**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Title**: Adherence to Oral Diabetes Agents for Individuals with Diabetes Mellitus

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Not applicable

**Date of Submission**: 1/31/2014

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| **Instructions**  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Maximum of 10 pages (*includes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.*** * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

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| **Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**  **Subcriterion 1a.** **Evidence to Support the Measure Focus**  The measure focus is a health outcome or is evidence-based, demonstrated as follows:   * Health outcome:[**3**](#Note3) a rationale supports the relationship of the health outcome to processes or structures of care. * Intermediate clinical outcome, Process,[**4**](#Note4) or Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence[**5**](#Note5)that the measure focus leads to a desired health outcome. * Patient experience with care: evidence that the measured aspects of care are those valued by patients and for which the patient is the best and/or only source of information OR that patient experience with care is correlated with desired outcomes. * Efficiency:[**6**](#Note6) evidence for the quality component as noted above.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement.  **5.** The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm) and [methods](http://www.uspreventiveservicestaskforce.org/methods.htm), or Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org/publications/index.htm).  **6.** Measures of efficiency combine the concepts of resource use and quality (NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**:

Outcome

☐ Health outcome: Click here to name the health outcome

*Health outcome includes patient-reported outcomes (PRO, i.e., HRQoL/functional status, symptom/burden, experience with care, health-related behaviors)*

X Process: Adherence to chronic medications

☐ Structure: **Click here to name the structure**

☐ Other: Click here to name what is being measured

**HEALTH OUTCOME PERFORMANCE MEASURE** *If not a health outcome, skip to* [*1a.3*](#Section1a3)

**1a.2.** **Briefly state or diagram the linkage between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.**

**1a.2.1.** **State the rationale supporting the relationship between the health outcome (or PRO) and at least one healthcare structure, process, intervention, or service**.

*Note: For health outcome performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

**intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measure**

**1a.3.****Briefly state or diagram the linkages between structure, process, intermediate outcome, and health outcomes**. **Include all the steps between the measure focus and the health outcome.**

The measure focus is on adherence to oral diabetes agents among patients with diabetes mellitus.[[1]](#footnote-1) Good adherence, defined as a PDC of 0.8 or higher, to oral diabetes agents is expected to lead to a reduction in adverse patient outcomes and other outcomes as follows:

Links of Process 🡪 Health Outcome

Improved communication and education regarding adherence to oral diabetes agents 🡪

Higher rates of good adherence to oral diabetes agents among persons with diabetes 🡪

Lower rates of hyperglycemia 🡪

Fewer microvascular and macrovascular complications due to hyperglycemia 🡪

Lower hospitalization rates, lower healthcare costs, and lower mortality rates

Summary

The desired outcomes for this measure are better adherence to oral diabetes agents among individuals with diabetes mellitus. Better adherence should result in a higher likelihood of glycemic control, resulting in fewer cardiovascular events and thus, fewer hospitalizations, lower costs, and fewer deaths.

**1a.3.1.** **What is the source of the systematic review of the body of evidence that supports the performance measure?**

X Clinical Practice Guideline recommendation – ***complete sections*** [***1a.4***](#Section1a4)***, and*** [***1a.7***](#Section1a7)

☐ US Preventive Services Task Force Recommendation – ***complete sections*** [***1a.5***](#Section1a5) ***and*** [***1a.7***](#Section1a7)

☐ Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)

X Other – ***complete section*** [***1a.8***](#Section1a8)

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** **Guideline citation** (*including date*) and **URL for guideline** (*if available online*):

American Diabetes Association (ADA). (2013). Standards of Medical Care in Diabetes—2013. *Diabetes Care, 36*(Supplement 1), S11-S66.

<http://care.diabetesjournals.org/content/36/Supplement_1/S11.full>

**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

The measure is supported by recommendations in the American Diabetes Association’s "Standards of Medical Care in Diabetes—2013" ([American Diabetes Association, 2013](#_ENREF_1)). Although the guidelines do not address the topic of medication adherence directly, recommendations regarding the use of a medication imply that the patient is taking the medication regularly.

