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Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients

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Abstract

Background Drug related problems have a significant clinical and economic burden on patients and the healthcare system. Medication review with follow-up (MRF) is a professional pharmacy service aimed at improving patient's health outcomes through an optimization of the medication.

Objective To ascertain the economic impact of the MRF service provided in community pharmacies to aged polypharmacy patients comparing MRF with usual care, by undertaking a cost analysis and a cost-benefit analysis.

Methods The economic evaluation was based on a cluster randomized controlled trial. Patients in the intervention group (IG) received the MRF service and the comparison group (CG) received usual care. The analysis was conducted from the national health system (NHS) perspective over 6 months. Direct medical costs were included and expressed in euros at 2014 prices. Health benefits were estimated by assigning a monetary value to the quality-adjusted life years. One-way deterministic sensitivity analysis was undertaken in order to analyse the uncertainty.

Results The analysis included 1403 patients (IG: $n = 688$ vs CG: $n = 715$). The cost analysis showed that the MRF saved 97 € per patient in 6 months. Extrapolating data to 1 year and assuming a fee for service of 22 € per patient-month, the estimated savings were 273 € per patient-year. The cost-benefit ratio revealed that for every 1 € invested in MRF, a benefit of 3.3 € to 6.2 € was obtained.

Conclusion The MRF provided health benefits to patients and substantial cost savings to the NHS. Investment in this service would represent an efficient use of healthcare resources.

Keywords Pharmaceutical services · Pharmacists · Medication review · Aged · Cost and cost analysis · Cost-benefit analysis

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Introduction

Drug related problems (DRP) and negative clinical outcomes related to medicines (NCOM) have a significant clinical and economic burden [1, 2], with the aged polypharmacy patients population being at high risk [3]. A direct positive correlation has been found between ageing, polypharmacy and an increased risk of DRP and NCOM. A recent study reporting the prevalence of DRP in aged patients using eight or more medications, found that 87% of the analysed patients had at least one DRP [3]. Another study found 8.9 DRPs per patient with a mean age of 81 years and using 15 medicines [4].

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These medication errors use social and health resources and generate costs to the healthcare system. Interestingly, a high percentage of NCOM are preventable, as evidenced in a Spanish study undertaken in a hospital setting [5]. These researchers estimated costs up to 14.5 € million for emergency department visits caused by preventable NCOM during 2003. Johnson and Bootman [6] estimated that the costs associated with drug-related morbidity and mortality in ambulatory care in the U.S. were $76.6 billion (in 1995 values, only direct medical costs). Other authors [7] updated these estimates to the year 2000, reporting costs of $177.4 billion. They concluded that given the economic and medical burden associated with DRP, the implementation of strategies for preventing drug-related morbidity and mortality were urgently needed.

An individualized review of patients' pharmacotherapy has been proven to be an effective strategy to avoid preventable NCOMs, reducing the clinical and economic burden [8]. A series of systematic reviews conclude that professional pharmacy services generally provide positive economic benefits, although there is high variability in both clinical outcomes and the subsequent cost-effectiveness analysis [9–12].

Medication review with follow-up (MRF) is a professional pharmacy service, where the pharmacist identifies patient's DRPs in order to prevent and resolve NCOMs [13]. We carried out the conSIGUE Program to assess the impact of the MRF on aged patients with polypharmacy and to promote the implementation of the MRF in community pharmacies [14]. MRF has been shown to be a cost-effective strategy through a cost-utility analysis [15]. However, policymakers requested other economic evidence different to the cost-utility analysis in the process of considering a change in health policy and a payment for the service.

The aim of this paper was to ascertain the economic impact of the MRF service provided in community pharmacies to aged polypharmacy patients by comparing MRF with usual care, by undertaking a cost analysis and a cost-benefit analysis.

