

## REVIEW

## A systematic literature review: prescribing indicators related to type 2 diabetes mellitus and cardiovascular risk management

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### SUMMARY

**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. Copyright © 2009 John Wiley & Sons, Ltd.

**KEY WORDS** — quality of care assessment; prescribing quality indicator; clinimetric properties; type 2 diabetes mellitus; cardiovascular risk management

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### 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.<sup>1–3</sup> 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.<sup>4,5</sup>

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.<sup>6</sup> 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.<sup>7</sup> Furthermore, there are indicators that link prescribing to clinical outcomes.<sup>8,9</sup>

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.<sup>10,11</sup>

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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.<sup>11</sup> 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.<sup>12,13</sup>

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 were 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 5121 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,<sup>8</sup> 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.

## 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).

Table 1. Definitions of clinimetric characteristics

Clinimetric characteristics	Definitions
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

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,<sup>4,5,14</sup> while others consisted of only PI.<sup>3,12,15–22</sup> In general, the assessment of various clinimetric characteristics of some indicator sets, e.g. ACOVE indicators, were described in several studies,<sup>23–25</sup> including adaptation of these indicators in different countries.<sup>26,27</sup> For sets of indicators that were updated several times, e.g. Beers' criteria and ACOVE indicators, we have included the latest version.<sup>25,28</sup>

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.<sup>29,30</sup> In six studies, authors reviewed randomized controlled trials to propose indicators.<sup>2,28,31–34</sup> In three studies a literature review was conducted to identify potential indicators.<sup>26,35,36</sup>

Face validity was addressed in 36 studies and assessed using different techniques including modified

Delphi,<sup>2,10,20,25–28,31,32,35–46</sup> nominal group,<sup>47,48</sup> focus group discussion,<sup>1,49</sup> surveys or panels of professionals,<sup>1,10,19,29,30,50–53</sup> continuous assessment of indicators using panels of various stakeholders,<sup>4,5,12,54</sup> or iterative process.<sup>55</sup>

Concurrent validity was assessed in four studies by comparing different data sources,<sup>24</sup> different PI,<sup>8,56</sup> and different data collection methods.<sup>57</sup> Medical records provided more detailed clinical information for quality assessment than administrative data, although scores for individual indicators did not change across sources.<sup>24</sup> 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.<sup>57</sup> Sequential quality indicators provided more accurate estimates of quality of care compared to cross-sectional measures.<sup>8,56</sup>

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.<sup>23</sup> Three studies used a composite score based on PI,<sup>22,58,69</sup> while others also included other process indicators. Some concluded that higher scores were associated with better-controlled risk factor levels<sup>31,59</sup> or better survival,<sup>23</sup> while others found at most weak associations.<sup>14,22,58</sup>

