**RCT**

**Potential PURL Review Form**

**PURL Jam Version**

**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]**  **Steroids for COPD—but for how long? *J Fam Pract.* 2014;63:29-32.** | | | | | | | |
| **1.** Citation | Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial.  Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T, Duerring U, Henzen C, Leibbrandt Y, Maier S, Miedinger D, Müller B, Scherr A, Schindler C, Stoeckli R, Viatte S, von Garnier C, Tamm M, Rutishauser J.  JAMA. 2013 Jun 5;309(21):2223-31. doi: 10.1001/jama.2013.5023.  PMID:  23695200 | | | | | | |
| **2.** Hypertext link to PDF of full article | http://www.ncbi.nlm.nih.gov/pubmed/?term=Short-term+vs+Conventional+Glucocorticoid+Therapy+in+Acute+Exacerbations+of+Chronic+Obstructive+Pulmonary+Disease+The+REDUCE+Randomized+Clinical+Trial+Leuppi+JD%2C+etal | | | | | | |
| **3.** First date published study available to readers | 6/5/13 | | | | | | |
| **4.** PubMed ID | 23695200 | | | | | | |
| **5.** Nominated By | Other: | | | | | | |
| **6.** Institutional Affiliation of Nominator | Other: | | | | | | |
| **7.** Date Nominated | 5/22/13 | | | | | | |
| **8.** Identified Through | Other: JAMA | | | | | | |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland | | | | | | |
| **10.** Nomination Decision Date | 5/31/13 | | | | | | |
| **11.** Potential PURL Review Form (PPRF) Type | RCT | | | | | | |
| **12.** Other comments, materials or discussion |  | | | | | | |
| **13.** Assigned Potential PURL Reviewer | Anne Mounsey, MD | | | | | | |
| **14.** Reviewer Affiliation | Other: UNC | | | | | | |
| **15.** Date Review Due | 7/24/13 | | | | | | |
| **16.** Abstract | International guidelines advocate a 7- to 14-day course of systemic glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease (COPD). However, the optimal dose and duration are unknown.  OBJECTIVE:  To investigate whether a short-term (5 days) systemic glucocorticoid treatment in patients with COPD exacerbation is noninferior to conventional (14 days) treatment in clinical outcome and whether it decreases the exposure to steroids. DESIGN, SETTING, AND PATIENTS REDUCE: (Reduction in the Use of Corticosteroids in Exacerbated COPD), a randomized, noninferiority multicenter trial in 5 Swiss teaching hospitals, enrolling 314 patients presenting to the emergency department with acute COPD exacerbation, past or present smokers (≥20 pack-years) without a history of asthma, from March 2006 ntthrough February 2011.  INTERVENTIONS:  Treatment with 40 mg of prednisone daily for either 5 or 14 days in a placebo-controlled, double-blind fashion. The predefined noninferiority criterion was an absolute increase in exacerbations of at most 15%, translating to a critical hazard ratio of 1.515 for a reference event rate of 50%. MAIN OUTCOME AND MEASURE: Time to next exacerbation within 180 days.  RESULTS:  Of 314 randomized patients, 289 (92%) of whom were admitted to the hospital, 311 were included in the intention-to-treat analysis and 296 in the per-protocol analysis. Hazard ratios for the short-term vs conventional treatment group were 0.95 (90% CI, 0.70 to 1.29; P = .006 for noninferiority) in the intention-to-treat analysis and 0.93 (90% CI, 0.68 to 1.26; P = .005 for noninferiority) in the per-protocol analysis, meeting our noninferiority criterion. In the short-term group, 56 patients (35.9%) reached the primary end point; 57 (36.8%) in the conventional group. Estimates of reexacerbation rates within 180 days were 37.2% (95% CI, 29.5% to 44.9%) in the short-term; 38.4% (95% CI, 30.6% to 46.3%) in the conventional, with a difference of -1.2% (95% CI, -12.2% to 9.8%) between the short-term and the conventional. Among patients with a reexacerbation, the median time to event was 43.5 days (interquartile range [IQR], 13 to 118) in the short-term and 29 days (IQR, 16 to 85) in the conventional. There was no difference between groups in time to death, the combined end point of exacerbation, death, or both and recovery of lung function. In the conventional group, mean cumulative prednisone dose was significantly higher (793 mg [95% CI, 710 to 876 mg] vs 379 mg [95% CI, 311 to 446 mg], P < .001), but treatment-associated adverse reactions, including hyperglycemia and hypertension, did not occur more frequently.  CONCLUSIONS AND RELEVANCE:  In patients presenting to the emergency department with acute exacerbations of COPD, 5-day treatment with systemic glucocorticoids was noninferior to 14-day treatment with regard to reexacerbation within 6 months of follow-up but significantly reduced glucocorticoid exposure. These findings support the use of a 5-day glucocorticoid treatment in acute exacerbations of COPD. | | | | | | |