Methodology

Study design

A cluster randomized controlled trial was carried out in 178 community pharmacies in 4 Spanish provinces (Guipúzcoa, Granada, Las Palmas and Tenerife) between November 2011 and July 2013, with 6 months of fieldwork in each province. Following a request for participation for all community pharmacies within a province, those willing to participate were randomly allocated into either the intervention group (IG) or comparison group (CG). Each pharmacy was required to recruit up to 10 aged polypharmacy patients, defined as those aged ≥65 years and taking 5 or more medications for at least 6 months. Neither patients nor pharmacists could be blinded due to the characteristics of the intervention. The sampling and the research methodology has been fully described previously [14]. The study was approved by the Clinical Research Ethics Committee of the Hospital Virgen de las Nieves of Granada (Spain) in November 2009. All patients were provided with an information sheet prior to the beginning of the study and informed consent was obtained.

A piggyback cost-benefit analysis and cost analysis were performed from the Spanish National Health System (NHS) perspective, with a time horizon of 6 months. Additionally, different extrapolations were made to estimate the outcomes depending on length of follow-up, number of patients receiving the MRF and a payment to pharmacies for delivering the service. The alternatives were a MRF service versus the usual care.

MRF service and study groups

Pharmacists allocated to the MRF group delivered the service according to national guidelines [13]. MRF starts with a patient interview, in which the pharmacist collects relevant information about health problems, medicines used, clinical and biological parameters, medication use, lifestyle habits, and patient concerns about diseases and medications. After performing a comprehensive medication review, the pharmacist identifies NCOMs and DRPs. An action plan is agreed with the patient and the physician if required.

Pharmacists in the MRF group received a 3-day training course covering clinical management of aged patients, MRF methodology, communication with patients and doctors, study protocol and documentation forms.

A specifically trained pharmacist, called the practice change facilitator, [16] supported pharmacists of the IG in the provision of the MRF, identifying barriers specific to each pharmacy and providing solutions. Additionally, the practice change facilitator ensured fidelity using process indicators to the intervention and supported pharmacists of both study groups on doubts about documentation forms.

Patients included in the CG received usual care. The usual care in the Spanish community pharmacy setting consists of dispensing medicines prescribed by physicians and minor ailments advice [17]. During the 6 months of follow-up, patients in both study groups attended the pharmacy on a monthly basis. Study variables were systematically collected at every patient visit to the pharmacy. Neither patients nor pharmacists received any incentives for participating in the study.

Costs

The economic evaluation was conducted from a health system perspective. The following direct medical costs were included in the analysis: medication costs, emergency department (ED) visits costs and hospital admissions costs, the cost of pharmacists' time, pharmacist training, the investment of the pharmacy, and the cost of the practice change facilitator were also considered to establish the cost of the intervention. Costs are expressed in euros at 2014 prices. Prices from previous years were updated using the Spanish consumer price index.

The information about medicines used was obtained from the records completed by pharmacists during the monthly visits with patients and validated by the practice change facilitators. Retail prices of the medicines were used [18]. All the products registered as medicines in Spain, involving prescribed and over-the-counter medications, were included.

Patients reported the number of times they had visited the emergency department (ED) throughout the follow-up. The reference sources for the unit costs of ED visits were the tariffs of the regional health services [19–21].

Patients were required to report the number of hospital admissions during the follow-up. The list of Diagnosis Related Group (DRG) was requested from the regional health directorates and hospitals. When the information reported by patients and the one provided by official sources was discordant, the latter was accepted. The costs of DRG were taken from the Spanish NHS [22]. Three specialists in internal medicine independently assessed the causes of hospital admission and only those associated with drug related problems (DRP) were included in the analysis [23].

The time spent by pharmacists during the provision of the MRF was obtained from the pharmacists' data collection forms. Missing data were replaced with the median value of the variable, in order to avoid an underestimation of time costs. Costs for the pharmacists' time were calculated by multiplying the minutes spent during the provision of the service by the wage, depending on collective wage agreements in each province and the type of contract of employment [14, 24]. Time spent providing usual care was not recorded in the conSIGUE Program, therefore it was estimated using data previously described in the literature [25].