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
Ackermann <i>et al.</i> <sup>14</sup>	Studies published in peer-reviewed journals identified through the main search strategy 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 <i>et al.</i> <sup>15</sup>	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 <i>et al.</i> <sup>16</sup>	To determine prescribing indicators which were used by primary care groups under prescribing incentive schemes	UK	E	amb	-	-	-	-	-	-	+	-	-
Basger <i>et al.</i> <sup>18</sup>	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 <i>et al.</i> <sup>50</sup>	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 <i>et al.</i> <sup>32</sup>	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 <i>et al.</i> <sup>10</sup>	To assess face validity of quality indicators being used or proposed for use in general practice by health authorities	UK	N/A	amb	-	+	-	-	-	-	+	-	-
Campbell <i>et al.</i> <sup>33</sup>	To develop review criteria to assess the quality of care for adult asthma, stable angina, and non-insulin dependant diabetes mellitus	UK	I	amb	+	+	+	-	-	-	-	-	-
Campbell <i>et al.</i> <sup>51</sup>	To field test the reliability, validity and acceptability of review criteria for angina, asthma, and type 2 diabetes mellitus	UK	N/A	amb	-	+	-	-	-	+	+	+	-
Campbell <i>et al.</i> <sup>39</sup>	To develop common quality standards for cardiovascular prevention and risk management across Europe	UK	I	amb	+	+	+	-	-	-	-	-	-
Cheng <i>et al.</i> <sup>36</sup>	To propose quality indicators that could be applied when treating vulnerable elders for stroke	US	N/A	both	-	+	+	-	-	-	-	-	-
DiSalvo <i>et al.</i> <sup>52</sup>	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 <i>et al.</i> <sup>19</sup>	To develop a set of indicators of prescribing quality for elderly inpatients in Australian hospitals	Aust	I	hosp	+	+	+	-	-	+	+	-	-
Fick <i>et al.</i> <sup>28</sup>	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 <i>et al.</i> <sup>47</sup>	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 <i>et al.</i> <sup>61</sup>	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 <i>et al.</i> <sup>60</sup>	To study the applicability of secondary care prescribing indicators to primary care and measure prescribing quality	UK	both	amb	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Hutchinson <i>et al.</i> <sup>29</sup>	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	+	+	+	-	-	-	-	-	-	-	-	-	-	-
Idanpaan-Heikkila <i>et al.</i> <sup>35</sup>	To develop a set of quality indicators for cardiac care	Fin	E	both	+	+	+	-	-	-	-	-	-	-	-	-	-	-
Jencks <i>et al.</i> <sup>68</sup>	To create a monitoring system for a range of measures of clinical performance that supports quality improvement	US	E	both	-	-	-	-	-	+	+	-	-	-	-	-	-	-
Katz <i>et al.</i> <sup>49</sup>	To explore the feasibility of using administrative data to develop process indicators for measuring quality in primary care	Can	I	amb	+	+	+	-	-	-	+	-	-	-	-	-	-	+
Kerr <i>et al.</i> <sup>8</sup>	To determine the relative accuracy of quality assessment in diabetes using simple intermediate outcome versus tightly linked quality measures	US	N/A	amb	-	-	-	+	-	-	+	-	-	-	-	-	-	-
MacKinnon <i>et al.</i> <sup>40</sup>	To develop a set of Canadian clinical indicators of preventable drug-related and care-related morbidity for type 2 diabetes	Can	I	amb	+	+	+	-	-	-	-	-	-	-	-	-	-	-
Majumdar <i>et al.</i> <sup>41</sup>	To rigorously develop and validate a set of quality indicators for type 2 diabetes mellitus for researchers or decision-makers	Can	both	amb	+	+	+	-	-	-	-	-	-	-	-	-	-	-
Martirosyan <i>et al.</i> <sup>20</sup>	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 <i>et al.</i> <sup>34</sup>	To suggest performance indicators that could monitor use of important primary care interventions	UK	E	amb	+	-	+	-	-	-	-	-	-	-	-	-	-	-
McColl <i>et al.</i> <sup>62</sup>	To test the feasibility of deriving comparative indicators in all practices within a primary care group	UK	E	amb	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Mehta <i>et al.</i> <sup>64</sup>	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	-	-	-	-	-	-	+	-	-	-	-	-	-	+
Milchak <i>et al.</i> <sup>48</sup>	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 <i>et al.</i> <sup>42</sup>	To propose a new set of quality indicators for the care of hypertension in vulnerable elders	US	N/A	both	-	+	+	-	-	-	-	-	-	-	-	-	-	-

(Continues)

Table 2. (Continued)

