Effectiveness of audit and feedback in addressing over prescribing of antibiotics and injectable medicines in a middle-income country: an RCT

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Received: 3 September 2018 / Accepted: 4 February 2019 / Published online: 21 February 2019
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Abstract

Overprescribing of antibiotics and injectable medicines is common in ambulatory care in many low- and middle-income countries. We evaluated the effects of three different interventions in improving physician prescribing. We conducted a four-armed randomized controlled trial with one-month and three-months follow-up. General physicians, pediatricians, and infectious disease specialists were included in this study if they had an outpatient office in Tehran, Iran. The study involved two behaviorally guided interventions: “new-design audit and feedback (NA&F)”; “printed educational material (PEM)” and an existing intervention of “routinely conducted audit and feedback (RA&F)”. The theoretical framework underpinning the intervention was the theory of planned behavior. Main outcome measures were the percentage change in the proportion of prescriptions containing injectable dexamethasone; oral amoxicillin and cefixime. NA&F reduced the proportion of prescriptions particularly those containing dexamethasone injectable and cefixime (1.64, 0.99 absolute percentage change, $p = 0.006$, $p = 0.01$ respectively). PEM reduced the proportion of prescriptions containing cefixime (0.93 absolute percentage change $p = 0.04$). Other primary outcomes had no significant differences. A secondary outcome measure showed overall prescribing of injectables also reduced (absolute risk reduction: 3%). Overall, the study provides strong evidence that using theoretical insights in the development of the intervention improved prescribing behavior that lasted at least three months after the intervention. The design, format, and presentation of messages in feedback forms significantly influence the impact of audit and feedback on physician prescribing. While the interventions were effective, the impacts on inappropriate prescribing were modest and limited. In settings with rampant problems of overprescribing, intensive interventions are required to substantially improve prescribing patterns.

Keywords Effectiveness of audit and feedback · Physician’s prescribing indicators · Rational medicine use interventions

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Introduction

Improving access to and use of medicines is an important policy goal for health systems around the world [1]. Households in many low- and middle-income countries (LMICs) face important barriers that impede access to medicines [2]. The major barriers are financial (ability to pay) and availability. Governments around the world are struggling to keep pharmaceutical expenditure under control [3], while at the same time striving to ensure access to medicines. Recent evidence suggests that the biggest growth in pharmaceutical costs is in middle-income countries. The concept of providing access to medicines also implies that the medicines are prescribed and used appropriately [4]. Without appropriate use, medicine availability and affordability may bring limited benefits to society. In many LMICs the picture of access to medicines is compounded by the double-burden of limitations in their affordability and availability as well as in their inappropriate use [5].

Overprescribing of antibiotics and injectable forms of medicines are common concerns in many LMICs and may result in unwanted patient outcomes and wastage of health care resources [6]. In Iran, prescriptions that include injectable forms of systemic corticosteroids- often as pain relievers- are a common concern. Other concerns are the over-prescription of effective medications without relevant indications (e.g. antibiotics for viral diseases) and failure to prescribe the most effective, safe, and cost-effective antibiotic in class, with evidence of inappropriate use of broad-spectrum antibiotics (very expensive) to treat simple upper respiratory tract infections [7].

Iran's relatively high antimicrobial use, almost 50% of prescriptions include at least one antibiotic, appears to be partially responsible for the increasing rate of antibiotic resistance, yet prescribing of broad spectrum antibiotics continues to increase. There are currently no national guidelines on antibiotics usage. There is also no restriction on antibiotics use, such as occurs in other countries such as in some Nordic countries [8]. Although many studies have assessed the effects of different interventions in improving physician prescribing, transferring their results to different settings remains challenging for two main reasons: the interventions are often poorly defined and developed, and they often originate from a limited number of high-income countries [9, 10].