The costs related to the investment of the pharmacy required to provide the MRF service during the 6 months of study were obtained through a questionnaire completed by pharmacy owners in the MRF group [24] (questionnaire available in [14]). Only the percentage of costs attributable to the MRF was considered. Investment of pharmacies on fixed and variable costs besides the cost of attendance of the pharmacists to the 3 half-days training course were included.

In order to allocate the proportional part of the cost to every patient, the mean cost of investment per pharmacy was divided by the mean number of patients included in the MRF service per pharmacy (7.9 ± 2.4 patients/pharmacy). The investment of pharmacies in the CG was assumed to be null.

Costs of practice change facilitators were met by official pharmacist associations in each province. The cost for the practice change facilitator's time was estimated by multiplying the working hours by the wage depending on the type of contract of employment per province, and adding the travel expenses to the pharmacies. Practice change facilitators were estimated to spend two thirds of their time with pharmacists in the IG and one third with pharmacists in the CG. The time spent in the CG was allocated to completing and validating data collection forms. However, since this expenditure was not attributable to the provision of the MRF, the cost of the practice change facilitator in the CG was considered to be null and the proportional part was discounted in the IG.

Benefits

Patients' health-related quality of life was measured with the quality-adjusted life years (QALY). Patients in both study groups completed the EQ-5D-3L questionnaire at every visit of the patient to the pharmacy [26], and utility indexes associated with each health state were estimated using the time trade-off method [27].

In this cost-benefit analysis, a monetary value obtained through empirical research was assigned to the QALY. The assignment of a monetary value to the QALY has been the objective of several studies, and the study recently published by Robinson et al. collected data from 9 European countries, including Spain [28]. The authors adapted the "chained" approach, using first the time trade-off and standard gamble methods to elicit utilities for health states and then estimating the willingness to pay (WTP) per QALY. They suggested that the WTP per QALY ranged from $18,247 to $34,097 (US dollars, 2013) and we assigned this monetary value to the QALYs obtained in our study.

Sensitivity analysis

One-way deterministic sensitivity analysis was undertaken in the base case of the cost analysis in order to analyse the uncertainty and to explore the impact of varying the input parameters. The alternative values of the parameters were their upper and lower variations (for costs related to medication, emergency department visits, pharmacy time

and investment of the pharmacy), logical values (hospital admissions without cause-effect screening and the number of patients that could be attended by each pharmacy in actual practice) and arbitrary and conservative values in remaining ones (length of follow-up and practice change facilitator time). Fourteen scenarios were analysed through these alternative values.

The following assumptions were used to calculate the number of patients that could be included in the MRF service in actual practice: a community pharmacy in Spain serves a mean of 2500 patients [29]; 16% of the population are aged patients using polypharmacy [30, 31], and 60% of these patients would accept the provision of service. The MRF service could be delivered to 240 patients per annum and 120 in 6 months. These calculations were conservative since the proportion of aged polypharmacy patients is higher in pharmacies than in the general population.

Statistical analysis

Student's *t*-test was used to analyse the differences between IG and CG, and a Chi-square test or Fisher's exact test was used to assess the differences in frequency distribution. The adjustment of the variables that were significantly different at baseline was performed through an analysis of covariance. All analyses were conducted using the Statistical Package for the Social Sciences (SPSS v. 18.0 for Windows XP, Microsoft, USA), Microsoft Excel 2010 and STATA version 12 (StataCorp LP, College Station, TX, USA).

Results

Study groups and patients

A total of 1474 patients were enrolled in the study. Patient recruitment, flow and dropouts are shown in Fig. 1. Data on 1403 patients meeting the inclusion criteria and allocated into the IG ($n = 688$) or CG ($n = 715$) were included in the analysis. Patients were recruited by 178 community pharmacies with the mean number of patients in each pharmacy 7.9 (SD: 2.4).

