Savings, scaling and sustainability: increasing the impact of de-implementation strategies

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General introduction

There is an increasing interest in reducing low-value care worldwide.(1) Low-value care is either care that is not beneficial for patients or care for which the value does not offset the risks or costs given the available alternatives.(2) Low-value care practices risk preventable adverse events and waste limited resources. For example, inappropriate drug prescriptions risk side-effects, inappropriate intravenous catheters risk infections, inappropriate laboratory testing risk false positive results and subsequent downstream testing, unnecessary follow-up consultations waste time of patients and doctors, and inappropriate upper endoscopies are on top of all rather unpleasant.(3-5) Prevalence estimations of inappropriate diagnostic testing range from 0.09% to 97.5%.(6) Additionally, the impact of reducing low-value care practices also varies, ranging from saving a few euros by preventing an inappropriate vitamin test to reducing the workload for healthcare professionals and potential harm for patients by reducing an inappropriate surgical procedure.(7, 8) Overall, low-value care is a pressing matter in healthcare systems and it limits the capacity to provide high-value care.(1)

National and international de-implementation programs have been reducing low-value care since the last two decades. The Choosing Wisely campaign started raising awareness about low-value care in the United States in 2011 and has reached over 30 countries.(9) In the Netherlands, the national program *To do or not to do?* (in Dutch: *Doen of laten?*) actively de-implemented low-value care from 2015 to 2023. In the first part, the program focused on reducing eight types of low-value care, increasing knowledge of de-implementation, and raising awareness. In the subsequent four years, 15 other types of low-value care were reduced, the volume of multiple low-value care practices was measured, and insights were gained about the long-term sustainability of de-implementation strategies. Effective strategies were also scaled and spread to other healthcare professionals.(10)

De-implementation research has led to a better understanding on how to successfully reduce low-value care. Grimshaw et al. developed a framework supporting policy makers and healthcare professionals to *de-implement wisely*.(11) The de-implementation process was divided into in five phases: 1. the identification of low-value care, 2. identification of local priorities, 3. identification potential de-implementation strategies, 4. evaluation of the strategy and 5. the spread of effective strategies. Notably, the sustainability of effective strategies was not considered as a separate phase, but briefly mentioned in the last phase. Spreading and scaling have, however, a different aim and require therefore a different approach. The main focus of spreading is expanding the reach regionally by raising awareness and tempting potential adopters to adopt the strategy.(12) The main focus of sustainability is to maintain the strategy and its effects locally.(12) Therefore, I have adapted the framework and split these processes to emphasize the differences. In addition, since there is a considerable overlap between identification of low-value care

and the local priorities, these phases were merged. This is shown in figure 1. The first three phases are widely studied, while less attention is paid on the evaluation of the societal benefits, the scaling and the sustainability of de-implementation strategies. Optimizing these aspects could increase the impact of de-implementation efforts considerably. Therefore, the general objective of this thesis is to enhance the understanding of capturing societal cost savings, the scaling of projects, and the long-term sustainability of effective strategies.

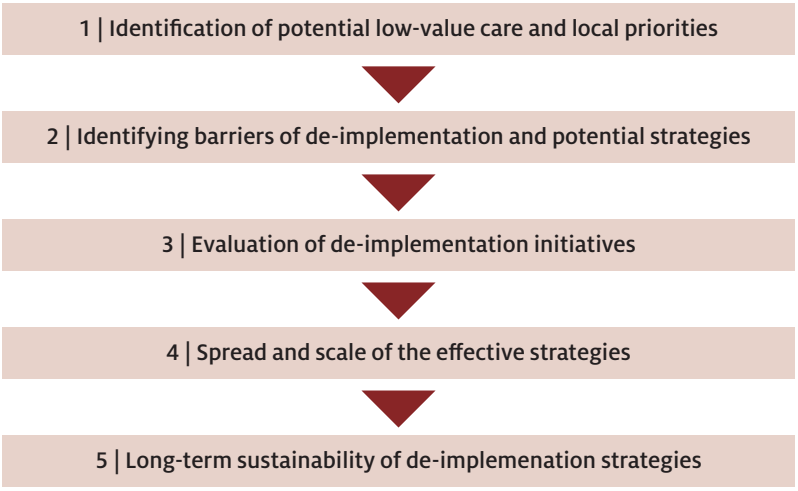

Figure 1 | Phases of de-implementation, adapted from 'de-implementing wisely: developing the evidence base to reduce low-value care by J.M. Grimshaw et al.' (11)

Phase 1 | Identification of potential low-value care and local priorities

There are several ways to identify low-value care practices.(1) A commonly used method is the screening of existing literature and clinical guidelines.(13-16) During the prioritization process, healthcare providers are typically asked to identify the most relevant low-value care practices.(14, 17, 18) An example is a survey among professionals to score several criteria of the identified low-value care practices. Used criteria are: the prevalence of the practice, the potential harm for patients, and potential costs.(14, 16) Also the delphi method is used to seek consensus about the most relevant low-value care.(19) Although patients or patient representatives can participate in the prioritization process, they are less commonly involved and their role may be limited.(19, 20) This, while patients are the receivers of low-value care.

The volume of inappropriate care is an important criterion; if the low-value care practice is rarely prevalent, reduction may not be priority.(15) However, determining the volume

of low-value care can be challenging.(6) It requires a clear and measurable definition of when care is appropriate or inappropriate. This definition is not always clear because the value of care often occurs along a continuum.(21) The value of treatments and diagnostic tests depend on the symptoms and characteristics of the patient. This makes volume measuring in large databases challenging.

Phase 2 | Identifying barriers of de-implementation and potential strategies

After low-value care is prioritized, it should be reduced. De-implementation strategies can facilitate the reduction of low-value care practices. These strategies are preferably tailored to the barriers and facilitators of a specific context.(11, 22) A recent review identified barriers and facilitators in 81 articles.(22) The barriers were related to healthcare provider characteristics, such as knowledge, attitude and behaviour, patients characteristics, organizational contexts, social contexts, and economic political context.(22) More specifically, frequently identified barriers are patient expectations, clinical uncertainty, inadequate information management, financial disincentives, negative staff attitudes and anxiety to change practice, and lack of time.(17, 22, 23)

There are various strategies to reduce low-value care aiming to initiate a behavioural change of patients, healthcare professionals or both.(24) Frequently used strategies are audit and feedback, patient education, education for healthcare professionals and a combination of these strategies. (25) Most strategies do not target all identified barriers.(26, 27) Therefore, it would be interesting to know the comparative effectiveness of the strategy types. Is one type of strategy more often effective than others? **Chapter 2** provides an overview of the effectiveness of strategies aiming to reduce inappropriate prescribing.

Phase 3 | Evaluation of de-implementation strategies

The effectiveness of strategies can be determined by measuring the reduction of the total volume of a care practice or the volume of the low-value care specifically. The volumes can be compared to the situation before the intervention or to a control group. De-implementation strategies are frequently effective in reducing volumes of inappropriate care.(24) However, the actual effects for patients and society rarely studied. For patients, de-implementation may translate in to less burden, harm of side-effects and less risk of complications.(28) These effects are, however, more difficult to measure than the volume reduction. Adverse events are less common than the low-value care itself, and studies therefore require a larger sample size to demonstrate positive effects on these outcomes.(3) From a society perspective large scale de-implementation would improve the quality of care by replacing low-value care with high value care and may save healthcare related costs. These positive effects are even more challenging to measure and therefore often only estimated. Nevertheless, de-implementation studies regularly claim that reducing a

particular care practices will save society millions of dollars. For example, the spending on low-value care was estimated to range from $75.7 to $226 billion in the United States.(29, 30) In addition, Shrank et al. estimated that the nationwide scaling of seven effective de-implementation strategies could save $12.8 billion to $28.6 billion annually.(30) Another study promised the National Health Service (NHS) to save 150 million euros if five low-value surgeries would be phased out.(31) In **chapter 3** we explain why such estimations do not reflect the actual savings potential of de-implementation.

In times of rising healthcare spending, policymakers and healthcare organizations are seeking effective methods to bend the cost curve while preserving or even improving the quality of care.(32, 33) Although the primary aim of most the quality improvement initiatives is enhancing quality of care, occasionally substantial cost-savings are anticipated for society.(24, 34-37) However, the translation of such theoretical savings of quality improvement initiatives into actual societal cash savings is complex and often not achieved.(38)

Four stages in the process of capturing societal savings can be extracted from the literature: 1. Reducing capacity, 2. Reducing departmental expenses, 3. Reducing hospital expenses, 4. Reducing insurer costs.(34, 38-42) These stages represent a potential pathway from an initiative towards cost-savings, however real-world scenarios may also be driven by the hospital's or insurer's investments. Various mechanisms are described to complicate the process, but comprehensive understanding of capturing societal cost savings is lacking. In **chapter 4**, we studied the barriers and facilitators of the four stages by using prehabilitation as a test case. Prehabilitation is a lifestyle improvement program that is offered to patients prior to major surgery. Prehabilitation has shown to reduce the number of surgical complications, reoperations and the average length of hospital stay.(43-45) Moreover, a recent review revealed evidence that prehabilitation can be cost-effective compared to usual care.(46)

Phase 4 | Spread and scale of the effective strategies

Many de-implementation projects start locally, and the spread of these strategies rarely occurs spontaneously.(47) Expanding the target population and implementing the strategies in more healthcare organizations have the potential to substantially increase the strategy's impact. Everett Rogers first introduced his Diffusion of Innovations theory in 1962, and it is applied in many fields, including healthcare.(47) This theory describes the spread of innovations from innovators through early adopters, early majority, late majority and laggards.

Innovators bring new innovations, such as new de-implementation strategies, in a health system. **Early adopters** are local role models and the first to approve the innovators' ideas. These are the first targets for raising awareness in spreading strategies. **Early majority** are 'not the first by which the new is tried, nor the last to lay the old aside.' They will soon follow after there is evidence of the effectiveness of strategies. **Late majority** approach innovations with skepsis and caution. They do not adopt a strategy until a majority has already done so. **Laggards** have strong traditional values and make decisions mostly based on what has been done in the past. They are the most cautious in adopting strategies.(47)

Rogers' theory describes various facilitators to spread of innovations. Although there are several similarities, de-implementation interventions are not equivalent to innovations. Healthcare innovations provide new possibilities, for example, additional diagnostic tests or new options for treatment.(47) De-implementation, on the other hand, aims to discontinue the provision of low-value care.(2, 48) Consequently, de-implementation is complicated by psychological biases. People unconsciously tend to favor information that confirms their beliefs.(49) This confirmation bias applies especially to de-implementation, since it requires clinicians to abandon clinical practices they previously thought to be evidence-based.(49, 50) The abandonment of care could also be experienced as a loss, even if it concerns care without value for the patient. Additionally, de-implementation is also affected by loss aversion, the tendency to avoid loss.(51) Moreover, the barriers for de-implementation differ as well.(52) For example, providing low-value care can be lucrative for healthcare providers and organizations due to current payment systems, such as fee-for-service payment.(53, 54) The differences between implementation and de-implementation result in a different focus regarding intervention strategies and may also be relevant for the dissemination process.(55, 56) Because of the nuances between implementation and de-implementation, we studied which factors influence the spread of de-implementation strategies and how these can be used to facilitate the spreading and scaling. This is described in **chapter 5**.

One of the de-implementation strategies we have scaled is the TRIODE project: a web-based patient education tool for dyspeptic patients.(57) The e-learning was effective in reducing inappropriate upper gastrointestinal tract (GI) endoscopies by increasing knowledge and providing self-management recommendations. However, the strategy was stopped after the study period, because it did not fit the daily practice, and depended on one physician-researcher and temporary funding. A scaling team adapted the e-learning to fit the daily practice. In addition, during the evaluation of the project, doctors and patients recommended to make the tool also available for patients in primary care. The scaling team interviewed multiple general practitioners and concluded that the e-learning should be placed on an already existing platform that is reliable and accessible

to patients and doctors. These conclusions let to a collaboration with Thuisarts.nl, the patient information site of the Dutch College of General Practitioners.(58) The e-learning was modified to fit the broader public and the design of Thuisarts.nl. The broadening of the target population and the adjustments raise the question whether the tool is still effective in improving self-management and reassuring patients. This question is addressed in **chapter 6**.

Phase 5 | Long-term sustainability of de-implementation strategies

When strategies are effective and have proven their value, results should also sustain in the long term. In literature, we find many quality improvements, including de-implementation strategies, that have been proven effective.(24) There are, however, only a few studies that also report the long-term effects.(24, 59) The benefits of a strategy are rarely reported for post-intervention periods longer than a year, and even fewer studies report the effects after the post-intervention period.(24, 35, 59, 60). Achieving sustainable results is challenging and is considered as one of the most important translational research problems.(61)

There is currently no consensus about what long-term sustainability is, and how it should be determined. There are various definitions of long-term sustainability with different viewpoints. Moore et al. defined sustainability as: 'after a defined period of time, a program, intervention or implementation strategies continue to be delivered and/or individual behavior change (i.e. clinician, patient) is maintained; the program and individual behavior change may evolve or adapt while continuing to produce benefits for individuals/systems'.(62) This comprehensive definition presents multiple perspectives on long-term sustainability: the patients, healthcare providers, and the strategy.

The patients: Has the patient's behavior changed and did the same patient not receive the avoided low-value care after a period of time? This perspective is particularly interesting for patient-targeted strategies, like the above mentioned TRIODE project.(57) After completing the e-learning, 60% of the participants cancelled the upper GI endoscopy. The researchers collected data up to 12 months to determine the sustainability and the participants did not receive an upper GI endoscopy after completing the e-learning. From the patients perspective, long-term sustainability is achieved for at least a year.

The healthcare provider: Has the behavior of healthcare professionals changed permanently? Do new patients also receive less inappropriate care from the same healthcare providers? This lens is especially of interest when the de-implementation strategy was aimed at healthcare professionals. The TRIODE project did not directly impact the healthcare professionals or the organization. They knew about the project, but they were not involved in the de-implementation and did not have to change their

behavior during the intervention period. Therefore this project will probably have had a minimal impact on the level of the healthcare organization.

The strategy: Is the strategy still used? Has the strategy been adapted to be feasible to maintain in the long-term? And if the intervention has been adjusted, did the effectiveness maintain? The TRIODE e-learning was not embedded in the hospitals. All participants were selected by a researcher who manually screened referral letters to include patients. This screening stopped after the end of the study, and subsequently the strategy also ended.

These perspectives show that the long-term sustainability depends on the definition and the desired outcome. For participants of the e-learning, there was a positive long-term effect. However, the healthcare professionals did not need to change their behavior and the strategy ended. Therefore, no future patients did benefit from this strategy.

In the first halve of the program *To do or not to do*, five de-implementation strategies proved their effectiveness, including the *RODEO* strategy.(63) This strategy reduced the volume of laboratory testing with an average of 11% in four hospitals. We aimed to study the sustainability of this strategy. **Chapter 7** describes the long-term effects from different perspectives: the volume reduction, the trend of the laboratory testing during the follow-up, and the continuation of strategy components. Additionally, influencing factors were identified.

Outline of the thesis

This thesis aims to contribute to the understanding of the last phases of three the de-implementation process: the achievement of societal cost savings, the spread of effective strategies and the long-term sustainability of successful initiatives. The outline is presented in figure 2.

Figure 2 | Thesis outline per de-implementation phase

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Effectiveness of interventions aiming to reduce inappropriate drug prescribing: an overview of interventions

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Abstract

Objective

Inappropriate prescribing of drugs is associated with unnecessary harms for patients and healthcare costs. Interventions to reduce these prescriptions are widely studied, yet the effectiveness of different types of interventions remains unclear. Therefore, we provide an overview regarding the effectiveness of intervention types that aim to reduce inappropriate drug prescriptions, unrestricted by target drugs, population or setting.

Methods

For this overview, systematic reviews (SRs) were used as the source for original studies. EMBASE and MEDLINE were searched from inception to August 2018. All SRs aiming to evaluate the effectiveness of interventions to reduce inappropriate prescribing of drugs were eligible for inclusion. The SRs and their original studies were screened for eligibility. Interventions of the original studies were categorized by type of intervention. The percentage of interventions showing a significant reduction of inappropriate prescribing were reported per intervention category.

Key findings

Thirty-two SRs were included, which provided 319 unique interventions. Overall, 61.4% of these interventions showed a significant reduction in inappropriate prescribing of drugs. Strategies that were most frequently effective in reducing inappropriate prescribing were multifaceted interventions (73.2%), followed by interventions containing additional diagnostic tests (antibiotics) (70.4%), computer interventions (69.2%), audit and feedback (66.7%), patient-mediated interventions (62.5%) and multidisciplinary (team) approach (57.1%). The least frequently effective intervention was an education for healthcare professionals (50.0%).

Conclusion

The majority of the interventions were effective in reducing inappropriate prescribing of drugs. Multifaceted interventions most frequently showed a significant reduction of inappropriate prescribing. Education for healthcare professionals is the most frequently included intervention in this overview, yet this category is least frequently effective.

Introduction

Inappropriate prescribing of drugs is associated with unnecessary healthcare costs, and risk of side effects for patients(1). These side effects can lead to harmful consequences such as falls, hospitalization, and an increased one-year mortality rate(2). The prevalence of inappropriate prescribing of drugs is high. For example, 18.5% of elderly and up to 46.5% of the people living in long-term care facilities received one or more potentially inappropriate drug.(3, 4) Avoiding these inappropriate prescriptions can have a large impact on patient outcomes and lead to a substantial reduction in healthcare costs(5, 6). Inappropriate prescribing is defined as the prescription of medication where risk outweighs benefit, failure to use a safer alternative drug, the misuse of a drug including incorrect dosage and duration of treatment, use of drugs with significant drug–drug and drug–disease interactions and finally the omission of beneficial drugs(7).

The presence of inappropriate prescribing indicates that the existence of a clinical practice guideline does not necessarily lead to guideline adherence(8, 9). An example is the increasing prescription of acid suppressant medication in children with infant colic and gastro-esophageal reflux (disease)(10, 11). Research indicates that proton pump inhibitors should not be prescribed in infants, given the lack of evidence for its effectiveness, the side effects and the lack of studies that prove its safety on the longer term(12). This is clearly described in (inter)national guidelines and by the U.S. Food and Drug Administration(13-16).

Another example is overprescribing of antimicrobial drugs. Inappropriate use of antibiotic drugs is correlated to antibiotic resistance(17). The harm of antibiotic resistance is underlined by a recent study, which estimated that antibiotic resistance contributed to the death of 33,110 people in the European Union(17). Of all antibiotic prescriptions 8.8% - 23.1% could be considered as inappropriate in primary care in England(18), whereas this is estimated to be up to 76% for some medical conditions in the United States(19).

Many different barriers for reducing inappropriate prescribing have been identified, such as patient expectations, clinical uncertainty, inadequate information management, administrative complaints, financial disincentives, negative staff attitudes, and anxiety to change practice(20). Numerous interventions have been developed to overcome these perceived barriers. The impact of these interventions is described in various systematic reviews (SRs), focusing on specific settings, interventions or patient populations(21-24). However, the comparative effectiveness of interventions for reducing inappropriate prescribing is unclear. Therefore, we aimed to identify effective intervention types for reducing inappropriate prescribing, without restrictions regarding setting, type of drugs

or targeted population. This could guide healthcare professionals and policy makers towards the most suitable approach for their own initiatives in reducing inappropriate prescribing of drugs.

Methods

For this overview, SRs were used as source for original studies. The review protocol was registered in the PROSPERO database (registration number CRD42016038131). In addition to the protocol, original studies of the SRs were included for analyses of the effectiveness of interventions. Results are reported based on PRISMA guidelines(25).

Data sources and search strategy

In collaboration with a medical information specialist, we developed a search strategy for EMBASE and MEDLINE. The search strategy consisted of synonyms for inappropriate prescribing combined with a filter for systematic reviews. The full search strategy is described in appendix 1. The databases were searched from inception to August 2018. In addition, the reference lists of included SRs were checked for eligible articles.

Eligibility criteria

SRs were eligible for inclusion if the aim of the review was to evaluate the effectiveness of interventions to reduce inappropriate prescribing or potentially inappropriate prescribing. This had to be stated in the objectives or method section. All types of interventions were eligible if targeted at healthcare professionals, patients or general public, either at an individual or organizational level. All types of outcomes regarding unnecessary or inappropriate prescribing were accepted, but outcomes of individual interventions had to be reported. No restrictions were made concerning patient characteristics, medical conditions and settings. We defined SRs as literature reviews written by more than one author, in which the authors reported the search terms, searched in two or more databases, and reported a table of included studies. Reviews that did not fulfil these criteria and reviews of low methodological quality (AMSTAR score 3 or less) were excluded(26-28). No language restrictions were applied.

Subsequently, we screened the original studies that were included in the SRs, following the PICO structure as presented in table 1. The aim of the original studies had to be implementation of one or more intervention(s) to reduce (potentially) inappropriate prescribing of medication. The intervention had to be explicitly described, and outcomes had to be reported as prevalence of (potentially) inappropriate prescribing before and after the intervention, or compared to a control group. The study was excluded if the intervention or outcomes were not clearly described in the SR, and the original study

was not available to clarify this. There were no restrictions regarding study design of the original studies.

Table 1 | PICO structure

P	All patients, unrestricted by characteristics, medical conditions or setting
I	All types of interventions aiming to reduce (potentially) inappropriate prescribing of all types of drugs
C	Any control group or pre-intervention group
O	All types of outcomes regarding unnecessary or inappropriate prescribing

Selection of the SRs and original studies

Duplicate references were removed, and title and abstract of the remaining references were screened for potential relevance. The inclusion criteria were applied to the full texts of the SRs. The selection process was carried out by a team of reviewers; each article was checked by at least two independent reviewers (NS, HV, ML, DK, SVD). Inclusion of the original studies was conducted by two reviewers (DK and SVD) after duplicate studies were removed. Disagreement was resolved by discussion.

Methodological quality of the SRs

The methodological quality of the SRs was assessed using the AMSTAR instrument by at least two reviewers independently (NS, HV, ML, DK, SVD) (26, 27). Consensus was reached by discussion between the reviewers.

Data extraction

For each included SR the following information was extracted by one reviewer and checked for accuracy by a second reviewer: objective, inclusion criteria, search date, population, setting, type of interventions, outcomes, number of included studies and participants, risk of bias of the included SR, results of the studies, quality of the evidence, and conclusion. All original studies of the SRs were extracted. Subsequently, the interventions of original studies and their outcomes were listed.

Data analysis

In order to compare the effectiveness of different types of interventions, we used the results of the included studies of the systematic reviews. If the intervention showed a significant ($p<0.05$) reduction in inappropriate prescribing, it was defined as effective and therefore successful. The significance had to be stated in numbers or described by the authors, otherwise the effect was labeled as 'not reported'. All studies that did not include a statistical analysis, were considered as 'not significant' in the analysis. All interventions were categorized by type, which was based on the EPOC taxonomy(29): additional

diagnostic testing, audit and feedback, computer interventions, education for healthcare professionals, patient-mediated interventions, multidisciplinary (team) approach, multifaceted interventions and other interventions. Interventions including both education for healthcare professionals and feedback were classified in the intervention category 'Audit and feedback', because we considered education an integral part of audit and feedback. Computer interventions included computerized alerts, recommendations and decision support systems. The setting of the intervention was categorized by type: hospital, outpatient setting and long-term care facility. Outpatient settings included primary care, care provided in medical clinics and community pharmacies. Long-term care facilities included healthcare homes, elderly homes, nursing homes and residential homes.

Results

Our search resulted in 4,066 references after de-duplication. Out of 134 articles that were assessed in full-text, 32 systematic reviews met our inclusion criteria. A flow diagram is presented in figure 1. The included systematic reviews are listed in table 2 and, with more detail, in appendix 2. The results of the methodological quality assessment of the SRs with the AMSTAR instrument are presented in appendix 3. We extracted 513 original studies from the systematic reviews, which studied 546 interventions. After removing duplicate interventions (n=167) and interventions of studies that did not meet our inclusion criteria (n=59), we were able to identify 319 unique interventions (figure 2). All interventions are listed more detailed in appendix 4. The significance was reported for 299 interventions, 20 interventions that did not report a statistical analysis were considered as not significant. The results per intervention category are presented in table 3 and figure 3.

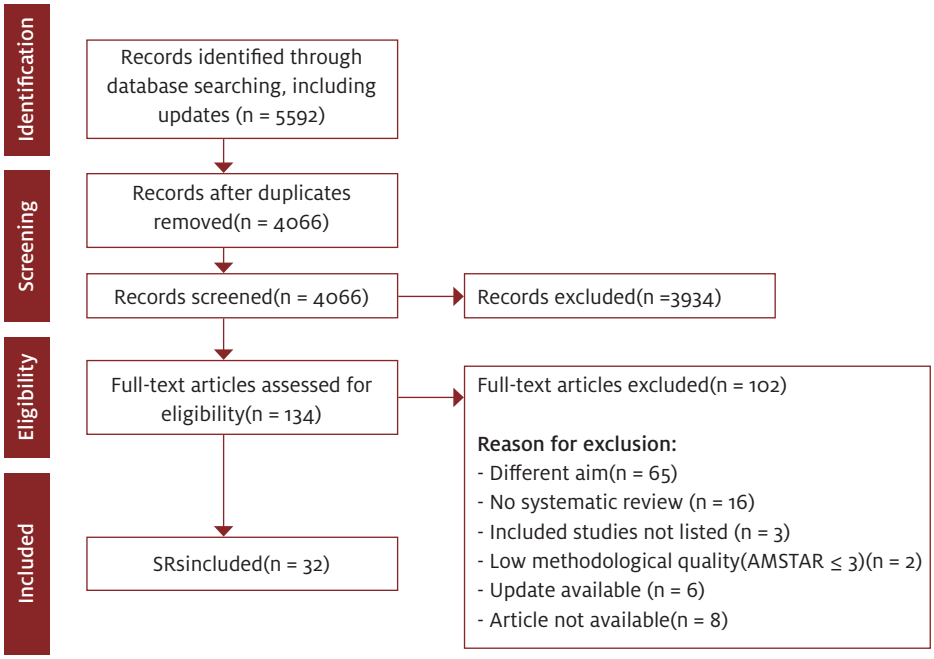

Figure 1 | Flow diagram inclusion of systematic reviews

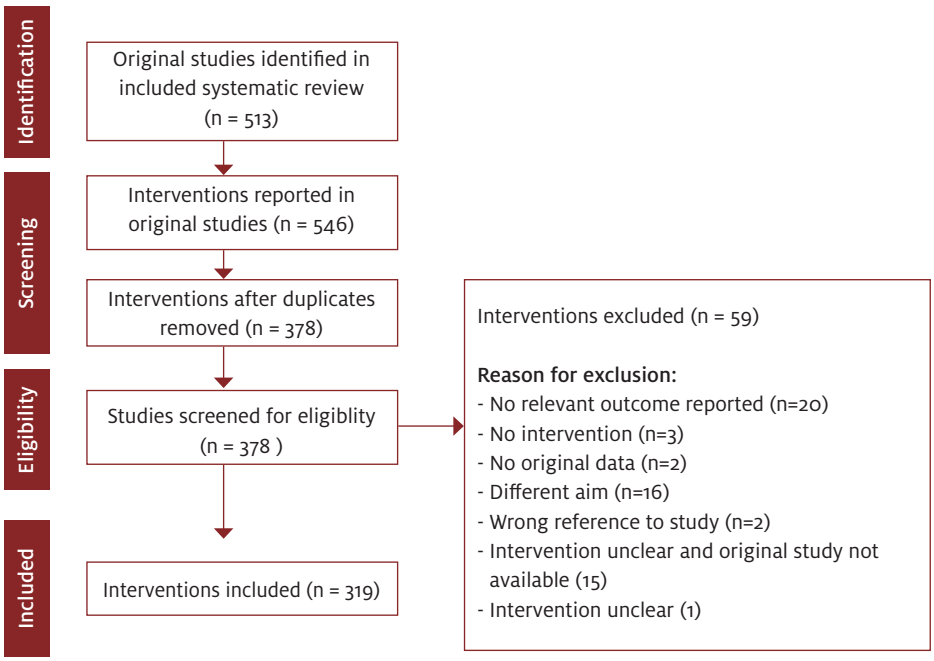

Figure 2 | Flow diagram included interventions

Table 2 | Details of the included systematic reviews

First author, year of publication	Focus	Multifaceted intervention	Additional diagnostic testing	Patient-mediated interventions	Audit and feedback	Computer interventions	Multidisciplinary approach	Education for healthcare professionals	Other	Excluded	Total number of interventions
Alldred 2016 (47)	Long-term care facilities						6	2	2	1	**12**
Arnold 2005 (48)	Outpatient Antibiotics	8		5	12	1		10	3	11	**50**
Arroll 2003 (49)	Outpatient Antibiotics			5							**5**
Birkenhager 2018 (24)	Long-term care facilities Psychotropic drugs							5	1	5	**11**
Castelino 2009 (50)	Elderly	2				1	7			1	**11**
China 2013 (51)	Outpatient	1						14			**15**
Cross 2016 (52)	Antibiotics	3		6	2	1				2	**14**
Dalton 2018 (53)	Elderly Hospital					8					**8**
Davey 2017 (23)	Hospital Antibiotics		12		1	2	3	5		6	**29**
Diep 2018 (54)	Hospital Intravenous Immunoglobulin								3		**3**
Forsetlund 2011 (55)	Elderly Long-term care facilities	1					7	11	1		**20**
Haastrup 2014 (56)	Primary care Proton pomp inhibitors			2					3	1	**6**
Hill-Taylor 2016 (40)	Elderly						1		3		**4**
Holstiege 2015 (57)	Outpatient Antibiotics					8					**8**
Johansson 2016 (22)	Elderly Polypharmacy				1		19	2	2	1	**25**
Lainer 2013 (58)	Outpatient					8	1			1	**10**
Lane 2018 (59)	Outpatient Antimicrobial prescribing	1							1	1	**3**

First author, year of publication	Focus	Multifaceted intervention	Additional diagnostic testing	Patient-mediated interventions	Audit and feedback	Computer interventions	Multidisciplinary approach	Education for healthcare professionals	Other	Excluded	Total number of interventions
Loganathan 2011(60)	Long-term care facilities					2	6	7		1	**16**
Marcum 2010 (61)	Long-term care facilities				1	2	7	7		1	**18**
McDonagh 2018 (62)	Outpatient Antibiotics for respiratory tract infection	1	2	1	2	2		4		2	**14**
McDonagh 2016 (21)	Outpatient Antibiotics for respiratory tract infection	15	13	10	6	7		13	1	4	**69**
Ostini 2011 (63)	Pre-existing inappropriate prescriptions	1		5	1	1	2			2	**12**
Page 2017 (64)	Hospital					23					**23**
Patterson 2014 (65)	Elderly Polypharmacy			1		1	8		1	1	**12**
Ranji 2008 (35)	Outpatient Antibiotics	6		18	12	3		12	2	2	**55**
Saha 2018 (66)	Outpatient Antibiotics				4			3			**7**
Tesfaye 2017 (67)	Chronic kidney disease					6	8	1	2	5	**22**
Thillainadesan 2018 (68)	Elderly Hospital						6		3		**9**
Thompson Coon 2014 (69)	Long-term care facilities						3	12		7	**22**
Vodicka 2013 (41)	Outpatient Antibiotics	2	1	1	1	3		4		5	**17**
Walsh 2016 (70)	Elderly Hospital						5				**5**
Yourman 2008 (71)	Elderly	2				4	3			1	**10**

LTC = long term care facility; CRP = C-reactive protein, PPI = proton pomp inhibitor.

Table 3 | Interventions per category and reduction of inappropriate prescribing

Intervention category	Focus of inappropriate prescribing	Description of interventions	Interventions with significant reduction/total (%)	Interventions with significant reduction/total (%) per setting
Multifaceted interventions (n=41)	Antibiotic prescribing (n=31) Other (n=10)	One or more educational aspect(s) in the intervention (n=40) Organizational interventions (n=1) Most common combination: Patient education and education for healthcare professionals (n=14)	30/41 (73.2%)	Hospital: 1/2 (50.0%) Outpatient: 28/37 (75.7%) LTC: 1/2 (50.0%)
Additional diagnostic testing (n= 27)	Antibiotic prescribing (n=27)	Testing one or more infection parameter(s) (n=22) Rapid testing: influenza (n=1) Rapid testing: streptococcus (n=4)	19/27 (70.4%)	Hospital: 9/12 (75%) Outpatient: 10/15 (66.7%) LTC: None
Computer interventions (n=52)	Drug interactions, allergies, dosing, double prescriptions, contraindications (n=38) Antibiotic prescribing (n=14)	Computer alerts and recommendations (n=29) Computer decision support (n=23)	36/52 (69.2%)	Hospital: 24/30 (80.0%) Outpatient: 10/20 (50.0%) LTC: 2/2 (100%)
Audit and feedback (n=24)	Antibiotic prescribing (n=21) Polypharmacy (n=1) Benzodiazepine (n=2)	Audit and feedback with education clinician (n=22) Audit and feedback (n=2)	16/24 (66.7%)	Hospital: 0/1 (0.0%) Outpatient: 15/22 (68.2%) LTC: 1/1 (100%)

Intervention category	Focus of inappropriate prescribing	Description of interventions	Interventions with significant reduction/total (%)	Interventions with significant reduction/total (%) per setting
Patient-mediated interventions (n=32)	Antibiotic prescribing (n=27) Other (n=5)	Patient education (n=17) Mass media campaigns (n=7) Delayed prescribing (n=8)	20/32 (62.5%)	Hospital: None Outpatient: 20/32 (62.5%) LTC: None
Multidisciplinary (team) approach (n=56)	Various	(re)forming a multidisciplinary team (n=16) Medical review by specialist (e.g. pharmacist, geriatrician) other than prescriber (n=40)	32/56 (57.1%)	Hospital: 17/21 (81.0%) Outpatient: 5/18 (27.8%) LTC: 10/17 (58.8%)
Education for healthcare professionals (n=70)	Antibiotic prescribing (n=38) Other (n=32)	Various types of educational meetings and trainings (n=70)	35/70 (50.0%)	Hospital: 5/6 (83.3%) Outpatient 22/42 (52.4%) LTC: 8/22 (36.4%)
Other (n=17)	Various	Review tools (n=5) Decision support (n=6) Tapering PPI (n=1) Request form (n=1) Providing epidemiological data (n=1) Extra notes in medical record (n=1) Reporting renal function (n=2)	8/17 (47.1%)	Hospital: 3/5 (60.0%) Outpatient: 2/8 (25.0%) LTC: 3/4 (75.0%)

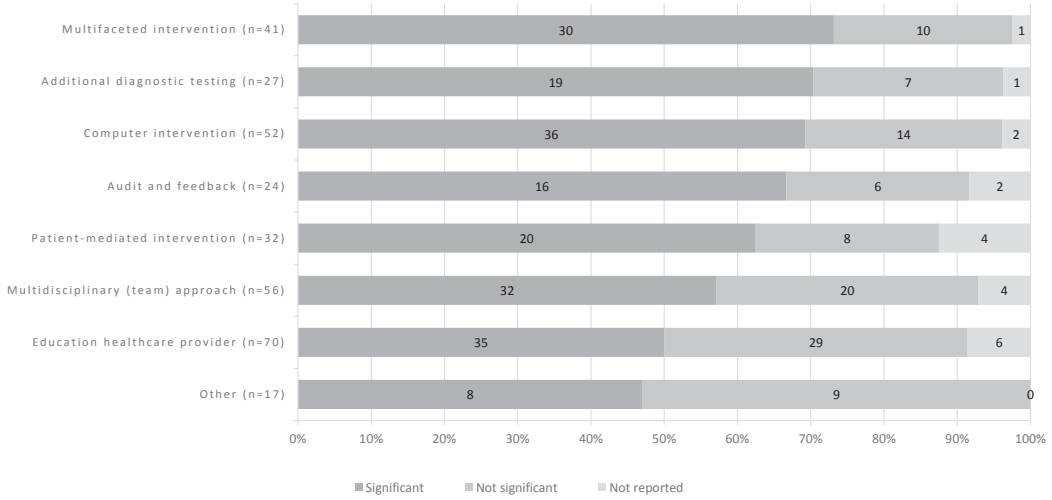

Figure 3 | Number of interventions per category, reported as significantly reducing inappropriate prescribing, no significant reduction or significance not reported

Overall, 61.4% (196/319) of the interventions significantly reduced inappropriate prescribing, 32.3% (103/319) of the interventions did not lead to a significant reduction, and there was no significance reported for 6.3% (20/319) of the interventions. Intervention types that most often significantly reduced inappropriate prescribing were multifaceted interventions (73.2%, 30/41) and interventions containing an additional diagnostic test in (70.4%, 19/27). In the other categories, percentages of interventions that significantly reduced inappropriate prescribing were 69.2% (36/52) for computer interventions, 66.7% (16/24) for audit and feedback, 62.5% (20/32) for patient-mediated interventions, 57.1% (32/56) for a multidisciplinary (team) approach, and 50.0% (35/70) for education for healthcare professionals. In the category other interventions, various types of interventions were placed, which resulted in small numbers of intervention types and mixed results. This is further explained in the description below.

In a hospital setting, 76.6% (59/77) of the interventions were significantly effective, compared to 57.7% (112/194) of the interventions in an outpatient setting and 52.1% (25/48) of the interventions conducted in long-term care facilities. Antibiotics were the most frequently targeted drugs with 140 interventions in outpatient settings, 26 interventions in hospitals, and four interventions in a long-term care facility. There was some variation in the percentage of significantly effective interventions over time: 58.8% (30/51) for interventions published before 2000, 62.0% (103/166) for intervention published between 2000-2010, and 61.8% (63/102) for interventions published after 2010. Details per intervention category are described below.

Multifaceted interventions (n=41)

Multifaceted interventions included two or more aspects in the applied strategy. Thirty-nine interventions contained an educational facet, targeted at patients and/or healthcare professionals. One intervention consisted of a change in disease management, including extended visits of physician and a pharmacist visit, and one intervention was a utilization control program. Inappropriate antibiotic prescribing was targeted in 31 interventions. The most common combination was patient education and education for healthcare professionals (n=14). Thirty-seven interventions were conducted in an outpatient setting, two interventions were conducted in a long-term care facility and two in a hospital. In 73.2% (30/41) of the multifaceted interventions a significant reduction of inappropriate prescribing was measured. Thirty interventions were targeted at both patients and healthcare professionals, of which 76,7% (23/30) showed a significant reduction of inappropriate prescribing. The combination of patient education and education for healthcare professionals were significantly effective in 64.3% (9/14) of the interventions. Providing feedback as one aspect of a strategy was significantly effective in 72,7% (8/11) of the interventions.

Additional diagnostic testing (n=27)

All interventions in this category targeted inappropriate antibiotic prescribing, either by starting antibiotic treatment less often or shortening the duration of the treatment. All interventions included tests for one or more infection parameter(s) or implemented rapid testing for influenza or streptococcus. In 70.4% (19/27) of the interventions with additional diagnostic testing, a significant reduction of inappropriate antibiotic prescribing was reported. In outpatient settings this was in 66.7% (10/15) of the interventions and in hospital settings in 75.0% (9/12) of the interventions.

Computer interventions (n=52)

Interventions in this category included computerized alerts and recommendations and computer decision support systems. A total of 52 computer interventions were studied and of which 69,2% (36/52) significantly reduced inappropriate prescribing. Of 30 interventions that were applied in hospitals, 16 interventions were computerized alerts, eight interventions were computer-generated recommendations and six interventions contained a computer decision support system that was studied. Computer interventions were mainly implemented to reduce inappropriate prescribing due to drug-drug interactions, double prescriptions, inappropriate dosing, and drug-allergy interactions. In hospital settings, 80.0% (24/30) of the interventions were reported to significantly reduce inappropriate prescriptions. In outpatient settings, 20 interventions were studied, of which 15 interventions concerned implementation of a computer decision support system and five interventions implementation of computerized alerts or recommendations. Of all computer interventions in outpatient settings, 50.0% (10/20)

was significantly effective in reducing inappropriate prescribing. Two interventions were conducted in long-term care facilities and both significantly reduced inappropriate prescribing.

Audit and Feedback (n=24)

Audit and feedback was used in 24 interventions, of which 22 interventions were combined with education for clinicians. Twenty-two interventions were conducted in an outpatient setting, one in a hospital and one in a long-term care facility. Twenty-one interventions were targeted at antibiotic treatment. Of all interventions, 66,7% (16/24) resulted in a significant reduction of inappropriate prescribing. Both interventions that provided feedback without education did not significantly reduce inappropriate prescribing of antimicrobial drugs.

Patient-mediated interventions (n=32)

This category included patient education, mass media campaigns and delayed prescribing. All patient-mediated interventions were targeted at outpatients or general public. The majority of the interventions focused on reducing antibiotic use (n=27). Of all patient-mediated interventions, 62.5% (20/32) showed a significant reduction of inappropriate prescribing of drugs. Patient education resulted in a significant reduction of drug prescription in 52,9% (9/17) of the interventions. Mass media campaigns were all targeted at antibiotics, and were significantly effective in 71.4% (5/7) of the interventions. Delayed prescribing is defined as providing the patient with a prescription with advice on when to use it. All delayed prescriptions were prescriptions for antibiotic treatment. In 75.0% (6/8) of the interventions using delayed prescribing, a significant reduction was seen in antimicrobial drugs usage.

Multidisciplinary (team) approach (n=56)

In this category, interventions consisted of a specialist (e.g. pharmacist or specialist geriatric care) performing a medication review, or forming or re-forming a multidisciplinary team. Overall, a multidisciplinary approach showed a significant reduction in inappropriate prescribing in 57.1% (32/56) of the interventions. A team approach resulted in a significant reduction of inappropriate prescribing in 68.8% (11/16) of the interventions and a medication review by a specialist in 52.5% (21/40) of the interventions. In most interventions in outpatient settings, a pharmacist conducted the medication review to reduce polypharmacy. This led to a significant reduction of inappropriate prescriptions in 27.8% (5/18) of the interventions. In long-term care facilities and hospitals, both forming a multidisciplinary team and a pharmacist reviewing medication were studied. In respectively 58.8% (10/17) and 81.0% (17/21) of the multidisciplinary interventions a significant reduction of inappropriate prescribing was observed.

Education for healthcare professionals (n=70)

The category education for healthcare professionals contains the most interventions (n=70) of all categories. Education for healthcare professionals was significantly effective in reducing inappropriate prescribing in 50.0% (35/70) of the interventions. In long-term care facilities, education for healthcare professionals was effective in 36.4% (8/22) of the interventions, in outpatient settings in 52.4% (22/42) and in hospital settings in 83.3% (5/6). Educational interventions for healthcare professions working in hospitals and outpatient were mostly targeted at antibiotic prescribing, respectively 6/6 and 28/42.

Other (n=17)

Seventeen interventions could not be listed in the defined categories. Medication review tools as intervention resulted in a significant reduction of inappropriate prescribing in 80.0% (4/5). Interventions in which a decision support tool was used, reduced prescription of inappropriate drugs in 33.3% (2/6). Other significantly effective interventions were the introduction of a request form for intravenous immunoglobulin (n=1), and extra patient administration (n=1). Interventions without a significant reduction were: tapering medication (n=1), feedback with epidemiological data (n=1) and reporting renal function (n=2).

Discussion

In this study we presented an overview of the effectiveness of interventions aiming to reduce inappropriate prescribing of medication. Overall, 61.4% of the included interventions were reported to result in a significant reduction of inappropriate prescribing. Most frequently effective were multifaceted interventions and interventions with additional diagnostic testing. Educational interventions solely targeted at healthcare professionals were most studied, yet those resulted least frequently in a significant reduction of inappropriate prescribing.

For antimicrobial drugs, additional diagnostic testing and multifaceted interventions showed to be most frequently effective in reducing inappropriate prescriptions. These strategies could therefore be used to tackle the growing problem of antibiotic resistance. This is also reflected in another review for additional diagnostic testing(30). However, the overuse of diagnostic tests should be taken into consideration, since some medical conditions are clinical diagnoses, and consequently laboratory testing is not recommended by guidelines(31, 32). Therefore, in some cases in outpatient settings, multifaceted interventions may be preferred. It should be noted that our data did not include multifaceted interventions targeting antibiotic prescribing in hospitals. Additional diagnostic testing, however, did show positive results for reducing inappropriate antibiotic prescription in hospitals.

Education for healthcare professionals is the most applied intervention in our results, nevertheless only 50.0% of the interventions in this category was successful. The limited effectiveness of this intervention is in accordance with an earlier study(33) and could be explained by different mechanisms. For example, the lack of knowledge may not be the main underlying problem for inappropriate prescribing, other factors are more dominant in the context of inappropriate prescribing(34), the education was of low quality or was not repeated sufficiently(24, 33, 35). However, if education targeted at healthcare professionals is combined with feedback, it tends to be effective more often. This may be explained by the theory that feedback provides insight in one's own routines, which is, after awareness, the next step towards behavioral change(36).

Furthermore, our results suggested that patients are an important factor in inappropriate prescribing. To illustrate, interventions targeted at patients are more often successful than education for healthcare professionals. Moreover, interventions targeting both patients and healthcare professionals are more frequently effective in reducing inappropriate prescribing, compared to interventions that are not targeted at patients. The finding that patients have an important role is supported by other literature as well(37-39). Therefore, we suggest to consider targeting patients as a facet of an intervention to reduce inappropriate prescribing.

Notable differences were reported in effectiveness of interventions between interventions conducted in hospitals, outpatient settings and long-term care facilities in all intervention categories. Interventions in hospitals tend to be successful more often compared to interventions conducted in outpatient settings. Contributable factors could include: study design (including sample size), quality of the study, design of the intervention, or defined outcome measures. For example, studies in long-term care facilities relatively often had a randomized controlled design, compared to studies performed in a hospital setting (appendix 4). The differences in effectiveness between settings may also be explained by the degree to which the intervention was integrated in daily practice of healthcare professionals(40). Interventions in outpatient settings often demanded more effort and/or extra steps of the healthcare professionals(41). For example, in interventions with a multidisciplinary approach in an outpatient setting often a pharmacist participated as medication reviewer. This collaboration was not further integrated into the daily activities (42), whereas in hospital settings integration was often enhanced by the use of pre-existing routine meetings(43, 44). This also applied to computer interventions: in hospital settings, alerts automatically popped up, in contrary to the manually controlled systems often used in outpatient settings(41, 45, 46).

Implications for practice

This review provides an overview of different types of interventions to reduce inappropriate prescribing. We did not find an intervention type that was effective in all settings. This suggests that interventions should be tailored to the context, by targeting barriers and facilitators. However, based on our results, we do suggest to conduct interventions with multiple facets. Moreover, we suggest to only use education for healthcare professionals as part of a multifaceted strategy.

Strengths and limitations

To our knowledge, this is the first review presenting an overview of interventions to reduce inappropriate prescribing of drugs, unrestricted by target drugs, population or setting. A few limitations should be reported. First, this paper reports whether the intervention in the original study significantly reduced inappropriate prescribing of drugs. Due to heterogeneity in reported outcome measures, meta-analysis could not be performed. By defining an intervention as 'successful' if it significantly reduced inappropriate prescribing, some nuances about the clinical impact of the effect are likely overlooked. In addition, whether an intervention significantly reduces inappropriate prescribing, depends on the sample size and the choice of outcome measures. Second, the inclusion of the original studies in this review depended on the inclusion criteria of the systematic reviews. This resulted in sets of included studies based on a specific intervention, patient population or drug. Although we may have missed interventions that are not included in systematic reviews, this review presents a wide range of intervention types and many interventions. Therefore, this may not influence representativeness. Third, the methodological quality was only assessed for systematic reviews and not for underlying studies.

Conclusion

This study showed that 61.4% of the interventions reported a significant reduction of inappropriate prescribing of drugs. The most frequently effective interventions were multifaceted strategies and additional diagnostic testing. Education for healthcare professionals is the most frequently included intervention in this overview, yet this category is least frequently effective in reducing inappropriate prescribing. Further research should focus on defining favorable contexts for interventions to improve the effectiveness of these interventions.

