hoe VBHC op dit moment wordt geïmplementeerd in de zorg. Bij VBHC ligt de nadruk op uitkomsten. Maar om verbeteringen te monitoren en te identificeren zijn proces- en structuurindicatoren belangrijk. Met de groeiende populariteit van VBHC worden uitkomstindicatoren vaak losgekoppeld van proces- en structuurindicatoren. Maar voor een bestendiging van VBHC is een integrale aanpak nodig waarin uitkomst- proces- en structuurindicatoren terugkomen en elkaar versterken. Daarnaast ontbreekt binnen VBHC een systematische aanpak om verbeterinterventies te identificeren en te selecteren. Op dit moment wordt benchmarking van uitkomstindicatoren gezien als de belangrijkste aanpak om verbetering in het kader van VBHC te identificeren. Benchmarking is echter niet de laatste stap, laat staan een doel op zich, maar slechts het begin; de eerste stap voor het identificeren van verbeterinterventies. Door benchmarking uit te breiden met diepgaande data-analyses kunnen trends en patronen worden geïdentificeerd. We laten in dit hoofdstuik zien dat het belangrijk is om het meten en standaardiseren van uitkomsten te koppelen aan bestaande kwaliteitsverbeteringsmethodieken voor procesverbetering.

In hoofdstuk 9 worden de belangrijkste bevindingen van dit proefschrift, enkele methodologische onderwerpen en de implicaties van de bevindingen voor praktijk, vervolgonderzoek en beleid besproken. De resultaten van dit onderzoek laten zien hoe onderzoek naar uitkomsten van zorg kan dienen als startpunt voor het implementeren van verbetercycli om de uitkomsten continu te monitoren en te verbeteren. Uitkomstmetingen zijn in Nederland van groot belang geworden. Ze bevorderen de betrokkenheid van zorgverleners, dagen hen uit om na te denken over hun (bijdrage aan de) resultaten en prikkelen tot verbetering. De toegevoegde waarde van procesmeting mag echter niet worden ondergewaardeerd: zonder inzicht in de relatie tussen proces en uitkomst, geen betere uitkomsten van zorg!

DATA MANAGEMENT

The data obtained during the PhD at the St. Antonius Hospital in collaboration with the Radboud University medical center (Radboudumc) are archived according to the Findable, Accessible, Interoperable and Reusable (FAIR) principles [1].

For this overall thesis a non-medical scientific research declaration was obtained from the Medical Research Ethics Committees United of the St. Antonius Hospital with the following reference number: W15.006.

Initially, raw and processed data was stored digitally on a local server of the Department of Value-Based Healthcare of the St. Antonius Hospital. All data archives are stored on the local server in secured sub-files which are only accessible by the associated senior staff members.

The raw and analyzed research data of Chapter 3-8 are stored in secured digital files on a local server of the Department of Value-Based Healthcare. The digital raw data generated for the analysis of Chapter 5 are stored on REDCap as part of the local account of the Department of Cardiology. Only the associated staff has access to the data. The analyzed data are stored on the local server of the Department of Value-Based Healthcare within designated secured files only accessible for associated researchers. The data collected on protein intake were collected via a secured digital questionnaire platform, voedselvragenlijsten.nl, of Wageningen University. The digital questionnaires are saved in the secured environment of the food questionnaire platform of the Wageningen University. The paper questionnaires and informed consent forms are saved in the sub-archive of the St. Antonius Hospital (Centraal Archief, Industrieweg 14, 3433 NL Nieuwegein). The data will be stored for 15 years after termination of the study (July 15th, 2019). The study was approved by the Medical Research Ethics Committees United under reference number W16.170. All data generated or analyzed in this thesis are included in submitted or published articles and additional data is available upon request from the associated corresponding author.

1 Wilkinson MD, Dumontier M, Aalbersberg IJ, *et al.* The FAIR Guiding Principles for scientific data management and stewardship. *Sci data* 2016;3:160018.

DANKWOORD

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De allerlaatste woorden zijn natuurlijk voor Frederick: Seg, nun schreibe ich an den letzten Worten dieser These. Gemeinsam haben wir die ersten Worte Niederländisch gelernt als wir uns vor fünf Jahren zusammen entschieden in Utrecht zu bleiben. Mittlerweile, tauschen wir Worte auf vielen verschiedenen Sprachen miteinander aus, oftmals ein Mix aus Deutsch, Niederländisch und Englisch. Dein aufrichtiges Interesse und die unzähligen Abende in denen wir über unsere Arbeit philosophiert haben, haben mir die Kraft gegeben es bis hier hin zu schaffen. Danke, dass du mich jeden Abend Tränen lachen lässt, durch deine Lösungen meine Sorgen beiseiteschiebst, immer parat stehst für jeden Schabernack und mich bei Bedarf mit beiden Füßen wieder auf den Boden der Tatsachen zurück bringst. Ich freue mich jetzt schon auf die nächsten Abenteuer in unserem gemeinsamen Leben!

ABOUT THE AUTHOR

Nina Zipfel, born on September 1st, 1990 in Toenisvorst in Germany, grew up in Erkelenz, Germany. In 2007, she spent a year in the United States where she received the American High School Diploma from Cannon Falls High School. After returning to Germany, Nina completed her secondary school diploma, from Cusanus-Gymnasium in Erkelenz in 2010. Shortly thereafter, she moved to Maastricht, the Netherlands, to study European Public Health at Maastricht University. As part of the Bachelor program, she studied Physiotherapy and Nursing for one semester at Semmelweis University in Budapest, Hungary. After graduation from the Bachelor program in 2013, Nina studied Epidemiology for her Master's Degree at Maastricht University. She completed her Master with an internship on the trends of Cannabis in Europe at the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in Lisbon, Portugal, in 2014. As her interest in research grew stronger, she started working as a student assistant as part of the EnCoRE study on colorectal cancer survivors at the GROW School of Maastricht University in 2014. During her studies she worked as a teaching assistant for the Bachelor Program 'European Public Health' from 2013 to 2015.

