

Cost-Effectiveness Analysis of Implementing a Secondary Prevention Programme in Those Patients Who Visited an Emergency Department for Drug-Related Problems

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Research article

Keywords: Adverse drug event, Emergency care, Polypharmacy, elderly, cost-effectiveness; Health economics

Posted Date: June 29th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-659198/v1>

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Abstract

Background: To evaluate the cost-effectiveness of a secondary prevention programme in patients admitted to the Emergency department due drug-related problems (DRPs)

Methods: A decision model compared costs and outcomes of patients admitted to the Emergency department with drug-related problems included in Anatomical Therapeutic Classification (ATC) groups A, B or C was designed, based on the results of a randomized clinical trial (NCT03607097). Model variables and costs, along with their distributions, were obtained from the trial results and the literature. The study was performed from the perspective of the National Health System including only direct costs. The Incremental Cost-Effectiveness ratio (ICER) was analysed regarding the ability of the programme to reduce emergency department revisits. Uncertainty in ICERs was evaluated with probabilistic sensitivity analyses.

Results: According to the results of the proposed model, the implementation of a secondary prevention programme for DRPs reduces the cost associated with Emergency Department revisits, with an annual net benefit of €87,639. Considering a mortality rate attributable to readmission for DRPs of 4.7%, the cost per life-years gained (LYG) with the implementation of this program was €2,205. In the short term, the reduction in the number of revisits due to the implementation of the programme was the variable that most affected the model, with the benefit threshold value corresponding to a relative reduction of 12.4% of the number of revisits in patients with DRPs to obtain benefits with the implementation of this type of programme.

Conclusions: Implementing a secondary prevention programme is cost-effective on patients admitted to the emergency department with DRPs. Implementation costs will be exceeded by reducing revisits to the emergency department.

Introduction

Drug-related problems (DRPs), defined as pharmacotherapy failure in patients owing to drug efficacy, safety, or availability problems, are a major public health issue. It is estimated that approximately 5–10% of hospital admissions and 30% of Emergency Department (ED) visits result from DRPs, and most are considered preventable [1–4].

Several studies published over the last decade have demonstrated that the implementation of multidisciplinary programmes focused on the primary prevention of DRPs can be effective strategies to reduce the risk of hospital admission [5–7]. However, the available evidence on the efficacy of secondary prevention programmes in patients who suffer a first DRPs episode is limited. Therefore, we designed a clinical trial (Clinical Trials.gov: NCT03607097) in a public tertiary hospital to determine the impact of a multidisciplinary action on patients who visit the ED with DRPs, whose results have been published recently [8]. Despite the high number of studies that show the healthcare impact of these programmes, there is limited information on the efficiency of this type of intervention. The reduction in the number of

hospital assistances secondary to the implementation of these programs implies a lower cost for the public health system.

Cost-effectiveness analyses are a useful tool to guide on the selection of efficient strategies for health institutions and healthcare administrators. The aim of our study was to determine the cost-effectiveness of the implementation of a secondary prevention programme for DRPs in patients attended in an ED by extrapolating the patient-level data collected from the Medication Code trial

Methods

In the present study, we conducted a cost-effectiveness analysis of the implementation of a multidisciplinary healthcare programme for the secondary prevention of DRPs in patients attending an ED from a Catalan healthcare payer perspective. Specifically, the programme developed a set of interventions at different levels of healthcare (collectively referred to as 'Medication Code') with the objective of reducing the 30-day revisits of patients attended in the ED for DRPs caused by medicines from the Anatomical Therapeutic Chemical (ATC) categories A (Alimentary tract and metabolism), B (Blood and blood forming organs) or C (Cardiovascular system). These interventions included actions aimed at improving the patient's chronic prescriptions (interview with the patient and a review of their chronic medication treatment), therapeutic adherence (including the delivery of written information on the medication treatment plan and a telephone consultation 48 h after discharge), and coordination between different levels of healthcare (including sending an email to the next healthcare provider explaining the reason for the consultation any changes in the medication treatment). Patients in the control group received the standard care in ED, consisting of medication review and prescriptions validation.

For this purpose, an economic model was developed to determine the effects on the short-term (time horizon: 30 days) implementation of the programme in a 644-bed public tertiary university hospital that attends 140,000 emergencies per year. The development of the model was based on the results of the 'Medicine Code' Clinical Trial (Clinical Trials.gov: NCT03607097) [8]. According to the results of this clinical trial, the population that consults the hospital emergency services for DRPs is mainly aged (average age: 80.3 (12.4) years), polymedicated (median: 9 (IQR:6–12)), being antithrombotic drugs the majority involved in these episodes. The model considered the context of the National Health System and included only direct medical costs (Table 1). The costs assumed for the implementation of the programme included the salaries of two full-time clinical pharmacist specialised in the management of patients with DRPs.

