Improving the Success of Mailed Letter Intervention Programs to Influence Prescribing Behaviors: A Review

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ABSTRACT

BACKGROUND: Educational interventions have long been used as a means of influencing prescribing behavior. Various techniques including educational mailings, academic detailing, prescriber feedback with or without disclosing patient-identifying data, and supplemental patient information have been used to promote appropriate prescribing habits, reduce costs, and optimize patient care. While the effects of educational intervention programs are widely reported, little information is available regarding the effectiveness of various mailed intervention techniques.

OBJECTIVE: To review the effectiveness of mailed intervention programs and identify factors that may promote successful outcomes.

METHODS: A literature search was conducted via PubMed for reports of mailed intervention programs published through May 2012. Specific search terms included “drug utilization review,” “drug utilization,” “Medicaid,” “prescribing feedback,” “mailed physician intervention,” and “mailed physician communications.” Identified publications that met the following criteria were selected for inclusion: (a) evaluated printed educational materials disseminated via postal mail, (b) occurred in an outpatient setting, and (c) measured intervention impact on prescribing patterns, health care utilization, or economic outcomes. Publications that met all 3 criteria were abstracted for intervention strategy, follow-up period, data source, intervention target, prescriber acceptance of intervention, and effect on prescribing patterns, health care utilization, and economic outcomes.

RESULTS: A total of 40 published reports regarding 39 unique interventions met inclusion criteria. The majority (34/39 [87.2%]) of studies were conducted in state or federally funded programs; only 5 programs involved private insurers. All programs used follow-up periods of ≤ 12 months after final intervention mailing. A total of 26 of the 39 unique interventions reported a positive impact on at least 1 target outcome. Programs that included a second recipient such as pharmacists ($n=4$) reported a greater impact as compared with interventions mailed to prescribers alone. Programs that provided patient-identifying data had a higher success rate than those that supplied prescriber feedback and/or educational materials (21/25 [84.0%] vs. 5/14 [35.7%]); it should be noted that 2 of the 5 successful programs that provided nonpatient-identifying materials also used academic detailing. Programs that sent education material and/or prescriber feedback pertaining to multiple medication classes or disease states had minimal impact on prescribing patterns ($n=4$). However, targeting 1 specific disease or medication supported by appropriate evidence resulted in favorable change in a short period of time. Additionally, providing recommendations that were supported by widely accepted clinical guidelines or literature were also associated with a high rate of success. A subset of programs that sought to evaluate health care utilization ($n=5$) and economic impact ($n=9$) observed little change in measured outcomes. Evaluation of prescriber response forms conducted by 7 programs revealed that changes

in therapy occurred in approximately 50% of patients with prescribers who intended to accept intervention recommendations.

CONCLUSIONS: Though the degree of heterogeneity between articles prevents provision of definite results, it appears that a well-constructed mailed intervention program has the potential to evoke significant changes in prescribing patterns. Prescribers appear to be receptive to mailed interventions; however, there are limited data to determine the association between acceptance and actual prescribing change. Future research should focus on identifying barriers that may prohibit acceptance of recommendations from translating into changes in therapy. Additionally, future projects should include longer assessment periods to determine the duration of impact following final intervention mailing and potential effect on health care and economic outcomes.

J Manag Care Pharm. 2012;18(8):627-49

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What is already known about this subject

- Retrospective drug utilization review is widely used by third-party payers and required of state Medicaid agencies to ensure the appropriateness of prescription drug use. Mailed letter interventions are often used to alert prescribers of potentially inappropriate prescribing, communicate therapeutic recommendations, and provide notification of potential for adverse effects. Intervention letters are assumed to have a direct effect on treatment of identified patients as well as a “spillover” effect onto other patients under the prescriber’s care.
- Previous publications evaluating the effectiveness of multifaceted interventions have focused heavily on the use of academic detailing or other forms of live educational outreach. Evaluations of mailed intervention programs alone have produced mixed results, and little information is available regarding the comparative effectiveness of various mailed intervention strategies.
- Figueiras et al. (2001) noted interventions that engage prescribers in personal contact (“active intervention”) are more effective than those that provide unsolicited mailed materials (“passive intervention”). The authors concluded that combining active and passive strategies and formulating materials to be personalized to the recipient appeared to be the most effective intervention design.

What this review adds

- This subject review discusses the overall effectiveness of mailed intervention programs published through May 2012 and identifies factors that may contribute to prescriber acceptance.
- Approximately 67% of identified programs reported a successful change in at least 1 measured outcome, including changes in prescribing patterns, health care utilization, and economic effects. Key factors associated with intervention success include (a) provision of patient-identifying data, (b) selection of recipients based on prescribing habits, (c) inclusion of a second intervention recipient, and (d) provision of focused recommendations that can be supported by widely accepted clinical guidelines or literature.
- Recipient response forms generally indicated acceptance of intervention programs. However, many programs reported only 50% of patients with a prescriber who indicated agreement with intervention recommendations had an actual change in therapy upon follow-up review.

Under the Omnibus Budget Reconciliation Act of 1990 (OBRA 90), state Medicaid programs are mandated to conduct drug utilization reviews to ensure beneficiaries are receiving safe and appropriate therapy.¹ Beginning in 1993, state Medicaid agencies were required to conduct retrospective drug utilization reviews on outpatient medications to identify potential overuse or unnecessary medication therapy. Since this time, the use of retrospective drug utilization review has expanded to health maintenance organizations (HMO), Medicare programs, Veterans Administration (VA) medical centers, and various health management programs outside of the United States.²⁻⁷ In addition to promoting safe and effective therapy, retrospective drug utilization review can also be used to coordinate care among physicians, reduce medication costs, and promote changes in prescribing behavior to reflect evidence-based recommendations.⁸⁻¹²

Medication-related concerns identified during retrospective drug utilization reviews may be communicated to prescribers using mailed intervention letters. Materials contained in intervention packets vary among programs, often according to targeted outcomes and/or availability of data, and may include patient-identifying data, prescriber feedback, educational information, and supplemental patient education materials. Although every program appeals to its stakeholders because the purpose of retrospective drug utilization reviews is to provide appropriate therapeutic coverage at the lowest possible costs, external reviewers may be driven by incentives to reduce costs for the parent organization and providing strategies focusing only on short-term savings. In the United States, patient-identifying information (i.e., patient names and/or prescription claims histories) are frequently provided in accordance with the Health Insurance Portability and Accountability

Act (HIPAA)^{2-4,8-25}; provision of such information is uncommon among programs conducted overseas. Programs outside of the United States commonly use prescriber feedback alone or in combination with educational materials to encourage changes in prescribing practices.^{5,6,26-30} Printed materials are often used in combination with academic detailing or other forms of educational outreach to create a multifaceted educational intervention.^{26,31,32}

The impact of educational intervention programs and retrospective drug utilization review has been widely reported in the literature.³³⁻³⁷ Intuitively, we expect that unsolicited printed materials would improve prescribing patterns, but it is difficult to quantify its association to improved clinical outcomes or health care resource costs. Previous systematic reviews reported that passive interventions, such as including unsolicited mailings, are not as effective as active interventions, such as academic detailing.^{34,38-42} No previously published subject reviews have examined the comparative effectiveness of various types of printed materials alone. The purpose of this review is to evaluate the effectiveness of mailed intervention programs that used primarily printed techniques and identify factors that have been associated with successful outcomes.

Methods

A comprehensive PubMed search was conducted in May 2012 using the following search terms: “drug utilization review,” “drug utilization,” “Medicaid,” “prescribing feedback,” “mailed physician interventions,” and “mailed physician communications.” No search limitations were set to include practices outside of the United States, as the purpose of this review was to identify factors that may influence prescribing behaviors. The search strategy is summarized in Figure 1.

Titles and abstracts were screened to identify studies that met the following inclusion criteria: (a) evaluated an educational intervention program in which at least 1 study group received only printed materials disseminated via postal mail, (b) occurred in an outpatient setting, and (c) aimed to measure intervention impact on prescribing patterns, health care utilization, or economic outcomes. After the initial screen, both authors reviewed the objectives and methods of identified articles to ensure each publication fulfilled the screening criteria.

During the full review, programs that exclusively measured impact of interventions mailed to nonprescribing practitioners, such as pharmacists or nurses, were excluded. Programs that specified inclusion of both physician and midlevel prescribers were included. Interventions provided via fax, e-mail, computerized physician reminders, patient chart, or verbal communication were excluded, as the purpose of this review was to evaluate the value of delayed recommendations. Publications that involved, but did not directly evaluate, the impact of a mailed intervention were also excluded. Additionally, the reference lists were manually reviewed for potential publications

FIGURE 1 Summary of Search and Selection Process

that were not identified during the electronic search. A similar review was performed for those identified reports.

Variables of assessment included follow-up period, data source, intervention targets, intervention materials, survey results of prescriber acceptance of the intervention provided, impact on prescribing patterns, impact on health care utilization, and impact on economic outcomes. All results were evaluated from the payer's perspective to determine the impact of direct correspondence-based programs. Throughout this review, the terms "significant" or "significance" was used to indicate a $P < 0.05$.