Table 1 shows the socio-demographic and clinical characteristics of patients at baseline and at last study visits. Patients in the IG used significantly more medicines, and had more health problems and uncontrolled health problems than in the CG at baseline ($p < 0.05$). All acute or chronic health issues were considered health problems, and the level of control was assessed by the pharmacists using information referred by patients and/or clinical and biological parameters. At the end of the study the number of uncontrolled health problems had

decreased in the IG more than 50% ($p < 0.001$), becoming similar to the CG. The number of patients with visits to ED or being hospitalised decreased in the IG, leading to significant differences between groups after the 6-month follow-up [23]. Utility scores were similar between groups at baseline; they remained constant in the CG while increased in the IG, leading to significant differences between groups as well.

Costs and cost analysis

Pharmacists spent a median of 350 min (interquartile range: 265–490 min) in the provision of the service per patient for all phases of MRF during the 6-month study. Time required to provide the usual care in Spain through the dispensing service with electronic prescription was estimated to be 4.2 min/patient visit to the pharmacy [25]. Taking into account the number of patients lost to follow-up, pharmacists would need 25 min/patient to provide usual care during the 6 months.

The investment needed by pharmacies to provide the MRF service in the conSIGUE Program was €210.8 (SD: 32.8) [14, 24], and the highest costs were associated with pharmacists' attendance on the training course. Amongst the 83 hospital admissions screened by the expert panel, 42 (50.6%) were related to medication (IG: 11, CG: 31; $p = 0.042$) [23].

The average cost of a practice change facilitator (wage plus travel expenses) was 1616.6 € per month. Taking into account that practice change facilitators worked 40 h per week, the mean cost per practice change facilitator was 0.169 €/min. Six practice change facilitators were employed with a total cost of 1.010 €/min.

Table 2 summarizes the unit and total costs for both groups. The highest cost was medication, with more than 60% of the total cost in both groups. The second most influential cost component was drug-related hospital admissions for the CG and pharmacy time for the MRF group. In the IG, the investment of the pharmacy had less weight.

The cost savings per patient of the base case are shown in Table 3. Cost differences between groups in medication, ED visits and hospital admissions were statistically significant ($p < 0.001$ for medication and ED visits and 0.018 for hospital admissions). The difference between total costs in both groups showed a cost saving for the NHS of 97 € per patient in 6 months.

In order to obtain a profit margin of 30%, which is the current margin paid to pharmacies for each product supplied by the NHS, pharmacies should receive 22 € per patient-month for providing the MRF [14, 24]. If health administration paid 22 € per patient-month, the net saving of the MRF service would be 273 € per patient-year.
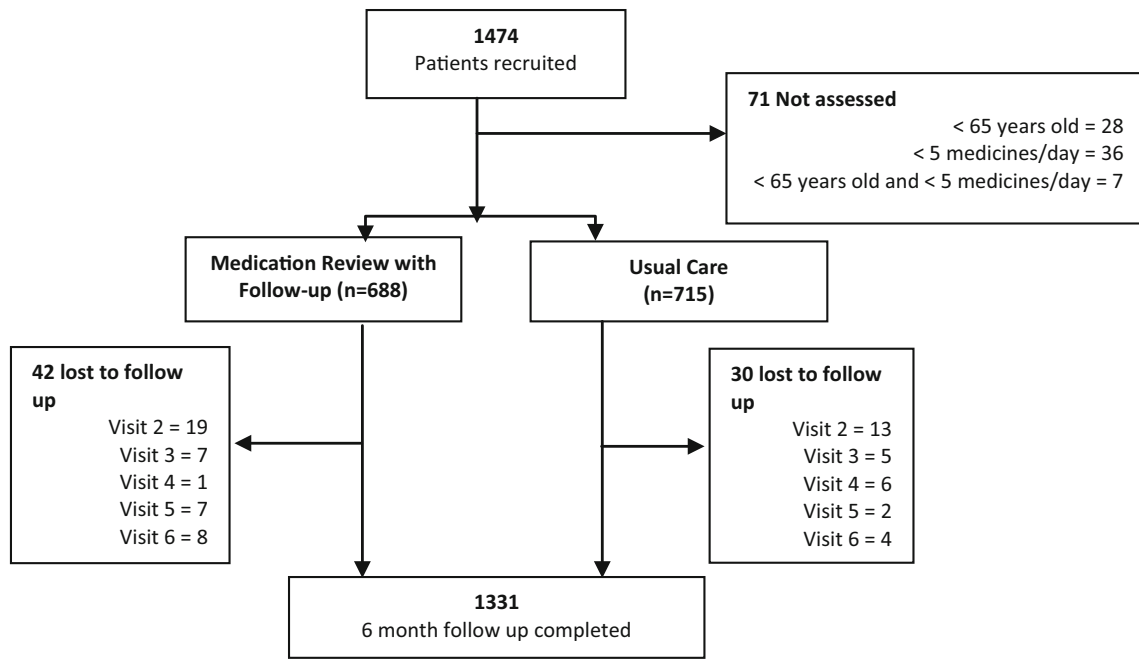
Fig. 1 Participants recruitment, flow and dropouts