| **17.** Pending PURL Review Date |  | | | | | | |
| **sECTION 2: Critical Appraisal of Validity**  **[to be completed by the Potential PURL Reviewer]**  **[to be revised by the Pending PURL Reviewer if needed]** | | | | | | | |
| **1.** Number of patients starting each arm of the study? | | 157 | | | | | |
| **2.** Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | | COPD patients presenting to the ED of 1 of 5 Swedish teaching hospitals with at least 2 of the following: change in baseline dyspnea, cough, or sputum quantity or purulence,15- 16 age older than 40 years, and a smoking history of 20 pack-years or more.Exclusion criteria were a history of asthma, ratio of FEV1 to forced vital capacity (FVC) greater than 70% as evaluated by bedside postbronchodilator spirometry prior to randomization, radiological diagnosis of pneumonia, estimated survival of less than 6 months due to severe comorbidity, pregnancy or lactation, and inability to give written informed consent. | | | | | |
| **3.** Intervention(s) being investigated? | | Methyl pred iv 40mg day 1 followed by Prednisone 40 mg qd from day 2-5  followed by matching placebo days 6-14. | | | | | |
| **4.** Comparison treatment(s), placebo, or nothing? | | Methyl pred iv day 1 then prednisone 40mg qd days 2-14y | | | | | |
| **5.** Length of follow up? Note specified end points e.g. death, cure, etc. | | 180 days | | | | | |
| **6.** What outcome measures are used? List all that assess effectiveness. | | The primary end point of this trial was time to next COPD exacerbation during a follow-up of 6 months, defined as an acute clinical deterioration beyond usual day-to-day variation, requiring interaction with a clinician | | | | | |
| **7.** What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc. | | A total of 56 patients (35.9%) reached the primary end point of COPD exacerbation in the short-term treatment group compared with 57 patients (36.8%) in the conventional treatment group. Time to reexacerbation did not differ between groups as demonstrated in the Kaplan-Meier plots. In a Cox regression analysis, the HR of reexacerbation between the short-term and conventional treatment group was 0.95 (90% CI, 0.70 to 1.29; P = .006) in the intention-to-treat and 0.93 (90% CI, 0.68 to 1.26; P = .005) in the per-protocol analysis, meeting our noninferiority criterion | | | | | |
| **8.** What are the adverse effects of intervention compared with no intervention? | | None | | | | | |
| **9.** Study addresses an appropriate and clearly focused question - ***select one*** | | Well covered  Adequately addressed  Poorly addressed  Not applicable    Comments: | | | | | |
| **10.** Random allocation to comparison groups | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: | | | | | |
| **11.** Concealed allocation to comparison groups | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: | | | | | |
| **12.** Subjects and investigators kept “blind” to comparison group allocation | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: | | | | | |
| **12.** Comparison groups are similar at the start of the trial | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: More women in conventiuonal group: 46.5% vs. 32.7% | | | | | |
| **14.** Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias. | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: More smokers in short-term treatment group favors the null hypothesis | | | | | |
| **15.** Were all relevant outcomes measured in a standardized, valid, and reliable way? | | Well covered  Adequately addressed  Poorly addressed  Not applicable  Comments: | | | | | |
| **16.** Are patient oriented outcomes included? If yes, what are they? | | Yes, COPD exacerbations | | | | | |
| **17.** What percent dropped out, and were lost to follow up? Could this bias the results? How? | | <4%; low dropout rate unlikely source of bias. Dropout was nondifferential | | | | | |
| **18.** Was there an intention-to-treat analysis? If not, could this bias the results? How? | | Yes | | | | | |
| **19.** If a multi-site study, are results comparable for all sites? | | Unknown | | | | | |
| **20.** Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity? | | No | | | | | |
| **21.** To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized. | | Patients presenting to ED with COPD exacerbation | | | | | |
