Effectiveness of Interventions to Teach Metered-Dose and Diskus® Inhaler Technique: A Randomized Trial

[1]Valerie G Press, [2]Vineet M Arora, [3]Kristin C Trela, [1]Richa Adhikari, [4]Frank J Zadravecz, [5]Chuanhong Liao, [6]Edward Naureckas, [6]Steven R White, [1]David O Meltzer, [7] Jerry A Krishnan

1. University of Chicago, Department of Medicine, Section of Hospital Medicine, Chicago, IL
2. University of Chicago, Department of Medicine, Section of General Internal Medicine, Chicago, IL
3. University of Michigan Medical School, Ann Arbor, MI
4. University of Illinois College of Medicine, Chicago, IL
5. University of Chicago, Department of Public Health Sciences, Chicago, IL
6. University of Chicago, Department of Medicine, Section of Pulmonary and Critical Care Medicine, Chicago, IL
7. Division of Pulmonary, Critical Care, Sleep, and Allergy, University of Illinois at Chicago, Chicago, IL

Corresponding Author:
Valerie G. Press, MD, MPH
University of Chicago Medicine
5841 S Maryland Ave, MC 5000, Chicago IL, 60637
Ph: 773-702-5170 Fx: 773-795-7398
Email: vpress@medicine.bsd.uchicago.edu

Author Contributions: Dr. Press had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design*: Press and Krishnan. *Acquisition of data*: Press and Trela. *Analysis and interpretation of data*: Press, Liao, Adhikari, Zadravecz, Krishnan. *Drafting of the manuscript*: Press, Trela, Zadravecz, and Adhikari. *Critical revision of the manuscript for important intellectual content*: Press, Arora, Meltzer, Naureckas, White, Krishnan. *Statistical analysis*: Press, Liao, Adhikari, Zadravecz. *Administrative, technical, and material support*: Trela, Krishnan. *Study supervision*: Press, Krishnan, Meltzer, Arora.

Funding: Dr. Press received funding from the National Cancer Institute (KM1CA156717) to support this project. Dr. Press is currently supported by a career development award from the National Heart Lung and Blood Institute (NIH K23HL118151). Dr. Arora received funding from the National Institutes on Aging Short-Term Aging-Related Research Program (T35AG029795) and National Institutes on Aging (K23AG033763). Dr. Meltzer received funding from the National Institutes on Aging Short-Term Aging-Related Research Program (T35AG029795), from the Agency for Healthcare Quality and Research through the Hospital Medicine and Economics Center for Education and Research in Therapeutics (U18 HS016967-01), from the National Institute of Aging through a Midcareer Career Development Award (K24 AG031326-01), from the National Cancer Institute (KM1 CA156717), and from the National Center for Advancing Translational Science (2UL1TR000430-06). Dr. Naureckas received funding from the National Institutes of Health (U10 HL098096) and National Institute of Allergy and Infectious Disease

(U19 A1095230). Dr. White received funding from the National Institute of Allergy and Infectious Disease (U19 AI095230). All other authors have no financial support to report.

Trial Registration: ClinicalTrials.gov identifier NCT01426581

Prior Presentations: This work has been presented in abstract form on May 21, 2013 at the American Thoracic Society Annual Meeting in Philadelphia, Pennsylvania; on September 13, 2014 at the Midwest Society of General Internal Medicine Annual Meeting in Chicago, IL (best research poster); on March 25, 2014 at Society of Hospital Medicine Annual Meeting in Las Vegas, Nevada (best research poster); and on April 25, 2014 at the Society of General Internal Medicine Annual Meeting in San Diego, CA.

Running Head: Interventions to Teach MDI and Diskus® Technique

Word Count: 3500/3500; Abstract 350=350; Refs: 26<80; Tables: 2; Figures: 4

Descriptor Number: 2.3 Health Education/Disease Prevention/Patient Education

MeSH Keywords: Patient Education as Topic; Asthma; Pulmonary Disease, Chronic Obstructive; Self Care

This article has an online data supplement, which is accessible from this issue's table of contents online at www.atsjournals.org.

Abstract

Rationale: The most effective approach to teach respiratory inhaler technique is unknown.

Objectives: To evaluate the relative effects of two different educational strategies (teach-to-goal instruction versus brief verbal instruction) in adults hospitalized with asthma or chronic obstructive pulmonary disease.

Methods: A randomized clinical trial was conducted at two urban academic hospitals. Participants received teach-to-goal or brief instruction in the hospital and were followed for 90 days after discharge. Inhaler technique was assessed using standardized checklists; misuse was defined as 75% or fewer of steps correct (≤9/12 steps). The primary outcome was MDI misuse 30 days post-discharge. Secondary outcomes included Diskus® technique, acute-care events at 30 and 90 days, and associations with adherence, health literacy, site, and patient risk (near fatal event).

Measurements and Main Results: Of 120 participants, 73% were female and 90% were African American. Prior to education, MDI misuse was similarly common in the teach-to-goal and brief intervention groups (92 vs 84%, p=0.2). MDI misuse was not significantly less common in the teach-to-goal versus brief instruction group at 30 days (54 vs 70%, p=0.11), but was immediately post-education (11 vs 60%, p<0.001) and at 90 days (48 vs 76%, p=0.003). Similar results were found with the Diskus® device. Participants did not differ across education group with rescue MDIs use or Diskus® device adherence at 30 or 90 days. Acute-care events were less common among teach-to-goal participants at 30 days (17 vs 36%, p=0.02), but not at 90 days (34 vs 38%, p=0.6). Participants with low health literacy receiving teach-to-goal were less

likely than brief instruction participants to report acute-care events within 30 days (15% vs. 70%, p=0.008). No differences existed by site or patient risk at 30 or 90 days (p>0.05).

Conclusions: In adults hospitalized with asthma or COPD, in-hospital teach-to-goal instruction for inhaler technique did not reduce inhaler misuse at 30 days, but was associated with fewer acute-care events within 30 days after discharge. Inpatient treatment-to-goal education may be an important first step toward improving self-management and health outcomes for hospitalized patients with asthma or COPD, especially among patients with lower levels of health literacy.

Clinical trial registered with ClinicalTrials.gov (NCT01426581)

Abstract Word Count: 348

Asthma and chronic obstructive pulmonary disease (COPD) are the most common lung diseases in the United States, with over one-million hospitalizations annually.[1] Medications delivered through respiratory inhaler devices are guideline-recommended for rescue and controller therapy to decrease symptoms, exacerbations, need for rescue medications, and to improve quality of life and lung function. [2--6] However, inhaler devices require multiple, sometimes complex, steps making them difficult to use.[7-11] Patients often do not know, or cannot effectively complete, these steps, resulting in misuse.[12,13]

Studies suggest that 28-68% of outpatients[14,15] and 62-86% of inpatients[13] misuse inhaler devices, placing patients at increased risk for poor health outcomes and future hospitalizations.[17,18] The cost of inhaler misuse accounts for $5-7 billion of the approximately $25 billion spent annually on inhalers.[16]

Current guidelines address this risk for misuse by recommending inhaler technique assessment and instruction during all health care encounters, including hospitalizations.[2,3] Hospital-based self-management education may be useful since experience with acute illness can be harnessed as a 'teachable moment.'[19] Teach-to-Goal (TTG) instruction,[12,13] based on the testing effect, allowing memory to be enhanced through the act of retrieving information while learning,[20] is comprised of tailored rounds of assessment and instruction to achieve the goal knowledge or skill.[7,12,13,21]

We demonstrated in a prior study that hospital-based TTG has greater efficacy than verbal instructions (brief intervention) immediately post-instruction in the hospital.[13] However, the longer-term duration of effects of hospital-based TTG on inhaler technique and acute care events after discharge home are unknown. This knowledge may help inform what methods of

education are most effective in improving outcomes after discharge among patients using inhalers.

