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

**Measure Number** (*if previously endorsed*)**:** 2371

**Measure Title**: Annual Monitoring for Patients on Persistent Medications

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 1/17/2014

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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 (*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). |
| **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.** 1a. Evidence to Support the Measure Focus The measure focus 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. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component.   **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.** 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).  **5.** 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. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see 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**: (*should be consistent with type of measure entered in De.1*)

Outcome

Health outcome: Click here to name the health outcome

Patient-reported outcome (PRO): Click here to name the PRO

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors*

Intermediate clinical outcome (*e.g., lab value*): Click here to name the intermediate outcome

Process: Laboratory monitoring for patients on persistent medications

Structure: Click here to name the structure

Other: Click here to name what is being measured

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

**1a.2.** **Briefly state or diagram the path 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) to at least one healthcare structure, process, intervention, or service (*i.e., influence on outcome/PRO*).**

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

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

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

*Identify population*: Individuals with persistent use of select therapeutic agents that pose risk for adverse drug events

*Monitor*: Provide at least annual appropriate monitoring tests for those with persistent medication use to identify risk of adverse drug events

*Intervene*: Adjust dosage or stop medication to reduce risk of adverse drug event

*Outcome*: Those with appropriate monitoring will have less risk of experiencing an adverse drug event

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

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)

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.*

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

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

Burden R and Tomson C. Identification, management and referral of adults with chronic kidney disease: Concise guidelines. Clin Med. 2005; 5(6): 635-42.

Federal Drug Administration (FDAa). **LANOXIN- digoxin tablet . Cardinal Health. 2013.**  Accessed December 6, 2013. Available at: <http://labels.fda.gov/>

Federal Drug Administration (FDAb).Lasix (furosemide) prescribing information. Bridgewater, nj: Sanofi-aventis. 2011. Accessed December 6, 2013. Available at: <http://labels.fda.gov/>

Hunt SA AW, Chin MH et al. Focused update incorporated into the acc/aha 2005 guidelines for the diagnosis and management of heart failure in adults: A report of the American college of cardiology foundation/American heart association task force on practice guidelines: Developed in collaboration with the international society for heart and lung transplantation. Circulation. 2009; 119(14): e391-479.

Lindenfeld J, Albert NM, Boehmer JP et al. Hfsa 2010 comprehensive heart failure practice guideline. Journal of cardiac failure. 2010; 16(6): e1-194.

Pinkerman C, Sander P, Breeding JE et al. Heart failure in adults. Institute for Clinical Systems Improvement (ICSI). 2013.

Smellie WS, Forth J, Coleman JJ et al. Best practice in primary care pathology: Review 6. Journal of clinical pathology. 2007; 60(3): 225-34.

Swedberg K, Cleland J, Dargie H et al. Guidelines for the diagnosis and treatment of chronic heart failure: Executive summary (update 2005): The task force for the diagnosis and treatment of chronic heart failure of the European society of cardiology. Eur Heart J. 2005; 26(11): 1115-40.

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

Clinical practice guidelines do not provide graded recommendations for annual monitoring of patients with persistent use of ACE inhibitors/ARBS, digoxin, and diuretics; however, several guidelines describe the risks of adverse drug events related to use of these medications and the importance of regular monitoring to avoid adverse drug events. We worked with researchers from Johns Hopkins Hospital Center for Medication Quality and Outcomes to review the current evidence and all relevant clinical practice guidelines to determine appropriate monitoring for patients with persistent use of ACE inhibitors/ARBs, digoxin, and diuretics. The initial search strategy included evidence-based and consensus-based guidelines, meta-analyses, and systematic reviews. A more detailed description of the search strategy can be found in section 1a.6.