**2013 American Diabetes Association guideline recommendations concerning the "Pharmacological therapy for hyperglycemia in type 2 diabetes":**

(page S22) Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes. (A)

(page S22) If noninsulin monotherapy at maximal tolerated dose does not achieve or maintain the A1C target over 3–6 months, add a second oral agent, a glucagon-like peptide-1 (GLP-1) receptor agonist, or insulin. (A)

**1a.4.3.** **Grade assigned to the quoted recommendation with definition of the grade:**

For the two recommendations quoted in 1a.4.2 from the "Standards of Medical Care in Diabetes--2013" by the American Diabetes Association (American Diabetes Association, 2013), the level of evidence is defined as follows:

A level of evidence of "A" for the ADA recommendations is defined as:

* Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:
  + Evidence from a well-conducted multicenter trial
  + Evidence from a meta-analysis that incorporated quality ratings in the analysis
* Compelling nonexperimental evidence, i.e., “all or none” rule developed by the Centre for Evidence-Based Medicine at the University of Oxford
* Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:
  + Evidence from a well-conducted trial at one or more institutions
  + Evidence from a meta-analysis that incorporated quality ratings in the analysis

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

For each recommendation in the "Standards of Medical Care in Diabetes--2013" by the American Diabetes Association (American Diabetes Association, 2013), the level of evidence is defined as follows:

A level of evidence of "A" for the ADA recommendations is defined as:

* Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:
  + Evidence from a well-conducted multicenter trial
  + Evidence from a meta-analysis that incorporated quality ratings in the analysis
* Compelling nonexperimental evidence, i.e., “all or none” rule developed by the Centre for Evidence-Based Medicine at the University of Oxford
* Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:
  + Evidence from a well-conducted trial at one or more institutions
  + Evidence from a meta-analysis that incorporated quality ratings in the analysis

A level of evidence of “B” for the ADA recommendations is defined as:

* Supportive evidence from well-conducted cohort studies
  + Evidence from a well-conducted prospective cohort study or registry
  + Evidence from a well-conducted meta-analysis of cohort studies
* Supportive evidence from a well-conducted case-control study

A level of evidence of “C” for the ADA recommendations is defined as:

* Supportive evidence from poorly controlled or uncontrolled studies
  + Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
  + Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)
  + Evidence from case series or case reports
* Conflicting evidence with the weight of evidence supporting the recommendation

A level of evidence of "E" for the ADA recommendations is defined as:

* Expert consensus or clinical experience

**1a.4.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.4.1*)**:**

The "Standards of Medical Care in Diabetes-2013" by the American Diabetes Association (American Diabetes Association, 2013) used rigorous methods to develop and maintain the recommendations and supporting evidence. The citation and URL for the methodology for grading recommendations (American Diabetes Association, 2013) are listed in Section 1a.4.1., above.

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

XYes **→ *complete section*** [***1a.7***](#Section1a7)

☐No **→ *report on another systematic review of the evidence in sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)***; if another review does not exist, provide what is known from the guideline review of evidence in*** [***1a.7***](#Section1a7)

**1a.5.** **UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1.** **Recommendation citation** (*including date*) and **URL for recommendation** (*if available online*):

**1a.5.2.** **Identify recommendation number and/or page number** and **quote verbatim, the specific recommendation**.

**1a.5.3.** **Grade assigned to the quoted recommendation with definition of the grade**:

**1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: the* *grading system for the evidence should be reported in section 1a.7.*)

**1a.5.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.5.1*)**:**

**1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** **Citation** (*including date*) and **URL** (*if available online*):

**1a.6.2.** **Citation and** **URL for methodology for evidence review and grading** (*if different from 1a.6.1*)**:**

**1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE supporting the measure**

**1a.7.1.** **What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?**

For the "Standards of Medical Care in Diabetes--2013" (American Diabetes Association, 2013), members of the ADA’s multidisciplinary Professional Practice Committee conducted a systematic search for studies related to the guideline section addressed by this measure: "Pharmacological therapy for hyperglycemia in type 2 diabetes." The evidence is summarized in the 2013 guidelines.

