**Meta-analysis – Systematic Review**

**Potential PURL Review Form**

**PURL Jam Version**

**Version #12 Sept 21, 2010**

**Think twice about nebulizers for asthma attacks**

***J Fam Pract*. 2014;63:321-322,346.**

**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  | Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma.Cates CJ, Welsh EJ, Rowe BH.Cochrane Database Syst Rev. 2013 Sep 13;9:CD000052.PMID: 24037768 |
| **2.** Hypertext link to PDF of full article  | http://www.ncbi.nlm.nih.gov/pubmed/?term=24037768 |
| **3.** First date published study available to readers  | 9/13/13 |
| **4.** PubMed ID  | 24037768 |
| **5.** Nominated By  | Jim Stevermer Other:  |
| **6.** Institutional Affiliation of Nominator  | University of Missouri Other:  |
| **7.** Date Nominated  | 10/2/13 |
| **8.** Identified Through  | Evidence Updates Other:  |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland |
| **10.** Nomination Decision Date  | 10/10/13 |
| **11.** Potential PURL Review Form (PPRF) Type  | Meta-analysis |
| **12.** Other comments, materials or discussion  |  |
| **13.** Assigned Potential PURL Reviewer  | Liz Ngyuen |
| **14.** Reviewer Affiliation  | University of Chicago Other:  |
| **15.** Date Review Due  | 11/14/13 |
| **16.** Abstract  | BACKGROUND:In acute asthma inhaled beta₂-agonists are often administered by nebulizer to relieve bronchospasm, but some have argued that metered-dose inhalers with a holding chamber (spacer) can be equally effective. Nebulizers require a power source and need regular maintenance, and are more expensive in the community setting.OBJECTIVES:To assess the effects of holding chambers (spacers) compared to nebulizers for the delivery of beta₂-agonists for acute asthma.SEARCH METHODS:We searched the Cochrane Airways Group Trial Register and reference lists of articles. We contacted the authors of studies to identify additional trials. Date of last search: February 2013.SELECTION CRITERIA:Randomized trials in adults and children (from 2 years of age) with asthma, where spacer beta₂-agonist delivery was compared with wet nebulization.DATA COLLECTION AND ANALYSIS:Two review authors independently applied study inclusion criteria (one review author for the first version of the review), extracted the data and assessed risks of bias. Missing data were obtained from the authors or estimated. Results are reported with 95% confidence intervals (CIs).MAIN RESULTS:This review includes a total of 1897 children and 729 adults in 39 trials. Thirty-three trials were conducted in the emergency room and equivalent community settings, and 6 trials were on inpatients with acute asthma (207 children and 28 adults). The method of delivery of beta₂-agonist did not show a significant difference in hospital admission rates. In adults, the risk ratio (RR) of admission for spacer versus nebulizer was 0.94 (95% CI, 0.61-1.43). The risk ratio for children was 0.71 (95% CI, 0.47-1.08, moderate quality evidence). In children, length of stay in the emergency department was significantly shorter when the spacer was used. The mean duration in the emergency department for children given nebulized treatment was 103 minutes, and for children given treatment via spacers 33 minutes less (95% CI, -43 to -24 minutes, moderate quality evidence). Length of stay in the emergency department for adults was similar for the 2 delivery methods. Peak flow and forced expiratory volume were also similar for the 2 delivery methods. Pulse rate was lower for spacer in children, mean difference -5% baseline (95% CI, -8% to -2%, moderate quality evidence), as was the risk of developing tremor (RR=0.64; 95% CI, 0.44-0.95, moderate quality evidence).AUTHORS' CONCLUSIONS:Nebulizer delivery produced outcomes that were not significantly better than metered-dose inhalers delivered by spacer in adults or children, in trials where treatments were repeated and titrated to the response of the participant. Spacers may have some advantages compared to nebulizers for children with acute asthma. |
| **17.** Pending PURL Review Date |  |
| **sECTION 2: Critical Appraisal of Validity****[to be completed by the Potential PURL Reviewer]** |
| **1.** What types of studies are included in this review? | RCT Other: Adults and children with acute asthma presenting for medical assistance in community setting, emergency room, inpatient admission who received B2 agonist via spacer or nebulizerExclusion criteria: studies on nonacute asthma, diff. drugs delivered, no separate data for asthma patients (vs chronic obstructive pulmonary disease patients), life-threatening asthma exacerbations |
| **2.** What is the key question addressed by this review? Summarize the main conclusions and any strengths or weaknesses. | Are spacers equivalent to nebulizers in delivering beta-agonists to adults and children with acute asthma exacerbations? |
| **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: 2 independent reviewers assessing risk of bias in the included trials (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting)Weighted treatment effect calculated using RevManRisk ratios for dichotomous outcomes, mean difference for continuous outcomes. Fixed effect model for continuous outcomes but also checked results with random effects modelResults were separated for adults and children due to heterogeneityResults from single-treatment trials were not pooled given concern about confounding due to uncertainty about relative doses delivered by spacer vs nebulizer. |
