**Metaanalysis – Systematic Review**

**Potential PURL Review Form**

**It’s time to use an age-based approach to D-dimer (*J Fam Pract*. 2014;63:155-156,158)**

**PURL Jam Version**

**Version #12 Sept 21, 2010**

**PURLs Surveillance System**

**Family Physicians Inquiries Network**

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| **SECTION 1: Identifying Information for Nominated Potential PURL** **[to be completed by PURLs Project Manager]** |
| **1.** Citation  | Schouten HJ, Geersing GJ, Koek HL, Zuithoff NP, Janssen KJ, Douma RA, vanDelden JJ, Moons KG, Reitsma JB. Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. BMJ. 2013 May 3;346:f2492. doi: 10.1136/bmj.f2492. PubMed PMID: 23645857; PubMed Central PMCID: PMC3643284. |
| **2.** Hypertext link to PDF of full article  | http://www.ncbi.nlm.nih.gov/pubmed/?term=23645857 |
| **3.** First date published study available to readers  | 5/3/13 |
| **4.** PubMed ID  | 23645857 |
| **5.** Nominated By  | Jim Stevermer Other:  |
| **6.** Institutional Affiliation of Nominator  | University of Missouri Other:  |
| **7.** Date Nominated  | 5/22/13 |
| **8.** Identified Through  | Other Other: BMJ TOC |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland |
| **10.** Nomination Decision Date  | 5/31/13 |
| **11.** Potential PURL Review Form (PPRF) Type  | Metaanalysis |
| **12.** Other comments, materials or discussion  |  |
| **13.** Assigned Potential PURL Reviewer  | Kate Kirley |
| **14.** Reviewer Affiliation  | University of Chicago Other:  |
| **15.** Date Review Due  | 6/27/13 |
| **16.** Abstract  | OBJECTIVE:To review the diagnostic accuracy of D-dimer testing in older patients (>50 years) with suspected venous thromboembolism, using conventional or age adjusted D-dimer cut-off values.DESIGN:Systematic review and bivariate random effects meta-analysis.DATA SOURCES:We searched Medline and Embase for studies published before 21 June 2012 and we contacted the authors of primary studies.STUDY SELECTION:Primary studies that enrolled older patients with suspected venous thromboembolism in whom D-dimer testing, using both conventional (500 µg/L) and age adjusted (age×10 µg/L) cut-off values, and reference testing were performed. For patients with a non-high clinical probability, 2×2 tables were reconstructed and stratified by age category and applied D-dimer cut-off level.RESULTS:13 cohorts including 12,497 patients with a non-high clinical probability were included in the meta-analysis. The specificity of the conventional cut-off value decreased with increasing age, from 57.6% (95% confidence interval 51.4% to 63.6%) in patients aged 51-60 years to 39.4% (33.5% to 45.6%) in those aged 61-70, 24.5% (20.0% to 29.7%) in those aged 71-80, and 14.7% (11.3% to 18.6%) in those aged >80. Age adjusted cut-off values revealed higher specificities over all age categories: 62.3% (56.2% to 68.0%), 49.5% (43.2% to 55.8%), 44.2% (38.0% to 50.5%), and 35.2% (29.4% to 41.5%), respectively. Sensitivities of the age adjusted cut-off remained above 97% in all age categories.CONCLUSIONS:The application of age adjusted cut-off values for D-dimer tests substantially increases specificity without modifying sensitivity, thereby improving the clinical utility of D-dimer testing in patients aged 50 or more with a non-high clinical probability. |
| **17.** Pending PURL Review Date | 6/27/13 |
| **sECTION 2: Critical Appraisal of Validity****[to be completed by the Potential PURL Reviewer]** |
| **1.** What types of studies are included in this review? | Other Other: Diagnostic cohort |
| **2.** What is the key question addressed by this review? Summarize the main conclusions and any strengths or weaknesses. | Do age-specific cut-offs for D-dimer improve the specificity of diagnosing VTE among patients with non-high clinical probability of VTE?Use of age-specific cut-offs (100 mcg/L per decade) has significantly better specificities for the diagnoses of VTE without any statistically-significant decrease in sensitivity. Specificities for conventional cut-off versus age-specific cut-off:-age 51-60: 57.6% v 62.3%, *P*= 0.005-age 61-70: 39.4% v. 49.5%, *P*<0.001-age 71-80: 24.5% v. 44.2%, *P*<0.001-age >80:    14.7% v. 35.2%, *P*<0.001A substantial number of unnecessary imaging studies could be avoided, particularly among the elderly, by using age-specific cut-offs.Strengths: well-powered, minimal heterogeneity which is explored and well-accounted forWeaknesses: The reference (gold-standard) did not uniformly include imaging so their may be overestimation of diagnostic accuracy, but any missed cases were clinically silent so this may not matter.  Also, they lumped together patients with suspected PE and DVT into one large cohort, but their analyses explored whether this might affect results, and it does not appear to be problematic. |
| **3.** Study addresses an appropriate and clearly focused question - ***select one*** | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments:  |
| **4.** A description of the methodology used is included. | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments:  |
| **5.** The literature search is sufficiently rigorous to identify all the relevant studies. | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments:  |
| **6.** Study quality is assessed and taken into account. | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments: Study quality was generally good, according to QUADAS-2 |
| **7.** There are enough similarities between selected studies to make combining them reasonable. | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments:  |
| **8.** Are patient oriented outcomes included? If yes, what are they? | This is a diagnostic study, so sensitivity and specificity are the primary outcomes. However, the authors employ a hypothetical cohort to estimate the number of unnecessary imaging studies that are avoided and the number of cases of VTE that would be missed using age-specific cut-offs. |
| **9.** Are adverse effects addressed? If so, how would they affect recommendations? | Again, a diagnostic study, but to explore the chance of missing a case of VTE, which is low and outweighed by the benefit of avoiding a large number of unnecessary tests. |
