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

**Measure Title**: Glycemic Control – Hyperglycemia

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

**Date of Submission**: 12/5/2013

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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 (*incudes 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 Intermediate clinical outcome: Glycemic Control – Hyperglycemia

☐ Process: Click here to name the process

☐ 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 inpatient hyperglycemia, an intermediate outcome. The desired outcomes for this measure are lower in-hospital mortality rates and infection rates and shorter lengths of stay. Appropriate glycemic control leads to a reduction in the intermediate outcome and other outcomes as follows:

Links of process – health outcome

Management of blood glucose levels in hospitalized patients 🡪

Lower rates of inpatient hyperglycemia 🡪

Lower in-hospital mortality rates and infection rates, and shorter lengths of stay

**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. IX. Diabetes care in specific settings. *Diabetes Care, 36*(Suppl 1), S45-S49. Retrieved July 25, 2013, from <http://care.diabetesjournals.org/content/36/Supplement_1/S11.full>

Qaseem, A., Humphrey, L., Chou, R., Snow, V., & Shekelle, M. (2011). Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline from the American College of Physicians. *Ann Intern Med, 154*(4), 260-267. Retrieved July 25, 2013, from <http://annals.org/article.aspx?articleid=746815>

Umpierrez, G. E., Hellman, R., Korytkowski, M. T., Kosiborod, M., Maynard, G. A., Montori, V. M., Seley, J. J., Van den Berghe, G. (2012). Management of Hyperglycemia in Hospitalized Patients in Non-critical Care Setting: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab, 97*, 16-38. Retrieved July 25, 2013, from <http://jcem.endojournals.org/content/97/1/16.full>

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

The measure is supported primarily by a recommendation in the following 2011 guideline:

The “Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline from the American College of Physicians” (Qaseem et al., 2011) offers the following recommendations regarding inpatient glycemic control on page 260:

* + Recommendation 1: ACP recommends not using intensive insulin therapy to strictly control blood glucose in non–surgical intensive care unit (SICU)/medical intensive care unit (MICU) patients with or without diabetes mellitus (Grade: strong recommendation, moderate-quality evidence).
  + Recommendation 2: ACP recommends not using intensive insulin therapy to normalize blood glucose in SICU/MICU patients with or without diabetes mellitus (Grade: strong recommendation, high-quality evidence).
  + Recommendation 3: ACP recommends a target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients (Grade: weak recommendation, moderate-quality evidence).

The measure is also supported by recommendations in two other recent guidelines:

“Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting: An Endocrine Society Clinical Practice Guideline” (Umpierrez et al., 2012, p. 17) includes the following recommendations:

* 3.1. We recommend a premeal glucose target of less than 140 mg/dL (7.8 mmol/liter) and a random BG of less than 180 mg/dL (10.0 mmol/liter) for the majority of hospitalized patients with non-critical illness. (strong recommendation/low quality evidence)
* 3.2. We suggest that glycemic targets be modified according to clinical status. For patients who are able to achieve and maintain glycemic control without hypoglycemia, a lower target range may be reasonable. For patients with terminal illness and/or with limited life expectancy or at high risk for hypoglycemia, a higher target range (BG <11.1 mmol/liter or 200 mg/dL) may be reasonable. (weak recommendation/very low quality evidence)

The “Standards of Medical Care in Diabetes—2013” (American Diabetes Association, 2013, pp. S45-S46) offers the following recommendations regarding inpatient glycemic control:

* + For critically ill patients: Insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold of no greater than 180 mg/dL (10 mmol/l). Once insulin therapy is started, a glucose range of 140–180 mg/dL (7.8–10 mmol/l) is recommended for the majority of critically ill patients. (Level of evidence=A)
  + More stringent goals, such as 110-140 mg/dL (6.1-7.8 mmol/L) may be appropriate for selected patients, as long as this can be achieved without significant hypoglycemia. (Level of evidence=C)
  + For non-critically ill patients: There is no clear evidence for specific blood glucose goals. If treated with insulin, the premeal blood glucose targets generally <140 mg/dL (7.8 mmol/L) with random blood glucose <180 mg/dL (10.0 mmol/L) are reasonable, provided these targets can be safely achieved. More stringent targets may be appropriate in stable patients with previous tight glycemic control. Less stringent targets may be appropriate in those with severe comorbidities. (Level of evidence=E)