The objectives of this two-center randomized clinical trial among inpatients with asthma or COPD were to compare the effects of hospital-based TTG compared to brief intervention on inhaler technique and acute care events at 30 and 90 days after discharge home. We hypothesized that among participants with asthma or COPD receiving inpatient education, MDI misuse would be significantly lower among TTG participants than brief intervention participants at 30-days post-hospital discharge. Some of the results of these studies have been previously reported in abstract form.[22-24]

Methods

Study Design and Randomization

We conducted a two-site block-stratified randomized clinical trial comparing TTG and brief intervention educational interventions. Participants were assigned to interventions stratified by site (hospital #1 and #2) and health literacy level (adequate, low, or insufficient vision to complete the health literacy assessment).[25] Study personnel were masked to intervention assignments. Participants received compensation for their time. The Institutional Review Boards at University of Chicago Medicine and Mercy Hospital and Medical Center, Chicago, approved the study.

Study Participants and Procedures

Patients were eligible if they were 18-years or older, hospitalized with a physician diagnosis of asthma or COPD, and were being discharged using a pressurized metered-dose inhaler (MDI) per the assenting primary clinical team. Patients were excluded if the treating physician did not provide assent or if the patient did not provide written informed consent.

A single, trained research assistant collected participant demographic data, health literacy level (Short Test of Functional Health Literacy in Adults [S-TOFHLA]),[10,25,26] and assessed vision (Snellen chart).[25,10] The research assistant assessed inhaler technique using previously validated standardized checklists for both MDI device use with aero chamber (kappa=0.94)[12] and the breath actuated Diskus® device (only among participants being discharged home on a Diskus® device in addition to their MDI).[12,13] Participants were asked about their rescue inhaler use at their 30 and 90 day follow-up visits, and missed doses of their Diskus® devices, when prescribed. Participants were considered high-risk if they reported a lifetime near fatal event (i.e., intensive care unit hospitalization and/or intubated).

Intervention

Participants were randomized to TTG or brief intervention and were provided instructions on 12-step MDI-with-spacer (all patients) and 10-step Diskus® (only those prescribed) instructions, as per our previously published approach [Figure 4]. Detailed descriptions and rationale are available as an online supplement.[13] The interventions were delivered by trained research educators who were masked to the other strategy to prevent contamination, and were

consistent across sites. Participants returned for in-person study visits at 30 (+/- 7) and 90 (+/- 14) days.

Outcomes

The primary outcome was MDI misuse at 30 days post-discharge. Secondary outcomes included MDI misuse immediately post-education and at 90 days; Diskus® misuse immediately post-education, and at 30 and 90 days; rescue inhaler use and adherence to inhaled controller medications; and post-discharge acute care events (self-reported all-cause emergency department [ED] visit or hospitalization) at 30 days or 90 days.

Statistical Analyses

Participant characteristics were described using proportions, mean (standard deviations [SD]), or median (interquartile range, IQR). We used two sample t-tests and Mann-Whitney U tests to compare baseline characteristics between groups, as appropriate. We used two sample t-tests of proportions to compare MDI misuse in each group over time and chi-square to evaluate MDI technique at each time-point post-discharge. Technique was dichotomized using our prior definition of MDI misuse (≤75% [≤9/12] steps correct).[12,13]

The study was powered at 80% for an effect size of ≥20% improvement of TTG compared to the brief intervention group. To ascertain whether baseline misuse and/or other patient characteristics factored into group differences at the 30 and 90 day time points, secondary analyses examined MDI misuse as a repeated measures variable, adjusting for

baseline MDI misuse, Diskus® use, health literacy, sex, and race using generalized estimating equations (GEE) model.[27]

A post-hoc sensitivity analysis evaluating MDI technique was performed using two additional 'misuse' cutoffs: 1) using chi-square to dichotomize misuse if participants only missed 'mission critical' steps as advised by pulmonary specialists, that would, if missed, result in no medication reaching the lungs (removing cap; activating inhaler); and 2) using linear regression of misuse based on the delta score at 30 days versus immediately post-education. Fisher exact tests were used to test for differences in acute care events between groups.

All analyses were performed using intention-to-treat analyses. Tests of significance used a two-sided p-value <0.05. STATA version 12 (College Station, Texas: StataCorp LP) was used.

Results

A total of 872 patients were screened to participate in the study, of whom 120 were eligible. Participants were randomized into TTG (n=62) or brief intervention groups (n=58) between September 2011 and February 2013 (Figure 1). Of the 120 participants, 100 were enrolled at hospital #1 and 20 were enrolled from hospital #2. Among enrolled participants, the median age was 48.5 years (IQR: 35-58); the majority were female and African American.

Most participants returned for their 30 day (n=107, 89%; TTG n=54, 87%; brief intervention n=53, 91%), and 90 day (n=103, 86%; TTG n=52, 84%; brief intervention n=51, 88%) follow-up visits. Only 32% of participants were prescribed a Diskus® for use post-discharge. Eighty-three percent of participants reported having a healthcare provider for their asthma or

COPD. Two-thirds were hospitalized at least once in the last year and nearly one-half had had a near-fatal event in their lifetime (Table 1). Baseline characteristics and inhaler technique (MDI and Diskus®) were similar in both the TTG and the brief interventiongroups (Figure 2a). The average time for TTG education was 6 minutes versus 2 minutes for the brief intervention group.

All 120 participants completed the pre- and post-education evaluations in the hospital. At 30 days after hospital discharge, there were no significant differences in participant characteristics between those who completed the assessments compared to those who were lost to follow-up (Table 2). However, participants with a prior near-fatal event (53% vs 24%, p=0.03) were more likely to return to the 90 day follow-up visit.

MDI technique improved immediately post-education with decreased proportions of misuse for both the TTG (92% to 11%, p<0.001) and the brief intervention groups (84% to 60%, p<0.001). However, the reduction in misuse was greater with the TTG group versus the brief intervention group (TTG 81% vs brief intervention 24%, p<0.001). (Figure 2a)

Post-Discharge MDI Technique

The proportion of participants who misused MDIs during the first 30 days after hospital discharge in the TTG group (54%) versus the brief intervention group (70%) was not significantly different (p=0.1). Among participants who received TTG education, the proportion of MDI misuse immediately post-hospital education versus 30 days after hospital discharge increased from 11% to 54% (p<0.001; Figure 2a). The proportion of misuse within the brief intervention group did not change significantly at 30 days versus immediate post-hospital education (70% vs

60%, p=0.1). At 90 days, the proportion of participants with MDI misuse was significantly lower in the TTG group versus the brief intervention group (48% vs 76%, p=0.004).

In multivariable analyses that accounted for baseline MDI misuse, use of Diskus® device, health literacy, sex, and race, the odds of MDI misuse in the brief intervention group at 30 days was 4.0 ([95% CI: 1.0-14.0], p=0.01) times the TTG group. At 90 days, results of multivariable analyses also suggested a higher odds of MDI misuse with brief intervention compared to TTG (OR 7.0 [95% CI: 2.0-21.0], p=0.001).

Our sensitivity analysis using the outcome of any MDI critical step missed found that the odds of MDI misuse was higher in the TTG group versus the brief intervention group post-education (OR 4 [95% CI: 0.48, 32] p=0.004). Using an outcome of number of MDI steps correct was significantly different in the TTG and brief intervention groups post-education (p<0.001) and at 90 days follow-up (p=0.01), with an average of 4.4 more steps correct post-education and 2.4 more steps at 90 days follow-up in the TTG group versus the brief intervention group. These data suggested that participants educated via TTG retained knowledge of critical steps in the use of MDI better than those educated using brief intervention.

