Prescribing quality indicators for type 2 diabetes management: development, validation and selection

Martirosyan, Liana

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Stellingen behorende bij het proefschrift

"Prescribing quality indicators for type 2 diabetes management: development, validation, and selection"

1. General practitioners and diabetologits disagree on what constitutes a good (first) drug choice for treatment of diabetic patients. (this thesis)

2. Use of diagnostic codes to identify patients with a certain condition overestimates the quality of provided care, if there is a diagnosis registration bias favoring patients already receiving the recommended treatment. (this thesis)

3. The more sophisticated a prescribing quality indicator is the more robust and the less feasible it is. (this thesis)

4. Health care providers do not prioritize prescribing indicators focusing on costs. (this thesis)

5. Doctors complain that the reasons for not complying with the guidelines are not taken into account, and the external stakeholders find fault that such reasons are not registered in medical records. (this thesis)

6. Relationships between prescribing indicators for diabetes care are not visible to the naked eye: in fact, the indicators cluster not on risk factor management, but rather on different levels of treatment intensification. (this thesis)

7. In science the credit goes to the man who convinces the world, not the man to whom the idea first occurs. *Sir Francis Darwin*

8. Every step you take, is a step away from where you used to be. *Brian Chargualaf*

9. We don't see things as they are, we see things as we are. *Anais Nin*

Liana Martirosyan, 15 december 2010

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Promotor:	Prof. dr. F.M. Haaijer-Ruskamp
Copromotores:	Dr. P. Denig Dr. J. Braspenning
Beoordelingcommissie:	Prof. dr. H.J. Bilo Prof. dr. N.S. Klazinga Prof. dr. M.L. Bouvy

Paranimfen:	Ruth de Smedt Liana Hakobyan

"Dedicated to:
My mother, Gayane Manrikyan, who has been my biggest support,
my husband Sascha Gross,
and my son Samuel"

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CHAPTER 1

General introduction

Type 2 diabetes mellitus: prevalence and burden

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disease with a dramatically increasing prevalence throughout the world and with no cure as of 2010. It is associated with an impaired glucose cycle, altering metabolism, and without adequate treatment serious complications may occur.[1;2]

The global prevalence of diabetes among adults is high, varying between 2.8 percent to 4 percent in the year 2000, and this number is expected to reach 350 million world-wide in 2030.[3] In the Netherlands, the prevalence of T2DM is estimated to be 41.6 per 1000 women and 40.1 per 1000 men. In 2007 there were 740.000 people diagnosed with diabetes mellitus, with 90% of them being diagnosed as having T2DM.[4] In addition, it is estimated that 30% of population aged over 60 have undiagnosed impaired glucose tolerance in the Netherlands.[5]

T2DM is an independent risk factor for several forms of cardiovascular disease (CVD) in both men and women.[6] The overall yearly mortality among patients with diabetes is 2.9%, with the most common cause of death being related to cardiovascular disease. When patients with diabetes develop clinical CVD, they sustain a worse prognosis for survival than do CVD patients without diabetes.[7;8]

Management of type 2 diabetes mellitus

As patients with T2DM have an increased risk for CVD, controlling several risk factors including hyperglycemia, which may give rise to secondary conditions is one of the main goals of diabetes management. Measurements of cholesterol, LDL, HDL and triglyceride levels may indicate dislipidemia, which may require treatment with lipid lowering medication. Measurement of the blood pressure and keeping it within strict limits by using diet and antihypertensive treatment protects against the retinal, renal and cardiovascular complications of diabetes. Annual eye and foot exams are recommended to monitor for progression of diabetic foot and diabetic retinopathy, etc.

Over the past 5-10 years, there have been substantial improvements in many processes of diabetes care (e.g., conducting laboratory tests at indicated intervals), but less dramatic improvements in intermediate outcomes (e.g., value of blood pressure or glycemic control). Indeed, recent studies have shown that substantial quality gaps in glycemic, blood pressure and lipid control exist in management of diabetic patients and are of considerable concern.[9;10]

Importance of prescribing in type 2 diabetes mellitus

Management of T2DM includes carefully managing diet, exercising, taking oral glucose lowering medication, using some form of insulin, and self-monitoring and may be further complicated by other factors such as presence of other risk factors and diseases. Carefully managing diet and

physical activity play an important role for diabetes and contribute to improved patients outcomes.[11] However, lifestyle modifications may not be sufficient for controlling the risk factors as the diseases progresses, and pharmacotherapy is in due course required for majority of diabetic patients.[12] Appropriate glucose and blood pressure control, lipid-lowering therapy, rennin-angiotensin aldosteron system (RAAS) inhibition, and antiplatelet treatment significantly reduce the risk of cardiovascular complications in diabetic patients.[13;14]

Despite the development of clinical guidelines describing key recommendations concerning appropriate pharmacotherapy in T2DM, many patients do not receive optimal drug treatment.[15-17] Undertreatment of diabetic patients has a large impact on individuals, societies, and health care costs.

Quality assessment in healthcare

Donabedian's classic paradigm for assessing quality of care was developed in 1988 and is based on a three-component approach—structure, process, and outcomes.[18] Structure refers to the attributes of the settings in which providers deliver health care, including material resources (e.g., electronic health records), human resources (e.g., staff expertise), and organizational structure (e.g., hospitals vs. outpatient clinics). For example, a health care provider may use a disease registry to track whether a patient with increased levels of cholesterol is receiving drugs for lowering cholesterol.
Process of care denotes what is actually done for the patient in terms of giving and receiving of care. Examples of processes of care include measuring and documenting clinical measurement values, such as glucose and blood pressure, prescribing medications to eligible patients, educating and empowering patients, etc.

Health outcomes are the direct result of a patient's health status as a consequence of contact with the health care system. For example, the patient's receiving the appropriate medications could decrease the chance of dying from a heart attack.

Donabedian's model proposes that each component has a direct influence on the next one, *i.e.* structure of care influence processes of care, and process of care determines outcomes of care. Prescribing is a typical example of health care process. In the field of diabetes care, pharmacotherapy is the best researched process of care in terms of its influence on health outcomes with a very good link established between the two dimensions of the paradigm.[19;20]

Assessing prescribing quality

Quality of health care can be improved without explicit quality assessment using different methods including peer-review[21], educational programs[22], use of standardized patients[23], implicit quality review[24], and on-site-visits.[25] While all these methods have their own advantages and can

constitute a method of choice in specific situations, they share two major disadvantages. First of all, none of these methods can be routinely applied as they require considerable man power, resource investment and are time consuming. Next, use of these methods does not provide a measurable basis for reliable comparisons over time or between providers that is crucial for continuous quality improvement and evaluation of interventions.

To overcome these limitations, prescribing quality indicators (PQI) are developed. A PQI is a measurable element of prescribing for which there is evidence or consensus that it can be used for measuring and hence improve quality of prescribing.[26] Usually, a PQI is defined as a percentage of patients that received the recommended drug treatment, with numerator comprising the number of patients actually receiving the treatment and denominator comprising the number of all patients for whom the treatment is appropriate. Prescribing quality indicators have explicitly defined criteria regarding what constitutes good quality of care, and the scores of the PQI can be compared over time and across different providers. Usually PQI are developed based on scientific evidence and/or acceptance by professionals in the field.[27] Therefore, they can be used to measure the compliance to drug recommendations as given in clinical guidelines. In addition, measurability of prescribing quality indicators provides a great opportunity for research, for example for comparison of indicator scores to assess their concurrent validity or by linking the scores of prescribing indicators to different patients outcomes for predictive validity assessment.[28]

Rationale for this thesis

Availability and validity of PQI for diabetes care

In the past decade there has been a lot of attention to diabetes care worldwide. In many countries, including the Netherlands, diabetes was among the first diseases for which disease management program have been developed.[29] Subsequently, a number of different quality indicators have been developed to monitor quality of diabetes care. Such indicators have been included in different national sets of indicators worldwide.[30;31] In addition, specific national and international projects involving quality indicators have been developed to improve quality of diabetes care.[32;33] Although some of these programs include prescribing quality indicators for diabetes management, a comprehensive set of prescribing indicators for diabetes care is lacking. In addition, there is lack of information on the validity of existing prescribing quality indicators of diabetes care.

Prescribing quality indicators for T2DM care have the potential to inform and improve quality of diabetes care.[34;35] However, to be useful, they have to meet a number of criteria. As a minimum, a PQI should reflect the best available evidence and be accepted by professionals in the field.[36] The data for calculating PQI should be readily available and collected on a routine basis. The PQI should be reliable and allow fair comparisons between health care providers. Information on these characteristics is necessary for choosing the best indicators in relation to the aim of quality assessment.[37]

An increasing number of quality indicators

PQI are demanded and used by different stakeholders, including policy makers, health insurance companies, professionals, and patient organizations. These stakeholders have to deal with an increasing number of quality indicators developed for a growing number of diseases.[38] This adds to the administrative and financial burden of collecting, reporting, and processing large amounts of quality information.[39] Application of scientifically sound methods to select the most relevant indicators is a key to reduce the workload and costs involved in quality assessment.

Objectives and structure of this thesis

In this thesis we describe the development, validation, and selection of prescribing quality indicators for diabetes care. We focus on three primary aims centered on pharmacological management of type 2 diabetes mellitus:

1. To develop a comprehensive, valid, and operationally feasible set of prescribing quality indicators for diabetes care
2. The improve the general understanding on clinimetric characteristics of PQI for diabetes care
3. To build up the knowledge on selection of relevant PQI from existing sets of indicators using different research methods

Chapter 2 presents the development of a set of prescribing quality indicators for diabetes care based on several international and national diabetes guidelines, and their validation in a panel of nationally recognized experts followed by a panel of diabetologists and general practitioners using the RAND Appropriateness Method (RAM). In addition, we assessed the operational feasibility of the selected PQI in the view of available data using electronic health records of T2DM patients.

In **Chapter 3** we assessed the impact of the type of clinical information used for identifying the target population (denominators) of several prescribing quality indicators. Patients with certain conditions, such as hypertension or being overweight are usually identified in electronic health records by using corresponding diagnostic codes. Alternatively these patients can be identified using elevated values of clinical measurements, *i.e.* blood pressure and body mass index. We studied how this choice of clinical information to define the target population affected the PQI scores and their ability to correctly identify treated and untreated T2DM patients.

In **Chapter 4** we reviewed existing PQI for T2DM and cardiovascular management. We conducted a systematic literature search in MEDLINE and EMBASE databases without language restriction, and reviewed clinimetric properties (face, content, concurrent, and predictive validity, operational feasibility, reliability, sensitivity to case-mix, and minimum sample size) of more than 200 extracted PQI. We grouped similar indicators and provided a classification of the subgroups based on their

clinimetrics. The study presents an overview of clinimetric characteristics for existing PQI and provides a short list of the indicators with the best validity results.

Chapter 5 summarizes the preferences for different prescribing quality indicators as expressed by important stakeholders in the Netherlands, such as the Healthcare Inspectorate, healthcare professionals (GPs, diabetologists, diabetes nurses, and pharmacists), patient representatives, and insurance companies. In a qualitative study, we explored the perceived importance of including PQI in quality assessment of diabetes care by different stakeholders and elicited the preferred types of PQI per stakeholder. In addition, we revealed the preferred way of receiving prescribing quality information by the included stakeholders.

In **Chapter 6** we describe a selection process of a minimal set of PQI for T2DM management using factor analysis. We show the value of this technique for reducing the number of prescribing quality indicators by identifying the relationships between prescribing quality indicators on a general practice level that might not be obvious otherwise.

Finally, in **Chapter 7** the findings, implications, and methodological considerations regarding the above mentioned studies are discussed. The recommendations for future research are provided in the same chapter.

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CHAPTER 2

Prescribing quality indicators of type 2 diabetes mellitus ambulatory care

Liana Martirosyan[1], Jozé Braspenning[2], Petra Denig[1], Wim JC de Grauw[3], Margriet Bouma[4], Fred Storms[5], Flora M Haaijer-Ruskamp[1]

[1]Department of Clinical Pharmacology, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands
[2]Centre for Quality of Care Research (WOK), University Medical Centre St Radboud, Nijmegen, the Netherlands
[3]Department of General Practice, Academic Research Network CMR NMP, University Medical Centre St Radboud, Nijmegen, the Netherlands
[4]Dutch College of General Practitioners, Utrecht, the Netherlands
[5]Dutch Institute for Healthcare Improvement, Utrecht, the Netherlands

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ABSTRACT

Background

Existing performance indicators for assessing quality of care in type 2 diabetes mellitus (T2DM) focus mostly on registration of measurements and clinical outcomes, and not on quality of prescribing.

Objective

To develop a set of valid prescribing quality indicators (PQI) for internal use in T2DM, and assess the operational validity of the PQI using electronic medical records.

Methods

Potential PQI for hypertension, hyperglycaemia, dyslipidaemia, and antiplatelet treatment in T2DM were based on clinical guidelines, and assessed on face and content validity in an expert panel followed by a panel of GPs and diabetologists. Analysis of ratings was performed using RAND/UCLA Appropriateness Method. Operational validity of selected indicators was assessed in a dataset of 3214 T2DM patients registered with 70 GPs.

Results

Out of 31 potential prescribing indicators, the expert panel considered 18 indicators as sufficiently valid, of which 14 indicators remained valid after assessment by the panel of GPs and diabetologists. Of these 14 indicators, one could not be calculated because of absence of eligible patients. For the remaining indicators, outcomes varied from 10% for timely prescribing of insulin to 96% for prescribing of any antihyperglycemic medication in patients with elevated HbA1c levels.

Conclusions

This study provides a set of face and content valid PQI for pharmacological management of patients with T2DM. While outcomes of some PQI were limited to patients with registration of clinical values, the selected PQI had good operational validity to be used in practice for assessment of prescribing quality.

INTRODUCTION

Efforts to measure and improve quality of care in outpatient settings have focused especially on care for chronic medical conditions, such as type 2 diabetes mellitus (T2DM). This has resulted in publication of clinical guidelines to assist doctors in management of diabetes, and the development of performance quality indicators. T2DM is a disease with a dramatically increasing prevalence throughout the world and serious complications may occur if the disease is not adequately treated[1;2]. Appropriate blood pressure control, lipid-lowering therapy, angiotensin-converting enzyme(ACE) inhibition, and antiplatelet drugs significantly reduce the risk of cardiovascular and microvascular complications in diabetic patients[3;4].

Quality information has been demanded not only by policy makers, consumers, and media, but also by health care providers themselves for internal use. In order to measure quality of prescribing in T2DM patients, valid prescribing quality indicators (PQI) are needed. Such PQI can be used by health care providers as a "screening tool" to help flag potential problem areas that need further investigation, for giving feedback to individual doctors, and to assess the impact of quality improvement initiatives. Although quality of care can be improved without explicit quality assessment, for example by peer review or educational programs, measurements provide valuable information for monitoring and feedback[5]. Quality improvement initiatives using quality measurements and achievable standards have been shown to improve diabetes outcomes, such as long term glucose control measurement[6;7].

Several sets of quality indicators for diabetes care have been developed. Many of them include outcome indicators or focus on processes of care, such as registration of clinical characteristics, but do not include any PQI.[8-10] PQI are process measures that can help to identify patients who may benefit from initiation or intensification of treatment. Such information is helpful for improving prescribing quality and dealing with so called 'therapeutic inertia'[11;12] Although some PQI for diabetes care are included in national sets of quality indicators[13;14], and some detailed PQI for T2DM management have been described[15;16], a comprehensive set of PQI for diabetes care is lacking.

We aimed to develop a set of PQI for pharmacological management in T2DM patients for internal use and to assess their operational validity using electronic medical records.

METHODS

Development of indicators

A list of 30 potential PQI for pharmacological management in T2DM was developed based on the latest versions of English language and Dutch diabetes guidelines[17-24]. Key guideline recommendations regarding drug treatment were transformed into potential indicators on the basis of measurability. Indicators comprised the number of patients actually receiving the drug

(numerator) over the number of patients for whom the drug was appropriate (denominator). Potential PQI were developed for the following areas: hypertension, hyperglycaemia, dyslipidaemia, antiplatelet treatment, and secondary prevention of cardiovascular disease (CVD). Developed indicators focused on undertreatment, drug choice, dosage, and safety.

Assessment of face and content validity

The face and content validity of potential indicators was assessed in a two-round expert panel followed by a panel of physicians from the field for whom the PQI were intended using the RAND/UCLA Appropriateness Method (RAM)[25]. The expert panel consisted of nationally recognized authorities from relevant specialties involved in ambulatory diabetes care: two GPs, two diabetologists, and a professor of endocrinology. The panel members had considerable practice and scientific experience and were members of Dutch College of General Practitioners, Dutch Institute for Healthcare Improvement, or Dutch Diabetes Association. For the field panel, fourteen general practitioners (GPs) and six diabetologists were recruited from two regions in the Netherlands.

Both panels were asked to rate the PQI on a 9-point scale for two criteria: reflection of the key recommendations in the guidelines, and relevance for patient health gain. Before rating the indicators, participants of both panels received background information including the evidence-base and definitions used for PQIs, and it was made clear that the potential PQI were intended for internal use.

In the first round, potential PQI were mailed to the experts for individual rating. In addition, experts were asked to suggest new indicators if they believed that important drug treatment recommendations were insufficiently addressed. The ratings were analyzed and PQI rated with disagreement were identified. In the second round, panel members met to discuss PQI rated with disagreement. The intention of the discussion was to resolve misinterpretations, and improve definitions of PQI. In case of ambiguity, the experts were asked to introduce changes in the definitions or wording of indicators. Discussion was facilitated by a moderator experienced in chairing expert panels. After the discussion, the definitions of PQI were refined, and the panellists were asked to rate the indicators a second time. Based on these second ratings, indicators classified as having insufficient validity were discarded. PQI considered valid by the expert panel were mailed to GPs and diabetologists participating in the third round. After analysis of their ratings, the final PQI were selected.

Operational validity

To assess operational validity, the selected PQI were calculated in a dataset extracted for the GIANTT project from electronic records of 3214 T2DM patients registered with 70 GPs working in 37 practices in the north of the Netherlands[26]. The dataset included information on demographics, prescribed

medication, comorbidities, physical examination and laboratory measurements as documented in medical records of GP practices and a regional diabetes facility, which offers support to GPs by providing 3-monthly and yearly diabetes follow-up examination of patients.

Analysis

A PQI was considered to be valid if it met the following predefined criteria: both panels rated it with median score of seven or more and without disagreement for either criterion[25]. Disagreement was analyzed using the interpercentile range between the first and last tertials adjusted for symmetry (IPRAS) method developed in the RAM[25]. The rationale behind this adjustment is that when ratings are symmetric with respect to the middle (5 on the 1-9 scale), the interpercentile range (IPR) required to identify disagreement is smaller than when they are asymmetric. The detailed formulas and examples for calculation of IPR and IPRAS are available on the RAND WebPage[27].

Operational validity was defined as the feasibility of calculation of PQI using electronic medical records. Indicators were calculated using SPSS for Windows version 11. For calculation of the PQI, we used values of blood pressure and HbA1c registered in the first half of 2004 and prescription data registered in the second half of 2004. This way we made sure that prescription occurred after observing elevated values of clinical measurements.

For albuminuria and BMI the last value in 2004 was used. Three PQI focusing on intensification of antihypertensive and antihyperglycaemic therapy were calculated in a longitudinal way by looking for patients who in spite of a treatment had two clinical values above target level in a period of any 4 months in 2004, and received treatment intensification in the following month. This approach has been selected since sequential indicators have been shown to provide better estimates of treatment intensification.[28] Detailed operational definitions for calculating all PQI are provided in the Appendix 2.

RESULTS

Selecting the face/content valid PQI

No indicator was discarded after the first round, but one new indicator was suggested. Therefore, in the second round the experts rated 31 indicators (Appendix 1). The panel of experts considered 18 indicators to be valid. The other 13 indicators were rated either with disagreement or with a median lower than seven for reflection of guidelines and patient health gain and were discarded (Table1). Reasons for disagreement identified during the discussion included: too much dependence on case-mix, insufficient evidence, irrelevance for ambulatory care, and disagreement on guideline recommendations (Table 1). In particular, there was disagreement between GPs and diabetologists regarding the recommendation from Dutch diabetes guidelines to prescribe thiazides as a first choice antihypertensive drug in T2DM patients without albuminuria. Diabetologists considered ACE-inhibitors as first choice drugs for diabetic patients irrespective of albuminuria.

Table 1. Discarded PQI

PQI considered as having insufficient validity by the expert panel	RKR		PHG		Reasons for disagreement provided by panellists
	M	D	M	D	
% of T2DM patients incident for hypertension without albuminuria prescribed a thiazide as a first choice drug	8	+	7	+	Not relevant for patient health gain in long term Thiazides are not a first choice drug for T2DM
% of T2DM hypertensive patients without albuminuria treated with a multiple drug regime including a thiazides	6	-	7	+	Not relevant for patient health gain in long term Thiazides are not a first choice drug for T2DM
% of T2DM patients with albuminuria and prescription of angiotensin receptor blocker (ARB) prescribed angiotensin converting enzyme (ACE) inhibitor before ARB prescription	7	+	6	+	ARBs are the first choice for RAS-inhibition Lack of evidence for ACE-inhibitors for all endpoints
% of T2DM hypertensive patients prescribed ά blockers in monotherapy	3	-	3	-	-
Percentage of T2DM patients receiving a drug regime including thiazide and β-blocker where thiazide is prescribed in a low dosage	5	-	5	+	Thiazides are not a good choice for T2DM β –blocker and ACE-inhibitor is better choice
% of T2DM patients with renal impairment, heart failure or impaired liver function prescribed metformin	8	+	7	+	Too sensitive to variety of patient characteristics
% of T2DM patients with recorded hypercholesterolemia triglyceride >2.3 mmol/l and LDL <3.0 mmol/l prescribed a fibrate	7	+	6	+	Lack of evidence: no endpoint evidence; No consensus on fibrates in the Netherlands and GPs should contact internists for prescribing a fibrate
% of T2DM patients over 40 years prescribed a statin	7	+	7	+	Age alone is not sufficient for prescribing a statin
% of T2DM patients without history of CVD but with high cardiovascular risk and well-controlled hypertension prescribed acetyl salicylic acid	7	+	5	+	Case-mix: High cardiovascular risk alone is not sufficient for prescribing acetyl salicylic acid
% of T2DM patients with uncontrolled hypertension prescribed acetyl salicylic acid	7	+	5	+	Lack of evidence
% of T2DM with diabetes and acute MI prescribed intensive insulin treatment	5	+	6	+	Relevant for hospital care
% of T2DM with diabetes and acute MI receiving thrombolytic therapy	5	+	6	+	Relevant for hospital care
% of T2DM with diabetes and coronary heart disease and present acute coronary symptoms prescribed combination of clopidogrel and acetyl salicylic acid	2	+	6	+	Relevant for hospital care No consensus on clopidrogel in the Netherlands
PQI considered as having insufficient validity by the field panel					
% of T2DM hypertensive patients receiving a drug regime including thiazides prescribed a thiazide in low dosage	8	+	6	+	Not relevant for patient health gain
% of all incident T2DM patients prescribed metformin as a first choice drug	8	+	7	+	More relevant for overweight patients
% of T2DM patients with impaired liver function or history of heart failure prescribed PPARγ-agonists (thiazolidinedions)	8	+	7	+	Too sensitive to variety of patient characteristics
% of T2DM patients aged ≤40 without history of CVD but who have 2 or more cardiovascular risk factors prescribed a statin	7	+	7	+	Case-mix: High cardiovascular risk alone (no overt CVD) is not sufficient for prescribing a statin

RKR- reflection of key recommendation in the guidelines; PHG- patient health gain; M- median rating for the criterion;D + a PQI was rated with disagreement on the criterion; D - a PQI was rated without disagreement on the criterion;MI- myocardial infarction; PPARγ-agonists - peroxisome proliferator-activated γ receptors'agonist

The field panel of GPs and diabetologists considered 14 indicators out of the 18 selected by the expert panel as being sufficiently valid. The four discarded PQI were rated with disagreement, because some members of the field panel gave low ratings to these PQI for reasons including lack of relevance for patient health gain and sensitivity to individual patient characteristics (Table 1). The final PQI covered the main aspects of pharmacological treatment in T2DM patients (Table 2).

Table 2. Outcome measures for the selected PQI

Definitions of PQI	Outcome measure, %, 95% CI (mid P)	Numerator and denominator
Hypertension management		
% of T2DM patients with systolic blood pressure ≥ 140 and prescribed any antihypertensive drug	81 (79-83)	1412/1749
% of T2DM patients prescribed a second antihypertensive drug from a different class if systolic blood pressure remained ≥ 140 with first class of antihypertensive drug	23 (20-27)	121/523
% of T2DM patients without hypertension with albuminuria prescribed ACE inhibitor or ARB	46 (31-60)	20/44
% of T2DM incident for hypertension patients with albuminuria prescribed ACE inhibitor or ARB as a first choice drugs	56 (39-72)	19/34
% of T2DM prevalent for hypertension patients with albuminuria prescribed a multiple drug regime containing ACE inhibitor or ARB	68 (60-74)	119/176
% of T2DM patients with hypertension and history of ischemic heart disease or myocardial infarction prescribed β-blocker	64 (58-70)	167/262
Hyperglycaemia management		
% of prevalent T2DM patients with HbA1c >7 % and prescribed any oral antihyperglycaemic agent or insulin	96 (95-97)	1166 /1215
% of prevalent T2DM patients not receiving insulin prescribed a second oral antihyperglycaemic drug from a different class if with one oral antihyperglycaemic drug HbA1c remained >7%	36 (31-41)	120/337
% of T2DM patients who are prescribed insulin if with combination of two oral drugs HbA1c remained >7 %	10 (7-136)	38/372
% of overweight incident T2DM patients prescribed metformin as a first choice drug	48 (32-63)	19/40
% of overweight prevalentT2DM patients prescribed a multiple drug regime containing metformin	73 (71-75)	1154/1577
Dyslipidaemia management		
% T2DM patients with high cardiovascular risk who are prescribed a statin	50 (49-52)	1506/2990
% of T2DM patients aged ≤40 with history of cardiovascular disease prescribed a statin	-	-
Antiplatelet treatment		
% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid	61 (56-65)	326/538

Hypertension was defined as diagnosis registered by GPs and/or average values of systolic blood pressure ≥140 mm/Hg;High cardiovascular risk:T2DM women age>60 years old and men >50 years old or/and with duration of diabetes ≥10 years or/and with uncontrolled hypertension or/and with albuminuria or/and HbA1c >7%;History of cardiovascular disease: history of myocardial infarction, ischemic heart disease, transient cerebral ischemia, stroke/cerebrovascular accident, or/and atherosclerosis/peripheral vascular disease as registered by GPs;Overweight patients: BMI ≥25

Operational validity

It was feasible to calculate 13 PQI using data routinely documented in medical records. One indicator focusing on prescription of statins to T2DM patients younger than 40 years and with history of cardiovascular disease could not be calculated because of lack of eligible patients (Table 2).
Five PQI required information on BMI and albuminuria, which were not available for over a third of patients. The other eight indicators were calculated based on variables available at least for 70% of patients (Table 3).