Results

Articles

A series of 5 PubMed searches using the phrases "drug utilization review," "drug utilization review and Medicaid," "prescribing feedback," "mailed physician communication," and "mailed physician interventions" retrieved 5,138 articles. Of these, 106 articles were considered potentially relevant. Upon further review, several articles were excluded due to duplicate findings ($n=40$) or multiple reports of the same data ($n=3$). Several abstracts ($n=26$) did not provide sufficient details to determine

if the intervention met review inclusion criteria, requiring full publications to be reviewed. An additional 3 articles were identified by reviewing the reference lists of abstracted publications. The literature review yielded a total of 40 published reports that met review criteria.

Study Characteristics

Design, Setting, and Follow-Up Period. Table 1 displays the characteristics of each of the 40 studies included in this review. The majority of the programs used randomized controlled or quasi-experimental designs, and nearly half were conducted in U.S. state Medicaid agencies. Most programs allowed for a null period of 1 month or more to account for letter distribution and incorporation of recommendations. Programs that included letter distribution in the post-intervention follow-up period are noted in Table 1. Follow-up periods were generally ≤ 12 months (36/39 [92.3%]); only 3 programs used extended follow-up periods during which they reported quarterly or bi-yearly results as well as overall impact from baseline to completion.^{3,4,43}

Audience. The majority of interventions were mailed to general

TABLE 1 Study Characteristics

Study	Study Design	Setting	Follow-Up Period (Months)	Intervention Recipients	Data Sources
Allard et al. (2001) ⁴⁷	RCT	Quebec, Canada	12 ^a	Prescribers	Survey responses from patient identified via health care database; prescription history as recorded by home visit nurse; health information obtained from prescribers
Anderson et al. (1996) ²⁶	RCT	British Columbia, Canada	6	Prescribers ^b	Triplicate Prescription Program (monitors prescribing of narcotics and certain anabolic steroids)
Avorn and Soumerai (1983) ³¹	RCT	Arkansas, New Hampshire, Vermont, and District of Columbia Medicaid	9 ^c	Prescribers ^b	Claims database
Bjornson et al. (1990) ⁴⁹	RCT	Minnesota Medicaid	4	Prescribers	Claims database
Coleman et al. (2003) ^{8,46}	QE	Connecticut Medicaid	6	Prescribers & pharmacists	Claims database
Collins et al. (1997) ¹³	QE	Wisconsin Medicaid	6	Prescribers & pharmacists	Claims database
Culbertson et al. (1999) ¹⁴	QE	Idaho Medicaid	6	Prescribers & pharmacists	Claims database
Dormuth et al. (2004) ⁴⁴	Clustered RCT	British Columbia, Canada	3 ^d	Prescribers	Claims database
Fick et al. (2004) ²	Randomized block	U.S. Medicare	6	Prescribers	Claims database
Groves (1985) ¹⁵	Cross-sectional	Florida Medicaid	3 ^e	Prescribers & pharmacists	Claims database
Guo et al. (1995) ⁹	QE	Alabama Medicaid	7	Prescribers	Claims database
Hoffman et al. (2003) ¹⁶	Retrospective cohort	U.S. HMO	6	PCP	Claims database
Hux et al. (1999) ²⁷	RCT	Ontario, Canada	6	Prescribers ^b	Claims database
Jing et al. (2011) ³	QE	Medicare and commercial Health Plan of New York	Physician arm: 21 ^f Patient arm: 12 ^f	PCP & patients	Claims database
Kaufman et al. (2005) ⁴	QE	Medicare and commercial Health Plan of New York	48 ^f	PCP ± prescriber if not the same	Claims database
Lee et al. (2004) ¹⁰	QE	Pennsylvania Medicaid	9	Prescribers	Claims database
Meyer et al. (1991) ¹⁷	RCT	Veterans Affairs Medical Center in Colorado	12	PCP identified as most frequent prescriber	Claims database and medical records database
Naughton et al. (2007) ³²	Clustered randomized trial	Eastern Regional Health Authority in Ireland	6	Prescribers	Claims database
O'Connell et al. (1999) ²⁸	Clustered RCT	Rural Australia	9 ^g	Prescribers	Claims database
Okano and Rascati (1995) ¹⁸	Clustered RCT	Texas Medicaid	6	Prescribers	Claims database
Owens et al. (2008) ⁵⁰	QE	Idaho Medicaid	6	Prescribers	Claims database
Pimlott et al. (2003) ²⁹	RCT	Ontario, Canada	6	Prescribers ^b	Claims database
Raisch and Sleath (1999) ¹⁹	QE	New Mexico Medicaid	3	Prescribers	Claims database
Rascati et al. (1996) ²⁰	Clustered RCT	Texas Medicaid	6	Prescribers	Claims database
Rokstad et al. (1995) ³⁰	QE	Counties of More and Romsdal, Norway	1	Prescribers	Physician recorded report of medications prescribed during patient visits; pharmacy recorded reports of medications written on study-specific prescription pads; administrative recorded reports of physician work hours
Schechtman et al. (1995) ⁴⁵	QE	Washington DC HMO	6	Prescribers	Claims database
Seltzer et al. (2000) ²¹	QE	Texas Medicaid	10	Prescribers	Claims database
Shatin et al. (2005) ⁵¹	Time series analysis	12 health plans affiliated with a U.S. managed health company	10	Prescribers	Claims database
Sleath and Collins (1997) ⁴⁸	QE	New Mexico Medicaid	3	Prescribers	Claims database

TABLE 1 Study Characteristics (*continued*)

Study	Study Design	Setting	Follow-Up Period (Months)	Intervention Recipients	Data Sources
Sleath et al. (1997) ²²	QE	New Mexico Medicaid	12	Prescribers & pharmacists	Claims database
Smith et al. (1997) ²³	Clustered RCT	Washington Medicaid	3	Prescribers or pharmacists if prescriber information was not available	Claims database
Søndergaard et al. (2002) ⁶	RCT	County of Funen, Denmark	12	Prescribers	Pharmacoepidemiologic and billing database
Søndergaard et al. (2003) ⁵	RCT	County of Funen, Denmark	12	Prescribers	Pharmacoepidemiologic and billing database
Starner et al. (2009) ²⁴	QE	Illinois, New Mexico, Oklahoma, Texas Medicare	1 day	Prescribers	Claims database
Vaegter et al. (2010) ⁴³	Time series analysis	Størstrom County, Denmark	84 ^h	Prescribers	Claims database
Woodward et al (2008) ⁷	QE	Australian Department of Veterans Affairs	Polypharmacy arm: 3 Drug interaction arm: 45 days	PCP identified as most frequent prescriber	Claims database
Zimmerman et al. (1994) ¹¹	QE	Wisconsin Medicaid	12	Prescribers	Claims database
Zuckerman et al. (2004) ²⁵	QE	Pennsylvania Medicaid	5	Prescribers	Claims database, meta-analysis by Yusuf et al. (1985) ⁵⁴ used to estimate event probabilities for economic analysis
Zuckerman et al. (2004) ¹²	QE	Pennsylvania Medicaid	6	Prescribers	Claims database

^aLetter distribution occurred throughout entire 12-month post-intervention follow-up period.

^bHigh-prescribing physicians.

^cIncluded 4 months for letter distribution.

^dPost-intervention period was 8 weeks for one 2-part mailing that was treated as a single intervention.

^eProfiles were reevaluated 3 months after intervention mailing. If an acceptable prescriber response or change in therapy has not occurred, the case is followed until a satisfactory outcome is achieved.

^fQuarterly evaluation throughout entire post-intervention follow-up period.

^gTwo 3-month post-intervention follow-up periods measured 3 months apart.

^hEvaluated every 6 months throughout entire post-intervention follow-up period.

HMO=health maintenance organization; PCP=primary care physicians; QE=quasi-experimental; RCT=randomized controlled trial.

physicians rather than specialists; few interventions specified inclusion of prescribers to include midlevel practitioners, such as nurse practitioners or physician assistants, as permitted by the practice law in the area. Interventions were most commonly sent exclusively to prescribers involved in the care of a patient who had received a target medication (32/39 [82.1%]). Five programs included the primary care provider as an intervention recipient regardless if they had prescribed the target medication,^{3,4,7,16,17} and 4 targeted those identified as “high-prescribers” based on a program-specified standard or in comparison to peers.^{26,27,29,31} Hux et al. (1999)²⁷ and Pimlott et al. (2003)²⁹ selected prescribers who had written ≥10 prescriptions for a target medication in a 2-month period, while Anderson et al. (1996)²⁶ selected those who had written excessively for target agents relative to the overall prescribing population. Programs (n=8) that selected prescribers based on geographic location rather than prescribing behavior were found to have little to no

impact on prescribing patterns.^{5,6,28,30,32,43-45}

In addition to targeting prescribers, several programs (n=6) also sent correspondence to pharmacies involved in the care of identified patients.^{8,13-15,22,23,46} Jing et al. (2011) was the only identified program that included both prescribers and patients as intervention recipients.³ Six of the 7 aforementioned programs concluded that inclusion of a second recipient to be more effective at achieving the targeted outcome as compared with prescriber recipients alone. Culbertson et al. (1999) was the only program to note no difference in effect when the same intervention material was sent to physicians and pharmacists as compared with physicians alone.¹⁴

Data Source. Despite known limitations, the majority of identified programs used prescription and medical claims databases to obtain medication use and diagnostic histories. Groves (1985) used a combination of computerized alert tools to identify patients with potentially inappropriate medications

followed by an audit by clinical pharmacists.¹⁵ Two (5.1%) programs utilized patient- or practitioner-reported information as a primary data source. After identifying patients from a government-supported health care database, Allard et al. (2001) utilized patient- and prescriber-reported medication and health information.⁴⁷ Rokstad et al. (1995) obtained information through physician recordings of medications prescribed, pharmacy reportings of medications prescribed on study-specific prescription pads, and physician staff recordings of physician work hours.³⁰ The use of multiple strategies may improve patient identification but did not always translate to improved prescribing patterns.

