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Cost-effectiveness analysis of implementing a secondary prevention programme in those patients who visited an emergency department for drug-related problems

Jesus Ruiz-Ramos[1,*], Ana Juanes-Borrego[1], Mireia Puig-Campany[2], Marta Blazquez-Andión[2], Laia López-Vinardell[1], Antonio Gilabert-Perramon[3], Josep María Guiu-Segura[3] and Maria Antonia Mangues-Bafalluy[1]

[1]Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[2]Emergency Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[3]Pharmacy and Medicine Department, Consorci de Salut i Social de Catalunya, Barcelona, Spain

*Correspondence: Jesús Ruiz-Ramos, Servicio de Farmacia, Hospital de la Santa Creu i Sant Pau, Calle San Quintin 89, 08025 Barcelona, Spain.
Tel: +34679131309; Email: jrzrms@gmail.com

Abstract

Objective To evaluate the cost-effectiveness of a secondary prevention programme in patients admitted to the emergency department due to drug-related problems (DRPs).

Methods A decision model compared costs and outcomes of patients with DRPs admitted to the emergency department. Model variables and costs, along with their distributions, were obtained from the trial results and literature. The study was performed from the perspective of the National Health System including only direct costs.

Key findings The implementation of a secondary prevention programme for DRPs reduces costs associated with emergency department revisits, with an annual net benefit of €87 639. Considering a mortality rate attributable to readmission of 4.7%, the cost per life-years gained (LYG) with the implementation of this programme was €2205. In the short term, the reduction in the number of revisits following the programme implementation 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 of patients with DRPs to obtain benefits.

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

Keywords: adverse drug event; emergency care; polypharmacy; elderly; cost-effectiveness; health economics

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. Approximately 5–10% of hospital admissions and 30% of emergency department (ED) visits are due to DRPs, and most cases are preventable.[1–4]

Several studies have demonstrated that the implementation of multidisciplinary programmes for the primary prevention of DRPs can be an effective strategy to reduce hospital admission.[5–7] However, the available evidence on the efficacy of secondary prevention programmes in patients who experience their first DRP episode is limited. Therefore, we designed a clinical trial in a public tertiary hospital to determine the effect of a multidisciplinary programme on patients with DRP-related ED visits, whose results have been published recently.[8] Despite the multitude of studies that show the healthcare effects of these programmes, information on the efficiency of this programme is limited. The reduction in the number of hospital assistances secondary to the implementation of these multidisciplinary programmes implies a lower cost for the public health system.

Cost-effectiveness analyses are useful tools to guide the selection of efficient strategies for healthcare institutions and administrators. Thus, this study aimed to determine the cost-effectiveness of a secondary prevention programme for DRP-related ED visits by extrapolating patient data collected from the Medication Code trial.

Methods

In this 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 included a set of interventions at different healthcare levels (collectively referred to as 'Medication Code') to reduce the 30-day ED revisits of patients with DRPs caused by medicines from the Anatomical Therapeutic Chemical (ATC) categories A (alimentary tract

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Table 1 Costs and variables considered in the model

	Intervention group	DRP code	References
ED assistance fee (€)	185	185	[10]
Hospital admission fee (€)	3000	3000	[11]
Annual healthcare specialist salary (€)	0	59 284	[11]
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	144 000	144 000	[12]
% DRP as cause of ED visit	21.0%	21.0%	[9]
% DRP caused by ATC categories 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)	85.4	85.4	[13]

Abbreviations: ATC, Anatomical Therapeutic Chemical classification; DRP, drug-related problems; ED, emergency department.

and metabolism), B (blood and blood-forming organs) or C (cardiovascular system). The programme included activities 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 about the medication treatment plan and a telephone consultation 48 h after discharge) and coordination between different healthcare levels (including sending an email to the next healthcare provider explaining the reason for the consultation and any changes in the medication treatment). The control group received standard care in the ED, consisting of medication review and prescription validation.