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
Muijters <i>et al.</i> <sup>43</sup>	To formulate and validate clinical prescribing indicators based on general practice guidelines	NL	I	amb	+	+	+	+	+	+	+	+	+
Oborne <i>et al.</i> <sup>21</sup>	To modify prescribing indicators, including appropriateness of prescribing algorithms developed in the hospital setting, for use in nursing homes	UK	I	amb	-	-	-	-	-	+	+	+	-
O'Brien <i>et al.</i> <sup>65</sup>	To examine the association between hospital sample sizes and observed performance on individual process-of-care measures	US	E	hosp	-	-	-	-	-	-	+	+	-
Persell <i>et al.</i> <sup>57</sup>	To evaluate the validity of performance measures for coronary artery disease using an ambulatory electronic health records	US	E	amb	-	-	+	+	-	+	+	-	-
Peterson <i>et al.</i> <sup>22</sup>	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 <i>et al.</i> <sup>3</sup>	To develop indicators based on prescription analysis in order to assess adherence to guidelines and monitor prescribing behavior	Germ	I	amb	+	-	-	-	-	-	+	+	-
Shekelle <i>et al.</i> <sup>44</sup>	To develop quality indicators for diabetes mellitus care in vulnerable elderly population	US	I	both	+	+	+	-	-	-	-	-	-
Solberg <i>et al.</i> <sup>55</sup>	To develop and test ambulatory care quality measures obtainable from administrative data	US	N/A	amb	+	+	-	-	-	-	+	+	+
Torreçilla-Rojas <i>et al.</i> <sup>59</sup>	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 <i>et al.</i> <sup>45</sup>	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 <i>et al.</i> <sup>27</sup>	To adapt a set of systematically developed US quality indicators for health care of vulnerable elders in the Netherlands	NL	I	amb	+	+	+	-	-	-	-	-	-
Voorham <i>et al.</i> <sup>56</sup>	To compare cross-sectional and sequential quality indicators for risk factor management in patients with type 2 diabetes	NL	both	amb	-	-	+	-	-	-	+	-	-
Wenger <i>et al.</i> <sup>25</sup>	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 <i>et al.</i> <sup>30</sup>	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	+	+	+	-	-	-	-	-	-

Author	Objective	Country	Setting	Developments	Face validity	Content validity	Concurrent validity	Predictive validity	Reliability	Operational feasibility	Sample size	Case-mix
Werner <i>et al.</i> <sup>58</sup>	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 <i>et al.</i> <sup>63</sup>	To investigate reactions to the use of evidence-based cardiovascular and stroke performance indicators within one primary care group	UK	I amb	-	-	-	-	-	-	+	-	-
<i>studies published in peer-reviewed journals identified through additional search</i>												
Asch <i>et al.</i> <sup>31</sup>	To develop and test a quality measurement system for women with hypertension	US	N/A amb	+	+	+	-	+	-	+	-	-
Asch <i>et al.</i> <sup>37</sup>	To examine the relationship between patients' characteristics and several domains of quality of care	US	N/A both	+	+	+	-	-	+	+	-	+
Higashi <i>et al.</i> <sup>23</sup>	To examine the link between quality of care that patients received and their survival	US	I both	-	-	-	-	+	+	+	-	-
MacLean <i>et al.</i> <sup>24</sup>	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 <i>et al.</i> <sup>9</sup>	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 <i>et al.</i> <sup>26</sup>	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	+	+	+	-	-	-	-	-	-
Aust-NPS <sup>1</sup>	To improve Australian health outcomes through the quality use of medicines	Aust	I amb	+	+	+	-	-	+	+	+	-
Dutch-CBO <sup>53</sup>	To develop quality indicators on efficacy and safety of diabetes care for external use	NL	E amb	+	+	+	-	-	+	+	-	+
NCQA-HEDIS <sup>4</sup>	To reliably compare the performance of health plans	US	E both	+	+	+	-	-	+	+	+	+
NHS-PING <sup>12</sup>	To produce and review sets of prescribing indicators issued by the Department of Health in the UK	UK	both amb	+	+	+	-	-	-	+	-	-
NHS-QOF <sup>5</sup>	To improve quality of care through a incentive scheme rewarding GP practices for how well they care for patients	UK	E amb	+	+	+	-	-	-	+	-	+
NQF <sup>54</sup>	To improve the quality of American healthcare by setting national priorities and goals for performance improvement	US	both amb	+	+	+	-	-	+	+	+	+
RAND Health <sup>46</sup>	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												
				37	36	37	4	6	13	40	13	9

+ Characteristic was addressed in the study; - characteristic was not addressed in the study.  
 \*Aust, Australia; Be, Belgium; Can, Canada; Germ, Germany; Fin, Finland; NZ, New Zealand; 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.

