ORIGINAL RESEARCH ARTICLE

Drug Saf 2012; 35 (8): 655-665
0114-5916/12/0008-0655/$49.95/0

Workshop- and Telephone-Based Interventions to Improve Adverse Drug Reaction Reporting

A Cluster-Randomized Trial in Portugal

Maria Teresa Herdeiro,[1,2,3,4] *Inês Ribeiro-Vaz*,[1,2] *Mónica Ferreira*,[4] *Jorge Polónia*,[1] *Amílcar Falcão*[5,6] and *Adolfo Figueiras*[7,8]

1 Northern Pharmacovigilance Centre, Faculty of Medicine, University of Porto, Porto, Portugal
2 Centre for Health Technology and Information Systems Research (Centro de Investigação em Tecnologias e Sistemas de Informação em Saúde – CINTESIS), Porto, Portugal
3 Health Technology Research Centre (Centro de Investigação em Tecnologias da Saúde – CITS), IPSN-CESPU, Gandra, Portugal
4 Centre for Cell Biology, University of Aveiro, Aveiro, Portugal
5 Centre for Neuroscience and Cell Biology – CNC, University of Coimbra, Coimbra, Portugal
6 Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal
7 Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Santiago de Compostela, Spain
8 Consortium for Biomedical Research in Epidemiology and Public Health (CIBER en Epidemiología y Salud Pública – CIBERESP), Barcelona, Spain

Abstract

Background: Spontaneous reporting of adverse drug reactions (ADRs) is the method most widely used by pharmacovigilance systems, with the principal limitation being the physician's underreporting.

Objective: This study sought to evaluate the results of workshop and telephone-interview interventions designed to improve the quantity and relevance of ADR reporting by physicians.

Methods: A cluster-randomized controlled trial was conducted on 6579 physicians in northern Portugal in 2008. Following randomization, we allocated 1034 physicians to a telephone-interview intervention, 438 to a workshop intervention and the remaining 5107 to the control group. At the workshop, a real clinical case was presented and participants were then asked to report on it by completing the relevant form. In the telephone intervention, participants were asked (i) whether they had ever had any suspicion of ADRs; (ii) whether they had experienced any difficulties in reporting; (iii) whether they remembered the different methods that could be used for reporting purposes; and (iv) whether they attached importance to the individual physician's role in reporting. We followed up physicians to assess ADR reporting rates to the Northern Pharmacovigilance Centre. In terms of relevance,

adverse reactions were classified as serious or unexpected. Statistical analysis was performed on an intention-to-treat basis, and generalized linear mixed models were applied using the penalized quasi-likelihood method. The physicians studied were followed up over a period of 20 months.

Results: Two hundred physicians underwent the educational intervention. Comparison with the control group showed that the workshop intervention increased the spontaneous ADR reporting rate by an average of 4-fold (relative risk [RR] 3.97; 95% CI 3.86, 4.08; $p < 0.001$) across the 20 months post-intervention. Telephone interviews, in contrast, proved less efficient since they led to no significant difference ($p = 0.052$) vis-à-vis the control group in ADR reporting (RR 1.02; 95% CI 1.00, 1.04). The effects of the interventions on the reporting rate of serious and high-causality ADRs indicated that the RRs associated with workshops were 6.84 (95% CI 6.69, 6.98; $p < 0.001$) for serious ADRs and 3.58 (95% CI 3.51, 3.66; $p < 0.001$) for high-causality ADRs.

Conclusions: Whereas telephone interventions only increased spontaneous reporting in the first 4 months of follow-up, workshops significantly increased both the quantity and relevance of spontaneous ADR reporting for more than 1 year.

Background

Adverse drug reactions (ADRs) are a significant public health problem and one of the major causes of morbidity and mortality, a situation magnified by the increasing use of health services in developed countries.[1-3] After a drug is marketed, previously unidentified important ADRs may occur. For this reason, postmarketing surveillance is essential for the discovery of new ADRs.[4] Spontaneous reporting of suspected ADRs by health professionals, followed by evaluation and incorporation into databases, is fundamental to drug safety surveillance and constitutes the most commonly used method for generating signals about unexpected and uncommon ADRs.[5]

Nevertheless, the effectiveness of the system is seriously compromised by underreporting, with serious repercussions on public health, triggering limitations on risk assessment and excessive delay in generating signals. Indeed, it is estimated that only 6% of all adverse reactions are reported.[6] The factors that influence underreporting, such as failing to perceive the importance of individual contribution to the overall knowledge of drug-treatment safety, lack of certainty about the diagnosis of a particular ADR, uncommunicative doctor-patient relationships, lack of time, interest and reporting forms, and fear of involvement in litigation have all been described as potential causes of underreporting behaviour.[7-12]