The model was developed based on the results of the 'Medicine Code' Clinical Trial (Clinical Trials.gov: NCT03607097).[8] The characteristics of the patients included in the clinical trial are described in Supplementary Table 3. According to these results, individuals who consult the hospital emergency services for DRPs are mainly 80.3 (12.4) years old, were polymedicated (median, 9 [interquartile range (IQR) 6–12)], and had antithrombotic drugs of which the majority were involved in these episodes. Among the 769 patients included in the analyses, 68 (8.8%) were readmitted within 30 days (control group, 40 of 386 [10.4%]; intervention group, 28 of 383 [7.3%]). In the adjusted model, the incidence of hospital readmission was lower in the intervention group than in the control group (odds ratio, 0.61 [95% confidence interval (CI), 0.37 to 0.97]; $P < 0.046$). Regarding the secondary variable, the frequency of ED revisits within 30 days after discharge was 18.1% [70 of 386] in the control group and 14.9% [57 of 383] in the intervention group.

For the cost-effective analysis, an economic model was developed to determine the effects of the short-term (30 days) implementation of the programme in a 644-bed public tertiary university hospital that attends 140 000 emergency cases per year, considering a frequency of 21% of DRP-related ED, of which 36.4% are caused by medicines from therapeutic categories A, B or C.[9] For the present analysis, a patient identification loss rate of 30% was assumed. 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 pharmacists who specialized in the management of patients with DRPs.

A decision tree was developed to simulate the clinical progression of patients who visited the ED (Figure 1); accordingly, patients who attended the ED for DRPs caused by medicines in categories 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 programme after hospital discharge, the possible reduction in the patient's length of hospital stay after the initial 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 visits. 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 programme. The cost per life-years gained (LYG) was calculated based on the prevention of death after a DRP-related revisit, considering a mortality rate of 4.7% attributable to admission for DRPs and a mean age of 80.3 years on ED attendance according to the results of the clinical trial,[7] with the life expectancy of 90.2 years in patients aged 80 years in Spain.[13] Cost-effectiveness was defined as a strategy that costs less than €27 000 per LYG based on the GDP per capita in Spain.[14, 15]

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%), revisit-associated costs (20%), number of annual ED visits (5%), patient identification loss rate (50%) and rates of visits for DRPs caused by drugs in categories A, B or C (20%).

A probabilistic sensitivity analysis was also performed to analyse the costs per prevented DRPs and LYG. The variables included in the analysis were the risk of revisit and readmission (50%), associated costs (20%), number of annual ED visits (5%), patient identification loss rate (50%) and rates of