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Appendix 1 | Search strategy

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)

1	((improv* or ameliorat* or amend* or better or appropriate* or inappropriate* or suboptimal or change) adj4 (medication or prescription or prescrib* or "drug administration" or medicate or "drug regimen" or medicative or pharma* or treatment recommendation$)).ti,ab.
2	exp Medication Errors/
3	exp Inappropriate Prescribing/
4	exp Guideline Adherence/
5	exp Physician's Practice Patterns/
6	1 or 2 or 3 or 4 or 5
7	MEDLINE or systematic review).tw. or exp meta-analysis/ or (search* adj12 (literature or database?)).ti,ab.
8	6 and 7

Embase Classic+Embase

1	((improv* or ameliorat* or amend* or better or appropriate* or inappropriate* or suboptimal or change) adj4 (medication or prescription or prescrib* or "drug administration" or medicate or "drug regimen" or medicative or pharma* or treatment recommendation$)).ti,ab.
2	exp medication error/
3	exp inappropriate prescribing/
4	(guideline adj3 adherence).mp.
5	(physician* adj3 pattern).mp.
6	1 or 2 or 3 or 4 or 5
7	MEDLINE.tw. or exp systematic review/ or systematic review.tw. or meta-analysis/ or (search* adj12 (literature or database?)).ti,ab.
8	6 and 7
9	limit 8 to (conference abstract or conference paper or conference proceeding or "conference review")
10	8 not 9

Appendix 2 | Description of included systematic reviews

Author and year	Alldred 2016
Objectives	To determine the effect of interventions to optimize overall prescribing for older people living in care homes.
Interventions	Various
Target drugs	All
Patient setting	Care homes
Data last search	May 2015
Amstar	11
Number of interventions listed for reducing inappropriate prescribing	12
Results	The interventions evaluated were diverse and often multifaceted. Medication review was a component of ten studies. Four studies involved multidisciplinary case-conferencing, five studies involved an educational element for health and care professionals and one study evaluated the use of clinical decision support technology. We did not combine the results in a meta-analysis due to heterogeneity across studies. Interventions to optimize prescribing may lead to fewer days in hospital (one study out of eight; low certainty evidence), a slower decline in health-related quality of life (one study out of two; low certainty evidence), the identification and resolution of medication-related problems (seven studies; low certainty evidence), and may lead to improved medication appropriateness (five studies out of five studies; low certainty evidence).We are uncertain whether the intervention improves/reduces medicine costs (five studies; very low certainty evidence) and it may make little or no difference on adverse drug events (two studies; low certainty evidence) or mortality (six studies; low certainty evidence). The risk of bias across studies was heterogeneous.
Conclusion	We could not draw robust conclusions from the evidence due to variability in design, interventions, outcomes and results. The interventions implemented in the studies in this review led to the identification and resolution of medication-related problems and improvements in medication appropriateness, however evidence of a consistent effect on resident-related outcomes was not found. There is a need for high-quality cluster-randomized controlled trials testing clinical decision support systems and multidisciplinary interventions that measure well-defined, important resident-related outcomes.

Author and year	Arnold 2005
Objectives	The main objective of this study was to systematically review the literature to find trials to enable an estimate of the effectiveness of interventions targeting professionals, when given alone or in combination, in improving antibiotic prescribing by healthcare providers; in the outpatient setting with both adults and children.
Interventions	Various
Target drugs	Antibiotics
Patient setting	Outpatient
Data last search	End of 2002
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	50
Results	Thirty-nine studies examined the effect of printed educational materials for physicians, audit and feedback, educational meetings, educational outreach visits, financial and healthcare system changes, physician reminders, patient-based interventions and multi-faceted interventions. These interventions addressed the overuse of antibiotics for viral infections, the choice of antibiotic for bacterial infections such as streptococcal pharyngitis and urinary tract infection, and the duration of use of antibiotics for conditions such as acute otitis media. Use of printed educational materials or audit and feedback alone resulted in no or only small changes in prescribing. The exception was a study documenting a sustained reduction in macrolide use in Finland following the publication of a warning against their use for group A streptococcal infections. Interactive educational meetings appeared to be more effective than didactic lectures. Educational outreach visits and physician reminders produced mixed results. Patient-based interventions, particularly the use of delayed prescriptions for infections for which antibiotics were not immediately indicated effectively reduced antibiotic use by patients and did not result in excess morbidity. Multi-faceted interventions combining physician, patient and public education in a variety of venues and formats were the most successful in reducing antibiotic prescribing for inappropriate indications. Only one of four studies demonstrated a sustained reduction in the incidence of antibiotic-resistant bacteria associated with the intervention.
Conclusion	The effectiveness of an intervention on antibiotic prescribing depends to a large degree on the particular prescribing behavior and the barriers to change in the particular community. No single intervention can be recommended for all behaviors in any setting. Multi-faceted interventions where educational interventions occur on many levels may be successfully applied to communities after addressing local barriers to change. These were the only interventions with effect sizes of sufficient magnitude to potentially reduce the incidence of antibiotic-resistant bacteria. Future research should focus on which elements of these interventions are the most effective. In addition, patient-based interventions and physician reminders show promise and innovative methods such as these deserve further study.

Author and year	Arroll 2003
Objectives	The aim of this study was to conduct a systematic review of the controlled trials of delayed antibiotic prescription for upper respiratory tract infections. We also explored the differences found between the studies, the potential for harm, and offer advice to clinicians for use in everyday practice
Interventions	Delayed prescription
Target drugs	Antibiotics
Patient setting	Outpatient
Data last search	April 2003
Amstar	9
Number of interventions listed for reducing inappropriate prescribing	5
Results	Four randomized controlled trials and one before–after controlled trial contributed to the review. The relative risk in the randomized trials for lower antibiotic usage when a delayed prescription was given ranged from 0.54 for the common cold to 0.25 for otitis media.
Conclusion	The consistent reduction in antibiotic usage in the five controlled trials included in this review suggests that delayed prescription is an effective means of reducing antibiotic usage for acute respiratory infections. The duration of delay for prescriptions ranged widely, from 1 to 7 days.

Author and year	Birkenhager 2018
Objectives	To assess the effect of multidisciplinary psychosocial interventions in nursing homes on the psychotropic drug prescription rate.
Interventions	Education/ coaching/ training
Target drugs	Psychotropic drugs
Patient setting	Nursing homes
Data last search	June 2017
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	11
Results	Analysis of 9 studies presenting antipsychotic drug use showed a significant decrease of antipsychotic drug use in the intervention group (RR 0.71, 95% CI 0.59e0.88), with a number needed to treat of 11. In 5 studies differences between intervention and control group of antidepressant drug use were presented. Meta-analysis of these 5 studies showed no significant effect (RR 0.82, 95% CI 0.64e1.02)

Conclusion	The pooled effect size of studies investigating psychosocial interventions on antipsychotic drug use revealed a significant decrease when compared with care-as-usual. Meta-analyses showed that interventions using educational components were not more effective than care-as-usual, but longer lasting interventions that involved a change of culture or process change were superior to care-as-usual interventions in lowering antipsychotic drug use. As stated before, this is in line with clinical findings that the education of care staff is important but of limited importance because of its short-term effects. Education has to be repeated and consequently implemented in daily practice to be effective. Longer lasting interventions that change culture and working processes with the aim of supporting care-workers to approach behavioral problems of residents differently lack the disadvantage of having only temporarily effects. A meta-analysis of studies analyzing the effects of psychosocial interventions on antidepressant drugs prescription did not show a significant decrease. Our results indicate that involvement of the physician in the psychosocial intervention is indispensable for obtaining and maintaining a reduction in the use of antipsychotic drugs.

Author and year	Castelino 2009
Objectives	To review the currently available literature on the impact of interventions by pharmacists on suboptimal prescribing in the elderly.
Interventions	Pharmacist interventions
Target drugs	All
Patient setting	All
Data last search	December 2008
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	11
Results	A broad range of tools was used to measure prescribing appropriateness; we found that a consensus on the best approach has not been reached. Most of the studies involving pharmacists showed significant improvement in suboptimal prescribing at one or more time points. However, most of these interventions were directed toward reducing the overuse or misuse of medications.
Conclusion	This review revealed some promising results of interventions involving pharmacists to optimize prescribing in the elderly. However, more studies on the effectiveness of interventions by pharmacists on improving all aspects of prescribing need to be performed.

Author and year	China 2013
Objectives	To synthesize current knowledge about the effectiveness and the magnitude of the effect, of Academic Detailing (AD), as a stand-alone intervention, at modifying drug prescription behavior of Family Physicians (fps) in primary care settings.
Interventions	Academic detailling
Target drugs	All
Patient setting	Primary care
Data last search	July 2010
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	15
Results	Five RCTS showed effectiveness, while 2 rcts reported a positive effect on some of the target drugs. Two observational studies found AD to be effective, while 2 did not. The median difference in relative change among the studies reviewed was 21% (interquartile range 43.75%) for rcts, and 9% (interquartile range 8.5%) for observational studies. The median effect size among the studies reviewed was - 0.09 (interquartile range 2.73).
Conclusion	AD can be effective at optimizing prescription of medications by family physicians.

Author and year	Cross 2016
Objectives	A systematic review was conducted to identify the components of successful communication interventions targeted at the general public to improve antibiotic use.
Interventions	Communication interventions
Target drugs	Antibiotics
Patient setting	All
Data last search	July 2015
Amstar	7
Number of interventions listed for reducing inappropriate prescribing	14
Results	12 of the 14 studies measured changes in antibiotic prescribing. There was quite strong (P<0,05 to 0,01) to very strong (P<0,001). evidence that interventions that targeted prescribing for RTIs were associated with decreases in antibiotic prescribing; the majority of these studies reported reductions of greater than 14% with the largest effect size reaching 30%.
Conclusion	Multi-faceted communication interventions that target both the general public and clinicians can reduce antibiotic prescribing in high-income countries but the sustainability of reductions in antibiotic prescribing is unclear.

Author and year	Dalton 2018
Objectives	The primary aim of this paper was to collect all currently available evidence of prospective controlled studies that have utilized computerized interventions capable of independently identifying potentially inappropriate prescriptions (PIP) and which aimed to improve the appropriateness of prescribing in hospitalized older adults (≥65 years). Second, we aimed to quantify the effect that these computerized interventions could have on reducing PIP in hospitalized older adults by conducting a parallel meta-analysis.
Interventions	Computer interventions
Target drugs	All
Patient setting	Hospital
Data last search	October 2017
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	8
Results	Reduction in patient with PIMs Three of the eight studies reported the exact number of patients that were prescribed PIMs as an outcome and so were amenable to quantitative analysis [10, 14, 18]. In these three studies, there were a total of 29,791 patients/patient visits (14,860 and 14,931 in the intervention and control arms, respectively). Given the heterogeneous types of intervention and considerable statistical heterogeneity between the study results (I2 = 82%; P = 0.004), a random-effects model was performed to provide a pooled estimate of effect. Our meta-analysis found that patients in the intervention group were less likely to be prescribed PIMs post-intervention (odds ratio 0.6, 95% CI: 0.38, 0.93) (Figure 2). These three studies were found to be at a low risk of bias, so we can be reasonably confident in the results of this meta-analysis. Reduction in PIMs prescribed Due to the variability in which the results were reported, a meta-analysis could not be performed for this primary outcome. Where it was possible to calculate, there was an ARR of 2–5.9% [10, 14, 15] and an RRR of 14–77.6% [10, 14, 15, 17] in PIMs prescribed across the studies. Overall, six studies showed a reduction in the number of PIMs prescribed when comparing the intervention and control groups, with five studies demonstrating statistically significant reductions (P < 0.01) [12–15, 17]. The only exception to this was the study by Boustani et al., whereby the intervention group still had a greater discontinuation rate in anticholinergic drug (PIM) orders vs the control group (48.9% vs 31.2%; P = 0.11) [12]. As previously mentioned, contamination may have been an issue in this study which may have reduced the difference found between the groups. Given the overall low risk of bias in these studies, we can be reasonably confident in the results provided.
Conclusion	Overall, our findings demonstrate that computerized interventions can be effective in reducing PIP in hospitalized older adults. Larger scale multicenter RCTs, at national and international levels, will be required to further demonstrate the benefit of these interventions across different institutions, ideally showing both cost-effectiveness data and clinically significant improvements in patient outcomes.

Author and year	Davey 2017
Objectives	To estimate the effectiveness and safety of interventions to improve antibiotic prescribing to hospital inpatients and to investigate the effect of two intervention functions: restriction and enablement.
Interventions	Various
Target drugs	Antibiotics
Patient setting	Hospital
Data last search	January 2015
Amstar	11
Number of interventions listed for reducing inappropriate prescribing	29 (total 89)
Results	For the persuasive interventions, the median change in antibiotic prescribing was 42.3% for the ITSs, 31.6%for the controlled ITSs, 17.7%for the CBAs, 3.5%for the cluster-RCTs and 24.7%for the RCTs. The restrictive interventions had a median effect size of 34.7% for the ITSs, 17.1% for the CBAs and 40.5% for the RCTs. The structural interventions had a median effect of 13.3% for the RCTs and 23.6% for the cluster-RCTs.
Conclusion	The results show that interventions to reduce excessive antibiotic prescribing to hospital inpatients can reduce antimicrobial resistance or hospital-acquired infections. The meta-analysis supports the use of restrictive interventions when the need is urgent, but suggests that persuasive and restrictive interventions are equally effective after six months.

Author and year	Diep 2018
Objectives	To explore if interventions to reduce inappropriate use is more successful for intravenous immunoglobulin (IVIG) due to a small number of labeled indications for IVIG and a smaller evidence base for efficacy in IVIG.
Interventions	Organizational interventions
Target drugs	intravenous immunoglobulin
Patient setting	Hospital
Data last search	June 2016
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	3
Results	All three studies were included in the meta-analysis for a total of 2100 episodes of IVIG transfusion (1013 pre-intervention and1087 post-intervention) as seen in Fig. 2. A random-effects meta-analysis was performed due to considerable heterogeneity in thes elected studies (X^2= 17.92, I^2= 89%). The risk ratio of inappropriate transfusions before interventions was 1.55 (95% CI 0.78-3.07) when compared to that after interventions.
Conclusion	Organizational interventions were ineffective at changing inappropriate IVIG use, but more high-quality studies describing the effects of these interventions are required before any conclusions can be drawn.

Author and year	Forsetlund 2011
Objectives	The purpose of the review was to identify and summarize the effect of interventions aimed at reducing potentially inappropriate use or prescribing of drugs in nursing homes.
Interventions	Various
Target drugs	All
Patient setting	Nursing homes
Data last search	April 2010
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	20
Results	20 RCTs were included from 1631 evaluated references. Ten studies tested different kinds of educational interventions while seven studies tested medication reviews by pharmacists. Only one study was found for each of the interventions geriatric care teams, early psychiatric intervening or activities for the residents combined with education of health care personnel.
Conclusion	Educational interventions may under certain circumstances reduce inappropriate drug use, but the evidence is of low quality. Due to poor quality of the evidence, no conclusions may be drawn about the effect of the other three interventions on drug use, or of either intervention on health-related outcomes.

Author and year	Haastrup 2014
Objectives	We therefore conducted a systematic review of clinical studies investigating discontinuation strategies and their effect on discontinuation rates in patients treated with PPIs.
Interventions	Various
Target drugs	Proton pump inhibitors
Patient setting	All
Data last search	December 2013
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	6
Results	All discontinuation regimens used in the studies differed, and several interventions have been tested in order to decrease use of PPIs. Discontinuations were reported across all studies ranging from 14% to 64% without deteriorating symptom control. Tapering seems to be a more effective discontinuation strategy than abrupt discontinuation.
Conclusion	Discontinuation of PPIs is feasible in a clinical setting, and a substantial number of the patients treated without a clear indication can safely reduce or discontinue treatment. Tapering seems to be the most effective way of doing this.

Author and year	Hill-Taylor 2016
Objectives	Our objective was to assess the effectiveness of STOPP/START criteria on prescribing quality and clinical, humanistic and economic outcomes in adults aged 65 years and older.
Interventions	Applying STOPP/START criteria
Target drugs	All
Patient setting	All
Data last search	June 2014
Amstar	9
Number of interventions listed for reducing inappropriate prescribing	4
Results	Meta-analysis found that the STOPP criteria reduced PIM rates in all four studies, but study heterogeneity (I2 = 86 7%) prevented the calculation of a meaningful statistical summary. We found evidence that use of the criteria reduces falls, delirium episodes, hospital length-of-stay, care visits (primary and emergency) and medication costs, but no evidence of improvements in quality of life or mortality.
Conclusion	STOPP/START may be effective in improving prescribing quality, clinical, humanistic and economic outcomes. Additional research investigating these tools is needed, especially in frail elderly and community-living patients receiving primary care.

Author and year	Holstiege 2015
Objectives	The aim of the present systematic review of RCTs and cluster-randomized trials (CRTs) is to evaluate the recent progress of Computerized Decision Support System (CDSS) as a tool to improve antibiotic prescribing in primary care.
Interventions	Computer-aided clinical decision
Target drugs	Antibiotics
Patient setting	Primary care
Data last search	November 2013
Amstar	7
Number of interventions listed for reducing inappropriate prescribing	8
Results	Proportions of eligible patient visits that triggered CDSS use varied substantially between intervention arms of studies (range 2.8–62.8%). Five out of seven trials showed marginal to moderate statistically significant effects of CDSS in improving antibiotic prescribing behavior. CDSS that automatically provided decision support were more likely to improve prescribing practice in contrast to systems that had to be actively initiated by healthcare providers.

Conclusion	CDSS show promising effectiveness in improving antibiotic prescribing behavior in primary care. Magnitude of effects compared to no intervention, appeared to be similar to other moderately effective single interventions directed at primary care providers. Additional research is warranted to determine CDSS characteristics crucial to triggering high adoption by providers as a perquisite of clinically relevant improvement of antibiotic prescribing.

Author and year	Johansson 2016
Objectives	The aim of the present study was to explore the impact of strategies to reduce polypharmacy on mortality, hospitalization and change in number of drugs.
Interventions	Various
Target drugs	Various
Patient setting	All
Data last search	March 2013
Amstar	10
Number of interventions listed for reducing inappropriate prescribing	25
Results	The majority of the included studies aimed at improving quality or the appropriateness of prescribing by eliminating inappropriate and non-evidence-based drugs. These strategies to reduce polypharmacy had no effect on all-cause mortality (OR 1.02; 95% confidence interval 0.84, 1.23). Only single studies found improvements, in terms of reducing the number of hospital admissions, in favor of the intervention group. At baseline, patients were taking, on average, 7.4 drugs in both the intervention and the control groups. At follow-up, the weighted mean number of drugs was reduced (0.2) in the intervention group but increased (+0.2) in controls.
Conclusion	There is no convincing evidence that the strategies assessed in the present review are effective in reducing polypharmacy or have an impact on clinically relevant endpoints. Interventions are complex; it is still unclear how best to organize and implement them to achieve a reduction in inappropriate polypharmacy. There is therefore a need to develop more effective strategies to reduce inappropriate polypharmacy and to test them in large, pragmatic randomized controlled trials on effectiveness and feasibility.

Author and year	Lainer 2013
Objectives	The objective of this paper is to provide a systematic review about the effects of Information Technology (IT) interventions on medication safety in primary care.
Interventions	IT interventions
Target drugs	All
Patient setting	Primary care
Data last search	March 2011
Amstar	6

Number of interventions listed for reducing inappropriate prescribing	10
Results	Of the six studies evaluating computerized provider order entry (CPOE) with clinical decision support (CDS) only 3 studies effectively reduced unsafe prescribing. Both pharmacist-led IT interventions decreased the prescription of potentially inappropriate medication or unsafe prescribing in pregnancy. No reduction of ADEs was achieved by a web program or a TeleWatch system intervention.
Conclusion	Only 5 of 10 RCTs revealed a reduction of medication errors. CPOE with CDS was effective if targeted at a limited number of potentially inappropriate medications. The positive results of pharmacist-led IT interventions indicate that IT interventions with inter-professional communication appear to be effective. The unequivocal results of the included RCTs stress the necessity of rigorous evaluation prior to large-scale implementation.

Author and year	**Lane 2018**
Objectives	We sought to determine whether locally relevant, realtime syndromic or microbiological infection epidemiology can improve prescribing by reducing diagnostic uncertainty.
Interventions	Various
Target drugs	Antibiotics
Patient setting	Outpatient
Data last search	April 2016
Amstar	10
Number of interventions listed for reducing inappropriate prescribing	3 (total n=12)
Results	The three studies that reported on antibacterial prescribing rates varied in the study design and included a cohort study with a historical control group (14), a retrospective cohort study (23) and a prospective cluster randomized controlled trial (25). A reduction in antibacterial prescribing was seen following a 3-year educational and surveillance program delivered by Temte et al. (14) to family practice residents with prescribing falling from 26.4% to 8.6% (P = 0.01) for upper respiratory infections. A reduction in antibacterial prescribing was reported by Hebert et al. (23) during a pandemic influenza period when compared with seasonal influenza periods: [odds ratio (OR) 0.72 (95% CI, 0.68 to 0.77), P < 0.001]. They also demonstrated that the likelihood of prescribing an antibacterial decreased as the number of febrile respiratory illness (FRI) cases that a physician had seen in the previous week increased—if 12+ patients were seen in the preceding week compared with 0–1 patients, antibacterial prescribing reduced [OR 0.57 (95% CI, 0.51 to 0.63), P < 0.001] (23). Shah et al. (25) reported a reduction in antibacterial prescribing following the introduction of an intervention providing clinicians with a syndromic heat map of influenza activity—they measured an absolute reduction in antibacterial prescribing of 5.1% during a period of moderate influenza activity (P < 0.05).

Conclusion	There is promising evidence that syndromic and microbiological epidemiological data can influence the use of antibacterials in primary care.

Author and year	Loganathan 2011
Objectives	The purpose of our review was to interpret the results of studies that have evaluated any type of strategy to improve prescribing in care homes.
Interventions	Various
Target drugs	All
Patient setting	Care homes
Data last search	April 2010
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	16
Results	The search strategy retrieved 16 studies that met the inclusion criteria. Four intervention strategies were identified: staff education, multi-disciplinary team (MDT) meetings, pharmacist medication reviews and computerized clinical decision support systems (CDSSs). Complex educational programs that focused on improving patients' behavioral management and drug prescribing were the most studied area, with six of eight studies highlighting an improvement in prescribing. Mixed results were found for pharmacist interventions. CDSSs were evaluated in two studies, with one showing a significant improvement in appropriate drug orders. Two of three studies examining MDT meetings found an overall improvement in appropriate prescribing. A meta-analysis could not be performed due to heterogeneity in the outcome measures.
Conclusion	Results are mixed and there is no one interventional strategy that has proved to be effective. Nevertheless, education including academic detailing seems to show most promise. A multi-faceted approach and clearer policy guidelines are likely to be required to improve prescribing for these vulnerable patients.

Author and year	Marcum 2010
Objectives	The objective of this study was to conduct a narrative review of the published literature, describing the current state of the art of medication prescribing in nursing homes and interventions for improvement.
Interventions	Various
Target drugs	All
Patient setting	Nursing home
Data last search	December 2009
Amstar	5

Number of interventions listed for reducing inappropriate prescribing	18
Results	Eighteen studies met the inclusion criteria for this review. Seven of those studies described educational approaches using various interventions (eg, outreach visits) and measured suboptimal prescribing in different manners (eg, adherence to guidelines). Two studies described computerized decision-support systems to measure the intervention's impact on adverse drug events (ADEs) and appropriate drug orders. Five studies described clinical pharmacist activities, most commonly involving a medication review, and used various measures of suboptimal prescribing, including a measure of medication appropriateness and the total number of medications prescribed. Two studies each described multidisciplinary and multifaceted approaches that included heterogeneous interventions and measures of prescribing. Most (15/18; 83.3%) of these studies reported statistically significant improvements in ≥1 aspect of suboptimal prescribing. Only 3 of the studies reported significant improvements in distal health outcomes, and only 3 measured ADEs or adverse drug reactions.
Conclusion	Mixed results were reported for a variety of approaches used to improve suboptimal prescribing. However, the heterogeneity of the study interventions and the various measures of suboptimal prescribing used in these studies does not allow for an authoritative conclusion based on the currently available literature.

Author and year	**McDonagh 2018**
Objectives	In this report, we summarize and update a large, complex comparative effectiveness review (CER) of the evidence of effectiveness of all potential interventions designed to reduce inappropriate antibiotic use for acute RTIs while not causing adverse consequences.
Interventions	Various
Target drugs	Antibiotics
Patient setting	All
Data last search	January 2018
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	14 (total n=95)
Results	Three education interventions, procalcitonin testing, and electronic decision support were the only interventions with evidence of improved prescribing without adverse consequences. Rapid strep testing for sore throat, rapid viral testing (multi-viral polymerase chain reaction) in adults, clinician education combined with audit and feedback, nurse telephone care combined with audit and feedback, rapid white blood cell count testing combined with delayed prescribing, and clinician communication training combined with electronic decision support and audit and feedback had low- to moderate strength evidence of improved prescribing outcomes but no evidence on potential harms. Clinician education alone and combined clinician and patient education, audit

	and feedback, CRP measurement, and academic detailing had low-strength evidence of reducing overall prescribing, but evidence regarding other outcomes was insufficient to draw conclusions. Clinic-based education for parents of children aged 24 months with AOM, public education campaigns aimed at adults, clinician education combined with audit and feedback, point-of-care testing for influenza in children, and tympanometry in children with suspected AOM had no impact on overall prescribing. Audit and feedback, patient education (a pamphlet), or the combination resulted in increased prescribing, although patient education alone and audit and feedback combined with patient education increased prescribing at a lower rate than in the control group. Using the adult algorithm for procalcitonin test results in children increased prescribing of antibiotics with a related increase in adverse events.
Conclusion	There is evidence that several interventions can effectively reduce inappropriate use of antibiotics in acute RTI without adverse consequences; the best evidence supports clinic-based education for parents, public campaigns for parents combined with clinician education, procalcitonin testing in adults, and electronic decision support.

Author and year	McDonahg 2016
Objectives	To assess the comparative effectiveness of interventions for improving antibiotic use for acute respiratory tract infections (RTI) in adults and children
Interventions	Antibiotics
Target drugs	All
Patient setting	All
Data last search	February 2015
Amstar	11
Number of interventions listed for reducing inappropriate prescribing	69 (total 132)
Results	Although reduction in antibiotic resistance is a major goal of these interventions, there were too few studies to assess this outcome. The few studies that attempted to assess appropriate prescribing had important limitations and lack of consistency in outcome definition and ascertainment methods across studies. Therefore, reduction in overall prescribing was the only commonly reported benefit across interventions. Actual use of antibiotics was also reported in too few studies to assess separately from prescribing. No intervention had high-strength evidence for any outcome. The best evidence, from an evidence base of 133 studies, including 88randomized controlled trials, was for four interventions with moderate-strength evidence of improved or reduced antibiotic prescribing compared with usual care that also had low-strength evidence of not causing adverse consequences. These were clinic-based parent education (21% overall prescribing reduction;

	similar return visits); public patient education campaigns combined with clinician education (improved appropriate prescribing; 7% reduction in overall prescribing; similar complications and satisfaction); procalcitonin for adults (12% to 72% overall prescribing reduction; similar continuing symptoms, limited activity, missing work, adverse events or lack of efficacy, treatment failure, hospitalizations, and mortality); and electronic decision support systems (improved appropriate prescribing and 5% to 9% reduction in overall prescribing; similar complications and health care use). Additionally, public parent education campaigns had low-strength evidence of reducing overall prescribing, not increasing diagnosis of complications, and decreasing subsequent visits. Other interventions had evidence of improved or reduced prescribing, but evidence on adverse consequences was lacking (streptococcal antigen testing, rapid multi viral testing in adults), insufficient (clinician and patient education plus audit and feedback plus academic detailing), or mixed (delayed prescribing, C-reactive protein [CRP] testing, clinician communication training, communication training plus CRP testing). Interventions with evidence of no impact on antibiotic prescribing were clinic-based education for parents of children 24 months or younger with acute otitis media, point-of-care testing for influenza or tympanometry in children, and clinician education combined with audit and feedback. Furthermore, limited evidence suggested that using adult procalcitonin algorithms in children is not effective and results in increased antibiotic prescribing.
Conclusion	The best evidence supports the use of specific education interventions for patients/parents and clinicians, procalcitonin in adults, and electronic decision support to reduce overall antibiotic prescribing (and in some cases improve appropriate prescribing) without causing adverse consequences, although the reduction in prescribing varied widely. Additionally, public parent education campaigns had low-strength evidence of reducing overall prescribing, not increasing diagnosis of complications and decreasing subsequent visits. Other interventions had evidence of improved prescribing but evidence on adverse consequences was lacking (streptococcal antigen testing, rapid multi-viral testing in adults), insufficient (clinician and patient education plus audit and feedback plus academic detailing) or mixed (delayed prescribing, CRP testing, clinician communication training, communication training plus CRP testing). Interventions with no impact on antibiotic prescribing were clinic-based education for parents of children ≤24 months with acute otitis media, point-of-care testing for influenza or tympanometry in children, and clinician education combined with audit and feedback. Furthermore, limited evidence suggested that using adult procalcitonin algorithms in children is not effective and results in increased antibiotic prescribing.

Author and year	Ostini 2011
Objectives	To identify effective strategies for stopping pre-existing prescribing in situations where continued prescribing may no longer be clinically warranted.
Interventions	Various
Target drugs	All
Patient setting	All
Data last search	January 2009
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	12
Results	Interventions that were found to be effective included patient mediated interventions (4 studies); manual reminders to prescribers (2 studies); educational materials being given to patients (2 studies)—in 1 case with GP support; a face-to-face intervention with individual prescribers; and 1 case of regulatory intervention. Audit and feedback were found to be effective in 1 study, but only partially effective in another. Other partially effective interventions included electronic reminders; educational materials sent to prescribers29; and educational meetings with prescribers combined with distance communication. Unlike other prescribing research, which typically involves multifaceted approaches, 9 of the 12 studies of interventions to stop prescribing looked at the effect of a single type of intervention.
Conclusion	It appears possible to stop the prescribing of a variety of medications with a range of interventions. A common theme in effective interventions is the involvement of patients in the stopping process. However, prescribing at the level of individual patients was rarely reported, with data often aggregated to number of doses or number of drugs per unit population, attributing any reduction to cessation. Such studies are not measuring the actual required outcome (stopping prescribing), and this may reflect the broader ambiguity about when or why it might be important to end a prescription. Much more research is required into the process of stopping pre-existing prescribing, paying particular attention to improving the outcomes that are measured.

Author and year	Page 2017
Objectives	To assess the evidence of the effectiveness of different categories of interruptive medication prescribing alerts to change prescriber behavior and/or improve patient outcomes in hospital computerized provider order entry (CPOE) systems
Interventions	Computerized alerts
Target drugs	All
Patient setting	Hospital
Data last search	February 2016
Amstar	6

Number of interventions listed for reducing inappropriate prescribing	23
Results	Just over half of the studies (53%, n= 17) reported a statistically significant beneficial effect from the intervention alert; 34% (n =11) reported no statistically significant effect, and 6% (n =2) reported a significant detrimental effect. Two studies also evaluated the effect of alerts on patient outcome measures; neither finding that patient outcomes significantly improved following alert implementation (6%, n=2). The greatest volume of evidence relates to three alert categories: drug-condition, drug-drug and corollary order alerts. Of these, drug-condition alerts had the greatest number of studies reporting positive effects (five out of six studies). Only two of six studies of drug-drug interaction and one of six of corollary alerts reported positive benefits.
Conclusion	This systematic review synthesized the current CPOE literature on the effectiveness of different CPOE interruptive medication prescribing alert categories to change prescriber behavior and/or improve patient outcomes. Just over half of the studies (53%, n = 17) reported a statistically significant beneficial effect from the intervention alert. The majority of alert categories were shown to improve outcomes in some studies, with some individual alert categories exclusively or mostly demonstrating benefits. However, there were also many studies where outcomes did not improve. Virtually no studies sought to investigate the impact on changes to prescriber behavior and outcomes overall when alerts from multiple categories are incorporated within the same system. The current evidence-base does not show a clear indication that particular categories of alerts are more effective than others in hospital CPOE systems. Subsequently organizations are left to make a decision on the amount and type of prescribing alerts to include in hospital CPOE systems with limited evidence to support these decisions.

Author and year	**Patterson 2014**
Objectives	This review sought to determine which interventions, alone or in combination, are effective in improving the appropriate use of polypharmacy and reducing medication-related problems in older people.
Interventions	Various
Target drugs	Various
Patient setting	All
Data last search	November 2013
Amstar	11
Number of interventions listed for reducing inappropriate prescribing	12

Results	Two studies were added to this review to bring the total number of included studies to 12. One intervention consisted of computerized decision support; 11 complex, multi-faceted pharmaceutical approaches to interventions were provided in a variety of settings. Interventions were delivered by healthcare professionals, such as prescribers and pharmacists. Appropriateness of prescribing was measured using validated tools, including the MAI score post intervention (eight studies), Beers criteria (four studies), STOPP criteria (two studies) and START criteria (one study). Interventions included in this review resulted in a reduction in inappropriate medication usage. Based on the GRADE approach, the overall quality of evidence for all pooled outcomes ranged from very low to low. A greater reduction in MAI scores between baseline and follow-up was seen in the intervention group when compared with the control group (four studies; mean difference -6.78, 95% CI -12.34 to -1.22). Postintervention pooled data showed a lower summated MAI score (five studies; mean difference -3.88, 95% CI -5.40 to -2.35) and fewer Beers drugs per participant (two studies; mean difference -0.1, 95% CI -0.28 to 0.09) in the intervention group compared with the control group. Evidence of the effects of interventions on hospital admissions (five studies) and of medication-related problems (six studies) was conflicting.
Conclusion	It is unclear whether interventions to improve appropriate polypharmacy, such as pharmaceutical care, resulted in clinically significant improvement; however, they appear beneficial in terms of reducing inappropriate prescribing.

Author and year	Ranji 2008
Objectives	We conducted a systematic review of studies of strategies to reduce unnecessary antibiotic prescribing in outpatient practice.
Interventions	Various
Target drugs	Antibiotics
Patient setting	Outpatient
Data last search	March 2007
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	55
Results	Quality improvement interventions are effective for reducing the unnecessary prescribing of antibiotics in ambulatory practice, with quantitative analyses demonstrating a median absolute reduction in overall prescribing rates of 9.7% (IQR, 6.6–13.7%).
Conclusion	Quality improvement efforts are effective at reducing antibiotic use in ambulatory settings, although much room for improvement remains. Strategies using active clinician education and targeting management of all ARIs (rather than single conditions in single age groups) may yield larger reductions in community-level antibiotic use.

Author and year	Saha 2018
Objectives	This systematic review aims to determine whether pharmacist led or pharmacist-involved interventions are effective at improving antibiotic prescribing by General Practitioners (GPs)
Interventions	Pharmacist led or pharmacist involved interventions
Target drugs	Antibiotics
Patient setting	Outpatient
Data last search	February 2018
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	7 (total n=8)
Results	Antibiotic prescribing rate (APR) reductions (OR 0.86, 95% CI 0.78–0.95, moderate-certainty evidence) and antibiotic prescribing adherence rate (APAR) improvements (OR 1.96, 95% CI 1.56–2.45, high-certainty evidence) were observed at 6months median intervention follow-up. High-quality randomized trials reduced the APR (OR 0.92, 95% CI 0.90–0.94) and increased the APAR (OR 2.55, 95% CI 2.16–3.01). Interventions were successful in decreasing the APR (OR 0.93, 95% CI 0.90–0.95) and increasing the APAR (OR 1.72, 95% CI 1.04–2.84) when implemented by a pharmacist–General practitioner team. Interventions involving pharmacist–infectious disease professional teams also decreased the APR (OR 0.81, 95% CI 0.66–1.0) and increased the APAR (OR 2.36, 95% CI 1.87–2.96). General practitioner (GP) education plus prescribing feedback, and group meetings were effective in both outcomes, whereas GP education, academic detailing and workshop training were effective in APAR outcome. However, substantial heterogeneity was demonstrated.
Conclusion	Antibiotic stewardschip programs involving pharmacists are effective in decreasing antibiotic prescribing and increasing guideline-adherent antibiotic prescribing by GPs.

Author and year	Tesfaye 2017
Objectives	This systematic review aims to summarize the prevalence of Inappropriate prescriptions (IP) in patients with CKD and examine its association with adverse clinical outcomes; to compare the relative effectiveness of available interventions in reducing IP and associated adverse clinical outcomes; and to identify factors contributing to IP.
Interventions	Various
Target drugs	All
Patient setting	All
Data last search	June 2016
Amstar	6
Number of interventions listed for reducing inappropriate prescribing	22 (Total n=49)

Results	Forty-nine studies from 23 countries met the inclusion criteria. An IP prevalence of 9.4%-81.1% and 13%-80.50% was reported in hospital and ambulatory settings, respectively; whereas, in long-term care facilities the prevalence ranged between 16% and 37.9%. Unsurprisingly, IP was associated with adverse drug events like increased hospital stay (Mean [SD] of 4.5 [4.8] vs 4.3 [4.5]) and high risk of mortality [40%]. Twenty-one studies reported the impact of interventions on IP; manual and computerized alerts were the main forms of interventions (n=19). The most significant reduction in IP was observed when physicians received immediate concurrent feedback from a clinical pharmacist (P<.001). Polypharmacy, comorbidities, and age were identified as predictors of IP.
Conclusion	Inappropriate prescribing has led to poor patient outcomes. Although pharmacist-based and computer-aided approaches have shown promising results, there is still room for improvement. Future studies should focus on developing a multifaceted intervention to address the widespread prevalence of IP and associated clinical outcomes in CKD patients.

Author and year	Thillainadesan 2018
Objectives	The aim of this systematic review was to investigate the efficacy of deprescribing interventions in older inpatients to reduce PIMs and impact on clinical outcomes.
Interventions	Various
Target drugs	All
Patient setting	Hospital
Data last search	April 2017
Amstar	7
Number of interventions listed for reducing inappropriate prescribing	9
Results	Seven of the nine studies reported a statistically significant reduction in PIMs in the intervention group. There was no change in one study where there were zero PIMs on admission and discharge, and in the other study a reduction in PIMs that was not statistically significant was observed. There was significant heterogeneity in outcome measures and reporting. Few studies reported on the impact of deprescribing interventions on clinical outcomes. Reported clinical outcomes included drug-related problems (n = 3), quality of life (n = 2), mortality (n = 3), hospital readmissions (n = 4), falls (n = 3) and functional status (n = 2). Most studies reported a benefit in the intervention group that was not statistically significant. No notable harm was observed in the intervention group. There was a high risk of bias in the included studies.
Conclusion	The evidence available suggests that deprescribing interventions in hospital are feasible, generally effective at reducing PIMs and safe. However, the current evidence is limited, of low quality and the impact on clinical outcomes is unclear.

Author and year	Thompson Coon 2014
Objectives	The purpose of this systematic review was to assess the effectiveness of interventions used to reduce inappropriate prescribing of antipsychotic medications to individuals with dementia resident in care homes to help to inform the provision of services
Interventions	Various
Target drugs	Antipsychotic medication
Patient setting	Care homes
Data last search	November 2012
Amstar	7
Number of interventions listed for reducing inappropriate prescribing	22
Results	Twenty-two quantitative studies (reported in 23 articles) were included evaluating the effectiveness of educational programs (n ¼ 11), in-reach services (n ¼ 2), medication review (n ¼ 4), and multicomponent interventions (n ¼ 5). No qualitative studies meeting our inclusion criteria were identified. Eleven studies were randomized or controlled in design; the remainder were uncontrolled before and after studies. Beneficial effects were seen in 9 of the 11 studies with the most robust study design with reductions in antipsychotic prescribing levels of between 12% and 20%. Little empirical information was provided on the sustainability of interventions
Conclusion	Interventions to reduce inappropriate prescribing of antipsychotic medications to people with dementia resident in care homes may be effective in the short term, but longer more robust studies are needed. For prescribing levels to be reduced in the long term, the culture and nature of care settings and the availability and feasibility of nondrug alternatives needs to be addressed.

Author and year	Vodicka 2013
Objectives	To assess the effectiveness of primary care based interventions to reduce antibiotic prescribing for children with Respiratory tract infections (RTIs).
Interventions	Various
Target drugs	Antibiotics
Patient setting	Primary care
Data last search	June 2012
Amstar	4
Number of interventions listed for reducing inappropriate prescribing	17

Results	Interventions combining parent education with clinician behavior change decreased AB prescribing rates by between 6–21%; structuring the parent–clinician interaction during consultation may further increase the effectiveness of these interventions. Automatic computerized prescribing prompts increased prescribing appropriateness, while passive information, in the form of waiting room educational materials, yielded no benefit.
Conclusion	Conflicting evidence from the included studies found that interventions directed towards parents and/or clinicians can reduce rates of AB prescribing. The most effective interventions target both parents and clinicians during consultations, provide automatic prescribing prompts, and promote clinician leadership in the intervention design.

Author and year	**Walsh 2016**
Objectives	The primary objective of this review was to collate all the available evidence on the effectiveness of pharmacist interventions on the quality of prescribing among older hospitalized patients.
Interventions	Pharmacist interventions
Target drugs	All
Patient setting	Hospital
Data last search	June 2014
Amstar	8
Number of interventions listed for reducing inappropriate prescribing	5
Results	No study focused specifically on dementia patients. Three trials reported statistically significant reductions in the Medication Appropriateness Index score in the intervention group (mean difference from admission to discharge = −7.45, 95% CI: −11.14, −3.76) and other potential inappropriate prescription (PIP) tools such as Beers Criteria. One trial reported reduced drug-related readmissions and another reported increased adverse drug reactions.
Conclusion	Multi-disciplinary teams involving pharmacists may improve prescribing appropriateness in older inpatients, though the clinical significance of observed reductions is unclear. More research is required into the effectiveness of pharmacists' interventions in reducing PIP in dementia patients. Additionally, easily assessed and clinically relevant measures of PIP need to be developed.

Author and year	Yourman 2008
Objectives	This systematic review was conducted to describe the impact of computer decision support (CDS) interventions designed to improve the quality of medication prescribing in older adults.
Interventions	Computer-aided clinical decision
Target drugs	All
Patient setting	All
Data last search	July 2007
Amstar	5
Number of interventions listed for reducing inappropriate prescribing	10
Results	Of the 10 studies testing CDS interventions, 8 showed at least modest improvements (median NNT 33) in prescribing, as measured by minimizing drugs to avoid, optimizing drug dosage, or more generally improving prescribing choices in older adults (according to each study's intervention protocols). Findings for the impact of CDS interventions on clinical outcomes were mixed and were reported for only 2 studies.
Conclusion	Various types of CDS interventions may be effective in improving medication prescribing in older adults, but few studies reported clinical outcomes related to changes in medication prescribing. Data from this study should help to guide refinement and testing of future CDS interventions that specifically target older adult populations that are taking multiple medications.