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

Drug-oriented PI	Face validity	Content validity	Reliability	Operational feasibility
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). <sup>3,16,43,47,50,59</sup>	+	+		+
% First choice drug class (e.g., biguanides) of all oral antidiabetic drugs. <sup>16,59</sup>	~	+		+
Patients on preferred drug classes (e.g., diuretics or $\beta$ -blockers) of all antihypertensives. <sup>47,59</sup>	+	+		+
Ratio of preferred: less preferred drugs (e.g., plain:combination diuretics) <sup>10</sup>	~			+
Number of prescriptions for (preferred) drugs per PU (or ASTRO-PU) <sup>10</sup>	~			+
Second step drugs				
Patients prescribed ARB and prior to this an ACE inhibitor of all patients prescribed ARBs. <sup>43</sup>	+	+		+
Non-first-choice or not preferred drugs				
Patients on long acting isosorbide nitrate, glibenclamide, combinations of diuretics or $\alpha$ -glucosidase inhibitor, etc. <sup>16,26,59</sup>	+	+		+
Dose/1000persons/day of lipid lowering drugs in elderly. <sup>47</sup>	+	+		
Patients on novelty drugs, such as ARBs or thiazolidinediones, of all patients receiving antihypertensives or oral glucose-lowering drugs. <sup>47,59</sup>	+	+		+
$\leq 0.6$ prescriptions/100 Pus for drugs with limited indications (e.g. cerebral and peripheral vasodilators) <sup>50</sup>	~	+		+
Safety indicators				
Drugs to be avoided (in elderly) (e.g., chlorpropamide, long acting sulphonylurea, short-acting nifedipine). <sup>4,15,19,21,23–28,52,60</sup>	+	+	+	~
Co-prescriptions to be avoided, e.g. of statins with macrolides, diuretic, ACE-inhibitor with potassium or NSAID, metformin with glibenclamide, etc. <sup>1,3,18,19</sup>	+	+	+	+
Correct dosing of drugs (under/overdosing and number of daily dosings)				
Prescription of high dose hydrochlorothiazide <sup>52</sup> prescription of low dose bendrofluazide <sup>16</sup>	+	+	+	+
Once- or twice- daily dosing of antihypertensives in elderly. <sup>23–27</sup>	+	+	+	+
Redundant prescribing				
patients prescribed more than 1 drug from the same therapeutic group simultaneously (e.g. thiazides) <sup>19,47</sup>	+	+	+	-
Cost-conscious prescribing or limited set of drugs prescribed				
Cost of treatment per unit. <sup>16,47</sup>	+	+		+
% Prescribed generic drugs. <sup>3</sup>				+
Change amlodipine to felodipine. <sup>16</sup>				+
Number of different brands with the same active substance <sup>3</sup> DU90% within a specific drug class. <sup>43</sup>	~	~		+

+ 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.

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.<sup>4,10,12,16,19,45,53,55</sup> 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.<sup>9,17,20,21,49,50,52,60–63</sup> Implicit assessment of operational feasibility occurred in all other studies when PI were calculated during assessment of other clinimetric characteristics, e.g. reliability or concurrent validity.<sup>3,8,14,15,22–24,31,34,37,43,51,56–59,64–67,68</sup>

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.<sup>9,21–24,37,49,51,57</sup> In some cases reliability was assessed theoretically during the indicator development process.<sup>4,17,53,54</sup>

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.<sup>14,16,22,34,50,57,62,65</sup> Two studies showed the influence of case-mix on performance scores.<sup>37,64</sup> Several approaches were proposed to minimize the effect of patient clinical or sociodemographic characteristics on PI outcomes, including statistical adjustment,<sup>4,37</sup> exclusion of indicators that are too much affected by such characteristics,<sup>53,55</sup> or exclusion of patients for reasons like contraindications, perceived side-effects,

or refusing medication.<sup>5,25</sup> Another approach to deal with case-mix was setting lower target levels.<sup>69</sup>

Sample size was addressed in 13 studies. Two studies showed that sample size can affect performance scores and hinder comparisons between individual providers.<sup>64,65</sup> Suggested solutions were exclusion of indicators or providers with small numbers,<sup>51,55,58,65</sup> use of hierarchical estimates,<sup>65</sup> or pooling data from several providers or time periods.<sup>1</sup> The minimal sample size suggested per indicator ranged from 5–10<sup>49</sup> to 30–60 patients.<sup>1</sup> Others suggested to include only providers with a certain number of patients,<sup>3,25,52</sup> but did not support this with calculations. A paper related to measures proposed by the National Quality Forum<sup>70</sup> 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 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.<sup>10,50</sup>