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

The “Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline from the American College of Physicians” (Qaseem et al., 2011) identifies the strength of each recommendation, using the following categories:

Strong = Benefits Clearly Outweigh Risks and Burden *Or* Risks and Burden Clearly Outweigh Benefits

Weak = Benefits Finely Balanced with Risks and Burden

For each recommendation in “Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting: An Endocrine Society Clinical Practice Guideline” (Umpierrez et al., 2012), the strength of the recommendation is identified as follows:

Strong = The Task Force has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm.

Weak = Requires more careful consideration of the person’s circumstances, values, and preferences to determine the best course of action.

The “Standards of Medical Care in Diabetes—2013” (American Diabetes Association, 2013) only identifies the level of evidence for each recommendation and does not grade the recommendation in Section 1a.4.2. as strong or weak. The levels of evidence supporting the three recommendations are A, C, and E. A level of evidence of A is defined as clear or supportive evidence from well-conducted, generalizable, randomized controlled trials; or compelling nonexperimental evidence. A level of evidence of C is defined as supportive evidence from poorly controlled or uncontrolled studies; or conflicting evidence with the weight of evidence supporting the recommendation. A level of evidence of E is defined as expert consensus or clinical experience.

**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.*)

The “Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline from the American College of Physicians” (Qaseem et al., 2011) identifies the quality of evidence and the strength of each recommendation, using the categories outlined in Table 1.

**Table 1. The American College of Physicians Guideline Grading System\***

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| --- | --- | --- |
| **Quality of Evidence** | **Strength of Recommendation** | |
| **Benefits Clearly Outweigh Risks and Burden *Or***  **Risks and Burden Clearly Outweigh Benefits** | **Benefits Finely Balanced**  **With Risks and Burden** |
| High | Strong | Weak |
| Moderate | Strong | Weak |
| Low | Strong | Weak |

\*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) workgroup. Source: Qaseem et al. (2011)

For each recommendation in “Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting: An Endocrine Society Clinical Practice Guideline” (Umpierrez et al., 2012), the strength of the recommendation and the quality of the evidence is identified as follows:

“The Clinical Guidelines Subcommittee of The Endocrine Society deemed the management of hyperglycemia in hospitalized patients in a non-critical care setting a priority area in need of practice guidelines and appointed a Task Force to formulate evidence-based recommendations. The Task Force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group, an international group with expertise in development and implementation of evidence-based guidelines. A detailed description of the grading scheme has been published elsewhere. The Task Force used the best available research evidence to develop some of the recommendations. The Task Force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase ‘we recommend’ and the number 1, and weak recommendations use the phrase ‘we suggest’ and the number 2. *Crossfilled circles* indicate the quality of the evidence, such that denotes very low quality evidence; low quality; moderate quality; and high quality. The Task Force has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm. Weak recommendations require more careful consideration of the person’s circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the values that panelists considered in making the recommendation; in some instances, there are remarks, a section in which panelists offer technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the panelists and their values and preferences; therefore, these remarks should be considered suggestions.”

The “Standards of Medical Care in Diabetes—2013” (American Diabetes Association, 2013) identifies the level of evidence for each recommendation, using the following categories:

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 Center for Evidence Based Medicine at 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 citations and URLs for the methodologies used to conduct the literature reviews and grade the recommendations are the same as those for the three guidelines listed in Section 1a.4.1.