Table 1
Costs and variables considered in the model.

| | Intervention | DRP Code | References |
|--|---------------------|-----------------|-------------------|
| | Group | | |
| ED assistance fee | 185 | 185 | [18] |
| Hospital admission fee | 3000 | 3000 | [19] |
| Annual healthcare specialist salary (€) | 0 | 59,284 | [19] |
| Annual cost per all DRP code personnel (€) | 0 | 118,568 | |
| ED Revisit | 14.9% | 18.1% | [8] |
| Hospital readmission | 10.4% | 7.3% | [8] |
| Mortality | 4.7% | 4.7% | [8] |
| Hospital-days | | | |
| Annual ED Visits | 144000 | 144000 | [20] |
| % DRP as cause of ED visit | 21.0% | 21.0% | [9] |
| % DRP caused by ATC groups A, B or C | 36.4% | 36.4% | [9] |
| % Patients lost | 30.0% | 30.0% | |
| Life of years Gained | | | |
| Mean age | 80.1 | 80.1 | [8] |
| Life expectancy (years) | 83.6 | 83.6 | [10] |

DRP: Drug-related problems; ED: Emergency department; ATC: Anatomical therapeutic classification

According to the results published in the literature, the frequency of ED visits owing to DRPs is 21%, of which 36.4% are caused by medicines from therapeutic groups A, B, or C [9]. According to the results of the clinical trial, the implementation of a health programme for patients with DRPs reduces the frequency of 30-day ED revisits by 17.6% (14.9% vs. 18.1%) and 30-day readmissions by 29.8% (7.3% vs. 10.4%)⁸. For the present analysis, a patient identification loss rate of 30% was assumed.

A decision tree was developed to simulate the clinical progression of patients attended in the ED (Fig. 1), according to which patients attended for DRPs for medicines in groups A, B, or C could be either treated or not by the 'Medication Code' programme. To simplify the model, the DRPs were considered mutually exclusive. As the study determined the effect of the intervention programme after hospital discharge, the possible reduction in the patient's length of hospital stay after the initial intervention programme was not considered in the model.

An incremental cost-effectiveness ratio (ICER) analysis was performed on the ability of the programme to reduce ED attendance. The ICER was calculated based on the costs assumed for the implementation of the programme in relation to the ED revisit cases with and without the implementation of the programme. The cost per life year gained (LYG) was calculated based on the prevention of death after a revisit due to DRPs, considering a mortality attributable to the admission for DRPs of 4.7% and a mean age of ED attendance of 80.3 years according to the results of the clinical trial⁷, being the life expectancy of 83.8 years in Spain [10].

The final model was calculated using Microsoft Excel v.14.5.9. A univariate sensitivity analysis (tornado diagram) was performed to establish the short-term robustness of the model to variables with uncertainty, including the risk of revisit and readmission (50%), costs associated with revisits (20%), number of annual ED visits (5%), patient identification loss rate (50%), as well as the percentage of visits caused by DRPs in A, B, or C groups (20%).

In addition, a probabilistic sensitivity analysis was performed to analyse the cost per prevented DRPs and per LYG. The variables included in the analysis were the risk of revisit and readmission (50%), the costs associated with these (20%), the number of annual ED visits (5%), the patient identification loss rate (50%), as well as the percentage of visits caused by DRPs in groups A, B, or C (20%). The variation in mortality related to DRPs was considered to be 20%. The analysis was performed using a Monte-Carlo simulation on the included uncertainty variables, simulating a cohort of 1,000 patients admitted to the ED unit, either after the implementation of the program or without it. Each point estimate contains random values within the considered range. All variable distributions were considered to represent beta distributions. The considered distribution values are presented in Table 2.