The effectiveness of Portugal's ADR reporting system, introduced in 1992, has likewise been affected by underreporting. In 2004, Figueiras et al.[13] delineated an educational intervention, purpose-designed to enhance physicians' knowledge of and attitudes to the country's voluntary ADR reporting system and improve their subsequent reporting behaviour.[7,10] This programme was evaluated in the northern region of Portugal by means of a cluster-randomized trial (CRT), which demonstrated that, while an educational intervention programme based on gaps in physicians' knowledge and attitudes is effective, such effectiveness tends to decline over time. Hence, novel educational interventions (workshops and telephone interviews) were implemented in 2008 among clusters allocated to the intervention groups in 2004. Accordingly, this study sought to evaluate the results of such workshop- and telephone interview-based educational interventions by analysing the quantity, relevance and duration of the effect of these interventions.

Methods

Study Population, Setting and Design

The study was conducted in the northern region of Portugal, covering a population of 6579 physicians, 25 hospitals and their respective outpatient centres. Fifteen of the hospitals were general medical hospitals, which cover a designated geographic catchment area; five were small satellite hospitals of general hospitals; and five were specialty hospitals (e.g. cancer, maternity, paediatrics). The study population included all National Health System physicians based in the northern region of Portugal, except for those not involved in any clinical activity (e.g. administrators, laboratory analysis), those working in substance abuse and rehabilitation centres or specialty hospitals that cover multiple geographical areas in the north Portugal region, and those working in the Northern Pharmacovigilance Centre (NPC) or any department having a specific voluntary ADR reporting programme (figure 1).

In 2004, a CRT was conducted in these same settings, involving four clusters allocated to the intervention and 11 clusters allocated to the control group. The methods designed and results have been described elsewhere.[13] Briefly, to prevent cross-contamination between the intervention and control groups, each cluster consisted of one reference hospital, small hospitals in the selected geographic area, plus the outpatient centre. In the intervention groups, 1-hour educational outreach visits[13] were undertaken, tailored to training needs identified in a previous study.[13]

In 2008, a second randomization was performed, covering the four groups that had been allocated to the intervention group in 2004. As a result, two clusters received the workshop intervention and two clusters the telephone-interview intervention (figure 1).

Interventions

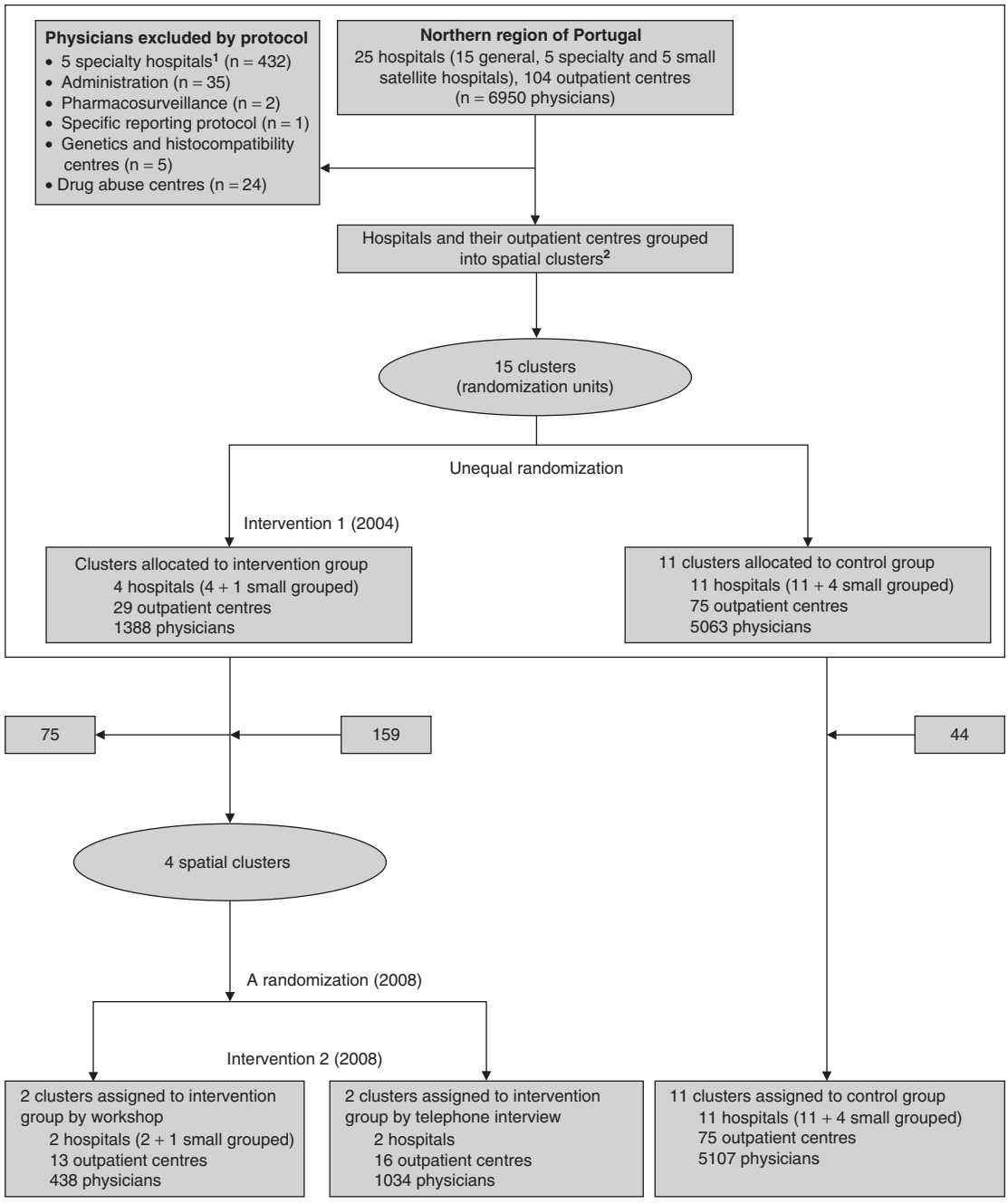
Telephone interviews consisted of a telephone conversation conducted according to a pre-established script (see Supplemental Digital Content, http://links.adisonline.com/DSZ/A72), which had been previously tested outside the intervention areas.