**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*)**:**

***Complete section*** [***1a.7***](#Section1a7)

**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*)**:**

***Complete section*** [***1a.7***](#Section1a7)

**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?**

The “Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline from the American College of Physicians” (Qaseem et al., 2011) investigated the literature to answer the following questions:

* “Does the use of intensive insulin therapy to achieve tight glycemic control compared with less tight glycemic control improve health outcomes in the following settings or patient populations: surgical intensive care until (SICU), medical intensive care unit (MICU), general surgical ward, general medicine ward, patients with myocardial infarction or acute stroke, and patients in the perioperative setting?”
* “What are the harms of strict glycemic control in the above subpopulations?”

The “Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting: An Endocrine Society Clinical Practice Guideline,” (Umpierrez et al., 2012) focused on reviewing evidence from the literature to establish “consensus recommendations for the management of hyperglycemia in hospitalized patients in non-critical care settings.”

The “Standards of Medical Care in Diabetes—2013” (American Diabetes Association, 2013) reviewed a large body of evidence that related to “screening, diagnostic, and therapeutic actions that are known or believed to favorably affect health outcomes of patients with diabetes.”

Although the guidelines provided a review of the body of the evidence supporting the recommendations listed in Section 1a.4.2, many of the studies that the guidelines evaluated were investigating the use of intensive insulin therapy and its impact on health outcomes, which did 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 inpatient hyperglycemia 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.8.1and 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 nine recent studies published in the medical literature that focus on the relationship between hyperglycemia and patient outcomes in the hospital setting.

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

Nine 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 studies from both types of searches were reviewed to identify those that addressed the relationship between inpatient hyperglycemia and patient outcomes and/or resource utilization. The 9 selected studies met the following criteria: the study measured hyperglycemia in the inpatient setting, the study reported patient outcomes and/or length of stay in subgroups defined by blood glucose levels, and the study was published in the last eleven years.

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

Summary of Recently Published Studies

The magnitude and direction of the association between hyperglycemia and patient outcomes were highly consistent in the nine studies that were recently published in the peer-reviewed literature. The evidence from these studies is directly relevant to the focus of the measure and target population. The focus of the nine studies and of the measure is on hyperglycemia in adult patients in the hospital setting.

Consistency and Magnitude of Effect Related to Mortality

Eight of the nine studies (Falciglia, Freyberg, Almenoff, D’Alessio, & Render, 2009; Frisch et al., 2010; Jackson, Amdur, White, & Mascata, 2012; Lee et al., 2012; McAlister et al., 2005; Pasquel et al., 2010; Rady, Johnson, Patel, Larson, & Helmers, 2005; Umpierrez et al., 2002), described below, reported results for mortality. All eight of these studies described consistent results: persons with hyperglycemia had a higher risk of mortality than those with normal or lower blood glucose levels. The odds ratios for mortality comparing patients with hyperglycemia and those with normoglycemia were of the same general magnitude in five studies: 2.13 for 200-300 mg/dL and 2.85 for >300 mg/dL compared to 70-110 mg/dL (Falciglia et al., 2009); 1.97 for >200 mg/dL compared to 80-120 mg/dL (Jackson et al., 2012); 2.2 for >180 mg/dL compared to ≤120 mg/dL (Pasquel et al., 2010); 1.5 for >144 mg/dL compared to a median of 118 mg/dL (Rady et al., 2005); 18.3 for new hyperglycemia and 2.7 for known diabetes (referent group not defined) (Umpierrez et al., 2002). Frisch et al. (2010) reported odds ratios for 30-day mortality for patients without diabetes by mean blood glucose after surgery: 10 for 200 mg/dL, 18 for 250 mg/dL, and 43 for 300 mg/dL (*p* <0.001; referent group not defined). Lee et al. (2012) reported the odds of in-hospital mortality increased by 7% for every 10 mg/dL increase in the mean blood glucose level and by 6% for every 10 mg/dL increase in the maximum blood glucose level. In a study of patients with community-acquired pneumonia, patients with an admission glucose >11 mmol/l (>198 mg/dL) had a 73% higher (95% CI 12-168%) mortality risk than patients whose admission glucose was ≤6.1 mmol/l (≤109.8 mg/dL) (McAlister et al., 2005).