Although the guidelines provide a review of the evidence supporting the recommendations listed in Section 1a.4.2, the studies included in the summary of the evidence focused on narrowly defined questions, which do not align with the focus of the measure. Therefore, an empirical search of evidence was conducted by the measure developer to find literature that addressed the relationship between adherence to oral diabetes agents and patient outcomes and/or resource utilization. Based on the studies found from the empirical search, the measure developer evaluated the quantity and quality of evidence and reported the findings in Sections 1a.8.1 and 1a.8.2.

**1a.7.2.** **Grade assigned for the quality of the quoted evidence with definition of the grade**:

Please see Sections 1a.4.2 and 1a.4.3.

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.**

Please see Section 1a.4.4.

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: Click here to enter date range

**QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5.****How many and what type of study designs are included in the body of evidence**? (*e.g., 3 randomized controlled trials and 1 observational study*)

**1a.7.6.** **What is the overall quality of evidence across studies in the body of evidence**? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

**ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7.** **What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence**? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

**1a.7.8.** **What harms were studied and how do they affect the net benefit (benefits over harms)?**

**UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9.** **If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review**.

**1a.8 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

In this section, we summarize the findings of six recent studies on the relationship between adherence of patients with diabetes to oral diabetes agents and patient outcomes and resource use.

**1a.8.1** **What process was used to identify the evidence?**

Six studies were identified using hand searches of reference lists of relevant clinical practice guidelines and other relevant articles and Web of Science citation searches of key articles. The abstracts and/or full-text articles from both types of searches were reviewed to identify those studies that addressed the relationship between adherence to oral diabetes agents among patients with diabetes mellitus and patient outcomes and/or resource utilization. The six selected studies met the following criteria: the study measured adherence to oral diabetes agents among patients with diabetes mellitus; the study reported patient outcomes, hospitalization rates, and/or resource use in subgroups defined by adherence levels; and the study was published in the last 10 years.

**1a.8.2.** **Provide the citation and summary for each piece of evidence.**

Consistency and Magnitude of Evidence

Concerning the six studies designed to address outcomes, the magnitude and direction of the association between good adherence with a variety of outcomes were highly consistent across studies reported in the recent peer-reviewed literature. Below we first summarize the consistency of the results for the various outcomes, and then we present the specific results for each study.

Several outcomes were measured in six studies of adherence to oral diabetes agents. Good persistence to OHA (oral hypoglycemia agents) was associated with achieving goal hemoglobin A1c levels (RR 1.07, 95% CI 1.06-1.09) ([Kim et al., 2010](#_ENREF_31)), and a 10% increase in a continuous measure of medication gaps (CMG) for metformin was significantly associated with an increase of 0.14% in HbA1c ([Pladevall et al., 2004](#_ENREF_38)). In another study, rates of work-related absenteeism were reported to be 8.8% lower among those adherent to oral antidiabetic medications ([Carls et al., 2012](#_ENREF_5)). Three studies reported results related to the risk of all-cause hospitalization. The risk was lower among patients with diabetes who were adherent to OHA: OR 0.71 (95% CI 0.51-0.98), p=0.0375) ([Colombi et al., 2008](#_ENREF_17)); or higher among those who were nonadherent to OHA: OR 1.38 (95% CI 1.21-1.58) ([Ho et al., 2006](#_ENREF_27)), and OR 1.21 (95% CI 1.13-1.31) ([Hong & Kang, 2011](#_ENREF_29)). The risk of diabetes, cardiovascular disease, or renal disease hospitalization and all-cause mortality were higher among patients with diabetes who were nonadherent to OHA: OR 1.26 (95% CI 1.08-1.47), and OR 1.40 (95% CI 1.01-1.95), respectively ([Hong & Kang, 2011](#_ENREF_29)).