Table 2
Probability values and fixed applied during probabilistic sensitivity analysis.

| Name | Data distribution | Point estimate of probability | Initial value considered | Range |
|--|-------------------|-------------------------------|--------------------------|-----------------|
| Hospital readmission reduction | beta | 29.8% | 50,0% | 14.9–44.7% |
| Revisit reduction | beta | 17.6% | 50,0% | 8.8–26.4% |
| Annual visits to ED | beta | 144,000 | 5,0% | 136.800-151.200 |
| Annual visits to ED caused by DRP | beta | 21,0% | 20,0% | 16.8–25.2% |
| DRPs caused by drugs from ATC groups A, B or C | beta | 36.4% | 20,0% | 29.1–43.6% |
| DRPs mortality | beta | 4.7% | 20,0% | 3.8–5.6% |
| Patients Lost | beta | 30,0% | 50,0% | 15.0–45.0% |
| Annual Cost of DRP-Code implementation | uniform | 89,000 € | * | 89.000 € |
| Cost per ED visit | uniform | 185 € | * | 185 € |
| Cost per hospitalization | uniform | 3,000 € | * | 3,000 € |

¹DRP: Drug-related problem; EDD: Emergency Department

Results

According to the results of the proposed model, the implementation of a secondary prevention programme for DRPs reduces the cost associated with ED revisits, with an annual net benefit of €87,639 (CI95%:80,258 – 94,021) thus, representing the most significant option. Considering a mortality attributable to readmission for DRPs of 4.7%, the cost per LYG with the implementation of this program was €2,055 (CI95%:1,403-2,927).

The results of the univariate analysis are shown in Fig. 3. In the short term, the reduction in the number of revisits due to the implementation of the intervention programme was the variable that most affected the model, with the benefit threshold value corresponding to a relative reduction of 12.4% of the number of revisits in patients with DRPs to obtain benefits with the implementation of this type of programme. The results of the probabilistic sensitivity analysis are shown in Fig. 3 (cost per prevented revisit) and Fig. 4 (Cost per LYG).

Discussion

According to the proposed model, the implementation of a multidisciplinary team action programme to prevent revisits in patients attended in the ED for DRPs is a cost-effective strategy.

DRPs is a growing public health concern in an environment of increasingly polymedicated patients [11], with a significant impact both in terms of health and consumption of healthcare resources. Several studies conducted over the last decade have shown that DRPs prevention programmes can reduce both the number of hospital admissions and healthcare costs [12]. The results of our clinical trial support these findings, demonstrating that a secondary DRPs prevention programme reduces both the number of ED revisits and hospital readmissions. However, as with any health intervention, cost-effectiveness analysis is an important aspect to be considered in the decision-making process of DRPs prevention programme implementation.

The economic benefit of the implementation of primary DRPs prevention programmes has been confirmed by many published reports [13–16]. These studies have shown that these types of programmes have the potential that do not require additional resources. However, to date there are no published studies with complete pharmacoeconomic models of these types of interventions, often considering only costs associated with reducing the treatment cost and without appropriate sensitivity analyses. However, there are also no reports on the benefits of the implementation of a secondary DRPs prevention programme that is coordinated by an ED.

Our study demonstrates that a set of measures at different levels of care provide a significant economic benefit. It should be noted that the potential benefits of the implementation of this type of programme include not only a reduction in the number of ED revisits to the emergency room, but also an improvement in the quality of life of patients. Several studies have shown an improvement in the quality of life with an intervention programme for chronic treatments [14–17], which is a benefit to be considered after the investment made. However, the results of the clinical trial did not include this aspect in this group of patients, not allowing to perform a quality-adjusted year's analysis.

According to the proposed model, the higher the number of patients attending the ED for DRPs, the more likely is that the programme will be cost-effective; therefore, the implementation of this programme would be especially beneficial in those EDs with a high rate of DRPs, resulting from a high-risk population or a poor health care at other levels of care.

We identified several limitations in our study. First, there is an important variability in the frequency of ED visits caused by DRPs [4], affecting the efficiency of the model presented. Secondly, the model was designed based on the results of one clinical trial conducted in a single centre. It has been published a wide variability in the results obtained with the implementation of DRPs prevention programmes in terms of hospital revisits and readmissions [18]. However, it should be noted that the results obtained in the reference clinical trial are similar to those obtained by *Ravn-Nielsen et al* [4] with a similar intervention model. Therefore, we consider that the proposed economic model has sufficient clinical evidence.

Nevertheless, it should be considered that the interventions performed at discharge for pharmacotherapy optimisation programmes are very heterogeneous in the different hospitals; therefore, the results of other types of interventions that do not fit to the model used in this clinical trial require their own economic analysis. Moreover, the phenomenon of ED revisits is a complex issue that is affected by the structure of the healthcare system. To account for this variability, we included a wide range of cases in the sensitivity analysis, considering a variation in the reduction in hospital revisits and readmissions, as well as a 50% loss in patient identification. With this variation, we have included a range of values in which most cases could be found.