Consistency and Magnitude of Effect Related to Infection Rates

Three of the nine studies (Jackson et al., 2012; King, Goulet, Perkal, & Rosenthal, 2011; Pasquel et al., 2010) reported results related to the relationship between hyperglycemia and rates of infection (urinary tract infection, any type of postoperative infection, and pneumonia, respectively). All three of these studies reported consistent results: persons with hyperglycemia had statistically significantly increased rates of infection compared to those with normal blood glucose levels. The odds ratios for different types of infection, comparing patients with hyperglycemia and those with normoglycemia, were of the same general magnitude: 1.68 for urinary tract infection among those with BG >200 mg/dL (Jackson et al., 2012); 1.43 for postoperative infection among those with BG >250 mg/dL (King et al., 2011); and 3.6 for pneumonia among those with BG >180 mg/dL (Pasquel et al., 2010).

Consistency and Magnitude of Effect Related to Length of Stay

Three of the nine studies (Pasquel et al., 2010; Rady et al., 2005; Umpierrez et al., 2002) reported results for the association between length of stay and hyperglycemia. Of these three studies, two studies showed consistent results: persons with hyperglycemia had longer lengths of stay compared to those with normal blood glucose levels. In a retrospective study of medical and surgical patients receiving total parenteral nutrition (TPN) (Pasquel et al., 2010), patients with higher blood glucose levels during TPN had longer hospital (*p* =0.011) and intensive care unit (*p* =0.008) lengths of stay. In an observational study of 7,285 patients aged ≥18 years admitted to a single ICU in a tertiary-care teaching hospital between 1999 and 2003 (Rady et al., 2005), diabetic and nondiabetic patients who required glycemic control had longer hospital stays than those who did not require glycemic control (6.7 days, 8.0 days, and 4.4 days, respectively, both *p* <0.001). A similar pattern was observed in intensive care units for diabetic and nondiabetic patients who required glycemic control and those who did not require glycemic control (1.5 days, 1.6 days, and 1.3 days, respectively, both *p* <0.001). In a retrospective study of adult patients admitted to a community teaching hospital (Umpierrez et al., 2002), patients with new hyperglycemia (defined as hyperglycemia occurring during the hospitalization, but without prior history of diabetes) also had longer lengths of stay than the other groups (9.7 days compared to 5.5 days for diabetic patients and 4.5 days for normoglycemic patients, all *p* <0.01).

Detailed Results of Studies

Falciglia et al. (2009): This retrospective cohort study of 259,040 admissions across 173 medical, surgical, and cardiac ICUs in 113 VA hospitals from October 2002 to September 2005 found that hyperglycemia was associated with increased mortality, independent of illness severity. The selected admissions were taken from a larger cohort of 425,853 consecutive first admissions to VA ICUs during the time period. Patients with no computerized blood gas data, those with less than two serum glucose measures, and those whose mean glucose was less than 70 mg/dL were excluded from the study. In the cohort, 1.3%, 32.6%, 52.5%, and 13.6% were <40, 40-59, 60-79, and >79 years of age, respectively. The rate of unadjusted mortality at discharge from hospitalization was 11.2%. Mortality risk increased with increasing blood glucose. The unadjusted mortality rates for each of the mean glucose categories were: 7.3% (70-110 mg/dL), 10.2% (111-145 mg/dL), 14.8% (146-199 mg/dL), 17.3% (200-300 mg/dL), and 21.9% (>300 mg/dL), respectively. When compared to normoglycemic patients (70-110 mg/dL), the adjusted odds ratio for hospital mortality was 2.13 (200-300 mg/dL) and 2.85 (>300 mg/dL), respectively.

Frisch et al. (2010): This observational study of surgery patients (mean age of 56.5 years) found that perioperative hyperglycemia was associated with mortality after non-cardiac surgery. Medical records from all patients who underwent inpatient surgery at a tertiary academic center from January to June 2007 were reviewed. For 2,469 patients without diabetes, the odds ratios for 30-day mortality by mean blood glucose after surgery were 10 for 200 mg/dL, 18 for 250 mg/dL, and 43 for 300 mg/dL (*p* <0.001), but this relationship was not significant for patients with diabetes. Normoglycemic was not defined.