| **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: Cochrane Airways Group Specialised Register (includes CENTRAL, MEDLINE, EMBASE, CINAHL, AMED, PsycINFO, respiratory journals and meeting abstracts) |
| **6.** Study quality is assessed and taken into account. | [x]  Well covered [ ]  Not addressed[ ]  Adequately addressed [ ]  Not reported[ ]  Poorly addressed [ ]  Not applicableComments: Sources of bias were graded as high, low or unclear, also assessed heterogeneity |
| **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? | Yes:Primary Outcomes: hospital admission, duration of hospital admissionSecondary Outcomes: duration in emergency department, respiratory rate, pulse, tremor, lung function, blood gas, use of steroids, symptom score, relapse rates |
| **9.** Are adverse effects addressed? If so, how would they affect recommendations? | Yes:Tremor, change in pulse and risk ratio |
| **10.** Is funding a potential source of bias? If yes, what measures (if any) were taken to insure scientific integrity?  | No - funded by NHS Executive (North Thames and Eastern regions), ER Dept (University of Alberta), Garfield Weston Foundation and Canadian Institute of Health Research, St George's University London |
| **11.** To which patients might the findings apply? Include patients in the meta-analysis and other patients to whom the findings may be generalized. | Children (>2 yo) and adults with acute asthma exacerbations |
| **12.** In what care settings might the findings apply, or not apply? | Emergency room, inpatient, outpatient, maybe home? |
| **13.** To which clinicians or policy makers might the findings be relevant? | Pediatricians, intramuscular, family medicine, emergency room |
| **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. Asthma exacerbation in adults and adolescents Author. In: DynaMed [database online]. Available at: [www.DynamicMedical.com](http://www.DynamicMedical.com) Last updated: 6/7/13. Accessed 11/11/13Asthma exacerbation in children, 5/30/13, 11/11/13 |
| **3.**  Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences) | Metered-dose inhalers with spacer comparable to nebulizers for beta-agonist delivery |
| **4.** UpToDate excerpts |  |
| **5.** UpToDate citation/access date | Always use Basow DS as editor & current year as publication year.Title. Acute asthma exacerbations in children: Inpatient management Author. Mark Dovey, M In: UpToDate [database online]. Available at: <http://www.uptodate.com>. Last updated: 10/1/2012. Accessed 11/11/13 |
| **6.**  Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences) | Metered-dose inhalers with spacer comparable to nebulizers for beta-agonist delivery |
| **7.** PEPID PCP excerpts[www.pepidonline.com](http://www.pepidonline.com)username: fpinauthorpw: pepidpcp |  |
| **8.** PEPID citation/access data | Author. Title. In: PEPID [database online]. Available at: <http://www.pepidonline.com>. Last updated:. Accessed |
| **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.) | BTS 2011- recommends spacer over nebuliser |
| **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)[ ] 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. | Although current recommendations reflect findings of the Cochrane review, most settings are still using nebulizers over spacers. |
| 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 |  |
| **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 | This meta-analysis sought out to compare differences in beta-agonist delivery via nebulizer versus spacer for adults and children (>2 years old) with non life-threatening asthma exacerbations presenting to outpatient clinics and emergency rooms as well as patients already admitted to hospitals. Thirty-nine randomized controlled trials were reviewed including 729 adults and 1897 children in clinical settings throughout the world.Primary outcomes were hospital admission and duration of hospital admission. Secondary outcomes included duration of emergency room visit, side effects (tremor, change in pulse and respiratory rate), change in lung function, blood gases, relapse rate, symptom score and steroid use.Data for adults and children were analyzed separately due to significant heterogeneity. There was no significant difference in hospital admission in adults (RR=0.94, [0.61,1.43]; *P*=0.77) and children (RR=0.71, [0.47,1.08]; *P* =0.11) or in hospital admission duration in adults (MD=-0.60 [-3.23,2.03]; *P* =0.65) and children (MD=0.33. 95% CI [-0.10,0.76], *P*=0.13).The only significant differences in secondary outcomes were found among children and favor spacers: decreased emergency room visit duration (MD=-33.48 min=, [-43.32,-23.65], *P*<0.00001), lower % rise from baseline pulse (MD=-5.41, [-8.34, -2.48], *P*=0.0003) and lower incidence of tremor (RR=0.64, [0.44, 0.95], *P*=0.027). |
| 1. Criteria- note yes or no for those which this study meets

 | RELEVENT - YesVALID - YesCHANGE IN PRACTICE- YesMEDICAL CARE SETTING - YesIMMEDIATELY APPLICABLE - YesCLINICALLY MEANINGFUL - Yes |
| **3.** Bottom Line- one –two sentences noting the bottom line recommendation  | In adults, spacers are equivalent to nebulizers for delivery of beta-agonists for nonlife-threatening asthma exacerbations. For children, spacers produce fewer side effects (tachycardia, tremor) and can expedite emergency room visits compared to nebulizers. |
| **4.** Title Proposal | Spacers are just as effective, if not superior to nebulizers for asthma exacerbations. |
| **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 |  |