The script was efficient, in that it made for a fluid conversation between researcher and physician. The intervention lasted 3–8 minutes, depending on the degree of physician participation. A total of three attempts were made to call each physician by telephone, after which he/she was deemed impossible to contact. During the interview, physicians were asked whether (i) they had ever had any suspicion of ADRs; (ii) they had experienced any difficulty in reporting; (iii) they remembered the different methods that could be used for reporting purposes (telephone, fax, email or internet); (iv) they attached importance to the individual physician's role in reporting; (v) they remembered any cases of an alert (such as cyclooxygenase-2 inhibitors and statins cases) in which reporting had played a vital role; and finally (vi) they had any questions concerning the reporting system. Following the telephone interview, each participant was sent support material, which included one letter of acknowledgment, one ADR spontaneous report form and one NPC presentation folder to the desired address.

Workshops, on the other hand, consisted of a brief presentation lasting approximately 1 hour, including definitions of pharmacovigilance, ADRs and their impact on public health, followed by a more in-depth approach to spontaneous ADR reporting and physicians' attitudes to and knowledge of the practice. Based on previous results,[7] a clinical case was presented and each physician was invited to discuss it. Thereafter, an ADR form was completed with the data of the case presented and the support of the summary of product characteristics (SPC). In addition, one attendance certificate, one NPC presentation folder and one ADR report form were distributed to the physicians attending the sessions.

Control Group

Eleven clusters from the control group were not subjected to either intervention. Nevertheless, because the NPC co-manages an awareness programme with the Portuguese National Medicine and Health Product Authority (Autoridade Nacional do Medicamento e Produtos de Saúde, I.P. – INFARMED), which is responsible for



1 Specific hospitals (cancer, maternity, etc.) that cover multiple geographical areas in the north Portugal region were excluded from the study because of the possibility of cross-contamination.

2 Each cluster consisted of one reference hospital plus the outpatient centre and small hospitals in its catchment area.

Fig. 1. Flow of participants through the trial.

conducting awareness campaigns among northern health professionals, there was the possibility that some of the control and intervention clusters had attended such programmes.

Follow-Up

Outcomes assessed included an indicator of reporting quantity (total number of reports) in addition to four indicators of reporting relevance. In the current study, the following were deemed relevant: serious ADRs (life-threatening or resulting in death, congenital abnormality, hospital admission, disability and/or incapacity); definitive or probable ADRs; and unexpected ADRs (unknown ADRs that are not described in the SPC). These relevance criteria were adopted by the Portuguese System of Pharmacovigilance, following the WHO guidelines.[14] Reports were assessed after validation by the regulatory body, which attributed degrees of probability as follows: definitive, probable, possible, improbable, conditional or unclassified. The follow-up period started post-intervention and was deemed at an end in 2009. All data were certified according to WHO procedures and were sourced from the Portuguese Health Authority (NPC). Data were made available for study purposes only, by attributing a code number to the physicians so as to prevent further identification and ensure confidentiality. This educational intervention trial was approved by the Northern Regional Health Authority (letter no. 005015 of 13 March 2007) and the hospital ethics committee (letter no. 1539 of 25 May 2007 and letter of 28 January 2008).

Statistical Analysis

All statistical analyses were performed on an intention-to-treat basis.[15] This meant that, once assigned to an intervention group, subjects were included in the analysis as part of that group regardless of whether or not they attended the intervention. Inclusion of all randomized subjects in the statistical analysis prevents any selection bias incurred by physicians' non-attendance during the intervention.