Jackson et al. (2012): Investigators used data from the Veterans Affairs Surgical Quality Improvement Program database for 7,576 and 5,773 colectomy procedures to study the effect of operative day glucose and postoperative day-1 blood glucose, respectively, on patient outcomes. Mean patient age for the study groups ranged from 67.3 to 70.6 years. Based on multivariate analysis, postoperative day-1 blood glucose levels >200 mg/dL were associated with death (OR 1.97, 95% CI 1.23-3.15), cardiac arrest (OR 2.31, 95% CI 1.08-4.98), myocardial infarction (OR 3.94, 95%CI 1.64-9.58), and urinary tract infection (OR 1.68, 95% CI 1.08-2.63), compared to those with blood glucose equal to 80-120 mg/dL.

King et al. (2011): This retrospective cohort study analyzed 1999-2004 data on 55,408 patients with diabetes having a variety of non-cardiac surgeries at Veterans Health Administration facilities (mean age of 64.8 years). The rate of postoperative infections was 8.0% overall. Higher blood glucose levels were associated with increased rates of postoperative infectious complications (*p* <0.001). In the sample, 72% of patients had a mean serum glucose level of at least 150 mg/dL during the first 24 hours after surgery. Patients with 24-hour mean postoperative glucose levels of 150 to 250 mg/dL had a greater risk of infection, when compared to those with 80 to 110 mg/dL (adjusted incidence rate ratio 1.22, 95% CI 1.04–1.43; *p* = 0.01). Patients with glucose levels >250 mg/dL had an even higher risk of postoperative infection (adjusted incidence rate ratio: 1.43; 95% CI 1.19–1.71; *p* < 0.001).

Lee et al. (2012): This retrospective study of 3,132 patients from 17 hospitals who had invasive cardiovascular surgery found that higher mean and maximum blood glucose levels were associated with increased risk of in-hospital mortality. Data were extracted from the electronic health records of patients ≥18 years of age (mean age of 66 years) who underwent surgery from 2000 to 2006 and were admitted to the ICU within three days of admission. Among survivors and non-survivors, the mean blood glucose levels during the 72-hour observation period were 198 and 221 mg/dL, respectively, and the maximum blood glucose levels were 256 and 326 mg/dL, respectively (*p* <0.001 for both). For mean blood glucose models, the odds of in-hospital mortality increased by 7% for every 0.56 mmol/L (10.08 mg/dL) increase in the mean blood glucose level (OR 1.07, 95% CI 1.01-1.12). In the maximum blood glucose model, the odds of mortality increased by 6% for every 0.56 mmol/L (10.08 mg/dL) increase in the maximum blood glucose level (OR 1.06, 95% CI 1.03-1.08). Hyperglycemia was defined as fasting blood glucose ≥126 mg/dL or random ≥198 mg/dL; normoglycemia was not defined.

McAlister et al. (2005): In this prospective cohort study of consecutive patients admitted with a clinical diagnosis of community-acquired pneumonia (CAP) to six hospitals from November 2000 to November 2002, hyperglycemia at admission was independently associated with adverse outcomes. Patients admitted directly to the ICU were excluded. The final sample included 2,471 patients with a median age of 75 years. Compared with patients with an admission glucose <11 mmol/l (<198 mg/dL), patients with an admission glucose >11 mmol/l (>198.2 mg/dL) had an increased risk of death (13% vs. 9%, *p* =0.03) and in-hospital complications (29% vs. 22%, *p* =0.01). In-hospital complications included “any nonmetabolic complications, cardiac complications (acute coronary syndromes and/or heart failure), and nosocomial infections (i.e., in sites other than the lungs).” Compared with patients whose admission glucose was ≤6.1 mmol/l (≤109.8 mg/dL), patients with an admission glucose >11 mmol/l (>198 mg/dL) had a 73% higher (95% CI 12-168%) mortality risk and 52% (95% CI 12%-108%) higher in-hospital complication risk. For each 1 mmol/l (18 mg/dL) increase in admission glucose, the adjusted risk of in-hospital complications increased 3% (95% CI 0.2–6%) in the entire cohort and 5% (95% CI 1–9%) in those with a history of diabetes. The adjusted risk of in-hospital mortality increased 8% (95% CI 1–15%) per mmol/l in those with a history of diabetes.