Intervention Strategies

Most programs (34/39 [87.2%]) evaluated change as compared with pre-intervention prescribing behavior or in comparison with a control group who received no intervention materials. Of these, 14 were randomized controlled trials. Ten programs compared changes in prescribing behavior between multiple intervention strategies. Fick et al. (2004) demonstrated that providing patient-identifying intervention material along with a list of alternative medications was more effective than mailed educational material alone.² Meyer et al. (1991) found no difference among a patient-identifying intervention that provided general or specific recommendations.¹⁷ Both studies took precautions to avoid cross-contamination of the intervention groups. Additionally, no difference was found among interventions that provided various forms of nonpatient-identifying information, such as educational material or prescriber feedback.^{5,6,45} Combining nonpatient-identifying intervention materials with academic detailing produced mixed results.^{26,31,32} Table 2 describes the association between mailed intervention and change in prescribing as reported in each study included in this review.

Target Medications. Focusing an intervention on specific medications appears to be a successful means of impacting prescribing behavior. Okano and Rascati (1995)¹⁸ and Raisch and Sleath (1999)¹⁹ used similar intervention techniques to address inappropriate prescribing of antiulcer agents. Okano and Rascati focused the intervention on a single target and successfully reduced the use of dual antiulcer therapy.¹⁸ When Raisch and Sleath expanded target criteria to include long-term and high-dose therapies without an appropriate diagnosis, no impact was seen on the use of dual antiulcer therapy.¹⁹ Three programs that targeted an extensive list of unrelated medications and/or disease states had minimal impact on prescribing behavior.^{28,43,44} The exception to using broad targets is Groves, who successfully used patient-specific recommendations to evoke change in prescribing among patients identified as at-risk for drug-related adverse effects.¹⁵

Several authors noted that it may be difficult to prompt

discontinuation of agents that have been used on a long-term basis; this may be particularly true for sedative hypnotics.^{13,24,29,48} One report found that patient demand deterred 26% of prescribers from intervening on long-term use of sedative agents.⁴⁸ Additionally, both prescribers and patients may have a decreased perception of potential harm associated with agents that have been used on a long-term basis.²⁹ Aside from the potential impact of chronic use, there appeared to be no difference in success rates between interventions that recommended initiation or discontinuation of a medication.

Intervention Materials. Provision of patient-identifying information appears to be a major factor contributing to the success of an intervention. Patient-identifying material ranged from simply identifying a patient by name to providing detailed prescription and medical claims histories or medication adherence reports. Twenty-one of the 25 programs that provided some form of patient-identifying data were considered to have a significant impact on prescribing.^{2-4,7-16,18-23,25,48} It should be noted that Meyer et al. considered their patient-identifying intervention to be unsuccessful because changes in prescribing patterns were no longer significant at 6 and 12 months post-intervention.¹⁷ Though Bjornson et al. (1990) provided patient-identifying data, the data differed from each of the successful interventions—instead of providing information regarding all eligible patients, they included a medication history profile for one patient under each physician's care and monitored for prescribing changes within that single identified profile.⁴⁹

Most programs that used patient-identifying data opted to make generalized recommendations that could be applicable to their entire target population.^{2-4,7-14,16,18-25,48,49} For example, the intervention conducted by Zuckerman et al. (2004) alerted physicians of the identified patient's potential for acetaminophen overuse, discussed the associated risks, and suggested adjusting therapy to meet recommended daily standards.¹² Such a method appears to be an effective intervention tactic, as 20 of 22 programs (90.1%) that provided this type of recommendation were successful. Programs that provided exclusively patient-specific recommendations often enlisted a team of physicians and pharmacists who carefully reviewed profiles and developed customized therapeutic suggestions.^{15,47} Kaufman et al. (2005) was unique in that they provided a telephone follow-up to the subset of physicians identified as the highest volume prescribers during which they offered patient specific recommendations.⁴ Only 1 program sought to compare the impact of such interventions and found no difference between generalized versus patient-specific recommendations.¹⁷

Several programs measured the impact of incorporating academic outreach into a mailed intervention.^{4,26,31,32} In this review, all direct, nonmailed communications were classified as academic outreach and included live group education, individual visits from academic detailers, and telephone

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Allard et al. (2001) ⁴⁷	PIP per Quebec Committee on Drug Use in the Elderly ⁵⁵	Patients >75 years with >3 unique medications divided into intervention (n = 136) and control (n = 130). Intervention patient profiles reviewed by team of 2 physicians, 1 pharmacist, and 1 nurse. Recommendations and supporting references were mailed to prescribers on behalf of 80 patients.	Mean number [SD] of PIP per patient decreased by 0.24 [0.69] in intervention and 0.15 [0.52] in control (P = NS as compared with baseline and <0.001 as compared with control). Number of patients with ≥1 PIP decreased 18 (14.2%) in intervention and 8 (6.9) in control (P = NS as compared with baseline and 0.049 as compared with control). No difference in number of different medications or global assessment of medication use between groups.
Anderson et al. (1996) ²⁶	Narcotics and other analgesics, narcotic antitussives, certain anabolic steroids	Physicians (n = 18) received mailed notification that they had been identified as a high prescriber of regulated analgesics relative to peers. Physicians (n = 18) received mailed notification and attended an educational workshop. Physicians (n = 18) served as a control group.	Mean number [SD] of prescriptions issued per physician decreased by 29.2 [32.1] (25% reduction) in mailed intervention alone and by 33.4 [37.3] (33% reduction) in mailed intervention + education. (P < 0.01 for both as compared to control and NS between groups). 3.8 (3%) increase in number of prescriptions issued observed in control.
Avorn and Soumerai (1983) ³¹	Cerebral and peripheral vasodilators, cephalixin, propoxyphene	Physicians (n = 132) received a cover letter followed by a series of 3 educational bulletins without literary or visual appeal alone (n = 66) or in addition to a series of 6 visually and literary appealing educational “unadvertisements” and supplemental patient education material (n = 66). Physicians (n = 141) received academic detailing in addition to all print materials. Physicians (n = 140) served as a control group.	Mailed only prescribed an average of 251 fewer units of target drugs as compared with control (P = NS) and mailed + academic detailing prescribed an average of 782 fewer units as compared with control (P < 0.001). No differences observed for various forms of mailed materials alone.
Bjornson et al. (1990) ⁴⁹	Hydralazine, isosorbide dinitrate, prazosin	Physicians (n = 288) received a cover letter, published clinical trial on pharmacologic management of congestive heart failure, a patient medication history profile, and response form. Physicians (n = 288) served as a control group.	In both groups, 5 (0.9%) physicians prescribed a full change in therapy for the identified patients, and 23 (4%) prescribed a partial change in therapy for the identified patients (P = NS for both and combined effect).
Coleman et al. (2003) ⁸	SABA, inhaled corticosteroids, leukotriene modifiers, mast-cell stabilizers, oral corticosteroids, long-acting beta2-agonists	Prescribers and pharmacies of patients (n = 35) identified as high dose SABA users received a cover letter, patient medication profile, and an educational insert. Patients identified as normal dose SABA users (n = 510) served as a comparison group.	46% of patients in the intervention group were no longer considered high-dose SABA users (P < 0.001). Prior to the intervention, fewer intervention patients received ≥1 long-term controller agent (78 [58%] vs. 491 [96%] for intervention and comparison, respectively; P < 0.001); no difference between groups following intervention (87 [65%] vs. 360 [71%], respectively; P = NS). No pre-post difference in intervention for any target long-term controller agent (P = NS). Prior to intervention, more patients in the intervention group had claims for office visits (P < 0.001). No difference between groups following intervention (P = NS) and a within-group decreases in both intervention and comparison groups (P < 0.05). Prior to the intervention, more patients in the comparison group had claims for physician services (P < 0.001). No difference between groups following intervention (P = NS) within-group decrease in comparison group (P < 0.05). No between or within group differences for hospital visits, emergency department visits, or hospitalized days.