Table 3. Completeness of the dataset for variables used to calculate PQIs

Name of the variable	% of patients with a registered value
Age	100%
Gender	100%
Duration of diabetes	99%
Systolic blood pressure	80% (in the first half of 2004)
HbA1c	70% (in the first half of 2004)
BMI	65% (in 2004)
Albuminuria	43 % (in 2004)

The best performance was observed for the indicators focusing on prescribing any antihypertensive or antihyperglycaemic drugs. The lowest PQI outcomes were observed for timely intensification of antihypertensive or antihyperglycaemic treatment.

DISCUSSION

Out of 31 potential prescribing indicators derived from diabetes guidelines, fourteen were assessed by both expert and field panel as sufficiently valid for internal quality assessment. Thirteen of them were feasible to calculate using data available from electronic medical records.

To our knowledge, this is the first study that aimed to develop a set of PQI for diabetes care. We used the RAM methodology, which is considered the best method for systematically combining recommendations from clinical guidelines with opinion of health care providers[29], to develop PQI that are face and content valid. Another strong point in the assessment of validity was the use of IPRAS to measure disagreement between participants in both rounds, as this method has shown excellent sensitivity and good specificity to measure the degree of dispersion among ratings[25]. In addition, we followed a procedure of discussing reasons for disagreement, and improving definitions and wordings of the indicators before the final rating. This ensured that ambiguity was not the reason for disagreement or rejection of indicators.

It was our objective to develop and validate indicators for internal use by health care providers treating patients with T2DM. We selected the PQI using two different panels. The additional assessment of the prescribing indicators as selected by the experts in a field panel ensures

acceptability of indicators for everyday practice by those for whom the indicators are actually intended. The majority of the indicators validated by the expert panel were also selected by the field panel.

A limitation of our method is that panel members from different groups may have different judgments which affects the ratings[30]. Judgments made by any expert panel may not be representative for all health care professionals. However, in our study we had two different panels, making the final selection of indicators more reliable and generalizable. Our results show the significance of combining evidence with expert and field opinion. In particular, we found that diabetologists and GPs disagreed on some recommendations in guidelines. Since our aim was to select indicators for which there was a consensus between both groups, indicators considered relevant by only some experts were not included in the final selection. In addition, we used a selection of seven diabetes guidelines for this PQI development. Therefore, it is possible that PQI based on relevant recommendations from other guidelines were not considered. There is, however, international consensus on the key clinical recommendations for diabetes care in different guidelines[31]. Our PQI covered these central recommendations.

In all five areas of pharmacological management, several indicators of undertreatment and/or drug choice were considered valid. Except for aggressive management of hyperglycaemia, these were indicators with evidence grade A[23]. None of the indicators focusing on dosage or safety reached sufficient face and content validity because of disagreement with the recommendations or expected influence of other patient characteristics which may not always be documented in records.

Two PQI selected in our study were also considered face or content valid in previous studies, and some are being used at national level, i.e. PQI focusing on prescribing ACE-inhibitors in T2DM hypertensive patients with albuminuria[13;14;32;33] and prescribing β-blockers in T2DM patients with history of myocardial infarction[14;34-36]. The PQI focusing on prescribing ACE-inhibitors before prescribing ARBs did not reach face and content validity in our study, but was considered valid previously[37]. PQI focusing on hypertension and hyperglycaemia undertreatment have been selected also by other panels albeit with higher targets e.g. 150 for systolic blood pressure and 9% for HbA1c[32]. This can be explained by emerging evidence and by the differences in diabetes guidelines regarding specific recommendations in different countries[38]. None of the proposed PQI was included in the set of diabetes quality measures owned by the National Committee for Quality Assurance[36] or in the Australian set of indicators of quality prescribing in general practice[13]. This implies that the proposed set of indicators can be seen as a welcome addition to the existing sets of indicators.

Operational validity for most of PQI was good. Only one PQI could not be measured because of

absence of young T2DM patients with history of cardiovascular disease in our dataset. We combined clinical information stored in two data sources to enhance completeness of data collection, but some variables were not available for all patients, possibly because they are not measured each year. Missing data are a problem of any clinical registry. However, it was shown that proportion based PQI are robust to data loss up to 35% of an entire sample[39]. Considering that our PQI are also proportion based and any change in denominator will cause change in numerator, the PQI based on variables available for at least 70% of patients can be considered sufficiently generalizable. The outcomes of PQI based on albuminuria and BMI with data missing for 43 and 57 % of patients respectively may not reflect prescribing quality for whole population in this particular dataset. Nevertheless, they can be used by doctors to identify potential problems among patients with available clinical information. Some patients who are eligible for particular treatment may be missed, but those who meet the eligibility criteria for treatment (denominator) are expected to be prescribed an appropriate medication scheme (numerator).

Although we did not aim to assess quality of prescribing in this study, outcome measures for many PQI showed room for improvement. More problems were seen regarding prescribing of statins, acetyl-salicylic–acid, and timely intensification of antihypertensive and antihyperglycaemic treatment. However, it should be noted that we used a dataset of 2004, and prescribing patterns may have changed since then.
In contrast, performance for some PQI was very good, e.g. PQI focusing on prescription of any antihyperglycaemic agent showed very high outcome (96%). If a PQI shows such high performance over time for the same health care provider, it may be retired, since there is no potential for further improvement, as recently happened to one of the National Committee for Quality Assurance measures[40].

The main restriction for the use of these disease-oriented PQI is availability of patient clinical information, which is not present in all administrative datasets. However, improvement of measurement and registration of clinical values as a part of quality improvement, and development of new data collection methods will provide databases for effective use of the PQI in the future. PQI are by definition proxy measures of prescribing quality. There will always be patient and clinical characteristics that will legitimate deviations from the recommended treatment[6]. Finally, the recommendations in guidelines change over time, and PQI should be periodically updated to reflect the best evidence.

The study provides a set of face and content valid PQI for pharmacological management in T2DM that were tested for internal use by health care providers. This set can be used to make health care providers aware of specific areas of prescribing that may be suboptimal, including issues of undertreatment and drug selection.

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Appendix 1 Preliminary Prescribing Quality Indicators for Type 2 Diabetes Mellitus (T2DM) management

Definition of indicators	Domain	Evidence Grade
Hypertension management		
% of T2DM patients with systolic blood pressure ≥ 140 and prescribed any antihypertensive drug	undertreatment	A
% of T2DM patients prescribed a second antihypertensive drug from a different class if systolic blood pressure remained ≥ 140mm/Hg with 1st class antihypertensive drug	undertreatment	A
% of T2DM patients incident for hypertension without albuminuria prescribed a thiazide as a first choice drug	first choice drug	B
% of T2DM hypertensive patients without albuminuria treated with a multiple drug regime including a thiazide	drug choice	B
% of T2DM non-hypertensive patients prescribed (ACE) inhibitor or (ARB) if they have albuminuria	undertreatment	A
% of T2DM incident for hypertension patients with albuminuria prescribed ACE inhibitor or ARB as a first choice drugs	first choice drug	A
% of T2DM hypertensive patients with albuminuria prescribed a multiple drug regime including ACE inhibitor or ARB	drug choice	A
% of T2DM patients with albuminuria prescribed ARB prescribed ACE inhibitor before ARB prescription	first choice drug	B
% of T2DM hypertensive patients receiving a drug regime including thiazides prescribed a thiazide in low dosage	dosage	B
% of T2DM hypertensive patients receiving a drug regime including thiazide and β –blocker prescribed a thiazide in low dosage	dosage	B
% of T2DM hypertensive patients prescribed ά blockers in monotherapy	safety	B
Hyperglycaemia management		
% of prevalent T2DM patients with HbA1c >7% and prescribed any oral antihyperglycaemic agent or insulin	undertreatment	B
% of prevalent T2DM patients not receiving insulin who are prescribed a second oral antihyperglycaemic drug from a different class if with one oral antihyperglycaemic drug HbA1c remained >7%	undertreatment	B
% of T2DM patients who are prescribed insulin if with combination of two oral drugs HbA1c remained >7 %	undertreatment	B
% of all incident T2DM patients prescribed metformin as a first choice drug	first drug choice	B
% of overweight incident T2DM patients prescribed metformin as a first choice drug	first choice drug	A
% of overweight prevalent T2DM patients receiving a multiple drug regime including metformin	drug choice	A
% of T2DM patients with renal impairment, heart failure, or impaired liver function prescribed metformin	safety	B
% of T2DM patients with impaired liver function or history of heart failure prescribed PPARγ-agonists (thiazolidinedions)	safety	B

Definition of indicators	Domain	Evidence Grade
Dyslipidaemia management		
% T2DM patients with high cardiovascular risk risk prescribed a statin	undertreatment	A
% of T2DM patients over 40 years prescribed a statin	undertreatment	A
% of T2DM patients aged ≥40 without history of cardiovascular disease but who have two or more cardiovascular risk factors rescribed a statin	undertreatment	A
% of T2DM patients aged ≤40 with history of cardiovascular disease prescribed a statin	undertreatment	A
% of T2DM patients with recorded hypercholesterolemia triglyceride >2.3 mmol/l and LDL <3.0 mmol/l prescribed a fibrate	drug choice	A
Antiplatelet therapy		
% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid*	undertreatment	A
% of T2DM patients without history of cardiovascular disease but with high cardiovascular risk and well-controlled hypertension prescribed acetyl salicylic acid	undertreatment	B
% of T2DM patients with uncontrolled hypertension prescribed acetyl salicylic acid	safety	C
Secondary prevention of CVD in T2DM		
% of T2DM patients with hypertension and history of ischemic heart disease or myocardial infarction prescribed β-blocker	drug choice	A
% of T2DM with diabetes and acute myocardial infarction prescribed intensive insulin treatment	undertreatment	B
% of T2DM with diabetes and acute myocardial infarction receiving thrombolytic therapy	undertreatment	A
% of T2DM patients with coronary heart disease and present acute coronary symptoms prescribed combination of clopidogrel and acetyl salicylic acid	undertreatment	C

*This indicator was suggested by the experts and was added after the 1st Round

High risk includes T2DM women age> 60 years old and men > 50 years old or/and with duration of diabetes more than 10 years or/and with uncontrolled hypertension or/and with albuminuria or/and HbA1c > 7%; ACE angiotensin converting enzyme; ARB angiotensin receptor blocker

Grade A: evidence coming from at least one meta-analysis of RCTs

Grade B: evidence coming from prospective or case-control studies

Grade C: evidence coming from expert opinion or descriptive studies

Appendix 2 Operational definitions for calculation of prescribing quality indicators (PQI) for type 2 diabetes mellitus ambulatory care

- All patients in our database were patients with diagnosis of type 2 diabetes mellitus
- The international classification of primary care is used for coding of diagnosis[1]
- Medication is coded using Anatomical Therapeutic Chemical Classification System[2]

PQI for hypertension management

% of T2DM patients with systolic blood pressure≥ 140 and prescribed any antihypertensive drug

Inclusion criteria:
Patients with average systolic blood pressure (SBP) ≥ 140 in the period of 01/01/2004 -30/06/2004(first half of 2004)

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed the following antihypertensive (AH) groups: C02 (miscellaneous AHD), and/or C03 (diuretics), and/or C07 (beta-blockers), and/or C08 (calcium antagonists) and/or C09 (ACE inhibitors and ATII antagonists) in the period of 01/07/2004 –31/12/2004 (second half of 2004)
- no (0) if eligible patients are prescribed none of the mentioned medication groups in the mentioned time period

% of T2DM patients prescribed a 2nd antihypertensive drug from a different class if SBP remained ≥ 140mm/Hg with 1st class antihypertensive drug

Inclusion criteria:
Patients with prescription of one antihypertensive drug and with 2 sequential SBP >140 (time period between 2 SBP measurements is up to 4 months) in 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a second AH drug (i.e. added to first AH drug) within 5 months (starting from the date of the 1st SBP measurement)
- no, (0) if eligible patients were not prescribed (added) a second AH drug within 5 months (starting from the date of the first SBP measurement)

% of T2DM patients without hypertension with albuminuria prescribed ACE inhibitor or ARB

Inclusion criteria:
Patients without hypertension (no ICPC codes K85, K86 or K87) and with albuminuria in 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed any medication from C09 group (ACE inhibitors and ATII antagonists) in the second half of 2004
- no (0) if eligible patients were not prescribed any medication from CO9 group in the second half of 2004

1 ICPC-2, Interational classification of primary care, Second Edition, Oxford University Press, 1998
2 World Health Organization Collaborating Centre for Drug Statistics Methodology, 2007, available at http://www.whocc.no/atcddd/

% of T2DM incident for hypertension patients with albuminuria prescribed ACE inhibitor or ARB as a first choice drugs

Inclusion criteria:
Patients incident for hypertension (codes K85, K86 or K87 registered in 2004)

Outcome:
- yes (1) if first antihypertensive medication prescribed in eligible patients (who correspond to inclusion criteria) was a medication from CO9 group
- no (0) if eligible patients were prescribed other antihypertensive medication

% of T2DM prevalent for hypertension patients with albuminuria prescribed a multiple drug regimen containing ACE inhibitor or ARB

Inclusion criteria:
Patients with hypertension (SBP≥ 140 in the first half of 2004 or ICPC codes K85, K86 or K87) and with albuminuria in 2004 and prescribed more than 1 antihypertensive medication in the second half of 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a drug regimen that included any medication from CO9 group in the second half of 2004
- no (0) if eligible patients were not prescribed any medication from CO9 group in the second half of 2004

% of T2DM patients with hypertension and history of ischemic heart disease or myocardial infarction prescribed β-blocker

Inclusion criteria:
Patients with hypertension (SBP≥ 140 in the first half of 2004 or ICPC codes K85, K86 or K87) and history of ischemic heart disease (codes K75 or K76)

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a β-blocker in the second half of 2004 (any medication from CO7 group)
- no (0) if eligible patients were not prescribed any medication from CO7 group in the second half of 2004

PQI for hyperglycaemia management

% of prevalent T2DM patients with HbA1c >7 % and prescribed any oral antihyperglycaemic agent or insulin

Inclusion criteria:
Patients with average HbA1c > 7% in the first half of 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed any oral antihyperglycaemic medication (group A10B) or insulin (group A10A) in the second half of 2004
- no (0) if eligible patients were not prescribed any medication from group A10B or A10A in the second half of 2004

% of T2DM patients with prescription of one oral antihyperglycaemic drug and not receiving insulin who are prescribed a 2nd second oral antihyperglycaemic drug from a different class if HbA1c remained > 7.0%

Inclusion criteria:
Patients with prescription of one oral antihyperglycaemic drug and no insulin and with 2 sequential HbA1c >7% (period between 2 HbA1c measurements is up to 4 months) in 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a second (added) oral antihyperglycaemic drug within 5 months (starting from the date of the 1st HbA1c measurement)

- no (0) if eligible patients were not prescribed (added) a second antihyperglycaemic drug within 5 months starting from the date of the first HbA1c measurement

% of T2DM patients with 2 oral antihyperglycaemic drugs and not receiving insulin who are prescribed insulin if HbA1c remained > 7.0 %

Inclusion criteria:
Patients with prescription of two oral antihyperglycaemic drugs and no insulin and with 2 sequential HbA1c >7% (period between 2 HbA1c measurements is up to 4 months) in 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed (added) insulin within 5 months (starting from the date of the 1st HbA1c measurement)
- no (0) if eligible patients were not prescribed (added) insulin within 5 months starting from the date of the first HbA1c measurement

% of overweight incident T2DM patients prescribed metformin as a first choice drug

Inclusion criteria:
Incident diabetic patients (duration of diabetes <1 year in 2004) and body mass index (BMI) $\geq$ 25 in 2004

Outcome:
- yes (1) if the first drug prescribed to eligible patients (who correspond to inclusion criteria) was metformin (A10BA02)
- no (0) if eligible patients were prescribed another antyhyperglycaemic medication

% of overweight prevalent T2DM patients prescribed a multiple drug regime containing metformin

Inclusion criteria:
All T2DM patients (jn our case all patients are T2DM patients) with BMI $\geq$ 25 in 2004 and prescribed more than 1 antihyperglycaemic agent in the second half of 2004

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a drug regimen containing metformin (A10BA02) in the second half of 2004
- no (0) if eligible patients were not prescribed metformin (A10BA02) in the second half of 2004

PQI for dyslipidaemia management

% T2DM patients with high cardiovascular risk who are prescribed a statin

Inclusion criteria:
Patients with high cardiovascular risk (women aged >60 years and men >50 years old, or duration of diabetes ≥10 years, or average SBP≥140, or with albuminuria, or HbA1c ≥7%)

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a statin in the second half of 2004 (any medication from C10AA group)
- no (0) if eligible patients were not prescribed any medication from C10AA group in the second half of 2004

% of T2DM patients aged ≤40 with history of cardiovascular disease prescribed a statin

Inclusion criteria:
All T2DM patients younger than 40 years with history of cardiovascular diseases caused by atherosclerosis (codes K74, K75, K76, K89, K90, K91, K92)

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed a statin in the second half of 2004 (any medication from C10AA group)
- no (0) if eligible patients were not prescribed any medication from C10AA group in the second half of 2004

PQI for antiplatelet treatment

% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid

Inclusion criteria:
All T2DM patients with history of cardiovascular diseases caused by atherosclerosis (codes K74, K75, K76, K89, K90, K91, K92)

Outcome:
- yes (1) if eligible patients (who correspond to inclusion criteria) were prescribed acetyl salicylic acid (B01AC06 or B01AC06) in the second half of 2004
- no (0) if eligible patients were not prescribed acetyl salicylic acid (B01AC06 or B01AC06) in the second half of 2004

CHAPTER 3

Methods to identify the target population: implications for prescribing quality indicators

Liana Martirosyan[1], Onyebuchi A. Arah[2], Flora M. Haaijer-Ruskamp[1], Jozé Braspenning[3], Petra Denig[1]

[1]Department of Clinical Pharmacology, University Medical Center Groningen, University of Groningen, the Netherlands
[2]Department of Epidemiology, University of California, Los Angeles (UCLA), School of Public Health, Los Angeles, California, United States
[3] Scientific Institute for quality of Healthcare, Radboud University Nijmegen Medical Centre, the Netherlands

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ABSTRACT

Background

Information on prescribing quality is increasingly used by policy makers, insurance companies and health care providers. For reliable assessment of prescribing quality it is important to correctly identify the patients eligible for recommended treatment. Often either diagnostic codes or clinical measurements are used to identify such patients. We compared these two approaches regarding the outcome of the prescribing quality assessment and their ability to identify treated and undertreated patients.

Methods

The approaches were compared using electronic health records for 3214 diabetes patients from 70 general practitioners. We selected three existing prescribing quality indicators (PQI) assessing different aspects of treatment in patients with hypertension or who were overweight. We compared population level prescribing quality scores and proportions of identified patients using definitions of hypertension or being overweight based on diagnostic codes, clinical measurements or both.

Results

The prescribing quality score for prescribing any antihypertensive treatment was 93% (95% confidence interval 90-95%) using the diagnostic code-based approach, and 81% (78-83%) using the measurement-based approach. Patients receiving antihypertensive treatment had a better registration of their diagnosis compared to hypertensive patients in whom such treatment was not initiated. Scores on the other two PQI were similar for the different approaches, ranging from 64 to 66%. For all PQI, the clinical measurement -based approach identified higher proportions of both well treated and undertreated patients compared to the diagnostic code -based approach.

Conclusions

The use of clinical measurements is recommended when PQI are used to identify undertreated patients. Using diagnostic codes or clinical measurement values has little impact on the outcomes of proportion-based PQI when both numerator and denominator are equally affected. In situations when a diagnosis is better registered for treated than untreated patients, as we observed for hypertension, the diagnostic code-based approach results in overestimation of provided treatment.

BACKGROUND

In the last decade, many prescribing quality indicators (PQI) have been developed to measure whether the right drugs are prescribed to the right patients[1]. They are being used for quality improvement initiatives, and to identify and reward providers who meet predefined standards of quality. For assessing prescribing quality, it is important to correctly identify the target population, *i.e.* patients with a specific condition who should receive a specific treatment. . The validity of such identification depends not only on source of data but also on the type of information used to define a condition[2].

It has been recognized that the data source used can influence the outcome of the quality assessment. Administrative data, which are created mainly for billing purposes, often do not provide sufficient detail for reliable quality assessment[3-5]. Medical records provide a good alternative since they contain more detailed information although it can be difficult to extract all relevant information from this data source[6]. Aside from the data source, the operational definition of a condition may influence the outcome of the quality assessment. To identify the target population, *i.e.* patients in need of a specific treatment, either diagnostic codes or clinical measurements indicative of a disease or condition can be used. For example, to assess the quality of treatment in patients with hypertension, one can calculate the percentage of patients with the diagnosis of hypertension prescribed the recommended treatment[7-10], or the percentage of patients with elevated blood pressure levels being prescribed the recommended treatment[11-14].

These different approaches to define the target population give rise to several possible problems. Using information from recorded diagnoses can introduce bias due to incomplete registration when some patients with a condition do not have a corresponding diagnostic code registered in the data or due to incorrectly registered diagnostic codes[15;16]. Missing eligible patients is especially problematic for internal quality assessment, when health care providers use PQI as screening tools to identify patients who may benefit from the improved treatment. Using clinical measurements, on the other hand, may lead to missing patients with well-controlled disease states. In both cases, incorrect estimates of prescribing quality can occur when the accuracy of identification is not equal for treated and untreated patients. If this bias varies between providers, it can introduce misclassification on provider level and mislead pay-for-performance programs when better score on quality indicators is linked to financial incentives.

Little is known about the impact of the chosen approach to define the target population on the assessment of prescribing quality. The objective of our study was to compare the approach based on diagnostic codes registered in electronic health records (EHR) to the approach based on clinical measurements registered in EHR addressing the following questions:

1. Does the chosen approach affect prescribing quality scores?

2. What is the ability of the two approaches to identify well treated and undertreated patients?

For this study, existing PQI were selected focusing on glucose lowering and antihypertensive treatment in patients with type 2 diabetes mellitus. This is a field where both internal and external quality assessment are becoming priority for health care systems, and knowledge about the impact of the chosen approach to define the target population is important for accurate and meaningful quality measurement.

METHODS

Study setting and sample

In The Netherlands, patients are registered with a single general practitioner (GP) who has a gatekeeper role in coordinating their medical care. Almost all GPs used electronic health records. For our study, we used data from all T2DM patients registered with 70 GPs working in 37 practices in the North of the Netherlands. These GPs participate in the GIANTT project that collects routinely documented data, such as demographics, prescribed medication, diagnoses and clinical measurements, from the EHR of the patients. An approval to use the data for this study was obtained from the Steering Committee of the GIANTT project was obtained on April 7, 2006.

Patients with T2DM were identified through screening of the electronic medical records of the GPs using text terms for diabetes (including diab*, dm, type 2, type II), diagnostic codes for diabetes (ICPC-code T90.x)[17], record flags for diabetes, and diabetes medication (ATC-code A10)[18]. All identified patients were classified by a research assistant and verified by their GP as having type 2 diabetes mellitus using the WHO classification of diabetes[19]. In general, T2DM patients visit their GP every three months, and routine blood pressure measurements are usually conducted during these visits.

Data collection

An automatic data extraction method was used which was described previously, and is very sensitive (97-100%) in detecting relevant clinical measurement information, e.g. blood pressure and body mass index (BMI) values, irrespective of registration method or information system used by the GP[20]. The method relies on text recognition to ensure retrieval of information from 'free text' segments of the records in addition to data collection from structured tables, comparable to a manual chart review. Diagnoses are collected from the problem lists in the EHR where the GPs document medical problems pertaining to the patient using either the International Classification for Primary Care (ICPC)[17] coding or text lines, which were manually recoded into the corresponding ICPC codes by two researchers verified by an experienced GP. All participating GPs prescribed electronically, which means that the dataset included full information regarding prescribed medication.

Prescribing quality indicators (PQI)

We included PQI that have been developed for assessing prescribing quality in T2DM patients. These PQI were derived from evidence-based diabetes guidelines, and previously tested in expert panels[9;10;21;22]. For this study, we selected two PQI focusing on the treatment of patients with hypertension and one PQI focusing on glucose management in obese or overweight patients. Both hypertension and overweight can be defined using diagnostic codes or clinical measurement values, and the required information is commonly available in the EHR (table 1). These three PQI represent different aspects of prescribing in different subgroups of T2DM patients. For the first indicator (PQI-1), the clinical measurement is directly influenced by the recommended treatment which may result in missing patients with a well-controlled disease state when using clinical measurements. This is partly the case for PQI-2, although the recommended β-blocker may not be the main treatment prescribed for lowering the blood pressure. For PQI-3, there is no direct effect of the recommended treatment on the control of the condition.