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.<sup>15,19</sup> Since in specific cases there can be good reasons to use 'inappropriate'

drugs, these indicators were recommended for internal use to identify potential problems.<sup>19</sup> 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 PI because of the absence of eligible patients or lack of information on duration of prescriptions.<sup>19,60</sup>

Indicators focusing on cost were seldom assessed for face and content validity<sup>47</sup> or doubts were raised for their relation to quality.<sup>43</sup> 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.<sup>43</sup>

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.<sup>41,53</sup> 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 contra-indications to the recommended treatment from the indicator. Several of such PI with exclusion criteria, however, lacked face or content validity across different 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.<sup>25–27</sup> Furthermore, the operational feasibility of such indicators was found to be hampered in one study

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
Patients prescribed drugs for a specific indication				
Prescribed statins (or lipid lowering drugs):				
In patients with high cardiovascular risk or CVD <sup>1,3,12,16,18,20,30,35,39,47,54,55,61</sup>	+	+	+	+
In diabetic patients or treated with glucose lowering medication <sup>40,41,43</sup>				
Prescribed (a specific type of) glucose lowering treatment <sup>41,53</sup>	~	~		+
Prescribed daily aspirin (or antiplatelet drug or anticoagulants) in:				
Diabetic patients or treated with glucose lowering medication (and additional cardiac factor) <sup>14,26,40,41,44,47,54</sup>	+	+	+	+
Patients with history of CVD or high cardiovascular risk <sup>1,12,14,16,19,20,26,30,34,41,47,54,61-63</sup>				
Prescribed any antihypertensive treatment				
In patients with stroke <sup>26</sup>	+	+	+	+
In (elderly) patients with diabetes and hypertension or albuminuria <sup>41,53</sup>				
Prescribed ACE inhibitor (or ARB) of:				
In patients with CHD or history of MI <sup>5</sup>	+	+	+	+
T2DM patients <sup>40</sup>				
T2DM patients with hypertension and/or microalbuminuria or (macro)albuminuria <sup>1,5,12,18,20,26,33,41,44,47,51,53,61</sup>				
Prescribed $\beta$ -blockers to (diabetic) patients with MI or CHD <sup>4,16,18,20,26,30,42,47,54</sup>	+	+	+	+
T2DM or high cardiovascular risk patients received influenza immunization <sup>5,39,54,55</sup>	+	+	+	+
Appropriate treatment for patients with diabetes or CVD or hypertension or cardiovascular risk <sup>1,30,48,52</sup>	+	+	+	+
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 <sup>5,7</sup>	~	~	+	~
In elderly patients with IHD <sup>23-25</sup>				
Hypertension and kidney disease <sup>5</sup>				
(Elderly patients) with diabetes and microalbuminuria or proteinuria <sup>23-27,30</sup>				
(Elderly) patients with CHD (and diabetes or elevated LDL) prescribed lipid lowering drugs unless contraindicated <sup>23-25,57</sup>	+	+	+	~
Prescribed antiplatelet drug in patients with diabetes or CVD unless contraindicated or already on other anticoagulants <sup>5,18,23-27,29,32,37,39,46,57,60</sup>	~	~	+	~
Prescribed aspirin in elderly T2DM patients unless on other anticoagulants <sup>23-27</sup>	~	~		+
Prescribed $\beta$ -blockers in patients with coronary disease and/or MI (and hypertension) unless contraindicated <sup>5,23-25,27,29,32,35,39,57</sup>	+	+	+	~
% of eligible T2DM patients who received influenza immunization or refused immunization <sup>54</sup>	+	+	+	+
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 <sup>26,33,34,44,47,53,62,63,67</sup>	+	+	+	+
HbA1c above specified level (age dependent) <sup>20,33,51,67</sup>				
BP above specified level, average of 2 readings, last 3 readings above (age dependent) level <sup>20,31-33,37,39,46,53,67</sup>				
First-choice drug in patients with specific condition				
Prescribed first choice drug (e.g. metformin or first-choice antihypertensive) in (overweight) diabetic patients <sup>20,31,37,41,46,47</sup>	+	+	+	+
Drugs to be avoided in patients with specific conditions				
Glyburide to be avoided in elderly diabetic patients <sup>40</sup>	+	+		+
Thiazolidinediones to be avoided in diabetic patients with heart failure <sup>40</sup>				
Patients older than 75 years prescribed lipid lowering drugs for primary prevention <sup>3</sup>				