**Monitoring for Patients on ACE Inhibitors or ARBs**

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| --- | --- | --- | --- | --- |
| **Reference** | **Monitoring Parameter** | **Population** | **Monitoring Frequency** | **Rationale** |
| American College of Cardiology and the American Heart Association (Hunt 2009) | Serum potassium | Patients with heart failure | Serial monitoring | Use of ACE/ARB may lead to hyperkalemia which may complicate therapy and cause cardiac conduction disturbances |
| Renal function  Serum potassium | Patients using an ACE Inhibitor and potassium-sparing diuretic (aldosterone antagonist) | Renal Function: monthly for first 3 months and then every 3 months  Potassium: within 3 days and again at 1 week | Use of ACE/ARB Increases risk for hyperkalemia |
| Renal function  Serum creatinine | Patients with bilateral renal artery stenosis or using an nonsteroid anti-inflammatory drug | Renal Function: monthly for first 3 months and then every 3 months | Use of ACE inhibitor may increases serum creatinine level |
| Institute for Clinical Systems Improvement (Pinkerman 2013) | Serum creatinine  Blood urea nitrogen  Serum potassium | Patients age 18 years or older with heart failure | 1- to 4-weeks after initiation/dose increase then 1- to 2-times per year  IF elderly: 1- to 2-weeks after initiation/dose increase then 1- to 2-times per year |  |
| Best practice in primary care pathology/ European Task Force Guidelines (Smellie 2007; Burden 2005; Swedberg 2005) | Serum creatinine  Serum electrolytes | Low-risk patients with heart failure using ACE Inhibitors, ARBs, and diuretics | 1 – 2 weeks after each dose increase/relevant drug addition | To assess deterioration in kidney function associated with use of ACEIs or ARBs (patients with kidney disease and/or heart failure) |
| High-risk patients with heart failure using potassium-sparing diuretics or combination therapy or with existing renal dysfunction | 5 – 7 days after each dose increase/relevant drug addition |  |
| Serum potassium | Patients using an ACE Inhibitor and potassium supplements or potassium-sparing diuretics | Monitor frequently | Hyperkalemia occurred in approximately 1% of hypertensive patients |

**Monitoring for Patients on Digoxin**

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| **Reference** | **Monitoring Parameter** | **Population** | **Frequency** | **Rationale** |
| Heart Failure Society of America (Lindenfeld 2010) | Serum digoxin  (0.7 – 0.9 ng/mL) | Majority of patients except the elderly or those with impaired renal function | Monitoring in specific situations (see rationale) | Serum digoxin concentration < 1.0 ng/mL were associated with favorable outcomes whereas those > 1.2 ng/mL were associated with harm (B)  Monitoring should be considered when:  - a significant change in renal function occurs  - a potentially interacting drug is added or discontinued  - confirmation of suspected digoxin toxicity |
| Institute for Clinical Systems Improvement (Pinkerman 2013) | Serum digoxin | Elderly or renal-impaired patient with heart failure | Monitor at 1 – 2 weeks after initiation | Monitor to avoid digoxin toxicity: serum digoxin levels do not always correlate to symptoms of toxicity |
| Serum digoxin | Patients age 18 years or older with heart failure | 5- to 7-days after initiation/dose change | Monitoring also recommended for: suspected toxicity, suspected non-adherence, new or existing renal dysfunction, determination of therapeutic range |
| Serum creatinine  Electrolytes | Patients age 18 years or older with heart failure | Baseline and periodically thereafter |  |
| American College of Cardiology and the American Heart Association (Hunt 2009) | Serum potassium | Patients with heart failure and using a diuretic | Serial monitoring | Hypokalemia may cause fatal arrhythmias and increase the risk of digoxin toxicity |
| FDA Label (FDAa, 2013) | Serum digoxin | Adults with mild to moderate heart failure and for the control of resting ventricular rate in patients with chronic atrial fibrillation | Sample just before next scheduled dose of drug | Blood tests will be necessary to ensure digoxin dose is appropriate (therapeutic and toxic effect)  Dose of digoxin should be based on clinical grounds but serum digoxin concentration can be helpful to the clinician in determining the adequacy of digoxin therapy and in assigning certain probabilities to the likelihood of digoxin intoxication. |