Owing to the context used to calculate the cost (Catalan Health System) and considering the high variability in the salaries of clinical pharmacists and the cost of healthcare between countries, the economic results obtained in our study cannot be directly extrapolated to other contexts and should be adjusted to each particular healthcare system. It should also be considered that our model included a tertiary hospital, with sizeable ED attendance and an ageing population. Therefore, its extrapolation to smaller hospitals, as well as to those attending a younger population, could also be inappropriate. However, the results of the present study are enough consistent to ensure that the implementation of this type of programme is a highly efficient strategy.

Conclusions

DRPs are an emerging health problem given the increase in the number of polymedicated patients. Therefore, it is necessary to develop interventions that minimise their impact on patients and healthcare systems. The results of our study strongly support investing in a secondary DRPs prevention programme acting at different levels of healthcare is a cost-effective strategy.

Declarations

Funding's: This research has been supported by a grant from Instituto de Salud Carlos III (Ministry of Science and Innovation, Spain). IP PI18/00889.

Conflicts of interest/Competing interests (include appropriate disclosures): None of the authors has any potential financial conflict of interest

Availability of data and material: Not applicable.

Code availability (software application or custom code): Not applicable.

Authors' contributions: JR and AJ participated in the design of the study, data collection and performed the statistical analysis. MP and MMA were responsible for the coordination of the study, participated in its design and helped to draft the manuscript. LL and MB participated in specific literature collection. TG and JMG participated in the design of the study and statistical analysis. All authors read and approved the final manuscript.

Ethics approval (include appropriate approvals or waivers): This study was approved by the Clinical Research Ethics Committee of the Santa Pau Hospital (Hospital Santa Pau; Reference No: IIBSP-COD-2018-25)

Consent to participate (include appropriate statements): Not applicable.

Consent for publication (include appropriate statements): All authors have approved the manuscript before publication. No material of this article has been published elsewhere

Funding (information that explains whether and by whom the research was supported).

References

1. Baena MI, Faus MJ, Fajardo PC, Luque FM, Sierra F, Martínez-Olmos J, et al. Medicine-related problems resulting in emergency department visits. *Eur J Clin Pharmacol.* 2006;62:387–93. <https://doi.org/10.1007/s00339-007-4137-z>.
2. Ayalew MB, Tegegn HG, Abdela OA: Drug Related Hospital Admissions; A Systematic Review of the Recent Literatures. *Bull Emerg Trauma.* 7, 339–346. (2019). <https://doi.org/110.29252/beat-070401>.
3. Nivya K, Sri Sai Kiran V, Ragoo N, Jayaprakash B, Sonal Sekhar, M. Systemic review on drug related hospital admissions - A pubmed based search. - *Saudi Pharm J.* 2015;23:1–8. <https://doi.org/10.1016/j.jsps.2013.05.006>.
4. Patel P, Zed PJ. Drug-related visits to the emergency department: how big is the problem? *Pharmacotherapy.* 2002;22:915–23. <https://doi.org/10.1592/phco.22.11.915.33630>.
5. Ravn-Nielsen LV, Duckert ML, Lund ML, Henriksen JP, Nielsen ML, Eriksen CS, et al. Effect of an In-Hospital Multifaceted Clinical Pharmacist Intervention on the Risk of Readmission. *JAMA Intern Med.* 2018;178:375–82. <https://doi.org/10.1001/jamainternmed.2017.8274>.
6. Koshman SL, Charrois TL, Simpson SH, McAlister FA, Tsuyuki RT. Pharmacist care of patients with heart failure: a systematic review of randomized trials. *Arch Intern Med.* 2008;168:687–94. <https://doi.org/10.1001/archinte.168.7.687>.
7. Wei L, Yang X, Li J, Liu L, Luo H, Zheng Z, et al. Effect of pharmaceutical care on medication adherence and hospital admission in patients with chronic obstructive pulmonary disease (COPD): a randomized controlled study. *J Thorac Dis.* 2014;6:656–62.
8. <https://doi.org/10.3978/j.issn.2072-1439.2014.06.20>.
9. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US); 2000 Feb 29. Identifier NCT03607097, Integral Management of Healthcare Problems Related With Drugs in Polimedicated Patients: Medication Code; 2018 July 18 [cited 2021 Jan 15]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03607097>.
10. Queneau P, Bannwarth B, Carpentier F, Guliana JM, Bouget J, Trombert B, et al. Emergency department visits caused by adverse drug events: results of a French survey. *Drug Saf.* 2007;30:81–8. <https://doi.org/10.2165/00002018-200730010-00008>.