Appendix 3 | Methodological quality of included systematic reviews. Assessed with AMSTAR instrument

	# yes	A priori design?	Duplicate selection and data extraction?	Adequate search?	Publication status used as inclusion criterion?	Included and excluded studies listed?	Study characteristics reported?	Risk of bias assessed?	Risk of bias included in conclusions?	Appropriate methods to combine findings?	Publication bias assessed?	Conflict of interest reported?
Alldred 2016	11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Arnold 2005	8	Yes	Yes	Yes	Can't answer	Yes	Yes	Yes	No	Yes	No	Yes
Arroll 2003	6	No	Yes	Yes	Can't answer	No (incl)	Yes	Yes	No	Yes	Yes	No
Birkenhager 2018	8	Yes	Yes	Yes	No	No (incl)	Yes	Yes	Yes	Yes	Yes	No
Castelino 2009	6	Yes	Can't answer	Yes	Yes	Yes	Yes	Yes	No	NA	No	No
Chhina 2013	6	Yes	Yes	Yes	Can't answer	No (incl)	Yes	Yes	No	NA	No	Yes
Cross 2016	7	Yes	Yes	Yes	No	No (incl)	Yes	Yes	Yes	NA	No	Yes
Dalton 2018	8	Yes	Yes	Yes	No	No (incl)	Yes	Yes	Yes	Yes	No	Yes
Davey 2017	11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Diep 2018	6	No	Yes	Yes	No	No (incl)	Yes	Yes	Yes	Yes	No	No
Forsetlund 2011	8	Yes	Can't answer	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	Yes
Haastrup 2014	8	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	No	NA	Yes	Yes
Hill-Taylor 2016	9	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	Yes	Yes	No	Yes
Holstiege 2015	7	Yes	Yes	Yes	Can't answer	Yes	Yes	Yes	No	NA	Can't answer	Yes
Johansson 2016	10	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Lainer 2013	6	Yes	Can't answer	Yes	Can't answer	No (incl)	Yes	Yes	Yes	NA	Can't answer	Yes
Lane 2018	10	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	Yes	Yes	Yes	Yes
Loganathan 2011	6	No	Yes	Yes	Can't answer	No (incl)	Yes	Yes	No	Yes	Yes	Yes
Marcum 2010	5	No	No	Yes	Yes	No (incl)	Yes	No	No	Yes	Yes	No

McDonagh 2018	8	Yes	Yes	Yes	No	No (incl)	Yes	Yes	No	Yes	Yes	Yes
McDonahg 2016	11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ostini 2011	6	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	No	NA	Can't answer	No
Page 2017	6	No	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Yes
Patterson 2014	11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ranji 2008	6	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	No	NA	Can't answer	No
Saha 2018	8	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	Yes	Yes	Yes	Yes
Tesfaye 2017	6	No	Yes	Yes	Can't answer	No (incl)	Yes	Yes	No	Yes	No	Yes
Thillainadesan 2018	7	Yes	Yes	Yes	No	No (incl)	Yes	Yes	Yes	No	No	Yes
Thomspson Coon 2014	7	Yes	Yes	Yes	Can't answer	No (incl)	Yes	Yes	No	Yes	No	Yes
Vodicka 2013	4	Yes	No	Yes	No	No (incl)	Yes	No	No	NA	Can't answer	Yes
Walsh 2016	8	Yes	Yes	Yes	Yes	No (incl)	Yes	Yes	Yes	No	No	Yes
Yourman 2008	5	Yes	Can't answer	Yes	Yes	No (incl)	Yes	No	No	NA	Can't answer	Yes

Appendix 4 | Included interventions

Included intervention	From SR	Method	Patient setting	Intervention category	Type of drugs	Intervention	Number of patients in intervention group*	Comparison	number of patients in comparison group*	Outcome measure	Significant reduction
Agostini 2007	Dalton 2018	before/ after	Hospital	Computer intervention	other	Computer-generated recommendations	12153	care as usual	12356	Reduction in % patient with PIMs	Yes
Alder 2005	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	communication skills intervention	40	child nutrition intervention	20	antibiotic prescribing	Yes
Allard 2001	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	A multidisciplinary team analyzed the drug profile and diagnoses of the experimental group	136	care as usual	130	number of potentially inappropriate prescriptions	No
Andreeva 2014	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	CRP testing during consultation, with guidance on interpretation.	101	care as usual	78	antibiotics prescribing rate	Yes
Angunawela 1991 a	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Mailed educational newsletter	NR	Control group, not further specified.	NR	percentage antibiotic prescriptions of total prescriptions	No
Angunawela 1991 b	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Mailed educational newsletter and educational seminar	NR	Control group, not further specified.	NR	percentage antibiotic prescriptions of total prescriptions	No
Arroll 2002	Ranji 2008	RTC	Outpatient	Patient-mediated interventions	Antibiotics	delayed prescriptions	67	Immediate prescription	62	number of prescriptions used	NR
Ashe 2006	McDonahg 2016	before/ after	Outpatient	Patient-mediated interventions	Antibiotics	waiting room posters	360	care as usual	360	prescriptions per consultation	No
Atkin 1996	Chhina 2013	controlled trial	Outpatient	Education healthcare professionals	other	academical detailing	180	care as usual	104	mean number of medications prescribed concurrently per elderly patient	No

Avorn 1992	Birkenhager 2018	RTC	Long-term care facility	Education healthcare professionals	other	education health providers	431	NR, full text unavailable	392	psychoactive drug use	Yes
Awdishu 2015	Tesfaye 2017	RCT	Hospital	Computer intervention	other	real-time computerized decision support system	1579	care as usual	2489	proportion of orders that were appropriate adjusted to renal function	Yes
Baer 2013	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	procalcitonin guided antibiotic treatment (initiation, continuation, or termination of antibiotic treatment strictly guided by procalcitonin cut-off levels).	168	care as usual	169	Antibiotic prescription within 14 days of randomization	No
Bailey 1997	Ostini 2011	RCT	Hospital	Multidisciplinary (team) approach	Antibiotics	Pharmacist contact recommending discontinuation of iv antibiotics	51	care as usual	51	Action taken number of patients (discontinue antibiotic or switch to oral)	No
Ballard 2002	Thompson Coon 2014	controlled trial	Long-term care facility	Multidisciplinary (team) approach	other	Psychiatric liaison team reviewed patients directly and also provided support to facility staff	208	care as usual	125	proportion of residents taking neuroleptic medication	Yes
Bashir 1994	Ostini 2011	RCT	Outpatient	Patient-mediated interventions	other	brief advice on stopping benzodiazepine use in a clinic consultation and a self-help booklet	50	care as usual	55	Percentage of patients with reduction in benzodiazepine use at 6 months	Yes
Bauchner 2006	McDonahg 2016	RCT	Outpatient	Audit and feedback	Antibiotics	Audit and feedback with education for healthcare professionals	1368	education, without recom-mendations on the treatment	1138	Antibiotic prescriptions in adherence to guideline/ total antibiotic prescriptions	No

Baum 2010	Tesfaye 2017	before/ after	Hospital	Education healthcare professionals	Antibiotics	educational session for healthcare professionals and providing a list with drug prescription recommendations	85	care as usual	85	proportion of prescriptions with drugs that were not correctly adjusted to renal function	Yes
Bauraind 2004	Cross 2016	interrupt-ed time series	Outpatient	Patient-mediated interventions	Antibiotics	nationwide mass media campaign	Nationwide (Belgium)	Not reported as interrupted time series design.	NR	change in outpatient antibiotic sales	NR
Belongia 2001	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	other	Educational materials for patients, educational materials plus educational outreach (single session) for clinicians	107 884	care as usual	58 439	median number of prescriptions	Yes
Belongia 2005	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	other	mass media campaign (including television); educational meetings and distribution of written materials for public	all residents of Wisconsin	care as usual	all residents of Minnesota	median number of prescriptions	Yes
Bergkvist 2009	Walsch 2016	controlled trial	Hospital	Multidisciplinary (team) approach	other	Pharmacist added to an existing ward-level health care team	28	care as usual	25	MAI score	Yes
Bernal Delgado 2002	Chhina 2013	RCT	Outpatient	Education healthcare professionals	Antibiotics	academical detailing	378.52 prescriptions	care as usual	282.51 prescriptions	Relative reduction in the number of packages	No
Berner 2006	Lainer 2013	RCT	Outpatient	Computer intervention	other	computer decision support system with NSAID rule	34	computer decision support system	34	percentage cases unsafe prescription NSAID	Yes
Bernier 2014	Cross 2016	interrupt-ed time series	Outpatient	Patient-mediated interventions	Antibiotics	nationwide mass media campaign	Nationwide (France)	Not reported as interrupted time series design.	MR	change in antibiotic prescribing rate	Yes

Bernsten 2001	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Medical review by pharmacist	104	care as usual	86	Prescription drug use	No
Bexell 1996	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Educational seminars	1167	care as usual	1333	Average number of drugs	Yes
Bhardwaja 2011	Tesfaye 2017	RCT	Outpatient	Multidisciplinary (team) approach	other	a computer alert to pharmacists at the time of dispensing to possible errors in target drug selection and dosing for patients with renal insufficiency	3025	care as usual	3100	the proportion of medication errors was significantly	Yes
Bjerrum 2004	McDonahg 2016	observa-tional	Outpatient	Additional diagnostic testing	Antibiotics	C-reactive protein rapid test	NR		NR	antibiotics prescribing rate	Yes
Björnsson 2006	Haastrup 2014	RCT	Outpatient	Other	other	tapering omeprazole	51	omeprazole	46	rate of patients discounting ppi	No
Bladh 2011	Thillainadesan 2018	RCT	Hospital	Multidisciplinary (team) approach	other	Clinical pharmacist service including medication review with computer support system	164	care as usual	181	Potential Inappropriate Medication/ Patient	No
Bourgeois 2010	Vodicka 2013	RCT	Outpatient	Computer intervention	Antibiotics	Computerized decision support	9409	care as usual	2907	total antibiotic prescriptions	No
Boustani 2012	Dalton 2018	RCT	Hospital	Computer intervention	other	Computer-generated recommendations	199	care as usual	225	Reduction in % of PIMs	No
Breakell 2018	MCDonagh 2018	before/ after	Outpatient	Education healthcare professionals	Antibiotics	Education on National Institute for Clinical Excellence (NICE) guidance	51	care as usual	50	Patients receiving antibiotics	No
Bregnhoj 2009 a	Johansson 2016	RCT	Outpatient	Education healthcare professionals	other	interactive educational meeting	61	care as usual	72	number of prescribed drugs	No
Bregnhoj 2009 b	McDonahg 2016	RCT	Outpatient	Audit and feedback	Antibiotics	interactive educational meeting + feedback	79	care as usual	72	number of prescribed drugs	Yes
Briel 2006 a	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Interactive training in patient-centered communication skills; educational workshop with guideline distribution	NR, full text unavailable	NR, full text unavailable	NR, full text unavailable	visits at which antibiotic was prescribed	No

Briel 2006 b	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Educational workshop with guideline	NR, full text unavailable	NR, full text unavailable	NR, full text unavailable	visits at which antibiotic was prescribed	No
Bucci 2003	Patterson 2014	RCT	Outpatient	Multidisciplinary (team) approach	other	Pharmacist services	39	care as usual	41	change in MAI score	No
Cals 2009 a	McDonahg 2016	RCT	Outpatient	Education healthcare professionals	Antibiotics	training in enhanced communication skills	227	care as usual	204	antibiotic prescribing at index consultation	Yes
Cals 2009 b	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	c-reactive protein test	201	care as usual	230	antibiotic prescribing at index consultation	Yes
Cals 2010	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	c-reactive protein test	129	care as usual	129	Antibiotic use	Yes
Camins 2009	Davey 2017	RCT	Hospital	Education healthcare professionals	Antibiotics	academical detailing by specialized team	112	care as usual	138	% appropriate intervention vs control	Yes
Cates 1999	Ranji 2008	before/ after	Outpatient	Patient-mediated interventions	Antibiotics	delayed prescribing	988	care as usual	991	Median number of antibiotic prescriptions per month	Yes
Cavalieri 1993	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	geriatric assessment team	33	Usual care: residents managed by individual physicians without formal training in geriatrics.	36	Number of drugs	Yes
Chazan 2007	McDonahg 2016	before/ after	Outpatient	Multifaceted interventions	Antibiotics	Patient and clinician education interventions	82,314	care as usual	82,314	total antibiotic use	Yes
Chertow 2003	Tesfaye 2017	before/ after	Hospital	Computer intervention	other	real-time computerized decision support system	5490	care as usual	8950	fraction of appropriate prescriptions	Yes

Chowdhury 2007 a	McDonahg 2016	controlled trial	Outpatient	Education healthcare professionals	Antibiotics	educational materials for health care professionals	NR	care as usual	NR	Antibiotic prescriptions	NR
Chowdhury 2007 b	MCDonagh 2016	controlled trial	Outpatient	Audit and feedback	Antibiotics	Audit and feedback + educational materials	NR	care as usual	NR	Antibiotic prescriptions	NR
Christakis 2001	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	point-of care evidence-based message system	537	care as usual	423	Difference of percentage of antibiotic prescriptions for otitis media that were for <10 days between baseline and study period	Yes
Christ-Crain 2004	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	Procalcitonin guided treatment respiratory infection	124	care as usual	119	Relative risk of antibiotic exposure measured in percentage and patient-days	Yes
Christ-Crain 2006	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	Procalcitonin guided treatment community acquired pneumonia	151	care as usual	151	Initial appropriateness	No
Cioffi 2016	MCDonagh 2018	RCT	Outpatient	Additional diagnostic testing	Antibiotics	Rapid white blood cell testing plus delayed antibiotic prescribing versus	437	delayed prescribing	355	Patients receiving antibiotics	NR
Claesson and Schmidt 1998	Johansson 2016	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medication review in multidisciplinary teams	626	care as usual	1228	Mean no. of prescribed drugs	No
Coenen 2004	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	education clinician	292	care as usual	401	Percentage portion of patients receiving antibiotics	NR
Coleman 1999	Castelino 2009	RCT	Outpatient	Multifaceted interventions	other	Change of management. Extended visit with physician. Pharmacist visit. Patient self-management en support group	96	care as usual	73	rate of high-risk drug	No

Constantine 2007	Diep 2018	before/ after	Hospital	Multifaceted interventions	other	Bundle of optimization tools; pre-printed IVIG order form and education program	373	care as usual	339	Unlabeled and unclear IVIG transfusion episodes	Yes
Crotty 2004 a	Forsetlund 2011	RCT	Long-term care facility	Education healthcare professionals	other	Educational outreach	381	usual care	334	Percentage of residents prescribed and administered any psychotropic medication	No
Crotty 2004 b	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	56	care as usual	54	Medication Appropriateness Index score	Yes
Crotty 2004 c	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	50	Usual care. Both groups received a half day education	54	MAI (Medication Appropriateness Index) score	Yes
Dalleur 2014	Thillainade-san 2018	RCT	Hospital	Multidisciplinary (team) approach	other	Inpatient geriatrician consultation team using STOPP criteria	77	Inpatient geriatrician consulting team	81	Amount of Potential Inappropriate Medication	Yes
Davis 2007 a	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	point-of care evidence-based message system pediatric care center	882	care as usual	637	Difference of percentage of antibiotic prescriptions for otitis media that were for <10 days between baseline and study period	Yes
Davis 2007 b	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	point-of care evidence-based message system primary care pediatric clinic	729	care as usual	614	Difference of percentage of antibiotic prescriptions for otitis media that were for <10 days between baseline and study period	Yes

De burgh 1995	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	academical detailing	NR	care as usual	NR	benzodiazepine prescribing rate	No
De Santis 1994	Arnold 2009	RCT	Outpatient	Education healthcare professionals	Antibiotics	education healthcare professionals	313 prescriptions	care as usual	319 prescriptions	percentages of prescriptions of antibiotics for tonsillitis complying with those recommended in antibiotic guidelines	Yes
Diederichsen 2000	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	c-reactive protein test	414	clinical assessment	398	Frequency of antibiotic prescription	No
Ding 2013	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	Procalcitonin testing with decision support algorithm	33	care as usual	35	participants treated with antibiotics	Yes
Do 2016	MCDonagh 2018	RCT	Outpatient	Additional diagnostic testing	Antibiotics	C-Reactive Protein point-of-care testing	1017	care as usual	1019	patients used antibiotics within 14 days	Yes
Dowell 2001	Ranji 2008	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Delayed prescribing	95	immediate prescribing		collected prescriptions	No
Doyne 2004	Vodicka 2013	RCT	Outpatient	Multifaceted interventions	Antibiotics	academical detailing, patient education	NR	receipt of locally developed guidelines plus practice specific feedback	NR	antibiotic prescribing per 100 upper respiratory infections	No
Dranitsaris 2001	Davey 2017	RCT	Hospital	Multidisciplinary (team) approach	Antibiotics	educational outreach - review and recommend change	162	care as usual	147	Overall appropriate prescribing	No
Earthy 2000	Thompson Coon 2014	before/ after	Long-term care facility	Education healthcare professionals	other	education program	198	care as usual	198	proportion of residents taking neuroleptic medication	No

Esposito 2011	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	Rapid testing for procalcitonin and decision support algorithm	155	care as usual	155	% started on antibiotics	Yes
Falconnier 2001	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	other	education of physicians and pharmacist medication review and recommendations	806	care as usual	842	percentage of dosage regimens adjusted to renal function	Yes
Farag 2014	Tesfaye 2017	time series	Outpatient	Other	Antibiotics	estimated glomerular filtration rate reporting	604	no estimated glomerular filtration rate reporting	691	the average rate of antibiotic prescriptions dosed in excess of guidelines	No
Feasby 2012	Diep 2018	before/ after	Hospital	Multifaceted interventions	other	Utilization control program and IVIG request form	652	care as usual	646	Unlabeled and unclear IVIG transfusion episodes	No
Field 2009 a	Marcum 2010	RCT	Long-term care facility	Computer intervention	other	computerized decision support systems	400	care as usual	433	percentage of appropriate orders	Yes
Field 2009 b	Tesfaye 2017	RCT	Long-term care facility	Computer intervention	Antibiotics	clinical decision support system	400	care as usual	433	portion of final drug orders that were appropriate	Yes
Finkelstein 2001	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	2 meetings of the practice with a physician peer leader, using CDC-endorsed summaries of judicious prescribing recommendations; feedback on previous prescribing rates were also provided. Parents were mailed a CDC brochure on antibiotic use, and supporting materials were displayed in waiting rooms.	7050	control group received no feedback	6410	Difference in antibiotics prescribed per-person year (per child, adjusted):	Yes

Finkelstein 2008	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	physician behavior-change strategy that included guideline dissemination, small-group education, frequent updates and educational materials, and prescribing feedback. Parents received educational materials by mail and in primary care practices, pharmacies, and childcare settings.	66256	not further specified	77628	Antibiotic-use rates	Yes
Flottorp 2002	Ranji 2008	RCT	Outpatient	Multifaceted interventions	Antibiotics	Computer-based decision support system, educational meetings and written materials for providers; written and electronic educational materials for patients; financial disincentives for patients	7544	Intervention targeted for urinary tract infection	4825	use of antibiotics in patients with sore throat	Yes
Formoso 2013	Cross 2016	controlled trial	Outpatient	Patient-mediated interventions	Antibiotics	mass media campaign	1.15 million persons	care as usual	3.25 million	change in antibiotic prescribing	Yes
Forrest 2013	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	electronic health record based clinical decision support	83698	care as usual	55247	Difference of percentage of amoxicillin as first-line therapy for acute otitis media	No
Fossey 2006	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	181	No information about control group	168	average reduction of neuroleptic use	Yes
Francis 2009	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Patient education	256	care as usual	272	Antibiotics prescribed per consultation	Yes

Franktenthal 2014	Hill-Taylor 2016	RCT	Long-term care facility	Other	other	STOPP/START tool	183	care as usual	176	prevalence of one or more potentially inappropriate medication	Yes
Franz 2004	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	dissemination of guideline; structural, introduction of testing for C-reactive protein and interleukin-8 with decision support algorithm	656	care as usual	635	number of newborn infants who received antibiotic therapy	Yes
Frayha 1997	Diep 2018	before/ after	Hospital	Other	other	IVIG indication form	62	care as usual	28	Unlabeled and unclear IVIG transfusion episodes	Yes
Furniss 2000	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	158	care as usual	172	Mean number of prescribed drugs.	Yes
Galanter 2005	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	323 alerts	care as usual	87 situation that would have generated an alert.	Likelihood of patient receiving at least a single dose of the contraindicated medication (%)	Yes
Gallagher 2011	Thillainade-san 2018	RCT	Hospital	Other	other	STOPP/START screening and recommendations by physicians	190	care as usual	192	Total amount of Potential Inappropriate Medication	Yes
Garcia-Gollarte 2014	Hill-Taylor 2016	RCT	Long-term care facility	Other	other	STOPP/START tool	516	care as usual	502	prevalence of one or more potentially inappropriate medication	Yes
Gerber 2013	McDonahg 2016	RCT	Outpatient	Audit and feedback	Antibiotics	clinician education coupled with audit and feedback of antibiotic prescribing to children with acute respiratory tract infections	246,338 patient visits	care as usual	231,674 patient visits	Broad-spectrum antibiotic prescribing	Yes

Ghibelli 2013	Dalton 2018	before/ after	Hospital	Computer intervention	other	Computer-generated recommendations	60	care as usual	74	Reduction in % of PIMs and % patient with PIMs	Yes
Gillespie 2013	Walsch 2016	RCT	Hospital	Multidisciplinary (team) approach	other	Pharmacist added to an existing ward-level health care team	182	care as usual	186	MAI score	Yes
Gjelstad 2013	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	clinician education, delayed prescribing, academic detailing	NR	a different intervention targeting prescribing practice for older patients	NR	antibiotics prescribing rates	Yes
Gleason 2004	Ostini 2011	controlled trial	Outpatient	Education healthcare professionals	other	Physician alert letter summarizing metformin contraindications and risks of continued use sent to physicians together with name of patient who uses metformin and has a contraindication diagnosis	712	Patients who use metformin, without a con-traindication diagnosis.	16,575	Percentage of patients for whom metformin was discontinued at 9 months	Yes
Gonzales 1999a	McDonahg 2016	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	Clinician education , audit and feedback, patient education	34978	care as usual	46767	Antibiotic prescription rates	Yes
Gonzales 1999b	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	Antibiotics	Distribution of educational materials to clinicians and patients	36404	care as usual	46767	Antibiotic prescription rates	No
Gonzales 2004	McDonahg 2016	controlled trial	Outpatient	Patient-mediated interventions	Antibiotics	educational materials were mailed to intervention practice households. Waiting and examination room posters were provided to intervention office practices.	155	care as usual	2,005	antibiotic prescription rates	No

Gonzales 2005	McDonahg 2016	controlled trial	Outpatient	patient-mediated interventions	Antibiotics	educational materials were mailed to intervention practice households. Waiting and examination room posters were provided to intervention office practices.	401	care as usual	1,152	Adjusted antibiotic prescription rates	Yes
Gonzales 2008	McDonahg 2016	controlled trial	Outpatient	Patient-mediated interventions	Antibiotics	Mass media campaign	2.2 million persons	care as usual	0.53 million persons	managed care-associated antibiotic dispenses per 1000 members	Yes
Gonzales 2011	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	point-of-care C-reactive protein	74	a Clinical Algorithm	65	antibiotic use	No
Gonzales 2013a	McDonahg 2016	RCT	Outpatient	Other	Antibiotics	Printed support tool	4640	care as usual	4145	Change in antibiotic prescribing (%)	Yes
Gonzales 2013b	McDonahg 2016	RCT	Outpatient	Computer intervention	Antibiotics	electronic decision support	3991	care as usual	4145	Change in antibiotic prescribing (%)	Yes
Gonzalez-Ochoa 1996 a	Ranji 2008	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Individual and group interactive educational meetings for patients	NR	care as usual	NR	Proportion of Patients Receiving Antibiotics	NR
Gonzalez-Ochoa 1996 b	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Educational seminar and distribution of written materials for clinicians	NR	care as usual	NR	Proportion of Patients Receiving Antibiotics	Yes
Gorgels 2005	Ostini 2011	controlled trial	Outpatient	Patient-mediated interventions	other	Long-term benzodiazepine users received letter from family practitioner with advice to gradually discontinue benzodiazepine use followed 3 month later by invitation to meet with family practitioner to evaluate benzodiazepine use	2595	care as usual	1821	Percentage reduction of benzodiazepine prescription at 21 months	Yes

Graham 2008	Chhina 2013	before/ after	Outpatient	Education healthcare professionals	other	academical detailing	NR	care as usual	NR	means of change in cox-2 rates. Daily dose/patient	yes
Griffey 2011	Dalton 2018	interrupt-ed time series	Hospital	Computer intervention	other	Computer-generated recommendations	739	care as usual	668	Reduction in % of PIMs	Yes
Guillemot 2005	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	Antibiotics	Mass media campaign; educational meetings and written materials for parents; educational outreach, educational meetings, and distribution of guidelines for clinicians	866	care as usual. no specific campaign on antibiotic use	680	rate of antibiotic use	Yes
Gurwitz 2008	Lainer 2013	RCT	Outpatient	Computer intervention	other	computerized provider order entry with computer decision support	NR	computerized provider order entry	NR	preventable events per 100 resident- months	No
Gutierrez 1994	Ranji 2008	controlled before/ after	Outpatient	Audit and feedback	Antibiotics	audit and feedback + clinician education	3891	care as usual	3613	% visits at which antimicrobial was prescribed	Yes
Hagen 2005	Thompson Coon 2014	interrupt-ed time series	Long-term care facility	Education healthcare professionals	other	education healthcare professionals	1190	No education	1124	use of psychotropic drugs	No
Hanlon 1996	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	medication review by pharmacist	105	care as usual	103	mean number of prescribed medications	No
Harris 2003 a	McDonahg 2016	before/ after	Outpatient	Multifaceted interventions	Antibiotics	education for health care professionals, posters and education for patients.	665	care as usual	554	antibiotic use	Yes
Harris 2003 b	McDonahg 2016	before/ after	Outpatient	Multifaceted interventions	Antibiotics	education for health care professionals and posters	229	care as usual	554	antibiotic use	Yes
Hassen 2009	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	Other	pharmacist joined physicians on their rounds	300	care as usual	300	proportion of prescriptions that were none complained with the guidelines	Yes

Hellstrom 2011	Walsch 2016	controlled trial	Hospital	Multidisciplinary (team) approach	other	Newly formed multi-disciplinary team including a pharmacist	106	care as usual	191	MAI score	Yes
Hemo 2009	McDonahg 2016	before/ after	Outpatient	Patient-mediated interventions	Antibiotics	Public campaign	84,979	care as usual	101,401	antibiotic use	Yes
Hemons 2015	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	NR	care as usual	NR	Relevant orders cancelled in response to alert	Yes
Hennessy 2002	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	Antibiotics	community-wide educational events and meetings, educational materials in high schools, mailed written materials to households	NR	unclear	NR	antibiotics courses per person	Yes
Hickman 2003	Ranji 2008	controlled before/ after	Outpatient	Multifaceted interventions	Antibiotics	Audit and feedback with educational outreach, educational meetings, and written materials for clinicians; written educational materials for patients	888	care as usual	142	rate of antibiotic prescribing of acute bronchitis	Yes
Hoa 2017	MCDonagh 2018	RCT	Outpatient	Education healthcare professionals	Antibiotics	Education plus posters and quizzes for clinicians	1279	care as usual	742	rate of antibiotic use	No
Holm 2015	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	Other	pharmacist medication review	79	no comparison group	no control group	before: Number of drug related problems, after: number of drugs not taken action on	NR
Hulgan 2004	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	NR	care as usual	NR	Percentage oraal/ totaal quinolone orders	Yes
Hux 1999	Arnold 2009	RCT	Outpatient	Audit and feedback	Antibiotics	mailed feedback + educational bulletins	NR	care as usual	NR	percentage of first-line drug use	Yes
Ilett 2000	Chhina 2013	RCT	Outpatient	Education healthcare professionals	Antibiotics	academical detailing	5182 prescriptions	care as usual	6666 prescriptions	number of antibiotic prescriptions in three months	yes

Joosten 2013	Tesfaye 2017	before/ after	Outpatient	Multidisciplinary (team) approach	other	estimated glomerular filtration rate alerts to community pharmacists	1369	no comparison group	no control group	acceptance rate of medication adjustments	NR
Juzych 2005	Ranji 2008	controlled trial	Outpatient	Education healthcare professionals	Antibiotics	education health providers	4429	care as usual	1970	prescribing rate	Yes
King and Roberts 2001	Johansson 2016	controlled trial	Long-term care facility	Multidisciplinary (team) approach	other	multidisciplinary case conference reviews	75	care as usual	170	Medication use	No
Kotynia 2005	Birkenhager 2018	RCT	Long-term care facility	Other	other	Decision support	53	care as usual	53	Psychotropic drug use	No
Kritchevsky 2008	Davey 2017	RCT	Hospital	Audit and feedback	Antibiotics	Education with comparative feedback	2225	comparative feedback	2238	moment and duration of antibiotics	No
Kroenke and Pinholt 1990	Johansson 2016	controlled trial	Hospital	Multidisciplinary (team) approach	other	specialist geriatric input and medication review	38	care as usual	41	change number of drugs	Yes
Krol 2004	Ostini 2011	RCT	Outpatient	Patient-mediated interventions	other	An intervention leaflet containing suggestions and advice to stop or reduce proton pump inhibitor use sent to patients by their general practitioner	59	care as usual	45	Percentage patients who stopped or reduced PPI use at 12 weeks	Yes
Krska 2001	Castelino 2009	RCT	Outpatient	Multifaceted interventions	other	education and medication review by pharmacist	168	care as usual	164	Decrease of portion of pharmaceutical care issues	Yes
Kuske 2009	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	89	No intervention related training	94	psychotropic drug use	No
Lacroix 2014	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	decision support lab score derived from PCT, C-reactive protein, and urine dipstick); structural, introduction of PCT testing	131	training	140	% patients receiving antibiotics	No
Lagerlov 2000	Arnold 2009	before/ after	Outpatient	Audit and feedback	Antibiotics	feedback and peer review groups	2500	care as usual	2732	Proportion of acceptable treated asthma	Yes

Lambert 2007	Cross 2016	before/ after	Outpatient	Patient-mediated interventions	Antibiotics	Mass media campaign	NR		NR	change in antibiotic prescribing rate. Items prescribed per 1000 population	Yes
Lampela 2010	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	comprehensive geriatric assessment	404	care as usual	377	Mean number of drugs	No
Lee 2014	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	181,064 prescriptions of high-alert medications	care as usual	176,353 prescriptions of high-alert medications	Percentage prescribed dosage above maximum	Yes
Lee 2017	MCDonagh 2018	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Patient education	457	care as usual	457	number of patients receiving antibiotics	No
Légaré 2010	McDonahg 2016	RCT	Outpatient	Education healthcare professionals	Antibiotics	intervention to improve communication clinician and patient	245	care as usual	214	Used antibiotics immediately after consultation	No
Légaré 2012	McDonahg 2016	RCT	Outpatient	Education healthcare professionals	Antibiotics	intervention to improve communication clinician and patient	181	care as usual	178	Used antibiotics immediately after consultation	Yes
Lenaghan 2007	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	home-based medication review by a pharmacist	68	care as usual	66	number of prescribed drugs	Yes
Lenander 2014	Johansson 2016	RCT	outpatient	Multidisciplinary (team) approach	other	pharmacist-led medication review in primary care: Patients in the intervention group received preparatory structured pharmaceutical advice (medication review) by a geriatrics pharmacist before a scheduled GP visits	107	usual care	102	Change in the number of drugs	yes
Lester 2015	Dalton 2018	before/ after	Hospital	Computer intervention	other	Computer-generated recommendations	9591	care as usual	3259	Reduction in % patient with PIMs	Yes

Lin 2008	Page 2016	before/ after	Hospital	Computer intervention	other	Modified alert	37040 orders	care as usual	42621 orders	% overridden	No
Linder 2009	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	Electronic Health Record integrated, documentation-based clinical decision support system	11954	care as usual	10007	Percentage of patients with an Acute Respiratory Infection who received an antibiotic prescription	No
Linder 2010	McDonahg 2016	RCT	Outpatient	Computer intervention	Antibiotics	Electronic health record feedback	NR	care as usual	NR	antibiotic prescribing	No
Link 2016	MCDonagh 2018	before/ after	Outpatient	Education healthcare professionals	Antibiotics	Education and communication training for clinicians	335	care as usual	217	rate of antibiotic use	Yes
Lipton 1992	Castelino 2009	RCT	Hospital	Multidisciplinary (team) approach	other	Pharmacist consultation	350	care as usual	356	less medication and inappropriate choice	Yes
Little 1997	Arroll 2003	RCT	Outpatient	Patient-mediated interventions	Antibiotics	delayed prescription	176	immediate prescription	184	number of prescriptions used	Yes
Little 2001	Ranji 2008	RCT	Outpatient	Patient-mediated interventions	Antibiotics	delayed prescription	150	immediate prescription	135	number of prescriptions used	Yes
Little 2005	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Delayed prescribing	272	immediate antibiotics	262	antibiotic use	Yes
Little 2013 b	McDonahg 2016	RCT	Outpatient	Other	Antibiotics	application of clinical scores	211	delayed prescribing	207	antibiotic use	Yes
Little 2013 c	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	rapid antigen test for patients with high clinical scores.	213	delayed prescribing	207	antibiotic use	Yes
Litvin 2013	McDonahg 2016	Observa- tional	Outpatient	Multifaceted interventions	Antibiotics	clinical decision support system and audit and feedback	NR	first time frame after the start of the intervention	NR	Inappropriate antibiotic use	No
Llor 2011 a	McDonahg 2016	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	Patient and clinician education interventions	NR	care as usual	NR	Antibiotic prescription	No
Llor 2011 b	McDonahg 2016	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	rapid testing and clinician education and patient education material	NR	care as usual	NR	Antibiotic prescription	Yes

Llor 2011 c	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	rapid antigen test	281	care as usual	262	Antibiotic prescription	Yes
Loeb 2005	Forsetlund 2011	RCT	Long-term care facility	Education healthcare professionals	Antibiotics	Educational meetings and workshops	2156	care as usual	2061	Number of antimicrobial prescriptions for suspected urinary tract infection per 1000 resident days	No
Long 2014	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	introduction of PCT testing	90	care as usual	90	% treated with antibiotics	Yes
Lundborg 1999	Arnold 2009	RCT	Outpatient	Education healthcare professionals	Antibiotics	education with massages based on national guidelines	2,353 prescriptions	care as usual	2,182 prescriptions	percentage prescriptions for first choice drugs for urinary tract infection	Yes
Macfarlane 2002	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Patient education + delayed prescribing	106	delayed prescribing	106	Antibiotic use in the next two weeks	Yes
Magin 2018	MCDonagh 2018	controlled trial	Outpatient	Education healthcare professionals	Antibiotics	Education of trainee general practitioners	217	care as usual	311	patients treated with antibiotics	No
Mahoney 2007	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	1452346 medication orders	care as usual	1390789 medication orders	Total amount, 12 months pre and post: drug allergy, single dose range, duplicate order	Yes
Mainous 2000 a	Ranji 2008	RCT	Outpatient	Multifaceted interventions	Antibiotics	Audit and feedback for clinicians; educational material for patients	7697	care as usual	12232	Proportion of Patients Receiving Antibiotics	Yes
Mainous 2000 b	Ranji 2008	RCT	Outpatient	Audit and feedback	Antibiotics	Audit and feedback	11596	care as usual	12232	Proportion of Patients Receiving Antibiotics	No
Mainous 2000 c	Ranji 2008	RCT	Outpatient	Patient-mediated interventions	Antibiotics	Written educational material for patients	9393	care as usual	12232	Proportion of Patients Receiving Antibiotics	Yes

Maltezou 2008	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	rapid antigen test	451	no laboratory testing	369	Antibiotic prescription	Yes
Maravic-Stojkovic 2011	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	reminders (circumstantial, decision support algorithm triggered by measurement of PCT); structural, introduction of PCT testing.	102	care as usual	103	% treated with antibiotics	Yes
Mattison 2010	Dalton 2018	before/ after	Hospital	Computer intervention	other	Computer-generated recommendations	not stated	care as usual	not stated	Reduction in % of PIMs and % patient with PIMs	Yes
Mc Callion 1999	Forsetlund 2011	RCT	Long-term care facility	Education healthcare professionals	other	Educational meetings and workshops	49	care as usual	56	use of psychotropic medication	No
Mc Ginn 2013	Holstiege 2015	RCT	Outpatient	Computer intervention	Antibiotics	Electronic Health Record integrated clinical prediction rules	586	Background information	398	Patients` age adjusted risk ratio of antibiotic prescribing	Yes
Mc Isaac 2002	Ranji 2008	RCT	Outpatient	Other	Antibiotics	Paper-based clinician decision support system	304	a similar form but without either the sticker or the chart prompts	317	unnecessary antibiotic prescription	No
McConnell 1982	Ranji 2008	RCT	Outpatient	Audit and feedback	Antibiotics	Audit and feedback followed by educational outreach and distribution of written materials	NR	care as usual	NR	mean number of tetracycline prescribing for upper respiratory infections	Yes

Mcisaac and Goel 1998	Ranji 2008	RCT	Outpatient	Other	Antibiotics	Paper-based clinician decision support system	184	The control forms followed the exact same checklist format except that the items constituting the score were simply listed along with other clinical signs or symptoms, and no management recommendations were made	212	antibiotic prescriptions	No
McNulty 2000	Arnold 2009	controlled trial	Outpatient	Audit and feedback	Antibiotics	audit and feedback + clinician education	71657 prescriptions	Microbiology tutorials	53867 prescriptions	change in amount of broad-spectrum antibiotic prescribed	No
McNulty 2010	McDonahg 2016	before/ after	Outpatient	Patient-mediated interventions	Antibiotics	Mass media campaign	1888 persons	care as usual	1830 persons	Reported antibiotic use	No
Meador 1997	Forsetlund 2011	RCT	Long-term care facility	Education healthcare professionals	other	Educational meetings and workshops	575	care as usual and waiting list	577	Use of antipsychotics	Yes
Meeker 2014	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	Clinicians had to sign a commitment letter that emphasized the clinician's commitment to guidelines for appropriate antibiotic prescribing. These letters were displayed in examination rooms for patients.	449	care as usual	505	Antibiotic prescribing rates for antibiotic-inappropriate acute respiratory infections	Yes

Melander 1999	Ranji 2008	controlled before/ after	Outpatient	Audit and feedback	Antibiotics	Audit and feedback followed by educational workshop with local opinion leaders	2050	care as usual	2622	number of antibiotics in percentage	NR
Melbye 1995	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	C-reactive protein testing	108	care as usual	121	antibiotics prescribing	No
Meredith 2002	Castelino 2009	RCT	Long-term care facility	Multidisciplinary (team) approach	other	Medication review by pharmacist	160	care as usual	157	medication use	Yes
Metlay 2007	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	performance feedback, clinician education, and patient educational materials	3,006 visits	care as usual	2,659 visits	antibiotic prescribing	NR
Meyer 2001	Ranji 2008	RCT	Outpatient	Education healthcare professionals	Antibiotics	Educational workshops	669	no training	657	Prescription with at least 1 antibiotic for upper respiratory tract infection of total prescriptions	Yes
Michalek 2014	Thillainade-san 2018	RCT	Hospital	Other	other	Application of FORTA	58	care as usual	56	Amount of Potential Inappropriate Medication	No
Midlov 2002	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	33	care as usual	172	number of drugs	No
Midlov 2006	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	academical detailing	NR	care as usual	NR	prescribing of benzodiazepine in elderly. Mean differences in percentage for active group minus the control. In prescribed defined daily doses	Yes
Milos 2013	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	pharmacist-led medication reviews	182	care as usual	187	Mean number of continuous drugs	Yes

Molstad 1989	Ranji 2008	controlled before/ after	Outpatient	Education healthcare professionals	Antibiotics	Educational workshop with development of clinical prescribing guideline	3729	care as usual	3441	rate patients prescribed antibiotics	Yes
Monane 1998	Yourman 2008	before/ after	Outpatient	Computer intervention	other	Alerts sent to pharmacists to identify inappropriate drug use in older adults	23269	no comparison group	no control group	rate of patients receiving potentially inappropriate drugs	NR
Monette 2007	Marcum 2010	RCT	Long-term care facility	Audit and feedback	other	audit and feedback and education healthcare professionals	1115	care as usual	1053	Percentage decrease of nonadherent antibiotic prescriptions	Yes
Monette 2008	Thompson Coon 2014	before/ after	Long-term care facility	Education healthcare professionals	other	educational program	90	care as usual	90	Proportion of antipsychotic users	NR
Monette 2013	Thompson Coon 2014	before/ after	Long-term care facility	Education healthcare professionals	other	educational program	293	care as usual	293	proportion of residents who discontinued antipsychotic medication	Yes
Murrie 2012	Haastrup 2014	before/ after	Outpatient	Patient-mediated interventions	other	Patient education	166	no control group	Not applicable	number of patients that reduced or stopped after 12 months	NR
Nash 2005 a	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	other	pharmacist review + feedback	51550	care as usual	67108	rate of excessive dosing of administered medications	Yes
Nash 2005 b	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	other	nurse review + feedback	51550	care as usual	73398	rate of excessive dosing of administered medications	Yes

Naughton 2001	Marcum 2010	before/ after	Long-term care facility	Education healthcare professionals	Antibiotics	education healthcare professional	226	care as usual	116	Percentage treatment according to indications	No
Naunton 2003	Johansson 2016	RCT	outpatient	Multidisciplinary (team) approach	other	pharmacist-conducted follow-up at home of high-risk elderly patients discharged from hospital	65	usual care	71	Number of prescribed medications	No
O'Connell 1999	Arnold 2009	RCT	Outpatient	Audit and feedback	Antibiotics	audit and feedback + clinician education	1294	care as usual	1146	Antibiotic prescribing rates	No
Olsson 2010	Johansson 2016	controlled trial	Long-term care facility	Other	other	Physician-led patient focused drug surveillance	135	care as usual	167	number of drugs	Yes
Olsson 2012 a	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Medication review by study physician	49	home visit by nurse	48	Number of drugs per patient	No
Olsson 2012 b	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Medication review by study physician and medication report	50	home visit by nurse	48	Number of drugs per patient	No
Ouldali 2017	Mcdonagh 2018	interrupt-ed time series	Outpatient	Audit and feedback	Antibiotics	Education clinician + feedback	134450	care as usual	61612	change in slope per 15-day antibiotic prescriptions per 1000 pediatric emergency departments	Yes
Paterno 2009	Page 2016	before/ after	Hospital	Computer intervention	other	Modified alert	31876	care as usual	39474	percentage not overridden	Yes
Patterson 2010	Forsetlund 2011	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	173	care as usual	161	Proportion of residents prescribed one or more inappropriate psychoactive (anxiolytic, hypnotic or antipsychotic) drugs	Yes

Paul 2006	Davey 2017	RCT	Hospital	Computer intervention	Antibiotics	computer decision support system	297	care as usual	273	more inappropriate psychoactive (anxiolytic,	Yes
Pell 2014	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	87 alerts	care as usual	66 alerts	hypnotic or antipsychotic drugs	Yes
Perez-cuevas 1996	Arnold 2009	controlled trial	Outpatient	Audit and feedback	Antibiotics	Audit and feedback + education healthcare professionals	65	care as usual	54	Percentage patients with rhinopharyngitis receiving an antibiotic prescription	Yes
Persell 2016 a	MCDonagh 2018	RCT	Outpatient	Computer intervention	Antibiotics	computer alerts with guidelines	558 patient visits	care as usual	57 patient visits	Antibiotic for non-antibiotic appropriate ARI	No
Persell 2016 b	MCDonagh 2018	RCT	Outpatient	Computer intervention	Antibiotics	computerized suggestions	461 patient visits	care as usual	57 patient visits	Antibiotic for non-antibiotic appropriate ARI	No
Persell 2016 c	Mcdonagh 2018	RCT	Outpatient	Audit and feedback	Antibiotics	audit and feedback	550 patient visits	care as usual	57 patient visits	Antibiotic for non-antibiotic appropriate ARI	No
Perz 2002	McDonahg 2016	Time series	Outpatient	Multifaceted interventions	Antibiotics	provider education, parent education, public education	NR	care as usual	NR	Changes in Antibiotic Prescription Rates	Yes
Peterson 1996	Chhina 2013	controlled trial	Outpatient	Education healthcare professionals	other	academical detailing	93220 prescriptions	care as usual	84527 prescriptions	ratio of NSAIDs to PCM in daily defined doses	Yes
Peterson 1997	Arnold 2009	controlled before/ after	Outpatient	Audit and feedback	Antibiotics	academic detailing + feedback	118	care as usual	118	ratio recommended/ not recommended antibiotics urinary tract infections	Yes
Peterson 2005	Dalton 2018	interrupt-ed time series	Hospital	Computer intervention	other	Computer-generated recommendations	2647	care as usual	2515	Reduction in % of PIMs	Yes

Pieper 2016	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	144	physicians received training about current guidelines	138	all psychotropic drug use	No
Pimlott 2003	Ostini 2011	RCT	Outpatient	Audit and feedback	other	Physicians mailed packages of feedback on their prescribing every 2 months for 6 months, together with educational material	168	Feedback on first-line antihyper-tension drug prescribing for elderly	206	Difference in percentage of prescriptions of benzodiazepines	Yes
Pitkälä 2014	Johansson 2016	RCT	Long-term care facility	Education healthcare professionals	other	of nurse training	118	care as usual	109	Change in the prevalence of harmful medication	Yes
Poehling 2006	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	rapid influenza testing	135	care as usual	170	% children treated	No
Polidori 2012	Page 2016	before/ after	Hospital	Computer intervention	other	Modified alert	NR	care as usual	NR	Alert adherence	NR
Pope 2011	Johansson 2016	RCT	Hospital	Multidisciplinary (team) approach	other	specialist geriatric provides feedback to primary physician	110	care as usual	115	number of drugs, before after	Yes
Pshetizky 2003	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	brief explanation to parents of patients	44	care as usual	37	rate of antibiotics purchase	Yes
Quartarolo 2007	Tesfaye 2017	before/ after	Hospital	Other	Antibiotics	reporting a calculated estimate of GFR to physicians	260	care as usual	198	rates of correct dosing of antibiotics	No
Raebal 2007 a	Lainer 2013	RCT	Outpatient	Computer intervention	other	pharmacy information management system	177	care as usual	276	Proportion of patients dispensed targeted medications	Yes
Raebal 2007 b	Yourman 2008	RCT	Outpatient	Computer intervention	other	Age-specific alerts sent to pharmacists when 1 of 11 potentially inappropriate drugs prescribed to older patients	29840	usual care	29840	Portion receiving a potentially inappropriate drug	Yes

Ray 1985	Arnold 2009	controlled before/ after	Outpatient	Education healthcare professionals	Antibiotics	education by physician counselor	372	care as usual	372	reduction of prescribing of contraindicated antibiotics and oral cephalosporins	NR
Ray 1987	Thompson Coon 2014	controlled trial	Long-term care facility	Education healthcare professionals	other	Educational program	2428	care as usual	4579	antipsychotic drug prescribing	No
Ray 1993	Loganathan 2011	controlled trial	Long-term care facility	Education healthcare professionals	other	Education healthcare professionals	228	care as usual	218	decrease of antipsychotic prescribing	Yes
Razon 2005	McDonahg 2016	before/ after	Outpatient	Education healthcare professionals	Antibiotics	Clinician education	2114	care as usual	1727	antibiotics for acute otitis media	Yes
Regev - Yochay 2011	Vodicka 2013	RCT	Outpatient	Education healthcare professionals	Antibiotics	Education healthcare professionals	43,677	care as usual	44,453	Antibiotic prescriptions per 100 patients per year	NR
Roberts 2001	Forsetlund 2011	RCT	Long-term care facility	Multifaceted interventions	other	Educational meetings , medication review and workshops	905	care as usual	2325	Percentage of residents being administered psychotropic medication	No
Roberts 2010	Tesfaye 2017	before/ after	Hospital	Computer intervention	other	clinical decision support system	509	care as usual	492	administered psychotropic	Yes
Rokstad 1995	Arnold 2009	controlled trial	Outpatient	Audit and feedback	Antibiotics	mailed feedback + recommendations	865 prescriptions	care as usual	1163 prescriptions	Mean number of defined daily dose of benzodiazepines for each patient	Yes

Roumie 2004	Ostini 2011	before/ after	Outpatient	Multifaceted interventions	other	personalized letters to patients from health service pharmacy summarizing Women's Health Initiative results, an alert placed in patients' electronic charts and summary for prescriber of Women's Health Initiatives results to accompany the electronic alert	92	immediately after the press release on the WHI study	NR	Discontinuation of hormone replacement therapy	Yes
Rovner 1996	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	42	nurse to patient ratio was increased	39	antipsychotics drug use	No
Rubin 2005	Ranji 2008	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	Patient education materials, media campaign, physician small group session, algorithms for diagnosis and management	a community in Utah	care as usual	the rest of rural Utah as a control community	proportion of upper respiratory tract infection treated with antibiotics	Yes
Samore 2005a	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	clinical decision support systems + Mass media campaign, educational meetings for clinicians, patient education	32490	care as usual	19310	Community-wide antimicrobial usage	Yes
Samore 2005b	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	Mass media campaign, educational meetings for clinicians, patient education	35420	care as usual	19310	Community-wide antimicrobial usage	No
Santoso 1996 a	Ranji 2008	controlled before/ after	Outpatient	Education healthcare professionals	Antibiotics	Educational outreach and educational workshop (single session) with distribution of educational materials	NR	care as usual	NR	Antibiotic usage	Yes
Santoso 1996 b	Ranji 2008	controlled before/ after	Outpatient	Education healthcare professionals	Antibiotics	Educational meeting and distribution of written materials	NR	care as usual	NR	Antibiotic usage	Yes

Schmader 2004	Walsch 2016	RCT	Hospital	Multidisciplinary (team) approach	other	Newly formed multi-disciplinary team including a pharmacist	202	care as usual	198	MAI score	Yes
Schmidt, 1998	Thompson Coon 2014	RCT	Long-term care facility	Multidisciplinary (team) approach	other	Multidisciplinary team meetings	626	care as usual	1228	Reduction in prescription of antipsychotic medications	Yes
Schnoor 2010	Davey 2017	RCT	Hospital	Education healthcare professionals	Antibiotics	educational meetings with dissemination of guideline; reminders (physical, posters, electronic and pocket versions of guideline)	275	care as usual	348	% guideline compliant for initial treatment	Yes
Schouten 2007	Davey 2017	RCT	Hospital	Education healthcare professionals	Antibiotics	educational meetings with dissemination of guideline; educational outreach by academic detailing	460	care as usual	338	%patients compliant with guideline for selected drug	Yes
Schuetz 2009	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	reminders (circumstantial, decision support algorithm with each PCT test); structural, introduction of PCT testing	628	care as usual	629	% patients treated	Yes
Sellier 2009	Page 2016	interrupt-ed time series	Hospital	Computer intervention	other	new alert	282	care as usual	321	Relevant orders cancelled in response to alert and inappropriate prescribing rate	No
Sellors 2003	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Pharmacist medication review	431	care as usual	458	mean number of drugs	No
Selvan 2010	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	9292	care as usual	6350	inappropriate prescribing rate	Yes

Senn 2004	Davey 2017	RCT	Hospital	Education healthcare professionals	Antibiotics	dissemination of questionnaire about guidelines; reminders (circumstantial and physical, questionnaire mailed to the resident in charge of patients who were receiving IV antibiotic treatment.	126	care as usual	125	% of patients discontinuing IV antibiotics and hazard ratio adjusted for patients' Karnofsky functional index	No
Shah 2014	Lane 2018	RCT	Outpatient	Other	Antibiotics	epidemiological data	NR	care as usual	NR	antibiotic prescribing rates	No
Sharp 2017	MCDonagh 2018	before/ after	Outpatient	Multifaceted interventions	Antibiotics	Electronic decision support (plus single education intervention)	11,458	care as usual	10,491	percentage receiving antibiotics	Yes
Simon 2006	Yourman 2008	interrupt-ed time series	Outpatient	Multifaceted interventions	other	Age-specific pop-up alert for drugs to avoid, with better alternative drugs, and academic detailing	24119	alerts alone	26805	Reduction of non-preferred drugs	No
Singh 2000	Davey 2017	RCT	Hospital	Multidisciplinary (team) approach	Antibiotics	CPIS criteria and expert approval for AB choice	39	care as usual	42	Total duration of all antibiotic treatment	Yes
Smabrekke 2002	McDonahg 2016	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	Patient and clinician education interventions	210	care as usual	124	Percent prescribed	Yes
Smeets 2009	McDonahg 2016	before/ after	Outpatient	Multifaceted interventions	Antibiotics	clinician education, communication training, audit and feedback, patient education	1000	care as usual	1000	antibiotic prescriptions	No
Smith 2006	Yourman 2008	interrupt-ed time series	Outpatient	Computer intervention	other	Drug-specific pop-up alert that recommended better alternatives	NR	care as usual	NR	Reduction of non-preferred drugs prescription per 10,000 patients	Yes
Solomon 2001	Davey 2017	RCT	Hospital	Education healthcare professionals	Antibiotics	educational meetings with dissemination of policy for necessary use; educational outreach by review and recommend change	125	care as usual	153	reduction of unnecessary levofloxacin or ceftazidime use.	Yes

Sorita 2015	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	648	care as usual	359	completed order (despite of high QTc, while high QTc is a contraindication)	Yes
Spaeder 2006	Lainer 2013	RCT	Outpatient	Computer intervention	other	TeleWatch system with clinic visits	25	clinic visits	24	Number of attempted titrations	No
Spinewine 2007	Walsch 2016	RCT	Hospital	Multidisciplinary (team) approach	other	Pharmacist added to an existing ward-level health care team	96	care as usual	90	MAI score	Yes
Spiro 2006	Ranji 2008	RCT	Outpatient	Patient-mediated interventions	Antibiotics	delayed prescriptions	138	standard prescription	145	Filled prescriptions	Yes
Stein 2001	Forsetlund 2011	RCT	Long-term care facility	Education healthcare professionals	other	Educational meetings and workshops	76	care as usual	71	Use of NSAIDs and acetaminophen the past seven days.	Yes
Stewart 2007	Ostini 2011	controlled trial	Outpatient	Patient-mediated interventions	other	General practitioners sent a patient information leaflet and a letter to chronic benzodiazepine users to outline disadvantages of long-term benzodiazepine use and invite patients to make appointment to discuss reducing or stopping use	1256	care as usual	6914	Difference in percentage reduction of defined daily dose per patient after 6 months	Yes
Stocker 2010	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	introduction of PCT testing	60	care as usual	61	treated with AB > 72 h	Yes
Stolz 2009	Davey 2017	RCT	Hospital	Additional diagnostic testing	Antibiotics	introduction of PCT testing	102	care as usual	106	Duration of AB use	Yes
Strikwerda 1994	Alldred 2016	RCT	Long-term care facility	Multidisciplinary (team) approach	other	Pharmacist medication review	61	care as usual	10	number of drugs	No