Audit and feedback refers to a summary of health care performance during a particular period of time with or without recommendations for clinical action. According to previous controlled trials, audit and feedback could moderately enhance the provided care [10]. Research has shown the slight effects of printed educational materials (PEMs), when used alone, in practice. Yet, considering the low costs of PEMs, their use might still be cost-effective [11]. One other limitation of prior research into audit and feedback is the lack of consideration of behavioral theory. Using a theoretical behavioral

framework to guide the intervention is considered to increase the likelihood of implementing successful interventions [12].

This trial was designed to test three different interventions for improving rational drug use indicators of general physicians, pediatricians and infectious disease specialists. The main objectives of the study were: 1) assessing the effectiveness of routinely conducted prescribing audit and feedback intervention in improving general physicians, pediatricians and infectious disease specialists prescribing behavior in comparison to printed educational materials and no intervention; and 2) assessing the effectiveness of new-design audit and feedback interventions in improving prescribing compared to the routinely conducted audit and feedback, printed educational materials and no intervention.

Methods

We conducted a four-armed randomized controlled trial: routinely conducted audit and feedback (RA&F), new-design audit and feedback (NA&F), printed educational materials (PEM) as well as a control arm. The reporting of the results follows the Consort recommendations [13]. The trial was registered in the Iranian Registry of Clinical Trials; Registration Number: RCT201106086740N1.

Setting and participants

General physicians, pediatricians, and infectious disease specialists were included in this study if they had an outpatient office in Tehran, Iran, and were in contract with one or both of the two main social health insurance organizations in the country because this provided reliable access to prescriptions data. The physicians were considered as strata as we collected data on prescriptions they had issued.

Physicians' prescription data were obtained from the claims pharmacies electronically submitted to the insurance organizations.

Interventions

The Theory of Planned Behavior (TPB) was used as the theoretical framework for developing interventions [14]. Details of the processes that were followed for intervention development have been described in the published study protocol [15]. In the new audit and feedback, a color coding method was used to attract physicians' attention to the main messages. In contrast, the routinely conducted audit-feedback intervention that was being used in the country as a standard approach contained a large collection of performance indicators compared with their peer groups, no color coding and no individually tailored messages to the prescribers.

Intervention delivery

Participants in the intervention arms received feedback reports or PEM (as applicable) via special delivery postage in June 2012. All the interventions were posted on the same day. We telephoned the physician office secretaries afterwards to ensure the letter had been delivered.

Outcomes

We selected three primary outcome measures relevant to common concerns over physician prescribing in Iran: the percentage change in the proportion of prescribed injectable dexamethasone, oral cefixime, and oral amoxicillin one and three months after interventions. Additionally, we considered a set of secondary outcome measures (average medicine items and price per prescription, proportion of prescriptions containing at least one injectable drug, antibiotic medicine items and corticosteroid medicine item) to assess whether changing behavior toward satisfying primary outcomes resulted in (unwanted) changes in other aspects of prescribing.

All outcomes were recorded at the patient level. Baseline data for the three months preceding the intervention, and data for one month and three months after the interventions were collected for all four arms of the study. All analyses were undertaken at the physician level and followed an intention-to-treat approach. We also conducted per-protocol analyses (excluding those physicians who had not received the interventions) as a sensitivity analysis.

Sample size

Dexamethasone injections were prescribed for about 14% of outpatients in Tehran. It is at the top of the first 10 medicines prescribed by physicians. Therefore, we considered it as the basis for sampling. We expected the interventions to decrease this rate to 10%. Assuming a study power of 80% and a statistical significance level of 5%, and a small prospect of loss to follow up, the number of participants in each study arm was calculated as 200 (i.e. a total 800 participants).