11. Instituto Nacional de Estadística. [Tablas de Mortalidad de la población de España por año, sexo, edad y funciones. INE base]. Retrieved from: <http://www.ine.es/>. Accessed on January 2020.
12. Lum MV, Cheung MYS, Harris DR, Sakakibara BM. A scoping review of polypharmacy interventions in patients with stroke, heart disease and diabetes. *Int J Clin Pharm.* 2020;42:378–92. <https://doi.org/10.1007/s11096-020-01028-x>.
13. Gillespie U, Alasaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, et al.: A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Arch Intern Med* 169, 894–900 (2009) <https://doi.org/10.1001/archinternmed.2009.71>.
14. Hou K, Yang H, Ye Z, Wang Y, Liu L, Cui X: Effectiveness of Pharmacist-led Anticoagulation Management on Clinical Outcomes: A Systematic Review and Meta-Analysis. *J Pharm Pharm Sci Publ Can Soc Pharm.* 20, 378 – 96 (2017). <https://doi.org/10.18433/J3SQ0B>
14. Wu WC, Taveira TH, Jeffery S, Jiang L, Tokuda L, Musial J, et al.: Costs and effectiveness of pharmacist-led group medical visits for type-2 diabetes: A multi-center randomized controlled trial. *PloS One.* 13, e0195898 (2018). <https://doi.org/10.1371/journal.pone.0195898>.
15. Sjölander M, Lindholm L, Pfister B, Jonsson J, Schneede J, Lövheim H, et al. Impact of clinical pharmacist engagement in ward teams on the number of drug-related readmissions among older patients with dementia or cognitive impairment: An economic evaluation. *Res Soc Adm Pharm RSAP.* 2019;15:287–91. <https://doi.org/10.1016/j.sapharm.2018.05.006>.
16. Hogg W, Lemelin J, Dahrouge S, Liddy C, Armstrong CD, Legault F, et al. Randomized controlled trial of anticipatory and preventive multidisciplinary team care: for complex patients in a community-based primary care setting. *Can Fam Physician Med Fam Can.* 2009;55:e76–85. <https://doi.org/10.1007/s00339-007-4137-z>.
17. Cooper JA, Cadogan CA, Patterson SMet al.: Interventions to improve the appropriate use of polypharmacy in older people: a Cochrane systematic review. *BMJ Open.* 2015;5(12):e009235. (2015) <https://doi.org/10.1007/s00339-007-4137-z>.
18. Diari Oficial de la Generalitat de Catalunya. [ORDEN SLT/63/2020, del 8 de marzo, por la que se aprueban los precios públicos del Servicio Catalán de la Salud]. Retrieved from <http://www.gencat.cat/dogc>. Accessed on Marhx 2020.
19. Sistema sanitari integral d'utilització pública de Catalunya. Taules salarials 2020. Retrieved from <https://ccoohospitalssantamaria.wordpress.com/2020/03/11/taules-salarials-siscat-2020/> Accessed on January 2020.
20. Memoria del Hospital Santa Creu i Sant Pau. 2019. Retrieved from <http://www.santpau.cat/es/web/public/memories-sant-pau>. Accessed on January 2020.