**Monitoring for Patients on Diuretics**

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| **Reference** | **Monitoring Parameter** | **Population** | **Frequency** | **Rationale** |
| American College of Cardiology and the American Heart Association (Hunt 2009) | Serum potassium | Patients with heart failure | Not specified | Hypokalemia is a common adverse effect of treatment with Diuretics and may cause fatal arrhythmias and increase the risk of digitalis (digoxin) toxicity, whereas hyperkalemia may complicate therapy with ACE Inhibitors, ARBs, and Potassium-Sparing Diuretics (Aldosterone Antagonists) |
| Serum potassium  Renal function | Patients with heart failure | 3 days, 1 week, 3 months, and then 3 month intervals | Subsequent monitoring should be dictated by the general clinical stability of renal function and fluid status  The addition or an increase in dosage of ACE Inhibitors or ARBs should trigger a new cycle of monitoring |
| Serum potassium Renal function | Patients with heart failure | Not recommended | Under circumstances where monitoring for hyperkalemia or renal dysfunction is not anticipated to be feasible, the risks may outweigh the benefits of the therapy in patients with current or prior symptoms of heart failure |
| Institute for Clinical Systems Improvement (ICSI) | Serum potassium  Electrolytes  Renal function | Patients with heart failure and hypotension | Not specified | NA |
| Heart Failure Society of America (Lindenfeld 2010) | Serum potassium | Patients with heart failure | Varied with study | In randomized controlled trials serum potassium was monitored more frequently after initial therapy and every 6 months after the first year of Potassium-Sparing Diuretic therapy in patients with diabetes or renal insufficiency or in those taking ACE Inhibitors or ARBs |
| Serum potassium Serum creatinine | Patients with heart failure | Within first few weeks of the treatment | See above rationale. |
| Electrolytes, especially serum potassium | Patients with heart failure and with eGFR <60 ml/min, baseline serum potassium  >4.3 mEq/L, diabetes mellitus, and prior use of antiarrhythmic drugs. | Not specified | See above rationale |
| FDA Label (FDAb, 2011) | Serum electrolytes (particularly potassium)  Serum creatinine  Blood urea nitrogen | Patients taking Laxis | frequently during the first few months of therapy and periodically thereafter | NA |

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

The recommendations in from the clinical practice guidelines in the above tables are not graded.

**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.*)

N/A

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

N/A

**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)?**

Yes **→ *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)

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**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)

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

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

A systematic review of the evidence specific to this measure was conducted by the Johns Hopkins Hospital Center for Medication Quality and Outcomes. This review is not yet published. A complete summary of the systematic review including all citations and the summary of each study can be found in the Supplemental Material (Question A.1).

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

The initial search strategy included evidence-based and consensus-based guidelines, meta-analyses, and systematic reviews related to appropriate monitoring for patients with persistent use of ACE inhibitors/ARBs, digoxin, and diuretics. Upon review, the search strategy was broadened to include randomized, controlled trials and cohort studies. It also included relevant studies listed in the selected articles. Two independent reviewers evaluated all selected articles to ensure quality. Where evidence included at least one large high quality randomized controlled trial, the researchers rated the evidence “sufficient.”

The following sources were used in the review:

1. Drug Databases
2. Literature Databases: Search terms were the drug class/name and the terms persistent medications, monitoring parameters, and therapeutic monitoring. No language restrictions were used in the literature review. The reference lists of selected articles were reviewed for relevant studies.

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

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

*If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.*

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

The evidence review sought to determine appropriate monitoring for patients with persistent use of ACE inhibitors/ARBs, digoxin, and diuretics. The evidence review looked for information regarding the impact of laboratory monitoring on outcomes considered to be adverse drug events, such as kidney damage, for those with persistent use of these drugs. Evidence was reviewed on the type and frequency of monitoring deemed appropriate for each medication.

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

Not graded.

