number of units (e.g. tablets, vials) of drug samples in all outpatient clinics was counted. The audit was repeated in November 2009 and July 2012. For each audit period, the total numbers of both units and doses of drug samples were calculated, and the average number of doses was estimated for liquids (0.5 mL/dose) and topical agents (0.5 g/dose). The number of doses of drug samples per patient visit was also calculated, to indicate potential exposure of patients to samples.

In total, 31 locations (i.e., health care units) were identified in 21 outpatient clinics. A total of 14 221 units of drug samples were counted in 2007, 8080 units in 2009, and 6989 units in 2012 (see details in Table 1). Although the number of units decreased over time, the number of doses increased, from 78 955 in 2007 to 75 487 in 2009 and 91 000 in 2012 (breakdown by clinic not shown), mostly because of a higher proportion of topical drugs in the dermatology clinic. The number of doses of drug samples per patient visit remained stable: 0.40 in 2007, 0.38 in 2009, and 0.41 in 2012.

In 2012, only 19% of doses documented during the audit were listed on the official hospital drug formulary; in addition, 4% of the doses were expired. Despite implementation of a Web-based intranet form to declare drug samples received from industry sales representatives, most doses of drug samples had not been declared to the pharmacy by hospital staff.

The availability of drug samples in outpatient clinics at the study hospital has remained stable for the past 5 years. It may seem feasible to prohibit the distribution of samples locally in outpatient clinics, but in fact, it is difficult to do so when such distribution is not prohibited by the pertinent regulatory authorities. For instance, physicians and medical residents often work in multiple hospitals, and their regulations regarding drug samples may vary. We believe that drug samples do not contribute to better patient care and should only be dispensed by retail pharmacies through a structured approach, with documentation of doses dispensed in the patient's record.

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Appropriateness of Triple Therapy after COPD Exacerbation

Dault and others[1] retrospectively examined discharge medications for patients who had been admitted to hospital for acute exacerbation of chronic obstructive pulmonary disease (COPD). Their primary objective was to determine the proportion of admissions for which the combination of long-acting ß$_2$ agonist, tiotropium, and an inhaled corticosteroid was prescribed. This so-called triple therapy is recommended in the Canadian COPD guidelines for patients with moderate to severe COPD and a history of recurrent exacerbations (one or more exacerbations per year, on average, for 2 consecutive years).[2] Presumably, however, some of the patients in the chart review published by Dault and others[1] were presenting with their first exacerbation of COPD. Thus, for a significant number of study participants, the prescription of triple therapy might not have been appropriate.

In the Canadian COPD guidelines,[2] the use of triple therapy in patients with moderate to severe COPD and a history of recurrent exacerbations is designated as having level 1A evidence. As alluded to by Dault and others,[1] the basis for this 1A level of evidence was the Canadian Optimal Therapy of COPD Trial,[3] which showed no significant reduction in the proportion of patients experiencing an exacerbation with triple therapy relative to tiotropium monotherapy (the primary end point). As pointed out by Suissa and others,[4] the results of the Optimal trial may have been influenced by the withdrawal of inhaled corticosteroids. In other words, patients who were receiving inhaled corticosteroids at the time of randomization and who were assigned to receive placebo would have experienced withdrawal from the regimen of inhaled steroids, with the possibility of a deleterious outcome, as has been demonstrated previously.[5,6]

Triple therapy is expensive, a factor that should be taken into account during selection of a therapeutic regimen for these patients. It has been my experience that maximal COPD therapy is often routinely prescribed during admission for an acute exacerbation, with little attention paid to the appropriateness of

the therapy or the patient's ability to afford the medication after discharge.

Finally, triple therapy is not without its own inherent risks. For example, analysis of data from the TORCH trial yielded similar values for number needed to treat (in terms of reduction in hospital admissions) and number needed to harm (in terms of cases of pneumonia).[7] This potential trade-off might be more favourable for a patient with a significant risk of recurrent exacerbation than for a patient presenting with a first exacerbation and no formal diagnosis of COPD.

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[Reply from authors:]

In response to Mr Manderville's letter, we would like to point out that the recommendation in the Canadian guidelines for chronic obstructive pulmonary disease (COPD) regarding use of the combination of a long-acting anticholinergic, a long-acting ß$_2$ agonist, and an inhaled corticosteroid (so-called "triple therapy") is applicable for all levels of exacerbation severity, including mild exacerbations treated at home.[1] Our study[2] focused on severe COPD exacerbations leading to hospital admission, and the mean number of admissions for an acute exacerbation of COPD in the previous year was about one per patient.

We agree that triple therapy should be prescribed for patients with COPD who are at significant risk of recurrent exacerbation, and we consider that our patients fell into that category, since having one hospital admission for COPD significantly increases the risk of readmission[3] and future exacerbation.[4] Although the Optimal trial did not show a significant reduction in total COPD exacerbations (i.e., all levels of severity), it did show a significant reduction in the risk of exacerbations leading to hospital admission, as a secondary end point.[5] The TORCH trial showed an increase in the absolute number of pneumonia cases among patients receiving inhaled corticosteroid therapy, but there was no associated increase in the risk of mortality, and there was a lower risk of hospitalization in the group treated with long-acting ß$_2$ agonist and inhaled corticosteroid relative to placebo.[6]

Finally, we agree that the cost of the medication should be taken into consideration, but overall, the reduction in rate of hospital admission and improvement in quality of life may outweigh this cost.

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