Generalized linear mixed models using penalized quasi-likelihood were applied to the statistical analysis.[16] This statistical method allows for longitudinal data analysis (repeated and multiple observations over time of each of many individuals) adjusted for the baseline values of the dependent variable. Such adjustment is vital in cases where study groups may become unbalanced due to the low number of random assignment units (i.e. as in our study, with only 15 clusters). To construct the models, we took the number of reports (total, serious, definitive or probable, unexpected, new drug-related) for each month as the dependent variable to control for initial heterogeneity among subjects, and the random distribution of spatial-clusters as the cluster effect. Given that the dependent variable is a count variable with variance higher than the mean, we applied negative binomial distribution.

To measure the intervention effect, a dichotomous indicator variable was created. This variable – denoted *period* – assumed a value of 0 for the baseline period, and a value of 1 for the months between the start of the intervention and end of follow-up. The intervention effect was evaluated on the basis of the interaction between the *group* (1 for intervention group, 0 for control group) and *period* variables. The reporting rates per 1000 physician-years were calculated by dividing the number of reports during the follow-up period by the number of physicians belonging to the study group during the same period. For analysis of the duration of the effect, another indicator variable was constructed with six categories (values of 0 for the baseline period; 1 for the first 4-month period post-intervention; and 2, 3, 4 and 5 for the ensuing periods, respectively). The intervention effect in each 4-month period was evaluated on the basis of the interaction between this indicator variable and the group variable. All analyses were performed using the R computer software programme. Results are expressed as relative risks (RRs) and their 95% CIs, indicating the extent to which reporting probability was increased by the briefing.

Results

Overall, 200 physicians underwent the educational intervention, 118 in the workshop and

82 in the telephone group (figure 1). The participation rate was 26.9% and 7.9% for the workshop- and telephone-intervention groups, respectively. The median follow-up period was 20 months. Table I shows physicians' characteristics by sex, age, medical specialty and workplace.

As against the control group, the telephone-intervention group had higher baseline reporting rates for total, serious and high-causality ADR categories, measured as reports per 1000 physician-years (table II). Lower reporting rates for serious and high-causality ADRs were observed for the workshop-intervention versus the control group (table II). With regard to the unexpected category of ADRs, the control group registered lower reporting rates than did the workshop- and telephone-intervention groups.

During the 20 months post-intervention, the workshop group increased their total ADR reporting (measured as reports per 1000 physician-years) 4-fold (RR 3.97; 95% CI 3.86, 4.08; $p < 0.001$ [table III]) compared with the control group and adjusted for baseline values, medical specialty and work setting. In the case of the telephone-intervention group, a non-statistically significant ($p = 0.052$) increase was observed in the total ADR reporting rate (RR 1.02; 95% CI 1.00, 1.04) compared with the control group. An increase was likewise observed in the reporting rates of unexpected and new drug-related ADRS (see table II), although it was not possible to calculate the effect measures since the models failed to converge (see table III). Moreover, concerning the telephone intervention group, there were periods (4-month periods) where a statistically significant decrease of the effect was observed compared with the control group due to numerical instability and low reporting rate.

Furthermore, the ADR reporting rate in the workshop-intervention group decreased during the follow-up phase of the intervention, and the RRs for total ADR reporting from the first to fifth 4-month period post-intervention were 12.40 (95% CI 11.86, 12.97; $p < 0.001$), 2.80 (95% CI 2.67, 2.93; $p < 0.001$), 3.93 (95% CI 3.74, 4.12; $p < 0.001$), 1.76 (95% CI 1.68, 1.84; $p < 0.001$) and 1.38 (95% CI 1.32, 1.45; $p < 0.001$), respectively (table IV).

Table I. Baseline characteristics of physicians, by study group[a]

Characteristic	Intervention group (n = 1472)		Control group (n = 5107)
	Workshop (438)	Telephone (1034)	
Sex			
Male	250 (57.1)	469 (45.4)	2446 (47.9)
Female	188 (42.9)	565 (54.6)	2661 (52.1)
Age			
Mean (SD)	49.31 (8.18)	46.29 (9.51)	48.55 (8.89)
Median (PCT 25, 75)	51 (44, 55)	46 (37, 54)	50 (41,55)
Medical specialty			
General medicine	184 (42)	245 (23.7)	1901 (37.2)
Medical	128 (29.2)	413 (39.9)	1840 (36)
Medical-surgical	53 (12.1)	142 (13.7)	646 (12.6)
Surgical	26 (5.9)	90 (8.7)	416 (8.1)
Other	11 (2.5)	58 (5.6)	163 (3.2)
Missing	36 (8.2)	86 (8.3)	141 (2.8)
Work setting			
Outpatient centre	198 (45.2)	219 (21.2)	1706 (33.4)
Hospital	240 (54.8)	815 (78.8)	3401 (66.6)

a Values are expressed as n (%) unless otherwise indicated.