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

N/A

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: 1989 – 2013

**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*)

|  |  |  |
| --- | --- | --- |
| ACE Inhibitor/ARB | Potassium/Creatinine | 4 Retrospective Cohorts (Miao 2011; Hurley 2005; Coleman 2010; Raebel 2007)  1 RCT (Brenner 2000) |
| Digoxin | Serum Digoxin | 6 RCT (Uretsky 1993; Packer 1993; Garg 1997; Young 1998; Krum 1995; Hurley 2005) |
|  | Potassium/Creatinine | Expert consensus (Hurley 2005; Pinkerman 2013; Hunt 2009) |
| Diuretics | Potassium/Creatinine | 2 RCT (Pitt 1999); (Pitt 2003) |

Brenner BM, Cooper ME, de Zeeuw D et al. The losartan renal protection study--rationale, study design and baseline characteristics of renaal (reduction of endpoints in niddm with the angiotensin ii antagonist losartan). Journal of the renin-angiotensin-aldosterone system: JRAAS. 2000; 1(4): 328-35.

Coleman JJ, McDowell SE, Evans SJ et al. Oversight: A retrospective study of biochemical monitoring in patients beginning antihypertensive drug treatment in primary care. British journal of clinical pharmacology. 2010; 70(1): 109-17.

Garg R and Gorlin R. The effect of digoxin on mortality and morbidity in patients with heart failure. The New England Journal of Medicine. 1997; 336(8): 525-33.

Hurley JS, Roberts M, Solberg LI et al. Laboratory safety monitoring of chronic medications in ambulatory care settings. Journal of general internal medicine. 2005; 20(4): 331-3.

Hurley JS, Roberts M, Solberg LI et al. Laboratory safety monitoring of chronic medications in ambulatory care settings. Journal of general internal medicine. 2005; 20(4): 331-3.

Krum H, Bigger J, Goldsmith R et al. Effect of long-term digoxin therapy on autonomic function in patients with chronic heart failure. Journal of American College of Cardiology. 1995; 25(2): 289-94

Miao Y, Dobre D, Heerspink HJ et al. Increased serum potassium affects renal outcomes: A post hoc analysis of the reduction of endpoints in niddm with the angiotensin ii antagonist losartan (renaal) trial. Diabetologia. 2011; 54(1): 44-50.

Packer M, Gheorghiade M, Young J et al. Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting-enzyme inhibitors. The New England Journal of Medicine. 1993; 329(1): 1-7.

Pitt B, Remme W, Zannad F et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med. 2003; 348(14): 1309-21.

Pitt B, Zannad F, Remme WJ et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized aldactone evaluation study investigators. N Engl J Med. 1999; 341(10): 709-17.

Raebel MA, McClure DL, Simon SR et al. Laboratory monitoring of potassium and creatinine in ambulatory patients receiving angiotensin converting enzyme inhibitors and angiotensin receptor blockers. Pharmacoepidemiol Drug Saf. 2007; 16(1): 55-64.

Uretsky B, Young J, Shahidi F et al. Randomized study assessing the effect of digoxin withdrawal in patients with mild to moderate chronic congestive heart failure: Results of the proved trial. Journal of American College of Cardiology. 1993; 22(4): 955-62.

Young J, Gheorghiade M, Uretsky B et al. Superiority of "triple" drug therapy in heart failure: Insights from the proved and radiance trials. Journal of American College of Cardiology. 1998; 32: 686-92.

**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*)

*ACE Inhibitors or ARBs*: There is sufficient quality evidence from several retrospective cohort studies, and the Reduction in Endpoints with the Angiotensin Antagonist Losartan (RENAAL) trial that that ACE inhibitors or ARBs can increase serum potassium concentrations.

*Digoxin*: There is sufficient quality evidence from multiple RCTs to support using annual serum digoxin concentration measurement as a monitoring parameter. There is less high quality evidence (expert consensus and FDA labels) to support monitoring of serum potassium and serum creatinine during digoxin therapy, however the clinical expert consensus is that the benefits of these tests outweigh the harms.