When examining potential differences between subgroups, no significant differences between sites were found for MDI technique at each time point analyzed. There were also no differences in MDI misuse between the TTG group and brief intervention group by health literacy group at 30 days; those with adequate health literacy had a lower odds of MDI misuse at 90 days in the TTG group compared to the brief intervention group (p=0.03) (Figure 2b).

We did not observe effect modification by health literacy on the association between MDI misuse and TTG versus the brief intervention group at post-education, 30 day, or 90 day

follow-up. Additionally, using multivariate analysis, after adjusting for sex, race, and health literacy level, the odds of MDI misuse remained significantly lower in the TTG group compared to the brief intervention group at post-education ($p<0.001$) and at 90 day follow-up ($p=0.005$), but not at 30 day follow-up ($p=0.06$). This analysis suggested that TTG was broadly applicable and superior to brief intervention for MDI in the different subgroups and literacy levels in our patient population.

Post-Discharge Diskus® Technique

Among patients who were prescribed a Diskus® device, TTG-based education was superior to the brief intervention with a significantly lower proportion of misuse immediately following education (5% vs 61%, $p=0.001$). In the TTG group, Diskus® misuse increased from 5% immediately post-education to 53% at 30 days post-discharge ($p=0.001$); there was no significant change in Diskus® misuse in the brief intervention group during the same time period (61% vs 59%, $p=0.9$). We did not observe a significant change in Diskus® misuse at 90 days compared to 30 days post-discharge in either TTG (90 days: 38% vs 30 days: 53%, $p=0.3$) or brief intervention groups (90 days: 62% vs 30 days: 59%, $p=0.5$). In addition, at 90 days, Diskus® misuse was common and not significantly different between the TTG and brief intervention groups (38% vs 63%, $p=0.2$).

Multi-inhaler (MDI + Diskus®) Technique

For patients using both MDI and Diskus® ($n=38$), 39% misused at least one device (15/38) and 18.4% (7/38) misused both devices post-education ($p=0.005$). We observed higher risk of

misuse for those using multiple devices at baseline (p=0.02), but not after teaching began (p>0.05). Among the 34 participants using both devices at 30 days post-discharge, we observed a significant association between MDI and Diskus® misuse (p=0.04). For instance, of the participants who misused at least one device (24/34, 71%), over half misused both devices (14/24, 58%).

Among the 32 participants using both devices at 90 days post-discharge, the association between MDI and Diskus® misuse remained (p=0.01). Of the 21 participants misusing at least one device (66%), 13 individuals misused both devices (62%).

Our analysis of confounding by multiple device use found no significant differences in misuse between TTG and brief intervention groups at any time point (post-education, p=0.06; 30 day post-discharge, p=0.19; 90 day post-discharge, p=0.06).

Acute Care Events Post-Discharge

Overall, 23% (28/120) of participants reported an acute care event at 30 days after hospital discharge (Figure 3). Fewer events (17%, 9/54) occurred in the TTG compared to the brief intervention group (36%, 19/53, p=0.03). At 90 days post-discharge, 36% (43/120) of participants reported an acute care event for any cause (36%, 43/120 reported an ED visit; 22%, 26/120 reported a hospitalization). There were no longer any differences in the proportion with acute care events in the TTG group compared to the brief intervention group (34% vs 38%, p=0.6).

Participants with low health literacy (n=23) were more likely than participants with adequate health literacy (n=79) to have had an acute care event within 30 days after discharge

(39% vs. 18%, p=0.03). However, among participants with low health literacy, those receiving TTG education were less likely than those receiving the brief education intervention to report an acute care visit within 30 days after discharge (15% vs. 70%, p=0.008). We did not find that TTG mitigated acute care visits among participants with adequate health literacy at 30 days (p=0.08). No differences by level of health literacy, within or across participant groups, were found for acute care events at 90 days. There were no differences by site or patient risk (high risk defined by at least one lifetime near fatal event) at 30 days or 90 days post hospital discharge (p>0.05).

Rescue Use and Controller Adherence Post-Discharge

Participants did not differ across TTG or brief intervention with respect to their use of rescue MDIs post discharge. Participants reported at the 30-day follow-up (n=107; TTG n=54, brief intervention n=53) visit that they had, on average, used their rescue MDIs on 2.5 of the last 7 days (TTG: 2.4 vs. brief intervention: 2.5, p=0.8), and 7.7 of the last 30 days (TTG: 7.9 vs. brief intervention: 7.6, p=0.8). Similarly, at the 90 day follow-up visit (n=103, TTG n=52, brief intervention n=51), participants reported, on average, that they used their rescue MDIs on 2.5 of the last 7 days (TTG: 2.3 vs. brief intervention: 2.8, p=0.3), and 9.2 of the last 30 days (TTG: 8.1 vs. brief intervention: 10.3, p=0.2).

Participants also did not differ with respect to adherence to their Diskus® device. Among the 34 participants returning at the 30-day follow-up visit (TTG n= 17, brief intervention n=17), exactly the same number of participants in each group (TTG n=4, brief intervention n=4) reported missing more than one dose of their Advair in each group (p>0.999). Among the 32

participants returning at the 90-day follow-up that used Diskus®, almost equal numbers of participants (TTG n=3, brief intervention=2) reported missing more than one dose in the last 30 days (p=0.6).

Discussion

To our knowledge, this study is the first in hospitalized patients with asthma or COPD to directly compare hospital-based education strategies on the durability and lasting effects of hospital-based education after discharge home for inhaler technique and acute care events. Two principal findings emerged. First, TTG is superior to a brief education intervention for reducing initial inhaler misuse. However, the overall benefit of TTG wanes such that the difference in MDI misuse between the two groups is not significant by 30 days. Second, the group that received TTG education was significantly less likely to have acute care events at 30 days (but not 90 days) after hospital discharge. Further, TTG appeared to be particularly protective for patients with low health literacy.

Importantly, together these findings suggest that TTG may be a superior initial strategy for inhaler instruction, and that there may be improved clinical outcomes to providing TTG inpatient inhaler education, especially for patients with lower health literacy levels, but that reinforcement of inhaler technique is required after discharge for long-lasting skills retention and improved health outcomes.

TTG's superior effect compared to a brief education intervention on reducing inhaler misuse among inpatients, initially reported in earlier work,[13] was re-demonstrated in this study.

However, this study newly found that these observed differences in MDI misuse between TTG and brief intervention at later time-points were smaller, and although the differences favored the TTG group at both 30 and 90 days, the differences were not consistently significantly different. Despite the decaying skills, however, TTG participants returned less often for acute care events within a month; this was true even for participants with low health literacy and did not differ with respect to medication adherence post-discharge. Of note, within three months differences in acute care utilization did not differ by group, despite differences in misuse; future work should explore the relationship to longer term skill retention and impact on clinical outcomes.

The implications of these two findings are that TTG not only provides initial improvement in inhaler technique, but also that these enhanced skills may persist long enough to provide initial post-discharge benefit. However, due to the declining skills and the lack of persistent differences in clinical outcomes by 3 months, additional educational sessions or "doses" may be needed for ongoing effective technique and longer term beneficial health outcomes.