Table 1. Definitions of the PQI according to the diagnostic code-based approach, the clinical measurement-based approach, and the reference method

	Diagnostic code-based	Clinical measurement-based	Reference (hybrid) method
PQI-1	Denominator:T2DM patients with diagnostic codes for hypertension	Denominator:T2DM patients with SBP≥140 mmHg	Denominator: T2DM patients with diagnostic codes for of hypertension OR SBP≥140 mmHg
	Numerator: Denominator AND prescription of any antihypertensive medication	Numerator: Denominator AND prescription of any antihypertensive medication	Numerator: Denominator AND prescription of any antihypertensive medication
PQI-2	Denominator: T2DM patients with diagnostic codes for hypertension and history of IHD or MI	Denominator:T2DM patients with SBP≥140 mmHg AND history of IHD or MI	Denominator:T2DM patients with diagnostic codes for hypertension OR SBP≥140 mmHg AND history of IHD or MI
	Numerator: denominator AND prescription of beta blocker	Numerator: Denominator AND prescription of beta blocker	Numerator: Denominator AND prescription of beta blocker
PQI-3	Denominator:T2DM patients with diagnostic codes for overweight OR obesity	Denominator: T2DM patients with BMI ≥25	Denominator:T2DM patients with diagnostic codes for overweight OR obesity OR BMI≥25
	Numerator: Denominator AND prescription of metformin	Numerator: denominator AND prescription of metformin	Numerator: denominator AND prescription of metformin

T2DM: Type 2 Diabetes Mellitus, IHD: Ischaemic Heart Disease, MI: myocardial infarction, SBP: Systolic Blood Pressure, BMI: Body Mass Index (weight in kilograms divided by height in meters-squared)

Data analysis

All the analyses were conducted using data from the EHR. The PQI were calculated using prescribing information from the second half of 2004. All preceding diagnosis information regarding hypertension (ICPC-codes K85, K86 and K87) and overweight or obesity (ICPC-codes T82 and T83) was used for the diagnostic code-based approach. For the clinical measurement-based approach, an average systolic blood pressure (SBP) of ≥140 mmHg during the first half of 2004 was used to define hypertensive patients, and the most recent BMI value in 2004 being ≥25 was used to define overweight patients. We used an average SBP≥ 140mmHg as a cut off value to identify patients with hypertension following the recommendations for treatment of T2DM patients with hypertension described in the Dutch Hypertension Guidelines for General Practitioners[23].

To check whether the inclusion of patients with an 'average' of only one elevated SBP value in the study period might be unjustified, we assessed how many of such patients had no preceding or next SBP values ≥140mm/Hg. This was the case for only 2% of the patients with elevated average SBP levels in the first half of 2004.

To select T2DM patients with history of ischemic heart disease or myocardial infarction (PQI-2) we have used ICPC codes K74, K76, and K75. All analyses were conducted using SPSS version 16.0 (SPSS, Inc., Chicago, Illinois).

To answer our first question, we calculated the PQI scores with 95% confidence intervals using only diagnostic codes or only clinical measurement values. The unit of analysis for calculation of the PQI scores was an individual patient, therefore the prescribing quality scores discussed in this paper are population level scores. We used mixed model analysis to adjust the scores of PQI and their 95% confidence intervals for correlation within GP practices. For our second question, we calculated the ability of each approach to identify 'well treated' patients (patients receiving the treatment as recommended), and 'undertreated' patients (patients in need of treatment but not receiving the recommended treatment). This was expressed as the proportion of 'well treated' (respectively 'undertreated') patients identified with either approach from the total number of 'well treated' (respectively 'undertreated') patients identified with the reference method, where we combined diagnostic codes with clinical measurement values (box1).

Finally, we repeated the analyses in a subset of patients that had at least one registered blood pressure or BMI value during the study period to assess the impact of incomplete registration of clinical measurements on the comparison of the two approaches.

RESULTS

The dataset included 3214 T2DM primary care patients with an average age of 67 years and diabetes duration of 6 years; 55% were women (Table 2). Of the patients, 32% had a registered diagnosis of hypertension, and 7% had a diagnosis of overweight. Blood pressure measurements were available for 80% of the patients, and BMI measurements for 66% of patients. Among patients with registered measurements, 55% had an average systolic blood pressure ≥140mmHg, and 55% had a BMI≥25.

Table 2 Characteristics of the study population (N=3214)

Characteristic	Value
Age, mean in years (SD)	67.1 (12.6)
Women, n (%)	1767 (55.0)
Duration of diabetes, mean in years (SD)	6.0 (5.6)
Registered diagnosis of hypertension, n (%)	984 (31.0)
Registered diagnosis of overweight or obesity, n (%)	213 (6.6)
Registered diagnosis of IHD or MI, n (%)	367 (11)
Registered systolic blood pressure, n (%)	2566 (79.8)
Registered Body Mass Index, n (%)	2106 (65.5)
Systolic blood pressure ≥140 mmHg, n (%)	1749 (54.4)
Body Mass Index ≥25, n (%)	1767 (55.0)

IHD: Ischaemic heart disease
MI: Myocardial infarction

Concurrence between registration of diagnostic codes and the corresponding clinical measurements was low. Among patients with an elevated systolic blood pressure, 62% (1086) did not have a registered diagnostic code for hypertension. In case of overweight, 92% (1624) of patients with BMI ≥25 did not have a registration of a corresponding diagnostic code (table 3).

Scores of PQI

The choice of approach affected the outcome of only PQI-1 focusing in prescription of any antihypertensive treatment. For this PQI the diagnostic code-based approach resulted in 12% higher prescribing quality score than measurement-based approach. For the remaining two indicators, the prescribing scores observed with different approaches were nearly identical (table 4).

Ability of identifying well treated and undertreated patients

The use of either diagnostic codes or clinical measurements to identify well treated or undertreated patients resulted in absolute differences in proportions of identified patients ranging from 15% to 84% (table 5). In all cases, the measurement-based approach identified more well treated and

Table 3 Eligibility agreement between registration of diagnoses and clinical measurements

	Diagnosis Yes	Diagnosis No	Total
SBP≥140	663	1086	1749
SBP<140	190	627	817
No SPB	131	517	648
Total	984	2230	3214
BMI≥25	143	1624	1767
BMI<25	5	334	339
No BMI	65	1043	1108
Total	213	3001	3214

SBP: Systolic Blood Pressure
BMI: Body Mass Index (weight in kilograms divided by height in meters-squared)

Table 4 Scores of prescribing quality indicators identified with different approaches

Prescribing quality indicators (PQI)	Outcome of the PQI, %, (95% CI) numerator/denominator	
	Diagnostic code-based	Measurement-based
PQI-1 Prescription of any antihypertensive medication in hypertensive T2DM patients	93(90-95) 1412/1749	81 (78-83) 905/984
PQI-2 Prescription of beta blocker in hypertensive T2DM patients with a history of IHD or MI	65(57-72) 100/155	64 (56-72) 125/194
PQI-3 Prescription of metformin in overweight T2DM patients	65(59-72) 39/213	66(62-69) 1154/1767

T2DM: Type 2 Diabetes mellitus
IHD: Ischaemic Heart Disease
MI: Myocardial Infarction

undertreated patients than the diagnostic code-based approach. For well treated patients, the proportion identified raised from 54% (diagnostic code-based) to 84% (measurement-based) for antihypertensive treatment in general (PQI-1), from 63% to 79% for beta blocker treatment after ischemic heart diseases (PQI-2), and from 12% to 97% for metformin treatment in overweight patients (PQI-3). Similarly, the proportion of undertreated patients identified increased from 21% (diagnostic code-based) to 88% (measurement-based) for PQI-1, from 60% to 75% for PQI-2, and from 11% to 95% for PQI-3 when clinical measurements were used (table 5).

Using the diagnostic code-based approach, a clear difference was observed in its ability to identify well treated versus undertreated patients for antihypertensive treatment in general (PQI-1). This approach identified 54% of the well treated but only 21% of the undertreated patients, indicating that the registration of a hypertension diagnosis in the EHR is more likely when drug treatment is initiated than when drug treatment is not (yet) initiated. Such bias was not observed for the other two PQI (table 5).

Table 5 Identification of well treated and undertreated patients using the diagnostic code-based and clinical measurement-based approach

Type of approach	Well treated patients proportion detected*, %	N	Undertreated patients Proportion detected**, %	N	N of eligible patients per PQI
PQI-1 Prescription of any antihypertensive medication in hypertensive T2DM patients					2070
Reference method	-	1687	-	383	
Diagnostic code-based, hypertension	54 (905/1687)	905	21 (79/383)	79	
Measurement-based, SBP≥140	84 (1412/1687)	1412	88 (337/383)	337	
PQI-2 Prescription of beta blocker in hypertensive T2DM patients with a history of IHD or MI					251
Reference method	-	159	-	92	
Diagnostic code-based, hypertension	63 (100/159)	100	60 (55/92)	55	
Measurement-based, SBP≥140	79 (125/159)	125	75 (69/92)	69	
PQI-3 Prescription of metformin in overweight T2DM patients					1837
Reference	-	1193	-	644	
Diagnostic code-based, overweight or obesity	12 (139/1193)	139	11 (74/644)	74	
Measurement-based, BMI≥25	97 (1154/1193)	1154	95 (613/644)	613	

T2DM: Type 2 Diabetes mellitus

SBP: Systolic Blood Pressure

BMI: Body Mass Index (weight in kilograms divided by height in meters-squared)

*Number of treated patients detected through the tested approach divided by the number of treated patients according to the reference method

**Number of untreated patients detected through the tested approach divided by the number of untreated patients according to the reference method

Subset analysis

We repeated the analyses in subsets of patients that had at least one recorded blood pressure measurement for PQI-1 (1939 of the 2070 hypertensive patients) and PQI-2 (227 of the 251 hypertensive patients with IHD or MI), and at least one BMI value for PQI-3 (1772 of the 1837 overweight patients). The PQI scores for the subset were quite similar to scores observed for the whole study population. According to the reference method, the prescribing quality scores

calculated for the subsets changed from 81% to 82% for PQI-1, from 63% to 64% for PQI-2, and remained 65% for PQI-3. For the diagnostic code-based approach, observed changes were 92% to 94% (PQI-1), 65% to 66% (PQI-2), 65% to 70% (PQI-3). As could be expected, the proportion of identified well treated and undertreated patients with the measurement-based approach increased for this subset of patients, and approached the reference method with proportions of 89%, 86%, 100% for well treated and 95%, 85%, 100% for undertreated patients.

DISCUSSION

Our study showed that prescribing quality scores do not necessarily change when using different approaches to define the number of patients eligible for treatment. However, when diagnosis is registered better for treated than for untreated patients, as was the case for hypertension, the diagnostic code-based approach resulted in overestimating the prescribing quality (93 versus 81%). In addition, it became clear that incomplete registration of diagnostic codes is a big problem for conditions such as hypertension and overweight, leading to the identification of low proportions of patients in need of treatment (11-60%) when using a diagnostic code-based approach.

In general, PQI are proportion-based measures which can be quite robust to changes in the numerator, as any change in the numerator causes changes in the denominator[24]. This was the case for the indicators focusing on the prescription of beta blockers and of metformin in specific patient groups (PQI-2 and PQI-3). However, for the indicator focusing on the prescription of any antihypertensive drug (PQI-1), the diagnostic code-based approach resulted in a higher score on prescribing quality compared to the clinical measurements-based and reference methods. The explanation of this finding is that the registration of the diagnostic codes for hypertension is more likely once antihypertensive treatment is prescribed, as was illustrated by the low percentage of untreated in comparison to treated hypertensive patients identified with the diagnostic code-based approach. A similar finding was observed in non-diabetic population, where treated patients also had a better registration of the diagnosis of hypertension[25].

In our study population, the clinical measurement-based approach identified higher proportion of patients who are in need of treatment compared to the diagnostic code-based approach. This is due to the fact that many patients with either high blood pressure or BMI levels did not have a registration of the corresponding diagnostic code in the EHR. Poor registration of conditions such as hypertension and especially overweight in the EHR seems to be a common problem[26,28]. It has therefore been advocated to use clinical measurements to improve documentation of such conditions[29]. Improved registration of diagnostic codes as a part of quality improvement programs may make diagnostic code-based PQI more reliable. It is important to realize, however, that the validity of registered diagnoses is influenced by many factors including the purpose of registration, skills and knowledge of the coder, insensitive coding schemes for registering specific diseases,

prioritizing the coding of some conditions over others by physicians, and completeness of a disease classification system[15;30].

Clinical measurement values appear to be a better choice for prescribing quality assessment, especially for internal quality assurance, when it is crucial to correctly identify as many patients who could benefit from the improved treatment. When the clinical measurement values are influenced by the recommended treatment, as is the case for PQI-1 and PQI-2, a clinical measurement-based approach for assessing the treatment may result in missing patients with well-controlled disease states. This is particularly a problem when patient eligibility and prescribed treatment are assessed cross-sectionally[14]. When prescribing is assessed in a sequential way (i.e. after the observed clinical measurement), as was done in our study, missing well-controlled patients appeared not to affect the quality scores. In situations where there are already much higher percentages of well-controlled patients, however, a measurement-based approach can result in lower prescribing quality scores in comparison to a diagnostic code-based approach.

In our study we used cut off levels of SBP ≥140mmHg to identify patients with hypertension as advised by Dutch hypertension guidelines. However, World Health Organization (WHO) and International Society of Hypertension (ISH) advised to use lower cut off levels of SBP to diagnose hypertension in T2DM patients[31]. Use of lower values of SBP to identify hypertensive patients may result in larger differences between the PQI scores when the different approaches are used.

We used a sensitive method for data abstraction from medical records. Registration of diagnostic codes was complemented by recoding diagnoses from text lines. Our reference method was based on a combination of available information about diagnosis and measurements documented in the EHR. Although EHR are often considered the gold standard for quality measurement, inadequate registration of both diagnoses and clinical measurements affects this reference method. Our subset analysis, however, showed that the prescribing quality scores were not affected by incomplete registration of clinical measurements. The PQI scores and proportions of identified patients may not be generalizable to other databases with different registration rates of clinical measurements or diagnostic codes but the identified problems are likely to occur in other settings. The registration rates in our dataset were similar to those described in other studies conducted in different parts of the world using EHR of both diabetic and general primary care population[25;32;33].

Finally, it has to be kept in mind that if these PQI are used for comparison of individual GPs, the number of eligible patients per PQI per GP may not be sufficient for reliable benchmarking. To address the problem of a small sample size per PQI, one could choose from several existing methods including pooling data from several health care providers or time periods or excluding indicators or health care providers with small patient numbers[21].

Although in our study setting the ICPC codes were used, we expect that the results of our study are also relevant for health care systems using the International Classification of Diseases (ICD), as this classification system also includes diagnostic codes for hypertension, overweight and obesity that could be combined or substituted with clinical measurement values.

CONCLUSION

To our knowledge, this is the first study addressing the impact of using different types of information to define a condition on the assessment of prescribing quality. With the increasing use of electronic health records, which offer more complete information than administrative data, EHR have the potential to provide sensitive estimates of healthcare quality. Our study shows some drawbacks of using either diagnostic codes or clinical measurement values from the EHR for prescribing quality assessment. Although both approaches resulted in missing patients who could benefit from the recommended treatment, the use of clinical measurements is more sensitive to screen for poorly treated patients. This is important for quality improvement purposes. When there is information bias in the documentation of diagnoses in relation to the treatment status, the use of diagnostic codes alone can mislead both policy makers and health care providers about the performance scores of quality indicators. In such cases, a combination of diagnostic codes and clinical measurement information is recommended for prescribing quality assessment.

Authors' contributions

LM originated the idea for this study, did the research proposal, data analysis, and prepared the manuscript. PD and HR-FM contributed to the research proposal, reviewed the analysis, and participated in the preparation of the manuscript. JB participated in the interpretation of the data and in the discussion of the paper. OAA participated in the data analyses and edited and reviewed the manuscript. All authors read and approved the final manuscript

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CHAPTER 4

A Systematic Literature Review: Prescribing Indicators related to Type 2 Diabetes Mellitus and Cardiovascular Risk Management

Liana Martirosyan M.D., MPH[1], Jaco Voorham MSc[1,2], Flora M.Haaijer-Ruskamp PhD[1], Jozé Braspenning PhD[3], Bruce H.R Wolffenbuttel M.D[4].,PhD, Petra Denig PhD[1]

[1]Department of Clinical Pharmacology, University Medical Centre Groningen, University of Groningen, the Netherlands
[2]Department of Epidemiology, University Medical Centre Groningen, University of Groningen, the Netherlands
[3]Scientific Institute for quality of Healthcare, Radboud University Nijmegen Medical Centre, the Netherlands
[4]Department of Endocrinology and Metabolism, University Medical Centre Groningen, University of Groningen the Netherlands

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ABSTRACT

Purpose

Valid prescribing indicators (PI) are needed for reliable assessment of prescribing quality. The purpose of this study is to describe the validity of existing PI for type 2 diabetes mellitus and cardiovascular risk management.

Methods

We conducted a systematic literature search for studies describing the development and assessment of relevant PIs between January 1990 and January 2009. We grouped identified PI as drug- or disease-oriented, and according to the aspects of prescribing addressed and the additional clinical information included. We reviewed the clinimetric characteristics of the different types of PI.

Results

We identified 59 documents describing the clinimetrics of 16 types of PI covering relevant prescribing aspects, including first-choice treatment, safety issues, dosing, costs, sufficient and timely treatment. We identified three types of drug-oriented, and five types of disease-oriented PI with proven face and content validity as well as operational feasibility in different settings. PI focusing on treatment modifications were the only indicators that showed concurrent validity. Several solutions were proposed for dealing with case-mix and sample size problems, but their actual effect on PI scores was insufficiently assessed. Predictive validity of individual PI is not yet known.

Conclusion

We identified a range of existing PI that are valid for internal quality assessment as they are evidence-based, accepted by professionals, and reliable. For external use, problems of patient case-mix and sample size per PI should be better addressed. Further research is needed for selecting indicators that predict clinical outcomes.

INTRODUCTION

Appropriate drug prescribing has been recognized as an important quality of care issue in the management of chronic conditions. Insight into the quality of prescribing is demanded by health care providers, payers, and the public. Such information is used for internal quality improvement through audit, feedback, and benchmarking in educational contexts.[1-3] External stakeholders use prescribing information for comparison of health care providers, and to implement performance-based reimbursement programs that reward health care providers for meeting preset targets.[4,5]

To measure quality of prescribing, prescribing indicators (PI) have been developed. Distinct types of PI exist that address different aspects of prescribing quality, such as recommended drug-choice, ineffective drugs or timely treatment.[6] There are drug-oriented PI which focus on the drugs prescribed irrespective of the indication, and disease-oriented PI looking at the prescriptions in relation to a specific condition.[7] Furthermore, there are indicators that link prescribing to clinical outcomes.[8,9]

Although there are no consensus-based criteria for the development of quality measures, they are expected to reflect the best available evidence, to be relevant, and to be accepted by the professionals in the field.[10,11] Effective use of PI requires understanding of what aspect of prescribing is measured, how the indicators were developed, and whether their clinimetric characteristics, *e.g.* validity and reliability, were assessed.[11] The requirements regarding these characteristics might depend on the aim of the indicator. For internal purposes, PI need to be relevant for healthcare providers: they have to be specific and sufficiently detailed to show potential problems and capture pertinent changes in prescribing. However, to make fair comparisons between health care providers for external use, *e.g.* by third party payers, there are additional requirements, like adjustment for patient case-mixes and having adequate number of patients per provider.[12,13]

A large number of PI have been developed in recent years for chronic conditions, such as type 2 diabetes mellitus (T2DM) and cardiovascular risk management. These conditions where one of the first for which disease management programs, as well as quality assurance programs were developed. We have focused on these conditions as they are closely related. While the prevalence of T2DM and cardiovascular diseases is dramatically increasing, appropriate pharmacological treatment of risk factors can prevent complications in both diabetic and non-diabetic populations.

For reliable measurement of prescribing quality valid indicators are needed. In spite of a large number of existing PI for T2DM and cardiovascular risk management, no information is available on their validity. The purpose of this study is to identify the various types of existing PI, and describe their clinimetric evaluation. The results of this study will help health care providers and policy makers to choose the most appropriate PI for quality assessment by pointing out their clinimetric

values as well as possible limitations.

METHODS

Search and selection strategy

We performed a systematic search in MEDLINE and EMBASE databases without language restrictions from January 1990 to January 2009 for studies focusing on the development or assessment of quality indicators including PI related to T2DM or CV risk management (Appendix 1). In addition, we hand searched the WebPages of professional organizations that have sets of quality indicators in English speaking countries and the Netherlands. PI was defined as a measurable element of prescribing that can be used to assess quality or efficiency of treatment at drug, patient or provider level.

Two reviewers independently screened the titles and abstracts of 5,121 retrieved manuscripts and excluded papers not focusing on T2DM or CV risk management. Using full copies of the papers, we excluded reviews, letters, commentaries, studies that did not include any PI and studies that merely used indicators to assess prescribing quality without assessment of clinimetrics.

Classification of papers and indicators

All selected papers were independently reviewed and classified by two researchers in a two-stage process, focusing first on classification of studies, and secondly, on classification of the PI identified from the studies. Disagreement between reviewers was resolved through discussion.

On study level, we recorded whether and how clinimetric properties, *i.e.* face, content, concurrent, and predictive validity, operational feasibility, reliability, robustness to case-mix, and minimal sample size needed, were assessed (Table 1). Furthermore, we recorded the aim and intended setting for the indicators. We classified the identified indicators as drug- or disease-oriented. We further grouped indicators according to the different aspects of prescribing addressed, and the type of clinical information included. As it has been argued that sequential assessment of prescribing in reaction to a clinical event or outcome would provide more meaningful indicators than simple cross-sectional assessment of the prescribed treatment,[8] we also divided the indicators regarding this aspect. In case of similar indicators, differing slightly in the way of formulation, we provided a general description of the indicator with some typical examples. At this generic indicator level, we reported the studies that have included such an indicator, as well as the outcomes regarding validity, reliability, and operational feasibility. Results on these clinimetrics were classified as 'positive' when all referenced studies reported the clinimetric to be present, 'negative' when the clinimetric was shown to be absent, and 'doubtful' if mixed or inconclusive results were reported.

Table 1. Definitions of clinimetric characteristics

Definitions of Clinimetric Characteristics	
Content validity	PI are based on literature review or evidence-based clinical guidelines
Face validity	PI are assessed and accepted by a group of experts or professionals in the field
Concurrent validity	PI correspond to a gold standard or other measures
Predictive validity	PI have the capacity for predicting patient (intermediate) outcomes
Operational feasibility	Feasibility of calculation of PI is demonstrated or defended in the view of available data
Reliability	PI yield the same outcome when measured by different persons or at different times
Case-mix adjustment	Patient-related attributes are controlled, minimized or checked to make measurement of prescribing quality as comparable as possible across providers or organizations seeing different mixes of patients
Minimal sample size	Minimal sample size per PI required for prescribing quality assessment is provided or solution to deal with small numbers is offered
Aim of the indicators described in studies	
Internal	Indicators are meant for use by health care providers for quality improvement, educational purposes and internal audit
External	Indicators are meant for use by policy makers for pay for performance, public reporting, or comparison across states or against national averages
Both	Indicators can be used for both internal and external quality assessment
N/A	Aim is not mentioned by the authors
Intended setting	
Ambulatory care	To assess quality of prescribing in primary and outpatient care or in nursing homes
Hospital care	To assess quality of prescribing in hospital setting
Both	To assess quality of prescribing in hospital and ambulatory care

RESULTS

We identified 46 studies published in peer-reviewed journals. By screening the references of these papers, we identified six additional published studies. From the WebPages of professional organizations, we found seven relevant documents that had not been formally published. Our final cohort thus included 59 papers focusing on the assessment of PI related to T2DM or CV risk management (Table 2).

Many studies described sets of quality indicators including not only PI but also indicators focusing on other aspects of care, *e.g.* screening, referral, etc. In some sets, PI were underrepresented,[4,5,14] while others consisted of only PI.[3,12,15-22] In general, the assessment of various clinimetric characteristics of some indicator sets, *e.g.* ACOVE indicators, were described in several studies,[23-25] including adaptation of these indicators in different countries.[26,27] For sets of indicators that were updated several times, *e.g.* Beers' criteria and ACOVE indicators, we have included the latest version.[25,28]

The development of indicators was described in 37 studies, which always included assessment of face and/or content validity. The other studies focused on the assessment of clinimetrics of previously developed PI.