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (*continued*)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Collins et al. (1997) ¹³	Dipyridamole and related agents (defined as aspirin, sulfinpyrazone, and ticlopidine)	Intervention packet contained letter identifying potential dipyridamole problem, reference information on dipyridamole use, list of patient names seen by the physician and/or pharmacist, and patient dipyridamole drug use histories. Physicians alone (n = 203) received intervention for long-term care (n = 181) and ambulatory (n = 99) patients. Pharmacists alone (n = 157) received intervention for long-term care (n = 149) and ambulatory (n = 132) patients. Physicians (n = 182) + pharmacists (n = 147) received intervention for long-term care (n = 91) and ambulatory (n = 120) patients. Long-term care (n = 342) and ambulatory (n = 235) patients served as a control group.	42 (46.2%) long-term care (OR: 2.10; $P < 0.025$) and 47 (39.2%) ambulatory patients (OR: 3.81; $P < 0.025$) in the physician-pharmacist group had no claim for dipyridamole. 57 (31.5%) long-term care (OR: 1.31; $P = \text{NS}$) and 30 (30.3%) ambulatory patients (OR: 2.22; $P < 0.025$) in physician-only group had no claim for dipyridamole. 37 (24.8%) long-term care (OR: 0.92) and 30 (22.7%) ambulatory patients (OR: 1.67) in pharmacist only group had no claim for dipyridamole ($P = \text{NS}$ for both). 87 (25.4%) long-term care and 36 (15.3%) ambulatory patients in control group had no claim for dipyridamole.
Culbertson et al. (1999) ¹⁴	Cimetidine, famotidine, lansoprazole, nizatidine, omeprazole, ranitidine, sucralfate	Intervention packets which contained a cover letter, educational material, medication profiles of patient identified as receiving potentially inappropriate antiulcer therapy, and a response form were sent to physicians and/or pharmacies. Physicians (n = 113) received intervention regarding 138 patients. Physicians (n = 187) + pharmacies (n = 79) received intervention regarding 329 patients. Physicians (n = 158) + pharmacies (n = 60) received intervention and follow-up calls regarding 248 patients.	12.4% decrease in dose ^a in physician alone, 8.0% decrease in physicians + pharmacists, 14.0% decrease in physicians + pharmacists + follow-up call: 14.0% decrease ($P < 0.01$ for all). Percent change greater in physician + pharmacist + follow-up call as compared with physician + pharmacist ($P < 0.05$) but not physician alone ($P = \text{NS}$).
Dormuth et al. (2004) ⁴⁴	Cimetidine, metronidazole/(amoxicillin or tetracycline), aspirin/ibuprofen/naproxen, isosorbide dinitrate, thiazide diuretics, inhaled corticosteroids, CCB, long-acting BDZ, hormones, clonazepam/alprazolam, diazepam, finasteride	Physicians (n = 258) received a series of educational bulletins that provided a clear recommendation for prescribing each target medication or class. Physicians (n = 241) received the educational bulletin 3-8 months later with the exception of a 2-part series that was mailed after 8 weeks and served as a control group.	Trends in prescribing of target medication to newly treated patients proceeded in direction suggested by mailing 1.3 times more likely in intervention group (95% CI 1.13-1.52). No single letter was associated with a significant impact on prescribing behavior.
Fick et al. (2004) ²	1997 Beers criteria list of agents to avoid in older adults ⁵⁶	All in-network PCPs (n = 355) received mailed educational material and a copy of the 1997 Beers criteria. ⁵⁶ 3 months later, physicians (n = 170) received a personally addressed letter listing patients > 65 years who received ≥ 1 PIP as well as a detailed educational brochure. Intervention packets were sent quarterly for 12 months. Physicians who had not written a PIP received acknowledgement. Physicians (n = 185) served as a control group.	Number of patients who received ≥ 1 PIP decreased from 3,364 (19.4%) at baseline to 3,007 (17.9%) ($P < 0.001$).

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (continued)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Groves (1985) ¹⁵	NSAIDs, tricyclic antidepressants, antipsychotic tranquilizers, antihypertensive and diuretics, antidiabetic agents, cardiac agents	Computer-generated medical history profiles identified patients at risk for drug interactions, adverse reactions, and potential overuse/underuse of medications. A team of 4 pharmacists and 1 physician conducted monthly reviews of identified profiles to determine if a intervention was necessary. If warranted, a patient-specific letter describing the problem was mailed to the prescribing physician, diagnosing physician, and dispensing pharmacist. The review committee followed up on each case until a satisfactory outcome was reached.	After 9 months, 443 (54%) of cases were considered resolved (as defined by a change in therapy or receipt of an acceptable prescriber explanation for continuation in therapy).
Guo et al. (1995) ⁹	Nizatidine, sucralfate, famotidine, omeprazole, ranitidine, cimetidine	Prescribers (n = 118) were sent a cover letter, profile of patient identified as receiving potentially inappropriate antiulcer therapy, and a comment form. Prescribers (n = 3776) who did not prescribe potentially inappropriate antiulcer therapy served as a comparison group.	Significant downward trend in days of therapy ^b throughout follow-up period ($P = 0.038$). Decrease in days of therapy ^b significant in fifth month of 8-month follow-up period ($P < 0.05$). No significant changes noted in other individual months.
Hoffman et al. (2003) ¹⁶	Medications with high-abuse potential (not specified)	PCPs of patients (n = 94) that triggered ≥ 3 categories of abuse potential alerts within 1 calendar quarter received a prescription profile for each identified patient and a letter that recommended reevaluation of the patient's medication use. Patients (n = 89) triggering 1-2 abuse potential alerts within 1 calendar quarter served as a matched comparison group.	Mean number [SD] of high-abuse prescription claims per patient per month decreased by 3.06 [4.61] in intervention and 1.96 [2.64] in comparison ($P < 0.05$). Mean number [SD] of prescribers per patient decreased by 2.2 [3.26] in intervention and 1.36 [2.43] in comparison ($P < 0.05$). Mean number [SD] of prescription claims per member per month decreased by 4.97 [4.43] in intervention and 3.72 [4.68] in comparison ($P = \text{NS}$).
Hux et al. (1999) ²⁷	Pencillins, macrolides, trimethoprim-sulfamethaxazole, tetracycline, first-generation cephalosporins, ciprofloxacin, norfloxacin, cefaclor, others (not specified)	Physicians (n = 134) received prescriber feedback displaying individual and peer antibiotic prescribing patterns as well as guideline-based educational materials every 2 months for 6 months. Physicians (n = 116) received prescribing profiles on 1 occasion after the completion of feedback in the intervention and served as a control group.	Proportion of first-line antibiotics use increased by 2.6% in intervention and decreased by 1.7% in control ($P < 0.01$).
Jing et al. (2011) ³	Miscellaneous antidiabetic and antihypertensive agents	Quarterly letters and medication profiles were sent to PCPs of potentially nonadherent patients. After 4 quarters, supplemental educational material was also mailed to patients.	Prescribers alone: number of potentially nonadherent patients decreased from 10,722 (35.6%) at baseline to 9,701 (30.8%) over 3 calendar quarters ($P < 0.001$). Prescribers + patients: number of potentially nonadherent patients decreased from 9,701 (30.8%) at baseline to 9,086 (27.7%) over 4 calendar quarters ($P < 0.001$).
Kaufman et al. (2005) ⁴	Quarters 1-9: amitriptyline, cyclobenzaprine, diazepam, indomethacin, meprobamate, methocarbamol, methylodopa, propoxyphene Quarters 10-16: amitriptyline, cyclobenzaprine, diazepam, dicyclomine, disopyramide, hyoscyamine, indomethacin, meprobamate, methocarbamol, methylodopa	Physicians received quarterly intervention packets that contained a cover letter, list of patients >65 years who received a PIP, name of PIP received, and a list of formulary alternatives. Each quarter, a clinical pharmacist contacted the highest volume prescribers via telephone to offer recommendations. All in-network providers and pharmacists received mailed educational information.	Number of patients who filled ≥ 1 PIP decreased from 2,871 (5.3%) to 1,451 (2.2%) ($P < 0.001$). Number of patients who received ≥ 1 of the 7 agents that were targets throughout the entire intervention decreased from 1,398 (2.6%) to 390 (0.6%) ($P < 0.001$).