Participants' decay of inhaler technique was not surprising, as skill decay is expected with complex tasks, based on the cognitive psychology literature.[28] Decay of skills are based on many factors, including the nature of the task and time between use.[29]

Teach-to-goal may have an advantage over brief intervention, through its repeated cycles, as TTG provides for an opportunity of 'overlearning' [29] and uses the cognitive psychology phenomenon of the 'testing effect' that can mitigate skill decay.[20,29] This may be observed when looking within groups between the 30-days post discharge proportion with MDI misuse

compared to baseline misuse: MDI misuse at 30 days post discharge among TTG participants was half what it was before TTG education, while brief intervention misuse was only down by about a tenth from baseline. However, even TTG's use of 'overlearning' and the testing effect phenomenon would not be expected to be sufficient to completely overcome decay. Therefore, repeated dosing of skill education is supported both by clinical guidelines that suggest assessing and teaching self-management skills at all health encounters, and by psychology literature that says that regular repetition is required to avoid decay.[29] Since the misuse largely plateaued by 30 days, most of the skill decay had already likely occurred. Therefore, the ideal time for the repeated education would be before one month post-discharge.

Strengths and Limitations

Our study had multiple strengths, including random allocation to two different educational strategies, masking of research personnel to avoid contamination of educational interventions between study groups or biased collection of outcomes, and high post-discharge follow-up rates.

The study also has potential limitations. Findings from our largely high-risk, nearly half of whom had a prior near-fatal respiratory exacerbation, African American study population, may not be applicable to other patient populations. The interventions in our study were delivered by trained research staff; whether such interventions are effective when delivered by trained clinical staff needs study. We assessed acute care events after hospital discharge and inhaler use and adherence based on self-report. Problems with recall and lack of objective verification may result in less accurate data. However, follow-up rates at 30 days were similarly

high in both groups (nearly 90%) and it is unlikely that patients in the two groups would have differential recall. Future work can employ objective adherence monitoring for MDIs.

Our sample size for participants using Diskus® was only ome- third of the enrolled population, therefore, the findings regarding Diskus®, including multiple inhaler use results, require further study. Participants with both asthma and COPD were included in this study and important differences by sub-population may exist, whether due to disease type, age or other potential mediators. Future work can delineate if and how the effects of TTG versus brief intervention differ among the two groups. Further, our patient population had a high rate of life-time near fatal events, indicating a patient population that may learn differently than a healthier population. Effects of TTG on outpatients' ability to learn and retain inhaler technique skills is warranted.

Finally, while TTG is a relatively inexpensive strategy compared with expenses associated with exacerbations, the need for in-person educators may be cost and/or time prohibitive in some settings. Therefore, future work can explore the development of alternate strategies that allow for harnessing the strengths of TTG without resource burden of personnel.

Conclusions

These findings emphasize the need for self-management training for inhaler technique at all health care encounters. Results of our study provide justification for developing and implementing hospital-based strategies, such as TTG, to educate patients about use of their respiratory inhalers, but also suggest the need for post-discharge education, such as when patients present for care in the ambulatory setting, or even at home. Strategies including novel

technology-based educational platforms that can be provided initially in the hospital and then extended post-discharge may add value to chronic disease self-management education.

Our data emphasize the critical need for post-discharge educational reinforcement of hospital-based education. The ideal timing, method, and location of this additional education, in addition to more robust evaluation of inhaler technique skill on adherence and health outcomes is important future work.

Acknowledgements

We thank the members of the Data and Safety Monitoring Board. We thank the University of Chicago Asthma and COPD Center for their support and the University of Chicago Pulmonary Function Lab staff for their generous provision of space for follow-up visits. We thank Jeffrey Charbeneau for his assistance with the power calculations and randomization schedule. We thank Matthew Churpek for his expertise in post-hoc analysis. We thank Nicole Twu, Danielle Blazek, Dan Nichols, Paul Staisiunas, Kimberly Beiting, Lisa Spampinato, and Laura Ruth Venable for their assistance with the project.

References

1. Morbidity & Mortality: 2012 Chart Book on Cardiovascular, Lung, and Blood Diseases. 2014. Available at: http://www.nhlbi.nih.gov/files/docs/research/2012_ChartBook.pdf. Accessed October 18, 2014.
2. Global Initiative for Chronic Obstructive Lung Diseases. Available at: http://www.goldcopd.com/. Accessed October 27, 2014.
3. National Heart Lung and Blood Institute. Guidelines for the Diagnosis and Management of Asthma (EPR-3). 2014. Available at: https://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/. Accessed October 18, 2014.
4. Celli BR, Thomas NE, Anderson JA, Ferguson GT, Jenkins CR, Jones PW, Vestbo J, Knobil K, Yates JC, Calverley PM. Effect of Pharmacotherapy on Rate of Decline of Lung Function in Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med* 2008;178(4):332-338.
5. Mathison DA, Koziol JA. Utility and Efficacy of Fluticasone Propionate and Salmeterol Inhaled from a Single Inhaler for Persistent Asthma. *J Asthma* 2005;42(10):829-831.
6. Brocklebank D, Wright J, Cates C. Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering corticosteroids in asthma. *BMJ* 2001;323(7318):896.
7. Paasche-Orlow MK, Riekert KA, Bilderback A, Chanmugam A, Hill P, Rand CS, Brancati FL, Krishnan JA. Tailored education may reduce health literacy disparities in asthma self-management. *Am J Respir Crit Care Med* 2005;172:980–986.
8. Thompson J, Irvine T, Grathwohl K, Roth B. Misuse of metered-dose inhalers in hospitalized patients. *Chest*1994;105:715–717.
9. Palen J, Klein JJ, Herwaarden CLA, Zielhuis GA, Seydel ER. Multiple inhalers confuse asthma patients. *Eur Respir J* 1999;14:1034–1037.
10. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest* 1998;114:1008–1015.
11. Dahl R, Backer V, Ollgaard B, Gerken F, Kesten S. Assessment of patient performance of the Handihaler® compared with the metered dose inhaler four weeks after instruction. *Respir Med* 2003;97:1126–1133.
12. Press VG, Arora VM, Shah LM, Lewis SL, Ivy K, Charbeneau J, Badlani S, Naureckas E, Mazurek A, Krishnan JA. Misuse of Respiratory Inhalers in Hospitalized Patients with Asthma or COPD. *J Gen Intern Med* 2011;26(6):635-642.
13. Press VG, Arora VM, Shah LM, Lewis SL, Charbeneau J, Naureckas ET, Krishnan JA. Teaching the use of respiratory inhalers to hospitalized patients with asthma or COPD: a randomized trial. *J Gen Intern Med* 2012;27(10):1317-1325.
14. Fink JB, Rubin BK. Problems with inhaler use: a call for improved clinician and patient education. *Respir Care* 2005;50(10):1360-1374; discussion 1374-1375.

15. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest* 1998;114(4):1008-1015.
16. Cisternas MG, Blanc PD, Yen IH, Katz PP, Earnest G, Eisner MD, Shiboski S, Yelin EH. A comprehensive study of the direct and indirect costs of adult asthma. *J Allergy Clin Immunol* 2003;111(6):1212-1218.
17. Gottlieb DJ, Beiser AS, O'Connor GT. Poverty, race, and medication use are correlates of asthma hospitalization rates. A small area analysis in Boston. *Chest* 1995;108(1):28-35.
18. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *Eur Respir J* 2002;19(2):246-251.
19. Cohen DJ, Clark EC, Lawson PJ, Casucci BA, Flocke SA. Identifying teachable moments for health behavior counseling in primary care. *Patient Educ Couns* 2011;85(2):e8-e15.
20. Roediger HL, Karpicke JD. The Power of Testing Memory: Basic Research and Implications for Educational Practice. *Perspect Psychol Sci* 2006;1(3):181-210.
21. Kripalani S, Bengtzen R, Henderson LE, Jacobson TA. Clinical Research in Low-Literacy Populations: Using Teach-Back to Assess Comprehension of Informed Consent and Privacy Information. *IRB Ethics Hum Res* 2008;30(2):13-19.
22. Press VG, Arora VM, Constantine K, Naureckas E, White SR, Krishnan JA. Effectiveness Of Teaching Respiratory Inhaler Technique (ETRAIN): A Randomized Trial. Am J Respir Crit Care Med 187;2013:A5022.
23. Press VG, Arora VM, Constantine KL, Naureckas ED, White SR, Meltzer DO, Krishnan JA. Effectiveness and Durability of a Patient-Centered Hospital-Based Approach to Provide Instruction on Inhaler Technique for Patients with Asthma or COPD: A Randomized Comparative Effectiveness Trial. Journal of Hospital Medicine. 2014;9(suppl 2).
24. Press VG, Arora VM, Constantine KL, Naureckas ED, White SR, Meltzer DO, Krishnan JA. Forget me not: A randomized trial of the durability of hospital-based education on inhalers for patients with COPD or asthma. J Gen Intern Med 2014;29:S102.
25. JR Nurss, RM Parker, MV Williams, DW Baker. *Short Test of Functional Health Literacy in Adults (STOHFLA).* Peppercorn Books & Press; 2001.
26. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. *Patient Educ Couns* 1999;38(1):33-42.
27. Liang K, Zeger S. Longitudinal data analysis using generalized linear models. Biometrika. 1986;73(1):13–22.
28. Arthur W Jr, Bennet W Jr, Stanush PL, McNelly TL. Factors that influence skill decay and retention": A qualitative review an analysis *Human Performance* 1998;11(1):57-101.
29. Kneebone R. Evaluating clinical simulations for learning procedural skills: a theory-based approach. Acad Med. 2005 Jun;80(6):549-53.

Table 1: Participant Characteristics

	All participants n=120	Brief intervention n=58	Teach-to-goal n=62
Sociodemographics			
Age, years (median [IQR])	48.5 (35-58)	49 (39-57)	48 (35-59)
Asthma (vs COPD)	82 (68%)	36 (62%)	46 (76%)
Female	88 (73%)	41 (71%)	47 (76%)
African American*	108 (90%)	52 (90%)	56 (90%)
Hispanic or Latino	10 (8%)	5 (9%)	5 (8%)
Ever smoker†	83 (69%)	41 (71%)	42 (68%)
Insufficient vision‡	18 (15%)	8 (14%)	10 (16%)
Less-than adequate health literacy§	23 (23%)	10 (20%)	13 (25%)
Post-discharge inhaler prescribed			
MDI	120 (100%)	58 (100%)	62 (100%)
Diskus®	38 (32%)	18 (31%)	20 (32%)
Study Site			
Hospital #1	100 (83%)	49 (84%)	51 (82%)
Hospital #2	20 (17%)	9 (16%)	11 (18%)
Healthcare Services			
Healthcare provider for asthma/COPD care‖	99 (83%)	51 (88%)	48 (77%)
Hospitalized in the last 12 months (≥1 time, excluding study period)	79 (66%)	34 (59%)	45 (73%)
Near-fatal respiratory event(≥1 ICU admission or intubation for asthma or COPD)	59 (49%)	26 (45%)	33 (53%)

All data are presented as n (%) unless otherwise indicated. Abbreviations; COPD, Chronic Obstructive Pulmonary Disease; MDI, metered-dose inhaler.

*Other races: White (12%), American Indian or Alaska native (1%), native Hawaiian or other Pacific Island(1%)

†Ever smoker defined as >100 lifetime cigarettes vs never smoker

‡Insufficient vision defined as worse than 20/50 vision in both eyes using Snellen

§Health literacy was assessed in 102 participants; brief intervention (n=50); treat-to-goal (n=52); remaining subjects had insufficient vision to complete assessment (x=18); less-than adequate health literacy was defined as score of <23/36 on Short Test of Functional Health Literacy (STOHFLA)

‖Identified either a general physician, specialist physician (pulmonologist or allergist), or nurse practionner as providing care for participants' asthma or COPD.

Table 2: Comparison of participants completing the study vs. those lost to follow-up

Characteristic	Completed 30 day follow-up			Completed 90 day follow-up		
	Yes, n=107	**No, n=13**	***p***	**Yes, n=103**	**No, n=17**	***p***
Age, years (median)	48	50.6	0.4	48	51	0.4
Female	79 (74%)	9 (69%)	0.7	75 (73%	13 (77%)	>0.99
African American	97 (91%)	85	0.6	95 (92%)	13 (76%)	**0.07**
Ever-smoker*	73 (68%)	10 (77%)	0.8	69 (67%)	14 (82%)	0.4
Insufficient vision†	15 (14%)	3 (23%)	0.4	13 (13%)	5 (29%)	0.1
Inadequate HL‡	21 (23%)	2 (20%)	>0.99	21 (23%)	2 (17%)	>0.99
Hospitalized in the last 12 months (≥1 time, excluding study period)	71 (66%)	8 (62%)	0.8	69 (67%)	10 (59%)	0.6
No provider§	17 (16%)	4 (31%)	0.2	18 (17%)	3 (18%)	>0.99
Near-fatal respiratory event(≥1 ICU admission or intubation for asthma or COPD)	54 (50%)	5 (38%)	0.6	55 (53%)	4 (24%)	**0.03**
Site (HP1 vs. HP2)	91 (85%)	9 (69%)	0.2	86 (83%)	14 (82%)	>0.99
Asthma vs. COPD	76 (71%)	6 (46%)	0.1	73 (71%)	9 (53%)	0.3

All data presented as n (%) unless otherwise indicated. Baseline (BL) completers (C): n=120; 30 day completers (C): n=107; loss to follow-up: (L) n=13; 90 day completers (C): n=103; loss to follow-up (L): n=17.

*Ever smoker defined as >100 lifetime cigarettes vs never smoker

† Insufficient vision defined as worse than 20/50 vision in both eyes using Snellen

‡ Health literacy was assessed in 102 participants; brief intervention (n=50); TTG (n=52); remaining subjects had insufficient vision to complete assessment (x=18); less-than adequate health literacy was defined as score of <23/36 on Short Test of Functional Health Literacy (STOHFLA)

§ Did not identify a general physician, specialist physician (pulmonologist or allergist), or nurse practionner as providing care for participants' asthma or COPD.

Figure Legends

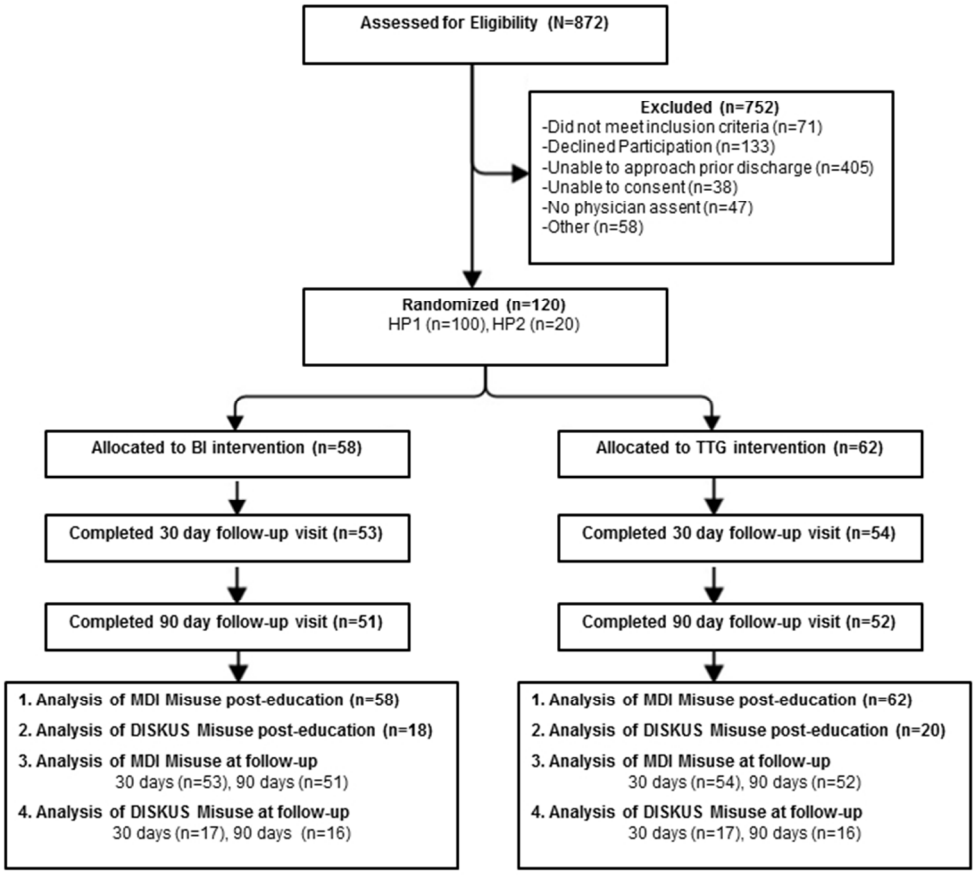
Figure 1. Participant flow – Initial assessment through primary outcome analysis