Strom 2010 a	Page 2016	RCT	Hospital	Computer intervention	other	Modified alert	995	care as usual	986	Percentage not reordering an alert-triggering drug within 10 minutes after the alert.	No
Strom 2010 b	Davey 2017	RCT	Hospital	Computer intervention	Antibiotics	Computer decision, hard stop, that would not allow concomitant orders of warfarin and trimethoprim-sulfamethoxazole.	194	care as usual	148	the proportion of desired responses (i.e. not reordering the alert-triggering drug within 10 minutes of firing)	Yes
Sturgess 2003	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Pharmacist medication review	110	care as usual	81	mean number of drugs	No
Such Diaz 2013	Tesfaye 2017	before/ after	Hospital	Multidisciplinary (team) approach	other	pharmacist provided recommendations	NR	care as usual	NR	Percentage of appropriate orders	Yes
Takemura 2005	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	immediate testing for C reactive protein and leucocyte count	147	no advance testing	154	Antibiotics received	Yes
Tamblyn 2003	Yourman 2008	RCT	Outpatient	Computer intervention	other	Age-specific pop-up alerts for 159 prescribing problems	6284	care as usual	6276	Number of PIM started per 1000 visits	Yes
Tamblyn 2008	Lainer 2013	RCT	Outpatient	Computer intervention	other	automatic computer decision support system	1899	on demand computer decision support system	1550	Portion of patients with one or more prescribing problems	No
Taylor 2003	McDonahg 2016	RCT	Outpatient	Patient-mediated interventions	Antibiotics	a pamphlet and a videotape promoting the judicious use of antibiotics	174	brochures about effective injury prevention	184	Mean number of antibiotics prescribed per patient diagnosed	No
Taylor 2005	Vodicka 2013	RCT	Outpatient	Patient-mediated interventions	Antibiotics	patient materials + personalized videotape message	252	patient materials	247	number of diagnoses and antibiotic prescriptions	No

Teich 2000	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	64594 orders	care as usual	263549 orders	Alert for recommend drug within the class. Percentage nizatidine of all H2 blocker orders	Yes
Temte 1999	Lane 2018	controlled trial	Outpatient	Multifaceted interventions	Antibiotics	epidemiological data + education	NR	care as usual	NR	antibiotic prescribing rates	Yes
Terrell 2009	Dalton 2018	RCT	Hospital	Computer intervention	other	Computer-generated recommendations	1793	care as usual	1925	Reduction in % of PIMs and % patient with PIMs	Yes
Terrell 2010	Lainer 2013	before/ after	Hospital	Computer intervention	other	Computer decision support	2647	care as usual	2515	Portion of targeted medications excessively dosed	Yes
Testad 2010	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	113	care as usual	98	antipsychotics drug use	No
Testad 2016	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	118	care as usual	156	antipsychotics drug use	No
Thompson 1984	Marcum 2010	before/ after	Long-term care facility	Multidisciplinary (team) approach	other	pharmacist prescribes medication	67	care as usual	72	number of drugs per resident	Yes
Tomson 1997	Chhina 2013	controlled trial	Outpatient	Education healthcare professionals	other	academical detailing	NR	care as usual	NR	Ratio of inhaled ß agonist to inhaled steroid in daily defined doses	No
Trygstad 2005	Patterson 2014	before/ after	Long-term care facility	Multidisciplinary (team) approach	other	pharmacist medication review	5160	care as usual	2202	number of beers list drugs	No
Trygstad 2009	Patterson 2014	controlled before after trial	Long-term care facility	Multidisciplinary (team) approach	other	pharmacist medication review	8087	care as usual	NR	number of beers list drugs	No
Ulfvarson 2003	Marcum 2010	RCT	Long-term care facility	Multidisciplinary (team) approach	other	Medication review by clinical pharmacist and cardiologist	43	Control group, not further specified.	37	Number of drugs not taken action on	NR

Van der Linden 2017	Thillainade-san 2018	RCT	Hospital	Multidisciplinary (team) approach	other	Pharmacist using RASP (Adjusted STOPP in Older Patients) and medication review	91	care as usual	81	Amount of Potential Inappropriate Medication	Yes
Van Driel 2007	McDonahg 2016	RCT	Outpatient	Education healthcare professionals	Antibiotics	Clinician education interventions	204	care as usual	204	% patient prescribed an antibiotic	No
Van Eijk 2001 a	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	group academical detailing	12734	care as usual	16201	rate of incidence prescriptions of high anti cholinergic antidepressants per 1000 person	Yes
Van Eijk 2001 b	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	individual academical detailing	17143	care as usual	16201	rate of incidence prescriptions of high anti cholinergic antidepressants per 1000 person	Yes
Veninga 2000	Arnold 2009	RCT	Outpatient	Audit and feedback	Antibiotics	feedback and education healthcare professional	2875 prescriptions	care as usual	3132 prescriptions	decrease of duration of treatment in defined daily dose/prescription	Yes
Vervloet 2015	Vodicka 2013	RCT	Outpatient	Audit and feedback	Antibiotics	guidelines, patient communication skills, antibiotic prescribing rate feedback.	59483	care as usual	94767	antibiotic prescription rate	Yes
Vida 2012	Thompson Coon 2014	before/ after	Long-term care facility	Education healthcare professionals	other	educational program	308	care as usual	308	proportion of residents who discontinued antipsychotic medication	NR
Vinks 2009	Johansson 2016	controlled trial	Outpatient	Multidisciplinary (team) approach	other	Pharmacist medication review	98	care as usual	98	mean number of drugs	NR
Vinnard 2013 a	McDonahg 2016	controlled trial	Outpatient	Education healthcare professionals	Antibiotics	Clinician education interventions	103	care as usual	216	change in antibiotic prescribing	Yes
Vinnard 2013 b	McDonahg 2016	controlled trial	Outpatient	Patient-mediated interventions	Antibiotics	patient education (patient mailing)	91	care as usual	216	change in antibiotic prescribing	No

Walker 1998	Davey 2017	RCT	Hospital	Multidisciplinary (team) approach	Antibiotics	Pharmacist recommendation in chart	25	care as usual	25	number of patients changed to oral antibiotic therapy	Yes
Weber 2008	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Geriatrician medication review	207	care as usual	413	mean number of drugs	No
Wehling 2016	Thillainade-san 2018	RCT	Hospital	Other	other	Application of FORTA	202	care as usual	207	Potential Inappropriate Medication/ patient	Yes
Weiss 2011	McDonahg 2016	before/ after	Outpatient	Education healthcare professionals	Antibiotics	Clinician education interventions	1000	care as usual	1000	Absolute change of antibiotic prescriptions	Yes
Welchen 2004	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	clinician education, communication training, audit and feedback, patient education	905	care as usual	818	adjusted antibiotic prescription rates % change in mean number of antibiotic prescriptions per 1000 patients	Yes
Westbury 2010	Thompson Coon 2014	controlled trial	Long-term care facility	Multifaceted interventions	other	education healthcare professionals, feedback, medication review, team	863	care as usual	715	proportion of residents taking antipsychotic medication	Yes
Wetterneck 2011	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	4013	care as usual	4147	Incidence of related medication errors	No
Wilf-miron 2012	Saha 2019	before/ after	Outpatient	Audit and feedback	Antibiotics	Group meetings with education en feedback	47500	care as usual	44375	antibiotic prescription rate	Yes
Williams 2004	Johansson 2016	RCT	Outpatient	Multidisciplinary (team) approach	other	Pharmacist medication review	63	care as usual	77	mean number of drugs	Yes

Wilson 2003	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	Workshops for clinicians, clinicians received feedback and guidelines and patient information including handouts and posters. Parents participated in focus groups. Parents were provided with guidelines and education through newsletters	24	guidelines and implementation package for healthcare providers. Parents were provided with guidelines and education through newsletters	30	mean change in antibiotic prescription per 100 Medicare services	Yes
Witt 2004	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	academical detailing	NR	Postal distribution of asthma medication guidelines	NR	Number of daily defined dose of beta agonist	No
Woods 2014	Page 2016	before/ after	Hospital	Computer intervention	other	new alert	18019 orders	care as usual	13164 orders	percentage atypical orders	Yes
Worrall 2007a	McDonahg 2016	RCT	Outpatient	Additional diagnostic testing	Antibiotics	Rapid antigen test	120	care as usual	141	% Of visits where antibiotics were prescribed	Yes
Worrall 2007b	McDonahg 2016	RCT	Outpatient	other	Antibiotics	decision rules	170	care as usual	141	% Of visits where antibiotics were prescribed	No
Worrall 2007c	McDonahg 2016	RCT	Outpatient	Multifaceted interventions	Antibiotics	rapid antigen test and decision rules	102	care as usual	141	% Of visits where antibiotics were prescribed	yes
Wutzke 2007	McDonahg 2016	before/ after	Outpatient	Multifaceted interventions	Antibiotics	Radio, television, and newspaper campaign. Implemented seasonally with community-based education sessions. Information was mailed to all general practices and community pharmacies	nationwide	care as usual	nationwide	Proportion of the community reporting taking antibiotics when ill with last cough, cold, or flu	Yes

Zermansky 2006	Johansson 2016	RCT	Long-term care facility	Multidisciplinary (team) approach	other	medical review by pharmacist	331	care as usual	330	Number of changes in medication per resident,	Yes
Zwar 1999	Ranji 2008	RCT	Outpatient	Audit and feedback	other	Audit and feedback followed by educational outreach session with distribution of written materials	NR	an intervention on an unrelated topic	NR	benzodiazepine prescribing per 100 encounters.	Yes
Zwar 2000	Chhina 2013	RCT	Outpatient	Education healthcare professionals	other	academical detailing	NR	academical detailing on unrelated topic	NR	benzodiazepine prescribing per 100 encounters.	No
Zwijsen 2014	Birkenhager 2018	RCT	Long-term care facility	Education healthcare professionals	other	education health providers	308	care as usual	65	antipsychotics drug use	Yes

**Number of patients, unless stated otherwise.*
AB: antibiotics, CRP: c-reactive protein, MAI: medication appropriateness index, NR: not reported, NSAID: non-steroidal anti-inflammatory drug, PCM: paracetamol, PCT: procalcitonin, PIM: potentially inappropriate medication, RCT: randomized controlled trial, SR: systematic review.

3

Why reducing low-value care fails to bend the cost curve, and why we should do it anyway

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Background

Low-value care does not benefit the patient, but it is potentially harmful, may not reflect patient preferences, and may result in considerable costs. Several US studies have estimated the nationwide costs of medical waste, including low-value care, at hundreds of billions of dollars.(1, 2) Health systems can reduce low-value care by targeted de-implementation interventions, of which many have been proven successful.(3, 4) Studies into de-implementation occasionally estimate substantial cost savings to the health system, claiming it will save society millions of dollars. For example: a de-implementation strategy reducing vitamin D testing could directly save up to 1.5 million Canadian dollars per year in Alberta(5); four Dutch departments of internal medicine could save 1.2 million euros a year by reducing inappropriate laboratory testing(6); avoiding inappropriate imaging could save Massachusetts 50-100 million dollars annually(7); and stopping five low-value general surgery services could save the English National Health Service (NHS) over 150 million euros per year.(8) Evidently, these potential savings attracted the attention of policymakers. Reducing low-value care has been adopted, for example, by the Dutch government to 'bend the healthcare cost curve' while simultaneously increasing the quality of care. Could this be the panacea to ailing health systems? Or are these promises too good to be true? In this perspective, we argue that calculating generous savings by reducing low-value care is wishful thinking.

It is frequently assumed that de-implementing low-value care practices causes a decline in medical use, which induces cost savings. These savings are commonly expressed as the value of foregone reimbursements, and subsequently interpreted as direct societal cost savings. This reasoning suffers from several fallacies. We address five mechanisms that provide insight into why the actual savings potential is substantially lower than these standard calculations.

Care Substitution

Roemer's law – a bed built is a bed filled – states that hospital utilization depends on the availability of care.(9) De-implementation of low-value care can induce care substitution. For example, de-implementation of knee arthroscopies for patients with degenerative osteoarthritis frees up the time of an orthopedic surgeon, other team members, and the operating theatre. This opens up capacity for other surgical procedures. If these are of high value, it results in more overall value for approximately the same price. But de-implementation can also provoke a supplier-induced demand of other low-value services: the orthopedic surgeon may perform more low-value shoulder operations.(10) The gains of de-implementation evaporate in this scenario. In order to obtain actual cost savings, volume of care needs to be reduced. Thus, care substitution should be discouraged. In the real world of the internal budgetary politics in hospitals, however, active volume reductions are rare.(11) Healthcare organizations need to decide and actively plan how the freed capacity will be used, otherwise de-implementation will neither increase value-for-money nor result in cost savings.

Not All Estimated Savings Are Realistic

The estimated savings of de-implementation interventions are frequently based on the total average reimbursed expenditures.(2, 6-8) These are, however, not representative of potential savings over either the short term or the long term. This can be explained by dividing hospital costs into four layers(12):

1) *Variable costs* are the costs of disposable equipment, drugs and medical devices that can be reduced fully, directly and immediately upon de-implementation. This category represents the direct cost savings of reducing low-value treatments.
2) *Semi-variable costs* are all costs that can be lowered if a sufficient reduction in the number of care practices is realized, for example salary costs of hourly employees. In such cases, a threshold of low-value procedures needs to be met: the minimal number in procedures needed before one can reduce work hours and subsequently also costs.
3) *Semi-fixed costs* do not change if the volume of care declines, because of a continuous obligation to pay. Examples of these are purchasing costs of reusable medical devices and salary costs of permanent employees. In the long term these costs have the potential to be reduced, but it typically takes a substantial time span to reach the threshold in volume reduction that would allow for scaling down.
4) *Fixed costs* are in essence insensitive to volume changes. For example, building-related costs and expenses on organizational overhead, like administration and ICT costs.

Reimbursements are average prices that cover all four cost categories, but the expected savings on the short term are only a small part of the reimbursed price. Roberts et al. estimated that the true variable costs account for only 16% of all hospital expenditures. (13) The variable costs are also relatively low for non-hospital care, such as diagnostic tests and general practitioner consultations. The remaining non-variable costs do not 'disappear' automatically: time is required before they can be reduced along with specific strategies that are hugely unpopular such as firing professionals or reducing their professional autonomy.(14) And despite all efforts, fixed costs remain since these are independent of volume changes.

Reducing Semi-variable And Semi-fixed Costs Is Difficult

Reaching the threshold to reduce semi-variable and semi-fixed costs is challenging. First, it could be difficult to determine relevant thresholds. With planned care such as cataract surgeries, hospitals could schedule fewer procedures and eventually meet the threshold to realize cost savings. This is, however, not an option for emergency or semi-acute care, such as trauma surgery. Hospitals need to have a minimum workforce to be able to cover peaks in this type of unplanned care. For some staff, particularly specialized doctors and nurses in small-hospital settings, scaling down is often not a viable option (i.e. those staff are part of hospital fixed costs).

Secondly, organizational resistance can prevent reaching the threshold to reduce staff. Waiting lists are a defence against cost-cutting management. Scaling down staff and capacity, while there is sufficient demand for care, can trigger resistance among professionals and patients: money is chosen over (valuable) care. In addition, long de-implementation periods hinder reaching thresholds. If 'time' becomes available, professionals will take up other tasks since doing nothing may undermine their professional integrity.(15) Their perceived workload will therefore not be reduced when the theoretical threshold is reached, also causing organizational resistance against scaling down workforce.

Payment Systems Hinder Wide-scale De-implementation

All healthcare systems partly rely on fee-for-service elements to incentivize adequate volume and prevent waiting lists. Fee-for-service systems contain a major financial disincentive for de-implementation. Especially on the short and medium term the loss

of revenue exceeds the amount of cost savings. Healthcare organizations have to either increase the prices of other care or substitute de-implemented care to avoid financial distress after large-scale de-implementation. Either way, the societal cost savings will be lower than saved reimbursements because of such compensation methods.

This especially applies for open-ended systems, where the total budget entirely depends on volume. However, even global payment systems such as the NHS in the United Kingdom rely on fee-for-service elements, for example when they contract private providers or when they seek to reduce patient backlogs. In NHS-type systems, de-implementation typically does affect hospital income in a less severe way, and any cost savings might increase profit margins. However, also in these cases a decrease in medical use does not automatically result in societal savings. To achieve societal savings, the hospital budgets should be reduced in response to de-implementation efforts. Shared-savings agreements are designed to do this and the results so far are promising.(16, 17) However, adjusting payment structures requires costly, complex and politically sensitive adjustments.

Reluctance Of Funding De-implementation Costs

The success of de-implementation depends on a tailored strategy that requires (substantial) financial resources both upfront and during the process. Since there is also no guarantee that a healthcare organizations will succeed in reducing costs, the question is who is willing to invest in de-implementation. Hospitals and healthcare professionals are unlikely to take the lead if they have to invest and take on the financial risk, especially if they do not profit from any cost savings when revenues decline. In order to provide guarantees, multi-year fixed revenue contracts could be employed. However, such agreements risk ratchet-effects, where payers aim to capture full benefits after the agreement period. The government and healthcare insurance companies may want to invest, but only if real cost savings are rendered. Given all uncertainties, payers may also be unwilling to fund upfront investments in de-implementation. Furthermore, in multiple-payer models competitors may refuse co-funding, as they may freeride on other payers' investments.

In addition to the costs of the de-implementation strategy, the alternative for low-value care practices also requires funding. For example, instead of the chronic use of opioids for knee osteoarthritis, patients are advised to exercise under supervision of a physical therapist. The cost of this alternative care reduces the potential societal payoffs of de-implementation.

In all cases, one needs to take the de-implementation costs and costs of complementary care into account, otherwise the cost-saving effects will be too optimistic from a societal perspective. Moreover, the government needs to take responsibility and invest in de-implementation. Without its support, other payers and healthcare organizations are unlikely to join a major investment in large-scale de-implementation.

De-implementation For Sustainable Healthcare

The sobering conclusion is that the savings potential of de-implementation interventions is unsure, but certainly considerably lower than claimed by policymakers and in the scholarly literature.(1, 2, 5-8, 18) Healthcare organizations face reimbursement reductions that will far exceed cost savings and require extensive efforts to realize. To overcome this, financial incentives of all stakeholders must be aligned, but this requires innovative payment methods and complex healthcare system changes.

This does not mean we should stop de-implementing low-value care. While obtaining cost savings is challenging, it may be possible with a long-term business plan containing active planning to suppress substitution and to reduce semi-variable and semi-fixed costs. Moreover, de-implementation has the potential to increase the value of care and stimulate efficient use of time and resources in healthcare. This is important in light of increasing shortages of healthcare professionals in almost all countries.(19) During the next decade, tough choices have to be made.(20) If these choices are not made, healthcare quality and safety will be compromised, hurting vulnerable populations the most. Efficient use of healthcare resources is an important requirement for a sustainable health system. Reducing low-value care enables an inevitable capacity shift to high-value care, if carefully planned. Moreover, actively substituting low-value care for high-value care faces less professional resistance than directly aiming for cost-savings. It does not result in substantial loss of revenue for providers and does not require a challenging reduction of semi-variable and semi-fixed costs. Individual patients still benefit from de-implementation through fewer adverse events and more high-value care, while society benefits by more value for money regarding healthcare taxes and premiums.
De-implementation of low-value care should not be adopted because of the opportunity for direct cost savings, but it should be enthusiastically embraced to improve the quality of care, reduce harm for patients, free up capacity for high-value procedures and to ensure future workforce sustainability.

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4

Stakeholders' perspectives on capturing societal cost savings from a quality improvement initiative: A qualitative study

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Abstract

Background

Besides improving the quality of care, quality improvement initiatives often also intend to produce cost savings. An example is prehabilitation, which can reduce complication rates and the length of stay in the hospital. However, the process from utilization reductions to actual societal cost savings remains uncertain in practice. Our aim was to identify barriers and facilitators throughout this process. We used the implementation of prehabilitation in a Dutch hospital as a test case.

Methods

We held 20 semi-structured interviews between June and November 2023. Eighteen stakeholders were affiliated with the hospital and two with different health insurers. Nine interviews were held face-to-face and 11 via Microsoft Teams. The interviews were recorded and transcribed. The first transcripts were inductively coded by two authors, the subsequent transcripts by one and checked by another. Differences were resolved through discussion.

Results

We identified 20 barriers and 23 facilitators across four stages: reducing capacity, reducing departmental expenses, reducing hospital expenses and reducing insurer expenses. All participants expected that the excess capacity will be used for other priorities. This was perceived as highly valuable and as an efficiency gain. Other barriers to capture savings included the fear of losing resilience, flexibility, status and revenue. Misalignment between service contracts among hospitals and insurers can hinder the ability to financially incentivize cost reductions. Additionally, some contract types can hinder the transfer of hospital savings to insurers. Identified facilitators included shared savings agreements, an explicit strategy targeting all stages, and labour shortage, among others.

Conclusion

This study systematically describes barriers and facilitators that influence the process of translating quality improvement initiatives into societal cost savings. Stakeholders expect that any saved capacity will be used for other priorities, including providing care due to the increasing demand. Capturing any cash savings does not occur automatically, emphasizing the need for a strategy targeting all stages.

Introduction

Health expenditure growth is expected to outpace gross domestic product (GDP) growth in most member countries of the OECD (Organization for Economic Co-operation and Development) during this decade. (1) Policymakers and healthcare organizations are seeking effective methods to bend the cost curve while preserving or even improving the quality of care. (2) Although for the majority of the quality improvement initiatives the primary aim is enhancing quality of care, occasionally substantial cost-savings are estimated. (3-7) For example, discontinuing five low-value general surgery services in the United Kingdom could lead to an annual cost reduction of €150 million. (8)

However, the translation of such theoretical savings of quality improvement initiatives into actual societal cash savings is complex and often not achieved. (9) This is challenging due to various reasons. For example, estimates of cost savings based on reimbursement prices overestimate true savings, because only variable costs, such as costs of disposable equipment and drugs, can be saved in short-term. (10, 11) One study found that these costs only cover 16% of total expenses in hospitals. (12) The majority of expenses, such as salary costs, purchasing costs of reusable medical devices and organizational overhead, are not directly saved when the volume of healthcare services is reduced. Moreover, since claims data do typically consist of cross-subsidies, the actual total costs may be either higher or lower than the official rates. Besides, the relation between external funding structures and internal allocation of resources is blurred. (13)

While improving quality of care may free up hospital capacity through shorter hospital stays and reduction of diagnostic tests and procedures, the capacity may be refilled with new treatments. Due to existing incentives in many healthcare systems, such substitution with other care occurs automatically. (9, 14-16) A way to achieve cash savings is to actively discourage care substitution. This requires an investment of time and resources. (17) Excess capacity should be gradually reduced until it reaches a threshold for downsizing, i.e. capacity reductions must be sufficiently large to scale down one single nursing shift, medical specialist, ward, etc.

Because marginal revenues typically exceed marginal costs by far, in fee-for-service type payment systems, scaling down costs is unlikely to be sufficient to cover for losses in hospital revenues. Under a fixed budget revenues are protected but cost savings that are not passed through to payers may shoulder organizational slack and not be returned to society, for example by reductions in taxes or insurance premiums. Moreover, since healthcare costs naturally increase due to demographic changes, new technologies and other structural drivers, it is difficult to establish the accurate benchmark. Cost savings can generally be interpreted as a lower hospital growth rate rather than actual reductions

in hospital costs. However, it is challenging deciding upon the appropriate benchmark to measure cost savings in terms of expected growth, historical growth or comparator hospitals. (18)

These problems may be solved by a well-designed process flanked by adequate incentives. However, little empirical evidence is available regarding the process to transform quality improvement programs into societal cost savings. (2) Our aim was to contribute to this gap by identifying the barriers and facilitators within the process. We used the implementation of prehabilitation in a university hospital in the Netherlands as a test case. Prehabilitation is a pre-operative multimodal lifestyle improvement program for patients undergoing major surgery. Research has shown that prehabilitation could reduce the number of surgical complications, reoperations and the average length of stay. (19-21) Moreover, a recent systematic review of economic evaluations revealed evidence that prehabilitation can be cost-effective compared to usual care. (22) However, these evaluations lack a comprehensive perspective on the costs and savings. (22)

Methods

Study design and scope

In this study, we conducted semi-structured interviews with relevant stakeholders of prehabilitation in an academic hospital in the Netherlands. Converting freed hospital capacity into societal cost savings is a multi-step process. Our objective was to identify barriers and facilitators associated with these steps. We considered reduced health insurers' costs as the main mechanism to obtain societal savings, given the non-profit structure and public financing of health insurers in the Netherlands (16). In June 2023, the local medical ethics review committee of the Radboud University Medical Center waived the review of this study as the Medical Research involving Human Subjects Act did not apply (file number: 2023-16520). The Consolidated Criteria for Reporting Qualitative Research (COREQ) were followed and the completed checklist can be found as S1 File. (23)

The test case

Prehabilitation is an important and well-known quality improvement initiative in the hospital. It was gradually implemented between 2021 and 2023 for all high-impact surgery care pathways in seven departments. The intervention consisted of an exercise program, dietetic consultation, psychological support, and smoking cessation support. Prehabilitation has shown positive results on the number of surgical complications, reoperations and the average length of stay. (19-21) Its effectiveness is currently investigated in large scale studies. The hospital financed the implementation and

prefinanced the intervention costs. The hospital agreed on a shared-savings agreement with health insurers, anticipating that after about five years after implementation the financial value of the freed capacity would compensate the investment of both health insurers and the hospital.

Setting

In the Netherlands, hospitals compete for contracts with insurers. (24) While there are ten health insurers in 2024, the four dominant insurers collectively hold approximately 90% of the market share, with variations in market shares across regions. (25) The majority of the hospitals are reimbursed through a hospital DRG-like (Diagnosis Related Group) system called DBCs (Diagnose-Behandel-Combinatie, or Diagnosis Treatment Combination). (24) Many insurers institute a global budgetary limit, either as lump-sum global budget or claims cost ceiling. (26) In the concerning hospital, the vast majority of the medical staff and employees are salaried on a fixed working hours contract.

Recruitment and sampling strategy

The stakeholders were recruited via purposive sampling based on experience, current position and department, and affinity with prehabilitation. While using expert sampling, we aimed to include experienced stakeholders from all relevant clinical and facilitating departments, as well as health insurers. We considered hospital managers to be experts, therefore we invited all hospital managers of the involved clinical departments: surgery, intensive care units and operation rooms. Of the facilitating departments (hospital sales, care administration, business administration), we invited employees who were consulted for the internal prehabilitation business case. We invited two persons working for different insurers. Both were involved in the implementation of prehabilitation. After each interview, the participants were asked to suggest stakeholders they deemed relevant for this study. The suggested persons were also invited. All stakeholders were invited per e-mail to participate in a semi-structured interview between the 13th of June 2023 and the 2nd of November 2023. A reminder was sent in case of no response after three to four weeks.

Data collection

The interviews took place between July 4th and November 22nd 2023. All participants provided verbal informed consent prior to the start of the interview, which was also recorded. Fifteen interviews were conducted by two female researchers DK (MD and MSc) and SvD (PhD), four interviews solo by DK, and one by DK and PJ (male, PhD). All interviewers have experience with qualitative research methods and were not previously involved in the prehabilitation program. The participants knew about their backgrounds and were aware of the study design and objectives. There was no prior relationship between the interviewers and the participants, other than that most participants worked for the same hospital as the interviewers.

The topic guide can be found as S2 File. DK preformed an unstructured literature search to identify possible steps in the process of capturing societal savings and potential barriers and facilitators. DK, NS, SvD and PJ discussed the literature, and shared knowledge and experiences. During iterative meetings, Dk, NS, SvD and PJ identified four stages in the process of capturing societal savings: 1. Reducing capacity, 2. Reducing departmental expenses, 3. Reducing hospital expenses, 4. Reducing insurer costs. These stages were extracted from literature and represent a possible pathway towards societal cost savings. (3, 9-11, 13, 27) DK drafted a interview guide based on the topics discussed during the meetings. The interview guide was reviewed by five team members (SvD, NS, TK, GW and PJ) and adapted based on their feedback. The topic guide was pilot tested with two prehabilitation program managers and a few questions were added to the topic guide. The two pilot interviews were also included in the analysis. The topic guide was slightly adapted for each stakeholder to fit the stakeholders' experience and expertise. Additionally, after each interview, the topic guide was evaluated and extended when the interviewees mentioned new perspectives.

The interviews were preferably held during a face-to-face meeting. If that was inconvenient, the interviews were conducted via a video call using Microsoft Teams. Only the interviewers and participants were present during the interviews. Field notes were made during the interviews to direct further questions. Data saturation was defined as the point in coding when no new barriers or facilitators were identified in two subsequent transcripts. No new interviews were conducted after data saturation was reached. No repeat interviews were carried out and the transcripts were not returned for correction to the participants.

Data analysis

The interviews were audio-recorded during face-to-face meetings and video-recorded during video-calls. The recordings were transcribed ad verbatim and the transcripts were analysed in ATLAS.ti. Two authors (DK and SvD) performed a inductive content analysis using the constant comparative method. DK and SvD independently coded the first transcripts. Open coding was used to label barriers and facilitators. If participants mentioned that the presence of an influencing factor hindered the process, it was labelled as a barrier. If the presence would facilitate the process, it was labelled as a facilitator. The barriers and facilitators were categorized into the four stages: reducing capacity, reducing departmental spending, reducing hospital expenses, reducing insurer expenses. During the coding, it came apparent that the first stage consisted of multiple steps. DK and SvD inductively created substages to emphasize these required steps. This was discussed during multiple meetings. Agreement on the coding was reached after five transcripts and the other transcripts were coded by one author (DK) and checked by another (SvD). Differences were resolved in consensus meetings with DK and SvD. The results were discussed during a meetings with NS and PJ.

Results

We interviewed 20 stakeholders, 10 male and 10 female, of which the functions can be found in Table 1. Three invited professionals did not participate: one surgeon did not reply, one surgeon rejected due to lack of affinity with the subject, and one hospital sales manager rejected due to lack of time. Nine interviews were held face-to-face, and 11 interviews via Microsoft Teams. The duration of the interviews ranged from 27 to 62 minutes.

Table 1 | Function of participants and their relation with prehabilition

Function	Number*	Relation with prehabilitation
Medical doctor	6	Three were treating patients after prehabilitation Three were selected due to their second position
Hospital manager	4	All were responsible for the finances of departments that were affected by prehabilitation (surgery, operation rooms and intensive care units)
Program manager	3	Two were active prehabilitation program managers One was a former prehabilitation program manager and active program manager of other quality improvement initiatives
Hospital administrator	3	Two were consulted during the development of business case of prehabilitation, one was the financial advisor of a relevant department
Health insurer	2	Both were involved in the prehabilitation case
Nurse	2	Both nursed hospitalized patients after prehabilitation
Business controller	1	Was consulted during the development of business case of prehabilitation and during the implementation of prehabilitation
Hospital sales manager	1	Was involved in making agreements concerning prehabilitation
Internal strategy consultant	1	Was familiar with prehabilitation, no direct involvement with prehabilition, has experience with other quality improvement initiatives
Hospital board member	1	Was responsible for the financing of prehabilitation and external agreements

**20 respondents were interviewed, some participants have multiple functions, e.g., medical doctor and manager.*

From 20 interviews, we identified 20 barriers and 23 facilitators across the four stages: reducing capacity, reducing department spending, reducing hospital spending, reducing insurer spending. These can be found in Table 2. Each stage of the process was considered a prerequisite for advancing to the subsequent stage, all aimed at achieving societal cost savings by reducing insurer expenses. The first stage, reducing capacity, has three subcategories: creating excess capacity, preventing substitution with other care, and downsizing.

Table 2 | Barriers and facilitators per stage of the process of translating capacity savings into societal cost savings

Stage	Barrier	Facilitator
1. Reducing capacity	*Creating excess capacity*	
	- The perceived freed up capacity may be lower than the calculated capacity reductions	- Combining multiple initiatives allows reaching capacity reduction thresholds
	Preventing substitution with other care	
	- Demand for care exceeds existing supply - Substitution is highly valued - Supplier-induced demand allows substitution with other care - Financial incentives stimulate substitution - Non-financial incentives stimulate substitution	- Active management could prevent substitution - The drive to provide appropriate care could counter supplier-induced demand - Insurance agreements can counter unwarranted financial incentives
	Downsizing	
	- Hospital employees have an aversion towards downsizing - Minimum capacity constraints prevent downsizing - A high threshold must be reached before excess capacity can be scaled down - The hospital board has a restrained approach towards downsizing - Hospital employees have a preference to use excess capacity instead of downsizing	- Optimizing collaboration within the hospital can reduce the minimum capacity - Securing the department's income counters the fear of losing revenue - A strategy could facilitate downsizing - Labor market issues may lead to downsizing

2. Reducing departmental expenses	- Providing less care does not automatically lower departmental expenses - A high threshold most be reached before working hours can be reduced - Reducing expenses requires time - Insurance agreements do not directly impact the department's decision making	- The hospital board commits to achieving cost savings - A top-down cost-cutting strategy could reduce department budgets - Flexible staffing allows reductions in working hours - High turnover of personnel allows reductions in working hours - Trust that any savings will be well-utilized can motivate employees to reduce expenses - The department benefits from realizing savings, i.e., as part of shared-savings agreements
3. Reducing hospital expenses	- Reduced departmental expenses do not automatically reduce the hospital expenses - Hospitals have a reluctance to effectuate savings - The diversity of insurance agreements may misalign cost-cutting incentives	- Hospitals have authority to enforce budgetary constraints - A long-term cost-cutting strategy is needed for reducing hospital expenses - Securing the hospital's income counters the fear of losing revenue - Aligned agreements with all involved insurers could prevent free-rider behavior
4. Reducing insurer expenses	- DBC rates do not automatically decline when an initiative is effective - Agreements on the total hospital budget hinder transfers of cost savings	- The hospital's belief that savings need to be returned to society via insurers - There is a common responsibility to maintain affordable healthcare - Some agreements could to transfer savings from the hospital to insurer - Shared savings agreements could motivate hospitals to reduce costs - Scaling initiatives to other hospitals may increase societal cost savings

Stage 1 | Reducing Capacity

Creating excess capacity

The starting assumption is that a decrease in length of stay reduces the required hospital capacity. Some interviewees agreed with this, while others have questioned whether the nurses' workload decreases proportionally. In particular in the ICU, the first admission day has a higher workload than the following days. Reducing the length of stay may therefore have less impact on the capacity than preventing the admission. In addition, tasks like training patients to self-care and lifestyle adjustments, still needs to be performed before the hospital discharge. Consequently, the perceived excess capacity may be lower than

presumed. On the other hand, excess capacity can be enlarged by implementing multiple initiatives that reduce length of stay.

Preventing Substitution with Other Care

To reduce the created excess capacity, it is essential that any reductions in care are not filled with other care. However, most participants expect that the excess capacity will be used for other patients. It is frequently mentioned that the demand of care currently exceeds the available supply, and it is expected that the demand will further increase in the future. The interviewees emphasized that some specialized healthcare professionals are scarce and should therefore be deployed most efficiently. They considered the opportunity to provide more care with the same resources highly valuable.

> *'You have a whole operating room complex with all kinds of people ready to do various things. It is wasteful, also a societal waste, not to deploy those people effectively. So, you should let them operate as efficiently as possible. As long as there is demand, as long as there are waiting lists. But that should not be the basis of treatment decisions. It is more like: if people are already on the waiting list, then you want to help as many as possible.'*
>
> **Participant 13, hospital sales manager**

Interviewees expect additional supplier-induced demand as a consequence of available excess capacity. For example, indications for treatment may expand when capacity becomes available. Additionally, the presence of excess capacity reduces the pressure to discharge patients, which may lead to prolonged length of stay of other admitted patients. Participants perceive financial and non-financial incentives to provide care. For example, specialists need to reach target volumes to preserve their competence. On the other hand, providing less care is discouraged, because one may lose opportunities for research, their status, their patients, and departments may need to downsize their capacity. Furthermore, not using full capacity may conflict with other process indicators on which the departments are assessed, such as warm-bed time.

> *'If [the board] would say: "The ICU is now five million short, and we must reduce staff or whatever", that would be the most foolish thing there is. And then I am going to admit patients to the ICU, who do not belong there, for 3,500 euros. I can earn my money if I want to. I can earn it easily. What all ICUs are doing now is admitting their Medium Care patients to the ICU and billing them as ICU beds. That is what is happening in the Netherlands now.'*
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> **Participant 4, medical doctor**

The stakeholders also mentioned facilitators. Some participants deemed it possible to prevent substitution with active management and a top-down approach. Furthermore,

the drive to provide appropriate care and prevent inappropriate care could counter supplier-induced demand. For example, patients do not always benefit from additional care, especially in the case of ICU treatment. Moreover, the demand for intensive care is decreasing, further reducing substitution possibilities. Lastly, increasing care provision may not be profitable for the hospital if the insurer instated a budgetary cap.

Downsizing hospital capacity

To render cost savings, the hospital should minimize its expenses. A viable approach involves downsizing the departmental excess capacity. Participants have expressed negative associations with downsizing in general, and they offered barriers specifically for downsizing excess capacity.

The interviewees expressed an aversion towards downsizing in general. Downsizing is a sensitive matter, and the culture within an organisation and the behaviour of individuals can hinder the process. There are negative perceptions of downsizing, such as it being the start of a slippery slope. Participants stated that once you shrink, you will not be able to retrieve the capacity in the future. Downsizing is also associated with the risk of losing expertise, status, the market position of the departments and the hospital. Moreover, participants fear losing flexibility in providing care, and consequently foresee increasing problems with the planning and coordination.

> *'I would absolutely not be in favor of reducing eighteen beds by two or four. Soon, you will have nothing left, and I see it happening now at [department]. In the past, I had ten, twelve beds, and we could provide excellent service to the region. I have now been reduced to six. It is a disaster; it is a disaster to schedule your surgeries, and you have no flexibility anymore. But you are also nothing. You become almost a joke in the region. We need to create a [specialty] network now and we are bringing a six-bed facility. Honestly, I am ashamed.'*
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> **Participant 3, hospital manager**

Participants also mentioned barriers for reducing the excess capacity. First, the presence of excess capacity does not automatically mean that it can be reduced. A reduction in capacity typically requires reaching a certain threshold. Moreover, the downsizing potential is limited by factors such as the requirement of minimal staffing and the need for resilience in case of outbreaks or disasters. Moreover, various participants stated that the departments are already at a minimal capacity. In their perception, they cannot shrink any further, for example because of the need to meet volume norms and retain income. Not meeting these will have negative consequences for departments, such as a loss of revenue. Additionally, tertiary medical centres have certain responsibilities, such as unlimited accessibility for patients in need of tertiary care. If they fail, they risk losing their credibility. Moreover, some participants believe that excess capacity should not be

downsized, but the available time should be invested in quality enhancing tasks, such as innovating and teaching. And last, according to participants, the hospital board and the government currently do not make the necessary decisions in reallocating resources and do not steer towards downsizing.

Downsizing is facilitated by improved collaboration within the organization and within the region. This could for example reduce the minimal required staffing. Additionally, a top-down downsizing strategy, endorsed by healthcare professionals, could facilitate the process. This could involve for example establishing explicit agreements and incorporating follow-up mechanisms and data. Furthermore, there is an increasing shortage of nurses and operation room employees. If resigned staff cannot be replaced due to these shortages, downsizing is inevitable. Last, it is suggested that lump-sum payment agreements could overcome the barrier of risking loss of revenue.

Stage 2 | Reducing Departmental Expenses

Some participants stated that providing less care does not naturally lead to lower departmental expenditures. The costs saved directly are the variable costs, i.e., material costs. Some interviewees estimated that such costs are only a small percentage of the total departmental costs. The semi-variable costs, e.g., personnel costs, can eventually be reduced, but require reaching a substantial reduction in care. The participants mentioned that this may be difficult due to the small patient numbers in their hospital. In addition, it takes time before expenses can be lowered. The interviewees expect that healthcare professionals will substitute freed-up time with other valuable tasks before the threshold to permanently close a single bed is reached. Such substitution could reduce the perceived quantity of excess capacity. Furthermore, the interviewees mentioned the department's fixed costs, which cannot be reduced easily. As previously mentioned, departments require minimal staffing, for example to cover all shifts and to ensure quality and safety during the shifts. A participant estimated that the fixed costs alone already exceed 50% of total costs. In addition, clinical departments finance supporting departments, such as the operating rooms and the radiology department. Departments can reduce the number of required services, but this does not substantially reduce the expenses of the supporting departments. To avoid a negative balance, either the fees per services must increase or the free capacity must be used for providing other care. Some participants do not expect that departments will voluntarily reduce expenses. Therefore, a top-down approach may be necessary.

> *'If you really want to cut costs, then, of course, you have to do fewer things on a large volume. That is always the pain point in an academic medical center [...]. And for us, because we have small volumes, does it mean I have to remove a nurse's arm or a leg? Well, that often just does not work.'*
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> **Participant 12, hospital board member**

A few participants also pointed out that healthcare is a complex system, and that a change in one place can also have consequences somewhere else. For example, reducing spending on staffing can result in less flexibility in care delivery, and it can subsequently induce workload and extra costs for the coordination of care. Lastly, departments and healthcare professionals lack awareness about existing agreements with insurers, limiting the impact of these agreements.

> *'What I often see is that various initiatives are penny-wise and pound-foolish. So, we save fifteen cents with a specific procurement action, but then we do not realize that suddenly we have additional costs because we have added another provider with whom contracts are made, so someone else incurs those extra costs. [...] But also, for example, those five nurses that had been cut back [...], you can present that as a significant saving. I am afraid that it has also resulted in us not achieving the revenues because we simply could not accommodate the patients.'*
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> **Participant 7, hospital administrator**

There are also facilitators to lower departmental expenditures. The hospital board commits to achieve cost-savings with the implementation of prehabilitation, making the deployment of a cost-cutting strategy more likely. Moreover, reducing costs can be rewarded by shared-savings agreements that return part of the savings to the department. To stimulate capacity reductions, excess capacity in the ward and in the operating rooms can be adopted by other specialties. For example, IC nurses can work on the emergency department or the coronary care unit (CCU). In addition, workforce reductions could be achieved by phasing out through natural outflow due to a high turnover of nurses, rather than resorting to terminations. Furthermore, there is currently a shortage of nurses, causing understaffing. Apart from the potential negative consequences, this could also reduce departmental expenses. Another driver to reduce departmental spending is the trust that savings are purposefully spent. A participant stated that the value for money may increase when financial resources are reallocated towards other sectors, for example elderly care. Excessive spending on a few patients could be perceived as incompatible with budgetary constraints elsewhere. If the stakeholders trust that savings would be spent wisely, it could enhance their motivation to reduce costs.

Stage 3 | Reducing Hospital Expenses

Reducing departmental expenses does not necessarily reduce the total hospital costs. For example, when excess capacity is absorbed by other departments, e.g., when a nurse works in a different department, the total hospital spending remains unchanged. Participants stated that a multi-year plan is needed to effectuate the cost-savings. Another participant mentioned that the hospital board often does not specifically enforce case-based cost savings, while that is perceived as necessary.

'We chose to implement prehabilitation. That simply means that you have excess capacity in other areas. So, in those areas, you also need to achieve your savings. And if not, if you are not willing to do that, then you also need to have the courage to say: we do not want this and we stop offering prehabilitation. That is also an option'

Participant 9, strategy consultant

Dutch hospitals negotiate with multiple health insurers, resulting in various budgetary agreements. A participant mentioned that misalignment of incentives for downsizing and cost-cutting may consequently occur. For example, one agreement may consist of a lump-sum payment, securing the hospital's income while reducing excess capacity, while a cost ceiling agreement with a different insurer could reduce hospital income when excess capacity is reduced. In addition, participants deemed transferring departmental savings via the hospital to the insurers as complex. First, there is a lack of insight in how costs are structured, hindering monitoring actual cost-savings. Besides, some interviewees stated that there is a misalignment between internal budgeting and reimbursement, further complicating the transfer.

'Because from a specialization perspective, you focus on your production plan, and as a hospital, you focus on the required Full-Time Equivalents (FTEs), but there is an indirect link in that. It is not a one-to-one relationship. Additionally, you also deal with a whole cost price system. [...] So the question is: Are the savings of those few FTEs sufficiently reflected in the system that lies underneath it? Often, it is just rounded off.'

Participant 15, hospital administrator

Mentioned facilitators include a secured hospital income and aligned agreements with the involved insurers. This would enable the hospital to reduce expenses without the fear of incurring a loss. Additionally, the stakeholders emphasized the role of the hospital board. The board has the authority to enforce departmental budgetary constraints to reduce the hospital expenditure. In this scenario, the individual departments retain the authority to determine cost-cutting measures, which may not necessarily involve reducing excess capacity.

Stage 4 | Reducing Insurer Expenditures

Several participants stated that savings should be effectuated by the health insurers through lower premiums. In addition, a stakeholder deemed achieving hospital savings a prerequisite to transfer any savings to the insurers. Reduction of insurers' costs largely depends on the agreements between the hospital and the health insurers. Participants named reducing the DBC (the Dutch equivalent of Diagnosis Related Groups (DRGs)) rates or reducing the number of reimbursed DBCs as a way to transfer savings to society. However, they also stated that the DBC rates are not aligned with actual hospital costs

and health insurers lack insight in the hospital expenditures, therefore DBC rates do not automatically decline when an initiative is effective. Therefore, cost savings may depend on specific agreements with hospitals. These are, however, often lacking because the savings potential of a single quality improvement initiative may face too many transaction costs to be included in the negotiation process. Another participant stated that reducing the DBC rates or the number of DBCs does not automatically reduce insurer costs. Agreements are made on the level of both the DBC rate and the total hospital budget. Budgetary caps could hinder translating hospital savings to the insurer, because insurers may not have to reimburse the full costs or not reimburse at all when a cap is reached. Therefore, savings on the level of DBCs are not automatically transferred to the payers. Also, in case of lump sum agreements, lowering of rates or the number of DBCs does not influence the reimbursed amount.

Some participants also mentioned some agreements between hospitals and insurers that facilitate the transfer of savings. For example, an open-ended budget automatically reduces hospital expenditures in case of volume reductions or reductions in the DBC rate. Also shared-savings agreements could transfer part of the hospital savings, while additionally motivate stakeholders to reduce costs. However, within a shared savings model, participants wonder how much will be left when the savings are shared with all stakeholders. Moreover, interviewees of the hospital and an insurer mentioned free-rider behavior by other insurers. Therefore, aligned agreements of insurers is mentioned as a prerequisite. Another proposed solution is a multiyear agreement, because it can provide the hospital time to reduce their cost structure. However, participants mentioned that insurers are reluctant on such agreements, for example because of the uncertainties of price fluctuations. Last, innovation-specific agreements are also mentioned to transfer hospital savings to insurers.

> *'I personally find the shared savings model to be a good principle because, ultimately, they are societal costs. Or it has been contributed by society, so it should flow back in that direction. But, of course, it is quite elegant if the hospital benefits from it as well. I mean, that is just where it starts. Every change process is simply individuals asking themselves, 'What's in it for me?''*
>
> **Participant 9, strategy consultant**

Another facilitator is the common goal of stakeholders to keep healthcare affordable and innovative. It is perceived to be a societal responsibility to contain the healthcare spending. In addition, investments of insurers may lead to external pressure for hospitals to effectuate savings. And last, scaling the innovation to more hospitals is also seen as a way to enhance societal savings.

Discussion

Twenty barriers and 23 facilitators were identified in four stages to capture societal cost savings: reducing capacity, department expenses, hospital expenses and insurer expenses. In general, there is an aversion towards downsizing. Due to lack of incentives to reduce costs or top-down policies for downsizing, all participants expect that any excess capacity will be used to provide other care. Nevertheless, such substitution is perceived as valuable and a societal gain. Other mentioned barriers are fear of losing resilience, flexibility, status and revenue. Moreover, agreements with a budgetary cap and lump sum agreements may hinder the translation of the cost savings to the insurers. And last, misalignment of agreements between hospitals and health insurers creates financial barriers for downsizing and cost-cutting. Identified facilitators included shared savings agreements, a downsizing strategy, labor shortages, and a shared responsibility to secure affordable healthcare, among others.

The identified barriers indicate that monetizing savings for society does not occur automatically when an initiative is effective. Stakeholders expect that saved capacity will be used to provide other care. This aligns with existing literature describing supplier-induced demand in healthcare. (14, 15, 28, 29) Reducing length of stay only saves a small percentage of the expenditure directly, because personnel costs and fixed costs remain unaffected in the short term. (10) A study illustrated that a reduction of 12 beds, typical for a ward, enables personnel reorganization and substantially reduce semi-fixed costs. (27) However, such large-scale downsizing requires a large volume of excess capacity. This may require combining multiple quality improvement initiatives as part of a hospital-wide strategy. (9) Moreover, stakeholders mentioned the need for a strategy or active approach to achieve reductions on all four stages. For example, a strategy is also deemed necessary to subsequently transfer the hospital savings to insurers due to existing misaligned agreements and incompatible budgeting systems. (13, 30)

Another identified facilitator is to secure the departments and hospital's income. However, securing either the departments or hospital's income and achieving societal costs savings seem incompatible. Nevertheless, this may be possible when savings are interpreted as a reduction in hospital spending growth rate compared to a historical benchmark. Shared-savings agreements between parties may accommodate this, although past experiments yield mixed results. (9, 31, 32)

Downsizing is deemed controversial by participants. The stakeholders emphasize that the demand for care currently exceeds the supply and it is expected to further increase. (33) Substituting excess capacity with other necessary care may partly compensate for increasing demand. Therefore, providing more care with approximately the same

resources could also be considered as a societal gain of quality improvement initiatives. In addition, it may not be necessary to aim for downsizing, since increasing shortages of medical professionals may cause natural downsizing in the future. (33, 34) In this case, effective prehabilitation could offer the opportunity to increase efficiency, and thereby retaining the accessibility of care.