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (*continued*)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Lee et al. (2004) ¹⁰	SABA, salmeterol	Physicians (n=564) received a list of pediatric (5-18 years) patients with potentially inappropriate SABA (n=382) or salmeterol (n=35) use, patient-specific prescription and medical claims data, and a patient diary. 3 months post-intervention, a monograph that provided continuing medical education credits was sent to all physicians likely to treat pediatric asthma.	Among high-dose SABA users, use of SABA metered-dose inhaler decreased by 26.3% ($P<0.001$); no change among other dosage forms ($P=NS$). Use of mast-cell stabilizer metered-dose inhaler decreased by 36.9% and use of leukotriene modifiers increased by 36.6% ($P<0.05$ for all); no change among asthma controller agents. No change in emergency department visits or hospitalizations from baseline ($P=NS$). 18 (82%) of salmeterol-only recipients discontinued use or received a SABA.
Meyer et al. (1991) ¹⁷	All medications excluding topical, ocular, and medical supplies	Prescribers received simple intervention on behalf of patients (n=102) with ≥ 10 active prescriptions that consisted of a list of identified patients and a request to reduce number of medications. Prescribers received an intensive intervention on behalf of patients (n=104) that consisted of simple intervention material plus patient-specific recommendations for reducing polypharmacy and an estimate of patient's compliance with the drug regimen. Patients (n=88) served as a control group.	The number of medications was reduced in all groups at 4, 6, and 12 months in all groups ($P=0.001$). The combined effect of the two intervention was significant at 4 months ($P=0.03$), but not at 6 or 12 months ($P>NS$). No difference was observed between the simple and intensive intervention ($P=NS$).
Naughton et al. (2007) ³²	Antiplatelet agents, HMG-CoA reductase inhibitors	Prescribers (n=50) received feedback displaying number of CVD and diabetic patients not receiving recommended statin and antiplatelet therapy along with an educational bulletin aimed to improve appropriate prescribing. Prescribers (n=48) received academic detailing in addition to all mailed materials.	3% increase in statin use and 1% increase in anticoagulant use among CVD patients both groups (between group $P=NS$). 5% increase statin use in mailed only and 4% increase in mailed + academic detailing among diabetic patients (between group $P=NS$). 3% increase in anticoagulant use in mailed only and 2% increase in mailed + academic detailing among diabetic patients (between group $P=NS$).
O'Connell et al. (1999) ²⁸	ACE inhibitors, antilipidemic agents, H2RA, NSAIDs, and oral antibiotics	Prescribers (n=1,294) received 2 intervention packets 6 months apart that contained prescriber feedback displaying individual and peer prescribing rates. The first intervention included an educational newsletter on general prescribing issues and the second included information on antibiotic prescribing. Prescribers (n=1,146) served as a control group.	No significant differences were observed in prescribing patterns of any individual class of medications ($P=NS$). For all target agents, prescribing rates per 100 Medicare services per month increased from 77.7 to 79.2 in intervention and decreased from 77.8 to 77.6 in control ($P=NS$).
Okano and Rascati (1995) ¹⁸	Cimetidine, famotidine, nizatidine, ranitidine, omeprazole, sucralfate	Physicians (n=97) received intervention packets regarding patients (n=117) who received duplicate antiulcer therapy. Packets contained a letter stating there is no evidence supporting concurrent use of an H2RA or omeprazole with sucralfate and a profile for each identified patient. Patients (n=105; n=93 physicians) served as a control group.	55 (57.9%) of patients in the intervention group continued to receive concurrent therapy as compared with 73 (75.3%) in the control group ($P=0.011$).
Owens et al. (2008) ⁵⁰	Oral triptans, amitriptyline, atenolol, divalproex sodium, metoprolol, propranolol, timolol, topiramate, gabapentin, verapamil	Prescribers of patients (n=154) identified as potential candidates for prophylactic migraine therapy received a cover letter describing the program, an educational leaflet, and a response form.	27 (24.8%) patients received a claim for a prophylactic agent. 91 (83.5%) patients had ≥ 1 office visit.

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (continued)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Pimlott et al. (2003) ²⁹	Long- and short-acting BDZ	Physicians (n=168) received prescriber feedback displaying individual prescribing of BDZ to patients >65 years as compared with peers and "best practice standards" as well as educational information every 2 months for 6 months. Physicians (n=206) received similar packets on an unrelated topic and served as a control.	1.8 (0.7%) decrease in mean number of long-acting BDZ in intervention increase of 1.3 (1.1%) in control (P=0.036). 1.6 decrease in mean number of all BDZ prescriptions in intervention and increase of 5.8 control (P=NS). No difference in concurrent prescribing of BDZ and other psychoactive agents (P=NS).
Raisch and Sleath (1999) ¹⁹	H2RAs, sucralfate, other antiulcer agents (not specified)	Prescribers with ≥3 patients (n=381) identified as recipients of potentially inappropriate antiulcer therapy received a cover letter describing the program, profiles of identified patients, and educational material. Half of the prescribers with 1-2 identified received the intervention (n=143 prescribers regarding 156 patients) and half served as a control comparison group (n=137 prescribers regarding 156 patients).	52 (33.3%) intervention and 28 (17.9%) control patients did not receive an antiulcer agent (P<0.01). 8 (24.2%) of intervention and 6 (23.1%) control patients had improvements in use of duplicate therapy (P=NS). 11 (9.8%) intervention and 0 (0%) control patients had improvements in use without diagnosis (P<0.01). 52 (47.3%) intervention and 24 (24%) control patients had improvements in use of acute dose without diagnostic justification (P<0.001).
Rascati et al. (1996) ²⁰	cimetidine, famotidine, nizatidine, ranitidine, omeprazole, sucralfate	Intervention packets that contained a letter stating that literature does not support use of duplicate antiulcer therapy and profiles of identified patients (n=174) were sent to prescribers (n=184). Patients (n=161) served as a control group.	61 (47.7%) intervention and 85 (64.4%) control patients continued to receive duplicate therapy (P=0.007).
Rokstad et al. (1995) ³⁰	BDZ, barbiturates, antihistamines, trimethoprim, sulfonamides, trimethoprim-sulfa, extended spectrum penicillins, nitrofurantoin	Physicians (n=51) received prescriber feedback displaying individual and peer prescribing rates of target medications as well as expert recommendations treatment of insomnia and acute cystitis. Physicians (n=60) served as a control group.	Decrease in mean number of defined daily dose ^c for short-, medium-, and long-acting BDZ, BDZ tranquilizers, barbiturates, and increased use of antihistamines and antidepressants in intervention group (P<0.05 for all). No change in number of prescriptions for insomnia agents (P=NS). Decrease in mean number of defined daily dose ^c for sulphonamides in intervention group (P<0.05). No change for other antibiotics (P=NS). Increased number of prescriptions for trimethoprim, decrease in number of prescriptions for trimethoprim-sulfa in intervention group (P<0.05).
Schectman et al. (1995) ⁴⁵	Cimetidine	Physicians (n=63) received an educational memorandum followed by a "reminder memo" alone or in addition to prescriber feedback displaying individual H2RA prescribing patterns. Physicians (n=12) were excluded from the intervention and used to check for secular trends.	Proportion of new cimetidine prescriptions increased from 21% at baseline to 30% (P<0.001) in intervention and decreased from 21.6% to 17.6% in excluded group (P=NS). No difference between mailed education + feedback and mailed education alone (P=NS).
Seltzer et al. (2000) ²¹	BDZ, barbiturates, acetylcholinesterase inhibitors, chloral hydrate, ethchlorvynol, ethinamate, glutethimide, methyp-rylon, paraldehyde, zolpidem	Physicians (n=291) with patients (n=244) identified as receiving potentially excessive sedative hypnotic therapy received a patient-identifying letter that described guidelines for sedative hypnotic use.	37 (47.4%) patients with responding prescribers who indicated an intent to modify therapy no longer had claims for sedative/hypnotics.
Shatin et al. (2005) ⁵¹	Tramadol, selective serotonin reuptake inhibitors, tricyclic antidepressants	A single Dear Health Professional letter regarding co-prescribing of tramadol and antidepressants was sent to prescribers.	Number of patients with a claim for an antidepressant within 30 days of a first tramadol prescription claim decreased from 1,061 (22.2%) pre-intervention to 844 (19.0%) post-intervention (P=NS).

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (*continued*)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Sleath et al. (1997) ²²	Sedatives (not specified)	Physicians (n=211) received educational information and prescription and medical profiles for patients (n=269) identified as recipients of long-term sedative therapy.	49% of patients with physicians who responded to intervention with intent to change therapy had a change in therapy. 40% of patients with physicians who responded to intervention with no intent to change therapy had a change in therapy. 35% of patients with a physician who did not respond to intervention had a change in therapy.
Smith et al. (1998) ²³	Triazolam, temazepam, estazolam, quazepam, flurazepam Nontarget alternative medications: other BDZ (i.e. diazepam), barbiturates, chloral hydrate	Physicians and/or pharmacists involved in the care of patients (n=99) identified as recipients of long-term sedative hypnotic therapy received a cover letter, guidelines for sedative hypnotic use, patient profiles, and prescriber feedback displaying individual and peer prescribing rates of target agents (pharmacists did not receive prescriber feedback). Patients (n=89) served as a control group.	Mean dose ^d decreased by 8.1 (27.6%) in intervention and 2.4 (8.5%) control (P=0.04). Mean number of prescriptions decreased by 0.9 (26.5%) in intervention and 0.1 (2.9%) in control (P=0.004). Mean number of tablets per prescription decreased by 5.5 (13.4%) in intervention and 2.9 (7.2%) in control (P=NS). 11 intervention and 4 control patients discontinued therapy with a target agent (P=NS). More patients in the intervention group began using sedating antihistamines as compared with control (6 [6.8%] vs. 1 [1.3%]; P=0.08) and nontarget benzodiazepines (8 [9.4%] vs. 0 [0%]; P=0.01).
Søndergaard et al. (2002) ⁶	SABA, inhaled corticosteroids	Physicians received asthma management guidelines and prescriber feedback displaying number of patients using various amounts of SABA and inhaled corticosteroids (n=77) or number of patients who received a SABA as compared to other area practices (n=74). Physicians (n=141) received information on an unrelated topic and served as a control group. All groups received 3 interventions, sent 3 months apart.	Neither patient count data (HR=0.77; P=NS) nor aggregate feedback (HR=0.79; P=NS) had an impact on prescribing inhaled corticosteroids to repeat SABA users. Neither patient count data (HR=0.108; P=NS) nor aggregate feedback (HR=0.92; P=NS) had an impact on prescribing inhaled corticosteroids to first-time SABA users.
Søndergaard et al. (2003) ⁵	Narrow spectrum penicillin (penicillin V), broad spectrum penicillins, macrolides, fluoroquinolones	Physicians (n=155) received educational material on diagnosis and treatment of upper respiratory infections and prescriber feedback displaying individual prescribing rates of antibiotics as compared with peers. Physicians (n=144) received mailed educational material alone and served as a control group.	0.6% decrease in prescribing rate of all antibiotics in intervention as compared with control (P=NS). 0.02% increase in fraction of narrow-spectrum penicillin prescriptions in intervention as compared with control (P=NS).
Starner et al. (2009) ²⁴	Determined according to National Committee for Quality Assurance list of drugs to avoid in elderly	7,963 intervention letters alerting physicians of PIP received by patients (n=13,198) ≥65 years.	5,403 (48.8%) target medications claims were defined as discontinued.
Vaegter et al. (2010) ⁴³	Antacids, anti-diabetic drugs, cardiac disease drugs, diuretics, beta-blockers, CCB, sex hormones, antibiotics, NSAIDs, analgesics, neuroleptics, antidepressants, asthma management agents	Physicians (n=166) received prescriber feedback displaying individual prescribing rates and prescribing percentile as compared with other practices for each of the 13 target classes. Feedback was sent every 6 months for 7 years.	Little variance was observed among prescribing rates within practices, and large variations were noted between practices. Overall, intervention had no impact on prescribing patterns.