Clinimetrics addressed and methods used in the studies *(Table 2)*

Content validity was addressed in 37 studies. The most common approach to ascertain content validity of the PI was using recommendations from clinical guidelines. In two cases, authors first assessed the quality of available guidelines, and used the highest ranking guidelines to propose indicators.[29,30] In six studies, authors reviewed randomized controlled trials to propose indicators.[2,28,31-34] In three studies a literature review was conducted to identify potential indicators.[26,35,36]

Face validity was addressed in 36 studies and assessed using different techniques including modified Delphi,[2,10,20,25-28,31,32,35-46] nominal group,[47,48] focus group discussion,[1,49] surveys or panels of professionals,[1,10,19,29,30,50-53] continuous assessment of indicators using panels of various stakeholders,[4,5,12,54] or iterative process.[55]

Concurrent validity was assessed in four studies by comparing different data sources,[24] different PI,[8,68] and different data collection methods.[57] Medical records provided more detailed clinical information for quality assessment than administrative data, although scores for individual indicators did not change across sources.[24] However, frequent misclassifications occurred when using automated measurement in electronic health records (EHR) in comparison to manual medical record review, because the automated method missed diagnosis or contraindications information registered in free-text notes.[57] Sequential quality indicators provided more accurate estimates of quality of care compared to cross-sectional measures.[8,68]

Predictive validity of PI was assessed in six studies, all using composite indicator scores. In five studies the association between process of care and outcomes was assessed cross-sectionally. Only one study assessed the link between quality of care and survival of patients using a prospective design.[23] Three studies used a composite score based on PI,[22,65,67] while others also included other process indicators. Some concluded that higher scores were associated with better controlled risk factor levels[31,67] or better survival,[23] while others found at most weak associations.[14,22,65]

Operational feasibility was the most frequently assessed characteristic (40 studies), using theoretical, implicit and explicit approaches. In case of theoretical assessment, PI requiring information not available in existing databases were excluded during development.[4,10,12,16,19,45,53,55] Indicators that were explicitly tested for operational feasibility were applied to specific types of datasets or settings, *e.g.* administrative data, EHR or primary care and hospital settings.[9,17,20,21,49,50,52,56,58-60] Implicit assessment of operational feasibility occurred in all other studies when PI were calculated during assessment of

Table 2. Description of the included literature

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
	studies published in peer-reviewed journals identified through the main search strategy												
Ackermann e.a. [14]	To determine whether variation in the number of simple diabetes processes of care across provider groups is associated with variation in other quality indicators including cardiometabolic risk factor levels	US	E	amb	-	-	-	-	+	-	+	-	-
Anderson e.a. [15]	To provide an estimate of the extent of potentially inappropriate prescribing using explicit criteria and computerized drug benefit claims data, and assess its association with physician characteristics	Can	I	amb	-	-	-	-	-	-	+	-	-
Ashworth e.a. [16]	To determine prescribing indicators which were used by primary care groups under prescribing incentive schemes	UK	E	amb	-	-	-	-	-	-	+	-	-
Basger e.a. [18]	To develop a list of prescribing indicators for elderly Australians based on the most frequent medications prescribed to Australians, and the most frequent conditions	Aust	I	amb	+	-	+	-	-	-	-	-	-
Bateman e.a. [50]	To develop a range of criteria of prescribing quality, to set standards for these criteria, and apply these standards to practices	UK	E	amb	+	+	+	-	-	-	+	-	-
Burge e.a. [32]	To systematically develop quality indicators for primary care practice and chronic disease management of ischemic heart disease, hypertension, hyperlipidemia, and heart failure	Can	I	amb	+	+	+	-	-	-	-	-	-
Campbell e.a.1998[10]	To assess face validity of quality indicators being used or proposed for use in general practice by health authorities	UK	N/A	amb	-	+	-	-	-	-	+	-	-
Campbell e.a.1999 [33]	To develop review criteria to assess the quality of care for adult asthma, stable angina, and non-insulin dependant diabetes mellitus	UK	I	amb	+	+	+	-	-	-	-	-	-

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Campbell e.a.2002[51]	To field test the reliability, validity and acceptability of review criteria for angina, asthma, and type 2 diabetes mellitus	UK	N/A	amb	-	+	-	-	-	+	+	+	-
Campbell e.a.2008[39]	To develop common quality standards for cardiovascular prevention and risk management across Europe	UK	I	amb	+	+	+	-	-	-	-	-	-
Cheng e.a.[36]	To propose quality indicators that could be applied when treating vulnerable elders for stroke	US	N/A	both	-	+	+	-	-	-	-	-	-
DiSalvo e.a.[52]	To test the feasibility of developing and implementing measures of continuum of hospital through post discharge ambulatory care for patients with acute myocardial infarction, congestive heart failure and hypertension	US	I	both	+	+	+	-	-	+	+	+	-
Elliot e.a.[19]	To develop a set of indicators of prescribing quality for elderly inpatients in Australian hospitals	Aust	I	hosp	+	+	+	-	-	+	+	-	-
Fick e.a.[28]	To revise and update the Beers criteria for potentially inappropriate medication use in adults 65 years and older in the United States	US	I	both	+	+	+	-	-	-	-	-	-
Garjon Parra e.a.[47]	To work out a system of indicators for improvement of primary care prescription, by incorporating the values and views of the professionals issuing prescriptions	Spain	I	amb	+	+	+	-	-	-	-	-	-
Gribben e.a.[58]	To develop a set of non-invasive, evidence-based, population-based quality of care indicators for primary care in New Zealand and to test their feasibility	NZ	I	amb	+	-	+	-	-	-	+	-	-
Guptha e.a.[56]	To study the applicability of secondary care prescribing indicators to primary care and measure prescribing quality	UK	both	amb	-	-	-	-	-	-	+	-	-
Hutchinson e.a.[29]	To formulate and evaluate a method for developing, from clinical guidelines, evidence-based review criteria that are prioritized, useful and relevant to general practices to assess quality of care for the primary care management of coronary heart disease	UK	I	amb	+	+	+	-	-	-	-	-	-

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Idanpaan-Heikkila e.a.[35]	To develop a set of quality indicators for cardiac care	Fin	E	both	+	+	+	-	-	-	-	-	-
Jencks e.a.[66]	To create a monitoring system for a range of measures of clinical performance that supports quality improvement	US	E	both	-	-	-	-	-	+	+	-	-
Katz e.a.[49]	To explore the feasibility of using administrative data to develop process indicators for measuring quality in primary care	Can	I	amb	+	+	+	-	-	-	+	+	-
Kerr e.a.[8]	To determine the relative accuracy of quality assessment in diabetes using simple intermediate outcome versus tightly linked quality measures	US	N/A	amb	-	-	-	+	-	-	+	-	-
MacKinnon e.a.[40]	To develop a set of Canadian clinical indicators of preventable drug-related and care-related morbidity for type 2 diabetes	Can	I	amb	+	+	+	-	-	-	-	-	-
Majumdar e.a.[41]	To rigorously develop and validate a set of quality indicators for type 2 diabetes mellitus for researchers or decision-makers	Can	both	amb	+	+	+	-	-	-	-	-	-
Martirosyan e.a.[20]	To develop a set of prescribing quality indicators for pharmacological management in type 2 diabetes mellitus patients for internal use, and to assess their operational validity	NL	I	amb	+	+	+	-	-	-	+	-	-
McColl e.a.1998[34]	To suggest performance indicators that could monitor use of important primary care interventions	UK	E	amb	+	-	+	-	-	-	-	-	-
McColl e.a.2000[59]	To test the feasibility of deriving comparative indicators in all practices within a primary care group	UK	E	amb	-	-	-	-	-	-	+	-	-
Mehta e.a.[61]	To evaluate the degree to which hospital process performance ratings and eligibility for financial incentives are altered after accounting for hospitals' patient mixes	US	E	hosp	-	-	-	-	-	-	+	+	+

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Milchak e.a.[48]	To define a comprehensive set of reliable and valid process of care criteria reflecting the hypertension practice recommendations, and derive a scoring method	US	I	both	+	+	+	-	-	-	+	-	-
Min e.a.[42]	To propose a new set of quality indicators for the care of hypertension in vulnerable elders	US	N/A	both	-	+	+	-	-	-	-	-	-
Muijrers e.a.[43]	To formulate and validate clinical prescribing indicators based on general practice guidelines	NL	I	amb	+	+	+	-	-	-	+	-	-
Oborne e.a.[21]	To modify prescribing indicators, including appropriateness of prescribing algorithms developed in the hospital setting, for use in nursing homes	UK	I	amb	-	-	-	-	-	+	+	+	-
O'Brien e.a.[62]	To examin the association between hospital sample sizes and observed performance on individual process-of-care measures	US	E	hosp	-	-	-	-	-	-	+	+	-
Persell e.a.[57]	To evaluate the validity of performance measures for coronary artery disease using an ambulatory electronic health records	US	E	amb	-	-	-	+	-	+	+	-	-
Peterson e.a.[22]	To assess whether hospitals' overall measure of composite adherence to guidelines was associated with observed and risk-adjusted in-hospital mortality rates	US	E	hosp	-	-	-	-	+	-	+	-	-
Schubert e.a.[3]	To develop indicators based on prescription analysis in order to assess adherence to guidelines and monitor prescribing behavior	Germ	I	amb	+	-	-	-	-	-	+	+	-
Shekelle e.a.[44]	To develop quality indicators for diabetes mellitus care in vulnerable elderly population	US	I	both	+	+	+	-	-	-	-	-	-
Solberg e.a.[55]	To develop and test ambulatory care quality measures obtainable from administrative data	US	N/A	amb	+	+	-	-	-	-	+	+	+

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Torrecilla-Rojas e.a.[67]	To define and validate a battery of prescription indicators on the use of anti-hypertensives, lipid-lowers, diabetes drugs and insulin, as measurements of family doctors' quality of prescription	Spain	I	amb	+	-	+	-	+	-	+	-	-
Tu e.a.[45]	To develop an updated set of indicators to measure and improve quality of care for patients with acute myocardial infarction	Can	both	hosp	+	+	+	-	-	-	+	-	-
Van der Ploeg e.a.[27]	To adapt a set of systematically developed US quality indicators for health care of vulnerable elders in the Netherlands	NL	I	amb	+	+	+	-	-	-	-	-	-
Voorham e.a.[68]	To compare cross-sectional and sequential quality indicators for risk factor management in patients with type 2 diabetes	NL	both	amb	-	-	-	+	-	-	+	-	-
Wenger e.a. [25]	To update and increase the comprehensiveness of the Assessing Care of Vulnerable Elders (ACOVE) set of process-of-care quality indicators	US	I	both	+	+	+	-	-	-	-	+	+
Wens e.a.[30]	To search for potential evidence-based indicators within diabetes-care guidelines and convert them into a manageable tool for assessing quality of diabetes care at the primary health-care level	Be	I	amb	+	+	+	-	-	-	-	-	-
Werner e.a. [65]	To determine whether quality measured with the process measures used in Hospital Compare are correlated with and predictive of hospitals' risk-adjusted mortality rates	US	both	hosp	-	-	-	-	+	-	+	+	+
Wilkinson e.a.[60]	To investigate reactions to the use of evidence-based cardiovascular and stroke performance indicators within one primary care group	UK	I	amb	-	-	-	-	-	-	+	-	-
	studies published in peer-reviewed journals identified through additional search												
Asch e.a. 2001[31]	To develop and test a quality measurement system for women with hypertension	US	N/A	amb	+	+	+	-	+	-	+	-	-

Author(s)	Objective of the study or organization	Country*	Aim of the indicators**	setting***	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Asch e.a. 2006[37]	To examine the relationship between patients' characteristics and several domains of quality of care	US	N/A	both	+	+	+		-	+	+	-	+
Higashi e.a.[23]	To examine the link between quality of care that patients received and their survival	US	I	both	-	-	-	-	+	+	+	-	-
MacLean e.a.[24]	To compare measurements of quality between medical records and administrative data using the Assessing Care of Vulnerable Adults (ACOVE) quality indicator set	US	both	both	-	-	-	+	-	+	+	-	-
Rodondi e.a.[9]	To better understand the potential utility and the feasibility of measuring therapy modifications in response to poor risk factor control as an additional measure of quality	US	N/A	amb	-	-	-	-	-	-	+	-	-
Steel e.a.[26]	To adapt a set of USA quality indicators to measure quality of care of older adults for use in patient surveys in England	UK	I	both	+	+	+	-	-	-	-	-	-
	papers found on webpages of professional organizations												
Aust-NPS[1]	To improve Australian health outcomes through the quality use of medicines	Aust	I	amb	+	+	+	-	-	+	+	+	-
Dutch-CBO[53]	To develop quality indicators on efficacy and safety of diabetes care for external use	NL	E	amb	+	+	+	-	-	+	+	-	+
NCQA-HEDIS [4]	To reliably compare the performance of health plans	US	E	both	+	+	+	-	-	+	+	+	+
NHS-PING [12]	To produce and review sets of prescribing indicators issued by the Department of Health in the UK	UK	both	amb	+	+	+	-	-	-	+	-	-
NHS-QOF [5]	To improve quality of care through a incentive scheme rewarding GP practices for how well they care for patients	UK	E	amb	+	+	+	-	-	-	+	-	+

NQF [54]	To improve the quality of American healthcare by setting national priorities and goals for performance improvement	US	both	amb	+	+	+	-	-	+	+		+	+
RAND Health [46]	To develop and test the Quality Assessment Tools system, a comprehensive, clinically based system for assessing quality of care for children and adults	US	both	both	+	+	+	-	-	-	-		-	-

Total number of times the clinimetric characteristics was assessed in all included studies	Development****	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
	37	36	37	4	6	13	40	13	9

*Aust-Australia, Be-Belgium, Can-Canada, Germ-Germany, Fin-Finland, NZ-New Zeeland, NL-the Netherlands, UK-United Kingdom, US -United States of America

**Indicators intended for: I=internal quality assessment; E=external quality assessment; N/A= aim was not explicitly mentioned; both= internal and external quality assessment

***Indicators intended for amb=ambulatory care, hosp=hospital care, both=both ambulatory and hospital setting

****New indicator(s) were developed as part of the study or project

\+ Characteristic was *addressed* in the study; - characteristic was *not addressed* in the study

other clinimetric characteristics, *e.g.* reliability or concurrent validity.[3,8,14,15,22-24,31,34,37,43,51,57,61-68]

The inter-rater reliability was evaluated in studies using manual chart review by means of kappa statistics. In all cases, good reliability was shown for manual data abstraction.[19,21-24,37,49,51,57] In some cases reliability was assessed theoretically during the indicator development process.[4,17,53,54]

Case-mix problems were addressed in nine studies, of which seven included indicators with external aim (Table 2). This issue was not addressed in other studies with a clearly mentioned external aim.[14,16,22,34,50,57,59,62] Two studies showed the influence of case-mix on performance scores.[37,61] Several approaches were proposed to minimize the effect of patient clinical or sociodemographic characteristics on PI outcomes, including statistical adjustment,[4,37] exclusion of indicators that are too much affected by such characteristics,[53,55] or exclusion of patients for reasons like contraindications, perceived side-effects or refusing medication.[5,25] Another approach to deal with case-mix was setting lower target levels.[70]

Sample size was addressed in 13 studies. Two studies showed that sample size can affect performance scores and hinder comparisons between individual providers.[61,62] Suggested solutions were exclusion of indicators or providers with small numbers,[51,55,62,65] use of hierarchical estimates,[62] or pooling data from several providers or time periods.[1] The minimal sample size suggested per indicator ranged from 5-10[49] to 30-60 patients.[1] Others suggested to include only providers with a certain number of patients,[3,25,52] but did not support this with calculations. A paper related to measures proposed by the National Quality Forum[69] provided guidelines for sample size calculations. It was shown that the minimal number of patients to get a reliability of 0.8 depends on the intraclass correlation coefficient (ICC), and could range from 36 for an ICC of 0.10 to 196 for an ICC of 0.02.

Types of PI and their reported clinimetrics

We identified in total 16 types of PI, including seven drug-oriented and nine types of disease-oriented PI. The same types of indicators were proposed for internal and external quality assessment. PI for T2DM were typically developed for ambulatory care, whereas PI for cardiac care and more general PI were also developed for hospital care.

Drug-oriented PI

The drug-oriented PI were grouped on different aspects of prescribing: first choice drug (classes), second-step drugs, non-preferred drugs, safety issues, dosing issues, redundant prescribing, and cost-conscious prescribing (Table 3). For almost all types, several generic indicators were identified, and five of them were tested in several studies. Indicators focusing on prescribing of first-choice or non-preferred drugs were both well-studied, and mostly rated as face and content valid, since they were derived from guideline recommendations. Regular updating was deemed necessary to reflect

Table 3. Classification of drug-oriented prescribing indicators as assessed in the studies

DRUG-ORIENTED PI	Face validity	Content validity	Reliability	Operational feasibility
1. First choice or preferred drugs or drug classes				
% first choice drugs (*e.g.*, enalapril or simvastatin) of all drugs prescribed within its therapeutic class (ACE inhibitors or lipid lowering drugs). [3,16,43,47,50,67]	+	+		+
% first choice drug class (*e.g.*, biguanides) of all oral antidiabetic drugs [16,67]	~	+		+
patients on preferred drug classes (e.g., diuretics or betablockers) of all antihypertensives [47,67]	+	+		+
ratio of preferred: less preferred drugs (*e.g.*, plain:combination diuretics) [10]	~			+
number of prescriptions for (preferred) drugs per PU (or ASTRO-PU) [10]	~			+
2. Secondstep drugs				
patients prescribed ARB and prior to this an ACE inhibitor of all patients prescribed ARBs [43]	+	+		+
3. Non-first-choice or not preferred drugs				
patients on long acting isosorbide nitrate, glibenclamide, combinations of diuretics or alpha-glucosidase inhibitor, etc. [16,26,67]	+	+		+
dose/1000persons/day of lipid lowering drugs in elderly [47]	+	+		
patients on novelty drugs, such as ARBs or thiazolidinediones, of all patients receiving antihypertensives or oral glucose-lowering drugs [47,67]	+	+		+
<=0.6 prescriptions/100 Pus for drugs with limited indications (e.g. cerebral and peripheral vasodilators) [50]	~	+		+
4. Safety indicators				
drugs to be avoided (in elderly) (*e.g.*, chlorpropamide, long acting sulphonylurea, short-acting nifedipine) [4,15,19,21,23,24,25,26,27,28,52,56]	+	+	+	~
co-prescriptions to be avoided, *e.g.* of statins with macrolides , diuretic, ACE-inhibitor with potassium or NSAID, metformin with glibenclamide, etc. [1,3,18,19]	+	+	+	+
5. Correct dosing of drugs (under/overdosing and number of daily dosings)				
prescription of high dose hydrochlorthiazide [52] prescription of low dose bendrofluazide [16]	+	+	+	+
once-or twice- daily dosing of antihypertensives in elderly [23,24,25,26,27]	+	+	+	+
6. Redundant prescribing				
patients prescribed more than 1 drug from the same therapeutic group simultaneously (*e.g.* thiazides) [19,47]	+	+	+	-
7. Cost-conscious prescribing or limited set of drugs prescribed				
cost of treatment per unit [16,47]	+	+		+
% prescribed generic drugs [3]				+
change amlodipine to felodipine [16]				+
number of different brands with the same active substance [3] DU90% within a specific drug class [43]	~	~		+

+ characteristic is present; - characteristic is absent; ~ characteristic is assessed but doubtful or mixed results; empty cell-no information is available on characteristic

PU: prescribing unit

ASTRO PU: Age, Sex and Temporary Resident Originated Prescribing Units

ARB: Angiotensin II receptor blocker

ACE-inhibitor: Angiotensin converting enzyme inhibitor

DU: drug utilization

emerging evidence for drug choice. PI expressing currently used ratios and number of prescriptions for specific drugs per prescribing unit (PU) were criticized, since there was no agreement about what defines quality in these cases.[10,50]

Safety indicators focused on potentially inappropriate drugs or drug combinations to be avoided, and both groups were widely studied. They were considered face and content valid but criticized for reflecting only a limited part of prescribing quality.[15,19] Since in specific cases there can be good reasons to use "inappropriate" drugs, these indicators were recommended for internal use to identify potential problems.[19] Indicators focusing on redundant prescribing, *e.g.* number of daily dosing or co-prescribing of more than one drug from the same therapeutic group, were studied in two and five studies respectively, which showed that this group of indicators is reliable, face and content valid. Difficulties were encountered regarding the operational feasibility of some safety and redundant prescribing indicators because of the absence of eligible patients or lack of information on duration of prescriptions.[19,56]

Indicators focusing on cost were seldom assessed for face and content validity[47] or doubts were raised for their relation to quality.[43] Furthermore, the value of the DU90% focusing on the number of different drugs prescribed within a drug class was disputed, because it does not discriminate between physicians, and high scores can be obtained while prescribing less preferred drugs.[43]

In summary, the drug-oriented indicators that have repeatedly shown face and content validity focus on: (a) proportions of first choice drugs within a therapeutic class, (b) drugs to be avoided, (c) number of preferred daily dosings. In general, drug-oriented PI have shown good operational feasibility.

Cross-sectional disease-oriented PI

We identified more than 30 generic disease-oriented indicators assessing prescribing in a cross-sectional way. They were grouped reflecting prescribing of: drugs for a specific indication (subdivided for different drugs), drugs for a specific indication unless contra-indicated (subdivided for different drugs), drugs for elevated risk factor levels, first-choice drug for a specific indication, and drugs to be avoided in specific patients (Table 4).

From the first group, the indicator "prescription of glucose-lowering treatment in diabetic patients" was criticized for not reflecting quality.[41,53] The other PI from this group were considered face and content valid but adjustment for case-mix was recommended to deal with patients that either do not require or should not receive the specified treatment. Alternatively, this could be solved by excluding patients with contraindications to the recommended treatment from the indicator. Several of such PI with exclusion criteria, however, lacked face or content validity across different

Table 4. Classification of cross-sectional disease-oriented prescribing indicators as assessed in the studies

CROSS-SECTIONAL DISEASE-ORIENTED PI	Face validity	Content validity	Reliability	Operational feasibility
1. Patients prescribed drugs for a specific indication				
prescribed **statins** (or lipid lowering drugs) : -in patients with high cardiovascular risk or CVD [1,3,12,16,18,20,30,35,39,47,55,54,58] - in diabetic patients or treated with glucose lowering medication [40,41,43]	+	+	+	+
prescribed (a specific type of) glucose lowering treatment [41,53]	~	~		+
prescribed daily **aspirin** (or antiplatelet drug or anticoagulants) in: - diabetic patients or treated with glucose lowering medication (and additional cardiac factor) [14,26,40,41,44,47,54] - patients with history of CVD or high cardiovascular risk [1,12,14,16,19,20,26,30,34,41,47,54,58,5960]	+	+	+	+
prescribed any **antihypertensive** treatment -in patients with stroke [26] -in (elderly) patients with diabetes and hypertension or albuminuria [41,53]	+	+	+	+
prescribed **ACE inhibitor (or ARB**) of: -in patients with CHD or history of MI [5] - T2DM patients [40] - T2DM patients with hypertension and/or microalbuminuria or (macro)albuminuria [1,5,12,18,20,26,33,41,44,47,51,53,58]	+	+	+	+
prescribed **beta blockers** to (diabetic) patients with MI or CHD [4,16,18,20,26,30,42,47,54]	+	+	+	+
T2DM or high cardiovascular risk patients received **influenza immunization** [5,39,54,55]	+	+	+	+
appropriate treatment for patients with diabetes or CVD or hypertension or cardiovascular risk [1,30,48,52]	+	+	+	+
2. Patients prescribed drugs for a specific condition unless contraindicated or not needed				
prescribed **ACE inhibitor or ARB** unless contraindicated to patients with: - CAD and diabetes [5,7] -in elderly patients with IHD [23,24,25] - hypertension and kidney disease [5] - (elderly patients) with diabetes and microalbuminuria or proteinuria [23,24,25,26,27,30]	~	~	+	~
(elderly) patients with CHD (and diabetes or elevated LDL) prescribed **lipid lowering drugs** unless contraindicated [23,24,25,57]	+	+	+	~
prescribed **antiplatelet** drug in patients with diabetes or CVD unless contraindicated or already on other anticoagulants [5,18,23,24,25,26,27,29,32,37,39,46,56,57]	~	~	+	~
prescribed **aspirin** in elderly T2DM patients unless on other anticoagulants [23,24,25,26,27]	~	~		+
prescribed **beta blockers** in patients with coronary disease and/or MI (and hypertension) unless contraindicated [5,23,24,25,27,29,32,35,39,57]	+	+	+	~
% of eligible T2DM patients who received **influenza immunization** or refused immunization [54]	+	+	+	+
3. Patients prescribed drugs for elevated risk factor level				
treatment of (diabetic) patients with concurrent high level risk factor: - cholesterol above specified level in (elderly) patients with diagnosis of CHD, diabetes or high cardiovascular risk [26,33,34,44,47,53,59,60,64] - HbA1c above specified level (age dependent) [20,33,51,64] - BP above specified level, average of 2 readings, last 3 readings above (age dependent) level [20,31,32,33,37,39,46,53,64]	+	+	+	+

4. First-choice drug in patients with specific condition				
prescribed first choice drug (e.g. metformin or first-choice antihypertensive) in (overweight) diabetic patients [20,31,37,41,46,47]	+	+	+	+
5. Drugs to be avoided in patients with specific conditions				
glyburide to be avoided in elderly diabetic patients [40]	+	+		+
thiozolidinedions to be avoided in diabetic patients with heart failure [40]				
patients older than 75 years prescribed lipid lowering drugs for primary prevention [3]				

+ characteristic is present; - characteristic is absent; ~ characteristic is assessed but doubtful or mixed results; empty cell-no information is available on characteristic
CVD: cardiovascular disease
CHD: coronary heart disease
MI: myocardial infarction
T2DM: type 2 diabetes mellitus
HbA1c: glycosylated hemoglobin
BP: blood pressure
ARB: Angiotensin II receptor blocker
ACE-inhibitor: Angiotensin converting enzyme inhibitor
LDL: low density lipoprotein

settings. For example, indicators focusing on prescription of ACE-inhibitors and aspirin in elderly patients with diabetes unless contra-indicated were accepted as face and content valid by expert panels in the USA and UK, but rejected by a Dutch panel.[25-27] Furthermore, the operational feasibility of such indicators was found to be hampered in one study using automated data collection methods, because information on contraindications entered as text data in medical records was missed.[57]

Another type of disease-oriented PI that was widely tested consists of indicators that focus on prescribed drugs in patients with an elevated risk factor level (Table 4). The cut-off levels varied depending on the literature used for developing the indicator, and in some cases age-dependent levels were specified.[33,51] Face and content validity was considered present but again case-mix problems were mentioned, especially regarding treatment in relation to cholesterol levels. In one case, this resulted in rejecting indicators that were considered too sensitive to patient case-mix.[53] We identified relatively few disease-oriented PI focusing on first-choice drugs or drugs to be avoided (Table 4).

In summary, the most widely assessed disease-oriented PI, showing good clinimetric results in different settings, focus on prescribed drugs for a specific indication or elevated risk factor, in particular: (a) statins in high cardiovascular risk patients. (b) aspirin or antiplatelet medication in high cardiovascular risk patients, (c) ACE-inhibitors in T2DM patients with hypertension and/or albuminuria, (d) beta blocker in patients with coronary heart disease or history of myocardial infarction, (e) treatment of patients with elevated HbA1c levels; (f) treatment of patients with elevated blood pressure levels.

Sequential disease-oriented PI

Among the 12 identified generic indicators that incorporate a sequential assessment strategy, we acknowledged four groups: treatment modification after an event, treatment modification after an event unless contra-indicated, start of a first-choice drug in specific patients, and continuum of post-discharge treatment (Table 5). These include indicators such as "if a patient has a certain risk factor level, then he should receive a treatment start or intensification", either with or without a defined maximal time period for such modifications. In two studies, a return to control without treatment modification was included in the indicators as adequate care.[8,9] Similar to the cross-sectional indicators, sequential indicators incorporated exclusions to deal with patients that have contraindications or already receive maximal treatment. All except one indicator were considered face and content valid. This one focused on treatment of elderly patients with an elevated LDL-level, which was considered valid by one panel but rejected by another.[25,27] Treatment modification indicators have shown concurrent validity,[8,68] and operational feasibility was good for the first three types of PI in this category. For PI focusing on the continuum of hospital through post discharge ambulatory care, the operational feasibility was hampered by the lack of adequate data systems.[52]

In summary, sequential PI focusing on treatment modifications after elevated risk factors (cholesterol, BP, HbA1c) showed face and content validity in several studies and settings, and are the only PI for which concurrent validity was shown.