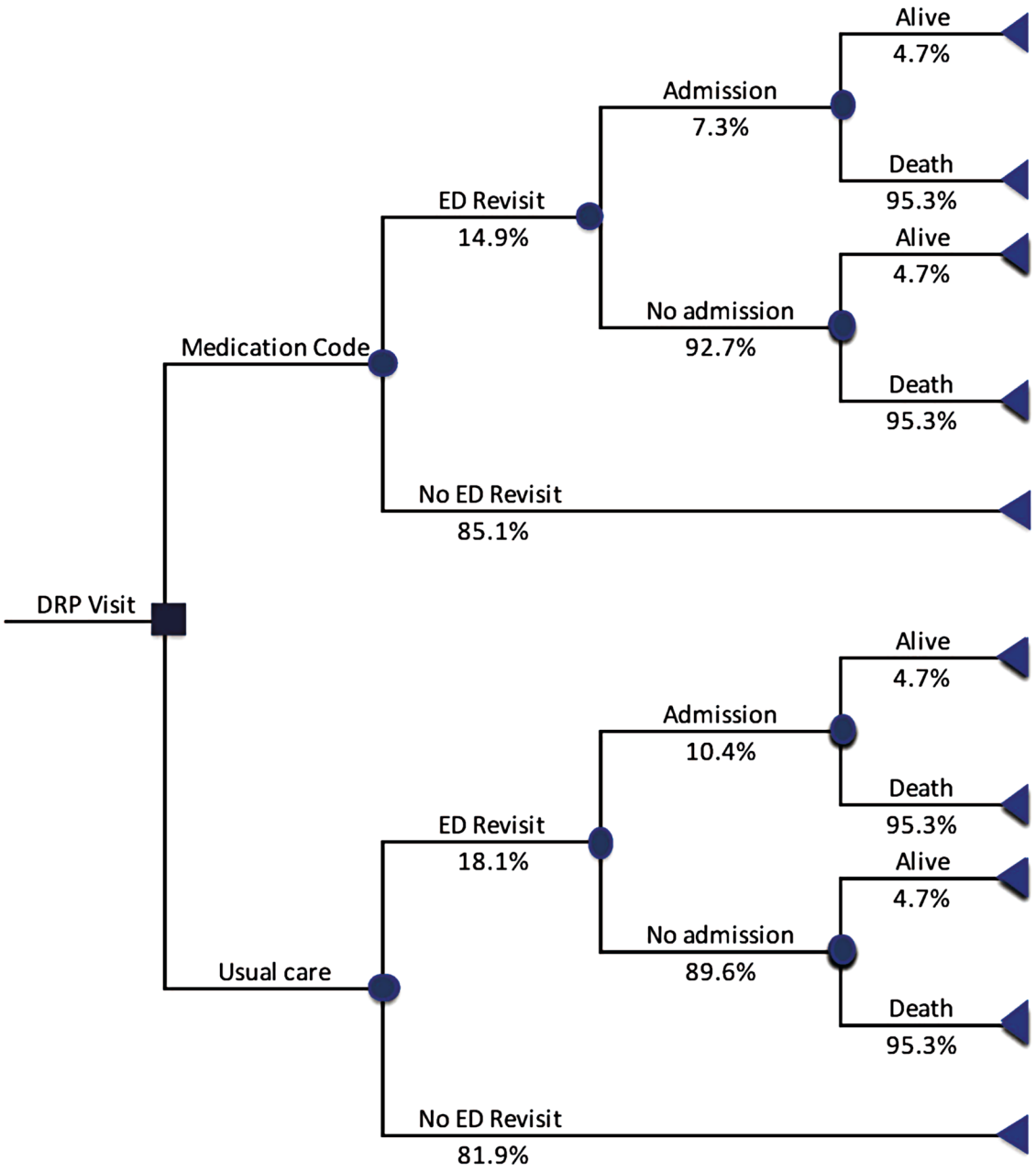

Figure 1 Short-term decision model with the probability coefficients assigned to each branch. DRP, drug-related problem; ED, emergency department.

visits for DRPs caused by drugs in categories A, B or C (20%). The variation in DRP-related mortality was considered 20%. The analysis was performed using a Monte Carlo simulation of the included uncertainty variables, simulating a cohort of 1000 patients admitted to the ED, either after or before the implementation of the programme. 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.

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 (95% CI, 80 258 to 94 021), thus representing the most significant option. Considering a mortality rate of 4.7% attributable to readmissions for DRPs, the cost per LYG with the implementation of this programme was €993.35 (95% CI, 572 to 1514), being considered a cost-effective strategy.

The results of the univariate analysis are shown in Figure 2. In the short term, the reduction in the number of revisits resulting from the programme implementation 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 for DRPs to obtain the benefits of the programme. The results of the probabilistic sensitivity analysis are shown in Figure 3 for the cost per prevented revisit and Figure 4 for the cost per LYG. The acceptability curve showed a greater than 90% probability that the model would be cost-effective for €3000 (Figure 5).

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

Name	Data distribution	Initial value considered	Point estimate of probability	Range (low–high)
Hospital readmission reduction	Beta	50.0%	29.8%	14.9–44.7%
Revisit reduction	Beta	50.0%	17.6%	8.8–26.4%
Annual visits to the ED	Gamma	5.0%	144 000	136.800–151.200
Annual visits to the ED for DRPs	Beta	20.0%	21.0%	16.8–25.2%
DRPs caused by ATC categories A, B or C	Beta	20.0%	36.4%	29.1–43.6%
DRP mortality	Beta	20.0%	4.7%	3.8–5.6%
Patients lost	Beta	50.0%	30.0%	15.0–45.0%
Annual cost of DRP code implementation	Gamma	€89 000	€89 000	€89 000
Cost per ED visit	Gamma	€185	€185	€185
Cost per hospitalization	Gamma	€3000	€3000	€3000

Abbreviations: ATC, Anatomical Therapeutic Chemical classification; DRP, drug-related problem; ED, emergency department.

