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Personalising adherence-enhancing interventions using a smart inhaler in patients with COPD: an exploratory cost-effectiveness analysis

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Four inhaler adherence clusters have been identified using the INCA audio device in COPD patients: (1) regular use/good technique, (2) regular use/frequent technique errors, (3) irregular use/good technique, and (4) irregular use/frequent technique errors. Their relationship with healthcare utilization and mortality was established, but the cost-effectiveness of adherence-enhancing interventions is unknown. In this exploratory study, we aimed to estimate the potential cost-effectiveness of reaching optimal adherence in the three suboptimal adherence clusters, i.e., a theoretical shift of clusters 2, 3, and 4 to cluster 1. Cost-effectiveness was estimated over a 5-year time horizon using the Irish healthcare payer perspective. We used a previously developed COPD health-economic model that was updated with INCA trial data and Irish national economic and epidemiological data. For each cluster, interventions would result in additional quality-adjusted life years gained at reasonable investment. Cost-effectiveness was most favorable in cluster 3, with possible cost savings of €845/annum/person.

INTRODUCTION

In chronic obstructive pulmonary disease (COPD), real-world adherence to maintenance therapy can be as low as 20%.[1] In contrast, trials report adherence rates of over 80% in most participants.[2] Previous studies showed that patients with high adherence have significantly better clinical and economic outcomes.[3] Consequently, interventions focusing on adherence enhancement have shown to be effective and cost-effective.[4,5] Yet, in these studies, only average adherence was assessed and no distinction was made between the different aspects of non-adherence. Optimal implementation of inhaled therapy involves both regular use as well as good inhaler technique.[6] In our previous work, we identified four distinct clusters of inhaler adherence that were associated with differential clinical outcomes.[7] Economic evaluations of adherence-enhancing interventions in each of those clusters have not been performed, but could help prioritizing specific target populations for tailored interventions. The aim of this follow-up study is to estimate the potential cost-effectiveness of reaching optimal adherence in each suboptimal adherence cluster.

RESULTS

The study's baseline population characteristics (*n* = 226) have been described elsewhere.[1,7] In short, cluster 1 had the lowest mortality during follow-up. Cluster 2 had the highest rate of antibiotic and/or oral steroids community prescriptions. The highest overall healthcare use was attributable to patients from cluster 3. Cluster 4 had the highest mortality (Fig. 1).

Cost-effectiveness

Cost-effectiveness analysis results are shown in Table 1. Adherence-enhancing interventions seem generally cost-effective, given all ICERs are below the Irish cost-effectiveness threshold of €45,000/QALY.[8] In other words, this means that all adherence-enhancing interventions would cost less than €45,000 to gain one life-year in perfect health. For each cluster, the theoretical intervention would result in additional life years and QALYs gained. Notably, for cluster 3, an intervention would be cost-saving (i.e., less costs and more QALYs).

DISCUSSION

We performed exploratory cost-effectiveness modeling to assess the potential economic benefits of improved adherence in three clusters of patients with suboptimal adherence. In all clusters, interventions seem cost-effective. Moreover, in patients with irregular use but good inhaler technique, a possible cost-saving of €845/annum/person could be yielded despite the higher cost of medication arising from better adherence.

Remote monitoring of adherence on a longitudinal basis provides an accurate evaluation of regularity of use as well as inhaler technique. The use of a technology, such as the one

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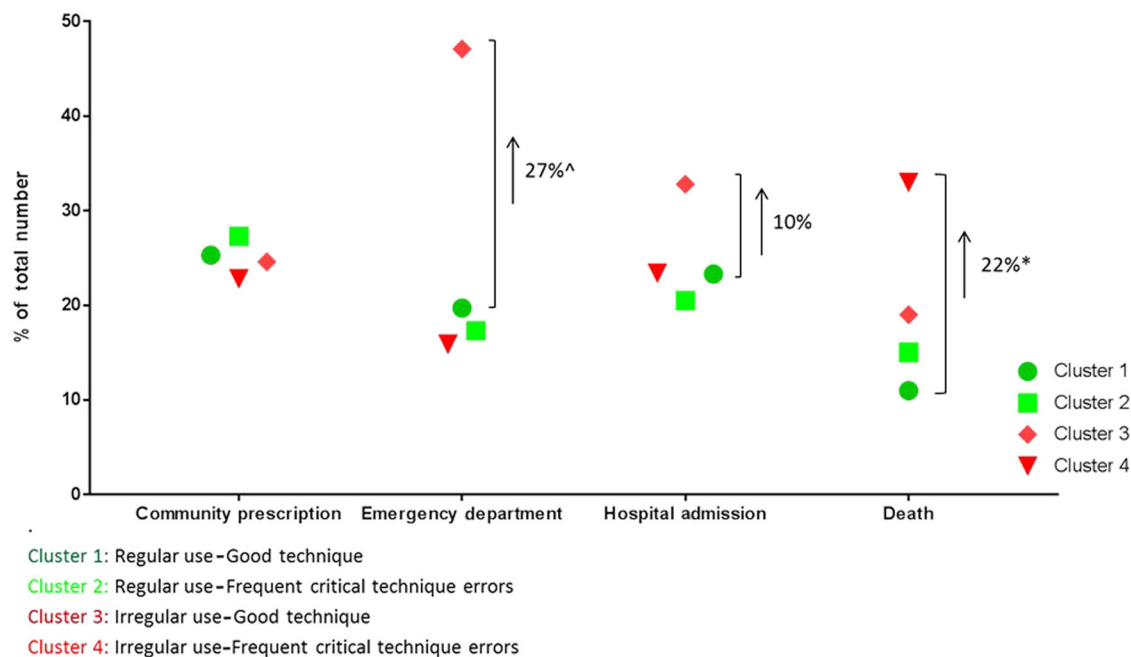JFM van Boven et al.