Randomization

The participants (strata) were randomized to one of the four study arms through the following procedure: The names of all eligible physicians who had an outpatient office in Tehran (about 6000 physicians) were first listed. Next, they were arranged in three groups: general physicians, pediatricians, and infectious disease specialists. In the next stage, these groups were used as the stratifying factor and participants were allocated to the study arms using a random number generator. We followed the

approach until each study arm had a minimum of 175 general physicians, 24 pediatricians, and 4 infectious disease specialists. Random numbers were generated and allocated to physicians by a member of the research team (AR) who was not involved in performing the interventions. The physician was the unit of randomization and analysis. While the participants were aware of the interventions, they were blinded to the data collection processes prior to the intervention and afterwards, including to the lengths of data collection and the indicators of interest for this research.

Statistical methods

We conducted the analyses at the strata level (physicians), as the intended unit of inference was the physician [16]. One-way analysis of variance, using physicians' demographic characteristics and pre-intervention rate of prescribing indicators, was applied to examine the comparability of the intervention and control groups at baseline. Chi-square tests were applied to evaluate categorical variables. Analysis of covariance was used to assess the effectiveness of the interventions. We evaluated the effects of the interventions on the percentage of prescriptions including on each of the mentioned drugs. To ensure the comparability of the arms, we compared the baselines between all outcome variables. The analysis followed a difference-in-the-difference approach and the effects of the interventions were calculated as the difference between the pre and post intervention periods at one and three months after the interventions compared with between the arms.

Ethical considerations

Data were extracted from the health insurance organizations' claims databases. We assessed the prescribing indicators for each participating physician, and sent individual feedback confidentially to those who were assigned to the relevant intervention arms for their personal review. All other analyses were conducted anonymously. The study was approved by the Ethics Committee of Pharmaceutical Sciences Research Center of Tehran University of Medical Sciences Ethics Committee Registration Number: 90–02–27-07.

Results

Participants flow

Figure 1 shows the flow of participants (strata) through the trial. Out of the 820 physicians that were selected, 809 participated in the trial. Eleven physicians withdrew after

Fig. 1 Participant flow

randomization. The characteristics of the intervention and control arms were similar at baseline (Fig. 1).

Baseline data

Data cleaning was conducted and values with large differences in average (extreme outliers) were extracted. Appendix Table 4 shows demographic and practice characteristics of physicians in the trial. The study groups had no significant differences in pre-intervention data, except for the average price per prescription (Table 1).

Primary outcomes

Table 2 summarizes the main study findings. Comparisons between the new-design feedback arm and the no intervention arm showed significant reductions in the percentage of prescriptions containing injectable dexamethasone (1.64 absolute difference in percent change; $p = 0.006$) and cefixime (0.99 absolute difference in percent change; $p = 0.01$). Moreover, the percentage of prescriptions containing cefixime (0.93 absolute difference in percentage change; $p = 0.04$) was significantly lower in the PEM arm than in the no intervention arm. We observed no other significant differences in any other primary outcome comparison (Table 2).

Secondary outcomes

Table 3 presents the secondary outcomes of the study. As seen, no significant differences were seen in secondary outcomes, except for the percentage of prescriptions containing at least one injectable drug which was significantly lower in the new-design feedback arm compared with the no intervention arm (-3.08 ; $p = 0.001$).

Discussion

This study is one of the few RCTs of audit and feedback interventions to improve physician prescribing in LMICs (10, 17, 18). In our study, we assessed two different audit and feedback formats and demonstrated that the NA&F was more effective in reducing inappropriate prescribing of injectables and certain antibiotics. Our study also involved a further intervention arm that received a PEM intervention. Again, we observed that a carefully designed and theory-based PEM was more effective than the routinely conducted audit and feedback, and the control group in reducing injectable dexamethasone prescriptions. Overall, the study provides strong evidence of using theoretical insights in the development of interventions to improve prescribing behavior that lasts at least three months after the intervention.