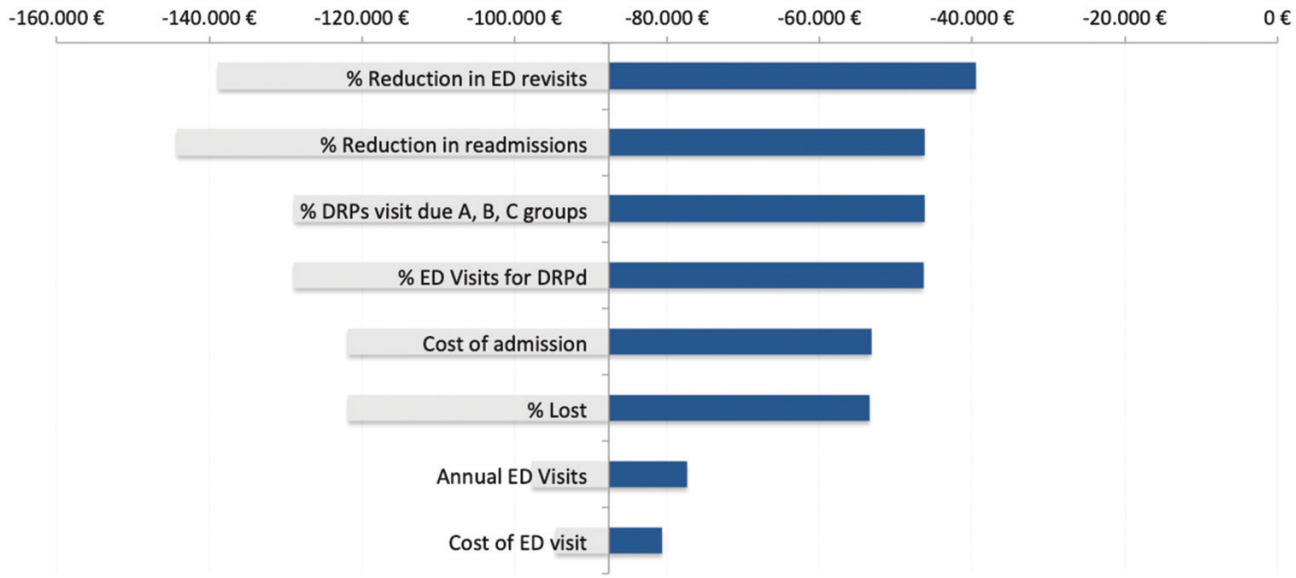

Figure 2 Results of a short-term univariate analysis. Each horizontal line represents how the variation of the variables affects the final result obtained in the model (−125 207€). The variations considered were risk of revisits and readmission (50%), associated costs (20%), number of annual visits to the emergency department (5%), percentage of losses in patient identification (50%), percentage of visits caused by drug-related problems of ATC categories A, B or C (20%).

Discussion

According to the proposed model, the implementation of a multidisciplinary programme to prevent revisits in patients with DRPs who attended the ED is a cost-effective strategy. With a decision-maker's willingness to pay €3000 for an additional LYG, there was a 90% probability of being cost-effective relative to the control for the self-reported health status measure. A high variability in the frequency of DRP-related ED visits and results from a single centre are the main limitations of the model. However, the similarity in the results to those of other published studies and the sensitivity analysis strengthened the present findings.

To the best of our knowledge, this study is the first to show that a secondary prevention programme for DRPs has an economic benefit for the healthcare system. However, our study has some limitations. First, there is an important variability in the frequency of DRP-related ED visits, affecting the efficiency of the model presented. Second, the model was designed based on the results of a single-centre clinical trial. The results obtained with the implementation of DRP prevention programmes varied in terms of hospital revisits and readmissions.[16] However, the results obtained in the reference clinical trial are similar to those obtained by Ravn-Nielsen *et al.*[5] with a similar intervention model. Therefore, we consider that the proposed economic model has sufficient clinical evidence. Nevertheless, the interventions performed at discharge for pharmacotherapy optimization programmes are very heterogeneous in different hospitals; therefore, the results of other interventions that do not fit the model used in this clinical trial require 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 various cases in the sensitivity analysis, considering a variation in the reduction in hospital revisits and readmissions and 50% loss in patient identification. With this variation, we have included a range of values in which most cases could be found.