Table 1 Socio-demographic and clinical characteristics of the patients at baseline and after the 6-month follow-up [mean (SD) unless otherwise reported]

	IG	CG	p value
Number of patients	688	715	–
Age (years)	75.3 (6.5)	74.9 (6.6)	0.243
Gender (female); n (%)	409 (60.1)	441 (61.7)	0.535
Number of medicines used			
Period 1	7.7 (2.5)	7.4 (2.4)	0.009
Period 6	7.5 (2.4)	7.3 (2.4)	0.204
Health problems			
Period 1	4.9 (1.8)	4.3 (1.5)	<0.001
Period 6	4.9 (1.8)	4.3 (1.5)	<0.001
Uncontrolled health problems			
Period 1	1.5 (1.3)	0.7 (1.0)	<0.001
Period 6	0.6 (0.9)	0.7 (0.9)	0.217
Patients in emergency department; n (%)			
Period 1	193 (28.1)	211 (29.5)	0.556
Period 6	90 (13.1)	173 (24.2)	<0.001
Patients hospitalised; n (%)			
Period 1	89 (13.4)	68 (9.9)	<0.044
Period 6	38 (6.2)	65 (9.8)	0.018
Utility scores			
Period 1	0.715 (0.28)	0.693 (0.31)	0.238
Period 6	0.768 (0.27)	0.693 (0.32)	<0.001

IG intervention group, *CG* comparison group, *SD* standard deviation

However, the saving obtained suggests that the service would be efficient even with a higher price than 22 € per patient-month. Based on annual estimates, the threshold price for the efficiency of the MRF is expected to be 45 € per patient-month. All the extrapolations are summarised in Table 4.

The sensitivity analysis showed that the MRF saved costs in 13 of 14 scenarios analysed. The MRF would achieve savings of 398 € per patient in the scenario where 240 patients were included in the service per pharmacy during 1 year. In this case, if the service was remunerated, savings per patient-year would be 326 € and each pharmacy would save 78,281 € per year.

Cost-benefit analysis

The cost-benefit analysis considered the health benefits obtained by the provision of MRF in addition to the costs savings (Fig. 2). The QALYs obtained were 0.3721 (0.12) in the IG and 0.3488 (0.15) in the CG (*p* = 0.002). Two scenarios were set up using the base case of the cost analysis, and the upper and lower limit of the estimated range for the monetary value of QALY in a European study [28]. The cost-benefit ratio indicated that MRF benefits were from 3.3 to 6.2 times higher than costs. When benefits in health were added, every case considered in the sensitivity analysis provided positive results for the MRF.