*Diuretics*: There is sufficient quality evidence from the Randomized Aldactone Evaluation Study (RALES) trial (Pitt 1999), the Eplerenome Post-AHI Heart Failure Efficacy and Survival Study (EPHESUS) trial (Pitt 2003) and other evidence and consensus based guidelines (Lindenfeld 2010; Hunt 2009; McDowell 2013) to support using serum creatinine and serum potassium as annual monitoring parameters for patients taking diuretics.

**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*)

*ACE Inhibitors or ARBs*: Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) are commonly used medications to treat hypertension. There is sufficient evidence from several retrospective cohort studies (Miao 2011; Hurley 2005; Coleman 2010; Raebel 2007), and the Reduction in Endpoints with the Angiotensin Antagonist Losartan (RENAAL) trial that that ACE inhibitors or ARBs can increase serum potassium concentrations (Brenner 2000). High serum potassium, known as hyperkalemia is a potentially fatal condition that can alter heart function and cause arrhythmias. Additionally, ACE inhibitors and ARBs can decrease renal function, for which serum creatinine is a commonly used clinical marker (Gottlieb 1992; Packer 1987; Burnier 1989; Hurley 2005; Coleman 2010; Raebel 2007). Therefore, serum potassium and serum creatinine are clinically useful monitoring parameters for these potentially serious safety concerns associated with the use of these drugs. Typically, if hyperkalemia or decreased renal function are observed, more frequent monitoring may be conducted or ACE inhibitor or ARB therapy may be withdrawn. The frequency of monitoring is dependent on the amount of time an individual has been taking the medication, but annual monitoring is the minimum appropriate frequency (McDowell 2013).

*Digoxin*: Digoxin is used to treat heart failure and abnormal heart rhythms. The evidence from multiple RCTs supports using an annual serum digoxin concentration measurement as a monitoring parameter (Uretsky 1993; Packer 1993; Garg 1997; Young 1998; Krum 1995; Hurley 2005). Digoxin toxicity is known to be a serious (potentially fatal) safety concern and there are a number of factors (e.g., decreased renal function or changes in serum electrolyte concentrations) that may precipitate toxicity, even in the setting of a stable dose over time. Although we recommend monitoring of serum potassium and serum creatinine during digoxin therapy, the clinical evidence to support this recommendation is less strong. However, it is generally accepted and agreed upon that hypokalemia poses a serious and potentially fatal risk to patients taking digoxin and diuretics (Hurley 2005; Pinkerman 2013; Hunt 2009). Additionally, digoxin is renally excreted therefore monitoring serum creatinine is critical for determining how quickly digoxin is being excreted. This is important for determining whether digoxin levels need to be adjusted based on renal function.

*Diuretics*: Diuretics are used to modify fluid volume in the body and correct fluid imbalances, which are commonly seen in patients with heart- and kidney-related conditions. Diuretics are used to improve liver, kidney and cardiac function. The evidence from the Randomized Aldactone Evaluation Study (RALES) trial (Pitt 1999), the Eplerenome Post-AHI Heart Failure Efficacy and Survival Study (EPHESUS) trial (Pitt 2003) and other evidence and consensus based guidelines (Lindenfeld 2010; Hunt 2009; McDowell 2013) supports using serum creatinine and serum potassium as annual monitoring parameters for patients taking diuretics. Hypokalemia (decreased potassium level) is a common adverse effect of treatment with diuretics and may cause fatal arrhythmias and increase the risk of digitalis (digoxin) toxicity. Hyperkalemia (increased potassium levels) may complicate therapy with ACE inhibitors, ARBs, and potassium-sparing diuretics (aldosterone antagonists) (Hunt 2009; Juurlink 2003; Juurlink 2004; Scensson 2004).

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

There were no harms associated with regular monitoring of serum potassium, serum creatinine and serum digoxin.

**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**.

The systematic review was conducted in Fall 2013, no additional studies have been published between time of systematic review and submission of this form in January 2014.

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**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.*

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

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