| **22.** In what care settings might the findings apply, or not apply? | | Primary care | | | | | |
| **23.** To which clinicians or policy makers might the findings be relevant? | | Primary care physicians and ED physicians | | | | | |
| **SECTION 3: Review of Secondary Literature**  **[to be completed by the Potential PURL Reviewer]**  **[to be revised by the Pending PURL Reviewer as needed]** | | | | | | | |
| **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.       Author.       In: DynaMed [database online]. Available at: [www.DynamicMedical.com](http://www.DynamicMedical.com) Last updated:      . Accessed | | | |
| **3.**  Bottom line recommendation or summary of evidence from DynaMed  (1-2 sentences) | | | | |  | | | |
| **4.** UpToDate excerpts | | | | |  | | | |
| **5.** UpToDate citation/access date | | | | | | Title. Management of acute exacerbations of COPD. Author. James Stoller IN:: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: May 2012. Accessed 06/25/2013 | | |
| **6.**  Bottom line recommendation or summary of evidence from UpToDate  (1-2 sentences) | | | Most exacerbations are treated with full dose therapy | | | | |
| **7.** PEPID PCP excerpts  [www.pepidonline.com](http://www.pepidonline.com)  username: fpinauthor  pw: pepidpcp | | |                 PO or IV                  Oral steroids associated with similar outcomes as intravenous (IV) steroids                  Ideal dose unknown                  40 mg prednisone qD 10-14 days effective                  Less side effects than higher doses | | | | |
| **8.** PEPID citation/access data | | | Author. Malaty and Ewigman Title. COPD In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated:. Accessed 06/25/2012 | | | | |
| **9.** PEPID content updating | | | 1. Do you recommend that PEPID get updated on this topic?  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):    2. 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.) | | | GOLD guidelines recommend 10-14 days of 30-40 mg prednisone | | | | |
| **11.** Citations for other excerpts | | |  | | | | |
| **12.**  Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences) | | | All recommend >5 days prednisone | | | | |
| **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)  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)  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)  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. | | | | Use of 5 day steroid course instead of 10-14 days for COPD exacerbation | | | |
| 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)  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)  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)  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)  1 2 3 4 5 6 7 | | | |
| **14.** Comments on your response in 4.13 | | | |  | | | |
| **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 | | | | REDUCE studied the use of 5-day versus 14-day administration of corticosteroids in adult patients with COPD exacerbation that presented to the Emergency Department at 5 Swedish teaching hospitals.  All consecutive patients between March 2006 – February 2011 with COPD exacerbation, aged 40 years and older, and at least 20 pack-years of smoking history were considered eligible.  COPD exacerbation was defined as presence of at least 2 of the following: change in baseline dyspnea, cough, or sputum quantity or purulence.  Patients with asthma, FEV1:FVC > 70%, pneumonia, estimated survival less than 6 months due to comorbidities and pregnant/lactating patients were excluded.  Time to next COPD exacerbation did not differ between the study groups (HR 0.95, 90% CI: 0.70 – 1.29).  Similar results were obtained in sensitivity analyses. | | | |
| 1. Criteria- note yes or no for those which this study meets | | | | RELEVENT - Yes VALID - Yes CHANGE IN PRACTICE- Yes  MEDICAL CARE SETTING – Yes  IMMEDIATELY APPLICABLE – Yes  CLINICALLY MEANINGFUL - Yes | | | |
| **3.** Bottom Line- one –two sentences noting the bottom line recommendation | | | | Five-day steroid course is noninferior to 10 to 14-day treatment | | | |
| **4.** Title Proposal | | | | Steroids for COPD exacerbation – Long versus short course treatment | | | |
| **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 Pending PURL—Forward to JFP Editor  3 Drop | | | |
| 1. 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 the 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.** Background/  Clinical Context/Introduction/Current Practice/ |  |
| **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 |  |