PCT = Percentile.

Table II. Adverse drug reaction reporting rate per 1000 physician-years[a] categorized by adverse drug reaction type and period, pre- and post-intervention

Reporting	Group	Period						
		Baseline	Post-intervention					
			Overall period	4-month period				
				First	Second	Third	Fourth	Fifth[b]
Overall	Workshop intervention	10.41 (10)	52.74 (39)	63.58 (20)	15.89 (5)	12.71 (4)	19.07 (6)	11.57 (2)
	Telephone intervention	19.89 (49)	22.73 (40)	17.05 (12)	9.94 (7)	8.52 (6)	7.10 (5)	28.41 (10)
	Control	10.28 (122)	11.96 (102)	4.08 (14)	6.12 (21)	3.50 (12)	10.21 (35)	11.56 (20)
Serious	Workshop intervention	3.12 (3)	21.64 (16)	25.43 (8)	3.18 (1)	6.36 (2)	12.72 (4)	0 (0)
	Telephone intervention	15.02 (37)	14.20 (25)	12.78 (9)	5.68 (4)	5.68 (4)	4.26 (3)	14.20 (5)
	Control	6.99 (83)	7.51 (64)	2.62 (9)	2.33 (8)	3.21 (11)	5.54 (19)	9.83 (17)
Unexpected	Workshop intervention	3.12 (3)	6.76 (5)	6.36 (2)	0 (0)	3.18 (1)	3.18 (1)	0 (0)
	Telephone intervention	3.24 (8)	3.98 (7)	1.42 (1)	4.26 (3)	1.42 (1)	1.42 (1)	2.84 (1)
	Control	1.60 (19)	2.35 (20)	0 (0)	1.46 (5)	0.87 (3)	2.33 (8)	2.31 (4)
High-causality	Workshop intervention	6.25 (6)	36.51 (27)	47.68 (15)	12.72 (4)	9.54 (3)	12.72 (4)	0 (0)
	Telephone intervention	14.61 (36)	15.91 (28)	8.52 (6)	9.94 (7)	7.10 (5)	4.26 (3)	19.89 (7)
	Control	6.41 (76)	9.85 (84)	3.50 (12)	4.67 (16)	2.62 (9)	9.04 (31)	9.25 (16)
New drug-related	Workshop intervention	4.16 (4)	13.52 (10)	12.72 (4)	6.36 (2)	6.36 (2)	3.18 (1)	5.78 (1)
	Telephone intervention	3.25 (8)	3.41 (6)	5.68 (4)	1.42 (1)	1.42 (1)	0 (0)	0 (0)
	Control	3.88 (46)	5.75 (49)	2.33 (8)	4.08 (14)	1.46 (5)	4.08 (14)	4.63 (8)

a [(No. of reports of a study group during a specific follow-up period (months))/(no. of physicians belonging to the study group during that follow-up period)∗(no. of months in that follow-up period)]∗1000∗12.

b Follow-up of all subjects was not complete.

Discussion

The results reported in this study indicate that workshop-based educational interventions significantly increased the quantity and relevance of spontaneous ADR reporting by physicians in the northern region of Portugal. Yet, the telephone-interview interventions proved less efficient. These results indicate that workshops can be a good strategy for reinforcing other interventions aimed at increasing and improving ADR reporting.

A number of papers have been published on the implementation of strategies for enhancing the spontaneous ADR reporting rate by physicians. These include (i) direct reporting by telephone;[17] (ii) creation of discussion groups;[18] (iii) availability of reporting forms;[19,20] (iv) financial incentives;[21,22] (v) solicited reporting;[23] and (vi) publication of bulletins and alerts in medical journals.[24] Nonetheless, we failed to locate any studies like ours, which reported educational interventions that feature workshops with the inclusion of a clinical case or telephone interviews. Our results show that determinants of physicians' attitudes to ADR underreporting can be modified, especially if certain strategies are implemented that establish the association between physicians' attitude-related 'seven deadly signs' proposed by Inman[8] and underreporting, as shown previously.[13]

Comparing baseline reporting in this study with that of a study conducted in 2004,[13] the rates, albeit similar, were a little higher in 2008, which suggests that the effect of the multifaceted outreach visit was gradually declining, despite the fact that the reporting rates in the clusters of the telephone-intervention group were twice as high, which could also be influenced by the fact that one of the two clusters included in the study bordered on the area in which the NPC is situated. If the effectiveness of workshops is compared with that of outreach visits, workshops will be seen to be less effective. This difference can be attributed to physicians' participation (47.2% vs 26.9%) in both interventions. This decline in

percentage participation may be due to the fact that the workshops address the same topics as the outreach visits, and the physicians and hospital teaching units do not feel the need to repeat the same subject matter. To increase reporting rates it is important to use different teaching-learning methods in order to motivate physicians and hospital teaching units to participate.