Detailed Results of Studies

[Carls et al. (2012](#_ENREF_5)): In this retrospective cross-sectional study of employees from medium and large employers in the United States (mean age of 49 years), those with diabetes who were adherent to oral antidiabetic medications experienced fewer days of absenteeism and short-term disability. Administrative claims data from 2004 to 2008 were used to identify patients with various chronic conditions including diabetes, based on having at least one visit where diabetes was listed as a diagnosis. For diabetes, the index prescription was defined as the earliest oral antidiabetic medication and employees were only included if they had at least one fill of the prescription. Adherence was measured as the percent of days covered (percentage of days with the relevant medication on hand during the 12-month follow-up period after the index prescription). Employees were considered to be adherent if medication was available for 80% or more of the days. There were 7,817 and 22,404 employees with diabetes who were eligible for the absenteeism and short-term disability cohorts, respectively. Adherent employees with diabetes had 2.9 fewer days absent from work than nonadherent employees with diabetes (29.0 vs. 31.9 days, p<0.001). Adherent employees with diabetes also had 2.1 fewer days of short-term disability compared to nonadherent patients with diabetes (4.9 vs. 7.0 days, p<0.001). In the multivariate model, adherence to oral antidiabetic medications was associated with absenteeism rates that were 8.8% lower than nonadherence (relative risk of 0.912 comparing adherence to nonadherence).

[Colombi et al. (2008](#_ENREF_17)): In this retrospective observational study of 2,052 patients with diabetes (mean age of 66 years), lower adherence to oral diabetes medications was associated with higher risk of all-cause hospitalization. Medical and pharmacy claims data from PPG Industries’ employees, retirees, and dependents with type 2 diabetes were obtained covering the years 2003 to 2005. The index prescription was the first prescription fill for an oral diabetes medication during the period, and patients were followed up a year before and after the index date. Adherence to medication was defined as an MPR of 80% or more during the year following the index date. The risk of all-cause hospitalization was lower in those who were adherent compared with those who were not in both of the age groups: those <65 years of age (OR 0.75 [95% CI 0.51-1.10], p=0.1435) and those ≥65 years (OR 0.71 [95% CI 0.51-0.98], p=0.0375).

[Ho et al. (2006](#_ENREF_27)): In this retrospective cohort study of 11,532 patients with diabetes mellitus being seen in a managed care organization (mean age 62-66 years), medication nonadherence for antihypertensives, statins and oral hypoglycemic agents was found to be associated with adverse outcomes. Patients enrolled in the diabetes registry as of September 2002 through the end of 2003 were included, and patient adherence based on automated pharmacy records was assessed during 2003. Outcomes were assessed from January 2004 through April 2005. Patient medication adherence was defined as a minimum of 240 days (80%) and a maximum of 365 days (100%) for one of the three medication classes. Nonadherence for antihypertensives was associated with increased risk for all-cause hospitalization (OR, 1.44; 95% CI 1.24-1.67) and all-cause mortality (OR 1.58; 95% CI 1.22-2.05). Nonadherence for statins was associated with increased risk for all-cause hospitalization (OR, 1.39; 95% CI 1.18-1.63) and all-cause mortality (OR 2.07; 95% CI 1.54-2.80). Nonadherence for oral hypoglycemic agents was associated with increased risk for all-cause hospitalization (OR, 1.38; 95% CI 1.21-1.58) and all-cause mortality (OR 1.39; 95% CI 1.07-1.82).

[Hong & Kang (2011](#_ENREF_29)): In this retrospective study of 40,082 patients 20 years of age and older (mean age 51-55 years) with type 2 diabetes, nonadherence to oral antihyperglycemic medication was found to increase the risk for hospitalization and increase healthcare costs. The study used data from the Korea National Health Insurance Claims Database from 2004 to 2007. Patients were included if they were first diagnosed with type 2 diabetes in 2004 and received at least one prescription for oral antihyperglycemic medications. Medication adherence was defined as an MPR of 80% or more. Nonadherent patients accounted for 70.6% of the total cohort for the first two years after the prescription. Patients who were nonadherent for the first two years had higher risks of all-cause hospitalization (OR 1.21, 95% CI 1.13-1.31); hospitalization for diabetes, cardiovascular disease, or renal disease (OR 1.26, 95% CI 1.08-1.47); and when compared to adherent patients, patients who were nonadherent for the first two years after prescription also had a higher risk of all-cause mortality (OR 1.40, 95% CI 1.01-1.95). Adherent patients had lower healthcare costs than nonadherent patients, with healthcare costs decreasing as adherence increased (determined by classifying MPR into four groups: <40%, 40%-60%, 60-80%, and >80%).