Figures

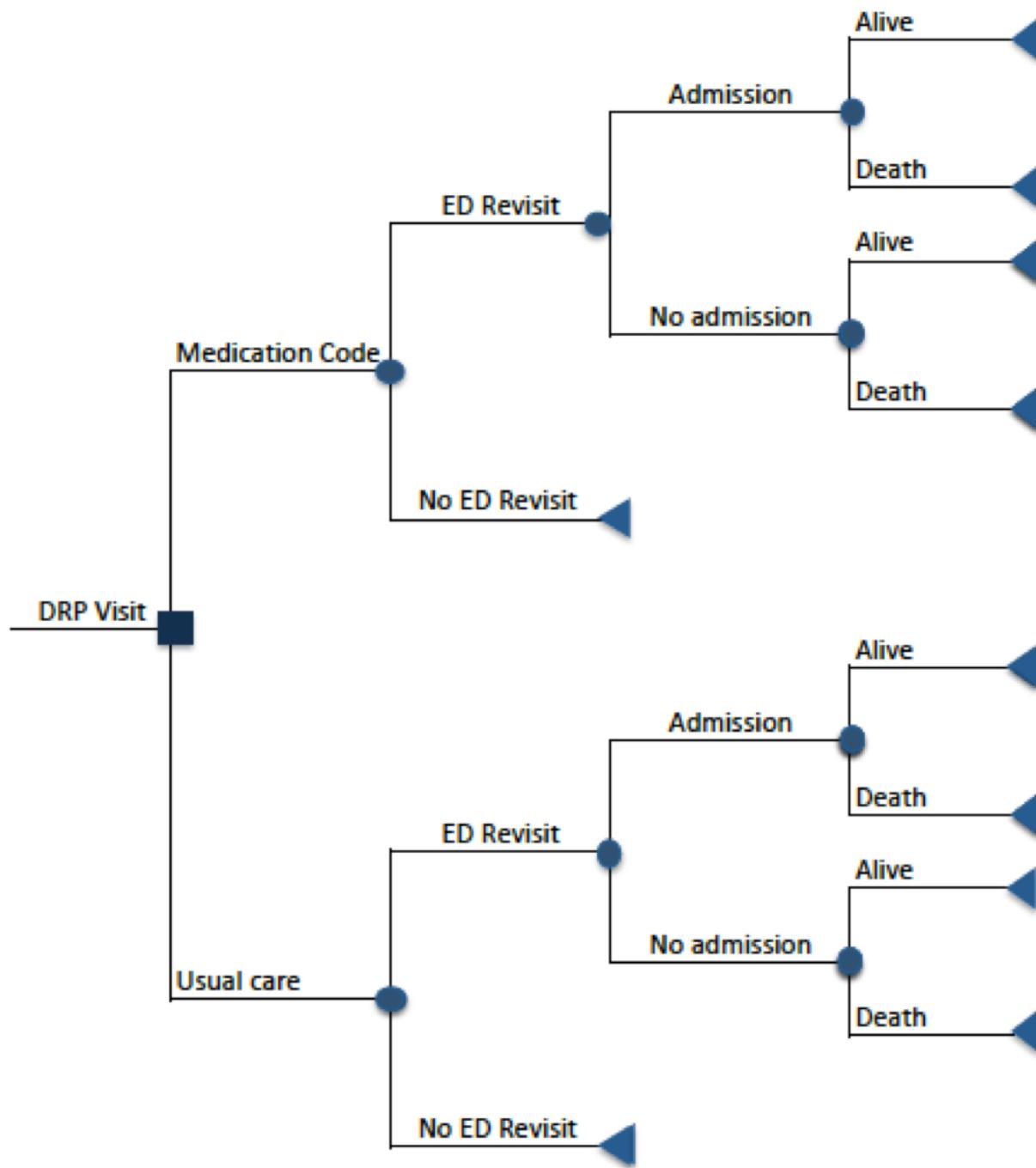


Figure 1

Short-term decision model. DRP= Drug-related problems; ED: Emergency department

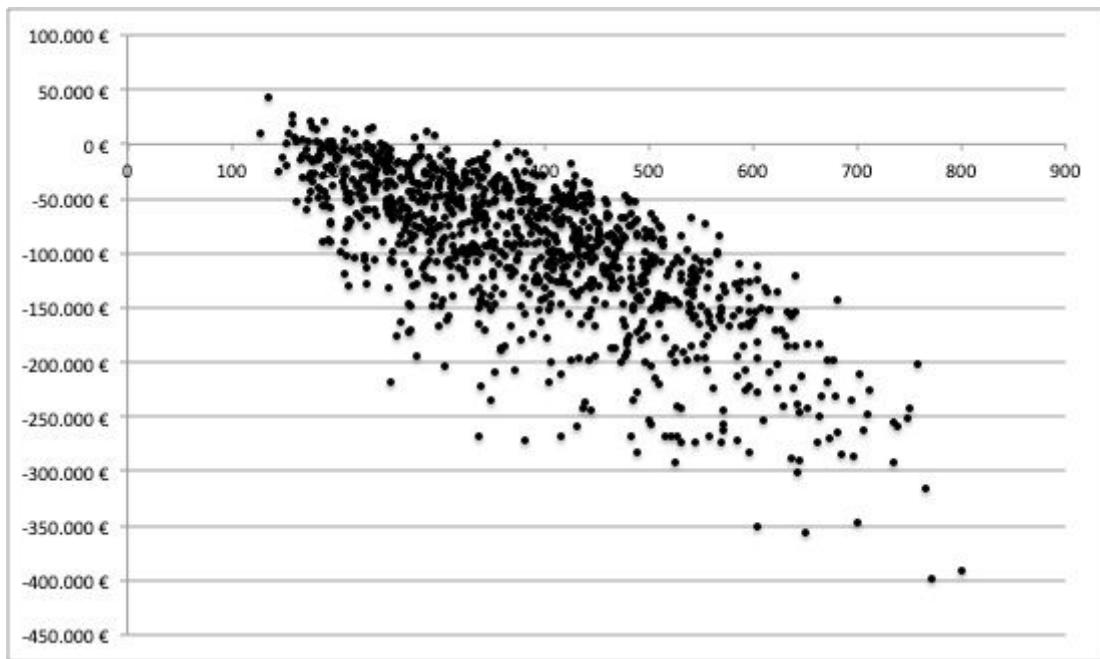


Figure 2

Results of short-term univariate analysis. Each horizontal line represents how the variation of the variables affects the final result obtained in the model (-125,207€). The variations considered were Risk of revisits and readmission (50%), costs associated (20%), number of annual visits to the emergency room (5%), percentage of losses in patient identification (50%), percentage of visits caused by Drug-related problems of ATC groups A, B or C (20%)