Figure 2A. Proportion of participants misusing either Metered Dose or Diskus® Inhaler

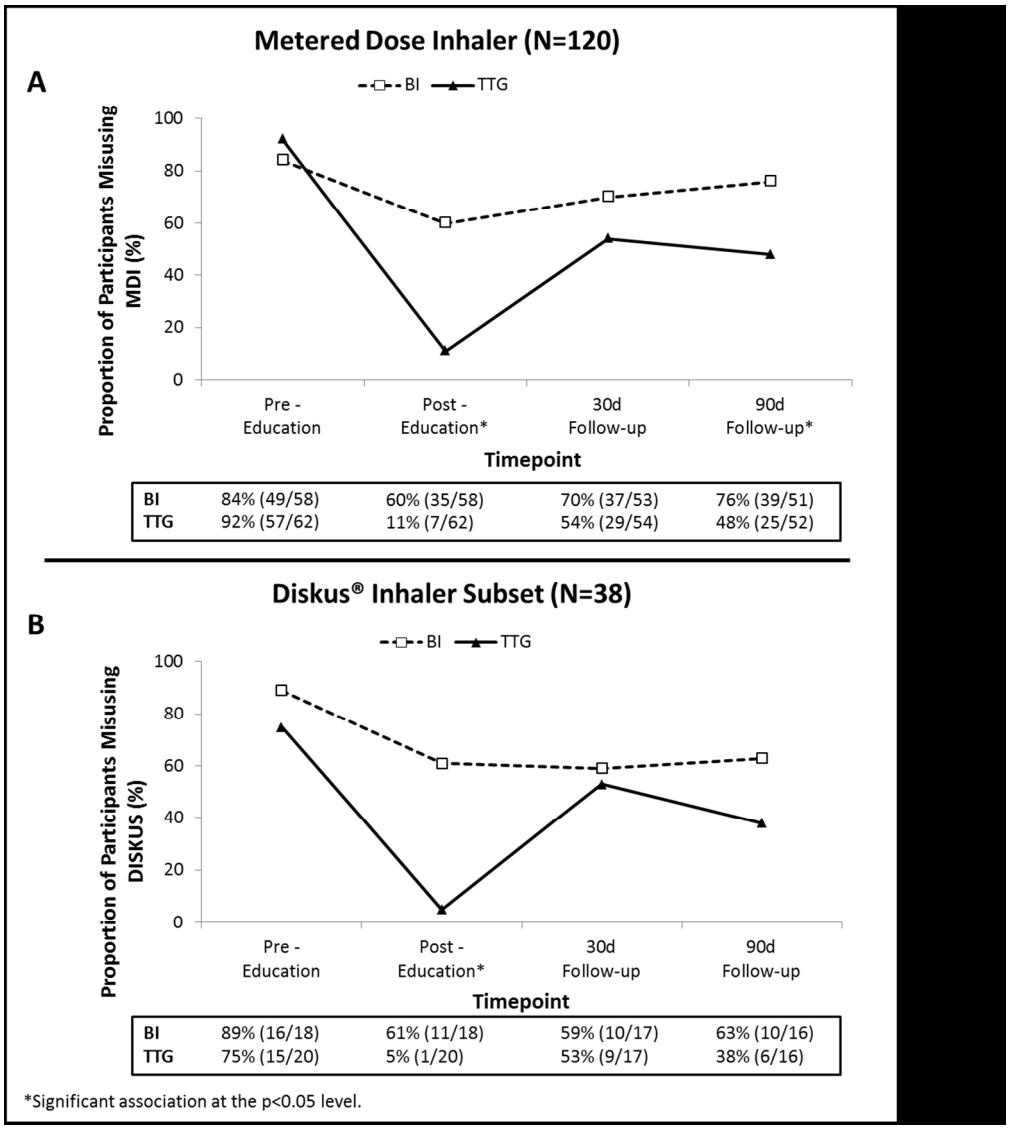
Figure 2B: Proportion of participants with (A) adequate literacy, (B) low literacy, and (C) Insufficient vision who misused Metered Dose Inhaler

Figure 3. Post-discharge acute care visits. 89% (n=107) of participants returned at 30 days post-discharge (54/62=TTG; 53/58=brief intervention) and 86% returned at 90 days (n=52/62 TTG; n=51/58 brief intervention).There were fewer acute care visits (Emergency Department visits and/or hospitalizations) among teach-to-goal vs. brief intervention participants (17%, 9/54 vs. 36%, 19/53, p=0.03) at 30 days but not at 90 days (40%, 21/52 vs. 43%, 22/51, p=0.64) post-hospital discharge**.**

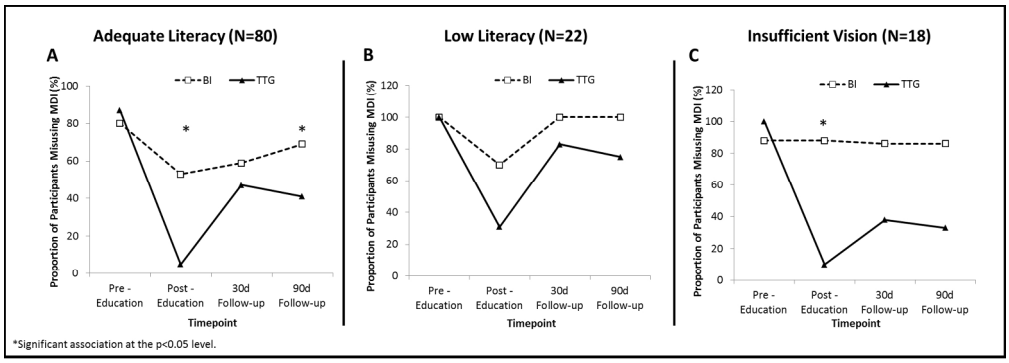
Figure 4. Intervention. *Disease education served as an attention control. Abbreviations: RA, research assessor; RE, research educator; TTG, teach-to-goal;