Inappropriate prescribing and use of antibiotics is a major concern in Iran [17], in the eastern Mediterranean region [18] and in many LMICs [19]. While we noted that the NA&F resulted in reducing the use of certain expensive antibiotics, none of the interventions was effective in reducing overall antibiotic use and amoxicillin use in particular. Amoxicillin is the most prescribed antibiotic in Iran and a reduction in its usage would have had important policy implications [17]. Previous studies have demonstrated the difficulties of improving antibiotic prescribing by physicians. A Cochrane review published in 2005 concluded that using “PEMs or audit and feedback alone resulted in no or only small changes in prescribing” [20]. The review concluded that the reasons behind inappropriate antibiotic prescribing were multi-factorial, and hence single-method interventions might not result in substantial improvements in antibiotic prescribing. Three studies conducted in Europe demonstrated significant improvements in antibiotic use when educational meetings and audit and feedback were used together [19]. A more recent RCT conducted in Ireland assessed the effects of postal delivery of prescribing feedback and

Table 1 Main and complementary outcomes in four evaluated arms, at baseline

Intervention arms		RA&F Arm	NA&F Arm	PEM Arm	Control Arm
Outcomes	Number of physicians	202	198	201	208
Mean items per prescription		3.04	2.97	3.01	3.08
SD		0.041	0.040	0.041	0.043
($\pm$ CI)		(2.96–3.12)	(2.90–3.05)	(2.93–3.09)	(2.99–3.16)
Mean price per prescription		41,674	41,504	45,907	47,817
SD		839.26	1213.52	2326.27	2310.22
($\pm$ CI)		(40019–43,329)	(39111–43,897)	(41320–50,494)	(43262–52,371)
Proportion of prescriptions including	Antibiotics	50.14	47.79	48.19	47.05
SD		1.01	1.13	1.00	1.14
($\pm$ CI)		(48.15–52.13)	(45.55–50.03)	(46.21–50.18)	(49.30–44.80)
	Injectable	41.67	43.33	40.40	42.05
		1.29	1.50	1.47	1.56
		(39.11–44.23)	(40.36–46.29)	(37.49–43.31)	(38.97–45.13)
	Corticosteroid	21.34	22.46	20.68	22.51
		0.96	1.02	0.98	1.17
		(19.44–23.23)	(20.44–24.49)	(18.74–22.61)	(20.19–24.43)
	Amoxicillin	5.95	5.07	5.17	5.67
		0.45	0.38	0.36	0.45
		(5.05–6.84)	(4.31–5.83)	(4.44–5.90)	(4.78–6.56)
	Cefixime	13.08	10.91	11.50	12.05
		0.68	0.59	0.64	0.66
		(11.73–14.44)	(9.73–14.44)	(10.24–12.77)	(10.73–13.36)
	Dexamethasone	9.59	11.40	10.46	11.45
		0.68	0.78	0.73	0.90
		(8.25–10.94)	(9.85–12.96)	(9.01–11.91)	(9.67–13.24)

RA&F Routinely Conducted Feedback Arm, NA&F New-Design Feedback Arm, PEM Printed Educational Material Arm, CI Confidence Interval

presenting the results of the feedback via educational outreach [21]. Both intervention approaches resulted in a similar 2%–3% reduction in antibiotic prescribing, although the study did not have a control no-intervention arm to rule out the effects of potential external factors influencing the observed reduction in both study groups. One interesting conclusion of this study was that the addition of educational outreach on top of audit and feedback did not further improve antibiotic prescribing [21]. Hence Arnold and Straus (2005) hypothesis that using different interventions together results in improving antibiotic prescribing needs to be further assessed in future studies. Patients and parents' demands are frequently cited as a main reason for physicians' antibiotic overprescribing [21, 22]. Future multi-faceted studies might benefit from conducting interventions that target physicians as well as patients and the public to improve rational use of antibiotics prescribing.