Table 2 Unit and total costs of both study groups (€, 2014) during 6-month follow-up

Item	Unit cost (€) and reference source	Number		Total cost (€)		% of total	
		IG	CG	IG	CG	IG	CG
Medication costs (no. packages)	Retail price[a]	29,353.00	29,974.00	425,460.7	459,157.7	63.34	62.73
Emergency department visits (no. visits)	58.55[b]	30	59	1756.5	3454.4	2.70	6.78
Andalusia	149.50[c]	41	58	6129.5	8671.0		
Basque Country	216.93[d]	47	173	10,195.7	37,528.9		
Canary Islands							
Drug-related hospital admissions (no. admissions)	Diagnosis Related Group[e]	11	31	64,846.4	215,382.5	9.65	29.43
Pharmacy time (cost/min)	0.443[f]	240,800.00	17,426.43	106,674.4	7719.9	15.88	1.05
Investment in MRF (per pharmacy)	210.8[g]	88	–	18,553.9	–	2.76	–
Practice change facilitator time (cost/min)	1.010[h]	37,661.04	–	38,112.9	–	5.67	
Total cost	–	–	–	671,730.1	731,914.5	100	100

IG intervention group, *CG* comparison group

[a] Spanish General Council of Colleges of Pharmacists [18]

[b] Tariffs of Andalusian health service [19]

[c] Tariffs of Basque Country health service [20]

[d] Tariffs of Canarian health service [21]

[e] Tariffs of Spanish National Health Service [22]

[f,g,h] Own data

Table 3 Mean costs per patient (€, 2014) during 6-month follow-up

Item	IG	CG	Mean difference[a]
Medication; mean (SE)[b]	615.5 (25.7)	661.3 (25.0)	−45.8
Emergency department visits; mean (SD)	26.3 (81.6)	69.5 (222.6)	−43.2
Hospital admissions; mean[c]	94.2	301.2	−207.0
Pharmacy time; MRF: median (Q_{25}–Q_{75})	155.1 (117.4–217.1)	11.1	144
Investment of pharmacy in MRF; mean (SD)	26.9 (3.8)	–	26.9
Practice change facilitator time; mean	27.7	–	27.7
Total	945.7	1043.1	−97.4

IG intervention group, *CG* comparison group, *SE* standard error; *SD* standard deviation

[a] Negative cost difference indicates cost saving related to MRF group

[b] Adjusted by the number of used medicines in period 1 (ANCOVA)

[c] Malet-Larrea et al. [23]

Discussion

The results of the present study show that MRF delivered in a community pharmacy setting targeted to aged polypharmacy patients has positive net benefits (between 420 € and 700 € per patient) and it saved 97 € per patient in 6 months. For every 1 € invested in MRF, the service returned a benefit from 3.3 € to 6.2 €.

The analysis showed that if MRF was implemented in clinical practice, a higher saving could be achieved. There were decreasing marginal costs of the intervention with the length of the follow-up and with the number of patients in the programme. Thus, the inclusion and maintenance of a higher number of patients during a longer period of time would generate more savings to the health care system. However, the sustainability of the service depends on its payment. Pharmacists would need a fee for service to deliver MRF to a higher number of patients and during a longer follow-up. Even if the health system remunerated pharmacists with 22 € per patient-month, savings per patient-year would amount to 326 €.

Diverse results have been found when assessing the cost-effectiveness of professional pharmacy services [32, 33]. Our results support the evidence suggesting that

Table 4 Summary of calculations and extrapolations

| Scenario	Time, unit of analysis and key assumptions	Variables and values	Cost-savings (€)[a]
(a) Base case scenario conSIGUE Program	6 months, patient	Medication: −45.8	−97
		ED visits: −43.2	
		Hospital admissions: −207.0	
		Pharmacy time: 144	
		Investment of pharmacy: 26.9	
		Practice change facilitator: 27.7	
		(Table 3)	
(b) Including fee for service	1 year, patient	Medication: −91.7	−273
	The fee for service calculation includes the cost of the intervention for the pharmacy; $22 \times 12 = 264$	ED visits: −86.3	
		Hospital admissions: −413.9	
		Practice change facilitator: 55.4	
		Fee for service: 264	
(c) Fee for service threshold analysis	1 month, fee for service	Medication: −91.7	−45
	Threshold: when cost-savings = 0	ED visits: −86.3	
		Hospital admissions: −413.9	
		Practice change facilitator: 55.4	
		= −536.58/12	
(d) Including a real number of patients ($n = 240$)	1 year, patient	Medication: −91.7	−398
	Intervention cost: share among 240 patients and extend follow-up visits time	ED visits: −86.3	
		Hospital admissions: −413.9	
		Pharmacy time: 190.9	
		Investment of pharmacy: 0.9	
		Practice change facilitator: 1.8	
(e) Including a real number of patients ($n = 240$) and fee for service	1 year, patient	Medication: −91.7	−326
	Former scenario with fee for service including cost of the intervention for the pharmacy ($22 \times 12 = 264$)	ED visits: −86.3	
		Hospital admissions: −413.9	
		Practice change facilitator: 1.8	
		Fee for service: 264	
(f) Including a real number of patients ($n = 240$) and fee for service	1 year, pharmacy	Medication: −91.7	−78,281
	Former scenario, per pharmacy with 240 patients	ED visits: −86.3	
		Hospital admissions: −413.9	
		Practice change facilitator: 1.8	
		Fee for service: 264	