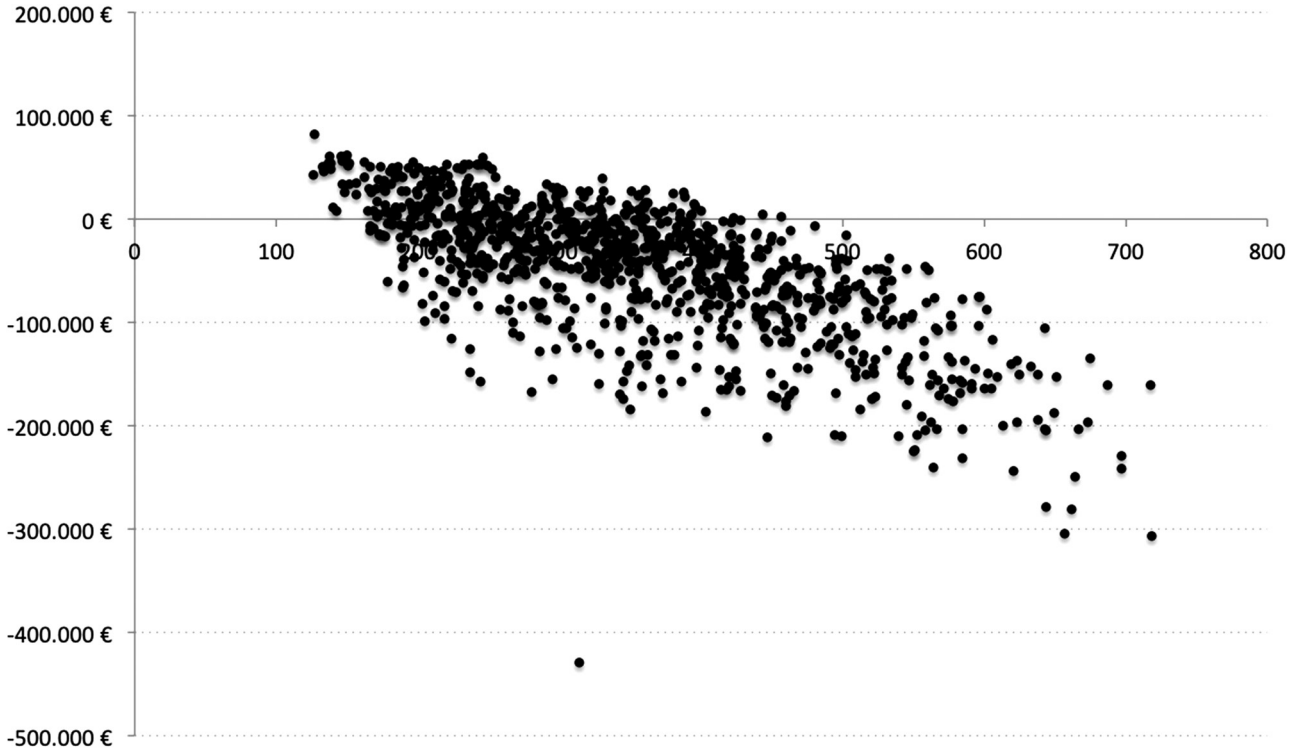

Figure 3 Incremental costs versus revisits prevented.