Pasquel et al. (2010): This retrospective study of medical and surgical patients receiving total parenteral nutrition (TPN) found hyperglycemia to be associated with increased hospital complications and mortality. The study population included 276 consecutive medical and surgical patients with a mean glucose of 139±85 mg/dL on admission. The mean age of these patients was 51 years. In multiple regression analyses, the likelihood of death was predicted by elevated pre-TPN blood glucose of 121-150 mg/dL (OR 2.2, 95% CI 1.1-4.4, *p* =0.030), 151-180 mg/dL (OR 3.41, 95% CI 1.3-8.7, *p* =0.01), or >180 mg/dL (OR 2.2, 95% CI 0.9-5.2, *p* =0.077), compared with those having mean blood glucose ≤120 mg/dL. Patients with higher blood glucose levels during TPN had longer hospital (*p* =0.011) and intensive care unit (*p* =0.008) lengths of stay. Blood glucose >180 mg/dL within 24 hours after TPN was associated with a higher risk of pneumonia (OR 3.6, 95% CI 1.6-8.4) and acute renal failure (OR 2.2, 95% CI 1.02-4.8), compared with those having blood glucose <120 mg/dL.

Rady et al. (2005): This observational study of 7,285 patients aged ≥18 years admitted to a single ICU in a tertiary-care teaching hospital between 1999 and 2003 found that poor glycemic control in nondiabetic patients was associated with increased insulin requirement and mortality. Electronic medical records were queried to identify patients with poor glycemic control, defined as glucose value of ≤144 mg/dL for less than 5% of the total hospital stay, and hospital death. The 1,083 diabetic patients (mean age of 70 years) and the 1,743 nondiabetic patients (mean age of 71 years) who required insulin for glycemic control were compared to each other and the 4,459 requiring no glycemic control (mean age of 70 years). Mortality was higher in nondiabetic patients than diabetic patients at any given insulin dose. Mortality increased for nondiabetic patients at median glucose levels of 145 mg/dL and for diabetic patients of >200 mg/dL. The control group (i.e., those requiring no glycemic control) had a median glucose level of 118 mg/dL (range 97-153 mg/dL) and a 5% mortality rate. Unadjusted mortality rates were 10% for nondiabetics compared to 6% for diabetics receiving glycemic control (*p* <0.001). Based on multivariate analysis, poor glycemic control (defined as >144 mg/dL for 95% of hospital stay) in diabetic and nondiabetic patients was independently associated with hospital mortality (OR 1.5; 95% CI 1.1-2.0).

Umpierrez et al. (2002): In this retrospective study of 1,886 consecutive adult patients admitted to a community teaching hospital, in-hospital hyperglycemia was common and was a marker of poor clinical outcome and mortality in patients with and without a history of diabetes. Patients admitted to the hospital between July and October of 1998, who had a recorded blood glucose measurement during the hospital stay, were included in the analysis. Among the patients, 223 (12%) were diagnosed with new hyperglycemia, 495 (26%) had a known history of diabetes at admission, and 1,168 (62%) were normoglycemic. The mean ages of these three study groups were 59 years, 63 years, and 54 years, respectively. “New hyperglycemia” was defined as patients without a prior history of diabetes who had “an admission or in-hospital fasting glucose level greater than 126 mg/dL or a random blood glucose level greater than 200 mg/dL on two or more determinations.” Patients with new hyperglycemia were more likely to be admitted to the ICU (29% vs. 9%, *p* <0.01), when compared to normoglycemic patients. Patients with new hyperglycemia also had longer lengths of stay than the other groups (9.7 days compared to 5.5 days for diabetic patients and 4.5 days for normoglycemic patients, all *p* <0.01). Mortality was also highest among patients with new hyperglycemia (16% compared to 3% in diabetic patients and 1.7% in normoglycemic patients, both *p* <0.001). After adjustment for patient and clinical characteristics, mortality rates among those with new hyperglycemia and those with diabetes were 18.3 times and 2.7 times higher, respectively, than the normoglycemic group. Normoglycemia was defined as normal plasma glucose and no previous history of diabetes; the article does not state blood glucose levels explicitly for the normoglycemic group.