Table III. Relative risk of reporting total, serious, high-causality, unexpected and new drug-related adverse drug reactions[a]

Independent variables	Adjusted RR (95% CI)[b]	p-Value
Effect of intervention on total no. of ADR reports		
Period	1.14 (1.13, 1.15)	<0.01
Group		
Workshop	0.92 (0.29, 2.91)	0.892
Telephone interview	1.72 (0.77, 3.88)	0.188
Intervention		
Workshop	3.97 (3.86, 4.08)	<0.001
Telephone interview	1.02 (1.00, 1.04)	0.052
Effect of intervention on reports of serious ADRs		
Period	1.05 (1.05, 1.06)	<0.001
Group		
Workshop	0.37 (0.09, 1.48)	0.159
Telephone interview	1.78 (0.73, 4.36)	0.207
Intervention		
Workshop	6.84 (6.69, 6.98)	<0.001
Telephone interview	0.93 (0.91, 0.94)	<0.001
Effect of intervention on reports of high-causality ADRs		
Period	1.52 (1.51, 1.54)	<0.001
Group		
Workshop	0.84 (0.25, 2.84)	0.780
Telephone interview	1.92 (0.82, 4.53)	0.134
Intervention		
Workshop	3.58 (3.51, 3.66)	<0.001
Telephone interview	0.75 (0.73, 0.76)	<0.001
Effect of intervention on reports of unexpected ADRs[c]		
Effect of intervention on reports of new drug-related ADRs[c]		

a RR for period is the adjusted RR of ADR reporting between the pre- and post-intervention periods in the control group. It assesses secular trends and possible contamination of the control group by the intervention group. RR for the group category is the adjusted RR of baseline ADR reporting between the intervention and control groups. RR for intervention measures the adjusted RR of ADR reporting for the intervention itself, as an interaction between the group variable and the period variable.

b RR adjusted for age, medical specialty and work setting.

c Values do not converge.

ADR = adverse drug reaction, **RR** = relative risk.

Our results are also in line with the conclusion of a systematic meta-analysis of randomized controlled trials, which indicated that physician's performance may be changed by many continuing medical education programmes,[25-27] and that such interventions are more likely to be effective if their aim is to modify behaviour rather than provide information. Traditional, passive, continuing medical education methods, such as didactic teaching conferences and learning-group presentations, have little or no impact on improving professional practices and are ineffective when it comes to changing physicians' behaviour.[26,27] Conversely, highly interactive learning methods that deliver interactive sessions designed to enhance physician participation, such as educational outreach visits,[28] workshops,[25,26] small discussion groups,[26,29] individualized training sessions,[26,29] practice-based interventions[27] and problem- or case-based learning,[30] are the most effective strategies. In particular, interactive educational workshops targeting qualified health professionals have been shown to be effective in improving professional practices and healthcare outcomes.[25] Hence, some components, such as tutor skills, enthusiasm and interactive educational materials, are considered pivotal to success in large-scale educational interventions.[13,30] In terms of results, the effectiveness of workshop interventions conducted in our study can doubtless be attributed to their interactive nature, particularly because they include models for the discussion of a practical case, which are fundamental to the success of the intervention.[26]

The results from this study show that telephone-based interventions proved to be less effective than workshop-based interventions. In our study, the ineffectiveness of telephone interviews can be linked to the low physician participation rate (our analysis was performed on an intention-to-treat basis), probably associated with methodological limitations due to the inherent difficulties involved in contacting physicians by telephone. Despite being easier to access telephone interviews at outpatient centres than at hospitals, certain outpatient centres allocate only 1 hour per week for physicians' external clinics, including the time spent attending to their own patients. In

Table IV. Relative risk of reporting total, serious, high-causality, unexpected and new drug-related adverse drug reactions, analysing the duration of effect for 4 months[a]