| **10.** Is funding a potential source of bias? If yes, what measures (if any) were taken to insure scientific integrity?  | No |
| **11.** To which patients might the findings apply? Include patients in the meta-analysis and other patients to whom the findings may be generalized. | Patients >50 with non-high clinical risk for VTE. Patients in ED or primary care. |
| **12.** In what care settings might the findings apply, or not apply? | ED and primary care |
| **13.** To which clinicians or policy makers might the findings be relevant? | ED physicians, primary care physicians, clinical pathologists |
| **SECTION 3: Review of Secondary Literature****[to be completed by the Potential PURL Reviewer]** |
| **Citation Instructions** | For UpTo Date citations, use style modified from <http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite> & AMA style. Always use Basow DS as editor & current year as publication year.EXAMPLE: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: <http://www.uptodate.com>.  {Insert dated modified if given.} Accessed February 12, 2009. {whatever date PPRF reviewer did their search.}For DynaMed, use the following style:Depression: treatment {insert search terms or title}. In: DynaMed [database online]. Available at: <http://www.DynamicMedical.com>. Last updated February 4, 2009. {Insert dated modified if given.}  Accessed June 5, 2009.{search date} |
| **1.** DynaMed excerpts |  |
| **2.** DynaMed citation/access date | Title. D-dimer testing for venous thromboembolism Author. In: DynaMed [database online]. Available at: [www.DynamicMedical.com](http://www.DynamicMedical.com) Last updated: 6/10/13. Accessed: 6/25/13 |
| **3.**  Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences) | They summarize this specific article and call it mid-level evidence. |
| **4.** UpToDate excerpts |  |
| **5.** UpToDate citation/access date | Always use Basow DS as editor & current year as publication year.Title: Diagnosis of acute pulmonary embolism Author: Thompson BT, Hales CA In: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: 2/5/13. Accessed: 6/25/13 |
| **6.**  Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences) | Nothing about age-specific cut-offs. |
| **7.** PEPID PCP excerpts[www.pepidonline.com](http://www.pepidonline.com)username: fpinauthorpw: pepidpcp | Use only to r/o DVT, NOT to confirm DVTPatients with low-to-moderate risk and Wells DVT score <2Negative D-dimer assay rules out DVT |
| **8.** PEPID citation/access data | Author. Title: D-dimer testing In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated:. Accessed 6/26/13 |
| **9.** PEPID content updating | 1. Do you recommend that PEPID get updated on this topic?[x]  Yes, there is important evidence or recommendations that are missing[ ]  No, this topic is current, accurate and up to date.If yes, which PEPID Topic, Title(s): D-dimer testing2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon () that should be updated on the basis of the review?[ ]  Yes, there is important evidence or recommendations that are missing[ ]  No, this topic is current, accurate and up to date.If yes, which Evidence Based Inquiry(HelpDesk Answer or Clinical Inquiry), Title(s):  |
| **10.** Other excerpts (USPSTF; other guidelines; etc.) |  |
| **11.** Citations for other excerpts |  |
| **12.**  Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences) |  |
| **SECTION 4: Conclusions** **[to be completed by the Potential PURL Reviewer]** **[to be revised by the Pending PURL Reviewer as needed]** |
| **1.** **Validity:** How well does the study minimize sources of internal bias and maximize internal validity? | Give one number on a scale of 1 to 7(1=extremely well; 4=neutral; 7=extremely poorly)[x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **2.** If 4.1 was coded as 4, 5, 6, or 7, 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? |  |
| **3. Relevance:** Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians?  | Give one number on a scale of 1 to 7(1=extremely well; 4=neutral; 7=extremely poorly)[x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **4.** If 4.3 was coded as 4, 5, 6, or 7,lease provide an explanation. |  |
| **5. Practice changing potential:** If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? | Give one number on a scale of 1 to 7(1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)[x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **6.** If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit. |  |
| 1. **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, educating or counseling a patient; or creating a system for implementing an intervention? | Give one number on a scale of 1 to 7(1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **8.** If you coded 4.7 as a 4, 5, 6 or 7, please explain.  |  |
| **9. 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? | Give one number on a scale of 1 to 7(1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **10.** If you coded 4.9 as 4, 5, 6, or 7, please explain why. |  |
| **11. Clinical meaningful outcomes or patient oriented outcomes:**  Are the outcomes measured in the study clinically meaningful or patient oriented?  | Give one number on a scale of 1 to 7(1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **12.** If you coded 4.11 as a 4, 5, 6, or 7, please explain why. |  |
| **13.** In your opinion, is this a Pending PURL? Criteria for a Pending PURL:* Valid: Strong internal scientific validity; the findings appears to be true.
* Relevant: Relevant to the practice of family medicine
* 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.
* Applicability in medical setting:
* Immediacy of implementation
 | Give one number on a scale of 1 to 7(1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL) [x] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6 [ ] 7  |
| **14.** Comments on your response in 4.13 | No validity concerns. Meets all criteria. |
| **SECTION 4.1: Diving for PURLs** **[optional for the potential PURL reviewer -if you wish to be the author on the summary]** |
| **1.** Study Summary- Please summarize the study in 5-7 sentences |  |
| 1. Criteria- note yes or no for those which this study meets