The NA&F intervention had a significant impact on reducing dexamethasone injectables prescribing (absolute risk reduction: 1.6%) as well as overall injectables prescribing (absolute risk reduction: 3%) compared with the control arm. Other interventions had no significant effects. The baseline rate of injectables prescribing in ambulatory settings in Iran is high (40%) as well as many other LMICs [23, 24]. Hence, any meaningful reductions in prescribing injectables have considerable financial and safety implications. We identified

only a few RCTs that had assessed the impact of different interventions on reducing injectables prescribing. In Indonesia, with a baseline injectables rate of about 70%, an intensive intervention involving interactive group discussions resulted in a significant 19% reduction in the intervention arm compared with the control arm [25]. A more recent RCT conducted in India using the same intervention, resulted in a significant 11% reduction in proportion of prescriptions containing injectables compared with the control. We found no RCT that assessed the effects of audit and feedback on injectable prescribing. Although the studies that assessed interactive group discussions observed more promising effects than our audit and feedback intervention, they are resource intensive and are not appropriate as routine interventions in settings with limited resources. As a comparison, our intervention seems appropriate as a national routine program if an infrastructure for electronic recording of prescriptions exists.

In our study, PEMs resulted in a significant reduction (absolute risk reduction: 1%) in prescribing cefixime oral forms compared with the control arm. No other significant effect was observed. These findings are similar to effectiveness observed in other interventional studies in which written educational content was disseminated among physicians to improve prescribing [25]. Considering that the incremental costs of disseminating printed materials are relatively small, it might still

Table 2 Primary outcomes for the study arms at baseline and 3 months after the intervention and within arm percentage changes

Interventions			Outcomes		
			Proportion of prescriptions include:		
			Amoxicillin	Cefixime	Dexamethasone
RA&F	Baseline		5.95	13.08	9.59
	SD		0.45	0.68	0.68
	($\pm$ %95CI)		(5.05–6.84)	(11.73–14.44)	(8.25–10.94)
	3 Month		5.11	11.56	8.25
	SD		0.37	0.60	0.59
	($\pm$ %95CI)		(4.37–5.85)	(10.37–12.76)	(7.08–9.42)
	% change		–0.84	–1.52	–1.35
NA&F	Difference in %change in comparison with (p value)	Control	0.15 (1.0)	–0.67 (0.39)	0.25 (1.0)
		PEM	–0.17 (1.0)	0.26 (1.0)	1.24 (0.39)
	Baseline		5.07	10.91	11.40
	SD		0.38	0.59	0.78
	($\pm$ %95CI)		(4.34–5.83)	(9.73–12.09)	(9.85–12.96)
	3 Month		4.16	9.07	8.16
	SD		0.29	0.47	0.62
PEM	($\pm$ %95CI)		(3.59–4.73)	(8.14–10.01)	(6.92–9.40)
	% change		–0.94	–1.84	–3.24
	Difference in %change in comparison with (p value)	Control	0.08 (1.0)	–0.99 (0.01)	–1.64 (0.01)
		PEM	–0.24 (1.0)	–0.06 (0.1)	–0.68 (1.0)
	Baseline		5.17	11.52	10.46
	SD		0.36	0.64	0.73
	($\pm$ %95CI)		(4.44–5.9)	(10.24–12.8)	(9.04–11.94)
Control	3 Month		4.50	9.72	7.94
	SD		0.30	0.58	0.60
	($\pm$ %95CI)		(3.94–5.10)	(8.57–10.87)	(6.75–9.14)
	% change		–0.67	–1.78	–2.56
	Difference in %change in comparison with (p value)	Control	0.32 (1.0)	–0.93 (0.04)	–0.96 (0.05)
	Baseline		5.67	12.05	11.45
	SD		0.45	0.66	0.90
	($\pm$ %95CI)		(4.8–6.6)	(10.73–13.36)	(9.7–13.24)
	3 Month		4.68	11.20	9.85
	SD		0.35	0.74	0.80
	($\pm$ %95CI)		(3.99–5.37)	(9.73–12.67)	(8.27–11.43)
	% change		–0.99	–0.85	–1.6

Comparisons are provided between the intervention arms with the no intervention arm; and between the RA&F and NA&F arms with the PEM arm. RA&F: Routinely Conducted Feedback Arm; NA&F: New/Design Feedback Arm; PEM: Printed Educational Material Arm; CI: Confidence Interval.

be worthwhile to pursue the intervention even if it only affected one prescribing outcome. To ensure this is the case, the cost-effectiveness of the intervention needs to be assessed.

