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**Title:** Optimizing chronic obstructive pulmonary disease (COPD) diagnosis and management to reduce healthcare costs: Systematic review and modeling

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**Body:** COPD represents an important burden to the National Health System (NHS) in Spain. The objective of this study is to estimate the gains in terms of COPD cost reduction achievable with simple measures directed towards improving COPD diagnosis and management. Based on the data extracted from a systematic review of the international literature on COPD healthcare resource use and costs (48 papers selected; 2002-2012; sources: MedLine/PubMed, Cochrane Library, ISI WOK, MEDES, IBECS, CSIC, Google Scholar), a model was built to estimate potentially avoidable costs (NHS perspective) due to: a) early COPD diagnosis by performing spirometry to 1% of the undiagnosed population, and reduction of COPD progression by improving treatment effectiveness as a result of implementing treatment guidelines; and b) reduction by 1% of either the non-persistent or non-adherent population. The model shows that the initial investment on performing spirometries and augmenting the proportion of diagnosed patients would be outweighed by the substantial gain derived from avoiding COPD progression to the next more severe stage in the diagnosed population. The cost reduction markup varies between 0.6 and 12 million Euros (2012), depending on the annual per patient cost estimate considered. Focusing the effort on improving patients' treatment persistence and adherence could further avoid 666€ and 601€ (2012) per patient and year, respectively. Earlier diagnosis and treatment effectiveness improvement are crucial to reduce COPD costs in the Spanish NHS. Comprehensive research on the costs of COPD and on the compliance of patients to treatment is needed in Spain.