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Title: Impact of adherence to treatment with tiotropium co-administered with fluticasone propionate/salmeterol combination in COPD patients

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Body: Introduction: Poor adherence to treatment has been considered a major factor contributing to sub-optimal COPD management. Objective: To assess the association between adherence to treatment and health care resource utilization (HCRU) in COPD patients treated with tiotropium (TIO) co-administered with fluticasone propionate / salmeterol combination (FSC). Methods: A retrospective observational cohort study utilizing administrative databases of the Quebec provincial health insurance of patients (age ≥ 40 years) with a diagnosis of COPD and ≥ 2 pharmacy claims for TIO + FSC dispensed from 1/1/2001 to 12/31/2010. Adherence to treatment was ascertained as compliance (medication possession ratio $\geq 80\%$) and persistence (no absence of treatment gap ≥ 30 days). Outcomes assessed were moderate exacerbations (ME), severe exacerbations (SE) and COPD HCRU. Multivariate logistic regression analyses (MLRA) were used to adjust for baseline characteristics. Results: A total of 11,148 subjects, proportions of compliant and persistent patients with TIO+FSC were 63% and 45% respectively. MLRA showed that adherence to TIO+FSC were associated with a significant ($p < 0.001$) reduction in risk of ME and SE. The adjusted Odds Ratio for compliant patients were: TIO (ME = 0.449, SE = 0.570) and FSC (ME = 0.546; SE = 0.749). Similar results were seen for persistence. Compliance and persistence with TIO+FSC were also associated with significant ($p < 0.001$) reduction in HCRU including rescue medication use and hospitalizations Conclusion: This study suggests that improved adherence to treatment with TIO+FSC is associated with decreased risk for exacerbations and lower HCRU in COPD patients.