Our study had limitations. As the data were derived from insurance databases, the physician selection was limited to those who had contracts with the insurers who comprise the majority of office-based practicing physicians in Iran. Other limitations included the accuracy of physicians' addresses, physicians' willingness to study the content of the pack properly and the reliability of the postage system in handing out the packs properly and correctly. These potential concerns would have affected the intervention groups in the same way; and

will affect the real use of the interventions in practice. We used a certified mail to make it possible to track the packages. The selected physicians were also checked for their addresses prior to sending the packages. We used attractive and engaging design for the PEM and asked the responsible authorities to sign the feedback forms' cover letters. These may have increased the chances of physicians paying enough attention to the contents.

Results of our study suggest that implementing the NA&F intervention is more likely to change the indicators of drug prescriptions than the two other interventions. It demonstrated that the design and format of the feedback form significantly

Table 3 Secondary outcomes for the study arms at baseline and 3 months after the intervention and within arm percentage changes

Interventions			Outcomes				
			Mean Items	Mean price	Proportion of Prescriptions including:		
					Antibiotics	Injectable	Corticosteroid
RA&F	Baseline		3.04	41,674	50.14	41.8	21.34
	SD		0.041	839.26	1.01	1.29	0.96
	(±%95CI)		(2.96–3.12)	(40019–43,329)	(48.15–52.13)	(39.11–44.23)	(19.44–23.23)
	3 Month		2.93	42,332	44.66	39.23	18.81
	SD		0.042	1152.55	1.01	1.31	0.88
	(±%95CI)		(284–3.01)	(40059–44,605)	(42.66–46.67)	(36.64–41.82)	(17.07–20.56)
	% change		–0.11	658	–5.48	–2.57	–2.53
	Difference in %change in comparison with (<i>p</i> value)	Control	0.05 (1.0)	1826 (1.0)	0.65 (1.0)	–1.08 (1.0)	0.56 (1.0)
		PEM	0.01 (1.0)	1949 (1.0)	–1.17 (1.0)	0.17 (1.0)	0.68 (1.0)
NA&F	Baseline		2.97	41,504	47.8	43.33	22.5
	SD		0.040	1213.51	1.13	1.50	1.02
	(±%95CI)		(2.90–3.05)	(39111–43,897)	(45.55–50.03)	(40.36–46.29)	(20.44–24.5)
	3 Month		2.86	42,040	42.27	38.76	18.18
	SD		0.039	1348.81	1.08	1.48	0.91
	(±%95CI)		(2.78–2.93)	(39381–44,700)	(40.13–44.41)	(35.83–41.69)	(16.39–19.98)
	% change		–0.11	536	–5.53	–4.57	–4.32
	Difference in %change in comparison with (<i>p</i> value)	Control	0.05 (1.0)	1704 (1.0)	0.6 (0.53)	–3.08 (0.001)	–1.23 (0.37)
		PEM	0.01 (1.0)	1827 (1.0)	–1.22 (1.0)	–1.83 (0.28)	–1.11 (1.0)
PEM	Baseline		3.01	45,907	48.19	40.4	20.7
	SD		0.041	2326.27	1.00	1.47	0.98
	(±%95CI)		(2.93–3.09)	(41320–50,494)	(46.21–50.18)	(37.49–43.31)	(18.74–22.61)
	3 Month		2.89	44,616	43.88	37.66	17.49
	SD		0.041	1911.51	0.99	1.41	0.84
	(±%95CI)		(2.81–2.93)	(40848–48,386)	(41.92–45.84)	(34.87–40.45)	(15.82–19.16)
	% change		–0.12	–1291	–4.31	–2.74	–3.21
	Difference in %change in comparison with (<i>p</i> value)	Control	0.04 (1.0)	–123 (1.0)	1.82 (0.11)	–1.25 (0.48)	–0.12 (1.0)
Control	Baseline		3.08	47,817	47.05	42.05	22.51
	SD		0.043	2310.22	1.14	1.56	1.17
	(±%95CI)		(2.99–3.16)	(43262–52,371)	(44.8–50.18)	(39–45.13)	(20.19–24.83)
	3 Month		2.92	46,649	40.92	40.56	19.42
	SD		0.048	2071.16	1.16	1.58	1.06
	(±%95CI)		(2.83–3.02)	(42566–50,733)	(38.61–43.22)	(37.43–43.69)	(17.31–21.53)
	% change		–0.16	–1168	–6.13	–1.49	–3.09