 | RELEVENT - VALID - CHANGE IN PRACTICE- MEDICAL CARE SETTING - IMMEDIATELY APPLICABLE - CLINICALLY MEANINGFUL -  |
| **3.** Bottom Line- one –two sentences noting the bottom line recommendation  |  |
| **4.** Title Proposal |  |
| **SECTION 5: Editorial Decisions** **[to be completed by the FPIN PURLs Editor or Deputy Editor]** |
| **1.** FPIN PURLs editorial decision(select one) | [ ]  1 Pending PURL Review—Schedule for Review [ ]  2 Drop [ ]  3 Pending PURL |
| **2.** Follow up issues for pending PURL Reviewer |  |
| **3.** FPIN PURLS Editor making decision  | [ ] 1 Bernard Ewigman[ ] 2 Sarah-Anne Schumann[ ] 3 John Hickner[ ] 4 Kate Rowland |
| **4.** Date of decision |  |
| **5.** Brief summary of decision |  |
| **SECTION 6: Survey Questions for SERMO, PURLs Instant Polls and Other Surveys****[To be completed by the PURLs Survey Coordinator and PURLs Editor]** |
| **1.** Current Practice Question for Surveys |  |
| **2.** Barriers to Implementation Question for Surveys |  |
| **3.** Likelihood of Change Question for Surveys |  |
| **4.** Other Questions for Surveys |  |
| **SECTION 7: Variables for Secondary Database Analyses**  |
| **1.** Population: Age, gender, race, ethnicity |  |
| **2.** Diagnoses |  |
| **3.** Drugs or procedures |  |
| **SECTION 8: Pending PURL Review Assignment****[to be completed by PURLs Project Manager]** |
| **1.** Person Assigned for  Pending PURL Review |  |
| **2.** Date Pending PURL Review is due |  |
| **SECTION 9: Pending PURL Review** **[to be completed by PURLs Pending PURL Reviewer]** |
| **1.** Did you address the follow up issues identified at the PURL Jam (Section 5.2). Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:  |
| **2.** Did you review the Sermo poll & Instant Poll results (if available)? Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:  |
| **3.** Did you modify Sections 2, 3, or 4? Add comments as needed. | [ ]  Yes[ ]  No[ ]  Not applicable Comments:   |

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| **SECTION 10: PURL Authoring Template** **[to be completed by the assigned PURL Author]** |
| **Author Citation Information** (Name, Degrees, Affiliation) |  |
| **1.** Practice Changer |  |
| **2.** Illustrative Case |  |
| **3.** Clinical Context |  |
| **4.** Study Summary |  |
| **5.** What’s New |  |
| **6.** Caveats |  |
| **7.** Challenges to Implementation |  |
| **8.**  Acknowledgment Sentence | The PURLs Surveillance System is supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.**If using UHC data:**We acknowledge Sofia Medvedev of University HealthSystem Consortium (UHC) in Oak Brook, IL for analysis of the National Ambulatory Medical Care Survey data. |
| **9.** References |  |