[Kim et al. (2010](#_ENREF_31)): In this retrospective study of 56,181 veterans who first filled a prescription for oral hypoglycemic agents between January 2000 and December 2002 (median age 63 years), persistence with refilling medications was associated with achieving goal A1C levels. Data for the study were obtained from the VA Pharmacy Benefits Management database. Patients were included if they filled at least two prescriptions starting at the baseline date and no prescriptions for diabetes prior to that date. Persistence was determined by the number of days supply of oral hypoglycemic agents. Non-persistence was defined as <0.80, good persistence ≥0.80-1.10, and overpersistence as >1.10. Glycemic control was the primary outcome variable. Meeting goal A1C was defined as having a level ≤7.0% versus having an A1C >7.0%. Improved A1C was defined as having an A1C lower than the baseline A1C level. Seventy-seven percent of patients had good persistence, and 25% of those were overpersistent. Good persistence was associated with achieving goal A1C (RR 1.07, 95% CI 1.06-1.09) and was associated with improved A1C (RR 1.06, 95% CI 1.05-1.07) when compared to nonpersistence. Overpersistent patients were less likely to achieve goal A1C levels (RR 0.95, 95% CI 0.94 to 0.97) or to improve A1C (RR 0.98, 95% CI 0.98- 0.99) when compared to those with good persistence.

[Pladevall et al. (2004](#_ENREF_38)): In this retrospective study of 677 patients 18 years of age and older (mean age 64 years), nonadherent patients experienced more adverse outcomes than adherent patients. Patients with a diagnosis of diabetes, hypertension, and dyslipidemia during the period of 1999 to 2001 and at least one prescription drug claim for an antidiabetic, lipid-lowering, or antihypertensive drug in those years were included. Health plan, administrative, and clinical data were used to identify patients. Nonadherence was measured for three classes of drugs: metformin, statins, and ACE inhibitors. Patients were classified as nonadherent when the percentage of the continuous measure of medication gaps (CMG) was 20% or higher. Rates of nonadherence were 43% for metformin. Average levels of outcomes were significantly higher in nonadherent patients compared to adherent patients. A 10% increase in CMG for metformin was significantly associated with an increase of 0.14% in HbA1c.

Summary of Recently Published Studies

Regarding the certainty or confidence in the estimates of benefits and harms to patients across studies in the body of evidence resulting from study factors, (a) study design/flaws, (b) directness/indirectness of the evidence to this measure, and (c) impression/wide confidence intervals due to few patients or events are addressed below.

Study Design/Flaws

We identified six recent studies that measured the association between adherence by patients with diabetes mellitus to oral diabetes medications and patient outcomes. The results of these studies are summarized above under "Detailed Results of Studies." The methodological quality of the body of evidence in this section was judged from the published articles about these studies.

The six studies described above are retrospective cohort studies based on claims data ([Carls et al., 2012](#_ENREF_5); [Colombi et al., 2008](#_ENREF_17); [Hong & Kang, 2011](#_ENREF_29); [Kim et al., 2010](#_ENREF_31); [Pladevall et al., 2004](#_ENREF_38)), or automated pharmacy data ([Ho et al., 2006](#_ENREF_27)). None of the studies was a randomized controlled trial; however, all of them controlled for confounders in estimating the association between adherence and patient outcomes or resource use. A variety of settings were represented by the studies: employed individuals ([Carls et al., 2012](#_ENREF_5)); employees, retirees, and dependents ([Colombi et al., 2008](#_ENREF_17)); members of a managed care organization ([Ho et al., 2006](#_ENREF_27)); enrollees in a national health insurance program in Korea ([Hong & Kang, 2011](#_ENREF_29)); and Veterans Affairs patients ([Kim et al., 2010](#_ENREF_31)); and an integrated delivery group ([Pladevall et al., 2004](#_ENREF_38)).