Comparisons are provided between the intervention arms with the no intervention arm; and between the RA&F and NA&F arms with the PEM arm. RA&F: Routinely Conducted Feedback Arm; NA&F: New-Design Feedback Arm; PEM: Printed Educational Material Arm; CI: Confidence Interval.

affects its effectiveness in changing prescribing behavior. The NA&F was developed on the basis of the most common medicine prescribing concerns on injectables systemic corticosteroids (mainly dexamethasone) prescribing, and antibiotics overuse especially the third generation antibiotics such as ceftriaxone (as an injectable) and oral cefixime forms. Additionally, a color coding method was used to attract physicians' attention to the main messages. In contrast, the routinely conducted audit-feedback intervention that was being used in the country as a standard approach contained a large collection of performance indicators comprised with their peer groups, no colour coding and no individually tailored

messages to the prescribers. Hence our study might also explain why some previous audit and feedback studies were ineffective in improving prescribing [26].

Conclusions

Based on the results of this study, we conclude that NF&A might have high impact on changing prescribing behaviour comparing with routine AU and PEM. In addition, careful attention to the format, design and the way the messages are conveyed in feedback forms are

important indicators of audit and feedback's potential success in improving prescribing behavior. The effects of study interventions on reducing injectables prescribing were modest and on antibiotics overprescribing were limited. Hence, it seems that in settings with rampant problems of medicines' overprescribing, there is a need to invest in intensive and perhaps multi-faceted interventions to substantially improve prescribing patterns.

Acknowledgements We thank the assistance of Ahmad Ali Mostofi for his useful assistance in data collection and taking part in designing the digital audit and feedback form.

Authors' contributions AR, FS designed the study with contributions from RD, AK, MH and MA. FS collected data and registered the study protocol. FS, AR and MH analysed the data. Ahmad Ali Mostofi designed the software format of audit and feedback forms. AR and FS were responsible for the data validation. FS and AR wrote the manuscript. The manuscript was revised based on comments from the other authors. All the authors approved the final manuscript. AR is the guarantor.

Compliance with ethical standards

Conflict of interest FS acted as the coordinator of the national committee on rational drug use at the Ministry of Health and Medical Education of Iran, which was in charge of implementing the routinely conducted audit and feedback intervention.

Ethical issues Trial registration: Iranian Registry of Clinical Trials Registration Number: RCT201106086740N1.

Pharmaceutical Sciences Research Center of TUMS Ethics Committee Registration Number: 90-02-27-07

Appendix

Table 4 Gender and specialty characteristics of physicians in study arms

Details		RA&F	NA&F	PEM	Control
Sex	Male	163	165	171	185
	Female	39	33	30	23
Specialty	General physician	175	171	174	178
	Pediatricians and infectious disease specialists	27	27	27	30

RA&F Routinely Conducted Feedback Arm, NA&F New-Design Feedback Arm, PEM Printed Educational Material Arm

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