ED visits emergency department visits

[a] Negative cost difference indicates cost saving related to MRF group

pharmacist interventions might be cost-effective and cost-saving [34–36]. For example, a recent study carried out in a hospital setting [36] found a cost-benefit ratio of 1:8.64 € for pharmacist interventions. Another study aimed at improving the quality of prescribing and the adherence to treatment by community pharmacists in patients with hypertension showed that benefits obtained were 10 times higher than costs [35]. In the Asheville project a similar service to MRF was delivered by community and hospital pharmacists over 6 years in patients with different chronic conditions such as asthma [37], hypertension and/or dyslipidaemia [38]. Similar results to the ones found in our study were achieved. The pharmacy service provided allowed not only clinical improvements (supported by a decrease in ED visits and hospital admissions) but also cost savings (direct cost savings averaged $725 per patient-year). Findings of the Asheville Project and conSIGUE Program are highly comparable due to the fact that the service provided was very similar, including the follow-up using scheduled consultations.

MRF is a well-defined service, which includes a comprehensive and systematic medication review and follow-

Fig. 2 Cost-benefit analysis (€, 2014) of the medication review with follow-up per patient in 6 months. The scenarios are given by the monetary value of QALY reported in the study by Robinson et al. [28]. *IG* intervention group. *CG* comparison group
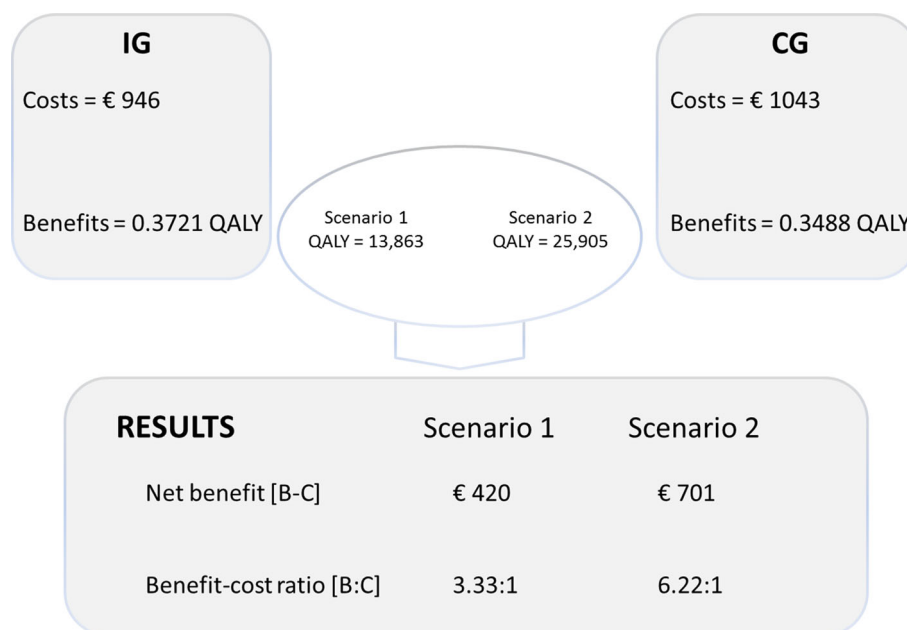
up of the patient. The provision of MRF requires a considerable investment of time, clinical knowledge and effort, since pharmacists are responsible for not only the process of the use of medicines, but also patients' health outcomes. Additionally, pharmacists in the conSIGUE Program were supported by a practice change facilitator. Consequently, the MRF provided in the conSIGUE Program achieved clinical results not found with other pharmacy services [39, 40].