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Fig. 1 Proportional contribution of each adherence cluster to all-cause clinical outcomes over the 12-month follow-up period (adjusted for the number of participants per cluster). Reported differences are the absolute differences in the proportion of events attributable to cluster 3 vs. cluster 1 for emergency department and hospital admission and cluster 4 vs. cluster 1 for death. ^ denotes $p = 0.05$, *$p < 0.05$

Table 1. Cost-effectiveness of enhancing adherence based on a 5-year time horizon

Cluster	Total costs	Intervention costs[a]	Medication costs	Healthcare costs	Life years	QALYs
Cluster 2: Regular use, frequent technique errors						
Intervention	€11,386	€184	€2901	€8300	3.75	3.00
Cluster 2	€10,150	€0	€2723	€7428	3.52	2.81
Difference	€1235	€184	€179	€872	0.23	0.19
ICER	€6520/QALY gained					
Cluster 3: Irregular use, good technique						
Intervention	€11,812	€184	€2936	€8692	3.80	3.03
Cluster 3	€12,657	€0	€2395	€10,262	3.40	2.70
Difference	−€845	€184	€541	−€1570	0.39	0.33
ICER	Cost-saving (i.e., less costs, more QALYs)					
Cluster 4: Irregular use, frequent technique errors						
Intervention	€13,075	€184	€3000	€9891	3.88	3.10
Cluster 4	€10,180	€0	€1918	€8261	2.98	2.36
Difference	€2896	€184	€1082	€1630	0.90	0.74
ICER	€3935/QALY gained					

ICER incremental cost-effectiveness ratio, *QALY* quality-adjusted life year
[a]Note that the mean per-patient intervention costs are slightly lower given some patients die within the first year and so do not cost the full €200

described in this report, identified four patterns of adherence and may give guidance as to how we might approach this challenge in a personalized manner. Hence, in the future, by providing personalized interventions to the highest risk groups we may both improve adherence and have a positive impact on both clinical and economic outcomes in those most in need, such as those in cluster 3. The need for personalized adherence-enhancing interventions has recently been highlighted.[9] They could include education and training on inhaler technique for those with frequent technique errors, patient reminders for those with irregular use due to forgetfulness, and shared decision-

making and motivational interviewing for those with irregular use due to a conscious, intentional decision.[9]

This study is a first attempt to estimate the cost-effectiveness of interventions in different adherence clusters, but was limited by the use of post hoc and short-term effectiveness data for the different clusters. Regarding generalizability, absolute costs may differ per country or setting, but we expect relative cluster results to be comparable. Our exploratory cost-effectiveness model estimates should be confirmed when long-term clinical intervention trial data become available, including extensive sensitivity and scenario analyses as well as analyses in a non-admitted primary care COPD population.

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CONCLUSION

Personalized adherence interventions targeting patient-specific regularity of inhaler use and inhaler technique could result in clinical and economic benefits for COPD patients.

METHODS

Study design

This was an exploratory cost-effectiveness analysis. Ethical approval for the clinical study was obtained from the Beaumont Hospital Ethics Committee.

Patient population

Patient selection and data collection has been described previously.[1] Briefly, hospitalized patients with COPD, prescribed salmeterol/fluticasone propionate (Seretide®, GlaxoSmithKline, Ireland), were included and written informed consent was obtained from all participants.

Inhaler adherence

Adherence was assessed using the INCA™ device that can track both timing and quality of inhaler use.[1] The INCA acoustic recordings allowed for identification of the following four adherence clusters:[7] (1) regular use/good technique, (2) regular use/frequent technique errors, (3) irregular use/good technique, and (4) irregular use/frequent technique errors. Cluster-specific healthcare utilization and mortality was studied previously[7] and is summarized in Fig. 1.

Cost-effectiveness analysis

The cost-effectiveness of enhanced adherence, i.e., the theoretical shift of patients from poor adherence (i.e., cluster 2, 3, or 4) to good adherence (i.e., cluster 1), was estimated. Therefore, a previously developed, described, and validated health-economic model[5] was used and populated with Irish and INCA-specific cost (for medication, intervention, and healthcare utilization) and effect (mortality and exacerbations) data (Appendix 1). The model has received a high-quality score in the latest COPD model review,[10] and estimates the incremental cost-effectiveness ratio (ICER) in terms of costs (2013, €) per quality-adjusted life-year (QALY) gained from the Irish healthcare payer's perspective assuming fixed per-patient intervention costs of €200 (authors' estimation). Three ICERs were calculated using cluster 1 as intervention and clusters 2, 3, and 4, respectively, as usual care scenarios. In line with recommendations,[11] a policy-relevant time horizon of 5 years was used, taking into account a 5% discount rate for both costs and effects as per Irish Health Information and Quality Authority guidelines (www.hiqa.ie).

Data availability statement

Detailed data and characteristics of the study population are available in ref. [1] and other data that support the findings of this study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

J.F.M.v.B. and R.W.C. designed the study. I.S., M.M., and E.M. were primarily involved in patient recruitment and management of the patients, R.B.R. was primarily involved in the audio analysis required for this manuscript. B.C., G.G., and K.B. were primarily involved in data collection and analysis. J.F.M.v.B. was primarily involved in the health-economic analysis and wrote the first draft of the manuscript. All authors provided input and approved the final manuscript. J.F.M.v.B. is the guarantor of the study.

ADDITIONAL INFORMATION

Competing interests: R.W.C. and R.B.R. are named on a patent for the INCA device.

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