+ 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.

using automated data collection methods, because information on contraindications entered as text data in medical records was missed.<sup>57</sup>

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.<sup>33,51</sup>

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.<sup>53</sup> 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, and (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.<sup>8,9</sup> Similar to the cross-sectional indicators, sequential indicators incorporated exclusions to deal with patients that have contra-indications 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.<sup>25,27</sup> Treatment modification indicators have shown concurrent validity,<sup>8,56</sup> 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.<sup>52</sup>

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.

## 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,<sup>19</sup> can be adjusted for use in primary care.<sup>60</sup>

### *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.<sup>26,27</sup> 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.<sup>8,56</sup>

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
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 <sup>9,32,37,46,56,67</sup>	+	+	+	+	+
Uncontrolled/above goal BP level -dependent of other risk factors e.g. diabetes- (and no return to control within 3–6 months) <sup>9,20,32,42,44,48,56</sup>					
Failed dietary/lifestyle modification (start oral glucose lowering or antihypertensive treatment) <sup>26,30,31,37,46</sup>					
Elevated HbA1c or fasting glucose level <sup>9,44,64,68</sup>					
Failed oral glucose lowering treatment (and no return to control within 3–6 months) <sup>20,30,37,40,46</sup>					
With history of CVD or high cardiovascular risk (antiplatelet or anticoagulant) <sup>36</sup>					
Pharmacologic or lifestyle intervention offered to elderly with diabetes and fasting LDL > 130 mg/dL (within 3 months) <sup>25,27</sup>	~	~		+	+
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) <sup>8,18,23–27,37,39,42,46</sup>	+	+	+	+	+
Patients with diabetes and proteinuria or patients with hypertension prescribed ACE inhibitor (or ARB) within 3 months unless contraindicated <sup>37,46</sup>	+	+		+	+
Start first choice treatment in specific patients					
Metformin in overweight incident diabetic patients <sup>20</sup>	+	+			+
ACE-inhibitor or ARB in incident hypertensive diabetic patients with albuminuria <sup>20</sup>					
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) <sup>4,22,35,45,49,52,58,64,65,68</sup>	+	+		+	~

+ 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.

No information is yet available on the predictive validity of individual PI. 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.<sup>8,57</sup> 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.<sup>64,71</sup> One should keep in mind, however, that medical records may not reflect all processes of care.<sup>72</sup> 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.<sup>15,50</sup> 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.<sup>60</sup> 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.<sup>43</sup> Disease-oriented PI can be calculated from administrative datasets and EHR.<sup>24,49,62</sup> Sequential disease-oriented

PI can be calculated from EHR.<sup>8,56</sup> 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.<sup>38</sup>

#### *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.<sup>70</sup>

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.<sup>69</sup> On the other hand, it has been recommended to stratify performance measurement by gender, since this allows to detect specific areas for improvement.<sup>73</sup> 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 PI.

## CONCLUSIONS AND IMPLICATIONS

We identified a large variety of PI 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 cannot 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.

## KEY POINTS

- A large variety of prescribing quality indicators exist that cover the important areas of prescribing for type 2 diabetes mellitus and cardiovascular risk management.
- Many drug and disease-oriented prescribing indicators are valid for internal quality assessment, since they have repeatedly shown face and content validity as well as operational feasibility.
- Prescribing indicators focusing on treatment modification in response to elevated risk factor levels seem more accurate measures of provided quality than commonly used cross-sectional indicators.
- Case-mix and sample size problems are insufficiently addressed, which limits valid application in external quality assessment.
- Predictive validity of individual prescribing indicators is not yet known.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## APPENDIX 1: DESCRIPTION OF THE 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 the time period from 1990 to January 2009.