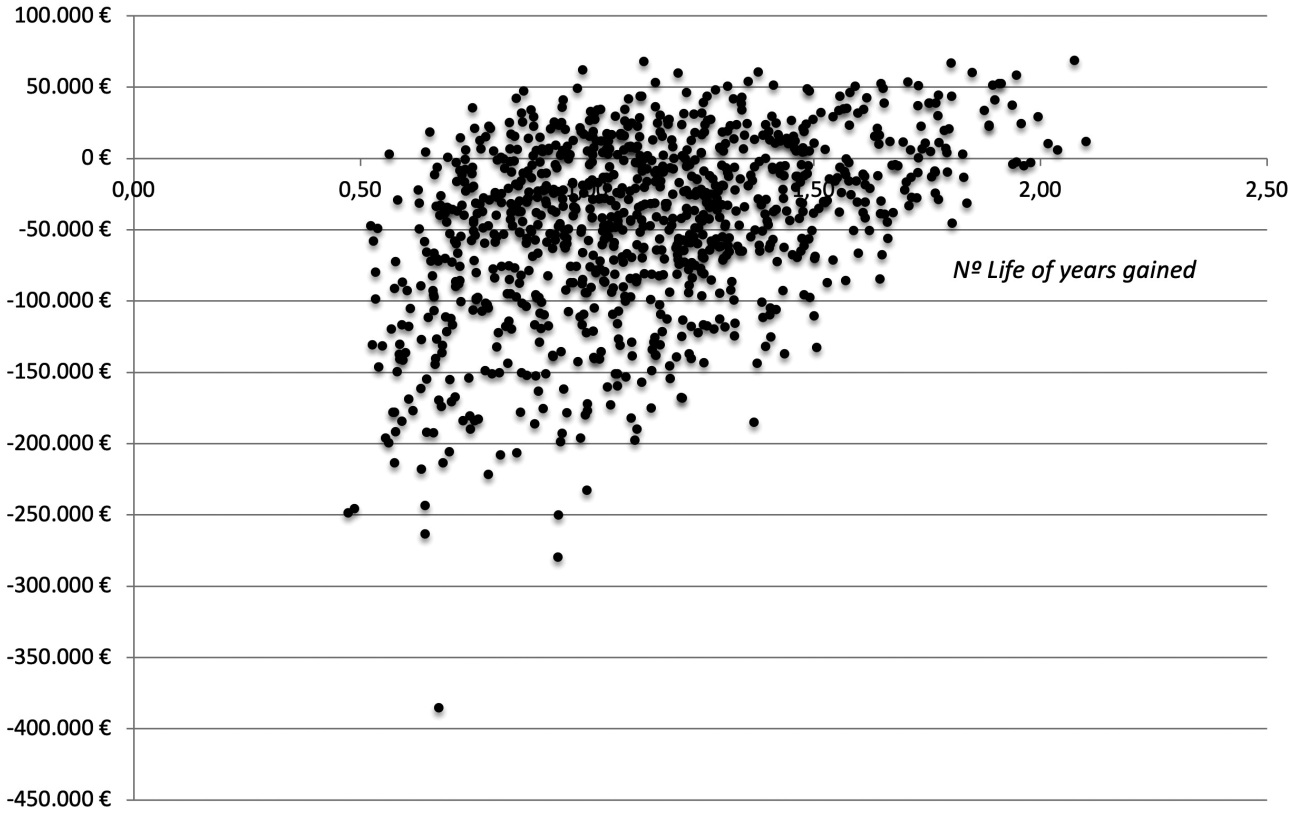

Figure 4 Incremental costs versus life-years gained (LYG).

DRPs are growing public health concerns in an increasingly polymedicated population,[17] with a significant effect on health and consumption of healthcare resources. Several studies have shown that DRP prevention programmes can reduce both the number of hospital admissions and healthcare costs.[15] The results of our clinical trial support these findings, demonstrating that a secondary DRP prevention programme reduces both the number of ED revisits and