Study Design

We identified nine recent studies that measured the association between inpatient hyperglycemia and outcomes in the hospital. The results of these studies are summarized under the section of “Consistency of Results across Studies” of this form. The methodological quality of the body of evidence in this section was judged from the published articles about these studies. Of the nine studies, one is a prospective cohort study of patients using medical chart abstraction (McAlister et al.,2005), and eight are retrospective studies using electronic health record data (Frisch et al., 2010; Lee et al., 2012; Rady et al., 2005), data collected for the study (Falciglia et al., 2009; Jackson et al., 2012; King et al., 2011), or medical record abstraction (Umpierrez et al., 2002) [one retrospective study (Pasquel et al., 2010) did not state the type of data used]. None of the studies was a randomized controlled trial; however, all of them controlled for confounders in estimating the association between hyperglycemia and patient outcomes. A variety of diagnoses and settings were included in the studies: medical, surgical, and cardiac ICUs (Falciglia et al., 2009), general surgery (Frisch et al., 2010), colectomy for cancer (Jackson et al., 2012); non-cardiac surgeries (King et al., 2011), cardiovascular surgery (Lee et al., 2012), community-acquired pneumonia (McAlister et al., 2005), medical and surgical patients receiving total parenteral nutrition (TPN) (Pasquel et al., 2010), ICU patients (Rady et al., 2005), and all diagnoses (Umpierrez et al., 2002).

Directness of the Evidence

Thresholds for hyperglycemia used in these studies were 180 mg/dL (Pasquel et al., 2010); 200 mg/dL (Falciglia et al., 2009; Jackson et al., 2012; Lee et al., 2012; McAlister et al., 2005; Rady et al., 2005; Umpierrez et al., 2002); and 250 mg/dL (King et al., 2011; McAlister et al., 2005; Rady et al., 2005).

Glycemic control measures were defined in a variety of ways. In seven of the studies, a mean or median of blood glucose values was used for a specific period of time: the entire stay (Falciglia et al., 2009; Rady et al., 2005); one day before, one day after surgery (postsurgery day one), and within the first ten days after surgery (Frisch et al., 2010); the operative day and postoperative day 1 (Jackson et al., 2012); 0-24 hours after surgery (King et al., 2011); at admission (McAlister et al., 2005); and on admission, pre-TPN, within 24 hours, and during days 2–10 of TPN (Pasquel et al., 2010).

Outcomes were reported for blood glucose categories (e.g., 70–110, 111–145, 146–199, 200-300 mg/dL, and >300 mg/dL) in four studies (Falciglia et al., 2009; Frisch et al., 2010; Jackson et al., 2012; King et al., 2011). In three studies, an algorithm based on blood glucose level was used to identify those at highest risk (Lee et al., 2012; Rady et al., 2005; Umpierrez et al., 2002). Another 2 studies used 1 or 2 specified thresholds to define hyperglycemia, such as 200 and 250 mg/dL (McAlister et al., 2005), and 180 mg/dL (Pasquel et al., 2010).

Eight of the 9 studies (Falciglia et al., 2009; Frisch et al., 2010; Jackson et al., 2012; Lee et al., 2012; McAlister et al., 2005; Pasquel et al., 2010; Rady et al., 2005; Umpierrez et al., 2002) included patients with and without diabetes. One study (King et al., 2011) restricted study participants to patients with diabetes.