Independent variables	RR (95% CI)[b]	p-Value
Effect of intervention on total no. of ADR reports		
4-month intervals		
First	0.80 (0.78, 0.81)	<0.001
Second	1.14 (1.12, 1.16)	<0.001
Third	0.67 (0.66, 0.68)	<0.001
Fourth	1.97 (1.94, 2.01)	<0.001
Fifth	1.14 (1.12, 1.16)	<0.001
Group		
Workshops	0.97 (0.30, 3.08)	0.954
Telephone interview	1.71 (0.76, 3.84)	0.197
Intervention in 4-month intervals		
Workshop		
First	12.40 (11.86, 12.97)	<0.001
Second	2.80 (2.67, 2.93)	<0.001
Third	3.93 (3.74, 4.12)	<0.001
Fourth	1.76 (1.68, 1.84)	<0.001
Fifth	1.38 (1.32, 1.45)	<0.001
Telephone interview		
First	2.11 (2.03, 2.18)	<0.001
Second	0.84 (0.81, 0.87)	<0.001
Third	1.38 (1.33, 1.43)	<0.001
Fourth	0.38 (0.36, 0.39)	<0.001
Fifth	1.31 (1.27, 1.36)	<0.001

a RR for period is the adjusted RR of ADR reporting between the pre- and post-intervention periods in the control group. It assesses secular trends and possible contamination of the control group by the intervention group. RR for the group category is the adjusted RR of baseline ADR reporting between the intervention and control groups. RR for intervention measures the adjusted RR of ADR reporting for the intervention itself, as an interaction between the group variable and the period variable.

b RR adjusted for age, medical specialty and work setting.

ADR = adverse drug reaction; **RR** = relative risk.

hospitals, telephone interviews are very difficult because physicians are not in one place for any extended period of time. A similar study performed on pharmacists[30] yielded interesting results, perhaps because telephone interviews can be more easily conducted with community pharmacists since they stay in the same place for long periods of time. A limitation in this study was that the clusters were not equivalent at baseline, inasmuch as the telephone-intervention group registered a higher reporting rate than the other groups. Although statistical analysis allows for adjustment to be made for such baseline differences, the fact that the baseline rate was higher might nevertheless have rendered increasing the reporting rate more difficult. This might explain why the telephone-intervention group registered a smaller increase.

With respect to duration of the effect, we, like other studies,[5,13] have found that purpose-designed educational interventions targeted at health professionals may well improve the quantity and quality of ADR reporting, yet the effectiveness of these interventions is significant for a limited period of time. Indeed, the point has been made that continuing education and reinforcing strategies are required to improve the impact of such interventions.[27] In our study, the workshop intervention showed itself to be effective for more than 1 year, which is in line with the duration of the effect of outreach visits.

Another limiting factor in this study resided in the database assessment and the lack of data on losses to follow-up. Similarly, important limitations should be borne in mind when it comes to interpreting the results reported here. For instance, the degree of external validity of these results is unknown, since many factors influence the effectiveness of educational interventions, such as health professionals' educational background, motivation and workload, the health system and trainer-related factors, e.g. their knowledge, assertiveness, motivation and communication skills.

Furthermore, the earlier educational interventions conducted in 2004[13] could account for the physicians' low workshop participation rate, possibly due to a lack of interest on their part due to the fact that they had previously received training on the same topic area. At all events, performing the analysis on an intention-to-treat basis means that low participation is already included in the assessment of effectiveness.

Conclusions

In view of the fact that interventions aimed at increasing and improving ADR reporting by physicians have a limited effect in time, it is es-

sential to resort to new interventions that enable a good level of reporting to be maintained. When designing these new interventions, it should be borne in mind that, in order for them to be attractive to the physicians, they must be implemented by using new teaching-learning techniques and, where possible, by gradually increasing the degree of interactivity. This study shows that telephone-based interventions are not effective for this purpose, whereas workshops, in which real clinical cases are used to complete a report form, can be a good method for conducting such interventions.

Acknowledgements

The authors wish to express their sincere thanks to the following: Professor Altamiro da Costa Pereira for his invaluable help in developing this study; Professor Adolfo Figueiras, whose work on this project was funded by the Consortium for Biomedical Research in Epidemiology and Public Health (CIBER en Epidemiología y Salud Pública [CIBERESP]) [AC08_008]; María Piñeiro (CIBERESP), who contributed greatly to the statistical analysis; and Professor Maria Teresa Herdeiro, whose work on this project was funded, in part, by Science and Technology Fund (Fundação para a Ciência e Tecnologia) grant SFRH/BPD/35746/2007 from the Portuguese Ministry of Science, Technology and Higher Education.

The authors declare that they have no conflicts of interest directly relevant to the contents of this study.