Healthcare decision-making may be improved by broadening the scope of the value of quality improvement initiatives. (35) The value of quality improvement initiatives may cover a broader range than cash savings and saved hospital capacity. (36) For example, prehabilitation may additionally reduce home care and could lead to earlier return to work. (20) Furthermore, the identified barriers suggest that monetizing capacity savings is difficult and that the saved amount may be lower than expected. This study suggests that the value of reducing length of stay is to be able to provide care for other patients. Therefore, only expressing the value in terms of costs saved lacks important nuances. By also focusing on the effects on the increased accessibility, healthcare decision making may be improved. Future research should focus on the value of care substitution and the impact of care substitution on the accessibility.

Strengths and limitations

To our knowledge, this is the first study that identifies barriers and facilitators through the entire process from an effective quality improvement initiative towards reducing societal costs. Additionally, a broad range of relevant stakeholders participated in this study. Some limitations apply. First, even though studies on prehabilitation show promising results, the effectiveness of our test case was yet unknown during the interview period. Consequently, certain questions were framed hypothetical, e.g., 'what if ...'. To substantiate expectations, participants were additionally asked for examples and experiences with other quality improvement initiatives. Secondly, with the exception of two insurer employees, all stakeholders were affiliated with the same hospital. Therefore, some barriers and facilitators may be context specific. Last, this article solely focuses on achieving societal cost savings through the described four stages and does not address the conversion of reduced health insurers' costs in societal savings in the form of lower premiums or governmental expenses. Nor does this article address alternative ways quality improvement initiatives could generate societal savings.

Conclusion

This study describes barriers and facilitators in the process of capturing societal cost savings across four stages: 1) reducing capacity, 2) reducing department expenses, 3) reducing hospital expenses, and 4) reducing insurer expenses. An encompassing

hospital strategy targeting these four stages is recommended, because societal cost savings do not occur automatically when hospital capacity is saved. Shared-savings agreements could facilitate the transfer of hospital cost savings to the health insurers. However, many barriers were encountered. Predominantly, stakeholders expect that any saved capacity will be used for other care due to increasing demand. However, such substitution with other care is also perceived as a societal gain. Framing financial gains of quality improvement initiatives in terms of addressing increasing demand may therefore be more accurate. This would require additional research into the value of care substitution.

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Supporting information

S1 File. Completed checklist of the Consolidated Criteria for Reporting Qualitative Research (COREQ).

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	7
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	7
Occupation	3	What was their occupation at the time of the study?	7
Gender	4	Was the researcher male or female?	7
Experience and training	5	What experience or training did the researcher have?	7
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	7
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	7
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	7
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	8

Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	6
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	6
Sample size	12	How many participants were in the study?	9
Non-participation	13	How many people refused to participate or dropped out? Reasons?	9
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	9
Presence of nonparticipants	15	Was anyone else present besides the participants and researchers?	8
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	9
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	7
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	8
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	8
Field notes	20	Were field notes made during and/or after the inter view or focus group?	8
Duration	21	What was the duration of the inter views or focus group?	9
Data saturation	22	Was data saturation discussed?	8
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?	8
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	8
Description of the coding tree	25	Did authors provide a description of the coding tree?	10
Derivation of themes	26	Were themes identified in advance or derived from the data?	7
Software	27	What software, if applicable, was used to manage the data?	8
Participant checking	28	Did participants provide feedback on the findings?	8

Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	13
Data and findings consistent	30	Was there consistency between the data presented and the findings?	11
Clarity of major themes	31	Were major themes clearly presented in the findings?	11
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	11

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

S2 File. Topic guide.

Introduction	– What is your position? – What are your thoughts on the prehabilitation program? – Did you observe any changes or effects of the prehabilitation program?
Excess capacity	The aim of prehabilitation is to reduce complication and consequently the length of stay. If this goal is achieved, it would lead to savings in hospital capacity. – What is the impact of reducing the length of stay on your workload? – What do you expect to happen with the newly available capacity? Can you provide an example where this happened? – Under what conditions can a bed remain unoccupied and not be refilled? - What can facilitate this? - What may preventing this? – Are there incentives to provide more care? - At the hospital level - At the department level - At the level of the healthcare professionals?
Downsizing	– Would you consider downsizing of in case substantial capacity savings? - What are reasons to do so? - What are reasons not to do so? - How would you feel if it happens? – Has labor shortages influenced the department's capacity? - What do you expect for the near future?
Reducing department expenses	– Could your department reduce expenses if prehabilitation is effective? - What can facilitate this? - What may preventing this? - Can you provide an example where this happened? – When would you be able to scale down staff? - Why would you do it? Why wouldn't you do it? - How would you feel if it happens? – What is the impact on the department's revenue when patients are discharged earlier? – What is the impact on the department's revenue when more new patients are admitted? – How do the department's revenues relate tot he hospital's revenues?
Reducing hospital expenses	– How can providing less care to a patients result in cost savings for the hospital? – Could the hospital reduce expenses if prehabilitation is effective? - What can facilitate this? - What may preventing this? - Can you provide an example where this happened?

Reducing societal expenses	– How can hospital cost savings be translated into savings for society? – Under what circumstances would the hospital be willing to pass on cost-savings to health insurers? – How can hospital cost savings be transfered to insurers - What can facilitate this? - What may preventing this? – Are initiatives like prehabilitation considered in agreement negotiations?
Conclusion	– Is there anything you like to add?

5

Development of the SPREAD framework to support the scaling of de-implementation strategies: a mixed-methods study

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Abstract

Objective

We aimed to increase the understanding of the scaling of de-implementation strategies by identifying the determinants of the process and developing a determinant framework.

Design and methods

This study has a mixed-methods design. First, we performed an integrative review to build a literature-based framework describing the determinants of the scaling of healthcare innovations and interventions. PubMed and EMBASE were searched for relevant studies from 1995 to December 2020. We systematically extracted the determinants of the scaling of interventions and developed a literature-based framework. Subsequently, this framework was discussed in four focus groups with national and international de-implementation experts. The literature-based framework was complemented by the findings of the focus group meetings and adapted for the scaling of de-implementation strategies.

Results

The literature search resulted in 42 articles that discussed the determinants of the scaling of innovations and interventions. No articles described determinants specifically for de-implementation strategies. During the focus groups, all participants agreed on the relevance of the extracted determinants for the scaling of de-implementation strategies. The experts emphasised that while the determinants are relevant for various countries, the implications differ due to different contexts, cultures and histories. The analyses of the focus groups resulted in additional topics and determinants, namely, medical training, professional networks, interests of stakeholders, clinical guidelines and patients' perspectives. The results of the focus group meetings were combined with the literature framework, which together formed the supporting the scaling of de-implementation strategies (SPREAD) framework. The SPREAD framework includes determinants from four domains: (1) scaling plan, (2) external context, (3) de-implementation strategy and (4) adopters.

Conclusions

The SPREAD framework describes the determinants of the scaling of de-implementation strategies. These determinants are potential targets for various parties to facilitate the scaling of de-implementation strategies. Future research should validate these determinants of the scaling of de-implementation strategies.

Introduction

Low-value care (LVC) is either care that is not beneficial for patients or care for which the value does not offset the risk or cost given the available alternatives. (1) LVC causes preventable adverse events for patients and wastes limited resources. (2-4) It has been estimated that 10-25% of healthcare spending in the United States is related to LVC. (5, 6) Prevalence estimations of inappropriate diagnostic testing range from 0.09% to 97.5%, indicating that the prevalence, along with the costs, highly depends on the type of care. (7) Nevertheless, LVC is a pressing matter in healthcare systems and limits the capacity to provide high-value care.

LVC can be reduced through targeted strategies, also called de-implementation strategies. (8, 9) For example, the number of opioid prescriptions have been reduced by providing comparative feedback with persuading messaging and action planning, and the use of an electronic patient education tool has reduced the number of inappropriate upper gastrointestinal endoscopies by 61%. (10, 11) In another study, the number of laboratory tests were reduced by 11% in four hospitals through a combination of strategies, namely, appointing role models, data feedback, education for healthcare professionals, intensified supervision of residents and changes in the order system, among others. (12) There are many more effective de-implementation strategies; a recent overview reported that 196 out of 319 strategies (61%) significantly reduced the number of inappropriate drug prescriptions, while another review showed that 11 out of 16 strategies (69%) significantly reduced the number of low-value medical tests. (13, 14)

To substantially increase the impact of such de-implementation strategies, the effective strategies should be scaled to other organizations and healthcare providers. (15) However, this rarely occurs spontaneously, and little is known about this process. (16, 17) This makes the scaling of these strategies challenging.

A commonly used theory is Rogers' theory of diffusion of innovations, which is also applied in healthcare settings. (18-21) Any idea, practice or object that is perceived as new can be considered an innovation. (18) The theory describes the spread of innovations from innovators through early adopters, the early majority, the late majority and laggards. Factors affecting the diffusion of innovations are categorized into three main domains: perceptions of innovation, characteristics of potential adopters, and contextual factors. (18)

It is unknown whether the determinants of scaling innovations also apply to the scaling of de-implementation strategies. The de-implementation of LVC can be considered innovative, as it aims to bring about change. However, de-implementation strategies are not equivalent to innovations. An innovation acts on a different level than a de-

implementation strategy. A healthcare innovation is an (evidence-based) intervention or care practice, while an implementation strategy is the method that enhances the adoption and implementation of the intervention. (22) The strategy aims to change the behavior of healthcare professionals and/or patients. Therefore, on one hand, scaling a de-implementation strategy is seen as spreading a method that aims to reduce LVC to other organizations and healthcare professionals. On the other hand, scaling a healthcare innovation is seen as spreading a care practice, such as an additional diagnostic test or new treatment option.

In addition, healthcare innovations provide new possibilities, while de-implementation aims to discontinue the provision of a care practice. (1, 18, 23) Consequently, de-implementation is complicated by psychological biases. People unconsciously tend to favor information that confirms their beliefs. (24) This confirmation bias applies especially to de-implementation, since the process requires clinicians to abandon clinical practices they previously thought to be evidence-based. (24, 25) The abandonment of care, even care with no additional value for the patient, could also be experienced as a loss. Therefore, loss aversion, i.e., the tendency to avoid loss, affects de-implementation as well. (8) In addition to these psychological aspects, there are also different barriers to de-implementation. (26) For example, providing LVC can be lucrative for healthcare providers and organizations due to current financial models, such as fee-for-service payments. (27, 28) These differences between implementation and de-implementation result in a different focus regarding strategies. (29, 30)

To enhance the de-implementation of LVC, several frameworks and models have been published. (17, 31-34) The main focus of these frameworks is either the process of de-implementation or the de-implementation strategy itself. (31, 35, 36) However, scaling a de-implementation strategy from one organization to another differs from the de-implementation process in one particular setting. In de-implementation, healthcare professionals identify LVC practices and target those they think are of importance. In scaling an effective strategy, the target is already fixed. Therefore, first, other individuals need to be convinced of the importance of targeting a particular LVC. In addition, they need to be convinced that the de-implementation strategy will also be effective in their organization and that it is worth investing valuable time in doing so. (18)

The literature on the scaling of de-implementation strategies is very limited. One framework describes this process as the last phase in de-implementation, yet it remains unclear which factors influence the scaling of de-implementation strategies and how these factors can be targeted. (17) However, there is substantial experience available in regard to scaling healthcare innovations. Therefore, we aim to use this knowledge to develop a determinant framework for the scaling of de-implementation strategies. (37)

Method

Study design

This study has a mixed-methods design. We performed an integrative review (38) because this method allowed us to systematically extract determinants from the literature. We defined determinants as influencing factors for scaling, including both barriers and facilitators. (37) First, we searched the literature for determinants of the scaling of de-implementation strategies. As these were not found, we also searched for the determinants of the scaling of healthcare innovations and interventions. We used the determinants of the scaling of healthcare innovations and interventions to build a literature-based framework. Subsequently, this framework was discussed in focus groups with de-implementation experts. The experts reviewed and adapted the framework for de-implementation strategies. This study was conducted in accordance with the applicable legislation according to the Research Ethics Committee of Radboud University Medical Centre (file number: 2021-7519).

LITERATURE-BASED FRAMEWORK

Literature search

We developed a search strategy for PubMed and EMBASE in collaboration with a medical information specialist (AT). The full strategy is described in Additional file 1. The search was conducted in PubMed and EMBASE for relevant literature published between January 1995 and December 2020.

Data screening and extraction

After duplicate articles were removed, two authors (among RBK, DVK or DK) independently screened the titles and abstracts of the remaining articles for relevance. Articles on the scaling of innovations or interventions in healthcare in OECD member countries were included. We excluded conference abstracts, commentaries, articles describing quality improvement in a specific organization, articles that were not available in English and articles that were published before 1995.

The full text of the remaining articles was screened for eligibility by one author (DVK or DK). After this screening, we noticed that determinants were rarely studied empirically. Therefore, we searched for determinants in all parts of the included articles, including the introduction and discussion. Relevant text passages were selected for further analysis if they contained information about factors or processes that influence scale up. To reach consensus about relevant passages, three authors (RBK, DVK and DK) independently highlighted the text passages that they considered relevant in the same five articles. Differences were discussed, and consensus was reached among the authors.

Subsequently, one author (DVK or DK) extracted the relevant fragments from the remaining included articles.

Data analysis

Qualitative analysis was performed in ATLAS.ti. One author (DK) performed conceptual labeling inductively by coding the determinants of the scaling process. A codebook was developed and continuously adapted during coding. Determinants were not coded if the definition was not clear or the association with the scaling process was not stated or demonstrated. All coded determinants were subsequently checked by another author (RBK or SVD). In a group meeting, three authors (DK, RBK and SVD) identified domains and subdomains, which were iteratively evaluated in two group meetings with all authors (DK, RBK, SVD, PPJ, GPW). None of the articles mentioned determinants of the scaling of de-implementation strategies; consequently, the literature-based framework solely discussed the determinants of the scaling of innovations and interventions.

FOCUS GROUPS

We aimed to convert our literature-based framework into a determinant framework for the scaling of de-implementation strategies. Therefore, we organized online focus groups with de-implementation experts who reviewed and complemented our framework. The completed Consolidated Criteria for Reporting Qualitative Research (COREQ) can be found in Additional file 2.

Participants and study procedure

Participants were purposively sampled based on their expertise in the de-implementation of LVC, their interest in the scaling of de-implementation strategies, and their country of residence. Expertise was defined as having past experience in advisory capacities concerning the de-implementation of LVC or direct involvement in de-implementation projects. Eighteen participants were invited by email to take part in a digital focus group, of which sixteen accepted the invitation. Two experts rejected the invitation, but both suggested another expert with a similar background who was willing to participate. In preparation for the focus group, the participants were asked to review the literature-based framework, answer questions about the relevance of the current determinants of de-implementation strategies, and add any potentially missing determinants. The preparation documents can be found in Additional file 3. During the focus groups, the experts discussed the relevance of the identified domains and subdomains of de-implementation strategies and whether the literature-based framework lacked determinants of the scaling of de-implementation strategies. The topic guide can be found in Additional file 4. Data saturation was reached after four focus groups. The focus groups were conducted by DK and either RBK or SVD.

Data analysis

The audio recordings were transcribed and analyzed in Atlas.ti. The codebook constructed for the literature-based framework was used as the basis for the coding. The initial coding was performed by DK and checked by either RBK or SVD. Differences were discussed in a consensus meeting with three authors (DK, RBK, SVD), who also discussed the adaptation of the previously identified domains and subdomains. The new domains and subdomains were evaluated in group meetings with all authors (DK, RBK, SVD, PPJ, GPW) until consensus was reached.

Patient and public involvement

There was no direct patient or public involvement in this study.

Results

The literature search identified a total of 2903 articles. After duplicate removal, the titles and abstracts of 1898 articles were screened. We selected 131 articles for full-text screening, of which 86 articles met our eligibility criteria. After a thorough screening of the full texts, text passages about scaling were found in 62 articles. Determinants could be identified in the passages extracted from 42 of these articles. This process is outlined in a flow diagram in (Figure 1). None of the articles discussed determinants of the scaling of de-implementation strategies. The determinants were categorized into four domains: scaling plan, external context, intervention and adopters. The literature-based framework is shown in Additional file 3.

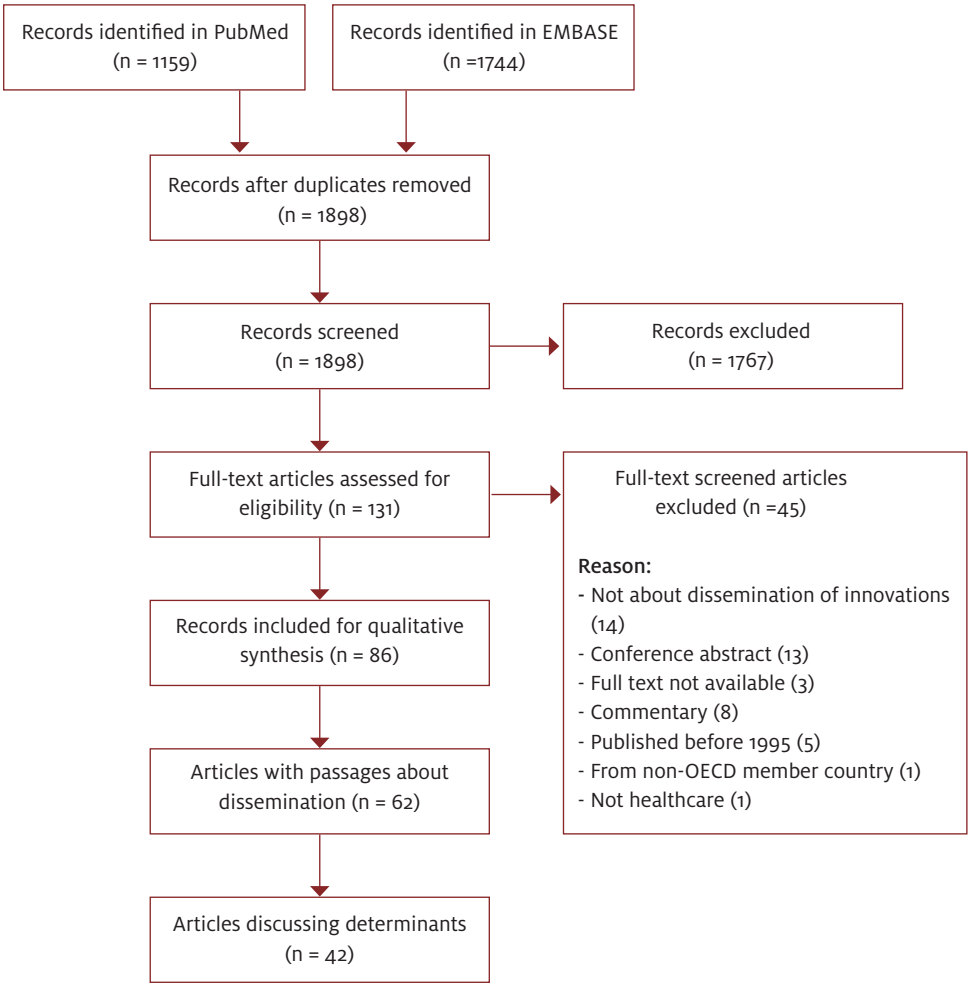

Figure 1 | Flow diagram

Study characteristics

A description of the articles that discussed determinants of the scaling of innovations is provided in Additional file 5. Twenty-seven studies collected empirical data. These studies were conducted in the United Kingdom, the United States, Canada, Australia, Israel or the Netherlands. Furthermore, determinants were found in nine perspectives and six literature reviews. The contribution of each article to the domains and subdomains is shown in Table 1.

Table 1 | Contribution to the subdomains of the literature-based framework per article

Author	Strategy			External context		Innovation		Adopters	
	Accountability	Raising awareness	Resources	Incentives for use	General needs and interest	Relative advantage	Feasibility	Adaptability	Project management
Barber, 2019 (39)	x	x	X				x	x	x
Barnett, 2011 (40)	x			X	x	x		x	x
Ben Chariff, 2020 (41)							x		
Benson, 2019 (42)						x	x		
Berwick, 2003 (43)						x	x	x	x
Carpenter, 2018 (44)	x								
Côté-Boileau, 2019 (45)	x		X			x	x	x	x
Crow, 2006 (46)								x	x
Dearing, 2018 (19)	x				x		x		x
Dearing, 2010 (47)		x					x		
Dengler, 2020 (48)		x			x		x	x	x
Fagan, 2019 (49)	x				x			x	x
Gardner, 2010 (50)	x						x	x	x
Greenhalgh, 2004 (51)	x					x	x		
Greilich, 2018 (52)	x								x
Hader, 2007 (53)					x	x		x	x
Harper, 2020 (54)	x						x		
Hayes, 2018 (55)						x	x	x	x
Hendy, 2013 (56)							x		

Jippes, 2010 (57)		x						x	
Jones, 2020 (58)	x		X			x	x	x	
Kelley, 2020 (59)	x	x	X	X	x	x		x	
Lee, 2020 (60)	x		X		x		x		
Leeman, 2020 (61)	x				x	x	x	x	x
Lorusso, 2020 (62)	x							x	x
Luz, 2020 (63)		x						x	x
Marshall, 2020 (64)				X				x	
Masso, 2016 (65)						x	x		
McGinty, 2020 (66)				X					
McKinlay, 2012 (67)				X	x				
Milat, 2015 (68)		x				x		x	x
Milat, 2012 (69)	x	x			x		x	x	x
Moroz, 2020 (70)	x						x	x	
Nguyen, 2019 (71)								x	x
Ono, 2018 (72)	x							x	
Ovretveit, 2017 (73)	x			X				x	x
Rhodes, 2020 (74)	x					x		x	x
Schrijvers, 2003 (75)	x	X					x	x	
Scott, 2008 (76)						x	x		
Sounderaja, 2020 (77)		X							
Suther, 2004 (78)						x	x		
Willis, 2016 (79)	x								x

Focus groups

Seventeen experts participated in digital focus groups held in April and May 2021. The characteristics of the participants are shown in table 2. All experts agreed that the determinants in the literature-based framework were also relevant for the scaling of de-implementation strategies. They provided nuances and examples of the determinants and added new topics to the framework, such as patients' perspectives, consequences of medical training and the importance of an alternative to the targeted LVC. Furthermore, they pointed out differences between innovations and de-implementation strategies and their consequences for scaling. The experts in the international focus group emphasized that while the determinants apply to various countries, the content and implications differ due to different contexts, cultures and histories. The results of the focus groups are summarized in Additional file 6.

Table 2 | Characteristics of the participating experts

Participant	Focus group	Country of residence	Profession				Organization					
			clinician or former clinician*	Researcher**	CEO	Policy maker or consultant	Health insurance provider	Hospital or GP practice	Patient organization	Choosing Wisely	University	Government
1	1	NL	x	X	X			x			x	
2	1	NL		X		X			x	x		
3	1	NL				X						x
4	1	NL	x	X				x		x	x	
5	2	NL	x			X	x			x		
6	2	NL	x	X				x		x		
7	2	NL	x	X				x				
8	3	NL		X							x	
9	3	NL	x	X				x		x	x	
10	3	NL	x			X	x					
11	3	NL	x			X			x			
12	4	NL		X						x	x	
13	4	US		X		X				x	x	
14	4	CA		X						x	x	
15	4	ES	x	X		X						x
16	4	IL		X						x	x	
17	4	NO		X							x	

*Among: nurse, medical doctor, physical therapist

***Among field of study: Healthcare, healthcare organization, health policy, health equity, behavioral science, philosophy of medicine*

CEO: Chief executive officer, GP: General practitioner, NL: Netherlands, US: United States of America, CA: Canada, ES: Spain, IL: Israel, NO: Norway.

Cluster of domains

The results of the focus groups were combined with the literature-based framework. This process resulted in the supporting the scaling of de-implementation strategies (SPREAD) framework. The determinants were classified into four domains: scaling plan, external context, de-implementation strategy and adopters. The four domains and their subdomains are shown in Figure 2 and Table 3. A detailed description is provided below.

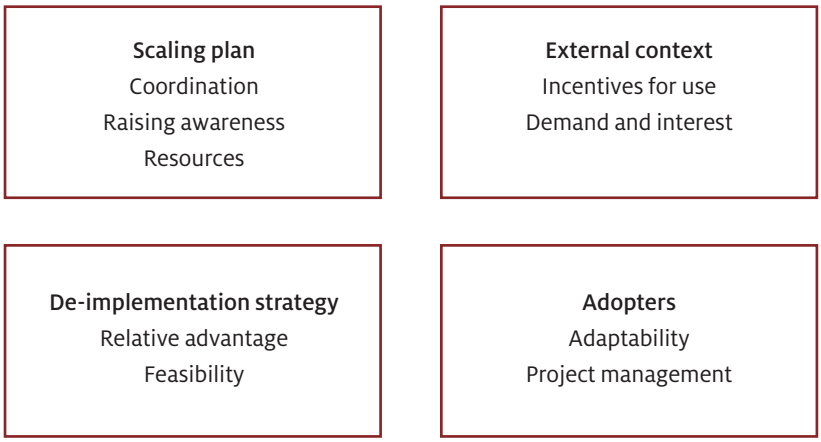

Figure 2 | Domains and subdomains

Table 3 | Domains, subdomains and determinants of the scaling of de-implementation strategies

	Domain	Subdomain	Determinants
1.	Scaling plan	Coordination	- Responsible team with commitment
			- Support
			- Partnerships
		Raising awareness	- Media campaigns
			- Professional and social networks
			- Opinion leaders
		Resources	- Financial resources
			- Sufficient time
			- Skilled team members
2.	External context	Incentives for use	- Political climate
			- Economic climate
			- Regulatory arrangements
			- Payment system
			- Clinical guidelines
		Demands and interest	- Demands of stakeholders
			- Interest of stakeholders
			- Public support
3.	De-implementation strategy	Relative advantage	- Gains - Investments
			- Risks
			- Evidence
		Feasibility	- Compatibility
			- Adaptability
			- Observability
			- Trialability
			- Complexity
4.	Adopters	Adaptability of the adopters	- Adopters' characteristics
			- Attitude toward intervention
			- Governance
			- Available resources
		Project management	- Accountability
			- Plan, monitor, evaluate, feedback and adapt
			- Clinical champions
			- Internal partnerships

SCALING PLAN

Coordination

The scaling of a de-implementation strategy requires a responsible team. While this team could consist of policy makers, health insurers, and healthcare professionals, patients and patient organizations could also lead the scaling process. The scaling team preferably partners with stakeholders and potential adopters of the intervention. Stakeholders differ per strategy; they include members from multiple disciplines and can be regional or national organizations. Stakeholders are not only the targets of a de-implementation strategy but also the ones who are indirectly affected by such a strategy. For example, an audit and feedback strategy requires an organization that provides data and a receiving healthcare professional. Other stakeholders are the ones who are affected if the strategy is effective at reducing low-value care, for example, patients, health insurers and the government. Therefore, patients and patient organizations are often important stakeholders that are valuable for scaling. A partnership with stakeholders should include a shared responsibility to increase the level of commitment. Moreover, scaling is facilitated by partnerships with organizations that have either a large end-user reach or powerful, active members in the target setting. Partnerships ideally start in an early stage, for example, in the developmental stage of the intervention or when the intervention is prepared for scaling. In addition to organizing partnerships, the scaling team should also provide support to adopters to make de-implementation as simple as possible. The support can include implementation training, technology support with benchmark data and creating a learning community. Such communities can exchange experiences, knowledge and insights about the strategy and its implementation.

Raising awareness

Potential adopters, including healthcare professionals and patients, must be made aware of the de-implementation strategy. These adopters can be reached through media channels and networks. Media campaigns not only spread information quickly but also shorten the time between awareness and use. Social and professional networks can also be addressed to raise awareness. Therefore, it is important to make use of the networks of the scaling team, the engaged stakeholders, and the intervention enthusiasts (opinion leaders). Moreover, peer-to-peer learning is more effective than innovators' own promotion of their interventions. This underlines the importance of opinion leaders in organizations other than the place of origin. Opinion leaders are persons within an organization or field who have earned respect by having high levels of competence. They have a strong amount of influence on individual attitudes toward interventions, which can be used to promote the scaling of the de-implementation strategy. In raising awareness, carefully framing of the de-implementation strategy is important since de-implementation can easily be interpreted as a cost-saving measure.

Resources

Resources are crucial for the scaling of de-implementation strategies. Financial resources are needed to execute the scaling plan, and the scaling team should have skilled members. These members should have required knowledge of the external context, including the relevant regulations. With this knowledge, financial and organizational barriers and facilitators can be addressed more effectively. In addition to financial and human resources, sufficient time is needed since scaling occurs slowly.

EXTERNAL CONTEXT

Incentives for use

Incentives for use are drivers of the use of de-implementation strategies, in addition to advantages of the strategy; they include a reduction of LVC and improved patient outcomes. They can act on all levels: individual, organizational and national. Examples of incentives are financial consequences, employment opportunities, regulatory arrangements, clinical guidelines, accreditation and scientific opportunities. Incentives for de-implementation are often lacking, while the provision of LVC is stimulated by, for example, current payment systems. De-implementation could therefore result in a financial disadvantage in some cases, which is a barrier to scaling. Therefore, incentives to reduce the amount of LVC and incentives for the use of de-implementation strategies should be added, while incentives for the use of LVC should be removed. Whether politicians and policy-makers create or remove incentives is influenced by multiple factors. For example, the economic and political climate can drive the strategic priorities of politicians and influence budget choices.

Demands and interest

Scaling is facilitated by a demand for the de-implementation strategy. A demand can start with an urge for less LVC from within society. This urge could stimulate organizations to look for ways to reduce the amount of LVC and could result in a demand for an effective de-implementation strategy. However, there are often conflicting demands in the case of de-implementation; there may be a simultaneous demand to keep providing LVC. This demand can come from all stakeholders, including patients, healthcare professionals, healthcare organizations, and the technology and pharmaceutical industry. All these stakeholders have their own interests, which may influence the demand for the provision of LVC. Additionally, even the availability of LVC can be a source of demand. Demands and interests are influenced by the perceptions of stakeholders. For example, hospitals could be interested in presenting themselves as providers of high-quality care. The common perception of high-quality care is more and innovative care, which could be perceived as contrary to reducing LVC. The perceptions of patients also influence their demands. For example, patients could feel like they have the right to receive care, even if it is of low-

value, because they pay insurance fees. Therefore, reducing LVC could be perceived as a loss to patients.

DE-IMPLEMENTATION STRATEGIES

Relative advantage

An effective de-implementation strategy leads to a reduction in the amount of LVC provided. The advantage of de-implementation strategies is therefore a reduction in the level of LVC, which indirectly improves patient outcomes. The relative advantage of the de-implementation strategy is the perceived advantage of the reduction of the targeted LVC compared to the current situation. De-implementation is facilitated if the targeted LVC is replaced with an alternative because healthcare professionals prefer to offer patients something more than a wait-and-see approach. Additionally, alternative care should be appealing and should not require more time and effort than the original plan for care. The advantages of de-implementation strategies can be further increased by limiting the risk of failing and decreasing the required investments to conduct the strategies, such as costs and workload. Furthermore, the gains of the strategy should be relevant to patients, adopters and adopting organizations. Examples of relevant gains for patients are an improved quality of life, better clinical outcomes, decreased burdens and favorable social outcomes, such as reassurance. Additional outcomes for healthcare professionals and organizations are higher quality performance and reduced costs or increased profits. In the case of partnerships, it helps if these parties also benefit from the strategy. The effects of the intervention must be substantiated by evidence about improved outcomes. Evidence is frequently challenged in the case of de-implementation, even when guidelines state that the targeted care is of low value. Therefore, it is important that there is strong supporting evidence.

Feasibility

The feasibility of a de-implementation strategy is determined by its compatibility, adaptability, observability, trialability and complexity. The goal of the strategy should be compatible with the existing values, beliefs, past experiences, and needs of potential adopters. Moreover, the influencing factors of providing LVC differ between hospitals and settings. Therefore, the local assessment of barriers and facilitators is essential, and strategies should be adapted according to these findings to fit the local needs and conditions. Adaptability provides the opportunity to modify the overall strategy to fit these local barriers and facilitators; therefore, it is also an important feature. Feasibility is also increased if the effects of the strategy are easy to observe and monitor because insights into the progression of the strategy motivate adopters to continue, and unforeseen effects can be identified and acted upon. Trialability, i.e., the ability to test a strategy on a small scale, lowers the initial investment and allows adaptors to experiment

with the strategy. Finally, the implementation of the strategy should be simple. A complex strategy can be simplified by implementing it in a stepwise manner.

ADOPTER OR ADOPTING ORGANIZATION

Adaptability

Adaptability is defined as an adopter's or adopting organization's capacity to change. It depends on the governance regarding change, the available resources and the adaptors' openness to change. The organization's governance could stimulate de-implementation through rapid decision-making and flexibility. Furthermore, de-implementation requires sufficient financial, technical and human resources from the adopting organizations and the time of individual adopters. Openness to change includes the perceived need for change, and it is associated with several adopter characteristics. Influencing characteristics are, for example, the adopter's age and attitude toward the de-implementation strategy, including his or her trust, confidence, optimism, commitment and support regarding the proposed change. Moreover, the ease of de-implementation depends on past experiences with a particular LVC and how it was promoted during medical training. The belief of the advantage of a particular procedure will be greater if the professional was trained by someone who was confident about its advantage. Consequently, the de-implementation of that procedure will be more difficult. On the organizational level, openness to change depends on the relative balance of the opponents and supporters of the change. This can be influenced by engagement strategies within the organization. Collaborations between stakeholders at various levels within an organization can help gain broad support for a de-implementation strategy.

Project management

Strategies must be embedded into organizations. This requires an accountable team composed of team members who have the authority to de-implement within their organization. De-implementation is facilitated by a plan and strong team leadership. Similar to the scaling plan, partnering with local end-users in early stages helps make strategies compatible with the current way of working. In addition to healthcare professionals, patients are often also end-users of de-implementation strategies. Involving patients is crucial to overcome their resistance to de-implementation. Furthermore, clinical champions who are enthusiasts of the strategy and are willing to promote and support it within their organizations should be selected. After implementation, continuous monitoring, evaluation and adaptation of the de-implementation strategy is recommended. Monitoring the impact and frequent evaluations of the strategy can both increase and sustain its gains. Providing feedback to users motivates the use of the strategy and sustains a positive perception.

Discussion

The SPREAD framework provides an overview of determinants that could be targeted to facilitate the scaling of a de-implementation strategy. These determinants are classified into four domains: scaling plan, external context, de-implementation strategy and adopters. First, scaling plans need to be coordinated by a team. This team should organize partnerships, support adopters, raise awareness among potential adopters, and gather resources. The external context preferably includes incentives for the use of a de-implementation strategy, whereas incentives for providing LVC should be removed. The use of de-implementation strategies is also stimulated by the demand for and interest in de-implementation or a specific strategy. Furthermore, the use of a de-implementation strategy ideally leads to advantages over the current situation, and its implementation should be feasible. Last, whether adopters adopt a de-implementation strategy also depends on their adaptability and local project management. Experts have emphasized that while the determinants are country-independent, they have implications that vary with context, culture and history.

Comparison with literature

Recently, an article was published about a scale-up program that aimed to reduce the prescription of potentially inappropriate medication at the emergency department. (80) No new determinants were described; the authors confirmed with focus groups the importance of the creation of a learning community, the need for buy-in from stakeholders, the use of data, continuous monitoring and providing feedback, and the adaptability of the strategy components, such as site-specific education.

Our literature search returned only one article that explicitly discussed the role of patients in the scaling of innovations. (39) Barber et al. described the importance of patients' support and the roles patients played during the scaling of a medical passport. Their findings were in accordance with the view of the de-implementation experts provided in the current study. They emphasized that patients are important stakeholders in LVC and that their support is crucial. By involving patients in the scale-up, support can be gained, and possible resistance can be overcome. The literature underlines this reasoning as well. For example, Augustsson et al. identified patient determinants of the de-implementation of LVC, and the majority of these determinants acted as barriers. (81) To overcome these barriers, Born et al. suggested partnering with patients and patient organization, which could build trust among patients and improve de-implementation strategies. (82) We emphasize that in addition to being partners, patients and patient organizations can also lead the scaling of a de-implementation strategy. Examples from several countries show that patient organizations can contribute to a reduction in the amount of LVC through the scaling of knowledge and tools that aim to increase shared decision making. (83)

All determinants of the scaling of innovations also apply to de-implementation strategies, according to the experts; we expected this shared application due to the resemblance between innovations and de-implementation strategies. The experts added several topics and determinants of de-implementation strategies to the framework, such as medical training, the presence of clear clinical guidelines, and patients' perspectives and roles. These factors are likely to also influence the scaling of innovations, despite not being described as determinants in our literature selection. We hypothesize that the main difference for scaling lies in the implications and importance of the determinants rather than the determinants themselves. For example, we identified 'compatibility with the values and beliefs of adopters' as a determinant of both innovations and de-implementation strategies. Some innovations are additional treatment options that naturally meet the values of healthcare professionals because they are trained to do something for their patients. (23, 84, 85) De-implementation strategies often aim at 'not doing', which could seem to undermine professional integrity. (86) This implies that de-implementation requires more attention and a different approach to meet the values and beliefs of healthcare professionals.

To our knowledge, this is the first determinant framework for the scaling of de-implementation strategies. Previous frameworks and reviews have focused on either the de-implementation process or the scaling of innovations or interventions. (34, 36) Our framework distinguishes itself from both types. Compared to determinant models on de-implementation, this framework adds topics such as a scaling plan and a coordination team responsible for the scaling and raising awareness among potential adopters. (31, 34, 81, 87) Compared to the literature on the scaling of innovations, e.g., Rogers' diffusion of innovations theory and the Consolidated Framework for Implementation Research, we have added several topics and nuanced the implications of the shared subdomains and determinants. (18, 21) For example, incentives could be created to support the use of an innovation, such as a payment system that covers its costs. (59) Incentives are also facilitators for scaling de-implementation strategies. This framework adds the recommendation to also remove incentives for the use of LVC to support the scaling of de-implementation strategies. In addition, the potential conflicts in demands are addressed in this study. The scaling of innovations is facilitated by the demand for the innovation. In the case of scaling de-implementation strategies, a demand for an effective strategy also acts as a facilitator; however, there are also demands to keep providing LVC, e.g., from the pharmaceutical industry. This complicates the scaling of de-implementation strategies.

Strengths and limitations

The methodology we applied to develop this determinant framework has several strengths. This framework is a result of a systematic analysis of recent literature, as well

as a critical review of de-implementation experts. The participating experts all have experience with the de-implementation of LVC and have a wide range of backgrounds and professions. Moreover, we included experts from multiple countries. There are, however, also limitations to consider. First, the Dutch experts were sampled from within our network because there are only a few people in the Netherlands who meet our criteria for de-implementation expertise. However, this is unlikely to have influenced the discussion between the experts because no sensitive topics were discussed. Furthermore, we included participants with a variety of backgrounds; however, for some professions, for example, hospital CEOs, we included only one person. However, some participants were collaborating closely with hospital boards and could therefore also reflect on institutional factors. In addition, there was an overrepresentation of experts from the Netherlands. Nevertheless, this framework is internationally relevant because the literature-based framework is based on international literature and all international experts agreed on the described determinants. The experts pointed out that the main difference between countries lies in the implications of the determinants rather than the determinants themselves. Finally, the identified determinants were only reviewed and confirmed by de-implementation experts. Future empirical studies should validate the determinants of the scaling of de-implementation strategies.

Conclusion

The SPREAD framework describes the determinants of the scaling of de-implementation strategies. The determinants are classified into four domains: scaling plan, external context, de-implementation strategy and adopters. All the identified determinants relevant to scaling healthcare interventions are also relevant to the scaling of de-implementation strategies. The determinants present opportunities for a variety of parties to move toward the successful scaling of de-implementation strategies. Future research should validate these determinants of the scaling of de-implementation strategies.

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Additional file 1 | Search strategy Embase and Pubmed

Embase

#	Searches
1	((disseminat* or upscaling or scale up or scaling up or spread* or diffus*) and (knowledge or guideline or intervention or innovation or policy)).ti,ab,kw. and (((health or healthcare).ti,ab,kw. and (innovation* or improvement*).ti.) or (intervention* and (scale or scaling)).ti.)
2	((obsole* or (("not" or "no longer") adj (effective or essential or efficient)) or ineffective or uneffective) and ("health system" or healthcare or care or policy or policies or practice or technology or procedure* or treatment* or intervention* or "health services" or strateg* or "clinical use" or referral* or diagnosis or regulatory or approach or prescrib* or therap*)).mp.
3	(low-value or overuse* or inappropriate or "old habits" or (overtest* or overdiagnos*)).mp.
4	2 or 3
5	(reduce or avoid or minimize* or discontinu* or minimis* or decreas* or stop or stopping or revers* or replace* or avert or "trim down" or (cut adj (down or back)) or substitute or decrement or ("de-implementation" or deimplementation or "do-not-do" or "deadopt*" or decommission*)).mp.
6	(disseminat* or scaling or upscaling or scale up or scaling up or scale or spread* or diffus*).ti,ab,kw.
7	(health or healthcare).mp.
8	(innovation* or improvement* or intervention*).mp.
9	4 and 5 and 6 and 7 and 8
10	1 or 9

Pubmed

#	Query
1	Search: (obsole*[tiab] OR ("not effective"[tiab] OR "not essential"[tiab] OR "not efficient"[tiab] OR "no longer effective"[tiab] OR "no longer essential"[tiab] OR "no longer efficient"[tiab) OR ineffective[tiab] OR uneffective[tiab]) AND ("health system"[tiab] OR healthcare[tiab] OR care[tiab] OR policy[tiab] OR policies[tiab] OR practice[tiab] OR technology[tiab] OR procedure*[tiab] OR treatment*[tiab] OR intervention*[tiab] OR "health services"[tiab] OR strateg*[tiab] OR "clinical use"[tiab] OR referral*[tiab] OR diagnosis[tiab] OR regulatory[tiab] OR approach[tiab] OR prescrib*[tiab] OR therap*[tiab])
2	Search: (low-value[tiab] OR overuse*[tiab] OR inappropriate[tiab] OR "old habits"[tiab]) OR (overtest*[tiab] OR overdiagnos*[tiab])
3	Search: (reduce[tiab] OR avoid[tiab] OR minimize*[tiab] OR discontinu*[tiab] OR minimis*[tiab] OR decreas*[tiab] OR stop[tiab] OR stopping[tiab] OR revers*[tiab] OR replace*[tiab] OR avert[tiab] OR "trim down"[tiab] OR ("cut down"[tiab] OR "cut back"[tiab]) OR substitute[tiab] OR decrement[tiab]) OR ("de-implementation"[tiab] OR deimplementation[tiab] OR "do-not-do"[tiab] OR "deadopt*"[tiab] OR decommission*[tiab])
4	Search: (disseminat*[tiab] OR scaling[tiab] OR upscaling[tiab] OR scale up[tiab] OR scaling up[tiab] OR scale[tiab] OR spread*[tiab] OR diffus*[tiab])
5	Search: (health[tiab] OR healthcare[tiab])
6	Search: (innovation*[tiab] OR improvement*[tiab] OR intervention*[tiab])
7	Search: #1 OR #2
8	Search: #7 AND #3 AND #4 AND #5 AND #6
9	Search: ((((disseminat* [tiab] OR upscaling [tiab] OR scale up [tiab] OR scaling up [tiab] OR spread* [tiab] OR diffus*[tiab]) AND (knowledge [tiab] OR guideline [tiab] OR intervention [tiab] OR innovation [tiab] OR policy [tiab])) AND (((health[tiab] OR healthcare[tiab]) AND (innovation*[ti] OR improvement*[ti])) OR (intervention*[ti] AND (scale[ti] OR scaling[ti]))))))
10	Search: #9 OR #8

Additional file 2 | Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Domain 1: Research team and reflexivity

Personal Characteristics

1. Interviewer/facilitator. Which author/s conducted the interview or focus group?
   - DK and either RBK or SDV
2. Credentials. What were the researcher's credentials? E.g. PhD, MD
   - DK: MD and MSc, RBK: MD and PhD, SVD: PhD
3. Occupation. What was their occupation at the time of the study?
   - DK, RBK and SV are researchers
4. Gender. Was the researcher male or female?
   - DK and SVD: female, RBK: male
5. Experience and training. What experience or training did the researcher have?
   - SVD and RBK conducted and published multiple qualitative studies, as research leader as well as researcher. DK followed a course 'Qualitative research methods and analysis' and has experience with qualitative research.

Relationship with participants

6. Relationship established. Was a relationship established prior to study commencement?
   - Yes. There are only a few people in the Netherlands that meet our criteria for de-implementation expertise. Therefore, we were obligated to recruit people from our network.
7. Participant knowledge of the interviewer. What did the participants know about the researcher? e.g. personal goals, reasons for doing the research
   - Additional file 3 contains all the information the participants received before the focus group.
8. Interviewer characteristics. What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic
   - The interviewers were performing several studies on reducing low-value care.

Domain 2: study design

Theoretical framework

9. Methodological orientation and Theory. What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis.

- The focus groups were part of a mix method study. First we performed an integrative review to develop a literature-based framework. The codebook conducted for the literature-based framework was used for deductive coding of the transcripts of the focus groups.

Participant selection

10. Sampling. How were participants selected? e.g. purposive, convenience, consecutive, snowball
    - We used purposive sampling to select participants.
11. Method of approach. How were participants approached? e.g. face-to-face, telephone, mail, email
    - Participants were invited by e-mail.
12. Sample size. How many participants were in the study?
    - Seventeen experts participated in our focus groups.
13. Non-participation How many people refused to participate or dropped out? Reasons?
    - One expert accepted the invitation, but did not show. He did not provide a reason. Two experts did not accept our invitation. One because of other obligations and the other because she did not met our criteria for de-implementation expertise. They spontaneously suggested a colleague with a similar background. We invited the suggested colleague, and they both participated.

Setting

14. Setting of data collection. Where was the data collected? e.g. home, clinic, workplace
    - Due to the COVID-19 pandemic, the focus groups took place digitally.
15. Presence of non-participants. Was anyone else present besides the participants and researchers?
    - No.
16. Description of sample. What are the important characteristics of the sample? e.g. demographic data, date
    - Characteristics of the participating experts are presented in table 2.

Data collection

17. Interview guide. Were questions, prompts, guides provided by the authors? Was it pilot tested?
    - The main questions were provided to the participant prior to the focus group meeting, see additional file 2. The interview guide was discussed with other researchers, but it was not tested.
18. Repeat interviews. Were repeat interviews carried out? If yes, how many?
    - No.

19. Audio/visual recording Did the research use audio or visual recording to collect the data?
    - The focus groups were audio recorded.
20. Field notes. Were field notes made during and/or after the interview or focus group?
    - Yes.
21. Duration. What was the duration of the interviews or focus group?
    - 53-57 minutes.
22. Data saturation. Was data saturation discussed?
    - Yes.
23. Transcripts returned. Were transcripts returned to participants for comment and/or correction?
    - No.

Domain 3: analysis and findings

Data analysis

24. Number of data coders. How many data coders coded the data?
    - Initial coding was performed by DK and checked by either RBK or SVD.
25. Description of the coding tree. Did authors provide a description of the coding tree?
    - Yes, see additional file 3.
26. Derivation of themes. Were themes identified in advance or derived from the data?
    - The focus groups were part of a mix method study. First we performed an integrative review to develop a literature-based framework. The codebook conducted for the literature-based framework was used as the basis for the coding. See additional file 3.
27. Software. What software, if applicable, was used to manage the data?
    - ATLAS.ti.
28. Participant checking. Did participants provide feedback on the findings?
    - No.

Reporting

29. Quotations presented. Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number.
    - There are no quotations presented in the main article.
30. Data and findings consistent. Was there consistency between the data presented and the findings?
    - Yes.
31. Clarity of major themes. Were major themes clearly presented in the findings?
    - Yes.
32. Clarity of minor themes. Is there a description of diverse cases or discussion of minor themes?
    - Yes.

Additional file 3 | Preparation focus groups

Summary of influencing factors in the dissemination of innovation

We have search the existing literature for factors the influence the dissemination of de-implementation interventions. Unfortunately we did not find any. Therefore we changed our scope to influencing factors of the spread of all kinds of innovations and interventions.

Methods

We have searched MEDLINE and Embase for articles between 1995 and December 2020. Articles on dissemination of innovations or interventions in healthcare in OECD member countries were included. We excluded articles that aimed quality improvement in a specific organization. We did a full-text screening on 88 articles, in which relevant text passages were highlighted in all parts of the included articles. Passages were selected and marked if they contained information about factors or processes that influence dissemination. We did a qualitative analysis on the extracted text passages: we have coded all factors that influenced the dissemination of an innovation or intervention, and identified themes and subthemes. These steps were iteratively evaluated in group meetings with the all authors.

The result

This resulted in a framework of influencing factors. All factors are categorized into four themes, which can be found in the table on the next page. You'll find a description of these factors on the following pages.