In fact, other studies showed even greater cost-benefit ratios such us those included in a series of systematic reviews 1:34.61, 1:17.0, 1:25.95, 1:75.84 [9–12]. However, these extreme values should be considered exceptional cases. The study design, included costs, type of pharmacy service and patients' characteristics have an undeniable impact on the results. For instance, the study reporting a cost-benefit of 1:75.84 assessed the impact of a pharmacokinetic service in hospitalised patients receiving aminoglycosides, a specific service in ill patients treated with narrow therapeutic range medicines. These patients were at a very high risk of complications, so there was every chance of avoiding higher clinical and economic burden than services like MRF, provided to ambulatory patients with chronic comorbidities. Nevertheless, the median values of cost-benefit ratios of the studies included in the reviews are similar to our cost-benefit ratio, endorsing our findings ($1:4.1, $1:4.68 and $1:4.81 [9]).

The main purpose of economic evaluations is for policymakers to make decisions. If policymakers and their political advisors do not have strong technical knowledge in health economics, the presentation of clear economic evaluations to inform the process of decision making is

required. In the consultations with policymakers, it was evident that the "cost per QALY" concept generated in the previous economic evaluation of the conSIGUE Program [15] was difficult to understand. In this analysis we translated this abstract concept to a more easily interpretable cost-benefit ratio. Furthermore, in this analysis we included more accurate costs and estimations of the economic impact that could be expected when implementing the MRF in actual practice.

The monetary value of health gain used in this analysis was obtained through empirical research rather than cost-effectiveness thresholds based on literature reviews [41] with lack of explicit scientific evidence [42]. The assignment of a monetary value to the QALY has been the objective of several studies [43–45]. However, these studies performed their estimations with a high level of variability. One of the most recent studies is the one developed by Robinson et al. [28] whose estimations have been used in the present study, and where the monetary value of QALY was estimated by the "chained" approach through data from 9 European countries, including Spain. Robinson et al. suggested that the willingness to pay (WTP) per QALY ranged from $18,247 to $34,097 (US dollars, 2013). In a previous study King et al. [44] found that the mean WTP per QALY ranged from $12,500 to $32,200 (2003 $US). These data obtained by contingent valuation are lower than the currently used cost-effectiveness thresholds, so the willingness of society to pay might have been overestimated when accepting cost-effectiveness thresholds. Alternatively, it is known that the WTP per QALY is higher for worse health status than for better ones [46]. In our study, patients' health status was better than in

Robinson's study, and therefore the cost-benefit ratio obtained using the lower limit of the monetary value of QALY (3.33:1) would be more likely to happen than 6.22:1.

The main limitation of the study could be that some direct medical costs such as visits to the physician, visits to specialist doctors and laboratory costs were not assessed in the conSIGUE Program, and therefore could not be included in this analysis. The number of visits to the physician is the indicator most likely to be affected by MRF service provision. However, several studies assessing similar services to MRF concluded that there are not significant differences in number of visits [47], cost [48] or both [49] of physician visits between intervention and comparison groups.

Conclusions

In the context of the economic pressure on the health care system, the identification and implementation of alternatives to increase the efficiency of health services and ensure the sustainability of the health system are required. Our study showed that MRF provided by community pharmacists, targeted to aged polypharmacy patients and compared to the usual care, avoids substantial costs to the NHS, besides providing health benefits to patients. Investment in the implementation of this service would represent an efficient use of healthcare resources, and a payment from the NHS to pharmacies for delivering MRF should be considered.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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