Directness of the Evidence

Measures of adherence and adherence thresholds used in these studies were the percentage (or proportion) of days covered (PDC) with an 80% threshold ([Carls et al., 2012](#_ENREF_5); [Ho et al., 2006](#_ENREF_27)); medication possession ratio (MPR) with 80% threshold ([Colombi et al., 2008](#_ENREF_17); [Hong & Kang, 2011](#_ENREF_29)); persistence with 80% threshold ([Kim et al., 2010](#_ENREF_31)); and a continuous measure of medication gaps (CMG) using a mean value ([Pladevall et al., 2004](#_ENREF_38)).

All six studies restricted the study sample to patients with diabetes mellitus. In addition, all six studies reported outcomes for adherent and nonadherent patients, using the adherence measures and thresholds listed in the paragraph above.

Several outcomes were measured in the six studies of oral antidiabetic agents: hemoglobin A1C levels ([Kim et al., 2010](#_ENREF_31); [Pladevall et al., 2004](#_ENREF_38)); days of absenteeism and short-term disability ([Carls et al., 2012](#_ENREF_5)); risk of all-cause hospitalization ([Colombi et al., 2008](#_ENREF_17); [Ho et al., 2006](#_ENREF_27); [Hong & Kang, 2011](#_ENREF_29)); and, risk of cause-specific hospitalization or all-cause mortality ([Hong & Kang, 2011](#_ENREF_29)).

The evidence from these studies is directly relevant to the focus of the measure and target population. The focus of the six studies and of the measure is on adherence of adult patients with diabetes mellitus to oral diabetes agents.

Age Distributions of Study Samples

The target population of the proposed measure is: all persons 18 years of age and older. In the six studies from the literature, all patients were 18 years of age and older. The mean ages of subgroups in the six studies ranged from 50 years ( Carls et al., 2012) to 66 years (Columbi et al., 2008).

Possible Imprecision

In the six studies, the sample sizes for patients with diabetes who were taking one or more of the medications ranged from 677 ([Pladevall et al., 2004](#_ENREF_38)) to 56,181 ([Kim et al., 2010](#_ENREF_31)) patients.

Citations for Other Sources of Evidence

Carls, G., Roebuck, C., Brennan, T., Slezak, J., Matlin, O., & Gibson, T. (2012). Impact of medication adherence on absenteeism and short-term disability for five chronic diseases. *Journal of Occupational and Environmental Medicine, 54*(7), 792-805.

Colombi, A., Yu-Isenberg, K., & Priest, J. (2008). The effects of health plan copayments on adherence to oral diabetes medication and health resource utilization. *Journal of Occupational and Environmental Medicine, 50*(5), 535-541.

Ho, P., Rumsfeld, J., Masoudi, F., McClure, D., Plomondon, M., Steiner, J., & Magid, D. (2006). Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Archives of Internal Medicine, 166*, 1836-1841.

Hong, J., & Kang, H. (2011). Relationship between oral antihyperglycemic medication adherence and hospitalization, mortality, and healthcare costs in adult ambulatory care patients with type 2 diabetes in South Korea. *Medical Care, 49*(4), 378-384.

Kim, N., Agostini, J., & Justice, A. (2010). Refill adherence to oral hypoglycemic agents and glycemic control in veterans. *Annals of Pharmacotherapy, 44*(5), 800-808.

Pladevall, M., Williams, L., Potts, L., Divine, G., Xi, H., & Lafata, J. (2004). Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. *Diabetes Care, 27*(12), 2800-2906.

1. The measure applies only to patients with type 2 diabetes. Therefore, the content of the form also focuses on patients with type 2 diabetes. [↑](#footnote-ref-1)