Expert group meeting

During the meeting, we will discuss the influencing factors, as presented in the table. We will focus on two main questions:

1. Do all factors that are described in the framework also influence the dissemination of de-implementation interventions?

2. Is this conceptual framework lacking any factors that influence the dissemination of de-implementation?

Table | influencing factors of the dissemination of innovations

Theme	Subtheme	Influencing factors
1. Strategy	Ownership	- Responsible team with commitment
		- Dissemination plan
		- Partnerships
	Reach of adopters	- Mass media campaigns
		- Social networks
		- Champions and opinion leaders
		- Homophily (peer to peer learning)
	Resources	- Financial resources
		- Skilled team members with knowledge of national context
		- Sufficient time
2. External context	Incentives for use	- Political and economic alignment
		- Regulatory arrangements
		- Adequate payment system
		- Economic climate
	General needs and interest	- General interest or need for a product
		- Public support
3. Innovation	Relative advantage	- Gain; relevant to performance, financial advantage, perceived benefit
		- Investments; costs and workload
		- Risks
		- Efficacy
		- Evidence
	Feasibility	- Compatible with: values and believes, local context, past experiences, and needs of potential adopters
		- Reinvention
		- Observability
		- Trialability
		- Complexity
4. Adopters	Adaptability of the adopters	- Governance; flexibility, fast-decision making and support
		- Available resources; financial, technical and human
		- Openness to change; need for change
		- Adopters characteristics; age, attitude
		- Partnerships
	Project management	- Accountability
		- Leadership
		- Plan, do, monitor, evaluate, adapt
		- Provide feedback
		- Opinion leaders and champions

Description of the factors within the themes and subthemes

STRATEGY

Ownership

Someone or a team should be responsible for the dissemination of the innovation. This team should make **a plan to disseminate** the innovation, and **partner with stakeholders and the potential adopters**. Which stakeholders depend on the innovation, they could be from multiple disciplines, and from provincial or national organizations. Partnerships preferably start in the developmental stage of the innovation or when the innovation is prepared for dissemination. The team should provide support to the adopters, including implementation training and technology support with benchmark data. This allows practices and local teams to target areas for improvement and monitor the effects on patient outcomes. Support can also be accomplished by facilitating a learning community. Such communities can exchange experiences, knowledge and insights about the innovation, implementation and adoption.

Reach of adopters

Potential adopters have to be made aware of the innovation. Ways to reach potential adopters are the use of **mass media campaigns and social networks**. Mass media campaigns spread knowledge fast and they could shorten the time between awareness and use. Social networks can also be addressed to create awareness. The social network of the dissemination team can be nurtured by the use of **champions and opinion leaders** (enthusiasts of the innovation), and by use of the networks of the engaged stakeholders. In reaching potential adopters, it should be taken into account that **peer to peer learning** is more effective than innovators promoting their own innovation. This underlines the importance of opinion leaders in the dissemination strategy. Opinion leaders are persons within an organization or field, who earned respect by high competence. They have strong influence on individual attitudes towards the innovation, which can be used in advantage of the dissemination of the innovation.

Resources

Resources are necessary for the dissemination of innovations. **Financial resources** are needed to execute the dissemination strategy, and the dissemination team should have **skilled members**. These members need to have knowledge of the external context in which the innovation is disseminated, with the current regulatory arrangements. With this knowledge, financial and organizational barriers and facilitators can be addressed more effectively. Dissemination occurs slowly, therefore **sufficient time** to disseminate is needed.

EXTERNAL CONTEXT

Incentives for use

Incentives are drivers for the use of an innovation, on top of the advantage of the innovation itself. They can act on an individual and organizational level. Incentives for use can, for example, be induced by **political activities**. Politicians and policy-makers could stimulate the use of an innovation by making facilitating **regulatory arrangements**, such as **a payment system** that covers the cost of the innovation. The willingness to create such incentives can be influenced by multiple factors. For example, the **economic climate** can drive strategic priorities of politicians and influence choices for budgeting.

General needs and interests

Dissemination is eased by a general demand for the innovation. A demand can start by an urge for change from within the society. This urge combined with public support could stimulate organizations to look for ways to achieve the change, and eventually, result in a demand for a specific innovation that facilitates the change.

INNOVATION

Relative advantage

Relative advantage is the perceived advantage of the innovation, compared to the situation without it. Not only should there be an **advantage** for patients, but also for the adopters, and/or the adaptors' organization. Sometimes it helps if even third parties advantage from it. The limitation of necessary **investments**, such as **costs** and **workload**, and the **risk of failing**, will increase the relative advantage further. The gains should be relevant to the adopter or the adopting organization. The innovation could for example increase the adaptors' performance or be financially beneficial by reducing costs or increasing profit. The **effects of the innovation** should be substantiated with **evidence** about improved outcomes without being a risk to patients.

Feasibility

The feasibility of the innovation is determined by its **compatibility, observability, trialability and complexity**. The innovation should be compatible with the existing values, beliefs, past experiences, and needs of potential adopters. Since organizations differ, it is necessary that the innovation can be modified by the adopters to fit with local needs and conditions. This **reinvention** should be allowed and supported. Moreover, the effects of the innovation should be easily observed and monitored; insights into the progression motivates the adopters to continue. This way, adopters can also act on unforeseen results. Trialability, the ability to test the innovation on a small scale, lowers the initial investment in the innovation and allows the adaptors to experiment. Lastly,

the innovation should be relatively simple. A complex innovation could be simplified by implementing it in a stepwise manner.

ADOPTER OR ADOPTING ORGANIZATION

Adaptability

Adaptability is the adopter's or adopting organization's capacity to change. It depends on the **governance** regarding the change implementation, **the available resources** and the adaptors' openness to change. The organization's governance can be supportive towards innovations, and stimulating implementation by showing flexibility and fast decision-making. Furthermore, sufficient financial, technical and human resources are needed for the implementation. Openness to change includes the perceived need for change and it is associated with several of the **adopter's characteristics**. Influencing characteristics are for example the adopter's age and attitude towards the innovation, including confidence, optimism, commitment and support to the proposed change. On an organization level, openness to change depends on the relative balance of opponents and supports of the change. This can be influenced with engagement strategies within the organization. **Partnerships** with people of different levels within the organization can help to gain broad support of the innovation.

Project management

The key is to fit the innovation into the organization. This requires someone or a team that is **accountable** for this implementation project. An implementation **plan** and strong **leadership** of this team can facilitate the implementation. Partnering with end-users in early stages helps to make the innovation compatible with the current way of working. Furthermore, one should nurture the social system of the organization with **opinion leaders and champions** and make use of their strong influence on individual attitudes towards an innovation. After implementation, **continuously monitoring, evaluating and adapting** is recommended. Monitor the impact and frequently evaluate the innovation to increase and sustain the gains. Provide **feedback** to the users to motivate the use of the innovation and sustain their positive perception.

Additional file 4 | Interview topic guide for focus groups

Introduction

- Confirm consent
- Introduction of researchers and participants, including: name, current employment and de-implementation expertise
- Study background, aim and purpose of the focus group
- Establish ground rules: cameras on, everyone unmute and respond freely to each other

Framework

- Room for questions of the participants about the framework
- Discussing first thoughts and general comments on the framework
- Discussing influencing factors per theme: strategy, external context, innovation, adopters
  - Do all factors that are described in [theme] also influence the dissemination of de-implementation interventions?
  - Is [theme] lacking any factors that influence the dissemination of de-implementation?
  - Are there factors are described in [theme], that should be more explicitly described?
- Encourage discussion by asking the participants to respond on each other
- Participants are asked for clarification if necessary

Conclusion

- Summary of main findings by researcher and opportunity for participants to respond
- Each participant is asked to provide a last comment or statement

Additional file 5 | Description of included articles

Author	Aim	Method	Country*
Barber, 2019 (34)	To ascertain how diffusion of an innovation, My Medication Passport, occurred and the roles played by patients in it	Case study	United Kingdom
Barnett, 2011 (43)	To explore innovators' experiences of the barriers to and facilitators of the implementation and diffusion of healthcare service innovations	Qualitative study	United Kingdom
Ben Chariff, 2020 (44)	To explore scalability assessment among primary care innovators to evaluate their preparedness for scaling up	Cross-sectional survey	Canada
Benson, 2019 (45)	To develop a set of user-reported measures to help understand how and why healthcare innovations spread	Perspective	N/A
Berwick, 2003 (46)	To explore the wider literature and theory of the dissemination of innovation to shed light on the specific case of health care	Perspective	N/A
Carpenter, 2018 (47)	To study the use of a learning community model to foster the adoption of health care innovations	Mixed methods evaluation	United States
Côté-Boileau, 2019 (48)	To improve our understanding of the spread, sustainability and scale-up of healthcare innovations	Scoping review	N/A
Crow, 2006 (49)	N/A	Perspective	N/A
Dearing, 2018 (17)	To identify the parameters of diffusion processes	Perspective	N/A
Dearing, 2010 (50)	To describe design activities that can be applied and combined for the purpose of spreading effective cancer communication innovations	Perspective	N/A
Dengler, 2020 (51)	To discuss the contemporary challenges of the safe implementation and dissemination of new innovations and call on colleagues to engage in this field	Perspective	N/A
Fagan, 2019 (52)	To recommend ways to further advance the scaling up of evidence-based interventions to improve public health and well-being at the population level	Perspective	United States
Gardner, 2010 (53)	To identify the factors influencing the uptake and establishment of continuous quality improvement processes into services	Case study	Australia
Greenhalgh, 2004 (54)	To summarize the findings of a systematic literature review of the diffusion of service innovations	Systematic review	N/A

Greilich, 2018 (55)	To describe a systematic approach to diffusion within perioperative medicine	Case study	United States
Hader, 2007 (56)	To understand why doctors did or did not implement innovations such as guidelines	Qualitative study	Canada
Harper, 2020 (57)	To investigate whether an intervention could be successfully adapted and scaled to other practice settings	Implementation study	United States
Hayes, 2018 (58)	To developed a practical model—the Highly Adoptable Improvement (HAI) Model—and supporting tools	Delphi method	United States and Canada
Hendy, 2013 (59)	To explore the gaps among evidence, management practices and the adoption of innovations	Longitudinal study	United Kingdom
Jippes, 2010 (60)	To examine the effects of a Teach-the-Teacher training course versus the effect that the structure of the social network has on the adoptive behavior of health care professionals	Controlled trail	Netherlands
Jones, 2020 (61)	To examine the potential for broader scale-up and dissemination of project HEAL using tools, models, and methodologies from a National Institutes of Health training program	Case study	United States
Kelley, 2020 (42)	To identify areas for health system improvement to promote the integration of innovative digital health technologies developed by small- and medium-sized enterprises	Qualitative Case Study	Canada
Lee, 2020 (62)	To obtain reflections from policy-makers on their experience of scaling up public health interventions	Qualitative study	Australia
Leeman, 2020 (63)	To describe a phased approach used to scale-up the complex, nurse-developed Connect-Home intervention across multiple settings	Perspective	N/A
Lorusso, 2020 (64)	To evaluate diffusion and gather feedback regarding staff perceptions of barriers to the uptake and effectiveness of multisensory environments	Qualitative study	United States
Luz, 2020 (65)	To develop and test the relationship between champions' personal social network structural and relational characteristics and innovation-project spread	Cross sectional study	Israel
Marshall, 2020 (66)	To present an in-depth exploration of the structural factors impacting practitioner experiences of managing HCV treatment and to shed light on how practitioners have chosen to respond to implementation challenges	Qualitative study	Australia

Masso, 2016 (67)	To describe how the results and lessons learned from evaluating a program were used to develop a conceptual framework for determining how to scale up innovations	Mixed method	Australia
McGinty, 2020 (68)	To describe a model for the coordinated deployment of numerous strategies to simultaneously implement multiple evidence-based interventions in vulnerable populations	Perspective	N/A
McKinlay, 2012 (69)	To describe six stages in the diffusion of retail clinics and consider sociopolitical influences that facilitate and impede their emerging potential	Case study	United States
Milat, 2015 (70)	To synthesize evidence on scaling up public health interventions into population-wide policy and practice and identify key success factors and barriers to the effective scale up of public health interventions	Literature review	N/A
Milat, 2012 (71)	To examine the perspectives of researchers and policy-makers regarding the concepts of 'scaling up' and 'scalability', to generate an agreed-upon definition of 'scalability' and to identify intervention and research design factors perceived to increase the potential for interventions to be 'scaled up'	Delphi study	Australia
Moroz, 2020 (72)	To identify the key factors involved in the spread and scale-up of a successful regional eConsult model	Qualitative study	Canada
Nguyen, 2019 (73)	To better understand the available evidence on the scale-up of normative change interventions for adolescent and youth reproductive health	Literature review	N/A
Ono, 2018 (74)	To identify the critical features of emerging health care extensions and the role they may play in diffusing other practice innovations and sustaining primary care	Mix method	United States
Ovretveit, 2017 (75)	To encourage more research into effective approaches to scaling up, to share some of the practical lessons from the authors' experience with improvers, and to give selected references and resources that are useful for scale-up programs and research	Perspective	N/A
Rhodes, 2020 (76)	To examine the implementation process of an evidence-based community-level intervention designed to increase HIV and STI prevention behaviors	Qualitative study	United States
Schrijvers, 2003 (77)	To search for the quickest way to disseminate health care innovation	Qualitative study	Netherlands

Scott, 2008 (78)	To determine which factors are associated with physicians' intention to use and actual usage of the Healthy Heart Kit.	Cross sectional survey	Canada
Sounderaja, 2020 (79)	To characterize the spread and use of the concept of 'disruptive innovation' within the healthcare sector	Systematic review	N/A
Suther, 2004 (80)	To assess whether primary care providers' perceptions of genomic medicine as an innovation influence their likelihood of adopting this innovation into primary care	Cross sectional survey	United States
Willis, 2016 (81)	To increase the understanding of how and under what conditions complex public health interventions may be scaled up.	Realist syntheses	N/A

Additional file 6 | Conclusion of focus groups

	Focus group 1	Focus group 2	Focus group 3	Focus group 4
Dissemination strategy				
Coordination	- There should be someone who takes the responsibility for de-implementation of low-value care - Patient organizations could be owners of a de-implementation intervention. - Patient organizations could promote the idea of de-implementation. - It is more difficult to drive the de-implementation, if one was once the promotor of care that is now target for de-implementation.	- Health insurance providers could lead the reduction of low-value care. - Professional associations have a responsibility to prioritize the de-implemention of low-value care. - De-implementation should be made as easy as possible for the adopters.	- The dissemination of de-implementation interventions can be facilitated by partnering with platforms that have a wide reach of adopters and power to stimulate the use of the intervention.	- It is not only ownership, but also partnership and sharing these responsibilities. - It is an advantage to have partnerships between the de-implementation intervention designers, researchers, and organizations who are not necessarily research-oriented. - Partner with those who have power and active members in those regions you want to disseminate the de-implementation intervention. - Co-sharing workload is also like a partnership, but we are trying create networks with different experts. - Partnerships are an opportunity to also involve the patients in the strategy part. - Partner with organisations that could create incentives, for example accreditation organisations.
Raising awareness	- It is important who the messenger is. - The use of mass media could also have negative consequences, as de-implementation could easily be interpreted as a cost saving measure. - Professional networks are even more important for healthcare professionals than social networks. - Social networks, including online social networks, could be important to reach patients.	- It is more difficult to find a healthcare professional who wants to be an opinion leader for de-implementation interventions than for innovations.		

Resources		- It takes time and money to disseminate de-implementation interventions.		
External context				
Incentives for use	- There are currently financial incentives that encourage the provision low-value care. These can be direct, but also more indirect, e.g. keep a device in service because it is not yet written off	- Besides adding incentives for de-implementation, incentive for low-value care should also be removed. - There are currently financial incentives that make providing low-value care profitable. - Not only could de-implementation lead to a decrease in profit, but it could also jeopardize one's employment. - Scientifically, de-implementation is valued less than innovation. - Dissemination of de-implementation interventions can be facilitated by letting patients pay for inappropriate care. - The national implementation agenda: that you force a hospital to choose a certain number of choices, "you just have to get started with this". People may not like that, but then it has to happen and then it happens, because it has to. - Medical guidelines facilitate in providing appropriate care. - Each type of low-value care has its own incentives.	- Besides adding incentives for de-implementation, incentive for low-value care should also be removed. - Medical guidelines facilitate in providing appropriate care, but there are not sufficient to accomplish de-implementation of low-value care.	- he national implementation agenda: that you force a hospital to choose a certain number of choices, "you just have to get started with this". People may not like that, but then it has to happen and then it happens, because it has to. - Accreditation can be used as an incentive for the use of de-implementation interventions.

Demands and interests	- A demand for low-value care can come from different stakeholders, e.g. patients and healthcare professionals. - A demand for low-value care can arise from a desired clinical outcome, but also from perceptions and assumptions. - Availability of low-value care is a source of demand. - The medical and pharmaceutical industry also have interests, and could propagate conflicting messages. - There is a discrepancy between the economic climate and the political climate in the Netherlands. Governmental organizations are focusing on limiting healthcare costs, while the general public thinks we should spend more on healthcare. - Patients are an important stakeholder concerning low-value care. - Include all stakeholders, also the ones that could disadvantage from the de-implementation intervention. - Pay attention to all interest in the healthcare sector.	- Demand and interests are influenced by the perception of stakeholders. - Exceptional care is perceived as more and better. - Each hospital creates its own innovations and interventions, and rarely adopt existing interventions. -Implementation is perceived as improvement and is therefore more exciting and superior. De-implementation is more difficult, because it requires discipline and regulation. - Patient could perceive low-value care as their right, because they pay for health insurance.	- Patients are an important stakeholder concerning low-value care. - Implementation is perceived as improvement and is therefore more exciting and superior. De-implementation is more difficult, because it requires discipline and regulation.	- The medical and pharmaceutical industry also have their interests, and they could propagate conflicting messages.

De-implementation intervention				
Relative advantage	- De-implementation could feel like a loss for patients. - Examples of patient relevant factors are: burden for patients, quality of life, clinical outcomes and reassurance. - De-implementation is easier, if there is an alternative of the particular low-value care other than 'wait and see'. - The alternative should be equally appealing as the targeted low-value care, for both patients and healthcare professionals. This depends on factors as quality, clinical outcomes, social outcomes e.g. reassurance, burden and complexity. - De-implementation is difficult if the alternative takes more time and effort than providing low-value care.		- De-implementation is easier, if there is an alternative of the particular low-value care other than 'wait and see'. - De-implementation is easier, if there is an alternative for low-value care, because healthcare professionals want to offer patients something. - De-implementation could feel like a loss for patients, therefore adequate patient education is essential. - Evidence showing that care is of low-value is always challenged, even if it is stated in guidelines. - Cognitive dissonance is an explanation for the fact that evidence has to be stronger in case of de-implementation: One reduces the evidence if it is not in accordance to their own observations.	- Symbolic value of the innovation: it is not cool enough or it does not appeal to the structure or the status-system. - Consider to replace low-value care with something, because to stop something is more difficult than to start something new.
Feasibility		- Each hospital has its own barriers. Preferably an intervention is adaptable and able to target these different barriers.	- Low-value care is a multifactorial problem. It is important to keep paying attention to the factors that are not targeted by the intervention during its dissemination.	

Adopters				
Adaptability of adopters	- The choices healthcare professionals make are influences by how they are trained and by whom. - Whether change of routines is possible, partly depends on the organization's culture. - Adopters need authority to change, to have the opportunity to change. - De-implementation requires time and money of the adopters and adopter's organization. - Patients could also be owner of a de-implementation intervention, yet there is a hierarchical difference. - Shared-decision making is important for de-implementation, but it requires time. - Patient education, tools and clinical decision support are useful for de-implementation - It requires effort to convince patients that reducing low-value care is in their interest, because de-implementation could feel like a loss to them.	- Focus also on younger doctors and medical training, since de-implementation can be more difficult for healthcare professionals who are practicing longer. They could experience a de-implementation as if they did something wrong for years. - It requires more intrinsic motivation to adopt an intervention than execute your own.	- Providing low-value care is taught in medical training. - Locale routines determine how healthcare professionals work. - De-implementation requires local support. - Defensive medicine, e.g. fear of claims or missing a sever diagnosis, is responsible for inappropriate care. - Healthcare professionals need skills to offer patients no tests or treatment. - De-implementation needs to meet the ethics and values of healthcare professionals.	- Where healthcare professionals are trained influences the ease of de-implementation. - Younger doctors are frequently more open to de-implementation. - Healthcare professionals are action-oriented individuals. Therefore individuals may be less receptive to a de-implementation intervention. - We tend to be more afraid of not doing things than over-doing things. The weight of doing something new and having a negative outcome is still better than the weight of not doing anything and having that same negative outcome. So the action of doing something is always perceived as better than not-doing. - You need to have trust with your organization to do a change. It's not only the confidence to the product, but also trust with your organization to do something different, you have to trust the data, trust the leadership and trust that they will put the patients safety first. - The historical trajectory is a factor, because in the organization that is used to do these kinds of changes it is easier than others.
Project management				- Any type of feedback from the patients or the system would promote the behavior change.

6

Evaluation of a real-world implemented web-based patient education tool for dyspeptic patients: a longitudinal survey study

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Submitted

Abstract

Objective

To explore if a real-world web-based patient education tool has the potential to support self-management and informed decision making in patients with functional dyspepsia.

Methods

The study was performed in the Netherlands between July 2022 and October 2023. The study consisted of two web-based questionnaires: the first was filled out directly after participants had finished the tool and the second three months thereafter.

Results

Ninety participants were included. Sixty percent of the participants felt (partly) reassured after finishing the tool and a minority changed their intentions of medical care seeking. The recommendations most frequently provided by the tool were dietary changes (83%), reducing stress or anxiety (70%) and increasing physical activity (62%). For each advised lifestyle change, 50%-77% of participants stated they were (extremely) likely to try it. The self-reported success rate after three months varied from 38% to 100% (n=59).

Conclusion

Informing patients via the web-based patient education tool has the potential to reassure patients, and support lifestyle changes and informed decision-making regarding medical care seeking.

Practice Implications

The education tool is publicly available, allowing many patients to benefit. Moreover, it is inexpensive and requires minimal maintenance. Therefore, implementing patient education in a real-world setting should be encouraged.

Introduction

Patient education can improve patients' knowledge and self-management, and enables patients to participate in healthcare decisions. (1, 2) In addition, targeted patient education is also a successful strategy to prevent low-value care. (3-6) Low-value care is care that does not benefit the patient, fit patients' preferences, or offset the risks or costs given the available alternatives. (7, 8). Upper gastrointestinal tract (GI) endoscopy for uncomplicated dyspepsia is a type of care that could be deemed low-value, because the yield is low and the outcomes rarely change clinical treatment. (9, 10)

A recent study evaluated the 'Trial to Reduce Inappropriate Oesophagogastroduodenoscopies for Dyspepsia' (TRIODE) strategy, which aimed to reduce inappropriate upper GI tract endoscopies. During this trial, a researcher offered dyspeptic patients referred for an upper GI endoscopy a web-based educational tool instead. This tool provided information about the stomach and advice for self-management to reduce symptoms. After completing the intervention, 61% of the participants cancelled the upper GI endoscopy. (4) Despite its effectiveness, the education tool was no longer used after the study period, because it did not fit into daily practice, and depended mainly on one physician-researcher and temporary funding. (4)

To increase the impact of implementation efforts, effective strategies should be embedded in daily practice and scaled to reach a larger population. (11) Many implementation initiatives start locally, and their spread rarely occurs spontaneously, as the example of TRIODE also shows. (12) During the evaluation of the TRIODE strategy, patients and healthcare providers agreed that the education tool should also be available for patients in primary care. Patients with dyspeptic symptoms should be informed about the mechanisms behind their symptoms and receive advice for self-management to reduce symptoms prior to them seeking medical care. (4, 13) Moreover, they agreed that the web-based education tool should be available in a real-world setting to reach a larger group of people with stomach complaints.

While the effect of interventions is often evaluated in a study setting, many interventions fail to make it to real-world implementation. (12) There is limited knowledge available of the effectiveness of real-world implemented strategies. We integrated the TRIODE tool into a well-known website with reliable patient information in the Netherlands. This study aimed to explore if the scaled web-based patient education tool has the potential to support both self-management and informed decision making in a real-world setting.

Methods

The adaption and implementation of the patient education tool

To implement the patient education tool in a real-world setting, some modifications were required. The aim was to make the tool publicly available on an already existing and well-known platform. Therefore, we collaborated with Thuisarts.nl. This is a national website focused on patient education, developed and maintained by the Dutch College of general practitioners (GPs). (14) It contains evidence-based information and recommendations based on guidelines for a broad range of medical situations. The website is widely used, receiving over 80 million visitors annually. (15) The education tool from the TRIODE study was modified to fit a broader public and to match the design of Thuisarts.nl. The modifications included a new design and a remake of the videos and animations, while the majority of the core message remained the same. The tool provided information about gastric function and dysfunction and personalized lifestyle recommendations to reduce the severity of patients' symptoms. In addition, it informed patients about the advantages, limitations and side-effects of diagnostic tests and various types of gastrointestinal medication. The tool was made publicly accessible on Thuisarts.nl at the beginning of 2022. (16)

Study design

We performed a survey study consisting of two questionnaires between July 2022 and October 2023. The first questionnaire was filled out directly after the participants had finished the web-based patient education tool and the second survey was sent out three months after.

Participants and data collection

The tool was aimed at non-pregnant adults, without a history of gastric bypass and alarming symptoms such as hematemesis and melena. An invitation to participate in our study was shown on the last page of the tool on Thuisarts.nl. Everyone who finished the patient education tool was eligible for participation in the study as no additional exclusion criteria were applied.

Prior to the start of the questionnaire, information on the study was provided. All participants provided informed consent at the start of the first questionnaire. At the end of the questionnaire, participants were asked to leave their e-mail address if they were willing to participate in the second questionnaire. Three months after completing the first questionnaire, participants received an invitation for the second questionnaire. Each participant who completed both questionnaires received a gift voucher.

Questionnaires

Two online questionnaires were developed for this study, see appendices 1 and 2. The aim of the questionnaires was to assess whether the tool has the potential to support patients' self-management and informed decision-making. In the first questionnaire (T=0) general patient characteristics were collected, as well as information about the duration of their stomach-related complaints, their medication use and the number of physician consultations in the last three months. Subsequently, questions were asked about the participants' intentions regarding self-management and desired medical care seeking, the extent to which they felt reassured by the information provided in the tool, and the severity of the symptoms. Most questions used a 5-point Likert scale, while possible responses for the reassurance question included: completely reassured, partly reassured, not reassured with the same level of concern, not reassured with more concern, and I have not felt concerned. The second questionnaire (T=1) consisted of questions about their self-management attempts and medical care seeking in the past three months, and the current severity of symptoms. Self-management was operationalized as patients' intentions regarding lifestyle change and to what extent they succeeded in this lifestyle change, desire to seek medical care seek in the past three months, and the current severity of symptoms.

Part of the questionnaire was developed by the research team based on the content of the education tool and the study's aim. All questions were discussed during an iterative process with four authors (DK, IA, TK, SVD) and checked by a linguist (SvS) to ensure readability and Dutch B1 level.

The severity of the upper gastrointestinal symptoms were assessed with a validated instrument: the patient assessment of upper gastrointestinal disorders-symptom severity index (PAGI-SYM). (17) This instrument was not available in Dutch. Therefore, we performed a forward-backward translation of the English version with the goal of obtaining a Dutch version at the Dutch B1 level. Two native Dutch translators independently translated the PAGI-SYM into Dutch. We held a consensus meeting with one of the translators, one linguist (SvS), and one researcher (DK). After consensus was reached, the instrument was translated back to English by a native English translator. Based on the backward translation, minor changes were made after consensus between four researchers (DK, IA, TK, SVD). The both questionnaires were tested by five volunteers which were selected via the network of the researchers. They completed the questionnaires in the presence of a researcher (DK) and were asked to comment on the questions and response options. Based on their feedback, the wording of a few questions was adapted.

Analysis

Descriptive analyses were used to define the level of reassurance and the intentions regarding self-management and medical care seeking at T=0 and T=1. To calculate the success rate of lifestyle changes, solely the patients who reported they had tried to change this aspect of their lifestyle were included.

Participants were excluded from the analysis when they ended the survey before answering any questions about self-management, medical care seeking or reassurance. All other responses were included, also when the participants preliminary ended the survey. Therefore, the total number of respondents may differ per question. Descriptive statistics were used to describe the number of participants who intended to seek medical care before using the tool and directly after using the tool, and whether they received medical care after three months. The responses from the 5-point Likert scale were consolidated into a 3-point scale by combining the two highest and two lowest options.

To report the number of participants that changed their intention to seek care after the education, we only included those who responded with 'definitely' and 'probably' regarding before education and changed to 'probably not' or 'definitely not' regarding after education, and vice versa. Changes from and to 'maybe' were excluded. The mean scores of the PAGI-SYM with Standard Deviation (SD) were calculated.

Results

Participant characteristics

A total of 188 persons clicked on the link leading to the study between July 2022 and July 2023, and 115 provided consent to participate. Ninety participants answered at least one question about self-management, medical care seeking or reassurance and were included in the analysis. Eighty-four participants completed all questions. The second questionnaire was started by 61 participants and completed by 59. The characteristics of the participants are presented in Table 1.

Table 1| Characteristics of the participants

	T=0	T=1
Mean age; years	N=84 49 (range: 18-84)	N=59 52 (range: 18-80)
Gender	N=84	N=59
Female; n (%)	66 (79)	46 (78)
Male; n (%)	17 (20)	12 (20)
Other; n (%)	1 (1)	1 (2)
Education level	N=84	N=59
Low; n (%)	13 (15)	9 (15)
Intermediate; n (%)	18 (21)	13 (22)
High; n (%)	53 (63)	37 (62)
Stomach complaints >6 months; n (%)	N=90 61 (68)	N/a
Gastrointestinal medication use; n (%)	N=90 68 (76)	N=59 44 (75)
Physician consultation in the last 3 months; n (%)	N=90 40 (44)	N=59 35 (58)
Symptom severity mean score (PAGI-SYM) (0-5)	N=88 2.00 (SD=0.96)	N=57 1.49 (SD=0.93)

N= Total number of participants, n= number of participants, PAGY-SYM= patient assessment of upper gastrointestinal disorders-symptom severity index, N/a = not applicable

Reassurance

After completing the tool, a majority felt either reassured (16%, 14/90) or partly reassured (44%, 40/90). Thirty-one percent (28/90) had the same concerns, 6% (5/90) did not have concerns prior to the education, and 3% (3/90) had increased concerns. The increased concerns were due to either unaddressed issues a perceived high risk of stomach cancer, or learning through the tool that alarm symptoms for a severe condition were present.

Intentions for lifestyle changes

Table 2 shows how likely participants (n=90) deemed themselves to follow the personalized lifestyle advice they received from the education tool at T=0. The most received recommendations concerned dietary changes (n=75, 83%), followed by reducing stress or anxiety (n=63, 70%) and increasing physical activity (n=56, 62%). For each recommendation, 50%-77% of participants stated they were likely or extremely likely to try it. Table 3 describes the number of participants that received advice on lifestyle changes and who tried and succeeded. Reducing alcohol intake, dietary changes

and increasing physical activity were the most tried interventions. The success rate of these recommendations was 75%, 94% and 88%, respectively.

Table 2 | Intentions for lifestyle changes (N=90)

Recommendations	(Extremely) likely (n, (%))	Neutral/ unknown (n, (%))	(Extremely) unlikely (n, (%))
Quit smoking (n=22)	11 (50%)	4 (18%)	7 (32%)
Reducing alcohol intake (n=37)	22 (59%)	8 (22%)	7 (19%)
Losing weight (n=50)	32 (64%)	7 (14%)	11 (22%)
Increasing physical activity (n=56)	43 (77%)	8 (14%)	5 (9%)
Reducing stress or anxiety (n=63)	37 (59%)	17 (27%)	9 (14%)
Dietary changes (n=75)	46 (62%)	24 (32%)	5 (6%)

Table 3 | Success rate of recommended lifestyle changes (N=59*)

Recommendation	Tried (n, (%))**	Succeeded (n, (%))***
Quit smoking (n=13)	2 (15%)	2 (100%)
Reducing alcohol intake (n=23)	17 (74%)	11 (75%)
Losing weight (n=32)	8 (25%)	3 (38%)
Increasing physical activity (n=38)	16 (42%)	14 (88%)
Reducing stress or anxiety (n=40)	12 (30%)	6 (50%)
Dietary changes (n=50)	36 (72%)	34 (94%)

**participants who received advice at T=0 and also completed the survey at T=1*
*** number of participants that tried a received recommendation*
****number of participants that succeed a tried recommendation*

Intentions of medical care seeking

Figure 1 shows the respondents' intentions before and after completing the online education tool. The majority of the participants did not change their intentions regarding seeking medical care. Of 90 responses, 8% to 14% of the participants changed their intention, which could be either deciding to seek care or opting not to. After three months, 40% of the participants that intended to consult their GP had done so. 96% of the participants received gastrointestinal medication. A minority of the patients that wanted a diagnostic blood test, helicobacter pylori test or endoscopy, had received it (respectively 25%, 18% and 18%).

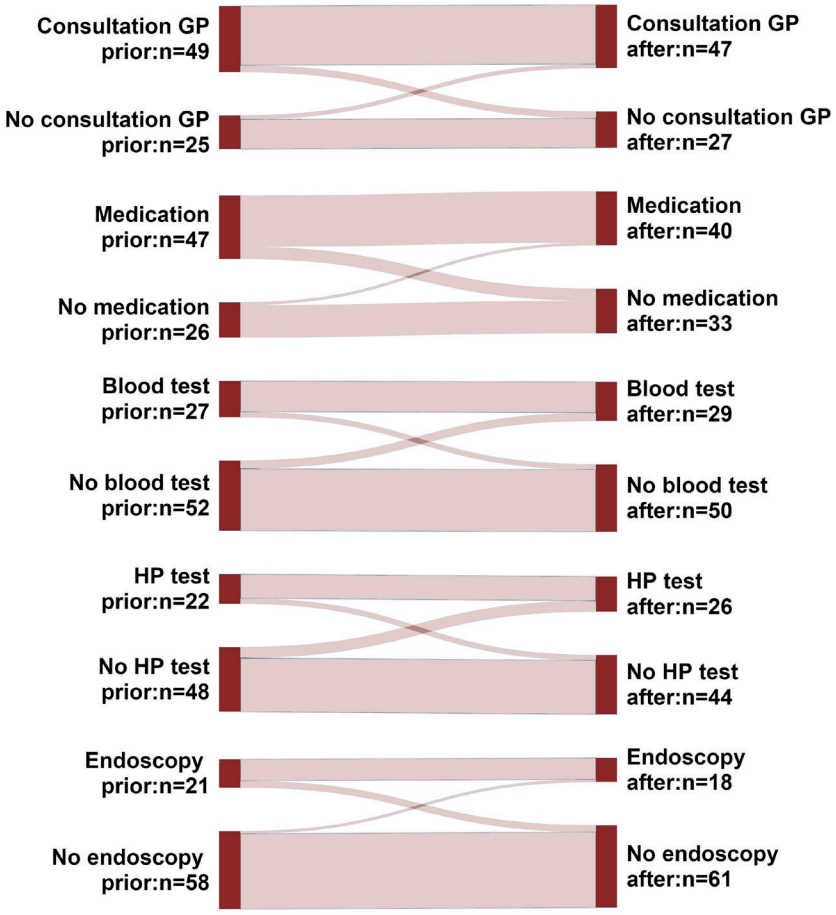

Figure 1 | Changes in participants' intentions to seek medical care before and after completing the education tool.

Discussion and conclusion

Discussion

Our study showed that informing dyspeptic patients via the web-based education tool has the potential to reassure patients, support recommended lifestyle changes to reduce symptoms, and support informed decision making regarding medical care. For each advised lifestyle change, over 50% of the participants stated they were either likely or extremely likely to try the recommended change. After three months, the self-reported success rate of the lifestyle changes varied from 38% to 100%. In addition, the participants reported a reduction of the severity of their symptoms three months after

the first survey. Thus, the education tool seems to be beneficial for dyspeptic patients after the real-world implementation.

A majority of the participants were willing to try recommended lifestyle changes in order to reduce their symptoms and a substantial portion also succeeded. Making and maintaining lifestyle changes is generally perceived as difficult and hindered by multiple factors, such as a lack of time, motivation and support. (18-21) Conversely, lifestyle changes are facilitated by awareness, knowledge and achieving results, among others. (18, 20, 21) Our education tool intended to increase knowledge and awareness of opportunities for self-management. Additionally, achieving results could also be an important driver in our case as participants reported a reduced severity of their symptoms after three months. Our results are in line with previous research revealing that self-management education programs can promote lifestyle changes, such as increasing physical activity, dietary changes and smoking cessation. (22, 23)

Health-related fears and concerns are associated with increased medical consultations and low-value care. (24-26) In some cases, the main reason to perform diagnostic tests is to reassure patients, which applies for upper GI endoscopies for dyspeptic patients. (27) However, studies have shown that performing an endoscopy does not always actually reassure patients, and educating dyspeptic patients could be more effective in reducing health anxiety. (4, 27) In our study, 60% of the participants felt reassured or partly reassured after finishing the education tool. Other studies also show the ability of patient education to reassure patients. A meta-analysis revealed that patient education could reassure patients and reduce health care visits. (28) However, it is important that advice is personalized, in order to prevent causing underuse of medical care.

In addition to reassuring patients, patient education can also provide patients with information on potential valuable care. In our study, some participants intended to seek medical care after the education, while prior they did not. This shows that educating patients about the indications, benefits and limitations of care could support decision-making about seeking care and may prevent underdiagnosis.

These promising results underline the importance of implementing patient education in real-world setting. The scaling of the patient education resulted in the real-world implementation of a tool that fits daily practice, is low-maintenance and is publicly accessible. The targeted population was expanded and the aim of the tool was broadened from reducing inappropriate upper GI endoscopies to informing patients about the nature of their complaints, possibilities of self-management and medical care. These changes can be part of the scaling process. (11, 12) As a consequence of these changes, our study had a different aim and different outcome measures were assessed. Instead

of measuring changes in the low-value use of endoscopies, we were interested in the effects on self-management and reassurance. Future research should focus on the effects of self-management on the appropriateness of care and on the long-term effects of implemented patient education.

Strengths and limitations

This survey study used carefully developed, comprehensible questionnaires. The validated questionnaire was translated using the forward-backward method, and all questionnaires were tested prior to use. The study also has several limitations. First, due to the real-world setting and the policy of the website to not collect user data, we lacked information about the total population using the tool. Although we were not able to check whether our sample is representative, a selection bias should be suspected. We suspect that patients who have a higher symptom severity, a higher education level, or a higher affinity with research and/or healthcare were more likely to participate.

Furthermore, we expect that patients who found the tool useful were more frequently willing to complete the second survey as well. The financial compensation would not have affected the decision to participate, as this was not mentioned until the start of the first questionnaire. Furthermore, there may be some recall bias because the participants were asked about their intentions of medical care seeking before receiving education after receiving it. Moreover, social-desirability bias also applies, which may cause over-reporting of successful lifestyle changes. However, the extent may be limited because the participation was anonymous and the compensation was regardless of the answers. Additionally, the sample was too small to perform sub-analyses and therefore the results should be interpret with caution. And lastly, a longer follow-up period with more respondents would provide more insight into the long-term effects of web-based patient education tool. Results of our study should therefore be interpreted with caution and long-term evaluations should be carried out to provide insight into the sustainability of the lifestyle changes.

Conclusion

This study shows that informing dyspeptic patients via a web-based patient education tool has the potential to reassure patients, and support lifestyle changes and informed decision making regarding medical care seeking. Long-term evaluations should be carried out to provide insight into the effectiveness of the tool and for which patient groups.

Practice implications

In its current form, the web-based education tool is publicly available on a well-known platform, allowing many dyspeptic patients to benefit from its use. Simultaneously, the

tool is inexpensive and requires minimal maintenance. Scaling of patient education in real-world settings should be actively encouraged, because it rarely occurs spontaneously. In addition, future research should focus on evaluating and improving the effectiveness of scaled strategies.

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Additional file 1

Questionnaire 1

1. How long have you had stomach complaints?
We are asking about how long you have had stomach complaints at least once a week.
a. Less than a week
b. 1 to 4 weeks
c. 2 to 6 months
d. 6 to 12 months
e. Longer than 1 year
f. I have no stomach complaints - end of the questionnaire

2. Have you visited a doctor for your stomach complaints in the last 3 months?
You can choose one or more answers.
a. No
b. Yes, a general practitioner
c. Yes, a gastroenterologist
d. Yes, an other doctor

3. Have you used medications for you stomach complaints in the last 3 months?
For example, acid reducers. This also includes medications that you can buy over-the-counter.
a. No → go to question 5
b. Yes, 1 to 15 times → go to question 4
c. Yes, more than 15 times → go to question 4
d. I don't know → go to question 5

4. Which medications have you used in the last 3 months?
You can choose one or more answers.
a. An antacid, such as Rennie, Maalox, Gastilox, or Antagel (aluminum hydroxide/ magnesium hydroxide or calcium carbonate)
b. A mucosal protector, such as sucralfate
c. An acid reducer, such as ranitidine or famotidine (an H2 blocker)
d. An acid reducer, such as pantoprazole or esomeprazole (a PPI)
e. I don't know
f. Other medication, namely: [...]

The following questions are about the situation before you used the education tool about stomach complaints.

5. Before using the tool, did you want to visit a general practitioner for your stomach complaints?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

6. Before using the tool, did you want to take stomach medications? This also includes medications that you can buy over-the-counter.
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

7. Before using the tool, did you want to ask your doctor for a blood test for your stomach complaints?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

8. Before using the tool, did you want to ask your doctor to be tested for the stomach bacteria?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

9. Before using the tool, did you want to ask your doctor for a camera examination of the stomach (endoscopy)?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

Now that you have used the tool, please indicate in these questions whether you are currently planning to do these things.

10. Do you want to visit a general practitioner for your stomach complaints?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

11. Do you want to ask your doctor for a blood test for your stomach complaints?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

12. Do you want to ask your doctor to be tested for the stomach bacteria?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

13. Do you want to ask your doctor for a camera examination of the stomach (endoscopy)?
a. Definitely
b. Probably
c. Maybe
d. Probably not
e. Definitely not

14. In the education tool, you received advice on how to reduce your stomach complaints. Indicate which recommendation you plan to follow.
You can also choose "I did not receive this recommendation."

	Definitely	Probably	Maybe	Probably not	Definitely not	I do not know	I did not receive this recommendation
Smoke less or quit smoking							
Drink less alcohol or stop drinking alcohol							
Lose weight							
Exercise more							
Reduce anxiety, depression, or stress							
Stop consuming certain foods or drinks							

15. Did the education reassure you?

a. Yes, completely

b. Partly

c. No, I still have the same concerns

d. No, I have more concerns. Reason: [...]

e. I did not have any concerns

16. How did you find this education tool?

a. Found it myself

b. Through the general practitioner

c. Through a gastroenterologist

d. Other, namely: [...]

17. What is your age?

[..] years

18. What is your gender?

a. Male

b. Female

c. Other

19. Which education level(s) have you completed?

Multiple answers possible

a. Primary school

b. Secondary school

c. Vocational education training

d. University for applied sciences

e. University

20. May we send you another questionnaire in 3 months about how your stomach complaints are progressing?
This questionnaire will be shorter than this one.
a. Yes, my email address is: [...]
b. No

21. Do you have any suggestions for improving the education tool?
[...]

Questionnaire 2

1. Have you visited a doctor for your stomach complaints in the last 3 months?
You can choose one or more answers.
a. No
b. Yes, a general practitioner
c. Yes, a gastroenterologist
d. Yes, an other doctor

2. Have you used medications for you stomach complaints in the last 3 months?
For example, acid reducers. This also includes medications that you can buy over-the-counter.
a. No → go to question 4
b. Yes, 1 to 15 times → go to question 3
c. Yes, more than 15 times → go to question 3
d. I don't know → go to question 4

3. Which medications have you used in the last 3 months?
You can choose one or more answers.
a. An antacid, such as Rennie, Maalox, Gastilox, or Antagel (aluminum hydroxide/ magnesium hydroxide or calcium carbonate)
b. A mucosal protector, such as sucralfate
c. An acid reducer, such as ranitidine or famotidine (an H2 blocker)
d. An acid reducer, such as pantoprazole or esomeprazole (a PPI)
e. I don't know
f. Other medication, namely: [...]

4. Did you have a camera examination of the stomach (endoscopy) in the last 3 months?
a. yes
b. no

5. Did you have a blood test for your stomach complaints in the last 3 months?

a. yes

b. no

6. Did you test for the stomach bacteria in the last 3 months?

a. yes

b. no

7. You received some recommendations for change in the education tool. Which changes did you make?

You can also chose 'I did not receive this recommendation' or 'I do not know whether I received this recommendation'.

	I tried and succeeded	I tried, but failed	I did not try	I did not receive this recommendation	I do not know whether I received this recommendation'
Smoke less or quit smoking					
Drink less alcohol or stop drinking alcohol					
Lose weight					
Exercise more					
Reduce anxiety, depression, or stress					
Stop consuming certain foods or drinks					

7

What is the long-term sustainability of a successful de-implementation strategy reducing inappropriate laboratory testing: a retrospective multicenter mixed-methods study

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Submitted

Abstract

Background

Many studies have reported strategies that successfully reduced inappropriate laboratory tests; however, the long-term sustainability of these methods has rarely been described. Our aim was to determine the sustainability of a successful strategy reducing laboratory test volume and to identify influencing factors.

Methods

We performed a retrospective mixed-methods study in the internal medicine department of three Dutch hospitals. The multifaceted strategy included educational activities, feedback, intensified supervision , changes in the order system, and active ambassadors. Quantitative data were collected in two hospitals from January 2015 to December 2019. This included a 22-month pre-intervention period, 14-month intervention period, and 22-month follow-up. The control group included five anonymous hospitals. The primary outcome was the number of laboratory tests per patient contact. The sustainability was tested using two analyses: I) an independent t-test to compare the volumes of the final year of the pre-intervention period and follow-up and II) a segmented linear regression analysis to determine the trend and changes in trend between periods. Additionally, semi-structured interviews were conducted with three local teams to identify contextual factors.

Results

The laboratory test volume in hospital 2 was significantly lower in the follow-up compared to the pre-intervention period, with a difference of -0.529 (95%CI: -0.881 to -0.178). The volume in hospital 1 decreased by -0.358 (95%CI: -0.770 to -0.0535), whereas the volume in the control hospitals increased by 0.283 (95%CI: -0.091 to 0.476). Both hospital 1 and 2 demonstrated a positive slope during follow-up, with regression coefficients of 0.058 (95%CI 0.030 to 0.086) and 0.030 (95%CI -0.001 to 0.060), respectively. Changes in the external context and organization hindered sustainability. Facets of the strategy that aligned with daily practice or were automated were better preserved than those that were less beneficial or required a substantial time investment.

Conclusions

In one of the two hospitals, the laboratory volume reduction was sustained during the final year of follow-up compared to the pre-intervention period. However, volume trends increased in both hospitals after the project ended. Continued monitoring of the desired outcomes and reacting to unwanted trends are recommended, because the local and external contexts change over time.

Introduction

Low-value care provides limited or no benefit to the patient, while it is potentially harmful. (1) An estimated 20% of all laboratory tests in hospitals could be considered low-value care. (2) These inappropriate laboratory tests risk false-positive results and can induce downstream diagnostic testing, affecting patients and increasing healthcare costs. (3) Inappropriate laboratory testing should therefore be prevented.

Since the start of the Choosing Wisely campaign in 2012, there has been growing attention towards low-value care and strategies to reduce it, known as de-implementation strategies. (4-6) Some of these strategies specifically target inappropriate laboratory testing. A recent systematic review described such strategies, which included audit and feedback, cost display, education, electronic medical record changes, and policy changes. (7) A vast majority of the studies reported a significant reduction in the overall laboratory testing volume or specific tests. One of the effective strategies was the RODEO strategy: Reduction of Unnecessary Diagnostics Through Attitude change of the Caregivers. (8) This multifaceted strategy resulted in a decrease of 11.4% in the volume of laboratory tests in the intervention group compared to an increase of 2.4% in the control group. (8) To increase the impact of the strategy, these results should be preserved in the long term. (9)

Achieving sustainable results is challenging and is considered one of the most important translational research problems. (10, 11) More research is needed in this field. For example, the benefits of a strategy are rarely reported for post-intervention periods longer than a year, and even fewer studies have reported the effects after the end of the post-intervention period. (12-15) Some studies suggest that sustainability can be achieved even when elements of the original study are discontinued. (16-19) For example, a multifaceted strategy successfully reduced the volume of laboratory tests and the costs in a university medical center. The intensity of the strategy was reduced in the long-term, but the achieved cost reduction was sustained. (18) This raises the question to what extent other effective strategies, such as the abovementioned RODEO strategy, have sustainable effects. Therefore, the objective of this study was to determine the sustainability of the RODEO strategy in reducing laboratory test volume and to identify factors that influence sustainability.
More specifically, we aimed to determine I) the difference in laboratory testing volume between the pre-intervention period and the follow-up period, II) the trend and changes in trend of the testing volume during our study period, III) to what extent the facets of the strategy were continued, and IV) which factors influenced the sustainability of the strategy.