In the one prospective study (McAlister et al., 2005), details related to outcomes were abstracted from the medical chart and all other data were prospectively collected in a standardized manner by trained research nurses. In the 8 retrospective studies (Falciglia et al., 2009; Frisch et al., 2010; Jackson et al., 2012; King et al., 2011; Lee et al., 2012; Pasquel et al., 2010; Rady et al., 2005; Umpierrez et al., 2002), the outcome measures were objectively assessed using standardized definitions and routinely collected repository or electronic health record (EHR) data.

The evidence from these studies is directly relevant to the focus of the measure and the target population. The focus of the 9 studies and the measure is inpatient hyperglycemia among adult patients.

The target population of the proposed measure is all persons 18 years of age and older. In the 9 studies from the literature, all patients were older than 18 years of age. The mean ages in the 9 studies ranged from 51 to 77 years.

Possible Imprecision

The sample sizes in these studies were moderate to very large, ranging from 276 to 259,040 patients [276 (Pasquel et al., 2010); 1,886 (Umpierrez et al., 2002); 2,471 (McAlister et al., 2005); 3,132 (Lee et al., 2012); 3,184 (Frisch et al., 2010); 7,285 (Rady et al., 2005); 7,576 (Jackson et al., 2012); 55,408 (King et al., 2011); 259,040 (Falciglia et al., 2009)]. One of the studies (276 [Pasquel et al., 2010]) had a moderate-sized sample, which may have contributed to wider confidence intervals.

Citations for Studies Listed in Section 1a.8.2.

Falciglia, M., Freyberg, R. W., Almenoff, P. L., D’Alessio, D. A., & Render, M. L. (2009). Hyperglycemia-related mortality in critically ill patients varies with admission diagnosis. *Crit Care Med, 37*(12), 3001-3009. doi: 10.1097/CCM.0b013e3181b083f7

Frisch, A., Chandra, P., Smiley, D., Peng, L., Rizzo, M., Gatcliffe, C., . . . Umpierrez, G. E. (2010). Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care, 33*(8), 1783-1788.

Jackson, R., Amdur, R., White, J., & Mascata, R. (2012). Hyperglycemia is associated with increased risk of morbidity and mortality after colectomy for cancer. *J Am Coll Surg, 214*(1), 68-80.

King, J., Goulet, J., Perkal, M., & Rosenthal, R. (2011). Glycemic control and infections in patients with diabetes undergoing noncardiac surgery. *Ann Surg, 253*(1), 158-165.

Lee, L., Emons, M., Martin, S., Faries, D., Bae, J., Nathanson, B., . . . Bode, B. (2012). Association of blood glucose levels with in-hospital mortality and 30-day readmission in patients undergoing invasive cardiovascular surgery. *Current Medical Research & Opinion, 28*(10), 1657-1665.

McAlister, F., Majumdar, S., Blitz, S., Rowe, B., Romney, J., & Marrie, T. (2005). The relation between hyperglycemia and outcomes in 2,471 patients admitted to the hospital with community-acquired pneumonia. *Diabetes Care, 28*(4), 810-815.

Pasquel, F., Spiegelman, R., McCauley, M., Smiley, D., Umpierrez, D., Johnson, R., . . . Umpierrez, G. E. (2010). Hyperglycemia during total parenteral nutrition: An important marker of poor outcome and mortality in hospitalized patients. *Diabetes Care, 33*(4), 739-741.

Rady, M., Johnson, D., Patel, B., Larson, J., & Helmers, R. (2005). Influence of individual characteristics on outcome of glycemic control in intensive care unit patients with or without diabetes mellitus. *Mayo Clin Proc, 80*(12), 1558-1567.

Umpierrez, G., Isaacs, S., Bazargan, N., You, X., Thaler, L., & Kitabchi, A. (2002). Hyperglycemia: An independent marker of in-hospital mortality in patients with undiagnosed diabetes. *Journal of Clinical Endocrinology and Metabolism, 87*(3), 978-982.