TABLE 2 Association Between Mailed Intervention, Prescribing Patterns, and Health Care Utilization (*continued*)

Study	Target Medications	Program Description and Intervention Materials	Effects of Mailed Intervention on Prescribing Behavior
Woodward et al. (2008) ⁷	Polypharmacy: all medications Drug interaction: all medications excluding those used on a short-term basis	Prescribers of patients (n=81) identified as receiving polypharmacy or a potential drug interaction (n=836) received a cover letter, patient profile, and practice guidelines.	Mean reduction of 2.2 unique medications and 4.67 claims per polypharmacy patient ($P<0.05$ for both). Mean reduction of 0.73 drug interaction pairs per patient ($P<0.001$).
Zimmerman et al. (1994) ¹¹	H2RA	Prescribers with >3 patients (n=195 long-term care; n=244 ambulatory) identified as recipients of high-dose long-term H2RA therapy received a cover letter stating concerns, journal references, a list of identified patients, and H2RA history profile for each identified patient. Prescribers with 3 identified patients (n=538 long-term care; n=1,202 ambulatory) served as a comparison group.	No difference in mean [SD] monthly H2RA dose ^a months post-intervention as compared with comparison in long-term care (15,575 [12,518] vs. 16,722 [9,957]) or ambulatory (17,133 [10,801] vs. 18,685 [11,340]) patients ($P=NS$ for both). Percent change greater in long-term care intervention at 6 months (40.2% vs. 31.8%; $P<0.05$) but not over 12-month post-intervention period (41.6% vs. 35.8%; $P=NS$). Percent change over 12-month post-intervention period greater in intervention than control (36.8% vs. 27.7%; $P<0.01$). No change in hospitalization rates for ulcer recurrence or gastrointestinal bleeding from baseline in either population ($P=NS$).
Zuckerman et al. (2004) ²⁵	Beta-blockers	Prescribers (n=157) received a cover letter, an educational newsletter offering continuing medical education credits, a list of post-AMI patients who were potentially nonadherent to beta-blocker therapy, and profiles for each identified patient. Prescribers (n=328) received mailed intervention packets regarding post-AMI patients without a claim for a beta-blocker. Prescribers (n=10,972) expected to treat post-AMI patients (excluding cardiologists) received the educational newsletter.	Beta-blocker use after 7 days increased from 46.4% to 49.6% and from 61.3% to 64.7% after 30 days ($P=NS$). Mailed intervention was associated with increased likelihood of being prescribed a beta-blocker by 16% ($P<0.01$). Percent of patients with beta-blocker adherence $\geq 80\%$ increased from 64.1% to 69.4% ($P=0.02$).
Zuckerman et al. (2004) ¹²	Acetaminophen	Physicians (n=833) received intervention concerning patients (n=624) identified as high-dose acetaminophen users. Packets contained a personalized cover letter, patient medication profiles, a list of prescription and nonprescription medications that contain acetaminophen, and a medication reconciliation form for patients. Patients (n=590) identified as high-dose users identified during a previous period composed a historical control group. In addition acetaminophen use was also compared with the entire Medicaid population.	Mean number of acetaminophen claims per patient decreased from 13.3 to 9.3 for high-dose users. ($P<0.001$). This was an average of 1 claim decline more than historical control group ($P=0.04$). Mean daily acetaminophen dose per patient decreased from 4.62 grams to 3.23 grams for high-dose users ($P<0.001$). Similar decline noted in historical control group ($P=NS$). Percent of patients with ≥ 2 acetaminophen claims decreased from 65.0% to 32.5% for high dose users ($P<0.001$). Similar decline noted in historical control group ($P=NS$). During the same period, there was a 9% decline in the proportion of high-dose acetaminophen uses among the entire Medicaid population and no difference in the number of claims or average daily dose.

^aAs measured by standardized normal therapeutic equivalent: ratio of total dose per 30 days to published compendia standards for usual daily dose for 30 days.

^bAs measured by real marginal value. Real marginal value was used to control for seasonal variations in use. Real marginal value = mean value in comparison population—each individual's mean value.

^cDefined daily dose: assumed average daily dose for primary indication.

^dAs measured in triazolam milligram equivalents.

^eAs measured in cimetidine milligram equivalents.

ACE=angiotensin-converting-enzyme; AMI=acute myocardial infarction; BDZ=benzodiazepines; CCB=calcium channel blockers; CI=confidence interval; CVD=cardiovascular disease; H2RA=histamine H2 receptor antagonists; HMG-CoA=3-hydroxy-3-methyl-glutaryl-CoA; HR=hazard ratio; NS=nonsignificant; NSAIDS=non-steroidal anti-inflammatory drugs; OR=odds ratio; PCP=primary care provider; PIP=potentially inappropriate prescribing; SABA=short-acting beta2-agonist; SD=standard deviation.

conferences. The potential benefit of academic outreach in addition to a mailed intervention is controversial; Avorn and Somerai (1983)³¹ noted added improvement among recipients who received outreach visits, while Anderson et al.²⁶ and Naughton et al. (2007)³² reported no added benefits.

A smaller subset of programs (n=10) provided prescriber feedback in lieu of patient-identifying data.^{5,6,26-30,32,43,45} Typically, feedback displayed individual prescribing patterns relative to that of peer prescribers. Pimlott et al. (2003) also provided a comparison to "best practice standards."²⁹ Schectman et al. (1995) was the only program that did not provide comparative data, as the authors believed the overall low volume of cimetidine use would discourage rather than encourage prescribing.⁴⁵

The impact of providing prescriber feedback alone appears to be minimal.^{6,43} Søndergaard et al. (2002) found neither feedback presented as patient count data or in the form of a comparative aggregate graph had an impact on prescribing patterns.⁶ Even when combined with educational material or academic detailing, the impact is questionable: Of the 9 programs^{5,23,26-30,32,45} that used prescriber feedback in combination with other techniques, 4 reported minimal to no improvements in prescribing patterns.^{5,28,29,32} Additionally, each of the 4 programs that provided educational materials alone were found to have little to no impact on measured outcomes.^{24,44,50,51} It should be noted that one program that reported positive outcomes used prescriber feedback in combination with patient-identifying data and educational material.²³

Along with providing educational material for prescribers, several programs also included supplemental educational material for patients.^{3,10,12,22,29,31} With the exception of Jing et al.³ (who mailed material directly to patients), supplemental patient material was supplied as part of the prescriber's intervention packet. Patient-targeted materials ranged from tips regarding medication use and/or disease-state management to fill-in-the-blank sheets for monitoring symptoms and medication reconciliation. Providing patient education material appears to contribute to intervention success, since the majority of programs that provided patient education materials were associated with significant improvements in prescribing behavior.^{3,10,12,22}

Frequency of intervention mailings appears to be a secondary factor of importance relative to target selection and the provision of patient-identifying data. Continuous mailings of educational material or prescriber feedback alone often had minimal impact on prescribing patterns.^{6,31,44,45} Conversely, multiple mailings that contained patient-identifying data and/or a combination of intervention materials had a higher success rate.^{2-4,16,27,31} Among these, two programs found mailings sent on a quarterly basis to be associated with continuous significant improvements in prescribing throughout the entire study period.^{3,4}

As displayed in Table 3, 20 of the identified programs

included a response form requesting recipient feedback regarding the intervention. Response rate among reporting programs ranged from 25% to nearly 90%.^{2,9,10,12,14,18,20,21,27,29,32,46,48-50} Generally, recipients viewed the intervention positively and often indicated intent to alter therapy based on the materials received. The majority of programs that reassessed patient profiles following response from mailings reported that an actual change in therapy occurred in approximately 50% of patients whose prescriber indicated intent to modify treatment.^{8,21,22,49} Exceptions to this finding include Culbertson et al.,¹⁴ who reported an average of 14.3% change among their 3 study groups, and Okano and Rascati¹⁸ and Rascati et al. (1996),²⁰ who reported changes of 73.3% and 81.2%, respectively.