Table 5. Classification of sequential prescribing indicators as assessed in the studies

SEQUENTIAL DISEASE-ORIENTED PI	Face validity	Content validity	Concurrent validity	Reliability	Operational feasibility
1. Treatment modification after indication or persistent high risk factor levels					
treatment start/modification offered to specific (high risk) patients with: - total cholesterol or LDL level above specified level (and no return to control within 3-6 months) or with hyperlipidaemia [9,32,37,46,64,68] - uncontrolled/above goal BP level -dependent of other risk factors e.g. diabetes- (and no return to control within 3-6 months) [9,20,32,42 44,48,68] - failed dietary/lifestyle modification (start oral glucose lowering or antihypertensive treatment) [26,30,31,37,46] - elevated HbA1c or fasting glucose level [9,44,64,68] - failed oral glucose lowering treatment (and no return to control within 3-6 months) [20,30,37,40,46] - with history of CVD or high cardiovascular risk (antiplatelet or anticoagulant) [36]	+	+	+	+	+
pharmacologic or lifestyle intervention offered to elderly with diabetes and fasting LDL>130mg/dL (within 3 months) [25, 27]	~	~		+	+
2. Treatment modification after indication or persistent high risk factor level unless not possible or needed					
treatment start/modification in patients with history of CVD or with elevated risk factor level (LDL, HbA1c, BP) unless contraindicated (and no return to control within 3 or 6 months) [8,18,23,24,25,26,27,37,39,42,46]	+	+	+	+	+
patients with diabetes and proteinuria or patients with hypertension prescribed ACE inhibitor (or ARB) within 3 months unless contraindicated [37,46]	+	+		+	+
3. Start first choice treatment in specific patients					
- metformin in overweight incident diabetic patients [20] - ACE-inhibitor or ARB in incident hypertensive diabetic patients with albuminuria [20]	+	+			+
4. Continuum of post discharge care					
patients with MI prescribed treatment (ACE-inhibitor, aspirin, clopidogrel, statin, or b-blocker) at discharge or after a specified time period (from 1 month up to 1 year) [4,22,35,45,49,52,62,61 65,66]	+	+		+	~

+ characteristic is present; - characteristic is absent; ~ characteristic is assessed but doubtful or mixed results; empty cell-no information is available on characteristic

BP: blood pressure

HbA1c: glycosylated hemoglobin

CVD: cardiovascular disease

LDL: low density lipoprotein

T2DM: type2 diabetes mellitus

MI: myocardial infarction

ACE-inhibitor: Angiotensin converting enzyme inhibitor

ARB: Angiotensin II receptor blocker

DISCUSSION

We have identified 16 types of PI covering important aspects of drug prescribing related to T2DM and CV risk management, including first-choice treatment, safety issues, dosing, costs, sufficient and timely treatment. Face and content validity, as well as operational feasibility were most frequently assessed. Less attention has been paid to predictive and concurrent validity, and case-mix issues were addressed mostly for PI intended for external use. Sample size problems were discussed for indicators with both aims, but the minimal sample size required per PI was seldom provided. There was no difference in the choice of indicators for internal or external quality assessment.

The PI that showed good results for their clinimetrics in different settings and studies, *e.g.* prescription of beta blockers in patients after myocardial infarction, share a good evidence base that does not leave room for disagreement between health care providers across the countries. Therefore, such indicators can be used for cross country comparisons of prescribing quality. Other indicators showing good clinimetric results, *e.g.* proportion of first choice drugs within a therapeutic class or treatment of patients with elevated risk factor levels, leave room for discussion which drugs to include as first choice, and which levels to consider as being elevated. Therefore, these indicators always need to be adapted to the prevailing evidence or guidelines. Sequential PI focusing on treatment modification after elevated risk factors are the indicators with the most extensive evidence of validity.

Most PI for T2DM and CV risk management have been developed for ambulatory care, *i.e.* both primary and secondary care. This is not surprising since the same treatment standards apply to both settings. It was shown that several drug-oriented PI that were initially used for hospital care,[19] can be adjusted for use in primary care.[56]

Validity assessment

The vast majority of the PI was based on review of literature or guidelines and was therefore considered content valid. Combining evidence with expert opinion appeared to be an established norm. This provides face validity and ensures acceptance of PI. Face validity of the same PI may vary according to differences in medical culture or expert panel.[26,27] Drug-oriented PI focusing on first-choice drugs or (co-)prescriptions to be avoided, and disease-oriented PI focusing on patients with a specific disease or risk factor level receiving treatment have shown face and content validity across a number of different settings. In addition, sequential disease-oriented PI focusing on treatment modifications showed concurrent validity.[8,68]

No information is yet available on the predictive validity of individual prescribing indicators. Studies assessing predictive validity used a composite measure score, which does not allow judging the contribution of individual indicators. Furthermore, the results on predictive validity were controversial. Since most studies used a cross-sectional design to investigate the association

between process of care and patient outcomes, it remains unclear if the observed associations were due to adequate treatment or to other unmeasured processes of care.

Feasibility and reliability

The operational feasibility of PI has seen much progress in the last decades. The use of EHR is increasing rapidly, and quality assessment using automated measures is replacing time consuming manual chart review. Automated data collection may lead to underestimating the quality of care when critical information is not captured. It was recommended that better recording of diagnosis, and development of specific codes for contraindications and patient choices, is needed before PI based on automated data collection can be used for external assessment.[8,57] On the other hand, the use of computerized methods that can reliably extract relevant information also from free text parts of such records shows promising results.[64,71] One should keep in mind, however, that medical records may not reflect all processes of care.[72] Especially when there is limited electronic prescribing or drugs are prescribed by several providers, data can be incomplete.

In general, operational feasibility of drug-oriented PI is good for prescription databases.[15,50] However, calculation of drug-oriented PI focusing on co-prescribing of drugs may not be possible in prescription databases if they do not contain information on duration of prescriptions.[56] Furthermore, in several European countries it is not possible to assess generic prescribing using pharmacy databases because generic substitution can take place on initiative of the pharmacist.[43] Disease-oriented PI can be calculated from administrative datasets and EHR.[24,49,59] Sequential disease-oriented PI can be calculated from EHR.[8,68] Problems with quality and availability of information were encountered in all types of datasets. In general, operational feasibility of the PI should be assessed in a new environment, as this largely depends on the particular dataset to be used for quality assessment.

All studies that assessed inter-rater reliability showed good agreement for PI. Their explicit nature and clear operational definitions, leaving little room for personal opinions, make PI reproducible when used by different assessors. This is in contrast to implicit review, where quality of care is assessed without predefined criteria using expert judgments.[38]

Sample size and case mix

The issue of sample size was addressed for PI with both aims. For internal assessment, the suggested number of patients was always a convenience or arbitrary number. In contrast, the minimal number of patients per PI intended for external comparisons should be justified to ensure sufficient power to detect differences. Although all organizations dealing with external assessment discussed this issue, explicit sample size calculations were presented only in one paper.[69]

Another issue that can limit external use of PI is patient case-mix. Several methods were suggested

to deal with this problem, including statistical adjustment or exclusion of patients. In general, both drug and disease-oriented PI can be sensitive to case-mix. Although incorporating exclusions of patients with contraindications partially solves the problem, the PI with such exclusions developed so far were often hampered by lack of face and content validity or operational feasibility. Some have argued that for internal quality assessment sophisticated case-mix adjustment may not be cost-effective, and therefore, basic age/sex adjustment might be sufficient.[12,70] On the other hand, it has been recommended to stratify performance measurement by gender, since this allows to detect specific areas for improvement.[73] For external use, however, other patient case-mix characteristics remain important that are currently not adequately addressed for the existing PI.

Limitations and strengths

Classification of the validity assessments was limited to the information provided in the publications. Almost all PI were assessed for face and content validity. However, because of the emerging evidence, some PI considered content valid several years ago, may not be valid anymore. Furthermore, few papers included details on PI that were discarded for lacking face or content validity.

The strength of our study was that we searched both Medline and Embase with no language restriction. We also included relevant documents from national professional organizations, but we may have missed some not formally published documents, in particular from non-English speaking countries. However, we trust that we have uncovered the most relevant themes, and that this review reflects current PI developments in diabetes and cardiovascular risk management. To our knowledge this is a first review that attempts to classify and report on the validity of prescribing indicators.

CONCLUSIONS AND IMPLICATIONS

We identified a large variety of prescribing indicators for T2DM and CV risk management that cover the important areas for prescribing, including recommended drug choices, safety issues, as well as timely and adequate pharmacological treatment of various risk factors. Our conclusion is that, in general, most developed PI are evidence-based and face valid but few were tested for concurrent or predictive validity. Small variations in indicators are seen between different studies and countries, due to differences in medical culture and emerging evidence. Since face and content validity depend on setting and time, existing indicators always need to be scrutinized before use in a new environment. Inter-rater reliability seems not problematic for PI assessment. Case-mix problems can affect most indicators. Problems with small sample size were especially observed for some safety issues. Operational feasibility can not be assumed without examining the available data. It seems especially problematic for PI focusing on redundant prescribing, continuity of care, and PI incorporating contraindications.

The challenge now faced by health care providers and policy makers is not to develop more PI, but to

choose the most relevant ones. Besides selecting PI with proven validity and operational feasibility, it is important to decide which aspects of prescribing one wants to address. It is to be expected that different stakeholders will differ in their views on the most relevant aspects. Our review provides a large number of PI that have shown good results regarding some basic clinimetrics, and examples of PI with positive assessments in various settings. The lack of information on predictive validity of individual PI is troublesome because of its importance for selecting indicators that are closely linked to clinical outcomes.

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Appendix 1 Systematic Search Strategy

Search strategy using embase.com (combined search in Embase and Medline)

1. (EMTREE terms: health care quality OR quality control)
AND
EMTREE terms: coronary artery atherosclerosis OR cardiovascular disease OR diabetes mellitus OR non insulin dependent diabetes mellitus OR ischemic heart disease OR heart infarction OR hypertension OR angina pectoris OR hyperlipidemia OR chronic disease
OR general practice OR primary health care OR general practitioner
AND
(Title words: (quality AND measure*) OR (quality AND assess*) OR indicator* OR perform* OR criteria OR profile*)

2. (EMTREE terms drug utilization OR prescription)
AND
(Title words: (quality AND measure*) OR (quality AND assess*) OR indicator* OR perform* OR criteria OR profile*)

3. 1 OR 2*
* for time period from 1990 till January 2009

CHAPTER 5

Stakeholder preferences regarding prescribing quality indicators: a qualitative study

Liana Martirosyan[1], Joekie Markhorst[2], Petra Denig[1], Flora M Haaijer-Ruskamp[1], and Jozé Braspenning[2]

[1]Department of Clinical Pharmacology, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands
[2]IQ Scientific Institute for Quality of Healthcare (IQ healthcare), University Medical Centre St Radboud, Nijmegen, the Netherlands

Submitted (shorter version)

ABSTRACT

Information on prescribing quality of diabetes care is required by health care providers, insurance companies, policy makers, and the public. Knowledge on preferences of all involved parties regarding type of prescribing quality information is important for effective use of prescribing quality indicators. Between June and December 2009 we conducted semi structured interviews with 16 key-informants representing eight different organizations in the Netherlands involved in healthcare quality improvement. The interview guide included topics on participants' opinions and preferences regarding existing types of prescribing quality indicators in relation to the aim of using quality information. Content analysis methods were used to process the resulting transcripts. Findings from this qualitative study of stakeholder preferences showed that indicators focusing on undertreatment were prioritized by all stakeholders. Furthermore, health care providers and policy makers valued prescribing safety indicators, insurance companies prioritized indicators focusing on prescribing costs, and patients' representatives valued indicators focusing on interpersonal side of prescribing. All stakeholders preferred positive formulation of the indicators to motivate health care providers to participate in health improvement programs. A composite score was found to be most useful by all stakeholders as a starting point of prescribing quality assessment. Lack of information on reasons for deviating from guidelines recommendations appeared to be the most important barrier for using prescribing quality indicators. According to the health care providers, there are many legitimate reasons for not prescribing the recommended treatment, and these reasons are not always taken into account. The specific preferences of stakeholders found in this study can assist in minimizing the number of relevant PQI and providing customized indicator sets. Furthermore, the implementation of an information system to register the reasons for not prescribing the recommended treatment will stimulate effective use of prescribing quality indicators.

INTRODUCTION

Insight into the quality care is demanded by healthcare providers (HCP), payers, and the public. These different stakeholders use quality information for different purposes such as internal quality improvement, cost containment, and accountability. There is general agreement that due to varying aims of using quality information, the different stakeholders have specific preferences for the type of quality information.[1-3] However, not much is known about their actual preferences. In this study, we searched for preferences among different stakeholders for prescribing quality indicators in diabetes care.

Appropriate drug prescribing has been recognized as an important quality of care issue in the management of chronic conditions, such as type 2 diabetes mellitus (T2DM). Diabetes is a chronic disease with a dramatically increasing prevalence throughout the world.[4] Appropriate pharmacological treatment of diabetes and related risk factors helps to reduce complications in patients with T2DM.[5]

To measure quality of prescribing in T2DM, a huge number of prescribing quality indicators (PQI) has been developed.[6] Despite this fact, PQI for T2DM management are largely underrepresented in national sets of quality measures that are used for external accountability in different countries. For example, the National Voluntary Consensus Standards for Adult Diabetes Care includes two PQI focusing on management of diabetic patients[7], and only these PQI were included in the Health Employer Data Information Set (HEDIS) of measures.[8] The Diabetes Quality Improvement Project, which was implemented in the United States as a comprehensive set of national diabetes quality measures, did not include any PQI for internal quality improvement or for accountability[9]. The PQI are also underrepresented in the Quality and Outcome Framework set of quality indicators in the United Kingdom with only one PQI relevant for diabetes care.[10] The Australian national set of diabetes indicators does not include any explicit PQI.(11) On the other hand, in some countries, for example, the United Kingdom and Australia, there are sets of internal quality indicators exclusively focusing on prescribing issues.[12;13] In the Netherlands, a similar situation exists with PQI mainly being used for internal quality improvement and only a few used for accountability purposes.[14;15]

The challenge now faced by the stakeholders is not to develop more indicators but to choose the most relevant ones. Among the existing PQI there are distinct types of PQI that address different aspects of prescribing relevant for care, *i.e.* PQI focusing on undertreatment, safety, first choice medication, and costs.[6] Previous studies investigating the preferences for PQI focused mostly on needs of one of the stakeholders, *i.e.* healthcare providers (HCP). It was found that PQI based on detailed patient clinical information are preferred to those based on aggregated data,[16] and that physicians rank evidence-based PQI higher than those based on costs.[17] However, knowledge is scarce regarding the types of PQI that are prioritized by other stakeholders. Furthermore, little is

known about the preferred format of the PQI. For instance, it is possible to focus either on numbers of patients receiving appropriate care or on patients receiving inappropriate care. Also, indicators can represent one specific item of care or can average several items into a composite score. The use of PQI could be more effective if we had a better understanding of ways to present quality information that are most meaningful to the stakeholders.

The aim of the current study was to explore whether the PQI are considered a relevant part of quality assessment of T2DM care, and which types of PQI should be included according to different stakeholders. In addition, we wanted to elicit the preferred way of receiving quality information as well as the perceived barriers regarding PQI use.

Study population

The present study draws on 16 semi-structured interviews with key informants representing (1) the public, (2) healthcare providers, (3) payers, and (4) healthcare inspectorate. These participants worked for eight organizations involved in healthcare quality measurement or improvement in the Netherlands. (Table 1)

Table 1. Number of participating stakeholders and their organization

Stakeholder	Organization	Interviewed key informants	Number of participants
The public	The Federation of Patients and Consumers Organization	Senior policy officer	1
		Medical advisor	1
Subtotal			*2*
Health care providers	Dutch Institute of Health Care Quality Improvement	Senior advisor/diabetologist	1
	Dutch College of General Practitioners	Authors of national diabetes guidelines for primary care/ primary care physicians	2
	Dutch Diabetes Federation	Diabetologist	1
		Diabetes nurse	1
	Royal Association for the Advancement of Pharmacy	Senior researcher/pharmacist	1
	Scientific Institute of Dutch Pharmacists	Senior manager/pharmacist	1
	Community health care providers	Primary care physician	1
		Diabetes nurse	1
Subtotal			*9*
Payers	Health insurance companies*	Health program manager	1
		Health care purchaser	1
		Medical advisor	1
Subtotal			*3*
Inspectorate	Dutch Health Care Inspectorate	Senior inspector	1
		Primary health care inspector	1
Subtotal			*2*
Total			16

*We have included three different insurance companies covering different geographical regions in the country

Purposive sampling was used to identify key informants from each organization, *i.e.* senior staff members who were engaged in quality of care issues within an organization. We have contacted our respondents directly or identified them through other members of the included organizations by asking them to suggest colleagues whose tasks are related to quality assessment or improvement. All participants received a letter containing information about the aim and methodology of the study.

Instrument and data collection

A semi-structured guide was used that included open-ended questions about aims of collecting and using quality information, and more specific questions related to opinions about and preferences for different types of existing PQI, the preferred way of receiving quality information, and factors limiting their use (Table 2). After eliciting opinions regarding existing types of PQI, on undertreatment, first choice-drug, safety and costs, we have asked the participants to choose the type(s) of PQI that were most relevant for their work and the reasons for their prioritization. The instrument was pilot-tested prior to the data collection.

Data collection was carried out between July-December 2009. The interviews were conducted face-to-face for 13 participants and by telephone for three participants who preferred to be interviewed this way. Interviews lasted on average 1.5 hours, ranging from one to two hours. The face-to-face interviews were conducted by two researchers; one was conducting the interviews and another one was making notes. The interviewer asked open-ended questions to reveal participants' views and preferences, and then probed for clarification or to explore new themes as they appeared. All interviews were recorded on digital recorders with permission of participants. All participants gave a written consent to participate in the interview. To ensure the accuracy of our data we used several techniques. First, the interviews were translated verbatim independently by the two researchers present at the interviews. The transcripts were compared and disagreement was resolved through discussion. Next, the accuracy of all transcripts was checked against the original recordings by an independent researcher. Finally, the transcripts of interviews were sent back to the interviewees who were asked to check their consistency and accuracy before the analysis.

Table 2. Topics covered in the interview guide

Current usage and aims of prescribing quality indicators
Opinions regarding the relevance of including PQI on assessment of quality of diabetes care
Opinions regarding and prioritization of existing types of PQI, *i.e.* focusing on undertreatment, safety, first drug choice, and costs
Opinions regarding formulation of the PQI (positive or negative)
Opinions regarding aggregation level of the PQI
Perceived barriers for implementation of PQI

Analysis

We analyzed data using a 5-stage iterative process to analyze each transcript: (1) familiarizing with data; (2) coding of the data; (3) description of the main categories; (4) linking of categories into major themes; and (5) interpreting the relations between themes.[18] First, the transcripts were read several times and parts of text that related to the same concepts were identified. Next, we coded data by giving descriptive codes to these concepts. Later, we grouped similar codes under the main themes. Finally, we organized our data by stakeholders to look across all parties in order to identify differences and similarities, and explored the relationships between recurring themes and aims of using quality information.

The transcripts were initially coded by the first co-author with regular discussion of an emerging framework for data coding with other co-authors followed by the second co-author's review of coding. We used qualitative analysis software (ATLAS.ti Win 6.1) to facilitate organization of data into codes, categories and themes.[19]

RESULTS

Usage and aims of prescribing quality indicators by the stakeholders

All interviewed stakeholders with the exception of the patient organization used some sort of PQI for T2DM management. Primary care physicians and diabetologists use PQI for T2DM management for internal quality improvement initiatives such as peer review. The representatives from the Dutch Health Inspectorate are primarily interested in investigating and following up on problems encountered in medical institutions. Therefore, they mainly use outcome quality indicators to identify the healthcare institutions that do not meet the minimal levels of predefined standards of quality. Recently, however, they launched a set of PQI for pharmacies to improve pharmaceutical care. Pharmacists in the Netherlands are increasingly being involved in pharmaceutical care and prescribing quality assessment, and are encouraged to search for patients not receiving the optimal treatment and alert physicians. For these purposes, they use various PQI for T2DM management and report the scores of these indicators to the Inspectorate. In addition, pharmacists report on PQI focusing on costs of medication to health insurance companies. Health insurance companies primarily collect PQI focusing on costs to provide financial incentives to the HCP that keep prescribing costs low. Finally, the patient organizations collect quality information to support patients when making HCP choices, and to develop policies where patients' preferences are taken into account. Currently, no PQI are used by patient organizations.

Relevance of including PQI on assessment of quality of diabetes care

PQI are an integral part of diabetes quality indicators set

All stakeholders stressed the importance of combining PQI with other quality indicators of diabetes care to obtain a comprehensive picture of provided quality. It was noted that since diabetes is a

chronic disease, there is a large number of factors that determine the final outcome of the treatment, and it is precisely the combination of all relevant processes that defines quality of diabetes care.

"The most important is overall treatment of an individual patient; therefore prescribing should be always seen in combination with other processes and outcomes of care." Diabetes nurse

"The prescribing quality for diabetes is as important as the eye or foot exam. All should be taken into consideration." Medical advisor/health insurance company

Some participants strongly argued against the use of PQI alone without other quality indicators, as different quality indicators of diabetes care are highly interrelated, *i.e.* the physicians need to measure and register certain clinical values first and subsequently make decisions about treatment options.

"I think that PQI should be seen as an integral part of quality of diabetes care and should never be considered separately from other quality indicators." Senior researcher/ Royal Association for the Advancement of Pharmacy

"...It is important only if combined with other quality indicators. Total care is more important then only the prescribing patterns." General practitioner

PQI reflect actions of healthcare providers

The HCPs noted that there is a lot of attention for quality indicators focusing on measurement and registration of HbA1c and other risk factors. Prescribing indicators, however, are more relevant as measures reflecting the actions of healthcare providers in response to observing elevated risk factors, as eventually most of the patients will need pharmacotherapy.

"The fact that you have measured the blood pressure is a process indicator, as well as the indicator of whether you measured the cholesterol. These process indicators are preconditions to carrying on. Currently, a lot of attention is still being paid to this type of indicators [focusing on registration of measurements] that are actually not very important. The point is: what do you do after observing elevated values of risk factors, and prescription indicators play an important role in this." General practitioner/Dutch College of General Practitioners

PQI reflect scientific evidence

All stakeholders believed that it is important to include PQI, because PQI usually reflect evidence-based recommendations. Moreover, the HCPs stated that prescribing is the most evidence-based part of diabetes treatment, as the other processes of care, *i.e.* registration of clinical measurements, lifestyle modification or diet are not so well researched in relation to patient outcomes as prescribing.

"...the evidence of education in relation to clinical outcomes is not so large, but prescribing has a lot more evidence and is a very important part of diabetes treatment." General practitioner/ Dutch College of General Practitioners

Opinions regarding and prioritization of existing types of PQI

PQI focusing on undertreatment

PQI focusing on undertreatment were prioritized by all stakeholders (Table 3). Room for improvement and reflection of guidelines was the most frequently mentioned reason for being interested in these PQI. The HCP found these PQI very relevant for their work, because undertreatment of diabetic patients remains a major problem.

> "I think that this type of information [information on undertreatment] is really important, because clinical inertia [initiation or intensification of therapy when indicated] is a big problem in treatment of type 2 diabetic patients. A good example is statines that are hugely underprescribed in patients with T2DM." Diabetolgist/ Dutch Institute for Healthcare Improvement

Pharmacists noted that they prefer these PQI because it is easy to improve these scores due to a large number of undertreated patients.

> "It is quite easy to improve on this type of indicators, and of course it is always nice for pharmacists to dispense more medications." Senior manager/Scientific Institute of Dutch Pharmacists

Representatives from health insurance companies mentioned that they find these PQI very important because they reflect the timeliness of start and intensification of treatment, and because undertreatment results in complications that add to the healthcare costs in long run.

> "When patients need certain treatment, they should be able to receive that treatment. In the end, poor care is more costly." Healthcare program manager/health insurance company

The representatives of the Inspectorate and the patient organization considered undertreatment of patients to be equal to the "wrong treatment", and noted that patients who are in need of therapy have the right to be prescribed the recommended treatment.

> "We are very much interested in PQI focusing on undertreatment, as it [undertreatment] can harm patients on the long run." Primary Healthcare Inspector/ The Healthcare Inspectorate

PQI focusing on safety

PQI focusing on safety were prioritized by the HCPs and the Inspectorate (Table 3). The HCPs mentioned that diabetic patients with kidney function impairment are at higher risk of adverse drug events, and therefore, safety issues in diabetic patients with kidney impairment are high on their agenda. Besides, the HCP noted that the average diabetic patient requires multiple drugs and has other conditions besides diabetes. Therefore, according to the HCP, safety PQI focusing drug-drug and drug-disease interactions are very important for assessing quality of diabetes care.

> "Safety is first, because I do not want to harm patients with the medication. Using safety PQI that reflect possible harm is very important for internal quality improvement." General Practitioner/

Dutch College of General Practitioners

"That is very important; as I see a lot of problems in people with kidney disease, or swollen ankles who get NSAIDs in high doses, and the kidney function collapses because of that. I think interactions between different [drug] classes are very important." Diabetologist/Dutch Institute of Healthcare Improvement

Pharmacists prioritized the PQI focusing on safety as they felt that they have the best knowledge on safety of medication and, therefore, they have the capacity to have a direct impact on improvement of patient's safety in relation to prescribed medication.

The representatives from the Inspectorate prioritized PQI focusing in safety, because pharmacotherapy involves many errors and suboptimal decisions, and patients will directly benefit from improvement of prescribing safety. In addition, it was noted that safety of healthcare is a priority for the Healthcare Inspectorate.

The participants from health insurance companies felt that safety should remain a prescribing area to be monitored and improved internally. Although they accepted the importance of safety PQI for diabetes care, in their opinion, judging these indicators requires professional knowledge which they lack.

"It is important that healthcare insurers do not take the place of healthcare providers and do not interfere too much in medication matters. I believe that professionals are perfectly able to improve on safety of prescribing themselves." Healthcare purchaser/Health insurance company

PQI focusing on first choice drug

The value of PQI focusing on the first choice drug as seen by the stakeholders was that they usually reflect guideline recommendations and include a safety component. However, no stakeholder found these PQI very relevant for their own aims. The payers referred to these PQI as being only important in situations when the first choice drug recommendations implied prescription of cheaper medication. The representatives from the Inspectorate mentioned that although these PQI usually have good face validity, they do not always reflect prescribing quality. In particular, they noted that a high grade of evidence is not always available to guide an evidence-based drug choice, and in such situations the final drug choice needs to be made by physicians. The HCPs had a similar opinion about the PQI focusing on the first choice drug. One participant argued that these PQI might be used for internal purposes and never for external accountability. The HCP argued that the first choice drug recommendations cannot be applicable to all patients, as there will be many patients that experience side effects, have contraindications, or refuse the recommended medications, making these PQI very sensitive to patient case-mix.

Another limitation of these PQI mentioned by the representatives of the Inspectorate and the

HCPs was the dynamic nature of the evidence supporting first choice drug recommendations. These participants noted that the recommendation in guidelines can change, because of emerging evidence recommending another first choice drug.

> "Fifteen years ago, a professional was considered incompetent if he used it [metformin] as there were too many side effects, whereas now it has become first-choice medication, which, of course, may change again." Senior Inspector/The Healthcare Inspectorate

In addition pharmacists mentioned that information on first choice drugs is not so crucial, as it often refers often to the choice from two drugs that can both be quite good, and therefore the difference is not as big as between safe and unsafe therapy.

