Cohort Study
Potential PURL Review Form
PURL Jam Version

PURLs Surveillance System
Family Physicians Inquiries Network

SECTION 1: Identifying Information for Nominated Potential PURL

A. Citiation: Juraschek SP, Daya N, Rawlings AM, Appel LJ, Miller ER 3rd, Windham BG, Griswold ME, Heiss G, Selvin E. Association of History of Dizziness and Long-term Adverse Outcomes With Early vs Later Orthostatic Hypotension Assessment Times in Middle-aged Adults. JAMA Intern Med. 2017 Sep 1;177(9):1316-1323. doi: 10.1001/jamainternmed.2017.2937. PubMed PMID: 28738139
B. Link to PubMed Abstract: https://www.ncbi.nlm.nih.gov/pubmed/?term=28738139
C. First date published study available to readers:9/1/2017
D. PubMed ID: 28738139
E. Nominated By: Jim Stevermer
F. Institutional Affiliation of Nominator: University of Missouri
G. Date Nominated: 7/24/2017
H. Identified Through: JAMA Internal Medicine
I. PURLs Editor Reviewing Nominated Potential PURL: Dean Seehusen
J. Nomination Decision Date: 8/5/2017
K. Potential PURL Review Form (PPRF) Type: Cohort Study
L. Assigned Potential PURL Reviewer: Bob Marshall
M. Reviewer Affiliation: Madigan Army Medical Center
A. Abstract: IMPORTANCE:
Guidelines recommend assessing orthostatic hypotension (OH) 3 minutes after rising from supine to standing positions. It is not known whether measurements performed immediately after standing predict adverse events as strongly as measurements performed closer to 3 minutes.

OBJECTIVE:
To compare early vs later OH measurements and their association with history of dizziness and longitudinal adverse outcomes.

DESIGN, SETTING, AND PARTICIPANTS:
This was a prospective cohort study of middle-aged (range, 44-66 years) participants in the Atherosclerosis Risk in Communities Study (1987-1989).

EXPOSURES:
Orthostatic hypotension, defined as a drop in blood pressure (BP) (systolic BP ≥20 mm Hg or diastolic BP ≥10 mm Hg) from the supine to standing position, was measured up to 5 times at 25-second intervals.

MAIN OUTCOMES AND MEASURES:
We determined the association of each of the 5 OH measurements with history of dizziness on standing (logistic regression) and risk of fall, fracture, syncope, motor vehicle crashes, and all-

cause mortality (Cox regression) over a median of 23 years of follow-up (through December 31, 2013).

RESULTS:
In 11 429 participants (mean age, 54 years; 6220 [54%] were women; 2934 [26%] were black) with at least 4 OH measurements after standing, after adjustment OH assessed at measurement 1 (mean [SD], 28 [5.4] seconds; range, 21-62 seconds) was the only measurement associated with higher odds of dizziness (odds ratio [OR], 1.49; 95% CI, 1.18-1.89). Measurement 1 was associated with the highest rates of fracture, syncope, and death at 18.9, 17.0, and 31.4 per 1000 person-years. Measurement 2 was associated with the highest rate of falls and motor vehicle crashes at 13.2 and 2.5 per 1000 person-years. Furthermore, after adjustment measurement 1 was significantly associated with risk of fall (hazard ratio [HR], 1.22; 95% CI, 1.03-1.44), fracture (HR, 1.16; 95% CI, 1.01-1.34), syncope (HR, 1.40; 95% CI, 1.20-1.63), and mortality (HR, 1.36; 95% CI, 1.23-1.51). Measurement 2 (mean [SD], 53 [7.5] seconds; range, 43-83 seconds) was associated with all long-term outcomes, including motor vehicle crashes (HR, 1.43; 95% CI, 1.04-1.96). Measurements obtained after 1 minute were not associated with dizziness and were inconsistently associated with individual long-term outcomes.

CONCLUSIONS AND RELEVANCE:
In contrast with prevailing recommendations, OH measurements performed within 1 minute of standing were the most strongly related to dizziness and individual adverse outcomes, suggesting that OH be assessed within 1 minute of standing.

B. Pending PURL Review Date**:** 10/1/2018

SECTION 2: Critical Appraisal of Validity

A. The study address an appropriate and clearly focused question. Well covered
Comments:

B. The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation. Not applicable
Comments:

C. The study indicates how many of the people asked to take part in it in each of the groups being studied. Well covered
Comments:

D. The likelihood that some eligible subjects might have the outcome at the time of enrollment is assessed and taken into account in the analysis. Not applicable
Comments:

E. What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed? Not applicable as there are not different arms of the study.