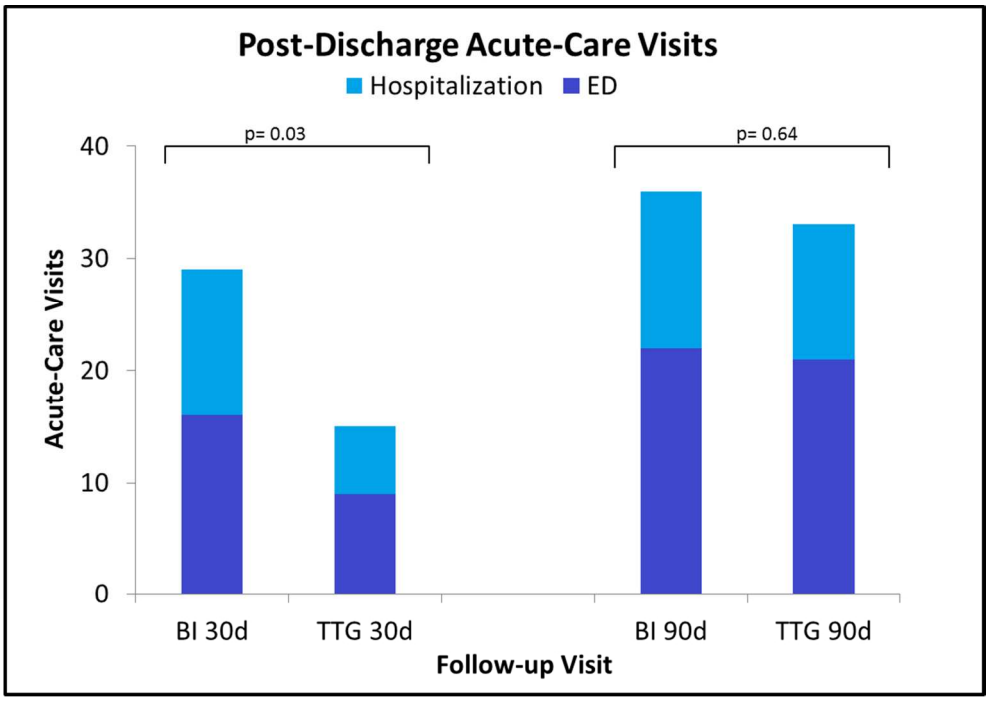
Participant flow – Initial assessment through primary outcome analysis
122x109mm (150 x 150 DPI)



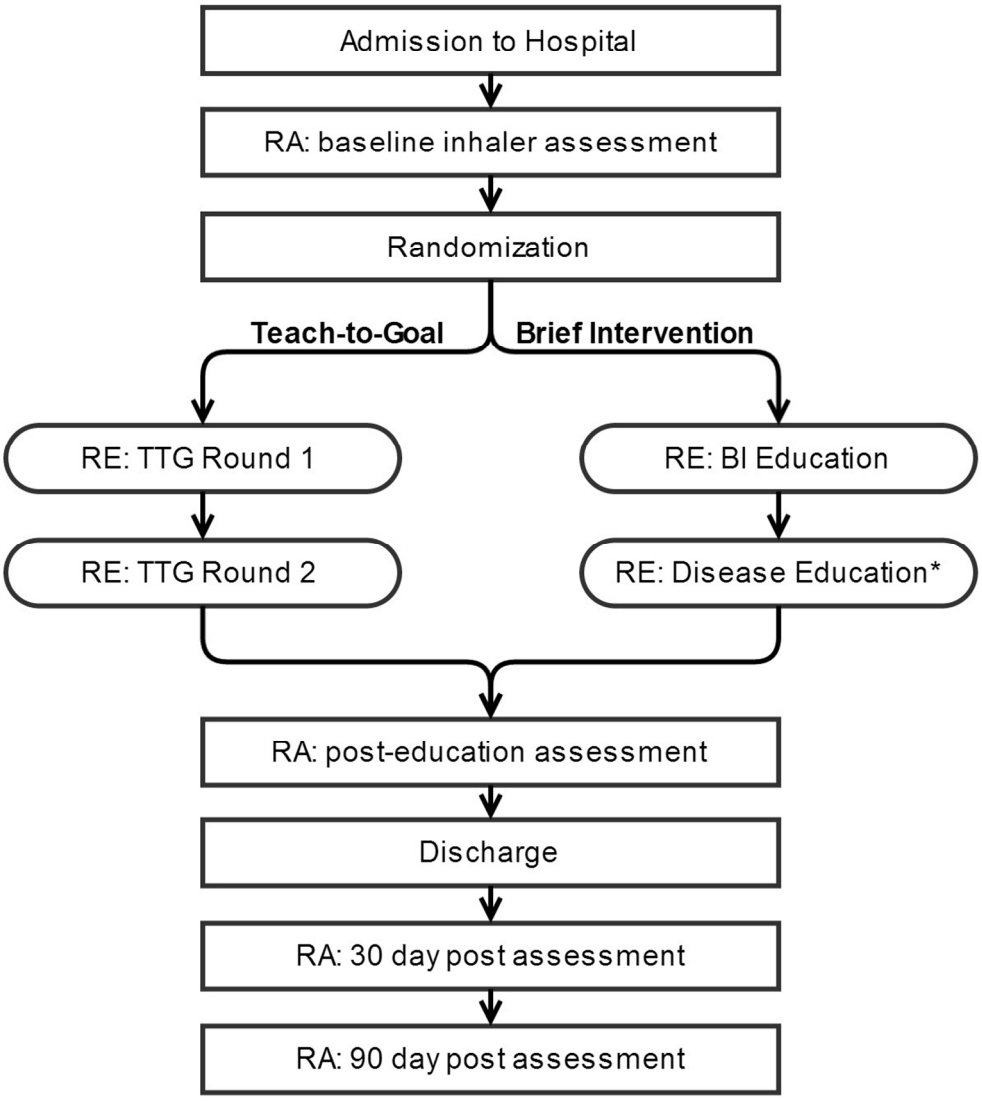
Proportion of participants misusing either Metered Dose or Diskus® Inhaler
218x244mm (150 x 150 DPI)



Proportion of participants with (A) adequate literacy, (B) low literacy, and (C) Insufficient vision who misused Metered Dose Inhaler
362x127mm (150 x 150 DPI)



Post-discharge acute care visits: 89% (n=107) of participants returned at 30 days post-discharge (54/62=TTG; 53/58=BI) and 86% returned at 90 days (n=52/62 TTG; n=51/58 BI).There were fewer acute care visits (Emergency Department visits and/or hospitalizations) among TTG vs. BI participants (17%, 9/54 vs. 36%, 19/53, p=0.03) at 30 days but not at 90 days (40%, 21/52 vs. 43%, 22/51, p=0.64) post-hospital discharge.
308x212mm (96 x 96 DPI)



Intervention
*Disease education served as an attention control. Abbreviations: RA, research assessor; RE, research educator; TTG, teach-to-goal; BI, brief intervention.

103x122mm (300 x 300 DPI)

Online Data Supplement

Effectiveness of Interventions to Teach Metered-Dose and Diskus® Inhaler Technique: A Randomized Trial

Valerie G Press, Vineet M Arora, Kristin C Trela, Richa Adhikari, Frank J Zadravecz, Chuanhong Liao, Edward Naureckas, Steven R White, David O Meltzer, Jerry A Krishnan

ONLINE SUPPLEMENT - FULL METHODS

Study Design and Randomization

A two-site block randomized, stratified clinical trial was used to compare the durability of two educational interventions to instruct hospitalized patients with asthma or COPD on respiratory inhaler technique. Random number generation was used to create the randomization schedule. Permuted block sizes were used. Investigators were masked to the block sequences. To ensure concealment, sequentially numbered envelopes were prepared by a project manager who assigned participants to interventions, stratified by site (hospital #1 vs #2) and level of health literacy (adequate, less-than-adequate, or insufficient vision to complete the health literacy assessment).[24] Study investigators and research assistants (RAs) were masked to the intervention assignments. Study participants received $25 for the inpatient study visit and $50 for each of the follow-up visits as compensation for their time. The study was approved by the Institutional Review Boards at University of Chicago Medicine and at Mercy Hospital and Medical Center, Chicago.