PQI focusing on cost

PQI focusing on costs related to prescribing were recognized as being relevant for the healthcare system by all stakeholders but they were prioritized only by health insurance companies. Other stakeholders, while accepting the importance of reducing costs attributed to prescribing, felt that it is not their responsibility to control costs and mentioned that costs should not be the main factor in the prescribing process. The participants from patient organization believed that costs do not have a relation to quality, since quality is meeting the needs of an individual patient without considering costs. Similarly, representatives of the Inspectorate noted that PQI focusing on costs are hardly interesting for them as these PQI do not reflect quality of provided care.

> "Costs and quality go together, but costs are not a priority for the Inspectorate. For instance, if the Inspectorate knows that a certain medication is more effective than another, less expensive medication, it prefers the more effective medication in spite of the higher costs. Indicators relating to costs are hardly interesting." Senior Inspector/The Healthcare Inspectorate

In general, all HCPs including pharmacists mentioned that is not their priority to know if the cheapest medication is prescribed. However, pharmacists mentioned that they do collect and report on PQI focusing on costs to ensure payments from the health insurance companies. All stakeholders that did not prioritize PQI focusing on costs agreed that prescribing a cheaper medication is only relevant in a situation when choosing from several drugs with similar effectiveness.

PQI focusing on communication between HCP and patients

Representatives of the patient organization noted that although there will always be patients who would like to know the very detail about provided quality of care, for an average patient it is difficult to judge the quality of care with the existing PQI. In addition to the PQI focusing on undertreatment, they prioritized a different type of PQI that would reflect effective communication between HCPs

and patients regarding the prescribed medication.The aspects considered as important were related to patients' participation in the treatment process, self-management, patients' empowerment and motivation to comply with the prescribed treatment, and provision of sufficient information about prescribed medication in an acceptable, understandable way.

"It is important to measure whether the [treatment] decisions have been shared with patients, for instance in deciding on the use of insulin. … Doctors have to motivate patients enough to ensure that the patients comply with the therapy and that together they achieve the aim." Senior policy officer/Federation of Patients and Consumer Organisations in the Netherlands

"The HCP should provide information about the prescribed medication, such as what to expect, common side-effects, etc. And most importantly, patients should believe in the medication prescribed by a doctor." Medical advisor/ Federation of Patients and Consumer Organisations in the Netherlands

Table 3. Prioritization of PQI by stakeholders in relation to their user aims

	Undertreatment	Safety	First choice drug	Cost	Communication
Stakeholder					
The public	✓				✓
Health care providers	✓	✓			
Payers	✓			✓	
Inspectorate	✓	✓			

Potential barriers for use of PQI

Reasons for deviating from the recommended treatment

The most frequently mentioned barrier for implementing PQI was the concern that reasons for not prescribing the recommended medication are ignored. The strongest opinions were expressed by the HCPs, who noted that many PQI are very sensitive to patient case-mix. Several patients may encounter side-effects to the recommended drugs, have contraindications, or simply refuse certain types of medication due to, for example, negative experiences in the past or influence of the media. There was a general concern raised by the HCPs that external bodies expect very high scores on indicators reflecting guideline recommendations, and that the external evaluators may not take into account all the legitimate reasons for not prescribing a recommended treatment to certain patients.

"Those things [side effects, contraindications and patient refusals] are part of the equation and were never understood by the government, insurance or whatever. They say oooh, you score 80% on metformin, that is very bad, it should be 100 %... ok, it is right it should be as high as possible, but there can be very good reasons not to prescribe the recommended treatment and that is true for many indicators". Diabetologist/Dutch Institute for Healthcare Improvement

The Inspectorate and insurance companies, however, did recognize that there might be many legitimate reasons for deviating form the recommended treatment. They mentioned that usually they do not have insight to reasons for deviations, and knowing this information would be very relevant for fair prescribing quality assessment.

Prescribing is a professional area

Representatives of insurance companies and the Inspectorate mentioned that for some specific types of PQI, such as focusing on safety, one would need sufficient professional knowledge to be able to judge the scores of the indicators. It was mentioned that lack of such knowledge could be solved by employing an expert panel. According to the representatives of the Inspectorate, the main reason why PQI are not yet collected from medical practices is a traditional belief that prescribing is a professional domain in which they, in their capacity as supervisors, should not interfere unless obvious problems are encountered. The majority of the HCPs supported this view as they believed that they are capable of improving prescribing quality internally by audits and peer-review without external interference.

> "Measuring the quality of prescribing is new and tricky for the Inspectorate. Some managers believe that prescribing is a professional domain in which they, in their capacity as supervisors, should not interfere. The Inspectorate does not have enough knowledge and will therefore not interfere. It is, of course, possible to put together an expert panel, but the most important point to discuss is whether or not prescribing should remain the privilege of professionals. " Senior Inspector/The Healthcare Inspectorate

> "Doctors will not trust external evaluators in assessing prescribing quality. Cost control is more or less accepted, but quality assessment - no. We are capable of improving quality at the local level, and not by interference of the Ministry and other external bodies." Community primary care physician

Operational feasibility

Although all stakeholders agreed that currently available data have the potential to provide information on the most important prescribing quality issues, operational feasibility was a frequently mentioned barrier to the actual use of PQI. In particular, many mentioned that the feasibility of calculating safety PQI is hampered, as additional clinical information is needed, such as kidney function, co-medication, etc. This type of information is not always available or easily retrievable from the registration systems. This was a particularly important issue for pharmacists. They believed to have the best knowledge related to medication safety issues but their involvement in prescribing quality improvement was limited by the lack of sufficient patient clinical data in the pharmacy registries.

"Prescription of certain medications in patients with impaired kidney and liver function requires a special attention, and pharmacists can be helpful in monitoring this. However, pharmacists normally do not have an access to the patients' clinical data." Senior researcher/ Royal Association for the Advancement of Pharmacy

Another important piece of information that, in particular, the HCPs and representatives of the patient organization felt was lacking, was the documentation of patient preferences for treatment, and socio-economic factors that might influence patient preferences. The HCP stressed the relevance of developing a registration system where this type of information could be entered in a systematic way, so it could assist shared-decision making and taking into account patient preferences.

Finally, the HCP mentioned that the numbers of PQI developed for different clinical areas is growing markedly, and there is great time burden for them to deal with such a large number of PQI. The same problem was identified by the key informants from the Inspectorate, who mentioned that a large number of existing indicators related to quality of prescribing makes the choice of the most relevant PQI difficult.

Preferences for a method to report the scores of PQI

Formulation of scores

A positive formulation of PQI scores was preferred by most participants and in particular by the HCPs. All HCPs mentioned that it is always better to start from the figures that focus on numbers of patients who are well treated, and only as a next step to discuss areas that need improvement. Starting with negative figures was thought as creating "a blaming culture" that can discourage and demotivate the HCPs from participation in quality improvement programs or from providing transparent data on quality.

"Try to be positive … What would be the incentive for those who perform worse than the others? If you put good guys in front and bad gays in the back, then everything is focused on the bad guys…Negative formulation creates chaos and negative attitude." Diabetologist/ Dutch Institute for Healthcare improvement

Insurance companies were well aware of this fact, and preferred using positive figures to make successful contracts with HCPs.

"Positive formulation is important for creating a positive and encouraging atmosphere in the communication with professionals. If you go to professionals and start off by presenting figures that represent good performance, this has a stimulating effect." Healthcare program manager/ Health insurance company

Aggregation level

When asked about preferences for aggregating PQI, all participants mentioned that both "composite" and individual scores are useful. The HCPs preferred a "fold out" system for internal quality assessment, where first a composite score is used to get a comprehensive overview, and next, it is folded out to the individual PQI level to identify potential areas for improvement. For external reporting, the HCPs preferred using only a composite score. The main underlying reason was the fear that external stakeholders may misinterpret the scores on individual PQI because they may fail to acknowledge the possible legitimate reasons for not prescribing the recommended treatment to certain patients. All external stakeholders, however, preferred to be informed on both aggregated and individual indicator level using a "fold out" system. The use of composite scores was considered to be convenient by providing a quick overview and eliminating the necessity of dealing with too many quality indicators. Despite this, the composite score was never considered informative enough. Information on an individual PQI level would be desired eventually, since only individual PQI scores ensure transparency of the provided care and identify areas that require special attention. Several participants mentioned that composite scores should ideally aggregate only indicators focusing on a similar topic, for example, safety or undertreatment.

DISCUSSION

Our study showed that all stakeholders consider PQI to be relevant for assessing quality of diabetes care. They all prioritized PQI focusing on undertreatment for their own aims. In addition, the HCPs and the Inspectorate prioritized PQI focusing on safety. No stakeholder prioritized PQI focusing on the first choice drug. For the remainder, the stakeholders had differing priorities for the types of PQI. Health insurance companies prioritized PQI focusing on costs, and the patient organization valued quality indicators that would reflect effective communication between patients and HCPs. Important barriers for using PQI were concerns that legitimate reasons for not prescribing the recommended treatment are overlooked, and relevant clinical information is not always available for adequate prescribing quality assessment. As for the preferred way of presenting scores of the PQI, we found that a positive formulation of indicators is very important for encouraging the HCPs to participate in prescribing quality improvement programs. A composite score averaging several PQI was considered a convenient way to start the process of prescribing quality assessment by all stakeholders, but scores on individual PQI were always preferred to inform quality improvement initiatives.

PQI are important tools for assessing quality of diabetes care

We found that all stakeholders stressed the importance of including PQI for assessment of diabetes care. The reasons brought forward by different stakeholders included the relatively high level of evidence available for PQI compared to other quality indicators, and prescribing being a vital component of T2DM management. Although carefully managing diet, exercising, and self-

monitoring contributes to improved health outcomes in diabetic patients,[20;21] for the majority of patients these interventions alone are not going to be sufficient. To avoid or minimize chronic diabetic complications, some sort of pharmacological treatment will then be necessary because of progressing nature of the disease.[22] Furthermore, there is an increased interest from the Healthcare Inspectorate in receiving information on quality and safety of medication use in the Netherlands. The recent endorsement of prescribing indicators for pharmacies confirms this trend. Similarly, the National Quality Forum in the United States acknowledged that there are too few measures available to improve the quality and safety of medication use and management, and endorsed 18 prescribing quality measures as a starting point. These measures focus on managing over-the-counter and prescription medication related to several conditions including diabetes.[23]

Preferences of stakeholders regarding PQI

Our results indicate that PQI focusing on undertreatment can be included in a uniform set of quality indicators appropriate for all stakeholders. For the rest, the stakeholders had differing preferences specific to their user aims. We have found that PQI focusing on costs were not interesting for the HCPs, and this is consistent with findings from other studies.[17;24] In the past, PQI on costs have been a part of internal quality improvement programs.[25;26] Auditing such information on prescribing appears to be less relevant for HCP nowadays, probably because health insurance companies now use different (reimbursement) strategies to control prescribing costs.

The PQI focusing on first choice drugs were not prioritized by any stakeholder. The drug choice recommendations are an important component of many clinical guidelines. However, PQI reflecting these recommendations are likely to be affected by patient case-mix and the changing evidence base. In comparison with the PQI that focus on undertreatment which look at prescribing any drug from a certain class, these PQI look at prescribing of a specific drug within a class. Therefore, it is more likely that the scores of such PQI is lowered because of patients experiencing side effects or having contraindications to a specific drug. In addition, the changing nature of evidence supporting the PQI focusing on first drug recommendations hampers comparisons of prescribing quality scores over time.

Patients and HCPs identified a gap regarding indicators measuring the interpersonal side of prescribing quality, *i.e.* shared decision making and respect for patients' preferences regarding the treatment options. Previous research has shown that patients value effective communication between HCP and patients in addition to technical measures of quality.[27] Although reliable measures for assessing patients' experiences and perspective do exist, they are not widely incorporated into quality assessment.[28] Knowing patients' experiences with their HCP is important, as there is evidence showing the link between positive attitudes of patients towards their HCP and improved patient outcomes.[29] To facilitate patients' involvement in the treatment process, it is important to

systematically register patient-related information, such as preferences for and experiences with (drug) treatment, in the medical records. Having such information may not only contribute to improved communication between HCPs and patients but will also provide the source for obtaining the type of quality information that patients value most.

The stakeholders agreed that PQI should be positively formulated to create an encouraging environment which is considered very important for participation of HCP in quality improvement programs. For the preferred aggregation level, we have found a discrepancy between HCPs and external stakeholders. The HCPs were reluctant to share the prescribing quality data on individual PQI level because of mistrust to the external evaluators. This is in line with other studies showing the unwillingness of physicians to share the quality data with the "general public".(30) We expect that allowing legitimate deviations from the recommended treatment could help to minimize this tendency.

Potential barriers for use of PQI

Our results indicate that lack of information on reasons why the HCPs do not comply with the drug treatment recommendations is a major barrier for effective use of PQI for all stakeholders. This finding echoes the results from other studies showing that adjustment to patients' case-mix is a concern for physicians when publishing quality information.[31;32] Such concerns from the HCPs' side are not unsubstantiated, as it has been shown that for a prominent proportion of patients in clinical practice there are legitimate reasons for not prescribing the recommended treatment.[33;34]

According to the Donabedian's Triad Model of healthcare quality assessment,[35] prescribing indicators are typical process indicators as they refer to the treatment of patients. In general, process indicators are considered to be less affected by clinical characteristics of patients compared to the outcome indicators.[36] That is particularly true for process indicators that show percentages of patients in whom certain laboratory measurements have been conducted, or who have received a foot or eye exam. With regard to sensitivity to patient case-mix, however, PQI may behave more like outcome indicators. Presence of comorbidities, patients' age, co-prescribed medications, contraindications, and possible side effects can all be relevant for the prescribing process, and subsequently the scores of PQI. Therefore, use of PQI requires the same caution with regard to patient characteristics as outcome indicators.

Limitations

There are some limitations to this study. We had a small number of participants for some stakeholders, and the participants may not necessarily be representative for all possible stakeholders in the country. However, we included the most relevant organizations in the Netherlands, and within these organizations we recruited the employees whose tasks were closely related to healthcare

quality assessment or improvement.

Conclusions

Prescribing quality indicators, especially those focusing on undertreatment, should be included in the quality assessment of diabetes care. Inclusion of PQI focusing on other aspects of prescribing quality will depend on the aim of the quality assessment. This study provides information on specific preferences of stakeholders which can assist in minimizing the number of relevant PQI and providing customized indicator sets. Development of information systems for documenting reasons for deviations and patient preferences are needed for a more widespread use of PQI for different aims.

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CHAPTER 6

Development of a minimal set of prescribing quality indicators for diabetes management

L. Martirosyan[1] MPH, F.M. Haaijer-Ruskamp[1] PhD, Jozé Braspenning[2] PhD and P.Denig[1] PhD

[1]Department of Clinical Pharmacology, University Medical Center Groningen, University of Groningen, the Netherlands
[2] Scientific Institute for Quality of Healthcare, Radboud University Nijmegen Medical Centre, the Netherlands

Submitted

ABSTRACT

Objective

To identify relevant prescribing quality domains of type 2 diabetes mellitus (T2DM) care for selection of a minimal set of prescribing quality indicators from a set of previously validated indicators.

Study design

Cross sectional study using electronic health records.

Methods

We used the principal factor analysis to identify the underlying dimensions of prescribing quality for 76 family practices participating to the GIANTT project in the Netherlands. From a set of 10 prescribing quality indicators covering various aspects of cardiovascular and metabolic management, we selected a subset of indicators with the highest loading within each identified dimension. Next, we evaluated the impact of using this subset on the quintile ranking of practices on their prescribing quality scores.

Results

We identified five prescribing quality dimensions in our dataset: two dimensions assessing initiation of pharmacotherapy for different risk factors in diabetic patients, two on stepwise intensification of treatment, and one on treatment of patients with cardiovascular disease. A composite score comprising the indicators selected from each of the dimensions showed good agreement with the composite score comprising all indicators with 82 % of family practices either not changing their position or shifting their ranking by only one quintile.

Conclusions

We showed that a minimal set of PQI for T2DM care should not just focus on management of different clinical risk factors, but should also reflect different steps of treatment intensification. The results of our study are relevant for stakeholders when selecting quality indicators to assess quality of prescribing in diabetic patients.

INTRODUCTION

The demand for accountability in health care and need for improving quality of provided care resulted in development of a large number of quality indicators for an increasing number of diseases.[1;2] Quality measurement and reporting have the potential to improve quality of care and reduce health care costs, but can also cause administrative and financial burden of collecting and reporting quality information. In addition, the number of quality indicators included in national sets is varying from country to country. For example, the number of quality measures included in Healthcare Effectiveness Data and Information Set (HEDIS) 2010 set in USA is about half of the number of indicators included in Quality and Outcome Framework in UK.[3;4] Although both sets are comprehensive, there is lack of understanding on what the number of indicators in such sets should be. Stakeholders using quality information, such as health care providers, policy makers, and payers, have to deal with a large number of quality indicators due to the growing number of different quality-reporting programs. In US hospitals, the administrative and financial burden of data collection has been considered to be very high, and different strategies are sough to reduce the number of quality indicators used[5] To reduce the burden of collecting and reporting quality information, it is important to select a minimum set of relevant quality indicators.[6;7] This paper describes the process and results of selecting a minimal set of prescribing quality indicators (PQI) for treatment of Type 2 diabetes mellitus (T2DM).

Currently, to evaluate and improve quality of drug treatment in T2DM patients, a large number of prescribing quality indicators exists worldwide.[8] Several approaches are available to make a selection of relevant prescribing indicators from a larger set. One can start choosing indicators based on stakeholders' specific preferences and areas of interest,[6;9] It is possible to further narrow down the choice of indicators based on clinimetric characteristics, such as the grade of evidence supporting the indicators, concurrent and predictive validity, and the availability of data[8;10] or discard all indicators that do not show room for improvement.[11]

Combining measures to a composite score is another way to reduce the number of indicators included in quality assessment. Composite scores provide an advantage of quick overview of the provided quality of care in a certain area.[12] However, they do not reduce the workload and financial burden of recording and collecting large amounts of data on an individual indicator level.

Another approach to systematically minimize the number of quality indicators is the use of data reduction techniques, such as factor analysis, allowing to uncover hidden relationships between different prescribing quality indicators.[13] Although such an approach has been shown to substantially reduce the number of indicators based on pharmacy registries, it has not been applied to reduce the number of indicators developed for a specific disease and based on electronic health records.

The aim of this study is to provide a minimal set of prescribing quality indicators (PQI) that can represent the quality of pharmacological management of T2DM patients on a healthcare provider level.

METHODS

Study Setting

In The Netherlands, patients are registered with a single family physician who has a gatekeeper role in coordinating their medical care. Almost all family physicians use electronic health records (EHR). We used a dataset extracted for the Groningen Initiative to Analyse Type 2 diabetes Treatment (GIANTT) project which provides information from electronic records of all T2DM patients registered in participating family practices in the north of the Netherlands.[14] For this study, we included the 76 practices that had eligible patients for all tested indicators in the year 2007 covering a total of 7944 T2DM patients.

The dataset includes information on demographics, prescribed medication, comorbidities, and physical examination and laboratory measurements as documented in the medical records. All participating physicians prescribe electronically, which means that the dataset includes full information regarding prescribed medication.

Prescribing Quality Indicators

In a previous study, a set of 14 indicators for assessing prescribing quality in T2DM was selected on face and content validity.[15] Two indicators were discarded from this original set due to a lack of eligible patients per family practice, *i.e.* focusing on patients younger than 40 with a history of cardiovascular disease (CVD), and on incident overweight T2DM patients. We modified one initial indicator focusing on prescription of statins in all diabetic patients with increased cardiovascular risk[15] to prescription of statins in patients with dislipidaemia to reflect changes in the Dutch diabetes guidelines regarding prescription of statins for the study time period.[16]

Statistical Analyses

We calculated the scores of PQI and their 95% confidence intervals (midP) using an individual family practice as a unit of analysis. The operational definitions of the PQI are described elsewhere.[15] There were three indicators focusing on the management of albuminuria with a renin-angiotensin-aldosterone system (RAAS) inhibitor in mutually exclusive subpopulations of T2DM patients, *i.e.* patients without hypertension, with incident hypertension and with prevalent hypertension. Since there were only 17 family practices that had eligible patients for all three indicators focusing on prescription of RAAS inhibitors, we combined them to one indicator to increase the number of eligible patients per practice for the factor analysis. (table2)

An exploratory factor analysis was conducted to identify the number of possible underlying dimensions. We used principal factor analysis to model correlation between indicators and show the extent to which they reflect the same underlying concepts. Next, we selected one PQI within each factor to represent a specific dimension of prescribing quality.

We evaluated models with different numbers of factors and selected the model with best conceptual coherence, total variance explained, and communalities of the PQI. The communality of each indicator, i.e. the sum of the squared factor loadings for all factors for a given variable, shows the amount of variance in a given PQI explained by the selected factors. Furthermore, we repeated the analysis in a subpopulation of family practices that had at least 70 T2DM patients to assess the influence of a practice size.

We selected the PQI with the highest loading within each factor to represent that specific dimension of prescribing quality. To evaluate the impact of selecting this subset of PQI on prescribing quality assessment at family practice level, we assessed the change in ranking of family practices using all or only this subset of indicators. For this, we calculated two composite scores for each family practice averaging scores of individual indicators, and ranked practices on these scores. The first composite score included all 10 initial PQI, and the second one included PQI selected by means of the factor analysis. Next, we ranked the family practices on the prescribing quality, distributed the composite scores using quintiles, and compared the differences in quintile allocation. We considered a difference of not more than one quintile as acceptable agreement. A difference of 2 quintiles was considered as intermediate agreement, whereas more than 2 quintiles were defined as poor agreement. SPSS version 16.0 for Windows was used for the analyses.

RESULTS

The average number of patients per family practice was 119 (mean 105, standard deviation 64). The table 1 provides general characteristics of T2DM patients included in the dataset. The scores of the prescribing quality indicators (PQI) calculated on a family practice level varied from 11% (SE 20) to 96% (SE 13).(table 2)

We carried out the principal factor analysis to identify the model providing the clearest interpretation of factors. We extracted two-, three-, four-, and five- factor solutions and considered the five-factor model the best interpretable and conceptually meaningful. The factors explained a substantial part of the total variance with a cumulative variance of 16% (one factor), 30% (two factors), 43% (three factors), 56% (four factors), and 67 % (five factors) (Table 3). No PQI was excluded from the analysis, as all indicators loaded across the factors with correlation coefficients greater than 0.5. Communalities were 0.6 or higher for all PQI.

Table 1 General characteristics of patient population (n=7944)

	Mean (Std. Error)
Age	66,3 (12,3)
Duration of diabetes (years)	5,7 (5,8)
Average systolic blood pressure (mm/Hg)	142,0 (17,3)
Glycated hemoglobin (HbA1c)	6,8 (0,9)
Total Cholesterol	4,4 (1,0)
Low density lipoproteins (LDL)	2,4 (0,9)
Body mass index*	29,9 (5,4)
Sex (female), %	52,8
Presence of albuminuria, %	12,7
History of myocardial infarction, %	14,4
History of cardiovascular disease (CVD)**, %	21,7

*Body mass index: weight in kilograms divided by height in meters-squared

** History of cardiovascular disease included history of myocardial infarction, ischemic heart disease, transient cerebral ischemia, stroke/cerebrovascular accident, and atherosclerosis/peripheral vascular disease as registered by family physicians

Table 2 Mean family practice scores of prescribing quality indicators forT2DM management (n=76)

	Prescribing quality indicators included in the factor analysis	**Mean PQI score, (SE)**	**Mean number of eligible patients per PQI (SE)**
1	% of T2DM patients with systolic blood pressure ≥ 140 and prescribed any antihypertensive drug	78.7 (8.8)	73.9 (5.6)
2	% of T2DM patients prescribed a second antihypertensive drug from a different class if systolic blood pressure remained ≥ 140 with first class of antihypertensive drug	24.8 (20.7)	13.5 (1.3)
3	% of T2DM patients with albuminuria prescribed RAAS-inhibitor	75.5 (16.5)	15.3 (1.4)
4	% of T2DM patients with history of ischemic heart disease or myocardial infarction prescribed β-blocker	63.3 (19.0)	25.7 (3.3)
5	% of not incident T2DM patients with HbA1c >7 % and prescribed any oral antihyperglycaemic agent or insulin	96.9 (4.0)	34.0 (2.5)
6	% of not incident T2DM patients not receiving insulin prescribed a second oral antihyperglycaemic drug from a different class if with one oral antihyperglycaemic drug HbA1c remained >7%	24.8 (16.5)	11.9 (1.0)
7	% of T2DM patients who are prescribed insulin if with combination of two oral drugs HbA1c remained >7 %	11.1 (18.0)	8.3 (1.0)
8	% of overweight prevalent T2DM patients prescribed a multiple drug regime containing metformin	70.1 (14.0)	64.0 (5.0)
9	% T2DM patients with LDL ≥ 2.5 or TC≥ 4.5 who are prescribed a statin	62.6 (12.6)	39.2 (2.9)
10	% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid	62.4 (19.7)	25.8 (3.3)

Table 2 (continued)

Prescribing Quality Indicators Merged to PQI3				
% ofT2DM patients without hypertension with albuminuria prescribed RAAS-inhibitor	54	(32)	4.8	(0.4)
% ofT2DM incident for hypertension patients with albuminuria prescribed RAAS-inhibitor	89	(31)	1.8	(0.3)
% ofT2DM prevalent for hypertension patients with albuminuria prescribed a multiple drug regime containing RAAS-inhibitor	78	(22)	9.8	(0.8)

T2DM:type 2 diabetes mellitus; RAAS-inhibitor: renin-angiotensin-aldosterone system inhibitor; HbA1c: glycosilated haemoglobin; LDL: low density lipoproteins; TC: total cholesterol

The first two factors focused on general first step drug treatment recommendations for majority of T2DM patients. The first factor named "starting treatment I" included three indicators reflecting, such as prescription of metformin, statin, and any antihypertensive medication. (table 3) The second factor, "starting treatment II", consisted of two other PQI focusing on treatment initiation of T2DM patients with specific risk factors, i.e. prescribing glucose lowering medication in patients with elevated HbA1c levels and prescribing renin-angiotensin system (RAS) inhibitors in T2DM patients with albminuria. . The fourth identified factor reflected treatment of T2DM patients with CVD, and comprised both PQI from our set of indicators concerning patients with a history of CVD, focusing on prescription of beta blockers and acetyl salicylic acid. Finally, there were two factors focusing on next steps of treatment intensification. The factor named "step 1 treatment intensification" included only one PQI focusing on adding a second drug in patients with hyperglycemia despite monotherapy with oral glucose lowering medication. The "step 2 treatment intensification" factor comprised a PQI focusing on adding a second class antihypertensive medication if one class was not sufficient to control the blood pressure, and a PQI on prescribing insulin in patients with uncontrolled HbA1c levels despite oral glucose-lowering treatment. Subanalysis limited to family practices that had at least 70 T2DM patients showed similar results with PQI loading across the same identified dimensions as for the total population.