In 2015, she started her PhD research project at the department of Value-based healthcare at the St. Antonius Hospital, Nieuwegein, the Netherlands in collaboration with the scientific research institute IQ Healthcare, Radboud University Medical Center, Nijmegen, the Netherlands. The project focused on investigating whether working with Value-based health care and patient-relevant outcomes leads to improved quality of health care. During her PhD, she joined the board of the organization "Jong Antonius" for young employees at the St. Antonius Hospital. She also is an active member of a young healthcare think tank called "Jonge Zorgdenktank" where she further expands her view and discusses health care issues with young professionals from various backgrounds. In 2018, she attended the specialized intensive seminar on Value-Based Health Care Delivery at Harvard Business School in Cambridge, United States of America. She has supervised MSc thesis students and co-taught a course as part of the medical studies at Radboudumc, Nijmegen. In 2019, she started as a postdoc researcher at the Coronel Institute of Occupation health at the Amsterdam university medical center where she continues her research focus on implementation and improvement science.

PhD Portfolio

Institute for Health Sciences
Radboudumc

Name PhD candidate: N. Zipfel	**PhD period: 01-02-2015 – 15-07-2019**
Department: IQ healthcare	**Promotor(s): Prof. G.P. Westert**
Graduate School: Radboud Institute for Health Sciences	**Co-promotor(s): Dr A.S. Groenewoud, Dr P.B. van der Nat, Dr B.J.W.M. Rensing**

		Year(s)	ECTS
	TRAINING ACTIVITIES		
a)	***Courses & Workshops***		
	- RIHS introductory course (Radboud University)	2015	1.5
	- Cochrane Systematic Review Course (Radboudumc)	2015	2.0
	- English Writing for Scientific publications (St. Antonius Hospital)	2015	0.5
	- Course presenting in English (St. Antonius Hospital)	2015	0.4
	- E-BROK basic course (St. Antonius Hospital)	2016	0.2
	- RIHS Scientific Integrity course (Radboud University)	2016	1.5
	- Value Based Healthcare Masterclass (Value in Care)	2017	0.2
	- Course Implementation Science in Health Care (Radboudumc)	2017	2.0
	- Course Introduction to R (Radboudumc)	2017	0.3
	- Course Analyzing Qualitative Research (Radboudumc)	2017	0.2
	- Career Guidance (Radboud University)	2017	1.75
	- Course longitudinal data analysis (St. Antonius Hospital)	2018	1.75
b)	***Seminars & lectures***		
	- EMGO+ Annual Meeeting/Care Day	2015	0.2
	- Seminar Value-based healthcare (VitalHealth)	2015	0.1
	- Radboud Research Round: Healthcare improvement science	2016	0.1
	- Value-Based Health Care and Cost-effectiveness (VGE, LUMC)	2017	0.1
	- Workshop 'Week of the Implementation', oral presentation	2018	0.5
	- Value-Based Health Care Delivery Intensive Seminar (Harvard Business School)	2018	2.0
c)	***Symposia & congresses***		
	- Santeon Symposium 'Zorg voor Uitkomst'	2015	0.1
	- Symposium 'Uitkomsten van onze zorg' (St. Antonius Hospital)	2015	0.1
	- Symposium 'The scientific basis for the evaluation of quality of hospital care (Erasmus MC)	2015	0.1
	- Meetbaar Beter Symposium	2015	0.1
	- Symposium 'Uitkomsten van onze zorg (St. Antonius Hospital)	2016	0.1
	- Meetbaar Beter Symposium	2016	0.1
	- ICHOM conference	2016	0.5
	- ISQua's 33rd International Conference, poster presentation	2016	1.5
	- Santeon Symposium 'Zorg voor Verbetering'	2017	0.1
	- Symposium 'Uitkomsten van onze zorg' (St. Antonius Hospital)	2017	0.1
	- PhD Retreat RIHS (Radboud University)	2017	0.5
	- Choosing Wisely 'Value added care conference'	2017	0.25
	- Symposium Netherlands Heart Registry (NHR)	2017	0.2
	- Science night, poster presentation (two) (St. Antonius Hospital)	2017	0.5
	- ISQua's 34th International Conference, poster presentation	2017	1.5
	- EHMA Annual Conference, oral presentation	2019	1.25
d)	***Other***		
	- Journal Club (St. Antonius Hospital)	2015-2019	2.0
	- Member 'Jonge Zorgdenktank'	2016-2019	3.5
	- Board member 'JongAntonius'	2018	1.0

	TEACHING ACTIVITIES		
e)	***Lecturing***		
	- Working groups CSI-Diabetes Mellitus PROM+VBC (Radboud University)	2018	0.4
f)	***Supervision of internships, other***		
	- Supervision student MSc Management Policy Analysis and Entrepreneurship in the Health and Life Sciences	2015	2.0
	- Supervision student MSc Healthcare policy and innovation management	2016	2.0
	- Supervision student MSc Healthcare policy and innovation management	2017	2.0
	- Supervision student MSc Nutrition and Health	2018	2.0
	- Reviewer for scientific publications	2019	0.1
TOTAL			**37.3**

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