Study Participants: Identification of Eligible Patients, Eligibility and Exclusion Criteria

RAs screened for admissions using each hospitals' respective electronic health record (EPIC and Cerner) Monday through Friday. Patients who were 18-years or older, hospitalized on an inpatient medical service, had a physician diagnosis of asthma or COPD as documented in the medical record and/or confirmed by inpatient primary team, and expected to be discharged home on an MDI by their inpatient physician, were eligible for inclusion. Patients who were

currently in an intensive care setting, lacked physician assent, or were unable to provide written informed consent were excluded from the study.

Study Procedures

Interviewers administered surveys to collect participant demographic data. Participants' baseline acute-care utilization for asthma or COPD was measured using the number of hospitalizations for asthma or COPD in the past 12-months and any lifetime near-fatal respiratory event (≥1 intensive care unit admission(s) and/or intubation).

The Short Test of Functional Health Literacy in Adults (STOFHLA),[1,2] a 36-item written comprehension test (scores: 0-36; less-than-adequate **or "low":** <23/36; adequate: ≥23/36) was used to measure health literacy, since inadequate health literacy is associated with poor inhaler technique.[1-3] Prior to administering the S-TOFHLA, vision was assessed (Snellen screening chart);[1,3] participants who used corrective-lenses were instructed to wear them. Vision worse than 20/50 in both eyes was defined as insufficient to complete the STOFHLA instrument.

Inhaler technique was assessed by a trained RA using detailed step-wise checklists for MDI (12-steps) **and when applicable, Diskus (10-steps),** described and published in our prior work.[4,5] The primary analysis used the definition of MDI misuse as performing <75% of steps correctly for the MDI (<9/12 steps).[4-7] However, due to the non-standardization of this variable, a sensitivity analysis evaluating inhaler technique was performed using two additional methods: 1) using only 'mission critical' steps**, that would, if missed, result in no medication reaching the lung** (removing cap and activating inhaler); and 2) using the delta score (0-12) at 30-days compared to post-education. Participants rated their confidence in their ability to use MDIs

using a 5-point Likert scale (1=strongly disagree to 5=strongly agree) using the following question: "I am confident that I know how to use this MDI respiratory inhaler correctly."[4] Inhaler confidence was dichotomized into confident (Likert scale 4-5) vs not confident (Likert scale 1-3).

Intervention [supplemental figure 1]

Upon completion of the baseline assessments, including baseline inhaler technique, vision, and health literacy assessments, participants were randomized to either TTG or BI. Research educators (REs) were trained only for their respective educational strategy (RE-TTG or RE-BI) and were masked to the other strategy.

Rationale: **The TTG intervention was chosen based on our prior work demonstrating its success as a hospital-based approach for teaching the use of respiratory inhalers.[4,5] For our randomized prior study examining only in-hospital efficacy of TTG (without post-discharge follow-up assessments), we considered a variety of alternative comparators to TTG, including usual care. However, there were several reasons that usual care was not a viable option, including that usual care may vary by institution and provider, many hospitals may not have standard assessment and education for inpatients prescribed respiratory inhalers, extremely high rates of misuse among inpatients have been establish indicating that some education should be provided, and TTG can be resource intensive. Therefore, we developed a standardized, resource-limited educational strategy, called "brief intervention" (BI) to compare to TTG.[5] Of note, in our prior study, BI did in fact decrease within group rates of**

inhaler misuse, therefore if anything, the BI group would push the results toward the null hypothesis.

TTG Intervention: The TTG educational strategy employed repeated rounds of assessment and demonstration-based education. First, masked RAs evaluated participants' baseline inhaler technique. The masked RA then left the room and a trained research educator (RE-TTG) provided a demonstration of correct inhaler use, followed by re-assessment of participants' technique (ie, "teachback"). The cycle was repeated for up to three rounds; round two occurred if participants did not demonstrate mastery (100% steps correct); round three occurred if participants still misused devices (<75% steps correct). Participants also received written instructions and a pamphlet describing basic information about their condition (asthma or COPD). After completion of the educational intervention, the RE-TTG left the room, and the masked RA re-entered the room and performed a post-education assessment of participants' inhaler technique.

BI Intervention: Participants randomized to BI also underwent an initial assessment by the masked RA. The RE-BI then provided the participant with simple verbal instructions (ie, read each step out-loud without any demonstration) as well as a copy of the written instructions. To make the treatments approximately equal in time, the BI group received verbal education on the pamphlet for their condition (asthma or COPD). After completion of the education, the RE-BI left the room, and the masked RA re-entered the room and performed a post-education assessment of the participants' inhaler technique.

Follow-up Visits

To evaluate durability of the hospital-based inhaler instruction, participants returned at 30-days (+/- 7days) and 3-months (+/- 2 weeks). At each visit, the RA re-evaluated participants' technique. In addition, the RA administered questionnaires regarding symptoms, utilization of acute-care services (defined as: ≥ 1 all-cause emergency department (ED) visits, hospitalizations**), and use of inhalers including both rescue MDIs and controller Diskus devices (when prescribed).**

Outcomes

The primary outcome, determined a priori, was MDI misuse at 30-days post-education. This study was designed to detect a 20% absolute difference in MDI misuse between TTG and BI arms achieving a power of 85%. Secondary outcomes included MDI misuse at other time-points (immediately after education in the hospital and 3-months post-discharge); all-cause acute-care events at 30-days and 3-months; and self-reported confidence for MDI use); and subgroup analyses by site and health literacy.

Statistical Analyses

Participant characteristics were described using proportions and measures of central tendency (mean, standard deviations [SD]; median, IQR). Two sample t-tests and Mann-Whitney U tests were used to compare baseline characteristics between groups as appropriate. Chi-squared and Fisher exact tests were used to test for differences in the prevalence of MDI misuse and acute

health-related events post-discharge in the TTG vs BI groups. The difference in MDI misuse between BI and TTG groups over time and their interaction as covariates was examined using a generalized estimation equations modeling (GEE) approach. The GEE model used a logit link function to analyze the dichotomized outcome of MDI misuse. A composite GEE model examined the effect of MDI misuse after controlling for prior use. Self-reported confidence for inhaler use was analyzed as a dichotomous variable using the McNemar test (before vs after) within BI and TTG, individually.

All analyses were performed with intention-to-treat analyses; tests of significance used a two-sided p-value of less than 0.05. All statistical analyses were performed using STATA version 12 (College Station, Texas: StataCorp LP).

References

1. JR Nurss, RM Parker, MV Williams, DW Baker. *Short Test of Functional Health Literacy in Adults (STOHFLA).* Peppercorn Books & Press; 2001.
2. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. *Patient Educ. Couns.* 1999;38(1):33-42.
3. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest* 1998;114(4):1008-1015.
4. Press VG, Arora VM, Shah LM, et al. Misuse of Respiratory Inhalers in Hospitalized Patients with Asthma or COPD. *J. Gen. Intern. Med.* 2011;26(6):635-642.
5. Press VG, Arora VM, Shah LM, et al. Teaching the use of respiratory inhalers to hospitalized patients with asthma or COPD: a randomized trial. *J. Gen. Intern. Med.* 2012;27(10):1317-1325.
6. Brocklebank D, Wright J, Cates C. Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering corticosteroids in asthma. *BMJ* 2001;323(7318):896.
7. Cisternas MG, Blanc PD, Yen IH, et al. A comprehensive study of the direct and indirect costs of adult asthma. *J. Allergy Clin. Immunol.* 2003;111(6):1212-1218.