Within each dimension we selected the indicator with the highest loading as the PQI that could represent that dimensions (PQI 1, 4, 5, 6, 7). To assess the influence of this selection of PQI on prescribing quality assessment, we ranked the family practices based on the composite scores of all initial PQI and the five PQI selected. Distribution of composite scores by quintiles showed that 81.5 % of family practices had an acceptable shift by either remaining within the same quintile or shifting only by one quintile; 10.5 % had an intermediate shift by 2 quintiles; and only for 8% of family practices there was poor agreement since they shifted by more than two quintiles.(table 4)

Table 3 Factor pattern coefficients from principal component analysis: five factor solution (n of family practices = 76)

	PQI	Factor loadings					Communalities
		Starting treatment I	Starting treatment II	Treatment of CVD	Step 1 treatment intensification	Step 2 treatment intensification	
1	% of T2DM patients with systolic blood pressure ≥ 140 and prescribed any antihypertensive drug	**,865**	,212	,041	,089	-,095	.811
2	% of T2DM patients prescribed a second antihypertensive drug from a different class if systolic blood pressure remained ≥ 140 with first class of antihypertensive drug	-,175	,254	,300	-,374	**,562**	.641
3	% of T2DM patients with albuminuria prescribed RAAS-inhibitor	,119	**,543**	,182	,438	,355	.660
4	% of T2DM patients with history of ischemic heart disease or myocardial infarction prescribed β-blocker	,143	,119	**,730**	-,068	-,162	.598
5	% of prevalent T2DM patients with HbA1c >7 % and prescribed any oral antihyperglycaemic agent or insulin	,070	**,790**	-,127	-,045	-,069	.652
6	% of prevalent T2DM patients not receiving insulin prescribed a second oral antihyperglycaemic drug from a different class if with one oral antihyperglycaemic drug HbA1c remained >7%	-,060	,007	,072	**,820**	-,062	.685
7	% of T2DM patients who are prescribed insulin if with combination of two oral drugs HbA1c remained >7 %	,033	-,123	-,149	,050	**,804**	.687
8	% of overweight prevalent T2DM patients prescribed a multiple drug regime containing metformin	**,546**	,502	,157	-,020	-,239	.633
9	% T2DM patients with LDL ≥ 2.5 or TC≥ 4.5 who are prescribed a statin	**,676**	-,198	-,123	-,225	,411	.731
10	% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid	-,121	-,192	**,727**	,210	,105	.636

Table 4 Agreement between composite scores per family practice based on five versus 10 PQI*

Composite score based on 10 PQI	Composite Score based on 5 PQI					
	1	2	3	4	5	Total
1	9	3	2	0	1	15
2	2	8	5	1	0	16
3	1	1	6	5	2	15
4	3	1	2	6	3	15
5	0	2	1	3	9	15
Total	15	15	16	15	15	76

* Rows represent quintile distribution of family practices based on a composite score of initial 10 PQI; Columns represent quintile distribution of family practices based on a composite score of the selected five PQI.
Dark grey cells represent family practice practices with acceptable agreement between two composite prescribing scores.
Intermediate grey cells represent family practice practices with intermediate agreement between two composite prescribing scores.
Light grey cells represent family practice practices with poor agreement between two composite prescribing scores.

DISCUSSION

By means of factor analysis we selected five PQI representing the identified dimensions within our dataset: two dimensions on initiation of treatment, two on treatment intensification steps, and one on the treatment of T2DM patients with a history of cardiovascular disease. A composite score based on these indicators showed good agreement for ranking the family practices on the assessed prescribing quality in comparison to a composite score bases on the initial 10 indicators.

One might expect that PQI focusing on management of the same risk factor, for example hypertension or hyperglyceamia, would correlate highly and would therefore constitute one dimension. Our study, however, showed that the PQI that loaded on the same factor often represented management of different clinical risk factors related to diabetes. Previous studies have shown that relationship between prescribing indicators is often unpredictable with very different prescribing indicators correlating to a high degree.[17] Instead of correlations within a risk factor, we observed relationships between different indicators which appear to be linked to different steps in treatment. The first two factors included PQI that assessed the first step in pharmacological treatment of T2DM patients such as initiation of antihypertensive and glucose lowering treatment, and prescription of statins and RAS-system inhibitors. The third and fifth factor reflected the second or third step in treatment of T2DM patients, assessing more aggressive management of uncontrolled risk factors. The fourth factor focused on secondary prevention of cardiovascular events in patients with known history of cardiovascular disease.

The composite score based on the five selected indicators showed in general good agreement with the score comprising all indicators, however, 8% of family physicians shifted by more than two quintiles. We had three very detailed indicators focusing in intensification of treatment that were triggered by a small number of patients even in large practices as they have multiple inclusion criteria. Such indicators have been shown to have a big influence on a composite score averaging indicators.[18] The composite score based on the selected five PQI included two indicators focusing on intensification of treatment. This could partially explain the poor disagreement between the two composite scores observed for few family practices.

We had complete and valid information on medication prescriptions of family practitioners for all their T2DM patients in our dataset, since they all prescribe electronically. Although we used a large dataset comprising electronic health records of 76 family practices with more than 7944 T2DM patients, our results may not be generalized to other datasets. We recognize that prescribing patterns of primary care doctors in different countries can be influenced by cultural differences,[19;20] and variation in national diabetes guideline recommendations that may vary both across and within countries.[21;22] Therefore, a confirmation of our findings in different datasets and countries is recommended.

To our knowledge, this is the first study to look at the dimensions of prescribing quality of T2DM care. Our study presents an additional approach for minimizing the number of indicators and reducing the financial and administrative burden for collecting and reporting quality of care information. The results of this study indicate that when making selection from initial set of indicators and developing a minimum set, it is important to include the PQI that represent different levels of treatment intensity, i.e. PQI focusing on start of treatment, intensification of treatment and management of T2DM patients with known cardiovascular disease.

Take-Away Points

Using factor analysis we selected five PQI indicators representing the dimensions of prescribing quality in our dataset and showed that this subset of indicators adequately reflects the overall prescribing quality on a family practice level.

- Factor analysis has an additional value for selecting a minimum set of prescribing quality indicators through identification of underlying dimensions of prescribing quality in T2DM
- A minimal set of PQI for T2DM care should integrate different treatment intensity levels of clinical risk factor management.

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CHAPTER 7

General Discussion

INTRODUCTION

This thesis fits into a growing body of research on healthcare quality indicators. The main aim of the research described in this thesis is to provide a valid and feasible set of prescribing quality indicators for type 2 diabetes management. In this chapter, the main findings from the particular studies are summarized, methodological strengths and limitations of the presented studies are addressed, and implications for implementation of the prescribing quality indicators and further research are discussed.

SUMMARY OF RESULTS

Objective 1: To develop a comprehensive, valid, and operationally feasible set of prescribing quality indicators for diabetes care.

What is already known?

- Prescribing quality indicators for T2DM management are underrepresented in national sets of quality indicators in many countries including the Netherlands.
- A comprehensive set of prescribing quality indicators for T2DM management does not exist.
- Validity, feasibility, and acceptability of indicators are essential for reliable measurement of (prescribing) quality.
- Choice of methods and data sources to identify the target population (*i.e.* eligible patients) for treatment may have important consequences on quality assessment scores.

What is new?

- A set of prescribing quality indicators for diabetes management was developed with proven face and content validity as well as operational validity, covering all important aspects of pharmacotherapy in T2DM patients.
- Use of clinical measurements provides a more sensitive approach than use of diagnostic codes to identify treated and especially untreated patients with hypertension and patients being overweight or obese.
- Use of diagnostic codes to identify eligible patients results in overestimation of prescribing quality scores in situations when diagnostic codes are better registered for treated than untreated patients.

Development of indicators

In **Chapter 2,** we described the development and validation of prescribing quality indicators (PQI) for hypertension, hyperglycaemia, dyslipidaemia, antiplatelet treatment, and prevention of secondary cardiovascular disease in T2DM patients for internal quality improvement in ambulatory setting. The indicators were derived from multiple diabetes guidelines and assessed in the panel of nationally recognized experts followed by a panel of GPs and diabetologists working in the field. Out of 31

potential prescribing indicators reflecting the main recommendations regarding pharmacological management of T2DM patients, the expert panel considered 18 indicators as sufficiently valid, of which 14 indicators remained valid after assessment of GPs and diabetologists.

Our results underline the importance of combining scientific evidence with expert and field opinion. We found that diabetologists and GPs disagreed on some first choice drug recommendations in the guidelines. Since our aim was to select indicators for which there was a consensus between both groups of professionals, indicators considered relevant by only some panel members were not included in the final selection. The final set included prescribing indicators focusing on all five areas of pharmacological management. Most of the selected indicators were supported by evidence classified as grade A. None of the indicators focusing on dosage or safety reached sufficient face and content validity. There was disagreement between experts on such indicators. The main reasons for disagreement and subsequent discarding of the indicators were lack of scientific evidence supporting an indicator, lack of clinical information on patient level that is necessary for calculating such indicators, and a high sensitivity of some indicators to patient case-mix.

Testing operational validity of the developed indicators

Operational validity for most of the PQI was good: we were able to calculate 13 out of 14 PQI using electronic health records of T2DM patients (**Chapter 2**). Many of our final indicators required information on clinical measurement values such as blood pressure, HbA1c, albuminuria, etc. For example, prescription of an additional class antihypertensive medication in patients with systolic blood pressure higher than 140 mm/Hg despite treatment with one class of antihypertensive medication. Not all needed information was available for all patients, possibly because some clinical measurements are not assessed or registered on annual basis. We concluded that the developed indicators can be used among patients with registered values for internal quality improvement initiatives.

Defining patients with specific conditions in need of treatment

The denominators of some of the developed indicators could be operationalized in our database by means of diagnostic codes or the clinical measurements values. For example, overweight or obese patients could be identified with an increased body-mass index (BMI) but also by using the diagnostic ICPC codes T82 and T83. Similarly, patients with hypertension could be identified by elevated blood pressure values or by the corresponding diagnostic codes (ICPC codes K85, K86, K87). We studied the effect of the different ways of operationalizing the denominators on the results of the indicators. (**Chapter 3**)

Using three indicators from our set of indicators as an example, we showed that in specific situations prescribing quality scores may differ depending on the method (diagnostic codes versus clinical

measurement values) to define target population. The choice of methods influences the indicator score when there is information bias favoring registration of diagnostic codes in patients who receive the recommended treatment. We observed such bias for the indicator measuring prescription of any antihypertensive medication in patients with hypertension. Patients with registered diagnostic codes for hypertension had a higher chance of being prescribed antihypertensive medication than patients without such codes but with elevated blood pressure values. Another relevant finding was that the clinical measurement-based approach had a higher ability to identify eligible patients who were not prescribed the recommended treatment compared to a diagnostic code-based approach. Use of diagnostic codes resulted in missing a higher number of undertreated patients that could benefit from the improved treatment compared to a clinical measurement-based approach.

Objective 2: To improve the general understanding on clinimetric characteristics of PQI for type 2 diabetes care and cardiovascular risk management.

What is already known?

- Many PQI have been developed, but there is no clear overview of their clinimetric characteristics.
- Requirements for indicators developed for internal or external use are different.

What is new?

- Content and face validity of most prescribing indicators for management of diabetes and cardiovascular risk factors is well established.
- Inter-rater reliability of prescribing indicators is high.
- Predictive validity of individual prescribing indicators is not yet known.
- Prescribing indicators focusing on treatment modification in response to elevated risk factor levels are more accurate measures of provided quality than commonly used cross-sectional treatment indicators.
- Case-mix and sample size problems are not always addressed for prescribing indicators used for external quality assessment.

Clinimetrics of existing PQI

In **Chapter 4,** we described the results of a systematic literature review to identify and classify existing prescribing indicators for diabetes and cardiovascular risk management. We classified the indicators in different types and summarized their clinimetric characteristics. We identified more than 200 distinct prescribing indicators, and grouped similar indicators to 16 subtypes of indicators covering first–choice treatment, safety issues, dosing, costs, sufficient and timely treatment. We provided the clinimetric characteristics as evaluated and documented in the literature on this subgroup level. As a result of our analysis, we came up with a short-list of specific indicators with the

best assessment results regarding different types of validity tested. These indicators were based on grade A evidence, and showed good clinimetrics in different settings. They focused on prescribing drugs for a specific indication, in particular (a) statins in high cardiovascular risk patients, (b) aspirin or antiplatelet medication in high cardiovascular risk patients, (c) ACE-inhibitors in T2DM patients with hypertension and/or albuminuria, (d) treatment of patients with elevated HbA1c levels, (e) treatment of patients with elevated blood pressure levels, and (f) b-blocker in patients with coronary heart disease or history of myocardial infarction.

We concluded that assessment of face and content validity, *i.e.* ensuring that the indicator is reflecting scientific evidence and is accepted by professionals has become the norm but additional validity testing is not that common. The reliability of prescribing indicators was found to be very good. Explicit definitions of indicators do not allow room for individual judgments on provided quality resulting in a high inter-rater reliability scores. These features enable the use of PQI for internal quality improvement initiatives. For external accountability purposes, however, this is not sufficient. We found that for many prescribing indicators used for external quality assessment no case-mix adjustment or minimal sample size calculation is provided. More attention has to be paid to these clinimetrics for reliable and fair comparisons across different health care providers. In addition, predictive validity of individual prescribing indicators is not established yet.

Objective 3: To build up the knowledge on stakeholder preferences and selection of relevant PQI from existing sets of indicators.

What is already known?

- The number of quality indicators is increasing due to the implementation of new disease management and quality improvement programs.
- Different stakeholders have a different perspective on quality of health care.
- Using large numbers of indicators introduces time, financial, and administrative burden for all involved stakeholders.
- Quality indicators have to correspond to the aims of quality measurement.
- Some stakeholders are interested in a smaller number of informative indicators.

What is new?

- All stakeholders indicate the importance of PQI for assessing overall quality of diabetes care.
- PQI focusing on undertreatment in diabetes are prioritized by all stakeholders, while the stakeholders differed in their preferences for prescribing indicators focusing on safety, costs, and first choice drug selection.
- A minimal set of PQI for T2DM care should not just focus on management of different clinical risk factors, but also reflect different steps of treatment intensification.

Selection of prescribing quality indicators based on specific preferences of involved stakeholders

In **Chapter 5,** we described the preferences for specific PQI for diabetes care. We concluded that the preferences of stakeholders are closely related to their aims for quality measurement. PQI focusing on undertreatment were considered relevant by all stakeholders, but otherwise the stakeholders had differing preferences. Health care providers and policy makers valued PQI focusing on the safety of medication, insurance companies prioritized indicators focusing on prescribing costs, and patients' representatives valued indicators focusing on the interpersonal aspects of prescribing. We found that the preferences of stakeholders also depend on their ability to control the issue described in the quality indicator. For example, pharmacists preferred indicators focusing on safety of medication, because they can directly contribute to the improvement of safety issues related to prescribed medication. Similarly, health insurance companies preferred indicators focusing on costs, because of their aim of cost containment in health care, and their ability to control costs through existing mechanisms such as reimbursement policies. Lack of documented information on reasons for deviating from guideline recommendations appeared to be the most important barrier for using prescribing quality indicators. Health care providers mentioned that there are many legitimate reasons for deviating from the guideline recommendation - and subsequently not achieving high levels on the prescribing indicators - ranging from side effects of the drug to the individual choice of patients. Patient representatives implied that they want their health care providers to prescribe the treatment based on specific patient situation. All stakeholders preferred positive formulation of prescribing quality indicators scores to encourage participation of health care providers in quality improvement programs. Composite scores were found to be a useful starting point for quality assessment, but individual indicators scores were preferred eventually by all stakeholders both for internal quality improvement and for external accountability purposes.

Selection of prescribing quality indicators based on prescribing quality domains identified through a data reduction technique

Chapter 6 presents the results of a data reduction technique to reduce the number of PQI for diabetes care. For this analysis we used our initial set of indicators described in **Chapter 2** with some modifications to increase the number of eligible patients per PQI in HGP practices. As a results of these modifications, the final set comprised 10 PQI. (Chapter 6) We explored the relationships between these PQI using factor analysis. We identified five prescribing quality dimensions in a dataset from 76 general practices: two dimensions assessing general pharmacotherapy of different risk factors related to T2DM, two on stepwise intensification of risk factor treatment, and one on treatment of diabetic patients with a known cardiovascular disease. It is important to highlight that the prescribing indicators were clustered on different levels of therapy intensification and not per clinical risk factor. Within each of the five identified dimensions, we selected the indicator with the highest loading to represent each dimension. We found that a composite score comprising these

five selected indicators showed good agreement with the composite score comprising all indicators at practice level. Using comparisons of rankings, 82% of the practices either did not change their position or shifting their ranking by not more than one quintile. This suggests that this set of five PQI can be used to represent prescribing quality as defined by the wider set of indicators.

METHODOLOGICAL CONSIDERATIONS

Within the research described in this thesis, a variety of methods has been applied, being a modified Delphi technique (RAND Appropriateness Method), a systematic literature review, cross-sectional analyses of prescribing quality scores using electronic health records (EHR), qualitative research methods, and a data reduction technique, *i.e.* factor analysis. Subsequently, the strengths and limitations of these methods are discussed.

Development of PQI using Rand Appropriateness Method

We have chosen the Rand Appropriateness Method for the development of our set of prescribing indicators as this is a systematic method allowing to combine scientific evidence with expert opinion.[1] In fact, we had several indicators based on guidelines that experts disagreed with and this resulted in discarding such indicators from the final set. Another strong point of this study is that we used IPRAS (Interpercentile Range Adjusted for Asymmetry) method to assess disagreement between experts during all rounds of indicator rating. This methods has shown 100% sensitivity with a good specificity after being tested in more than 16,400 theoretical indications and more than 6,500 real cases.[2]

As in any Delphi technique, the final selection of indicators is sensitive to the panel composition. It is known that panel members from different groups may have different judgments, which affects the ratings.[3] Judgments made by any expert panel may not be representative for all health care professionals. However, in our study, we had two different panels, making the final selection of indicators more reliable and generalizable.

Operational validity testing

We showed that the majority of the developed prescribing quality indicators had a good operational validity when electronic health records (EHR) are used for their calculation. We combined patient clinical information stored in two data EHR sources to enhance completeness of data collection.In addition, diagnoses were coded from text lines to improve the registration of diagnostic codes. It has to be born in mind, however, that EHR may not be widely available, limiting the use of indicators that are based on detailed clinical information.

We compared methods to identify target population using a reference method that was based on a combination of available information about registered diagnostic codes and clinical measurement values. Such a reference method is likely to be affected by inadequate registration of diagnostic

codes and clinical measurements. However, EHR are often considered the "gold standard" for quality measurement, and we chose this as the most complete source of information for prescribing quality assessment.

Literature review of clinimetric characteristics of existing PQI

We tried to make our systematic literature search as comprehensive as possible by including two major databases (MEDLINE and EMBASE), by having no language restriction for formally published papers, and by careful screening the grey literature, references of included papers from peer-reviewed journals, and relevant national WebPages. We had a sensitive search strategy with 88% (46 out of 52) of papers found through the main search strategy. However, we might have missed some documents, especially concerning grey literature from non English speaking countries.

We developed a system for classifying indicators based on their clinimetrics. We used a list of definitions for clinimetrics to identify their assessment, since in many studies the assessment of such clinimetric characteristics of the indicators was not the main objective of the study.

We grouped the large number of identified indicators into 16 main subgroups. These subgroups were created by aggregating similar prescribing indicators, for example, prescription of statins in patients with increased cardiovascular risk and prescription of statins in patients with history of cardiovascular disease. Presentation of clinimetric characteristics on a subgroup level does not give details regarding a specific individual indicator, *i.e.* the exact indicator definition and clinimetrics. However, we chose to present clinimetric characteristics of similar indicators on an aggregated, subgroup level for two main reasons. First of all, it summarizes the assessment of different clinimetrics for similar indicators in different countries, at different times and by different authors. This provides a more complete picture of assessed clinimetrics for a specific type of indicators. Next, the classification on subgroup level makes the provided overview more user friendly, *i.e.* instead of more than 200 individual prescribing indicators, 16 subgroups are presented.

Eliciting preferences of stakeholders regarding prescribing quality indicators

As there were no studies conducted previously to describe preferences of different stakeholders regarding prescribing indicators, a qualitative study was the most appropriate method to explore the preferences of stakeholders and to identify reasons for prioritizing specific indicators. In this study, we used several techniques to ensure credibility of our data including data and investigator triangulation.[4;5] A possible limitation of the study was the small number of representatives from some stakeholders that may limit generalizability of our findings. However, we involved the most relevant organizations, and within those organizations we identified the key informants. It is a relatively small group of people in the Netherlands who discuss possible sets of quality indicators. We are confident that we have recruited the most experienced stakeholders in regard to PQI for T2DM managment.

Use of factor analysis to reduce the number of PQI for T2DM management

Factor analysis can be a helpful technique for minimizing the number of prescribing quality indicators through identification of underlying dimensions of prescribing quality. The advantage of this method is identification of relationships between different prescribing indicators on a general practice level that are otherwise not visible. This allows not only reducing the number of prescribing indicators, but also identifies the most important dimensions of prescribing quality. We were able to reduce the number of prescribing quality indicators from ten to five. This might not be considered a significant reduction, but further reduction in the number of indicators would result in losing important domains that were supported by statistical analysis.

We confirmed the findings of this study by, repeating the analysis only for those practices that had at least 70 T2DM patients. The identified dimensions and loadings of indicators across the dimension did not change for this subset of general practices. In addition, we confirmed that the selected PQI reflect the overall prescribing quality by showing good agreement between the rankings of general practices based on composite scores comprising all initial indicators and the rankings based on the composite score comprising five PQI selected through the factor analysis.

IMPLICATIONS FOR IMPLEMENTATION OF PQI

Aims of using PQI

The developed set of prescribing quality indicators for T2DM ambulatory care(6) can be used for internal quality improvement by health care providers. (Table 1) The developed indicators are face and content valid, reliable, and operationally valid The majority (11 out of 14) of the selected indicators are supported by A grade evidence coming from the randomized controlled clinical trials that provide basis for many diabetes guidelines recommendations regarding pharmacotherapy in T2DM. All indicators in our set of PQI belong to the indicators with the best assessment results on clinimetrics out of all existing PQI for T2DM and cardiovascular risk management.[7] It is important, however, to realize that the final set of indicators should be updated over time to ensure that the indicators are reflecting the best available evidence. In general, it is recommended to update the quality indicators biannually or more frequently if new guidelines or evidence emerges.[8]

The developed PQI can be used for external quality assessment if the minimum sample size per PQI is known and available and case-mix adjustments are conducted to ensure reliable comparison between providers.

Table 1. Proposed set of prescribing quality indicators for T2DM management

% of T2DM patients with systolic blood pressure ≥ 140 and prescribed any antihypertensive drug
% of T2DM patients prescribed a second antihypertensive drug from a different class if systolic blood pressure remained ≥ 140 with first class of antihypertensive drug
% of T2DM patients with albuminuria prescribed RAAS-inhibitor
% of T2DM patients with history of ischemic heart disease or myocardial infarction prescribed β-blocker
% of not incident T2DM patients with HbA1c >7 % and prescribed any oral antihyperglycaemic agent or insulin
% of not incident T2DM patients not receiving insulin prescribed a second oral antihyperglycaemic drug from a different class if with one oral antihyperglycaemic drug HbA1c remained >7%
% of T2DM patients who are prescribed insulin if with combination of two oral drugs HbA1c remained >7 %
% of overweight prevalent T2DM patients prescribed a multiple drug regime containing metformin
% T2DM patients with LDL ≥ 2.5 or TC≥ 4.5 who are prescribed a statin
% of T2DM patients with history of cardiovascular disease prescribed acetyl salicylic acid

T2DM: type 2 diabetes mellitus; RAAS-inhibitor:Renin Angiotensin Aldosteron system inhibitors; HbA1c: Glucosylated Hemoglobin; LDL: Low density Lipoproteins; TC: Total Cholesterol

International comparability

The proposed set of PQI is also of international value, because it has been shown that existing diabetes guidelines share a considerable amount of recommendations,[9] and the selected indicators are based on the recommendations found in many national and international diabetes guidelines[10-15]. Before introducing this set of indicators in another country, however, it is recommended to re-test the face validity, as expert panels from different countries may have different ratings regarding the same indicator set.[16;17] The information on reliability, concurrent validity, and methods to adjust for case mix and improve sample size per indicator can be transferred and generalized to other countries and settings, as these properties are less prone to be influenced by expert opinion, health care systems or data availability. For example, the reliability of prescribing quality indicators with clear definitions once found to be very good does not need further assessment.

The proposed set of indicators requires detailed clinical data on a patient level that are usually available in medical records. In countries with no widely available EHR the use of our PQI would require manual medical record review. Therefore, prior to use in a new setting or country, the PQI should be tested for operational validity, as this characteristic largely depends on type and source of data used for calculation of indicators.[6;16;18]

We demonstrated that the use of diagnostic codes to identify eligible patients for prescribing quality assessment may overestimate the provided quality of care. This is likely to happen in

other countries and settings due to the presence of many factors influencing the registration of diagnostic codes, such as purpose of registration, skills and knowledge of the coder, prioritizing the coding of some conditions over others by physicians, and incompleteness of a disease classification system.[19;20] There are other conditions, different from hypertension and obesity that can also be identified by both diagnostic codes and clinical measurements, for example dyslipidemia, impaired liver and kidney function, etc. Future studies are needed to investigate the influence of the choice of a method to identify patients (diagnostic codes versus clinical measurement values) with such conditions on quality assessment scores.

The specific preferences of stakeholders regarding different types of prescribing quality indicators found in our qualitative study may not be generalizable to other countries due to differences in health care systems and possible different roles of stakeholders. The need to incorporate preferences of involved stakeholders for development and selection of quality indicators is acknowledged by several organizations developing indicators in different countries, and similar studies need to be conducted in other countries for selection of prescribing quality indicators.