References

1. Einarson TR. Drug-related hospital admissions. Ann Pharmacother 1993; 27 (7-8): 832-40
2. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998; 279 (15): 1200-5
3. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004; 329 (7456): 15-9
4. Lasser KE, Allen PD, Woolhandler SJ, et al. Timing of new black box warnings and withdrawals for prescription medications. JAMA 2002; 287 (17): 2215-20
5. Pedros C, Vallano A, Cereza G, et al. An intervention to improve spontaneous adverse drug reaction reporting by hospital physicians: a time series analysis in Spain. Drug Saf 2009; 32 (1): 77-83
6. Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. Drug Saf 2006; 29 (5): 385-96
7. Herdeiro MT, Figueiras A, Polonia J, et al. Physicians' attitudes and adverse drug reaction reporting: a case-control study in Portugal. Drug Saf 2005; 28 (9): 825-33
8. Inman WHW. Assessment drug safety problems. In: Gent M, Shigmatsu I, editors. Epidemiological issues in reported drug-induced illnesses. Honolulu, Ontario: McMaster University Library Press, 1976: 17-24
9. Smith CC, Bennett PM, Pearce HM, et al. Adverse drug reactions in a hospital general medical unit meriting notification to the Committee on Safety of Medicines. Br J Clin Pharmacol 1996; 42 (4): 423-9
10. Herdeiro MT, Figueiras A, Polonia J, et al. Influence of pharmacists' attitudes on adverse drug reaction reporting: a case-control study in Portugal. Drug Saf 2006; 29 (4): 331-40
11. Herdeiro MT, Polonia J, Gestal-Otero JJ, et al. Factors that influence spontaneous reporting of adverse drug reactions: a model centralized in the medical professional. J Eval Clin Pract 2004; 10 (4): 483-9
12. Lopez-Gonzalez E, Herdeiro MT, Figueiras A. Determinants of under-reporting of adverse drug reactions: a systematic review. Drug Saf 2009; 32 (1): 19-31
13. Figueiras A, Herdeiro MT, Polonia J, et al. An educational intervention to improve physician reporting of adverse drug reactions: a cluster-randomized controlled trial. JAMA 2006; 296 (9): 1086-93
14. World Health Organization, The Uppsala Monitoring Centre. Glossary of terms used in pharmacovigilance [online]. Available from URL: http://www.who-umc.org/graphics/25301.pdf [Accessed 2011 Feb 9]
15. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ 1999; 319 (7211): 670-4
16. Pinheiro JC, Bates DM. Mixed-effects models in S and S-PLUS. 3rd ed. New York: Springer, 2006
17. Vorcewest TE, Barstow L, Butcher B. System for voluntary reporting of adverse drug-reactions in a university hospital. Am J Hosp Pharm 1989; 46 (11): 2300-3
18. Sivaram C, Johnson S, Tirmizi SN, et al. Morning report: a forum for reporting adverse drug reactions. Jt Comm J Qual Improv 1996; 22 (4): 259-63
19. Castel JM, Figueras A, Pedros C, et al. Stimulating adverse drug reaction reporting: effect of a drug safety bulletin and of including yellow cards in prescription pads. Drug Saf 2003; 26 (14): 1049-55
20. McGettigan P, Golden J, Conroy RM, et al. Reporting of adverse drug reactions by hospital doctors and the response to intervention. Br J Clin Pharmacol 1997; 44: 98-100
21. Backstrom M, Mjorndal T. A small economic inducement to stimulate increased reporting of adverse drug reactions: a way of dealing with an old problem? Eur J Clin Pharmacol 2006; 62: 381-5
22. Gilroy GW, Scollins MJ, Gay CA, et al. Pharmacy-coordinated program that encourages physician reporting of adverse drug reactions. Am J Hosp Pharm 1990; 47: 1327-33
23. Gony M, Badie K, Sommet A, et al. Improving adverse drug reaction reporting in hospitals: results of the French Pharmacovigilance in Midi-Pyrenees region (Pharmaco-MIP) network 2-year pilot study. Drug Saf 2010; 33 (5): 409-16
24. Scott HD, Thacher-Renshaw A, Rosenbaum SE, et al. Physician reporting of adverse drug reactions: results of the Rhode Island adverse drug reaction reporting project. JAMA 1990; 263 (13): 1785-8

25. Thomson O'Brien MA, Freemantle N, Oxman AD, et al. Continuing education meetings and workshops: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2001: (2): CD003030
26. Davis D, O'Brien MA, Freemantle N, et al. Impact of formal continuing medical education: do conferences, workshops, rounds, and other traditional continuing education activities change physician behavior or health care outcomes? JAMA 1999; 282 (9): 867-74
27. Davis D, Thomson M, Oxman A, et al. Changing physicians performance: a systematic review of the effect of continuing medical education strategies. JAMA 1995; 274 (9): 700-5
28. Thomson O'Brien MA, Oxman AD, Davis DA, et al. Educational outreach visits: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2000; (2): CD000409
29. Figueiras A, Sastre I, Tato F, et al. One-to-one versus group sessions to improve prescription in primary care: a pragmatic randomized controlled trial. Med Care 2001; 39 (2): 158-67
30. Ribeiro-Vaz I, Herdeiro MT, Polonia J, et al. Strategies to increase the sensitivity of pharmacovigilance in Portugal. Rev Saude Publica 2010; 45 (1): 129-35

Correspondence: Professor *Maria Teresa Herdeiro*, Unidade de Farmacovigilância do Norte, Faculdade de Medicina, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. E-mail: therdeiro@med.up.pt