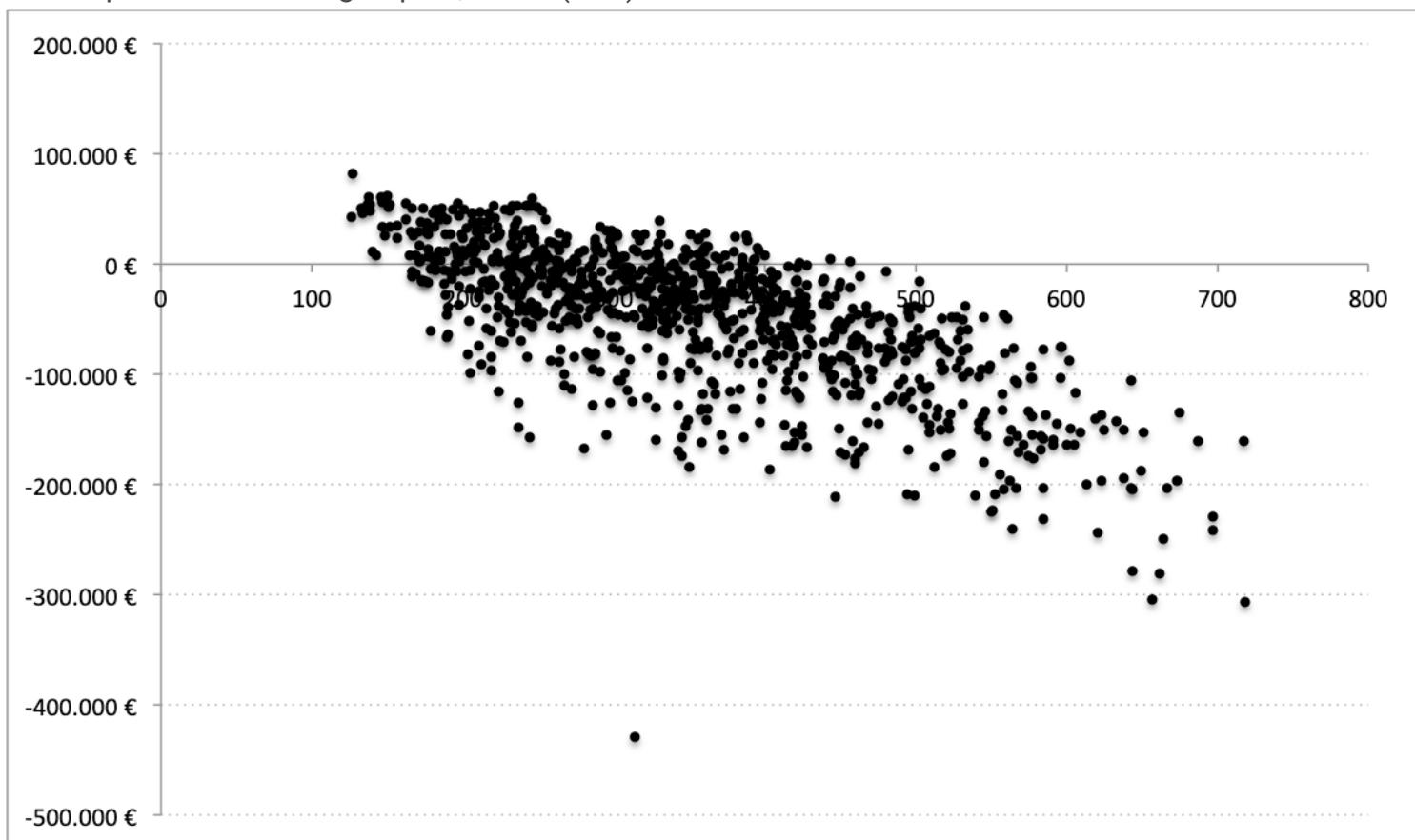


Figure 3

Cost of the intervention programme per re-visit avoided