Impact of Intervention

Effect on Prescribing Patterns. With the exception of 2 programs, the authors concurred with individual program interpretation of impact on prescribing patterns (Table 2). Of the 15 programs that used a randomized controlled design to measure impact on prescribing patterns, 8 (53.3%) reported a positive impact on at least 1 target outcome.^{2,18,20,23,26,27,31} Of the 21 remaining programs that used quasi-experimental or other observational designs, 18 (85.7%) reported positive results.^{3,4,8-16,19,21,25,30,45,48,50}

Exceptions to agreement with author interpretation include Owens et al. (2008)⁵⁰ and Starner et al. (2009).²⁴ Though the intervention conducted by Owens et al. was associated with an increase use of prophylactic therapy, this study relied heavily on surrogate markers and assumptions regarding the indicated use of target agents and was classified as questionable impact for the purpose of this review.⁵⁰ Starner et al. found their intervention to be associated with a significant decrease in target agent use; however, this was determined according to prescriptions claims data obtained on a single day 6 months post-intervention. This method was relatively restrictive (as compared with that employed by other programs) and therefore may not be representative of actual prescribing patterns.²⁴

Effect on Health Care Utilization. In addition to measuring effect on prescribing patterns, 5 programs also evaluated intervention impact on number of office visits, emergency room visits, and hospitalizations (Table 2).^{8,10,11,22,50} None of the programs noted changes in emergency room visits or hospitalizations. Increased office visits were observed by Sleath et al. (1997) and Owens et al., while Coleman et al. (2003) noted decreased office visits and use of physician services among both intervention and comparison groups.^{8,22,50}

Economic Impact. Table 4 displays the association between mailed intervention and change in economic outcomes. While most programs reported a downward trend in prescription costs, they often failed to reach statistical significance. Sleath et al. was unique in that they noted that an upward trend in costs

TABLE 3 Assessment of Prescriber Response

Study	Form Objectives	Response Rate	Prescriber Response	Association Between Response and Change in Prescribing Pattern
Bjornson et al. (1990) ⁴⁹	Assess awareness of published study. Assess intent to alter therapy based on study results. Identify additional factors that may influence decision to modify therapy.	53.1% (152/286); 49.3% (141/286) usable	95 (67.4%) of respondents indicate they were aware of the study clinical trial. 35.5% (50) intended to alter prescribing based on clinical trial results; 24.1% (38) did not intend to alter therapy; 19.1% (28) indicated decision would be patient dependent. Key factors include drug availability, professional training, experience with target drug's adverse event, size of mortality reduction, and comments by peers.	Slightly over one-half of patients with a responding physician who indicated intent to change had a full or partial change in therapy.
Coleman et al. (2003) ⁴⁶	Assess intent to intervene. Assess potential incorrect identification of prescribers or pharmacists.	47.3% (43/91)	21 (48.8%) intended to intervene. 6 (13.9%) indicated previous unsuccessful attempt. 6 (13.9%) did not intend to not intervene. 10 (23.3%) reported incorrect provider.	47.6% (10/21) of patients with physicians who indicated intent to intervene had a change in therapy.
Culbertson et al. (1999) ¹⁴	Assess intent to modify therapy.	44.8% (205/458)	Prescriber only: 23% reported intent to change therapy. Prescriber + pharmacist mailed intervention: 35% reported intent to change therapy. Prescriber + pharmacist mailed intervention + phone call: 44% reported intent to change therapy.	Prescriber only: 11% made change in therapy. Prescriber + pharmacist mailed intervention: 13% made change in therapy. Prescriber + pharmacist mailed intervention + phone call: 19% made change in therapy.
Fick et al. (2004) ²	Assess intent to modify therapy. Assess potential incorrect identification of prescribers.	71.2% (84/118)	211 (12.5%) indicated discontinuation of medication. 28 (1.7%) indicated decreased dose or frequency. 21 (1.2%) indicated prescribed an alternative medication. 1,327 (78.4%) indicated assessed patient with no change. 105 (6.2%) indicated other response.	NR
Guo et al. (1995) ⁹	Assess general comments regarding intervention.	68.6% (81/118)	NR	NR
Hux et al. (1999) ²⁷	Assess perceived value of intervention. Assess acceptability of intervention.	76.0% (76/100)	Respondents rated each of the following measures of data effectiveness as 4/5: usefulness of feedback as an education tool, impact on prescribing, motivation to learn about appropriate antibiotic use, willingness to participate in a similar program again. Factors most contributing to the acceptability of an intervention included confidentiality and data prepared apart from payer. Secondary factors included emphasis on efficacy rather than costs, obtaining prescriber consent, and access to program via fax. Tertiary factors included provision of continuing medical education credits.	NR

TABLE 3 Assessment of Prescriber Response (*continued*)

Study	Form Objectives	Response Rate	Prescriber Response	Association Between Response and Change in Prescribing Pattern
Lee et al. (2004) ¹⁰	Assess perceived value of intervention. Assess intent to modify therapy.	44.1% (249/564)	197 (50%) felt the intervention provided new information. 189 (70%) intended to use the patient education material provided. 190 (78%) felt supplemental education material will improve communication with patients. 185 (56%) intended to modify therapy for at least 1 patient.	NR
Naughton et al. (2007) ³²	Assess level of satisfaction with intervention. Assess willingness to continue receiving intervention. Assess perceived impact on practice. Assess general comments regarding intervention.	80.0% (88/110) for mailed intervention 89.9% (48/54) for academic detailing	Both groups expressed a high level of satisfaction with intervention, and there were no between-group differences in question responses ($P=NS$). All respondents who received postal bulletin indicated they would like to continue receiving mailed intervention, and 79 (84%) felt the feedback had impact on their practice. 39 (81%) receiving academic detailing indicated they would like to continuing receiving academic detailing with mailed intervention.	NR
Okano and Rascati (1995) ¹⁸	Assess agreement/disagreement with intervention. Assess potential incorrect identification of prescribers. Assess general comments regarding intervention.	67.5% (79/117)	39 (49.4%) agreed with the intervention. 23 (29.1%) disagreed with the intervention. 8 (10.1%) reported not my patient. 7 (8.9%) reported no longer seeing patient. 2 (2.5%) reported they did not prescribe the medication.	Profiles for 30 of the 39 patients with physicians who agreed with the intervention were available for evaluation after 6 months. Of these patients, 73.3% (22/30) had a change in therapy.
Owens et al. (2008) ⁵⁰	Assess perceived utility of migraine prophylaxis. Assess perceived value of intervention.	25.2% (41/163)	Approximately 90% believed prophylactic therapy to be "very effective" or "somewhat effective." Approximately 80% indicated the intervention was helpful.	NR
Pimlott et al. (2003) ²⁹	Assess level of satisfaction with intervention.	48.2% (81/168)	70% indicated they would participate in a similar mailed intervention program.	NR
Raisch and Sleath (1999) ¹⁹	Assess intent to intervene and intended method of intervention.	NR	NR	NR
Rascati et al. (1996) ²⁰	Assess agreement/disagreement with intervention. Assess potential incorrect identification of prescribers. Assess general comments regarding intervention.	71.2% (131/184)	64 (48.9%) agreed with the intervention. 25 (19.1%) disagreed with the intervention. 13 (9.9%) reported not my patient. 16 (12.2%) reported no longer seeing patient. 11 (8.4%) reported they did not prescribe the medication. 2 (1.5%) indicated "other" response.	Profiles for 44 of the 62 patients with physicians who agreed with the intervention and 21 of the 25 patient with physicians who disagreed with the intervention were available for evaluation. 18.2% (8/44) of patients with physicians who agreed continued to receive duplicate therapy as compared with 80.9% (17/21) among patients with physicians who disagreed ($P<0.001$).