Validity versus feasibility of PQI

In general, different clinimetric characteristics of PQI are interrelated. For example, prescribing indicators that are sensitive to case-mix issues may not be selected by experts during assessment (Chapter 2), and therefore such indicators will be considered as lacking face validity. Prescribing indicators that exclude patients that have side effects or contraindications to the recommended medication, partially remove the case-mix effect. However, these indicators require much clinical information that is not always available, and therefore are lacking operational validity. (Chapter 4) Similarly, indicators that incorporate longitudinal way of quality measurement, *i.e.* linking health care provider actions to patient clinical outcomes seem more accurate measures of provided care than commonly used cross-sectional indicators. Longitudinal indicators were the only type of indicators for which the concurrent validity has been shown, and there is a growing body of evidence showing that longitudinal indicators provide the fairest estimates of provided quality.[21;22] However, these indicators are more difficult to calculate than cross-sectional indicators, and they require availability of detailed clinical information hampering operational validity. In any case, the stakeholders need to make a trade off between the additional advantages provided by specific indicators and efforts to collect the necessary data for their calculation.

For prescribing quality assessment the choice of clinical information to reliably identify the patients with specific conditions is very important. Since our data showed that the combination of diagnostic codes and clinical measurement values is the most informative method to identify undertreated patients, we recommend this approach for internal quality assessment by health care providers to identify patients who may benefit from improved treatment. For external quality assessment, when

prescribing quality scores are used by policy makers for comparison across different health care providers, it is advised to avoid the use of diagnostic codes in situations where there is imbalance of diagnosis registration in relation to a treatment status of the patient. If there is no such imbalance, the choice of the method is not likely to influence the prescribing quality score, and both approaches can be used for prescribing quality assessment depending on which data are available or easier to obtain.

Relevance of prescribing quality indicators for assessment of diabetes care

Although prescribing quality indicators are still underrepresented in sets of quality indicators, our results showed that all stakeholders stressed the importance of including PQI for the assessment of diabetes care in the public domain. (Chapter 5) Recently there is an increased interest from different stakeholders in receiving information on quality and safety of medication use in the Netherlands. (Chapter 4) In 2008 financial incentives to general practitioners were introduced by some insurance companies for meeting prescribing indicators related to diabetes care.[23] In addition, the recent endorsement of prescribing indicators for pharmacies confirms this trend.[24] Similarly, the National Quality Forum in the United States acknowledged that there are too few measures available to improve the quality and safety of medication use and management, and endorsed 18 prescribing quality measures as a starting point. These measures focus on managing over-the-counter and prescription medication related to several conditions including diabetes.[25]

Selection of minimum set of prescribing quality indicators

Health care providers and other stakeholders have to deal with a large number of quality indicators due to the growing number of different quality-reporting programs. The administrative and financial burden of data collection and reporting is considered to be very high by health care providers, and different strategies are sought to reduce the number of quality indicators used. This thesis enables selection of prescribing quality indicators for T2DM management using three different approaches.

Selection of prescribing indicators based on their clinimetric characteristics, i.e. face, content, concurrent and operational validity is an important component of indicator selection process. Prioritization of clinimetric characteristics should reflect the aim of using prescribing indicators. Another step in the selection process is considering stakeholder preferences in relation to the aim of quality assessment.[3;26] Our results imply that prescribing quality indicators focusing on undertreatment issues would be the best candidates for inclusion in a uniform set of indicators for T2DM management intended for all involved stakeholders. The information on stakeholders' specific preferences for other prescribing indicators should be used for the development of customized sets of indicators for specific stakeholders.

Finally, factor analysis is a useful technique to reduce the number of prescribing quality indicators

developed for a specific condition or disease while not losing the overall picture of prescribing quality provided by general practitioners. As prescribing patterns of doctors may vary from country to country,[27;28] a confirmation of our findings in different datasets and countries is recommended. In addition, it would be interesting to explore whether the relationships of prescribing indicators for management of other chronic conditions follow the same pattern (i.e. cluster on different levels of treatment intensification) as for T2DM management.

Process (prescribing) indicators and health outcome indicators

According to the Donabedian's Triad Model of healthcare quality assessment,[29] improved process of care results in improved patients outcomes. However, process of care is only one determinant of successful health outcome. Differences in health outcomes might be observed due to case-mix, environment, lifestyle, *i.e.* diet, smoking, etc. In addition, different data collection methods may also explain differences in health outcomes. It is argued that outcome indicators should be only used situations where it is likely that variations in health care might lead to significantvariations in health outcome.[30] If theseconditions are not met, then alternative strategies such as process measurement are preferable for quality assessment and improvement.

Prescribing indicators are typical process indicators as they refer to the treatment of patients. The advantages of process measures are that they are more sensitive to differences in the quality of care and they are direct measures of quality. Prescribing quality indicators have a special position among other process indicators. Unlike indicators focusing on measurement and registration of clinical values (*e.g.* % of T2DM patients with blood pressure measurement), the PQI reflect the actions of health care providers in response to observing certain clinical values (*e.g.* % of T2DM patients with hypertension prescribed antihypertensive medication). For that reason, the PQI present a better opportunity for informing and improving quality of provided diabetes care.

In general, process indicators are considered to be less affected by clinical characteristics of patients compared to the outcome indicators.[30] This is particularly true for process indicators focusing on percentages of patients in whom certain laboratory measurements have been conducted, or who have received a foot or eye exam. With regard to sensitivity to patient case-mix, however, PQI require caution. Presence of comorbidities, patients' age, co-prescribed medications, contraindications, and possible side effects can all be relevant for the prescribing process, and subsequently the scores of PQI. Although information on predictive validity of individual prescribing indicators is lacking, prescribing is the best researched part of diabetes treatment, and it reflects the actions of health care providers. Therefore, prescribing indicators constitute a promising target for improving quality of diabetes care.

CONCLUSION

All stakeholders are convinced that prescribing quality indicators are necessary for assessment of quality of care provided to TDM patients. Therefore, a concise set of valid indicators is needed which can be measured in a reliable way. We have developed and tested a set of prescribing quality indicators for T2DM management that cover all pharmacological treatment areas relevant for diabetes management.

Based on our studies, we can recommend the use of the selected and validated 10 PQI that can be applied at the level of GPs or GP-practices. (Table 1) Criteria for selecting these indicators were good face and content validity, reliability, and operational feasibility (the definitions of the indicators are operational, and data needed for calculating the indicators are available). In addition, all 10 PQI are focusing on undertreatment, and therefore, they constitute the preferences of all stakeholders.
The selected indicators have been validated in different countries and by different authors for the clinimetric characteristics with good assessment results. The conducted systematic literature review did not provide any additional valid indicators.

When making further selection from this set of indicators and developing a minimum set, it is important to include the PQI from this set that represent different levels of treatment intensity, i.e. PQI focusing on start of treatment, intensification of treatment and management of T2DM patients with known cardiovascular disease.

If the selected indicators are to be used for external quality assessment, *i.e.* comparison of individual health care providers, it is important to mention that the necessary requirements for valid external quality assessment, *i.e.* sufficient sample size per PQI, adjustment for case-mix and longitudinal way of calculation, are not per se included in the definition of indicators, but rather should be taken into account and applied by indicator users.

FUTURE PERSPECTIVES

The ultimate aim of prescribing quality assessment regardless of stakeholders' perspective is patient health gain. To ensure the highest impact on patient intermediate and hard outcomes, it is necessary to focus on prescribing indicators with proven predictive validity. We have found that predictive validity is assessed for few prescribing indicators for T2DM management with controversial results. Most studies used a cross-sectional design to investigate the association between process of care and patient outcomes, and it remains unclear if the observed associations were due to adequate treatment or to other unmeasured processes of care. Well designed prospective studies are needed to assess predictive validity of individual indicators on a practice level. In addition, information on predictive validity of prescribing indicators will serve as another criterion for selection of prescribing indicators.

In the study on stakeholder preferences we have found that all stakeholders considered the lack of information on reasons for deviation from guidelines to be the most important barrier for use of prescribing quality indicators. Development of information systems to account for legitimate deviations from guidelines recommendations would provide better opportunities for fair and efficient prescribing quality assessment through use of prescribing quality indicators. This can be done for example, by adopting an exception reporting system similar to one used by the Quality and Outcome Framework in UK with development of coding system to register the reasons for not prescribing the recommended medication. The administrative burden could be counterbalanced by a healthier environment for external quality assessment.

Finally, guidelines or checklists for assessment of prescribing quality indicators need to be developed. We found that sometimes prescribing indicators are being used for external aim without sufficient testing. At the moment no standardized approach exists for assessment of clinimetric characteristics of prescribing indicators with different authors using different criteria for validation of indicators. Such a checklist should discriminate between clinimetric requirements for indicators with internal or external aims and should be described for different available data sources. Availability of such a checklist will serve two main purposes. First, it will enable assessment of prescribing indicators in relation to their aim before usage. Second, it will allow identifying gaps in assessment of indicators of choice, which can be filled by future research.

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Nederlandse samenvatting

In het afgelopen decennium is er wereldwijd veel aandacht besteed aan diabeteszorg. In veel landen, waaronder Nederland, was diabetes een van de eerste ziektes waarvoor een ketenzorg *disease management* programma werd ontwikkeld. Daarbij zijn verschillende indicatoren ontwikkeld om de kwaliteit van diabeteszorg te monitoren in verschillende nationale sets. Er bestaan specifieke nationale en internationale projecten over kwaliteitsindicatoren die zijn gericht op het verbeteren van de kwaliteit van diabeteszorg. Hoewel sommige van deze programma's ook voorschrijf -indicatoren voor diabetesmanagement bevatten, ontbreekt er nog een allesomvattende reeks. Bovendien ontbreekt informatie over de validiteit van de reeds bestaande voorschrijf-indicatoren voor diabeteszorg.

Omdat bij de meeste diabetici een juiste medicamenteuze behandeling de kans op cardiovasculaire complicaties kan verlagen, kunnen voorschrijf-indicatoren voor zorg aan mensen met diabetes mellitus type 2 (T2DM) in potentie de zorg informeren en de kwaliteit van diabeteszorg te verbeteren. Daarvoor moeten ze echter wel voldoen aan aan aantal criteria. Een voorschrijf-indicator moet tenminste gestoeld zijn op het beste bewijs voorhanden en worden geaccepteerd door de beroepsbeoefenaren. De data waarmee de voorschrijf-indicator wordt berekend moeten eenvoudig te verkrijgen zijn en systematisch verzameld worden. De indicator moet betrouwbaar zijn en het moet mogelijk zijn om een eerlijke vergelijking tussen zorgverleners te maken. Op basis van deze criteria kunnen de indicatoren gekozen worden die het meest geschikt zijn om de kwaliteit te beoordelen.

Voorschrijf-indicatoren worden vereist en gebruikt door verschillende belanghebbenden, zoals beleidsmakers, zorgverzekeraars, zorgverleners en patiëntenverenigingen. Deze belanghebbenden krijgen met een toenemend aantal kwaliteitsindicatoren te maken voor een groeiend aantal ziektes. De financiële en administratieve werkdruk neemt toe door gegevensverzameling, rapportage en het verwerken van grote hoeveelheden kwaliteitsinformatie. Het is daarom van belang wetenschappelijk degelijke methodes te gebruiken om de belangrijkste indicatoren te selecteren en zo de werklast en kosten van kwaliteitsbeoordeling zo beperkt mogelijk te houden.
In dit proefschrift is de ontwikkeling, validatie en selectie van voorschrijf-indicatoren voor diabeteszorg beschreven. De drie primaire doelen, hieronder beschreven, zijn gericht op de medicamenteuze behandeling van diabetes mellitus type 2.

- Het ontwikkelen van een alomvattende, valide en operationeel haalbare set van voorschrijf-indicatoren voor diabeteszorg.

- Het verbeteren van inzicht in de klinimetrische eigenschappen van voorschrijf-indicatoren voor T2DM-patiënten en cardiovasculair risicomanagement.

- Het opbouwen van kennis over het selecteren van relevante voorschrijf-indicatoren uit bestaande sets van indicatoren die in het publieke domein gebruikt kunnen worden.

In **Hoofdstuk 2** hebben we de ontwikkeling en validatie beschreven van voorschrijf-indicatoren voor hypertensie, hyperglycemie, dyslipidemie, behandelingen met trombocytenaggregatieremmers en de preventie van secundaire cardiovasculaire aandoeningen bij T2DM-patiënten in de ambulante setting. De indicatoren waren afkomstig van verschillende diabetesrichtlijnen en werden eerst besproken door een deskundigenpanel, daarna door een panel van praktijkdeskundigen. Van de 31 potentiële voorschrijf-indicatoren, gebaseerd op de belangrijkste aanbevelingen ten aanzien van de medicamenteuze behandeling van T2DM-patiënten, werden 18 indicatoren als voldoende valide beschouwd door de deskundigen. Daarvan bleven 14 indicatoren over nadat deze ook door de huisartsen en diabetologen in het veld waren beoordeeld.

Onze resultaten onderstrepen hoe belangrijk het is om wetenschappelijk bewijs met de mening van deskundigen en mensen in het veld te combineren. We zagen dat diabetologen en huisartsen onderling van mening verschilden over de aanbevelingen voor eerstekeusmiddelen in de richtlijnen. Aangezien het ons doel was om indicatoren te selecteren waar beide groepen het over eens waren, werden alleen die indicatoren in de definitieve selectie opgenomen. De definitieve set van indicatoren bestond uit voorschrijf-indicatoren die gericht zijn op alle vijf de gebieden van de medicamenteuze behandeling. Het grootste deel van de geselecteerde indicatoren is gestaafd met wetenschappelijk bewijs dat geclassificeerd is als klasse A. Zowel de indruks- als de inhoudsvaliditeit van de indicatoren gericht op dosering en veiligheid werden als onvoldoende beschouwd. Over deze indicatoren konden de experts het niet eens worden. De belangrijkste redenen voor onenigheid waren een gebrek aan wetenschappelijk bewijs om de indicator te ondersteunen, te weinig klinische patiëntengegevens die nodig zijn om zulke indicatoren te berekenen en het feit dat sommige indicatoren erg gevoelig waren voor casemix. De operationele validiteit van de meeste voorschrijf-indicatoren was goed: we konden 13 van de 14 indicatoren berekenen aan de hand van elektronische gezondheidsdossiers van T2DM-patiënten.

De noemers van sommige geformuleerde indicatoren konden geoperationaliseerd worden in onze database door middel van diagnostische codes of de klinische meetwaarde. In **hoofdstuk 3** namen we drie indicatoren uit onze set van indicatoren als voorbeeld en lieten zien dat kwaliteitsscores van voorschrijf-indicatoren niet noodzakelijkerwijs hoeven te veranderen bij een verschillende methode (diagnostische code of klinische meetwaarde) om de doelgroep te definiëren. De keuze voor een bepaalde methode beïnvloedt de indicatorscore echter wel als er informatiebias is door het bevorderen van registratie van diagnostische codes bij patiënten die de aanbevolen behandeling krijgen. Een dergelijke informatiebias kwam voor bij de indicator die het voorschrijven van antihypertensiva bij patiënten met hypertensie meet. Patiënten met een geregistreerde diagnostische code voor hypertensie kregen vaker antihypertensiva voorgeschreven dan patiënten zonder die code maar wel met een verhoogde bloeddruk. Een andere relevante bevinding was dat met behulp van de klinische meetwaardes er meer patiënten, konden worden geïdentificeerd die

niet de voor hen aanbevolen behandeling kregen, dan bij het gebruik van de diagnostische code. Bij het gebruik van diagnostische codes werden meer onderbehandelde patiënten gemist die hadden kunnen profiteren van de verbeterde behandeling dan bij gebruik van klinische meetwaarde.

In **hoofdstuk 4** beschreven we de resultaten van een systematische literatuurstudie om bestaande voorschrijf-indicatoren voor diabetes en cardiovasculair risicomanagement te identificeren en te classificeren. We classificeerden de verschillende soorten indicatoren en gaven een samenvatting van hun klinimetrische eigenschappen. We vonden meer dan 200 verschillende voorschrijf-indicatoren en groepeerden gelijksoortige indicatoren in 16 subtypes van eerste-keus behandeling, veiligheid, dosering, kosten en adequate en tijdige behandeling. We bepaalden de klinimetrische eigenschappen op dit subgroepniveau zoals beoordeeld en gedocumenteerd in de literatuur . Uiteindelijk kwamen we met een short-list van indicatoren die het meest valide werden bevonden. Deze indicatoren waren gebaseerd op bewijs van hoge kwaliteit en lieten goede klinimetrische eigenschappen zien in verschillende settings. Ze waren gericht op het voorschrijven van medicatie voor een specifieke indicatie, vooral (a) statines bij patiënten met een hoog cardiovasculair risico, (b) aspirine of trombocytenaggregatieremmers bij patiënten met een verhoogd cardiovasculair risico, (c) ACE-inhibitoren bij T2DM-patiënten met hypertensie en/of albuminurie, (d) bètablokkers bij patiënten met coronaire hartziekte of met in de voorgeschiedenis een myocardinfarct, (e) de behandeling van patiënten met een verhoogde HbA1c-waarde en (f) de behandeling van patiënten met een verhoogde bloeddruk.

In **hoofdstuk 5** beschreven we de voorkeuren voor specifieke voorschrijf-indicatoren in de diabeteszorg. We zagen dat de voorkeuren van belanghebbenden vooral te maken hebben met de doelstellingen die zij met de kwaliteitsmeting op het oog hebben, en die zijn verschillend voor de verschillende groepen. Alle belanghebbenden vonden de voorschrijf-indicatoren gericht op onderbehandeling relevant, maar verder hadden ze verschillende voorkeuren. Zorgverleners en beleidsmakers vonden de indicatoren gericht op medicatieveiligheid belangrijk, verzekeraars gaven de voorkeur aan voorschrijfkosten en patiëntenvertegenwoordigers waren meer gericht op de interpersoonlijke aspecten van het voorschrijven. Niet alleen is de voorkeur van belanghebbenden afhankelijk van het doel van de kwaliteitsmeting, maar ook van de mogelijkheid om invloed uit te oefenen op het aspect beschreven in de kwaliteitsindicator. De apothekers, bijvoorbeeld, gaven de voorkeur aan indicatoren gericht op medicatieveiligheid omdat ze direct kunnen bijdragen aan het verbeteren van de veiligheidsmaatregelen. Op dezelfde manier gaven de verzekeraars de voorkeur aan indicatoren gericht op kosten omdat hun doel kostenbeheersing is en ze hier ook actief aan kunnen bijdragen zoals bij het vergoeden van kosten. Het belangrijkste obstakel om voorschrijf-indicatoren te gebruiken bleek het gebrek aan gedocumenteerde informatie over redenen om af te wijken van aanbevolen richtlijnen. Zorgaanbieders noemden een aantal legitieme redenen om af te wijken van de aanbevolen richtlijnen – met als gevolg minder hoge waarden van

de voorschrijf-indicatoren – zoals de bijwerkingen van een medicijn of de individuele keuze van een patiënt. Patiëntvertegenwoordigers willen dat hun zorgaanbieders de behandeling baseren op de wensen van de individuele patiënt. Alle belanghebbenden gaven de voorkeur aan positieve formulering van voorschrijf-indicatorenscores om zorgverleners te stimuleren mee te doen aan kwaliteitsverbeteringprojecten. De belanghebbenden vonden samengestelde scores bruikbaar als beginpunt om de kwaliteit te beoordelen maar gaven uiteindelijk de voorkeur aan individuele scores voor zowel het verbeteren van de interne kwaliteit alsook voor het afleggen van externe verantwoording.

In **hoofdstuk 6** zijn de resultaten beschreven van een datareductietechniek om het aantal voorschrijf-indicatoren voor diabeteszorg te verminderen. We gebruikten een gemodificeerde versie van de set van indicatoren beschreven in **hoofdstuk 2** en onderzochten de relatie tussen de verschillende voorschrijf-indicatoren met behulp van factoranalyse. We identificeerden vijf dimensies van voorschrijf-kwaliteits in een dataset van 76 huisartsenpraktijken: twee dimensies beoordeelden de algemene farmacotherapie van verschillende risicofactoren met betrekking tot T2DM, twee beoordeelden de stapsgewijze intensivering van de behandeling van risicofactoren en een was gericht op de behandeling van diabetespatiënten bekend met een cardiovasculaire ziekte. Het is belangrijk om te benadrukken dat de verschillende dimensies eerder verschillende niveaus van therapie intensivering aangeven dan de afzonderlijke klinische risicofactoren. Binnen elk van de vijf dimensies kozen we de indicator met de hoogste factorlading om die dimensie weer te geven.. We vonden dat de samengestelde score uit deze vijf geselecteerde indicatoren op praktijkniveau grotendeels overeenkwam met de samengestelde score uit alle 10 oorspronkelijke indicatoren. Als we kijken naar de rangorde dan behield 82% van de praktijken dezelfde positie of verschoof hoogstens een kwintiel. Dit geeft aan dat de set van geselecteerde inidcatoren een goed beeld geven over de kwaliteit van de medicamenteuze behandeling van diabetes 2 per praktijk.

We zijn tot de conclusie gekomen dat voorschrijf-indicatoren noodzakelijk zijn voor de kwaliteitsbeoordeling van zorg aan T2DM-patiënten. Daar is een beknopte set van valide indicatoren voor nodig die op een betrouwbare manier gemeten kunnen worden. We hebben een set van voorschrijf-indicatoren ontwikkeld en getoetst die het gehele klinische gebied relevant voor diabetesmanagement behelst. Op basis van ons onderzoek adviseren we het gebruik van de 10 geselecteerde en gevalideerde voorschrijf-indicatoren (Tabel 1) die in huisartspraktijken gebruikt kunnen worden. Criteria om deze indicatoren te selecteren waren een goede indruks- en inhoudsvaliditeit, betrouwbaarheid en operationele uitvoerbaarheid (de definities van de indicatoren zijn operationeel en de data die nodig zijn om de indicatoren te berekenen zijn beschikbaar). Daarnaast richten alle 10 indicatoren zich op onderbehandeling en vertegenwoordigen zo de voorkeur van alle belanghebbenden.
De klinimetrische eigenschappen van de geselecteerde indicatoren zijn in verschillende landen

en door verschillende auteurs gevalideerd met goede beoordelingsresultaten. De uitgevoerde literatuurbespreking leverde niet meer valide indicatoren op.

Indien een verdere selectie uit deze set van indicatoren wordt gemaakt om een minimum set te formuleren, is het belangrijk dat indicatoren geselecteerd worden gericht op de verschillende fases van de behandeling, dat wil zeggen indicatoren gericht op het begin van de behandeling, het intensiveren van de behandeling en het beheer van T2DM-patiënten bekend met cardiovasculaire ziekte.

Als de geselecteerde indicatoren gebruikt worden voor externe kwaliteitsbeoordeling, dat wil zeggen voor het vergelijken van individuele zorgaanbieders, dan moet er rekening mee gehouden worden dat de eisen voor valide externe kwaliteitsbeoordeling, namelijk een voldoende steekproefgrootte per indicator, aanpassing voor casemix en longitudinale berekening, niet per se betrokken zijn bij de definitie van indicatoren. Daar moeten gebruikers steeds zelf rekening mee houden en zo nodig aanpassingen aanbrengen om ze geschikt te maken voor de eigen situatie. .

Tabel 1 Voorgestelde set van voorschrijf-indicatoren voor T2DM-management.

% van T2DM-patiënten met systolische bloeddruk ≥ 140 aan wie een antihypertensivum is voorgeschreven
% van T2DM-patiënten aan wie een tweede antihypertensivum is voorgeschreven uit een andere klasse als de systolische bloeddruk ≥ 140 bleef met eerste-keuze antihypertensivum
% van T2DM-patiënten met albuminurie aan wie een RAAS-inhibitor is voorgeschreven
% van T2DM-patiënten met een voorgeschiedenis van ischemische hartziekte of myocardinfarct en aan wie een bètablokker is voorgeschreven
% van niet-incidente T2DM-patiënten met een HbA1c-waarde van >7 % en aan wie een oraal antidiabeticum of insuline werd voorgeschreven
% van niet-incidente T2DM-patiënten die geen insuline gebruiken en aan wie een tweede oraal antidiabeticum werd voorgeschreven van een andere klasse als met een enkel oraal antidiabeticum de HbA1c-waarde >7 % bleef
% van T2DM-patiënten aan wie insuline werd voorgeschreven als in combinatie met twee orale medicijnen de HbA1c-waarde > 7% bleef
% van T2DM-patiënten met overgewicht die verschillende soorten medicatie gebruiken waaronder metformine
% T2DM-patiënten met LDL ≥ 2,5 of TC ≥ 4,5 aan wie een statine is voorgeschreven
% van T2DM-patiënten met een voorgeschiedenis van cardiovasculaire ziekte aan wie acetylsalicylzuur is voorgeschreven

T2DM: diabetes mellitus type 2; RAAS-inhibitor: renine-angiotensine-aldosterone systeem inhibitoren; HbA1c: glucosylated hemoglobine; LDL: lage dichtheid lipoproteine; TC: totaal cholesterol

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About the author

Liana Martirosyan (born 17 July, 1977 in Yerevan) has passed her secondary school exams at the Russian school # 150 in Yerevan, Armenia in 1993. In the same year she successfully passed the entry exams at the Yerevan State Medical University and started her medical studies at the faculty of preventive medicine. During the last three years of her medical studies Liana worked as a physician's assistant at the International Red Cross Rehabilitation Center in Yerevan assisting the treatment of patients after spinal cord injury, stroke and myocardial infarction. In 1999 she graduated from the Medical University with distinction diploma (cum laude) and afterwards completed the clinical residency program in medical microbiology at the National Institute of Armenia. During the years 2000-2005, Liana simultaneously worked as a doctor-microbiologist in one of the largest multiprofile hospitals in Yerevan (St. Grigory the Illuminator) and for the Center for High-risk Infections' Prevention in Armenia. During these years Liana was also teaching medical microbiology at Yerevan State Medical College #1. In 2003, next to her work as a doctor, Liana has entered a Master of Public Health Program at the American University of Armenia (affiliated with Johns Hopkins Bloomberg School of Public Health). In 2005 October she received her Masters Degree and in November moved to the Netherlands to work on the PhD thesis that resulted in this manuscript. Since February 2010 Liana works at the Netherlands Institute for Health Services Research (NIVEL) as a temporary adviser to WHO/European Region on an international project for influenza surveillance.

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