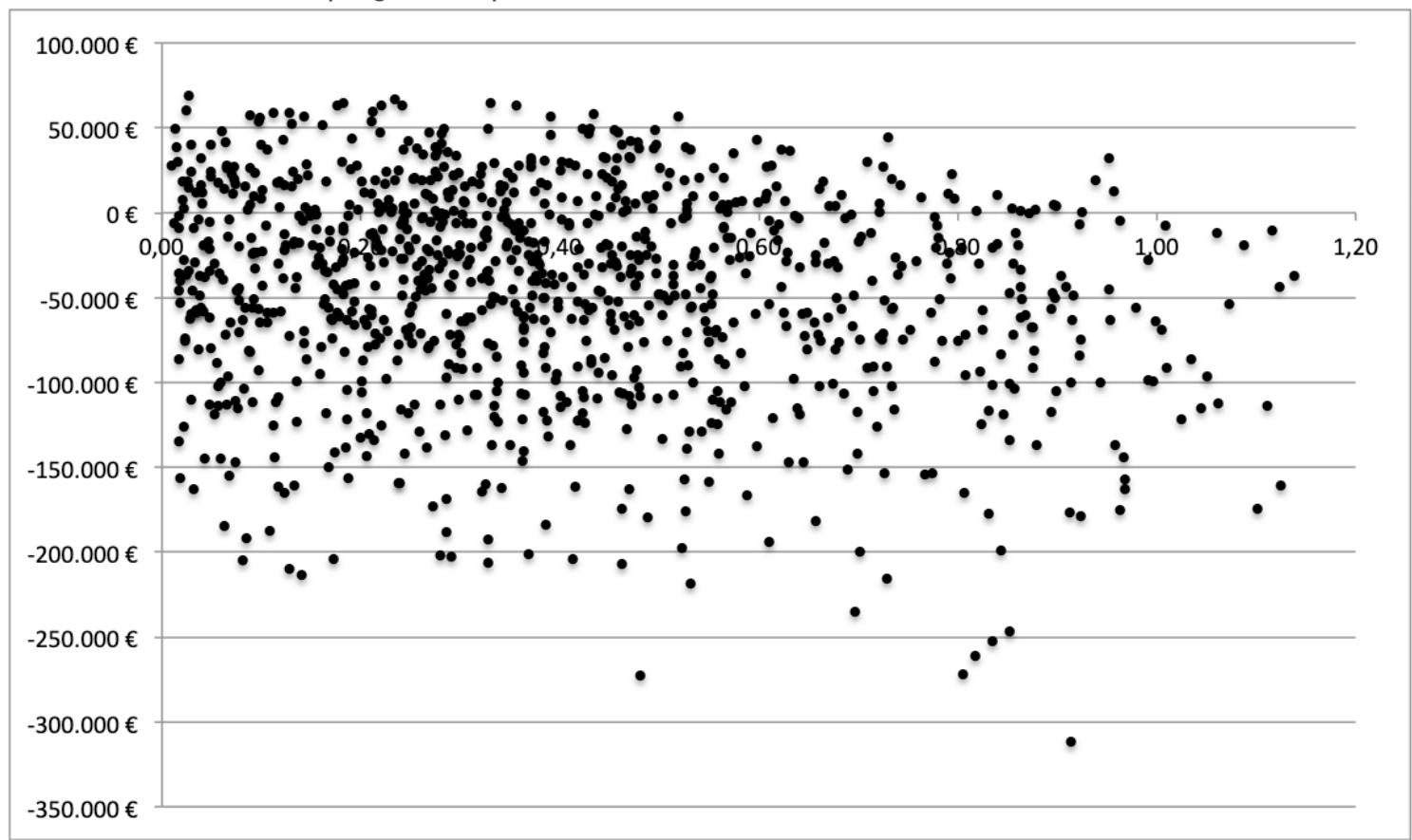


Figure 4

Cost of the intervention programme per life-year gained (LYG)