F. Comparison is made between full participants and those lost to follow up, by exposure status. Not applicable
Comments:

G. The outcomes are clearly defined. Well covered
Comments:

H. The assessment of outcome is made blind to exposure status. Not applicable
Comments:

I. Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome. Not applicable
Comments:

J. What are the key findings of the study? Measurement earlier than the current CPG is recommended and correlates with meaningful outcomes.

K. How was the study funded? Any conflicts of interest? Any reason to believe that the results may be influenced by other interests? This study was supported by a NIH/NIDDK Renal Disease Epidemiology Training Grant, and a collaborative study by the National Heart, Lung, and Blood Institute contract. No apparent conflict of interest. There is currently no evidence that supports any belief of influence from other interests.

SECTION 3: Review of Secondary Literature

A. DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995-. Record No. 114777, Orthostatic hypotension and orthostatic syncope; [updated 2018 Jul 31, cited 24 Sep 2018]; Available at http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=114777. Registration and login required.

B. Bottom line recommendation or summary of evidence from DynaMed: Classic orthostatic hypotension is ascertained by blood pressure measurement within three minutes of standing.

C. UpToDate. Editor: Basow DS. Literature review current through: Aug 2018. Access date: 25 Sep 2018. Title: Mechanisms, causes, and evaluation of orthostatic hypotension. Author: Kaufmann, Horacio, MD. In: UpToDate [database online]. Available at: http://www.uptodate.com. Last updated: Jun 05, 2015

D. Bottom line recommendation or summary of evidence from UpToDate: Postural (orthostatic) hypotension is diagnosed within two to five minutes of quiet standing (after a five minute period of supine rest).

E. Other excerpts: EFNS task force article

F. Citation Lahrmann, H. Portelli, P. Hilz, M. Mathias, C.J. Struhal, W. Tassinari. EFNS guidelines on the diagnosis and management of orthostatic hypotension; *European Journal of Neurology* 2006, 13: 930-936. doi:10.1111/j.1468-1331.2006.01512.x

G. Bottom line recommendation or summary of evidence from Neurology: Orthostatic hypotension (OH) is a reduction of systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg within 3 minutes of standing.

SECTION 4: Conclusions

A. **Validity**: Are the findings scientifically valid? Yes

B. If **A** was coded "Other, explain or No", please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results? N/A

C. **Relevance**: Is the topic relevant to the practice of family medicine and primary care practice, including outpatient, inpatient, obstetrics, emergency and long-term care? Are the patients being studied sufficiently similar to patients cared for in family medicine and primary care in the US such that results can be generalized?
Yes

D. If **C** was coded "Other, explain or No", please provide an explanation.

E. **Practice changing potential**: If the findings of the study are both valid and relevant, are they not a currently widely accepted recommendation among family physicians and primary care clinicians for whom the recommendation is relevant to their patient care? Or are the findings likely to be a meaningful variation regarding awareness and acceptance of the recommendation?
Yes

F. If **E** was coded as "Yes", please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

This has the potential to change practice as this demonstrates outcomes that can be reasonably predicted from earlier blood pressure measurement. Blood pressure measurements should be taken early and often and have the potential to impact patient outcomes.

G. **Applicability to a Family Medical Care Setting**:
Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc.), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or

referring for a procedure; advising, education or counseling a patient; or creating a system for implementing an intervention? Yes

H. Please explain your answer to **G**.

Taking orthostatic blood pressure measurements are easy to perform and commonly done in the office setting and should be done earlier compared to the current standard practice (waiting 2-3 minutes).

I. **Immediacy of Implementation**:
Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug, or other essentials available on the market? No

J. If **I** was coded "Other, explain or No", please explain why.

There are no major barriers to implementation. The cost/reimbursement of immediate implementation is not prohibitive.

K. **Clinically meaningful outcomes or patient oriented outcomes**:
Do the expected benefits outweigh the expected harms? Are the outcomes patient oriented (as opposed to disease oriented)? Are the measured outcomes, if true, clinically meaningful from a patient perspective?
Yes

L. If **K** was coded "Other, explain or No", please explain why.

M. In your opinion, is this a pending PURL? Yes

1. Valid: Strong internal scientific validity; the findings appear to be true.
2. Relevant: Relevant to the practice of family medicine.
3. Practice Changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
4. Applicability in medical setting.
5. Immediacy of implementation

N. Comments on your response for question M.
While this is practice changing, this study is focused on middle aged adults (age 44-66) and may not be generalizable to individuals outside this age group. One limitation is that they did not

differentiate those in the study who may have met the criteria at the later intervals. It would have been helpful to exclude those with diagnostic orthostatic hypotension by the current guidelines.