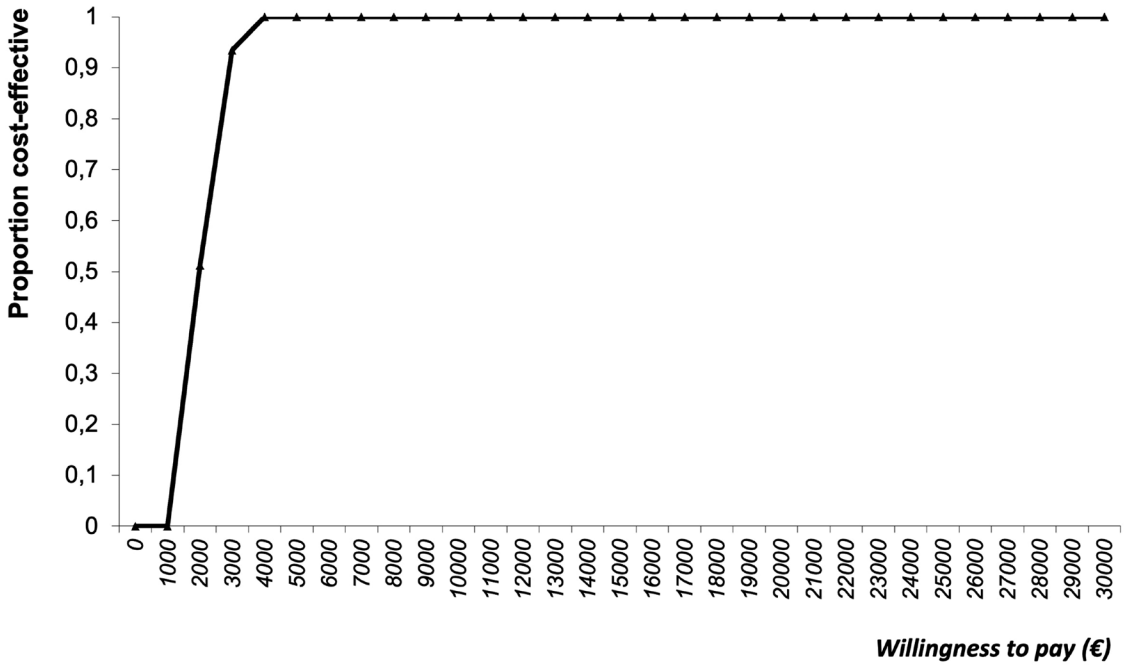

Figure 5 Predicted proportion of cost-effective services at the incremental willingness to pay per LYG. The incremental cost-effectiveness of implementing a 'Medication Code' programme was calculated and compared with the standard to compute an incremental cost-effectiveness ratio.

hospital readmissions. However, as with any health intervention, a cost-effectiveness analysis is an important aspect when deciding the implementation of DRP prevention programmes.

Many published reports have confirmed the economic benefit of the implementation of primary DRP prevention programmes.[16–19] These studies have shown that these programmes might not require additional resources. However, to date, no published studies have complete pharmacoeconomic models of these interventions, often considering only interventions associated with reducing the treatment cost and without appropriate sensitivity analyses. There are also no reports on the benefits of the implementation of a secondary DRP prevention programme that is coordinated by an ED.

Our study demonstrates that a set of measures at different care levels provide a significant economic benefit. The potential benefits of this programme include not only a reduction in the number of ED revisits but also an improvement in the quality of life of the patients. Several studies have shown an improvement in the quality of life using a programme for chronic treatments,[20–22] 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 an analysis of quality-adjusted years. Whether this is deemed cost-effective is dependent on the funder's 'willingness to pay' for the health outcomes gained. GDP has been used to consider the programme proposed as cost-effective. Several authors have criticized the use of this parameter to assess the value-for-money of an intervention, and different alternatives based on health opportunity cost using local data should be considered to make coverage decisions.[23]

Although the current analysis provides economic information that supports the implementation of the 'Medication Code' as a secondary prevention programme, a specific healthcare system is still needed to evaluate the feasibility and local cost ramifications of adopting this programme in different institutions. Costs will depend on the number of patients who attended the ED which is influenced by the number of patients who consult the emergency services for DRP, a variable influenced by the type of population reference in the health area. The modification of our model can assist in hospitals considering implementing this programme. On the contrary, owing to the context used to calculate the cost (Catalan Health System) and considering the high variability in the salaries of clinical pharmacists and healthcare costs between countries, the economic results in our study cannot be directly extrapolated to other contexts and should be adjusted to each healthcare system. However, the results of this study are consistent to ensure that the implementation of this programme is a highly efficient strategy, especially in EDs with a high rate of DRPs, resulting from a high-risk population or poor health care at other care levels.

Conclusions

DRPs are emerging health problems given the increase in the number of polymedicated individuals. Therefore, developing interventions that minimize their effect on patients and healthcare systems is necessary. The results of our study strongly support investing in a secondary DRP prevention programme at different healthcare levels, which is considered a cost-effective strategy.

Supplementary Material

Supplementary data are available at *International Journal of Pharmacy Practice* online.

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None.

Author Contributions

J.R.R. and A.J.B. participated in the design of the study, data collection and performed the statistical analysis. M.P.C. and M.B.A. were responsible for the coordination of the study, participated in its design and helped to draft the manuscript. L.L.V. and M.A.M.B. participated in the specific literature collection. A.G.P. and J.M.G.S. participated in the design of the study and statistical analysis. All authors read and approved the final manuscript.