Methods

For this study, the long-term sustainability was analyzed of a de-implementation strategy that effectively reduced inappropriate laboratory testing. (8) This article adheres to the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline for quality improvement studies. (20)

Study design and participating hospitals

We performed a retrospective mixed-methods study at the internal medicine department of three hospitals in the Netherlands. Four hospitals participated in the RODEO project between August 1st, 2016 and April 30th, 2018. (8) All four hospitals were invited to participate in this follow-up study. Three hospitals agreed to participate, while the clinical leader of the fourth hospital rejected the invitation for unknown reasons. This hospital did not achieve a significant reduction of laboratory testing in the primary study. Furthermore, one of the three participating hospitals could not provide reliable data. The data was deemed unreliable because: 1. the number of laboratory tests doubled in the first year, while other parameters did not; 2. The obtained data did not match the original data set, and multiple attempts to reproduce the original data failed; 3. anomalies were observed in other parameters, with unexplained spikes showing up to a tenfold increase. Therefore, this hospital was excluded from the quantitative analysis and solely included in the qualitative analysis. To maintain the anonymity of the non-participating hospital, the characteristics of all four hospitals are provided in Additional file 1.

In addition, for the quantitative analyses, a control group of five anonymous Dutch hospitals was generated by an information company that collects anonymized hospital data. The hospitals in the database were blinded for the researchers. Because the intervention group consists of only secondary care hospitals, all secondary care hospitals were included of which data was available during the entire study period of 58 months. Tertiary care hospitals were excluded due to their distinct patient population. The control group did not contain hospitals that were merged during the study period. Due to the blind formation of the control group, it is unknown whether conditions in the hospitals changed during the study period. However, possible changes were considered a normal aspect of the real world.'

The RODEO de-implementation strategy

A multifaceted strategy to reduce inappropriate laboratory testing was implemented in four hospitals. The strategy included educational activities, feedback, intensified supervision of residents, changes in the electronic order system, and an active clinical leader and local champion. The target population was internists and residents. The local teams consisted of: one or two internists as clinical leaders, residents as local champions,

a clinical chemist as an expert on appropriate testing, and a business controller who was responsible for providing data and supporting data interpretation. One hospital included a hospital manager who served as a project coordinator. The external coordinating team supported the local teams by organizing progress meetings and conferences. More specific details can be found in the study protocol of the original study. (21)

Timeline

In this follow-up study, data from the participating hospitals were collected for a study period of 58 months between January 2015 to December 2019: a 22-month pre-intervention period, 14-month intervention period, and 22-month follow-up period. For the intervention hospitals, these periods were determined before the data was collected and analyzed. The start of the pre-intervention period of the control group was set equal to hospital 2 based on data availability. Figure 1 shows the timeline of the study period.

The pre-intervention period: 22 months before the start of the RODEO project. The earliest start date of this period was limited by a national change in healthcare registration in 2014 which may have influenced the registration of contact moments. In the last 3 to 4 months of this period, the coordinating team prepared the local teams during a joint conference in which potential strategy components were discussed.

The intervention period: originally divided into a 6-month intervention and an 8-month post-intervention period, but according to the original study combined during the analysis. During the first 6 months, the local teams implemented strategy components and attended monthly progress meetings with the coordinating team. A second joint conference was held. During the following 8 months, all implemented strategy components were maintained and new ones were introduced. The progress meetings continued and a joint conference was held in which the sustainability of the project was discussed. Although on paper the intervention was only 6 months, there were clear spill over effect in the following months. Therefore we combined the two periods during analysis.

The follow-up period: 22 months after the project. The duration was limited by the start of the COVID-19 pandemic in the Netherlands in March 2020. During the follow-up period, the coordinating project team had stopped their involvement and the project relied on the local teams. Only the coordinating project team received funding for the project, while the local teams relied solely on voluntary efforts.

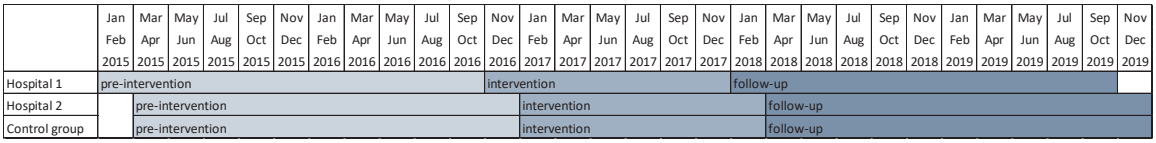

Figure 1 | Timeline of the study period in both intervention hospitals and the control group

Quantitative methods

Data and outcomes

The primary outcome was the laboratory test volume per patient contact. We collected the number of laboratory tests performed per month during the study period and standardized the volume per patient contact. Patient contacts included all daycare visits, long observations without overnight stays, first outpatient visits (including emergency department visits), repeat outpatient visits, and inpatient days. Telephone consultations were excluded because there was a change in registration during the study period, and therefore the data were not representative.

Data analysis

Two analyses were used to describe the sustainability of the RODEO strategy. First, we analyzed the difference in laboratory test volume between the final year of both the pre-intervention period and follow-up period using an independent t-test for each intervention hospital and the control group. A two-tailed p-value of < 0.05 was considered to indicate statistical significance. Second, we performed a segmented linear regression analysis to determine the trend of laboratory testing volume per patient contact during the three study periods and the changes in trends between the periods. Both analyses were performed using SPSS Statistics version 27.

Qualitative methods

Individual and group interviews were conducted to describe the context and the differences during the study period and follow-up. A completed Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist can be found in Additional file 2. (22)

Participants and study procedure

All members of the original local teams were invited via email for a semi-structured group interview or, if scheduling did not permit this, individual interviews. Team members were excluded if they worked in a different hospital at the time of recruitment than during the project (August 2021). This in practice meant that all residents were excluded from participation. The interviews took place in September 2021 and were

conducted digitally due to the COVID-19 pandemic. A medical doctor (DK) experienced in qualitative research conducted the interviews. The participants were informed about the interviewer's background, the study design and the study objectives. The topic guide can be found in Additional file 3. Data saturation does not apply because all potential participants were interviewed for this study.

Data analysis

The interviews were audio-recorded and transcribed. The transcripts were analyzed with MaxQDA 2022 (VERBI Software, 2021) and ATLAS.ti (22.0.11). Two authors (DK and AWB) independently coded all interviews deductively: factors that influenced the sustainability were classified into the domains and subdomains of a sustainability of innovations framework. (23) This conceptual framework is the result of a systematic review aiming to identify core factors in the sustainability of all types healthcare innovations. It consists of four domains: external context, local environment, organization, and innovation. The framework is available in additional file 5. For this study, the name of the fourth domain was changed to strategy. We distinguished between the intervention period and the follow-up period because the presence of these factors changed over time. All identified factors were formulated in a way that the presence of the factor would facilitate the sustainability. Differences were discussed in multiple consensus meetings with DK, AWB and SVD. To describe which factors were present during the intervention period and during follow up, member check was performed by DK for verification and to add missing information. A tailored version of table 3 and 4 was sent per e-mail to the clinical leaders of the three hospitals. Subsequently, during separate phone calls with the clinical leaders, the tables were reviewed and missing information was added.

Results

Quantitative results

Mean laboratory testing volume

The differences in the mean laboratory testing volume per patient contact between the last year of the pre-intervention period and the follow-up period are presented in Table 1. During the follow-up period, the mean testing volume of hospital 2 was significantly lower than during the pre-intervention period, with a difference of -0.529 (95% CI: -0.881 to -0.178, p=0.005). In hospital 1, the mean volume decreased non-significantly by -0.358 (95% CI: -0.770 to 0.0535, p=0.086), whereas the mean volume of the control hospitals significantly increased by 0.283 (95% CI: 0.091 to 0.476, p=0.006). The testing volume per month for the control group is shown in additional file 4.

Table 1 | Differences in the mean laboratory test per patient contact between pre-intervention period and follow-up period.

	Pre-intervention[a] Mean (95% CI)	Intervention[b] Mean (95% CI)	Follow-up[a] Mean (95% CI)	Difference pre-intervention vs follow-up (95% CI)
Hospital 1	11.871 (11.351 to 12.390)	10.606 (10.248 to 10.955)	11.512 (11.062 to 11.963)	-0.358 (-0.770 to 0.535)
Hospital 2	8.742 (8.236 to 9.248)	8.13 (8.009 to 8.253)	8.213 (7.915 to 8.510)	-0.529 (-0.881 to -0.178)[c]
Control group	10.846 (10.573 to 11.119)	10.252 (9.918 to 10.629)	11.130 (10.959 to 11.300)	0.283 (0.091 to 0.476)[d]

[a] The last 12 months of the follow-up period were compared with the last 12 months of the pre-intervention period, [b] last six months of the intervention period, [c] p=0.005, [d] p=0.006

Laboratory testing trends

The trend of laboratory tests per patient contact across the three studied periods is presented in Table 2 and visualized in Figure 2. In hospital 1, we observed a non-significant decreasing trend in laboratory tests during the pre-intervention period. During the intervention period, there was a significant decrease in laboratory tests, with a slope of -0.152 (95% CI -0.207 to -0.097, p<0.001). The change in slope with the pre-intervention period was -0.137 (95% CI -0.199 to -0.076, p<0.001), representing the effect of the intervention. However, during the follow-up period, there was a significant increasing trend of 0.058 (95% CI 0.030 to 0.086, p<0.001), indicating a diminished effect of the intervention in the long term.

Table 2 | Trend of laboratory tests per patient contact during pre-intervention, intervention and follow-up

	Hospital 1	Hospital 2
Pre-intervention		
Intercept (95% CI)	12.160 (11.793 to 12.528)	8.322 (7.920 to 8.724)
Trend before intervention (95% CI)	-0.015 (-0.043 to 0.013)	0.023 (-0.007 to 0.054)
Intervention		
Immediate change after start intervention (95% CI)	0.499 (0.083 to 1.080)	-0.183 (-0.819 to 0.454)
Trend during intervention (95% CI)	-0.152 (-0.207 to -0.097)[a]	-0.058 (-0.118 to 0.003)
Change in slope from pre-intervention slope (95% CI)	-0.137 (-0.199 to -0.076)[a]	-0.081 (-0.149 to -0.013)[b]
Follow-up		
Immediate change after end intervention (95% CI)	0.310 (-0.249 to 0.869)	-0.200 (-0.813 to 0.412)
Trend during follow-up (95% CI)	0.058 (0.030 to 0.086)[a]	0.030 (-0.001 to 0.060)
Change in slope from intervention slope (95% CI)	0.210 (0.149 to 0.272)[a]	0.087 (0.020 to 0.155)[c]

[a] p<0.001, [b] p=0.02, [c] p=0.012

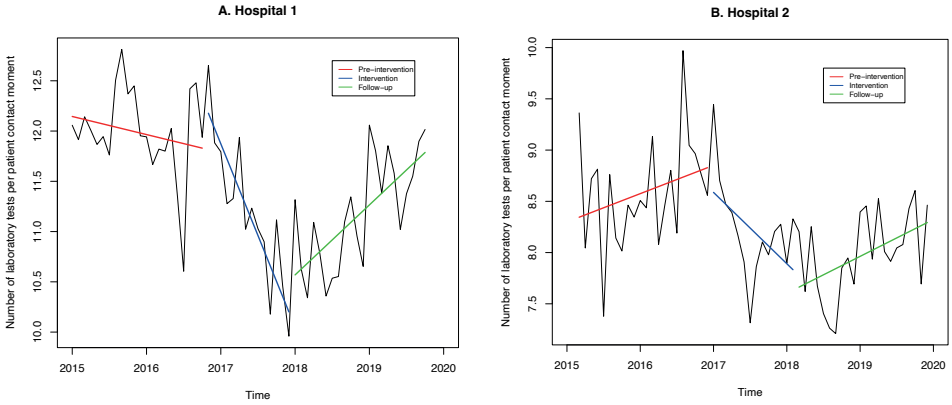

Figure 2 | Number of laboratory tests per patient contact per month. The black curve presents the number of laboratory tests per patient contact moment. The regression lines are presented for the three time periods: pre-intervention, intervention, follow-up.

The laboratory test volume of hospital 2 increased slightly (0.023, 95% CI -0.007 to 0.054, p=0.134) during the pre-intervention period, followed by a decreasing trend (-0.058, 95% CI -0.118 to 0.003, p=0.061) during the intervention period. A significant change in slope with the pre-intervention period (-0.081, 95% CI -0.149 to -0.013, p=0.020) indicates the effect of the intervention. During the follow-up period, there was an increasing trend of laboratory tests of 0.030 (95% CI -0.001 to 0.060, p=0.057). Moreover, the change in slope with the intervention period was 0.087 (95% CI 0.020 to 0.155, p=0.012). Together, these findings suggest a reduced effect of the intervention in the long term.

Qualitative results

Interviews and participants

Seven members of the local project teams were interviewed: three internists, one business controller, two clinical chemist and one hospital manager. One internist of hospital 3 rejected the invitation without providing a reason. We conducted a group interview with the local teams of both hospital 1 and 3. It was not possible to schedule a group interview with hospital 2, therefore two individual interviews were held.

Continuation of the strategy

Table 3 outlines the extent to which each facet of the strategy was continued in each hospital. The majority of the strategy was discontinued. Components that were continued on the same or lower level were: changes to protocols, educational sessions, supervision with attention for appropriate testing, active clinical leaders, changes in the order system. Only hospital intensified a strategy facet; more redundancy checks

were implemented because of their perceived effectiveness. The reasons for lessening or discontinuing facets were the required time investment or a perceived lack of effectiveness. For some facets, the team members were not able to indicate a specific reason for their discontinuing.

Table 3 | The extent to which facets of the strategy were continued during the follow-up period

Facets of the strategy	Hospital 1	Hospital 2	Hospital 3
Intensified supervision focused on appropriateness of diagnostic tests	↓	↓	↓
Education for residents about appropriateness of laboratory tests	=	↓	↓
Benchmark data presented to the staff and residents	X	X	X
Intensified involvement of the department of clinical chemistry	↓	X	↓
Monthly meetings of the project team	X	X	X
Posters	X	X	X
Mouse mats	X	X	X
Pocket cards showing the costs of laboratory tests	X	X	X
Changes in the electronic ordering system, i.e. minimal retests intervals, alerts, order sets	=	↑	=
Changes in local protocol and working agreements	=	=	=
Clinical leader: internist as team member and role model	↓	=	↓
Local champion: resident as team member and role model	X	X	X

↓: lessened, ↑: intensified, X: stopped, =: maintained

Influencing factors

Thirty-three factors were identified that influenced the sustainability. Table 4 outlines all influencing factors and the differences between the intervention period and follow-up. The factors are classified into three domains: local environment, organization and strategy. The factors are explained in more detail below and interview quotations that support the factors are provided in Additional file 6.

Table 4 | Identified facilitating factors for the sustainability of the RODEO strategy. The presence of the factors during the intervention period and follow-up are presented for each hospital.

	Hospital 1		Hospital 2		Hospital 3	
	Intervention	Follow-up	Intervention	Follow-up	Intervention	Follow-up
Local environment – Partners/stakeholders *Level: regional, regarding multiple hospitals*						
Networking -Meetings with other hospitals about appropriate testing	•	○	•	○	•	○
Incentives -Alignment of financial incentives of the laboratory and hospital	•	•	○	○	•	•
Feedback -Provision of benchmark data of participating hospitals	•	○	•	○	•	○
Commitment -Support of board of directors for the project	•	•	•	•	•	•
Involvement -Involvement of a dedicated external research team in the project	•	○	•	○	•	○
Organization – Leader/Champion *Level: internal medicine department*						
Leadership -Presence of a project team	•	○	•	•	•	○
Organization – Staff *Level: internal medicine department*						
Supervision -Providing positive feedback during supervision of residents	•	•	•	•	•	•
Support -External research team supported the internal data evaluation	•	○	•	○	•	○

Skills evaluation/monitoring						
-Presence of skills for meaningful interpretation of data	•	○	•	•	○	○
-Monitoring of data was done periodically	•	○	•	•	•	○
Motivation						
-Staff and residents have intrinsic motivation to improve the appropriateness of diagnostic tests	•	•	•	•	•	•
-Residents have intrinsic motivation to participate in the project	•	•	•	•	•	○
Involvement						
-All staff members are committed to the project	•	•	•	•	○	○
-The laboratory is committed to the project	•	•	•	○	•	○
Trust						
-The staff members trust the validity of the data	•	N/a	•	•	○	N/a
Strategic planning						
-The project members have a plan to achieve sustainable effects	○	○[a]	•	•	•	○[a]
Goals						
-The goal is awareness and critical thinking about diagnostic testing	•	•	•	•	•	•
-The goal is a reduction total volume of laboratory testing	•	○	•	•	•	○
Information						
-The project is focused on improving quality of care instead reducing costs	•	•	•	•	•	•
Knowledge						
-Knowledge about the appropriateness of tests is increased by educational sessions	•	•	•	•	•	•
Staffing						
-Consistence of the team: low turn-over of residents	○	○	○	○	○	○
-Consistence of the team: low turn-over of staff members	•	•	•	•	•	•
Beliefs						
-Appropriate testing is perceived important on the department	•	•	•	•	•	•
Innovation – Process						
Compatibility						
Education regarding appropriate testing is compatible with resident training	•	•	•	•	•	•
Spreading						
Elements of the strategy are disseminated to other departments	•	•	•	•	•	•

Innovation – Characteristics						
Perceived effectiveness of the strategy						
- The reduction of specific tests is perceived as substantial	•	N/a	•	N/a	•	N/a
- The cost reduction is perceived as substantial	○	N/a	○	N/a	○	N/a
- The reduction of the total volume of laboratory tests is perceived as substantial	•	N/a	•	N/a	•	N/a
- The increase of awareness for appropriate laboratory testing is perceived as substantial	•	•	•	•	•	•
- The increase of awareness for appropriate diagnostic tests is perceived as substantial	•	•	•	•	•	•
Innovation – Resources						
Time						
The project members feel that they had sufficient time for project	•	○	○	○	○	○
The clinical leaders feel that there is sufficient time for appropriate testing	•	•	•	○	•	•
The project has priority over other projects and activities	•	○	•	•	•	○

• = present, ○ = not present. N/a = not applicable

[a] *There was no plan to achieve sustainable effects, but they intended to continue the educational sessions about appropriate testing and attention for appropriate testing during supervision.*

Local environment – Partners and stakeholders

Hospital 2 mentioned a misalignment between the financial interest of the laboratory and the aim of reducing laboratory testing. This was mainly overcome by the strong intrinsic motivation of the team members and did not change during the study period. The hospital board was supportive in all hospitals during both periods, but was not actively involved. The main difference between the intervention and follow-up period was that the coordinating team was no longer involved. The interviewees emphasized that the coordinating team motivated them and prioritized the project. Moreover, with the withdrawal of the coordinating team, the network meetings and data sharing between the teams stopped as well.

Organization – Leaders and staff

All hospitals had an active project team during the intervention period. After the end of the study, only the project team of hospital 2 continued its role. Therefore, the team meetings also stopped, leading to the discontinuation of the project monitoring and evaluation in hospital 1 and 3. However, all project members were still motived to raise awareness about inappropriate testing during the follow-up period. In hospitals 1 and 2 this was considered successful, in hospital 3 less so. Hospital 2 additionally aimed to sustain the volume reduction of laboratory tests during the follow-up, whereas hospital 1 and 3 did not. The main reasons for this were a lack of trust in the data validity and challenges in translating the data into clinical relevance. During both periods, the interviewees described a high turnover of residents which hindered the sustainability. They emphasized the importance of repetition of education on this topic during both periods. Last, the project team of hospital 2 planned to sustain the effects of the strategy by continuing the education for residents, automating facets of the strategy, monitoring the effects and reacting to unwanted trends. Hospital 3 aimed for continuing resident education and routinizing the focus on appropriate testing during supervision, grand rounds, morning handovers and other clinical meetings. The project team of hospital 1 solely planned the continuation of the resident education.

Strategy – process, characteristics and resources

Strategy components compatible with daily practice were: focus on overuse of diagnostics during supervision, morning handovers, grand rounds and the educational sessions for residents. These existing moments were additionally used to address appropriate testing. This facilitated the continuation of these strategy components. All interviewees perceived the strategy as effective in raising awareness and reducing inappropriate testing. None of the participants thought the project resulted in substantial cost savings.

However, the interviewees noted that the project was time consuming. Interviewees from hospitals 2 and 3 felt they did not have sufficient time for the project during the

intervention period nor follow-up, while the team members of hospital 1 felt they had sufficient time for the project during the intervention period but not during follow-up. The required time investment was not compensated for and was additional to their usual workload. Additionally, one internist mentioned that the current workload limits doctors from thinking critically about the appropriateness of all the requested tests. Participants of hospitals 1 and 3 mentioned that after the project had ended, other important topics were prioritized over appropriate testing. Hospital 2 kept prioritizing appropriate diagnostic testing during the follow-up period, and in addition expanded their focus to appropriate care, including diagnostic testing and treatment.

Discussion

In one of two intervention hospitals included in the quantitative analysis, the reduction in the laboratory testing volume was sustained during the final year of the follow-up period compared to the preintervention period. In the control group, the testing volume significantly increased during the same period. However, hospitals 1 and 2 did both show an increasing trend in laboratory tests during the follow-up period. This indicates that the effectiveness of the strategy was not fully sustained, even though awareness of appropriate testing remained, according to the project members. The majority of the facets of the RODEO strategy were discontinued or lessened during the follow-up period. Facets that were compatible with daily practice and automated were better preserved than facets that were perceived as not effective or that required a substantial time investment. The sustainability of the strategy was hindered by changes in the environment and the organization, such as the withdrawal of the coordinating project team and the high turn-over of residents.

Hospital 2 showed a better sustained test volume reduction than hospital 1. The interviewees from hospital 2 identified resident education, active ambassadors and order system changes as the most valuable strategy facets. A recent systematic review underlines that modifications in the electronic ordering systems are most often highly effective compared to other strategies.(7) Additionally, long-term ambassador engagement is also acknowledged as an important factor in the sustainability and can be facilitated by organizational support, appropriate compensation and opportunities for professional development. (24-26) Although both hospitals maintained resident education and the adjustments to protocols and working agreements, these components were insufficient to sustain a volume reduction in hospital 1. While education-based strategies are frequently studied, it seems to be the least successful strategy type.(7, 12) However, including education in a multi-faceted strategy tends to increase a strategy's effectiveness.(13)

In addition, certain facilitators remained during follow-up in hospital 2 but did not in hospital 1. First, the aim to reduce testing volume was maintained in hospital 2, as well as the prioritization of the project. Both factors may have enhanced the staff and resident engagement in the long-term. In addition, hospital 2 remained data driven, while hospital 1 discontinued the focus on data. Therefore, we hypothesize that a combination of ongoing engagement of ambassadors, permanent order system changes, a data-driven approach and education, is important for sustaining results. Further research is needed to verify necessary elements for the sustainability of de-implementation strategies.

Sustaining the effects while lowering the intensity of the strategy would be the optimal situation. However, it is difficult to predict the minimum required intensity to maintain the positive outcomes of the strategy. (10) Therefore, we recommend scaling down stepwise while monitoring and acting upon unwanted effects. Monitoring is also important because the local context evolves over time. (26) To detect the impact of these changes, monitoring of the desired outcomes remains necessary, so that unwanted trends can be identified and acted upon. This means the strategy will require a continued investment in the long term. This is also acknowledged in the literature. (10, 27) This required ongoing investment should be considered when designing and implementing de-implementation strategies to optimize its feasibility after the project is finished. (28, 29)

All hospitals were affected by the discontinuation of the a dedicated coordinating team. The RODEO researchers organized network meetings with the hospitals, supported the local teams with benchmark data and its interpretation, and ensured prioritization of this project in the participating hospitals. However, the influence of a coordinating research team between the study period and after is not always acknowledged in the literature about long-term sustainability. For example, a systematic review describing strategies for reducing inappropriate laboratory testing defined sustainability as a study conducted over more than one year, including the pre-intervention period. (7) These studies could also be considered as having a long study periods rather than measuring the long-term sustainability. This highlights the importance of applying a universal definition of sustainability to improve the comparability of studies.

The sustainability of a strategy can be described from various perspectives resulting in different outcomes. (30) In this study, we determined the difference in mean testing volume between the pre-intervention period and follow-up, as well as the trends in laboratory testing volume during the study periods. Hospital 2 managed to sustain the reduction in the final year of the follow-up period but also showed an increase of laboratory tests during follow-up. Therefore, the strategy needs to be intensified to sustain the volume reduction after our study period. In addition to these quantitative outcomes, the project members from both hospitals emphasized that their most

important outcome was the increased awareness of appropriate diagnostic testing. In their perception, this has been sustained in both hospitals.

Limitations

This study has a few limitations. First, the follow-up period was limited to 22 months due to the start of the COVID-19 pandemic. The patient population of the hospitals changed substantially during the pandemic, and consequently, the ordering of laboratory tests also changed. Furthermore, only two of the four hospitals that participated in the RODEO project were included in all parts of the study. One hospital rejected our invitation for participation, and the other could not provide reliable quantitative data for the entire time period. The hospital that rejected the invitation did not achieve a significant reduction during the original study. Therefore, participation bias must be considered during the interpretation of the study results. Moreover, this study lacks the perspective of the residents, as no residents were employed in the same hospital during both the intervention and follow-up period. It remains uncertain whether the residents who were involved in the project would have perceived the sustainability of the strategy outcomes and components the same way as the interviewed project members. Last, there may be some recall bias because the interviewees had to describe the situation up until three years earlier. However, the strategy was still a part of their daily activities. Therefore we suspect that this did not have a large impact on the results.

Conclusion

In one of two intervention hospitals the reduction in laboratory testing volume was sustained for almost two years after the end of the project. Despite the project members' perception that the awareness about appropriate testing remained high, both hospitals showed an increasing trend in the number of laboratory tests during follow-up. The strategy facets that were compatible with daily practice and that were automated were better maintained than the facets that were less effective or required a substantial time investment. This should be taken into account when designing de-implementation strategies. The organization and the context may change in the long term. Therefore, monitoring the desired outcomes and responding to unwanted trends is recommended. Additionally, continuing to raise awareness and repeated education is recommended because of the high turn-over of residents.

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Additional file 1

Characteristics of invited intervention hospitals[a]

	Zaans Medical Center[b]	Meander Medical Center[b]	North-West Hospital group	Spaarne Gasthuis
Annual emergency department visits for internal medicine, No	3000	4400	3800	6000
Annual outpatient department visits for internal medicine, No	25000	37600	36900	54200
Annual inpatient admissions for internal medicine, No	1800	2900	3000	4248
Internists, No	13	16	18	21
Residents, No	17	30	20	60

[a] *all invited hospitals are presented to ensure the anonymity of the non-participating hospital.*
[b] *Hospitals in quantitative analysis*

Additional file 2

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Domain 1: Research team and reflexivity

Personal Characteristics

1. Interviewer/facilitator. Which author/s conducted the interview or focus group?
   - DK
2. Credentials. What were the researcher's credentials? E.g. PhD, MD
   - MD and MSc
3. Occupation. What was their occupation at the time of the study?
   - Researcher
4. Gender. Was the researcher male or female?
   - Female
5. Experience and training. What experience or training did the researcher have?
   - DK conducted and published multiple qualitative studies.

Relationship with participants

6. Relationship established. Was a relationship established prior to study commencement?
   - Yes. They have met before during other meetings. These meetings were about sharing experiences of the RODEO project.
7. Participant knowledge of the interviewer. What did the participants know about the researcher? e.g. personal goals, reasons for doing the research
   - The participants were aware of the study design and study objectives.
8. Interviewer characteristics. What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic
   - The participants knew about her background and that she was affiliated with the Dutch program To Do or Not To Do (a national program to reduce low-value care), which also funded the original RODEO project.

Domain 2: study design

Theoretical framework

9. Methodological orientation and Theory. What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis.
   - We deductively coded the transcripts using a framework for the sustainability of innovations.

Participant selection

10. Sampling. How were participants selected? e.g. purposive, convenience, consecutive, snowball
    - We used purposive sampling to select participants.
11. Method of approach. How were participants approached? e.g. face-to-face, telephone, mail, email
    - Participants were invited by e-mail.
12. Sample size. How many participants were in the study?
    - Seven participants
13. Non-participation How many people refused to participate or dropped out? Reasons?
    - One internist refused to participate without providing a reason.

Setting

14. Setting of data collection. Where was the data collected? e.g. home, clinic, workplace
    - Due to the COVID-19 pandemic, the interviews took place digitally.
15. Presence of non-participants. Was anyone else present besides the participants and researchers?
    - No
16. Description of sample. What are the important characteristics of the sample? e.g. demographic data, date
    - Seven members of the original project teams were interviewed: three internists, one business controller, two clinical chemist and one hospital manager department participated

Data collection

17. Interview guide. Were questions, prompts, guides provided by the authors? Was it pilot tested?
    - The topic guide was discussed with the other researchers who were also involved in the RODEO project. It was not pilot tested.
18. Repeat interviews. Were repeat interviews carried out? If yes, how many?
    - No.
19. Audio/visual recording Did the research use audio or visual recording to collect the data?
    - The focus groups were audio recorded.
20. Field notes. Were field notes made during and/or after the interview or focus group?
    - Yes.

21. Duration. What was the duration of the interviews or focus group?
    - 41-58 minutes.
22. Data saturation. Was data saturation discussed?
    - Data saturation does not apply for the used method, because all potential participants were invited to participate.
23. Transcripts returned. Were transcripts returned to participants for comment and/or correction?
    - No.

Domain 3: analysis and findings

Data analysis

24. Number of data coders. How many data coders coded the data?
    - DK and AWB independently coded all interviews.
25. Description of the coding tree. Did authors provide a description of the coding tree?
    - Yes, table 4.
26. Derivation of themes. Were themes identified in advance or derived from the data?
    - Yes, the domains and subdomains of a sustainability of innovations framework were used.
27. Software. What software, if applicable, was used to manage the data?
    - ATLAS.ti and MaxQDA 2022
28. Participant checking. Did participants provide feedback on the findings?
    - Yes, a member check was done by phone with the clinical leaders of hospitals.

Reporting

29. Quotations presented. Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number.
    - There are quotes included to illustrate the findings. The quotes are identified with the role of the participants and the number of the hospital.
30. Data and findings consistent. Was there consistency between the data presented and the findings?
    - Yes.
31. Clarity of major themes. Were major themes clearly presented in the findings?
    - Yes.
32. Clarity of minor themes. Is there a description of diverse cases or discussion of minor themes?
    - Yes.

Additional file 3

Topic guide

- What did you think of the results you achieved with executed strategy during the RODEO project?
- Did you communicate about this result within the department and the hospital? If so, how did that go?
- Was there attention given to appropriate laboratory testing after RODEO?
- How did the period after RODEO go in terms of attention to appropriate laboratory testing? For example, was there discussion about maintaining the strategy components? If so, how did that go? If not, why not?
- Were targets set and/or a plan made to maintain the result? Why or why not?
- Have there been developments that influenced the sustainability of the RODEO results?
- If the study had continued for another year in the same setup, what effect would that have had? And why?

All strategy component will be discussed.

- For each strategy component that has been continued:
  - What is the reason you continued this intervention?
  - How did that go? Were there any difficulties? If so, what challenges did you encounter and how were they addressed?

- For each stopped strategy component:
  - What is the reason that this component was discontinued?
  - Who were involved in making this decision?

- What efforts were made to maintain the results?
- What hindered you to maintain the results
- What enabled you to succeed in this?
- What has stimulated the sustainability in your hospital, department and team?

Additional file 4

Number of laboratory tests per patient contact in the control hospitals

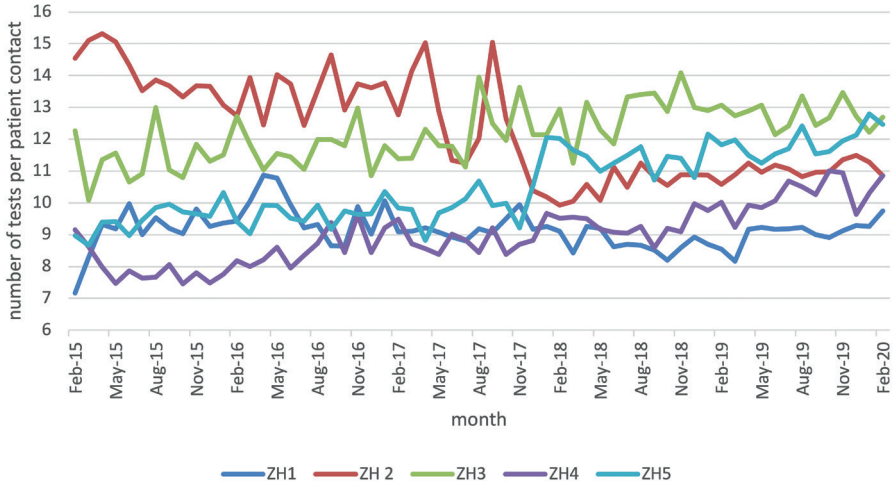

Figure 1 | Number of laboratory tests per patient contact of the control hospitals during the study period

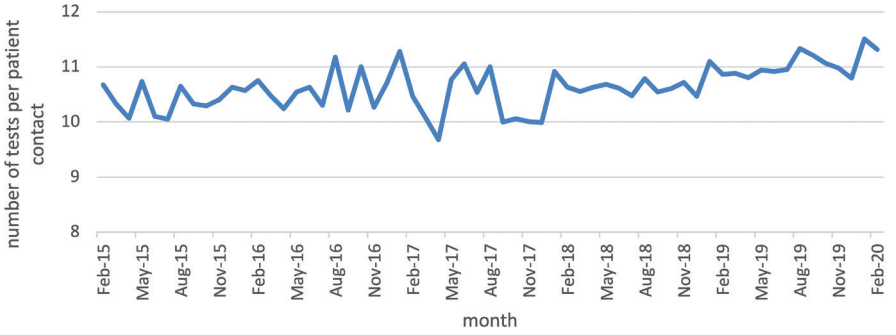

Figure 2 | Mean number of laboratory tests per patient contact of five control hospitals

Additional file 5

Framework sustainability of healthcare innovations by Crespo-Gonzalez et al. (1)

		Sustainability factors
External context/ environment	Socioeconomic and sociopolitical environment	Funding/Strategic funding/Funding stability/ Financing
		Policies/regulations/Legislations/Political Support
		Enabling environment/Access to care
Local environment	Partners (Stakeholders)	Partnership
		Communication/Feedback/Demonstration of innovation effectiveness/Incentives/Goals
		Networking/Involvement/participation/ engagement/commitment
	Community/Patients	Culture/beliefs/needs/Knowledge
		Motivation/Involvement/Trust/Participation/ Ownership
		Support/Sensitization/Perception of effectiveness
Organization	Staff	Training/Supervision/Support
		Skills evaluation/Monitoring
		Feedback/meetings
		Motivation/Involvement/Trust/Goals/Strategic planning
		Knowledge/Information
		Workload/Staffing
		Needs/Beliefs/Culture
		Incentives
	Leader/Champion	Organizational capacity/Governance
		Leadership
Innovation	Process	Adaptation/Adaptability/Improvement
		Program evaluation/Monitoring/Data evaluation
		Integration/Fit/Alignment/Compatibility
		Promotion/Spreading
	Characteristics	Benefits/Effectiveness/Legitimacy/Quality
		Complexity
		Demand
	Resources	Time
		Money/Financial
		Availability of materials/infrastructure
		Staff

Reference

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Additional file 6

Quotations with their corresponding influencing factor

Identified factors	Quotes
Local environment – Partners/stakeholders	
Networking Meetings with other hospitals about appropriate testing	'What I miss, for example, are the meetings we had with other hospitals, because that is where you get new ideas. You can not research everything on your own. [...] Some hospitals would come up with ideas like, 'The guideline says this, but why are we all doing it this way? This approach is just as effective, or it adds nothing to patient care. Why are we still doing it?' There are some ideas you just would not think of yourself. [...] I think it would be ideal if we could have such a meeting once every three months or twice a year.'- clinical leader hospital 2
Incentives Alignment of financial incentives of the laboratory and hospital	'[Our laboratory] is an external company, of which we are both clients and shareholders. So, the relationship is somewhat complicated. What they do at that company is offer more discounts the more you order. [...] Previously, we had agreements that were independent of the volume of tests. Because otherwise, you are not focusing on the patient, you are just trying to order more to get a discount. I did not think that was right. So, when we started ordering fewer tests, our costs actually increased.' - clinical leader hospital 2
Involvement Involvement of a dedicated external research team in the project	'[..] RODEO really helped us bring [appropriate testing] to the forefront. People became much more engaged with it. The fact that you are participating in a multicenter study helps motivate some people: 'Guys, we can not lay back. We have to move forward.' Sometimes we needed that kind of pressure.'- clinical leader hospital 2
Organization – Staff	
Skills evaluation/monitoring Presence of skills for meaningful interpretation of data	'Because those numbers are so abstract, you have no control over whether they actually reflect what you investigated. I found it challenging that it feels so disconnected from my control and experience as a doctor. I don't have a sense of what those numbers represent.' – clinical leader hospital 3.
Motivation Staff and residents have intrinsic motivation to improve the appropriateness of diagnostic tests	'I just enjoy it. So yes, I usually work more hours than my contract specifies, but I simply find it fun. It's too boring to only focus on one thing.' – hospital manager hospital 2

Strategic planning The project members have a plan to achieve sustainable effects	'The challenge is that you can have all the systems in place, but you must automate as much as possible; otherwise, you will constantly need to train new people. The turnover in large hospitals is even worse than ours, so you end up repeatedly saying, 'Hey, we didn't agree on this.' And then the next group comes in and says, 'Hey, what's this? We didn't agree on this.' Therefore, I believe the most important aspects are the resident training program, the redundancy checks and order set changes.' – hospital manager hospital 2 'You need to have ambassadors for the project. Without local champions, there are no ambassadors to guide the younger generation —the ones on the floor—to explain things to their younger colleagues. If a medical specialist address the topic, it has a different impact compared to when it comes from a peer. By educating and training the residents about appropriate care, you will still benefit from it in ten or fifteen years' - clinical leader hospital 2.
Goals The goal is awareness and critical thinking about diagnostic testing	What I feel is most important is that everyone takes the time to think about it. I had it in my mind that through [...] the education sessions, we were at least keeping that awareness alive: with every test I order, I need to consider whether it's really necessary – clinical leader hospital 3.
Staffing Consistence of the team: low turn-over of residents	'You have to repeat it 100,000 times. It is unbelievable. But the residents rotate every two years or so. It is surprising how little sticks over time; you constantly have to repeat things, which isn't a problem, but retention is an issue. At one point, we had a top 10 list from Rodeo posted on a piece of paper here, and I occasionally look at it. It is hanging in the handover room, and I'm always struck by how all ten points remain relevant..' – clinical leader hospital 1. I noticed that the residents no longer understood why we were doing it [education sessions about inappropriate testing], so they didn't find it very useful and weren't sure what to say. Then I thought: oh right, the entire group that was involved back then is gone, and now there is a whole new group of residents. I do find that a bit frustrating sometimes—feeling like you have to start all over again every two years' – clinical leader hospital 3.
Innovation – Process	
Spreading Elements of the strategy are disseminated to other departments	During the RODEO period, we also created a pocket card with the prices for the most commonly requested tests in internal medicine. Some other departments saw this pocket card and requested similar information for the tests relevant to their own departments – clinical chemist hospital 3

Innovation – Characteristics	
The cost reduction is perceived as substantial	'Basically, you save on [...] reagents [..] and staffing. However, reagents usually are not expensive, and to actually save on staffing, you would need to significantly reduce the workload—a lot less, in fact. So the real focus is not on cost savings, but on improving the quality of care, improve test orders, and reducing the burden on the patient'– business controller hospital 1.
Innovation – Resources	
Time	
The project members feel that they had sufficient time for project	'These kinds of projects take a lot of time and are very useful, but then the next moment there are [major changes] on the agenda. Suddenly, you find yourself involved in six working groups. So, if I had more time, I would definitely do it, but the time factor means you keep shifting from one thing to another, thinking, 'Alright, I've finished this, and then something else comes up.' – clinical chemist hospital 1.
The clinical leaders feel that there is sufficient time for appropriate testing	'As a doctor, you're always in a rush, and we are already moving much faster than before, but you can speed things up by simply checking one box, which orders the entire lab panel, and that is incredibly convenient. When you think critically, you must check six different boxes, but that extra time is just something you do not have' - clinical leader hospital 1.
The project has priority over other projects and activities	'[After the local champion of RODEO left], there was a resident with interest in polypharmacy who, of course, had the same enthusiasm as [the local champion] had for inappropriate testing. You think, 'That's great,' but then it fades away after two years. You have to be careful not to become cynical, but sustaining what you do is the most challenging part.' – clinical leader hospital 1.

8

General discussion

This thesis consists of de-implementation research and searches for opportunities to enhance the impact of future de-implementation efforts. It started with an overview of the effectiveness of various strategies reducing inappropriate drugs (**chapter 2**). Subsequently, we discussed various mechanisms that hinder the translation of capacity saving into cost savings (**chapter 3**) and we empirically studied which mechanisms influenced the achievement of societal cost-savings in the case of prehabilitation (**chapter 4**). Furthermore, we extracted determinants of successfully scaling innovations from the literature and assessed which ones were applicable for the scaling of de-implementation strategies (**chapter 5**). This resulted in a conceptual framework that was used to scale multiple de-implementation projects. In one of these projects, an information tool for dyspeptic patients, was scaled and the effects were evaluated in this thesis (**chapter 6**). And last, we studied the long-term effects of a strategy reducing inappropriate laboratory testing and identified factors influencing the continuation of the strategy in the long-term. (**chapter 7**).

In this chapter, I will reflect on the main findings and provide suggestions for both research and practice. Additionally, the limitations of doing research in real-world setting are discussed. The topics that will be addressed are the following:

- Savings: The value of not doing
- Scaling: Spread and scale to increase impact
- Sustainability: Securing future benefits
- Research in real-world setting
- Implications for future research
- Opportunities to increase impact

Savings: the value of not doing

De-implementation strategies encourage healthcare professionals to provide less low-value care. The effectiveness of such strategies is usually described by the achieved reduction of low-value care practices.(1-4) Therefore, this outcome was used in **chapter 2** to identify the most frequently effective strategy types. Multi-faceted strategies seem to be most frequently effective, and while education was the most studied strategy, it was also the least frequently effective one. Other reviews underline these findings, but additionally emphasize that integrating education into a multifaceted strategy enhances its effectiveness.(3, 5)

While the reduction of low-value care is an important outcome, it fails to describe the relevance of the de-implementation for patients and society.(6) Literature states that de-implementation strategies have the potential to save costs and resources, and prevent

adverse events.(1, 7-9) However, to determine whether such savings and gains have been achieved, additional outcome measures need to be assessed, such as the prevalence of side effects, patient-reported experience measures (PREMs), patient-reported outcome measures (PROMs), and real-world cost savings. (10) Even though improvement of these outcomes are among the claimed advantages of de-implementation, they are rarely studied.

The impact of de-implementation strategies on both quality of care and cost savings are frequently only estimated. The problem is that especially cost-savings are typically highly overestimated. For example: a de-implementation strategy to reduce vitamin D testing was estimated to save 1.5 million Canadian dollars per year; eliminating inappropriate imaging could lead to annual savings of 50-100 million US dollars; and phasing out five low-value general surgery procedures could save over 150 million euros per year.(11-13) In **chapter 3**, we discussed why such estimations exceed the actual savings potential. In case of societal savings estimations, a common assumption is that the total volume of the provided care declines proportionally after low-value care is reduced. This decline would automatically induce cost savings. Cost savings are often calculated by multiplying the number of reduced practices with the average unit cost. However, this number fails to accurately describe the true savings potential for several reasons: 1) the average unit costs do not resemble actual hospital costs, 2) the reduced low-value care may be replaced with other care, 3) payment systems hinder either de-implementation or the transfer of cost savings from organizations to society, and 4) de-implementation may also result in additional costs which are often not taken into account, such as project costs and expenses on the costs for the alternative of the de-implemented low-value care.

Accurately estimating cost savings is complex because the actual savings depend on context specific factors, including the financial structures and agreements. An example is the case of the RODEO strategy, of which we determined the long-term effects in **chapter 7**. The RODEO strategy successfully reduced the number of laboratory tests in four hospitals. However, the opportunity to reduce hospital expenses depend on the organization and agreements between the laboratory and the hospital. For example, a hospital can outsource laboratory testing and pay per test. In this case, a volume reduction will directly reduce hospital expenses. However, some hospitals with an outsourced laboratory agreed upon bulk discounts. This means that reducing laboratory tests may even cause a net increase in costs if the minimal test volume is not reached. For hospitals that own their laboratory, cost savings are also limited in the short term. These hospitals can initially only save the marginal costs of laboratory testing, such as the reagents and tubes. The marginal costs cover only a small portion of the total expenses, while the largest expense is labor costs. (14) Moreover, some tests are conducted simultaneously, irrespective of whether each of those tests is specifically individually requested. This means that reducing the requested number of some, but not all of those tests, will not result in actual cost savings since all tests will be conducted either way.

Achieving cost savings by reducing laboratory tests may be optimized when several aspects are considered. First, time, tubes and burden are saved when less often blood is drawn rather than ordering less tests per draw. Reducing the number of inappropriate drawings could therefore be a specific aim. Furthermore, some tests have high marginal costs due to the required reagents, therefore it could be interesting to focus on reducing these tests. In addition, some tests are not costly but are time consuming. Reducing these can substantially reduce the workload. And last, if you act on a large scale, a small reduction can already have a impact. Therefore frequently ordered tests may also be an interesting focus.

In **chapter 4** we identified factors influencing the translation of freed capacity to societal cost savings. We used a quality improvement initiative as a test case, because similar to de-implementation, it could reduce the required care provision and free up hospital capacity. The study shows that it is challenging to achieve societal cost savings by freeing up care capacity. Substantial cost savings rely mainly on scaling down workforce, and many stakeholders considered this undesirable due to the current shortage of healthcare professionals. (14) Moreover, all interviewed stakeholders expected that any free capacity will be used for either providing care to other patients or other valuable activities such as: spending more time with patients or for educational activities. Exiting literature underlines that the healthcare system incentivize providing other care rather than scaling down. (15, 16) Therefore, we argue that the value of quality improvement initiatives like prehabilitation is increasing the accessibility of care rather than reducing costs.

Acknowledging the real-world value of de-implementation projects is essential for policy decision making. In the case of de-implementation, policy makers calculated unrealistic cost savings estimations. Therefore, de-implementation was seen as lucrative cost cutting measure and presented as the solution for the budget deficit in the Dutch coalition agreement in 2021.(17) Beside the overestimation of potential savings, policy makers did not take into account that re-allocation of cost savings to other fields is complex and deemed to be unrealistic. (18)

As **chapter 4** shows, in some cases, the real-world value of not doing is the ability to provide other high-value care rather than achieving societal cost savings. Policy decision making would benefit from a broad perspective including the effects on accessibility of care as well. There is currently an increasing shortage of nurses, while simultaneously the demand for care is expected to increase in the next two decades. (19) Freeing up capacity would be highly valuable in areas suffering from a shortage of personnel when the free capacity is used for high value care. De-implementation holds the ability to contribute to this.

Scaling: Spread and scale to increase impact

The scaling of effective de-implementation strategies has two major advantages over starting a new project: the required investments are much lower, as is the risk of failing since the effectiveness is already proven. The scaling of projects occurs slowly, but often not at all.(20) In **Chapter 5**, we have identified determinants in four domains that can facilitate the scaling of successful de-implementation strategies. This framework was applied to support the scaling of several strategies of the Dutch national program To Do or Not To Do?. I will highlight aspects of a few scaling projects to illustrate the four domains: the scaling plan, the strategy, the adopters and the external context.

Scaling Plan

Someone or a team must be responsible for the scaling. This scaling team has several tasks: making potential adopters aware of the project and supporting them in implementation; evaluating and adjusting the original strategy; and stimulating implementation. For example, the RODEO strategy – of which the sustainability was studied in **chapter 7** – was scaled. The scaling was coordinated by a scaling team consisting of two program members and two key figures from the original project. Together, they created tools to support new teams: a toolkit, literature list, and a project plan template. Subsequently, the scaling team actively sought out interested internists and medical residents by reaching out within our professional network. For each interested local team, a presentation was held to get started. There was a lot of enthusiasm, but it proved difficult to translate this into the actual start of their project. Therefore, a learning network was created to motivate and inspire local teams. This turned out to be an essential part of the scaling strategy.