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Conflicts of Interest

None of the authors has any potential financial conflict of interest.

Code Availability

Not applicable.

Ethical Approval

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

Not applicable.

Consent for Publication

All authors have approved the manuscript before publication. No material of this article has been published elsewhere.

Data Availability

Not applicable.

References

1. Ruiz-Ramos J, Santolaya-Perrín R, García-Martín MªÁ et al. Prevalence of adverse drug events in emergency departments. FARMURG multi-center project. *Farm Hosp* 2021; 45: 176–9. https://doi.org/10.7399/fh.11596
2. Ayalew MB, Tegegn HG, Abdela OA. Drug related hospital admissions; a systematic review of the recent literatures. *Bull Emerg Trauma* 2019; 7: 339–46. https://doi.org/10.29252/beat-070401
3. Nivya K, Sri Sai Kiran V, Ragoo N et al. 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 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 et al. 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 Jet 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. https://doi.org/10.3978/j.issn.2072-1439.2014.06.20
8. ClinicalTrials.gov [Internet]. *Identifier NCT03607097, Integral Management of Healthcare Problems Related with Drugs in Polimedicated Patients: Medication Code*. Bethesda (MD): National Library of Medicine (US). 2000. [cited 2021 January 15]. https://clinicaltrials.gov/ct2/show/NCT03607097 (18 July 2018, date last accessed).
9. Queneau P, Bannwarth B, Carpentier F 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
10. Official Gazette of the Government of Catalonia (DOGC). *ORDER SLT/63/2020, of March 8, Approving the Public Prices of the Catalan Health Service*. http://www.gencat.cat/dogc (March 2020, date last accessed).
11. Comprehensive Health System for Public Utility in Catalonia. *Salary Schedules 2020*. https://ccoohospitalsantamaria.wordpress.com/2020/03/11/taules-salarials-siscat-2020/ (January 2020, date last accessed).
12. Hospital Santa Creu I Sant Pau Annual Memory 2019. *Hospital Santa Creu I Sant Pau (Barcelona, Spain)*. http://www.santpau.cat/es/web/public/memories-sant-pau (January 2020, date last accessed).
13. Statistics National Institute. *Mortality Tables of the Population of Spain by Year, Sex, Age and Function. INE Base*. http://www.ine.es/ (April 2022, date last accessed).
14. Marseille E, Larson B, Kazi DS et al. Thresholds for the cost-effectiveness of interventions: alternative approaches. *Bull World Health Organ* 2015; 93: 118–24. https://doi.org/10.2471/BLT.14.138206
15. The World Bank. *GDP per Capita, PPP (Constant 2011 International $)*. 2021. https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=ES (January 2021, date last accessed).
16. Hogg W, Lemelin J, Dahrouge S 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* 2009; 55: e76–85.
17. Lum MV, Cheung MYS, Harris DR et al. 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
18. Gillespie U, Alassaad A, Henrohn D et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Arch Intern Med* 2009; 169: 894–900. https://doi.org/10.1001/archinternmed.2009.71
19. Hou K, Yang H, Ye Z et al. Effectiveness of pharmacist-led anticoagulation management on clinical outcomes: a systematic review and meta-analysis. *J Pharm Pharm Sci* 2017; 20: 378–96. https://doi.org/10.18433/J3SQ0B
20. Wu W-C, Taveira TH, Dooley AG et al. Costs and effectiveness of pharmacist-led group medical visits for type-2 diabetes: a multicenter randomized controlled trial. *PLoS One* 2018; 13: e0195898. https://doi.org/10.1371/journal.pone.0195898
21. Sjölander M, Lindholm L, Pfister B 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 Social Adm Pharm* 2019; 15: 287–91. https://doi.org/10.1016/j.sapharm.2018.05.006
22. Cooper JA, Cadogan CA, Patterson SM et al. Interventions to improve the appropriate use of polypharmacy in older people: a Cochrane systematic review. *BMJ Open* 2015; 5: e009235. https://doi.org/10.1007/s00339-007-4137-z
23. Chi YL, Blecher M, Chalkidou K et al. What next after GDP-based cost-effectiveness thresholds? *Gates Open Res* 2020; 4: 176. https://doi.org/10.12688/gatesopenres.13201.1