For the scaling of a project aimed at reducing inappropriate vitamin orders, the scaling team needed to raise awareness among general practitioners (GP). A different approach was needed to reach the majority of the GPs. The scaling team published and article in a well read GP journal, the project appeared in several newsletters and it was mentioned in already existing educational programs provided by laboratories. (21)

The strategy

Potential adopters are more likely to embrace a de-implementation strategy if they are convinced that certain care does not add value to the patient, too much inappropriate care is being provided in their organization, and the strategy is effective. This requires strong evidence on all three points. Moreover, the project must be feasible and the time investment should be limited. The scaling team should evaluate the project and adjust it where necessary. An example of an adjusted strategy is the scaled education tool we studied in chapter 6. The original project was aimed at patients with inappropriate referrals for an upper gastrointestinal endoscopy. All participants were selected by a

researcher who manually screened the referral letters. This was not a feasible approach for the scaling. Therefore, the scaling team collaborated with the national patient information website thuisarts.nl (GPinfo.nl). (22) The e-learning was transformed into a patient education tool that is currently publicly available on thuisarts.nl and no longer requires manual screening.

Adopters

De-implementation strategies will be adopted by healthcare professionals who are motivated to change and are able to change. Healthcare providers who are aware of the negative consequences of certain healthcare services are more willing to stop those practices than others. It is the scaling team's task to identify these clinical leaders. One of the scaling projects of *To do or not to do*? aimed to reduce inappropriate use of catheters and infusions in hospitals. During the scaling, there was limited enthusiasm among doctors which were the initial project leaders. Conversely, nurses were highly motivated as they recognized the burden of inappropriate catheters. Therefore, a nurse was appointed as the scaling coordinator and reached out to enthusiastic colleague nurses. Changing the target group turned the scaling into a success.(23)

External Context

The external context may contain incentives to adopt a project, such as clear clinical guidelines, accreditation points for educational meetings, and project grants for de-implementation efforts. While it is possible to add such incentives, it may require a substantial time investment. For example, the coordinator of the vitamin project contacted Thuisarts.nl to update the online patient information to align with existing clinical guidelines. Additionally, the scaling team applied for accreditation of the online training, so that healthcare professionals received accreditation points upon completion. Furthermore, the uptake of scaling projects was also facilitated by increased awareness, which raised by multiple organizations. For instance, a national program *Zorgevaluatie en Gepast Gebruik* (Healthcare Evaluation and Appropriate Use) brought all stakeholders together and prioritized the appropriate use of care and the Dutch medical journal (NTvG) introduced a section 'healthy healthcare' in which articles about appropriate care were published. (24, 25)

These examples show how the SPREAD framework can be applied to scale projects. A scaling team should consider all determinants identified in **chapter 6** and address the ones relevant to their project. Similar to de-implementation, there is no one size fits all for scaling. (26) The examples show that the scaling of a strategy aimed at general practitioners required a different approach than a hospital based project. In addition, these examples also show that the scaling team needs to have access to financial funds. These funds are essential to adapt the strategy and compensate the time investment

of experts. However, a responsible team with sufficient funds is often lacking. Research funds and other sources of funding are mainly focused on starting new projects rather than the scaling of existing knowledge. As a consequence, new knowledge is gained, but existing knowledge is not implemented on a large scale.

The second domain shows that scaling requires adapting the strategy to fit the setting it is scaled to. However, modifications can change the effectiveness of the strategies. In **chapter 6**, we described the scaling of the education tool for dyspeptic patients and studied the effects of the adapted tool. The original education tool was modified reduce the manual labor, to fit a broader public and to match the design of *Thuisarts.nl*. The scaling resulted in a real-world implementation and broad usage of the educational tool. However, as a consequence of the modifications, the scaled tool had a different focus: to reassure dyspeptic patients, and to increase knowledge and awareness of opportunities for self-management. We found that a majority of the participants were willing to try recommended lifestyle changes in order to reduce their symptoms, and a substantial portion also succeeded. Moreover, the majority of the participants felt reassured after finishing the education tool. Because health-related fears and concerns are associated with increased medical consultations and low-value care, reassurance can be an important aim of patient-targeted de-implementation strategies. (27-30) And last, some participants intended to seek medical care after the education, while prior they did not. This indicates that the tool could support informed decision-making and may prevent underdiagnosis as well. These results emphasize the importance of scaling and real-world implementation of patient education.

Sustainability: securing future benefits

The impact of de-implementation efforts can be increased when the results sustain in the long-term. **Chapter 7** demonstrates that achieving long-term effects is feasible, but it requires continuous efforts. In addition, we found that the long-term sustainability was hindered by the withdraw of the coordinating research team, a high turnover of residents, and the required time investment. The original project was coordinated by an external project team. After their withdraw, the project was no longer externally supported and prioritized, and solely relied on the internal motivation of the local team. This resulted in a decreased intensity of the strategy in all hospitals. In addition, the strategy demanded a considerable time investment additional to their already high workload. Moreover, the time investment detracts from other valuable tasks and de-implementation efforts. The identified barriers were are similar to the ones regarding the sustainability of a strategy reducing peripheral intravenous catheters.(31) The authors concluded that the strategy remained effective five years after its start. No association was found between the

number of continued strategy components and the achieved results, indicating that it may be possible to maintain the effects while lowering the effort. However, finding the optimal balance remains challenging.

Long-term effects of strategies are rarely studied from the viewpoint of a changing context. (3, 5, 31) In chapter 7, we explicitly addressed the change by comparing influencing factors during the intervention period and the follow-up period. Contextual changes may impact the effectiveness of the strategy. For instance, continuous education on new topics is necessary to expand the focus. However, hospitals have a high staff turnover especially for residents who play an important role in test ordering. This implies that repetition of topics is also required to educate the new staff. Another significant change was the withdrawal of the external research team, which assisted with data interpretation, organized meetings on efficient diagnostics with other hospitals, and ensured project prioritization. Additionally, a change in the order entry system allowed individuals to create their own standard request packages. This led to an increase of the testing volume. Such changes need to be addressed to maintain achieved results. Not all changes are predictable, and even predictable changes may have uncertain impacts. Therefore, we recommend to continue monitoring and to respond to undesirable trends.

Conclusions about the sustainability depend on the chosen outcome measure, because the sustainability can be described from various perspectives: the patients, healthcare professionals/healthcare organizations, and the strategy.(32) From the patient's perspective, sustainability means not receiving the initially prevented low-value care practice after a period of time. From the perspective of a healthcare organisation, it means not providing low-value care to future patients. And from the perspective of the strategy, sustainability means maintaining the same effectiveness over time. In **chapter 7**, we assessed the sustainability from the perspective of the hospitals and the strategy. We found that in the final year less tests were performed compared to before the start of strategy. Thus, from this perspective, long-term sustainability was achieved because future patients received less low-value tests. However, we also observed that there is an increasing trend of laboratory testing, meaning that the effectiveness of the strategy is declining over time. Awareness of these different perspectives is crucial for a adequate interpretation and comparison of long term effects.

Research in real-world setting

We studied strategies and interventions that were implemented in clinical practice. This is important because clinical studies are frequently conducted within regulated environments and may apply strict inclusion criteria for the study population.(33-35).

However, it also means that some of our study designs were limited by the real-world setting. For example, in **chapter 7**, we retrospectively studied the long-term effects of a de-implementation strategy. The retrospective nature allowed us to study what happened in a real-world setting without interference of a research team. However, it also lead to a sole focus on the testing volume instead of also measuring the impact for patients or society. The hospitals could not retrospectively provide reliable data regarding the amount of blood samples, prevented downstream testing, or real-world cost savings. In addition, **chapter 6** also shows the methodological limitations of doing research in real-world setting. In the original study, the participants were selected based on their medical information and their referral for an upper gastrointestinal endoscopy. (34) The scaling team made changes to the education tool and made it publicly available on *Thuisarts.nl*. The availability of the tool was prioritized over a strong study design. Ideally, we would have collected data of the participants before, during and after using the tool, but this wat not compatible with making the tool publicly available. Furthermore, the scaled tool was aimed to inform patients about self-management and medical diagnostics and aimed at a broader audience. Therefore, we studied to what extend these goals were achieved. In contradiction to the original study, we did not assessed if the tool improved the appropriateness of care because this would require a different research design. This was also not compatible with making the tool available on *Thuisarts.nl*.

Implications for future research

This thesis contains important findings that can increase the impact of de-implementation strategies, and additionally revealed interesting areas for further scientific research.

- We concluded that for some cases, the real-world value of not doing is the ability to provide more high-value care. However, more evidence is needed on the situation after low-value care is reduced. What happens with the care capacity that is freed up by de-implementation efforts? In which circumstances leads reduction of low-value care to more high value care? Are efforts needed to prevent the replacement of low-value care with other low-value care practices? Answers to these questions can guide policy makers and healthcare organization to further increase the impact of de-implementation efforts on a societal level.
- De-implementation strategies are frequently studied within regulated environments and among selected patient populations. More research is needed to determine the effects of de-implementation strategies in real-world setting.
- Maintaining achieved results is challenging and hindered by the lack of time to prioritize the strategy. Therefore, future research should focus on finding the optimal balance between the long-term investments and the benefits of the strategy.

Opportunities to increase the impact of de-implementation efforts

The findings in this thesis provide various opportunities to increase the impact of de-implementation efforts. Because de-implementation requires time and financial investments, not all low-value care can be addressed at once. To increase the impact of de-implementation, I suggest to: 1) prioritize the de-implementation of low-value care based on the desired outcomes, 2) design strategies that will be scalable and sustainable, and 3) prioritize scaling of effective strategies.

1 | Prioritize based on desired outcomes

De-implementation of low-value care is not a goal, but a method, for example, to improve the quality of care. It is important to identify issues in healthcare and assess whether de-implementation is a suitable method to solve the problem. De-implementation of low-value care could be used to prevent harm for patients, free up care capacity or to reduce costs, but the impact varies among low-value care practices. Based on the desired outcomes, specific low-value care practices should be prioritized, for example:

- To prevent harm for patients, one should identify low-value care risking severe complications or low-value care with a high prevalence of complications.
- To free up care capacity, time consuming low-value care practices should be identified and de-implemented.
- To reduce costs in the shorter term, low-value care with a high variable costs should be targeted. For example, medication and care that requires expensive disposable products.

Some de-implementation projects discussed in this thesis do not meet these points. For example, a strategy reducing vitamin testing was scaled. Vitamin tests do not displace high value care, they do not cause severe side effects and reducing these tests not likely to save society considerable costs. That does not mean this project was low-value itself. First, many general practitioners recognized vitamin testing to be a highly prevalent low-value practice and they were motivated to reduce the testing volume. Therefore, this topic was a convenient start of de-implementation efforts at the general practitioners. In addition, raising awareness of inappropriate vitamin diagnostics created the opportunity to also discuss other low-value practices. Furthermore, valuable lessons were learned by studying and scaling the strategy. (23, 36) These lessons were shared nationally and internationally, which potentially increased the impact of other de-implementation efforts as well. And last, these and other positive results inspired the start of de-implementation in other fields, such as home-based nursing. (37) However, to increase the impact of future de-implementation efforts, I suggest to use de-implementation strategies to address a clearly defined problem and prioritize projects that can solve that problem.

2 | Design scalable and sustainable strategies

The impact of de-implementation strategies can be increased by scaling effective strategies and sustaining their results in the long-term. It is recommended to design de-implementation strategies based on an assessment of the barriers and facilitators. (26, 27) In addition to this, I would suggest to design strategies that are easy to scale and sustain. Based on chapter 5 and 6, the following aspects should be considered:

- Secure embedding in the daily practice. Projects that can be embedded in the daily practice are more likely to sustain and are more likely to be adopted.
- Limit the required time investment, especially after the implementation of the strategy.
- Limit the cost investment. Make sure the strategy does not require substantial ongoing financial investments that outweigh the financial or non-financial benefit.
- Ensure that the relevant outcomes are easy to monitor.

Scaling and sustaining both rely on de-implementation efforts of a local team, resulting in an overlap of important strategy aspects. In essence, the investment of time and resources should be limited for both targets. This may conflict with factors that enhance the effectiveness of a strategy. For example, some research suggests that more efforts would improve the effectiveness. (4, 38) This may not be compatible with the low efforts healthcare professionals are able and willing to invest in the long term.(31) Thus, it is necessary to find a balance between the required investments and the gains.

When designing a de-implementation strategy, it is important to have a long-term vision that considers the long-term feasibility and opportunities for scaling. Opportunities to embed the strategy in the normal practice is an important part of both scaling and ensuring the continuation, and can be simultaneously achieved. For example, many strategies consist of physicians education. If these education sessions and e-learnings are integrated with the existing accredited learning platforms, their reach can be enlarged and their continuation is guaranteed for a longer period. In case of patient education, websites like *Thuisarts.nl* could have a leading role in spreading information and maintaining the content up-to-date. This requires the collaboration with such organizations in early stages.

3 | Prioritize the scaling of effective de-implementation projects

Scaled projects are able to reach considerably more healthcare professionals and patients than local projects. (23) Therefore they have potentially more impact, while they require less financial investments. I suggest to use existing knowledge and de-implementation strategies, and invest in the scaling of effective projects. Without investments and a responsible team or organization, scaling will occur slowly or not at all. (20, 23) Therefore, funding organizations have an important role in funding the scaling

of effective strategies, while medical organizations have a role in the coordination of the scaling, i.e. a program such as Healthcare Evaluation and Appropriate Use, the National Health Care Institute, healthcare insurers or a medical federation. In the last decade, many initiatives have reduced low-value care practices and scaling these strategies can substantially increase their impact. (3, 9, 23, 39, 40)

Conclusion

This thesis revealed several opportunities to enhance the impact of de-implementation strategies. First, it should be noted that de-implementation of low-value care is not a convenient cost-cutting measure, but it can be used as a method to increase the quality and the accessibility of care. Second, to increase the impact of de-implementation efforts, the effective strategies should be scaled and implemented in real-world settings. This requires a dedicated team with sufficient time and financial resources. And last, the long-term effectiveness of strategies is not guaranteed and may requires ongoing efforts. To facilitate the long-term continuation, the required time investment should be limited. Therefore, we recommend designing de-implementation strategies with a long-term vision that considers the feasibility of continued efforts and the potential for scaling.

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A

Addendum

Summary

Samenvatting

Dankwoord

About the author

List of Publications

PhD Portfolio

Research Data Management

Summary

Low-value care refers to care practices that either provide no benefit to patients or where the risks and costs outweigh any potential benefits. Reducing low-value care can prevent harm to patients and potentially saves valuable resources as low-value care may limit the capacity to provide high-value care. Therefore, the interest in the de-implementation of low-value care has risen the last two decades.

There are five stages in de-implementation process: 1. identifying of low-value care, 2. designing de-implementation strategies, 3. evaluating strategies, 4. scaling effective initiatives, and 5. ensuring long-term effects. Many strategies have been proven to be effective in reducing inappropriate care, however less attention has been paid to the evaluation of the societal benefits, and the scaling and the sustainability of de-implementation strategies. Optimizing these aspects could increase the impact of de-implementation efforts considerably. Therefore, this thesis aimed to enhance the understanding of the de-implementation process, with the focus on achieving societal cost savings, scaling of effective initiatives, and ensuring their long-term sustainability.

This thesis starts by exploring if certain types of de-implementation strategies are consistently more effective in reducing low-value care than others in **chapter 2**. Strategies should be tailored to the relevant barriers and facilitators, however most strategies target only one or two barriers, such as lack of knowledge and awareness. In such cases, it would be helpful to know which strategy type has the most potential to reduce low-value care. Our overview revealed that multifaceted strategies were most frequently successful in reducing low-value drug prescriptions. Education for healthcare professionals was the most used strategy type, but also the least effective one with only halve of these strategies resulting in a decline. This underlines that solely increasing knowledge of healthcare professionals is often not enough to change their behaviour and routines. However, education may be a valuable component of a multifaceted strategy. Furthermore, our results suggest that involving patients may increase the effectiveness of de-implementation strategies.

In addition, our overview also shows that the effectiveness of de-implementation strategies is often determined by analysing the reduction of low-value care. While this is an important outcome, it fails to describe the relevance for patients and society. In the last years, de-implementation has been presented by policy makers as a method to enhance the quality of care while simultaneously reducing costs. However, the impact on both quality of care and cost savings are frequently only estimated instead of studied in the real world. This is a problem because especially cost-savings are typically highly overestimated. In **chapter 3**, we described various mechanisms that hinder achieving

societal cost-savings by reducing low-value care. In this perspective, we argue that the estimations are mostly based on the average unit costs which do not resemble actual hospital expenses. The potential cost savings of performing one surgery less are considerably lower than the average unit cost, because most costs are fixed or semi-fixed. Another barrier is the substitution of the reduced low-value care with other care, that may be of high-value but also low-value. This is a 'natural' phenomenon in healthcare systems that needs to be actively targeted. Moreover, payments systems act as a barrier. Fee-for-service systems financially stimulate providing more care, and are therefore a direct barrier of de-implementation. De-implementation in a global payment system can be profitable for the healthcare organizations, but any savings are not automatically transferred to society. And last, de-implementation may result in additional costs such as the project costs and costs for the alternative of the de-implemented care. These costs also need to be taken into account, but are often overlooked.

To increase the understanding of the process from freeing capacity to achieving societal cost savings, we interviewed stakeholders to identify relevant influencing factors in **chapter 4**. Prehabilitation was used as a test case for this study. It is a pre-operative lifestyle improvement program that holds the potential to reduce the number of surgical complications, reoperations and the average length of hospital stay. Moreover, studies revealed evidence that prehabilitation can be cost-effective compared to usual care. We identified 20 barriers and 23 facilitators across four stages: reducing capacity, reducing department expenses, reducing hospital expenses, and reducing insurer expenses. The stakeholders emphasized the presence of a general aversion towards downsizing driven by the fear of losing resilience, flexibility, status and revenue. All interviewees expected that any excess capacity will be used to provide other care. This was perceived as a highly valuable outcome, especially in the context of an increasing shortage of healthcare professionals and an increasing demand for care. Last, misalignment of agreements between hospitals and health insurers hindered opportunities for downsizing and cost cutting. Identified facilitators were shared savings agreements, a specific downsizing strategy, labor shortages and the shared responsibility to contain healthcare expenses. Overall, achieving societal cost savings requires an active approach to overcome the barriers. Besides improving the quality of care, we suggest that the real-world value of initiatives like prehabilitation is increasing the accessibility of care rather than reducing societal costs.

De-implementation strategies that achieve the desired results, should be scaled to increase their impact. While there is considerable attention for the spread of innovations, less is known about spreading de-implementation strategies. To fill this knowledge gap and enhance the spread of de-implementation efforts, we developed the SPREAD framework. This framework contains determinants of the scaling of de-implementation

strategies and is described in **chapter 5**. First, determinants of the scaling of innovations were extracted from existing literature and categorized into four domains: the scaling plan, the external context, innovation, and the adopters. Subsequently, during focus groups, experts discussed the relevance of the determinants for the scaling of de-implementation efforts. Moreover, the experts provided additional topics, such as: addressing low-value care during medical training, the use of professional networks, the support of important stakeholders, the presence of clear clinical guidelines, and the role for patients in the scaling of initiatives. The SPREAD framework consists of 36 determinants. We suggest forming a coordinating scaling team that considers all factors and addresses the relevant ones. The tasks of a coordinating team may include: making a scaling plan, organizing partnerships, raising awareness among potential adopters, and gathering financial resources. The strategy should be evaluated on the ability to fit a new context and making modifications may be beneficial. The external context preferably includes incentives to adopt a strategy, while incentives to provide low-value care should be removed. And last, target adopters that are willing and able to adopt the strategy and to reduce low-value care.

The SPREAD framework was used to scale effective de-implementation initiatives in the Netherlands. One of the scaled projects was an education tool for dyspeptic patients. The scaled tool is evaluated in **chapter 6**. The original tool successfully reduced the number of inappropriate upper gastrointestinal tract endoscopies by informing patients about the stomach, the benign nature of the complaints and self-management. To include patients, a researcher manually screened the referral letters. The scaling team aimed to reach a wider audience, while limiting the required time investment. This led to a collaboration with the national patient information website thuisarts.nl (GPinfo.nl) The tool was adapted to meet the standards of *thuisarts.nl*. The scaling resulted a real-world implementation and public availability of the tool.

The scaled tool was evaluated on the ability to reassure patients and to support self-management. A survey was conducted using two questionnaires: one that was filled out directly after the using the tool and one after three months. A majority of the patients felt reassured after using the tool and were willing to try recommended lifestyle changes. After three months, most participants reported that they succeed in changing their lifestyle. Some participants intended to seek medical care after the education, while prior they did not, and vice versa. This shows that educating patients about the indications, benefits and limitations of care could support informed decision making and may also prevent underdiagnosis. These results show the potential of scaling and real-world implementation of a de-implementation strategy.

Lastly, in **chapter 7**, we assessed the sustainability of a de-implementation strategy

reducing inappropriate testing. A multifaceted strategy led to an average reduction of 11% in laboratory testing volume among four hospitals. The strategy involved several components: modifications to the order system, education for residents, intensified supervision, increased involvement of the clinical chemistry department, and active clinical leaders and local champions. Our evaluation included a quantitative analysis of the testing volume and a qualitative analysis to identify influencing factors and assess changes during both the intervention period and follow-up. The study period consisted of a 22-month pre-intervention period, 14-month intervention period, and 22-month follow-up. One of the two intervention hospitals significantly maintained the volume reduction during the final year of follow-up compared to the pre-intervention period. Meanwhile, the control group showed a significant increase in testing volume. However, both intervention hospitals showed an upward trend in testing during follow-up, suggesting that the effectiveness of the strategy reduced overtime. despite the local teams emphasized an ongoing awareness of appropriate testing among the staff and residents. Most components of the strategy were either discontinued or reduced after the intervention period. Facets that were compatible into daily practice or automated were better maintained, than those that were perceived as ineffective or required substantial time. The sustainability of the strategy was hindered by changes in the environment and the organization, such as the withdrawal of the coordinating project team and the high turn-over of residents. Together, these results suggest that ongoing effort are needed to maintain the effectiveness. Therefore, the long-term plan should be considered when designing de-implementation strategies. This may involve a low required time investment, and periodically monitoring of the desired outcomes and responding to unwanted trends.

The findings of this thesis are discussed in **chapter 8**. This thesis provide several opportunities to enhance the impact of de-implementation strategies. First, we emphasize that de-implementation of low-value care is not a convenient cost-cutting measure, but it has the potential to increase the quality of care and the accessibility. Second, to increase the impact of de-implementation efforts, the strategies should be scaled and implemented in real-world settings. This requires a dedicated team with sufficient time and financial resources. And last, the long-term effectiveness of strategies is not guaranteed and may requires ongoing efforts. To facilitate the long-term continuation, the required time investment should be limited. We recommend to design de-implementation strategies with a long-term vision that considers the feasibility of continued efforts and the potential for scaling.

Samenvatting

Niet-gepaste zorg is zorg die geen toegevoegde waarde heeft voor de patiënt, of waarbij de nadelen niet opwegen tegen de voordelen. Het verminderen van niet-gepaste zorg, ook wel de-implementatie genoemd, kan onnodige bijwerkingen en complicaties voorkomen. Ook kan de-implementatie bijdragen aan een betere inzet van schaarse middelen, omdat niet-gepaste zorg waardevolle zorg kan verdringen. Mede door deze mogelijkheden is de interesse in de-implementatie van niet-gepaste zorg de afgelopen twee decennia sterk toegenomen.

Er zijn vijf stappen in het de-implementatieproces: 1. identificeren van niet-gepaste zorg, 2. samenstellen van een de-implementatie strategie, 3. evalueren van de strategie, 4. opschalen van effectieve initiatieven en 5. waarborgen van de effecten op lange termijn. Voorbeelden van de-implementatiestrategieën zijn: scholing voor zorgprofessionals, het verspreiden van patiëntinformatie, het verstrekken van spiegeldata, wijzigingen aanbrengen in het aanvraagsysteem, en de inzet van klinische leiders als ambassadeurs van een project. De effectiviteit van strategieën is veelvuldig onderzocht, maar er is nog weinig aandacht voor het meten van de maatschappelijke voordelen, het opschalen van strategieën, en het behoud van de effecten op lange termijn. De impact van de-implementatie initiatieven zou aanzienlijk kunnen worden vergroot wanneer deze drie aspecten worden verbeterd. Daarom is het hoofddoel van deze thesis om de-implementatie te verbeteren door inzicht te verkrijgen in: 1. de potentiële kostenbesparing, 2. het opschalen van effectieve initiatieven, en 3. het langdurig behouden van de positieve effecten.

Deze thesis begint met het verkennen van de effectiviteit van verschillende de-implementatiestrategieën. Bij voorkeur worden strategieën samengesteld op basis van alle relevante belemmerende en bevorderende factoren, zoals een gebrek aan bewustzijn en kennis. Echter, in de praktijk richten de meeste strategieën zich slechts op één of twee factoren, en wordt er vaak gekozen voor het geven van scholing. Wanneer niet alle belemmeringen weggenomen kunnen worden, is het nuttig om te weten welk type strategie het meest succesvol is. Onze literatuurstudie in **hoofdstuk 2** toonde aan dat strategieën die bestaan uit meerdere onderdelen het vaakst succesvol waren in het verminderen van niet-gepaste medicatievoorschriften. Scholing voor zorgprofessionals was de meest gebruikte strategie, maar tegelijkertijd ook het minst vaak succesvol. Dit bevestigt dat alleen het vergroten van kennis van zorgprofessionals meestal niet voldoende is om hun gedrag en routines te veranderen. Echter, scholing kan wel waardevol zijn als onderdeel van een strategie met meerdere componenten. Verder suggereren onze resultaten dat het betrekken van patiënten de effectiviteit van de-implementatie strategieën kan vergroten.

Ons overzicht in hoofdstuk 2 laat ook zien dat de meest gebruikte uitkomstmaat de afname van de hoeveelheid niet-gepaste zorg is. Dit is een belangrijke uitkomstmaat om de effectiviteit van een strategie te bepalen, maar het beschrijft niet het voordeel voor patiënten of de maatschappij. Veelal presenteren beleidsmakers de-implementatie als een manier om de kwaliteit van zorg te verbeteren en tegelijkertijd de maatschappelijke zorgkosten te verlagen. Echter, de verwachte kostenbesparing en de toename van kwaliteit worden vaak enkel geschat en niet in de praktijk gemeten. Dit is een probleem, omdat met name de kostenbesparing vaak sterk wordt overschat.

In **hoofdstuk 3** beschrijven we verschillende mechanismen die maatschappelijke kostenbesparingen belemmeren nadat niet-gepaste zorg is verminderd. We stellen dat de meeste schattingen zijn gebaseerd op declaratietarieven, en die komen niet overeen met de werkelijke ziekenhuisuitgaven. De potentiële besparing van één operatie minder uitvoeren is aanzienlijk lager dan het tarief dat ziekenhuizen ervoor mogen vragen, omdat de grootste kostenposten vaste of semi-vaste lasten zijn. Een andere belemmering is dat de ruimte die ontstaat bij het verminderen van niet-gepaste zorg wordt opgevuld met andere zorg. Dit is een 'natuurlijk' fenomeen in gezondheidssystemen dat actief moet worden tegengegaan om kosten te kunnen besparen. Bovendien vormen betalingssystemen ook barrières voor het de-implementeren zelf of voor het bereiken van een besparing. Daarnaast zijn er ook kosten verbonden aan de-implementatie zelf, zoals projectkosten. Tot slot wordt niet-gepaste zorg regelmatig vervangen door een alternatief. Deze alternatieve zorg moet ook betaald worden. Dergelijke kosten moeten ook meegenomen worden in de berekening van de netto besparing, maar dat wordt vaak niet gedaan.

Er is nog weinig bekend over hoe minder zorg verlenen kan leiden tot een maatschappelijke kostenbesparing. Daarom hebben we in **hoofdstuk 4** mensen geïnterviewd om beïnvloedende factoren te vinden. In deze studie hebben we prehabilitatie gebruikt als casus. Prehabilitatie is een preoperatief leefstijlverbeteringsprogramma en het heeft de potentie om het aantal complicaties, heroperaties en ligdagen te verminderen. Bovendien toonden studies aan dat prehabilitatie kosteneffectief kan zijn. We hebben 20 belemmerende en 23 bevorderende factoren gevonden. Deze zijn verdeeld over vier stappen: 1. het verminderen van zorgcapaciteit, 2. het verminderen van afdelingsuitgaven, 3. het verminderen van ziekenhuisuitgaven en 4. het verminderen van uitgaven van verzekeraars. De geïnterviewden identificeerde belemmerende factoren, zoals een algemene aversie tegen krimp. Krimp – het inleveren van faciliteiten of middelen – werd geassocieerd met het verlies van veerkracht, flexibiliteit, status en inkomsten. Daarnaast verwachten alle geïnterviewden dat de vrijgekomen capaciteit zal worden gebruikt om andere zorg te verlenen. Dit werd gezien als een zeer waardevolle invulling, vooral door een verwacht tekort aan zorgprofessionals en een alsmaar toenemende zorgvraag. Als

laatste hinderden de conflicterende afspraken tussen ziekenhuizen en zorgverzekeraars mogelijkheden voor krimp en kostenbesparing. Een gevonden bevorderende factor was een *shared savings* afspraak, waarbij de besparing wordt verdeeld tussen de afdeling, het ziekenhuis en de verzekeraars. Verder noemden de geïnterviewden een specifieke krimpstrategie, personeelstekorten en de gemeenschappelijke verantwoordelijkheid om zorguitgaven te beheersen. Wij concludeerden dat de ruimte die vrij wordt gemaakt door initiatieven zoals prehabilitatie waardevoller is als het gebruikt wordt voor andere zorg dan wanneer de ruimte wordt afgebouwd om kosten te besparen.

De impact van de-implementatie kan worden vergroot door succesvolle strategieën op te schalen. Er is veel bekend over het opschalen van innovaties, maar minder over het opschalen van de-implementatiestrategieën. Daarom hebben we in **hoofdstuk 5** het SPREAD-framework ontwikkeld. Dit framework bevat factoren die de opschaling van de-implementatiestrategieën beïnvloeden. Eerst hebben we uit de literatuur factoren gehaald die de opschaling van innovaties beïnvloeden. Deze factoren werden gecategoriseerd in vier domeinen: het opschalingplan, de externe context, de innovatie en de nieuwe gebruikers. Vervolgens hebben experts tijdens focusgroepen de relevantie van de gevonden factoren voor de opschaling van de-implementatie bevestigd en hebben ze het framework verder aangevuld. De toegevoegde onderwerpen waren onder andere: niet-gepaste zorg als onderwerp in de opleiding, gebruik maken van professionele netwerken, de steun van belangrijke partijen, de aanwezigheid van duidelijke klinische richtlijnen en de rol van patiënten tijdens het opschalen. Het SPREAD-framework bestaat uit 36 factoren. Om de opschaling goed te laten verlopen, stellen we voor om een coördinerend opschalingsteam te vormen. Dit team zou alle factoren langs kunnen lopen en zich kunnen richten op de relevante factoren. Andere taken van het team zijn: het maken van een opschalingsplan, het organiseren van samenwerkingsverbanden, het vergroten van het bewustzijn bij potentiële nieuwe gebruikers en het verkrijgen van financiële middelen. Daarnaast moet de originele strategie geschikt gemaakt worden voor opschaling. Ook moet er gekeken worden of de externe context stimulerender kan worden gemaakt. Het zorgsysteem kan bijvoorbeeld prikkels bevatten om te de-implementeren, die moeten worden gebruikt. Tot slot moet het opschalingsteam op zoek naar nieuwe gebruikers die gemotiveerd zijn om niet-gepaste zorg te verminderen, en die hiermee aan de slag kunnen.

Het SPREAD-framework is gebruikt om effectieve de-implementatiestrategieën op te schalen in Nederland. Één van de opgeschaalde projecten was een online patiëntinformatietool voor mensen met functionele dyspepsie. De oorspronkelijke strategie verminderde met succes het aantal niet-gepaste gastroscopieën door patiënten te informeren over de maag, de onschuldige aard van de klachten en de mogelijkheden voor zelfzorg. Om te bepalen voor wie de patiëntinformatie geschikt was, screende

een onderzoeker handmatig de verwijsbrieven. Voor de opschaling streefde het opschalingsteam ernaar om de doelgroep uit te breiden en tegelijkertijd de benodigde tijdsinvestering te verminderen. Dit leidde tot een samenwerking met de nationale patiënten informatiewebsite *Thuisarts.nl*. De tool werd aangepast naar de huisstijl van *Thuisarts.nl*. De opschaling resulteerde in een geïmplementeerde tool die voor iedereen toegankelijk is. De opgeschaalde tool is geëvalueerd in **hoofdstuk 6** op het vermogen om patiënten gerust te stellen en om zelfzorg te stimuleren. Er werden twee vragenlijsten afgenomen: één direct na het doorlopen van alle informatie en één na drie maanden. Een meerderheid van de patiënten voelde zich gerustgesteld na het gebruik van de tool en was bereid om de aanbevolen leefstijlveranderingen te proberen. Na drie maanden rapporteerden de meeste deelnemers dat ze erin waren geslaagd hun leefstijl te veranderen. Sommige deelnemers waren van plan om medische zorg te zoeken na de informatie, terwijl ze dat aanvankelijk niet van plan waren, en vice versa. Dit toont aan dat het informeren van patiënten over de indicaties, voordelen en beperkingen van zorg kan bijdragen aan het besluit om zorg te vragen. Doordat mensen eerst niet en later wel zorg willen zoeken, wordt er mogelijk onderdiagnostiek voorkomen. Deze resultaten tonen aan dat opschaling van patiëntinformatie bij kan dragen aan de zelfzorg en de beslissing om medische zorg te zoeken.

Ten slotte hebben we in **hoofdstuk 7** de langetermijneffecten van een strategie geëvalueerd die niet-gepast laboratoriumdiagnostiek heeft verminderd. De strategie bestond uit verschillende componenten: aanpassingen aan het ordersysteem, scholing voor arts-assistenten, geïntensiveerde supervisie met focus op gepaste zorg, intensievere betrokkenheid vanuit de klinische chemie en actieve internisten en arts-assistenten als ambassadeurs van het project. De strategie leidde tot een gemiddelde vermindering van 11% van het aantal laboratorium testen in vier ziekenhuizen. Wij hebben de langetermijneffecten op verschillende manieren geëvalueerd: een kwantitatieve analyse van het aantal testen in twee ziekenhuizen en een kwalitatieve analyse in drie ziekenhuizen om beïnvloedende factoren te identificeren tijdens de interventieperiode en de follow-up. De studie bestond uit een pre-interventieperiode van 22 maanden, een interventieperiode van 14 maanden en een follow-up van 22 maanden. Eén van de twee interventieziekenhuizen behield ook de reductie van het aantal testen 22 maanden na de interventieperiode. In dezelfde tijdsperiode was er in de controlegroep juist een significante toename van het aantal testen. Echter, beide interventieziekenhuizen toonden een oplopende trend in het aantal testen tijdens de follow-up periode. Dit laat zien dat de effectiviteit van de strategie in deze periode afnam, terwijl de lokale teams benadrukten dat het bewustzijn van passende zorg op de afdeling was gebleven. De meeste componenten van de strategie werden na de interventieperiode gestopt of verminderd. Componenten die goed in de dagelijkse praktijk pasten of waren geautomatiseerd, werden beter behouden dan die weinig effectief werden ervaren of

die veel tijd vereisten. De belangrijkste belemmeringen voor het behoud van de effecten waren veranderingen in de organisatie, zoals een hoge doorloop van arts-assistenten. Daarnaast was ook het stoppen van het externe coördinerende onderzoeksteam een belangrijke verandering. Op basis van deze resultaten, kunnen we concluderen dat er blijvende inspanningen nodig zijn om de effectiviteit van de strategie te behouden. Daarom moet bij het samenstellen van een strategie al nagedacht worden over de lange termijn. Het is belangrijk dat de benodigde tijdsinvestering minimaal is, dat de voortgang regelmatig gemonitord wordt en dat er wordt reageert als er een ongewenste trend wordt waargenomen.

In **hoofdstuk 8** bediscussieer ik de bevindingen in deze thesis. Samenvattend beschrijft dit proefschrift verschillende mogelijkheden om de impact van de-implementatie-strategieën te vergroten. Ten eerste benadrukken we dat de-implementatie van niet-gepaste zorg geen geschikte methode is om makkelijk kosten te besparen. Wel heeft de-implementatie de potentie om de kwaliteit van zorg te verbeteren en de toegankelijkheid te verhogen. Ten tweede moeten de effectieve strategieën worden opgeschaald om de impact van strategieën te vergroten. Dit vereist een coördinerend opschalingsteam met voldoende tijd en financiële middelen. En tot slot is de effectiviteit van strategieën niet gegarandeerd voor de lange termijn, en het behoud van de effecten vraagt om permanente inspanningen. Om de voortgang van de strategie te stimuleren, moet de benodigde tijdsinvestering beperkt blijven. Verder bevelen we aan om strategieën samen te stellen die lang vol te houden zijn. Ook zou er in een vroege fase al rekening gehouden moeten worden met de mogelijkheden voor opschaling.

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Mi amor, mi Dush. Danki pa ta ken bo ta. Stimabo. Pa semper.

About the author

Daniëlle Kroon was born in Emmeloord on the 29th of February in 1992. She grew up on a farm with her parents, two brothers and a rabbit. After finishing secondary school she left the potato city and moved to Amsterdam to study medicine at the University of Amsterdam. She did her research internship on the quality of anti-malaria drugs in Lambaréne, Gabon and additionally worked on multiple studies to improve the treatment of malaria. After her graduation, she started as a physician in the emergency department in *Ziekenhuisgroep Twente*. However, missing the tropical sun, she decided to pursue her career in the Caribbean, and worked in the emergency department in the Horacio Oduber Hospital in Aruba.

While working in both hospitals, she saw various opportunities to optimize the healthcare process and was eager to contribute to that. As a PhD-candidate and member of the *To do or not to do* team, she aimed to improve healthcare by reducing low-value care practices in the Netherlands. Because she fell in love with – and in – Aruba, she returned to the island after finishing her PhD thesis. She continued her career as a physician in the Horacio Oduber Hospital. She lives with her partner, dog, house gecko, and a garden full of palm trees and cacti.

List of Publications

Scientific publications

The long-term sustainability of a successful de-implementation strategy reducing inappropriate laboratory testing: a retrospective multicenter mixed-method study.
***D. Kroon**, A.W. Boerman, R.B. Kool, et al. Published in this thesis*

Evaluation of a web-based patient education tool for dyspeptic patients: a longitudinal survey study
***D. Kroon**, I.L Abma, M.A. Lantinga, et al. Published in this thesis*

Stakeholders' perspectives on capturing societal costs savings from a quality improvement initiative: a qualitative study.
***D. Kroon**, S. A. van Dulmen, N. W. Stadhouders, et al. PLoS ONE,19(9): e0310799.*

Inzet van bloedkweken en hun indicatie op SEH's. Tijd voor verandering?
***D. Kroon**, J. Van Kreij, D. Baden, et al. Ned Tijdschr Geneeskd. 2024;168:D8276*

Why reducing low-value care fails to bend the cost-curve, and why we should do it anyway
***D. Kroon**, N. W. Stadhouders, S. A. van Dulmen, et al. International Journal of Health Policy and Management, 2023; 12(Issue 1): 1-3.*

Development of the SPREAD framework to support the scaling of de-implementation strategies: a mixed-methods study.
***D. Kroon**, S. A. van Dulmen, G. P. Westert, et al. BMJ Open 2022;12:e062902.*

Effectiveness of interventions aiming to reduce inappropriate drug prescribing: an overview of interventions.
***D. Kroon**, N. F. Steutel, H. Vermeulen, et al. JPHSR, 2021, vol XX, 1-11.*

COVID-19: a window of opportunity for positive healthcare reforms.
*S. Auener, **D. Kroon**, E. Wackers, et al. International Journal of Health Policy and Management, 2020; 9(10): 419-422*

Serum lipids and lipoproteins during uncomplicated malaria: a cohort study in Lambaréné, Gabon.
*B.J. Visser, S.G. de Vries, R. Vingerling, M. Gritter, **D. Kroon**, et al. The American Journal of Tropical Medicine and Hygiene 96, 2017, pp 1205 – 1214*

The diagnostic accuracy of the hand-held Raman spectrometer for the identification of anti-malarial drugs.
*B.J. Visser, S.G. de Vries, E.B. Bach , J. Meerveld-Gerrits, **D. Kroon**, et al. Malaria Journal 2016, 15:160*

Assessing the quality of anti-malarial drugs from Gabonese pharmacies using the MiniLab ® : a field study
*B.J. Visser, J. Meerveld-Gerrits, **D. Kroon**, et al. Malaria Journal 2015, 14:273*

Efficacy and safety of artemisinin combination therapy (ACT) for non-falciparum malaria: a systematic review
*B.J. Visser, R.W. Wieten, **D. Kroon**, et al. Malaria Journal 2014, 13:463*

Other publications

How to Reduce Overuse in Healthcare: A Practical Guide [book]
S. A. van Dulmen et al. | *2023* | *Wiley-Backwell* | **Co-author of chapter 11 & 13**

Waarom stoppen met niet-passende zorg geen miljarden oplevert
***D. Kroon.**, et al. Zorgvisie 2023*
https://www.zorgvisie.nl/blog/waarom-stoppen-met-niet-passende-zorg-geen-miljarden-oplevert/

Zo schaal je een succesvol project landelijk op
***D. Kroon.** Zorgvisie 2024*
https://www.zorgvisie.nl/blog/opinie-zo-schaal-je-een-succesvol-project-landelijk-op/

PhD portfolio

Department: IQ healthcare
PhD period: 01/05/2019 – 01/01/2024
PhD Supervisor(s): Prof. dr. Patrick Jeurissen, Prof. dr. Tijn Kool, Prof. dr. Gert Westert
PhD Co-supervisor(s): Dr. Simone van Dulmen

TRAINING ACTIVITIES	HOURS
Courses	
RIHS Introduction course for PhD candidates (2019)	15
Action research (2019)	8
Endnote Workshop (2019)	1
Winteracademie Betaalbaarheid van Zorg (2020)	42
Qualitative research methods and analysis (2020)	5.6
RU Scientific writing for PhD students (2020)	84
Radboudumc – eBROK course (2021)	42
Principles of epidemiological data analysis (2021)	112
Regression analysis (2021)	112
Scientific integrity (2023)	20
Conferences	
Advancing the Science and Impact of Audit & feedback (2019)	8
RIHS PhD retreat (2019, 2021)	28
Skipr Congres: Doen of laten (2019)	20
Preventing overdiagnosis (2022) – *oral presentation and workshop*	32
ROHA conferentie (2022) – *2x workshop*	14
Congres Talma instituut 'De zorg onder druk' (2022)	8
Betaalbaarheid van Zorg: Vijftien jaar marktwerking (2022) – *oral presentation*	11
Doen of Laten? Eindconferentie (2023) – *2x oral presentation*	20
Other	
Peer review for scientific journals (5x; 2019-2024)	20
Opzetten en coördinatie Leernetwerk 'Doelmatige diagnostiek' (2020-2023)	40
Training Appropriate Care at AQUAS Barcelona (2022)	120

TEACHING ACTIVITIES	
Lectures	
'Passende zorg' session for honours program (2019, 2020)	6
'Evidence Based Practice' werkgroepen (2019)	6
Fellowship session: Choosing Wisely Canada: 'Sustainability and Scaling' (2023)	3
Supervision of internships / other	
Supervision research project 'Grant proposal' (2019)	45
Supervision internships of master students (4x; 2020 – 2023)	140
Total	**962,6**

Research Data Management

Ethics & Privacy

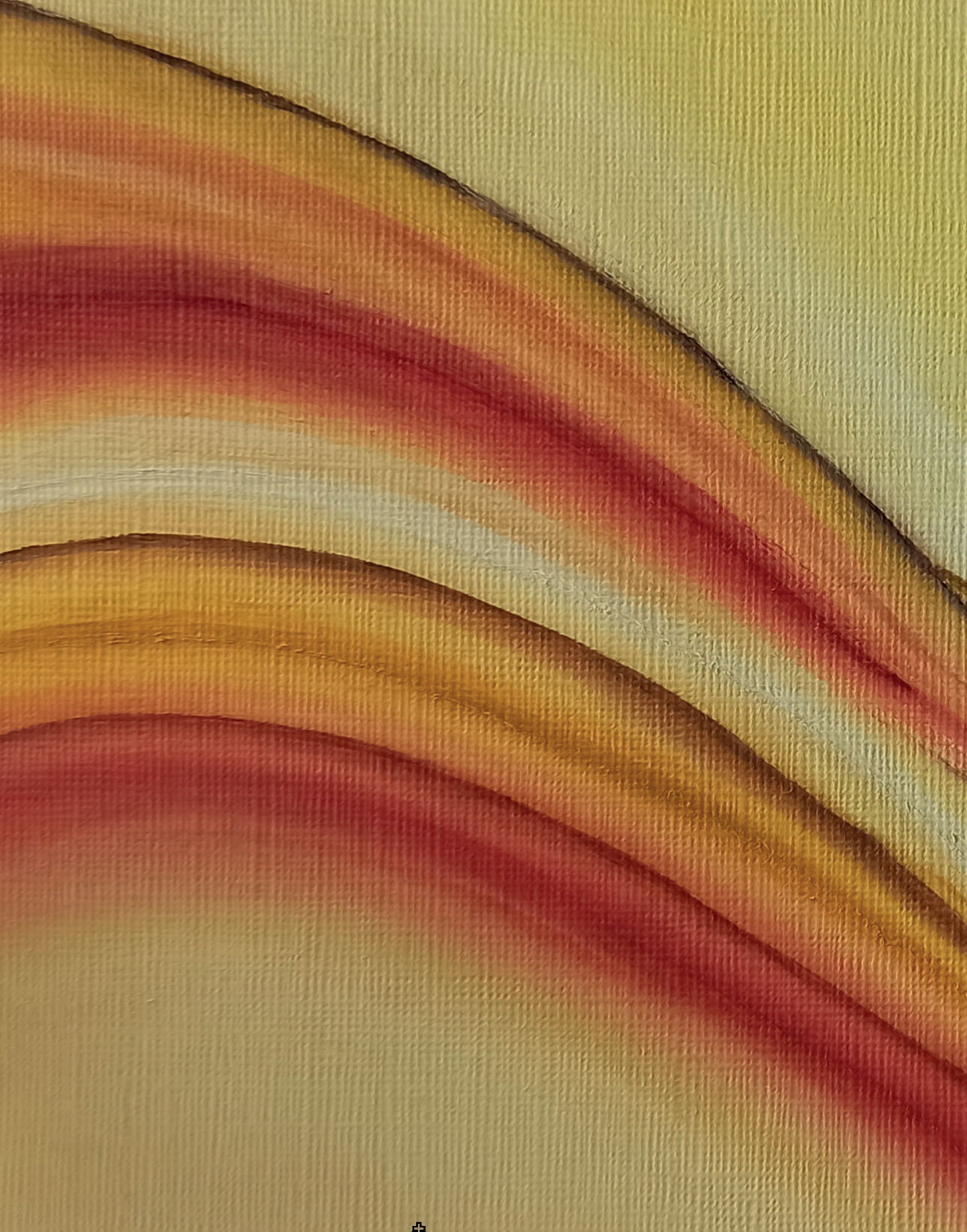
All studies in this thesis were conducted in accordance with the principles of the Declaration of Helsinki and guidelines of Good Clinical Practice. The Medical Ethics Review Committee of the Radboud University Medical Center approved the study described in chapter 5 (file number: 2021-7519). Additionally, the committee waived the need for approval for the studies in chapter 4 (file number: 2023-16520), chapter 6 (file number: 2022-13578) and chapter 7 (file number: 2021-8316), because the Medical Research involving Human Subjects Act did not apply. All studies were conducted in accordance with regulations concerning general data protection and the participants were not exposed to significant actions or additional interventions. Chapter 2 and 3 are literature-based studies and therefore did not require an ethics review.

Data collection and storage

We obtained informed consent from all participants prior to the interviews conducted for chapter 4, 5, 7. Additionally, all participants provided informed consent prior to the questionnaire used in chapter 6. Furthermore, the Medical Ethics Review Committee of the Radboud University Committee confirmed that informed consent of patients was not required for using the data of the hospitals in chapter 5. Some interview recordings were securely shared with authorized third parties through encrypted transfers, exclusively for transcription purposes. All collected data were pseudonymized and stored in a secured folder at the Radboudumc server of IQ health science department. Only authorized researchers have access to these data. Identifiable data were stored in a local secured folder of IQ health science department, separately from the pseudonymised data.

Availability of data

All studies are published open access with a Creative Commons Attribution licence (chapter 2, 3, 4 and 5), or will be published as such (chapter 6 and 7). Pseudonymised data used for chapters 4, 5, 6 and 7, syntaxes of chapter 7, and descriptive files of all chapters will be archived in a secure folder of IQ health science department. These files are available from IQ health for researchers who meet the criteria for access to confidential data. For access to the data used in chapter 7, additional permission is needed from the participating hospitals. Additionally, all used datasets are or will be archived in the Radboud Data Repository.



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