TABLE 3 Assessment of Prescriber Response (*continued*)

Study	Form Objectives	Response Rate	Prescriber Response	Association Between Response and Change in Prescribing Pattern
Seltzer et al. (2000) ²¹	Assess agreement/disagreement with intervention. Assess potential incorrect identification of prescribers. Assess general comments regarding intervention.	71.5% (208/291)	64 (40.4%) agreed with the intervention. 55 (26.4%) disagreed with the intervention. 18 (8.7%) reported not my patient. 16 (7.7%) reported no longer seeing patient. 17 (8.2%) reported they did not prescribe the medication. 18 (8.7%) indicated "other" response. Many physicians who disagreed or selected "other" indicated that chronic illness justified long-term treatment.	Profiles for 78 of the 84 patients with physicians who agreed with the intervention were available for evaluation. Of these, 47.4% (37/78) discontinued sedative/hypnotic therapy.
Sleath et al. (1997) ²²	Assess intent to intervene and intended method of intervention (i.e., counseling, providing spacer, etc.).	NR	NR	NR
Sleath and Collins (1997) ⁴⁸	Assess intent to intervene and intended method of intervention. Assess potential incorrect identification of prescribers. Gage recipient tone regarding intervention.	49% of physicians returned form regarding 47% (126) of patients	24 (19%) reported an intent to change therapy. 48 (38%) intended to monitor or counsel. 21 (17%) intended to recommend non-pharmacologic treatment. 33 (26%) reported no planned action due to patient demand. 14 (11%) reported no planned action because they had incorrectly received intervention. 2% of responses were positive in tone; 92% were neutral; and 6% were negative.	49% of patients with physicians who intended to act on intervention had a change in therapy. 40% of patients with physicians who planned no action had a change in therapy. 35% of patients with physicians who did not respond had a change in therapy.
Starner et al. (2009) ²⁴	Assess acceptance of program.	NR	NR	NR
Woodward et al. (2008) ⁷	Assess acceptance of program.	NR	NR	NR
Zuckerman et al. (2004) ¹²	Assess acceptance of program.	NR	NR	NR
Zuckerman et al. (2004) ²⁵	Assess willingness to modify therapy.	34.5% (287/833)	50% were willing to change therapy for at least 1 patient. 30% were unwilling to change therapy. 20% did not respond to question.	NR

NR = not reported.

of asthma-related health care utilization occurred in 1 of their 2 intervention groups.²² Though greater reductions were often observed among groups that received more intensive interventions, the added costs may result in a negligible net benefit.

Avorn et al. estimated the costs of their intervention, which incorporated both mailed materials and academic detailing, to be approximately \$100 per physician.³¹ With this taken into account, the net savings in target medications costs is reduced from \$105 to \$5 per physician. Similarly, Culbertson et al. noted additional costs decreased net prescription savings overall of their intensive intervention from \$107 to \$52 per patient.¹⁴

Discussion

Although evidence-based medicine is the cornerstone of today's clinical practice, successful treatment often relies on coordination of care between providers and patient adherence to prescribed therapies. Mailed interventions may promote coordination of care between prescribers and provide real-world information regarding patient prescription use. This review identified 40 publications that described the results of 39 distinct mailed intervention initiatives and links the effectiveness of letter interventions to various outcomes. Approximately 50% of the randomized controlled trials reported a positive impact

TABLE 4 Economic Impact of Mailed Intervention

Study	Mailed Intervention Materials	Effect Measure	Economic Impact of Mailed Intervention											
Avorn and Soumerai (1983) ³¹	Educational material ± supplemental patient education material ± academic detailing	Change in prescribing costs per physician (\$)	Academic Detailing + Mailed Intervention			Mailed Intervention		Control			P-Value			
			-105			NR		NR			0.002			
Collins et al. (1997) ¹³	Patient profile + educational information	Change in mean [SD] dipyridamole expenditure per long-term care patient (\$)	Physician Only			Pharmacist Only			Physician + Pharmacist			Control		
			Pre	Post	P-Value	Pre	Post	P-Value	Pre	Post	P-Value	Pre	Post	P-Value
		189.12 [72.52]	119.23 [107.19]	0.007	188.27 [77.29]	98.30 [98.01]	0.007	159.49 [77.50]	62.92 [94.67]	0.007	198.88 [68.91]	139.39 [110.73]	NS	
	Change in mean [SD] dipyridamole expenditure per ambulatory patient (\$)	122.62 [78.15]	84.69 [92.16]	NS	143.59 [78.49]	94.63 [90.92]	NS	146.26 [85.63]	85.05 [101.10]	NS	142.72 [83.22]	114.78 [94.52]	NS	
Culbertson et al. (1999) ¹⁴	Patient profile ± educational material	Mean change in cost of antiulcer medications per patient (\$)	Physician Only			Physician + Pharmacist			Physician + Pharmacist + Follow-Up Call					
			-55.87			-42.66			-107.75					
		Impact of various intervention techniques on antiulcer medication cost	Physician + pharmacist + follow-up call group had greater decrease in cost before and after intervention as compared with other study groups (<i>P</i> < 0.05).											
Guo et al. (1995) ⁹	Patient profile	Change drug reimbursement as measured by real marginal value ^a (\$)	Significant downward trend in drug reimbursement throughout follow-up period (<i>P</i> = 0.002). Decrease in drug reimbursement significant in 5 of the 7 follow-up months (<i>P</i> < 0.05).											
		Change in total drug reimbursement per prescriber per month (\$)	-112.73											
Hoffman et al. (2003) ¹⁶	Patient profile	Change in mean [SD] prescription drug costs per member per month (\$)	Intervention			Control			P-Value					
			-118.38 [296.00]			-39.07 [331.00]			NS					
		Change in medical costs per member per year (\$)	-1,413			-970			< 0.05					
Hux et al. (1999) ²⁷	Prescriber feedback	Change in median antibiotic cost	Increased by an average of over \$3 per prescription in control group as compared with no change in intervention group (<i>P</i> = 0.002).											
Sleath et al. (1997) ²²	Patient profile + educational material		Physician Only					Physician + Pharmacist						
			Pre		Post		P-Value	Pre		Post		P-Value		
		Change in mean [SD] cost of SABA (\$)	92.31 [47.43]		82.51 [84.26]		NS	74.96 [38.71]		61.14 [37.12]		< 0.05		
		Change in mean [SD] cost of asthma medications (\$)	157.53 [94.93]		138.55 [124.19]		NS	152.84 [95.83]		132.08 [91.06]		< 0.05		
		Change in mean [SD] cost of asthma-related health care use (\$)	81.25 [344.44]		229.94 [818.12]		NS	47.74 [93.00]		39.13 [90.35]		NS		
	Change in mean [SD] cost of asthma medications and health care use (\$)	238.78 [353.88]		361.50 [815.21]		NS	200.58 [137.76]		171.21 [127.31]		NS			

TABLE 4 Economic Impact of Mailed Intervention (continued)

Study	Mailed Intervention Materials	Effect Measure	Economic Impact of Mailed Intervention								
			Intervention			Comparison			P-Value		
			Pre	6 Months Post	12 Months Post	Pre	6 Months Post	12 Months Post	Pre	6 Months Post	12 Months Post
Zimmerman et al. (1994) ¹¹	Patient profile + educational material										
		Change in mean [SD] cost of H2RA in long-term care population (\$)	67.99 [12.04]	44.11 [32.25]	43.17 [31.97]	64.78 [14.99]	48.55 [25.50]	46.36 [27.62]	<0.005	NS	NS
		Change in mean [SD] cost of H2RA in ambulatory population (\$)	60.29 [15.06]	44.69 [27.60]	43.64 [31.66]	57.63 [18.14]	47.86 [31.86]	46.05 [32.01]	<0.05	NS	NS
Zuckerman et al. (2004) ²⁵	Patient profile + educational material	Estimated savings of beta-blocker use 7 days post-discharge (\$)	71,970								
		Estimated savings of beta-blocker use 30 days post-discharge (\$)	76,678								

^aReal marginal value was used to control for seasonal variations in use. Real marginal value = mean value in comparison population – each individual's mean value. H2RA = histamine H2 receptor antagonists; NR = not reported; NS = nonsignificant; SABA = short-acting beta2-agonist; SD = standard deviation.

to prescribing patterns as compared with nearly 86% that used quasi-experimental or other nonrandomized controlled designs.

Commonly, a change in prescribing was defined by the presence or absence of a medication claim or dose change of a target agent. Such changes were often used as surrogate markers for improvements in health care and/or economic outcomes. While claims data can provide information regarding change in prescribing, it is not necessarily predictive of impact on long-term clinical or economic outcomes. Few programs attempted to evaluate impact on health care or economic outcomes, and ones that did often reported trends that failed to achieve statistical significance; a finding that was also observed by Hennessy et al. (2003).³⁵ With the exception of one program, utilization tended to trend downward. Sleath et al. reported an interesting finding in their physician-only intervention group: an increase health care utilization (and associated costs) during the post-intervention period.²² This finding demonstrates that it is possible for an intervention to prompt an initial increase in utilization as additional medications and prescriber services may be required to address issues brought to light through intervention materials.

The lack of statistical significance observed for economic outcomes may be due in part to the relatively short follow-up periods used by the majority of identified programs. Additionally, the fact that interventions are based on individual

transactions makes it difficult to quantify outcomes that may have been influenced by external circumstances outside the control of their program. It is possible that changes in hard outcomes may occur over longer periods of time; however, this brings into question the duration of impact following cessation of mailed intervention programs. Meyer et al. reported the effects of their one-time intervention mailing decreased to a point of nonsignificance after 6 months and continued to trend downwards at 12 months post-intervention.¹⁷ Though many others have reported significant effects at 6 and 12 months post-intervention, none evaluated the impact beyond 12 months of final intervention mailing. Several programs that provided continuous well-constructed mailings over an extended period (i.e., 12 months) achieved and maintained significant results throughout the entire intervention period.^{2-4,16} Such a program may be well equipped to evaluate economic outcomes.

This review identified several key factors that may contribute to intervention success, perhaps the most important being provision of patient-identifying data. Eighty-four percent of reviewed programs that used this method reported a significant impact on prescribing patterns. Comparatively, programs that provided prescriber feedback alone or in combination with other nonpatient-identifying materials had a lower rate of success. Intuitively, one could see how supplying prescribers with a list of identified patients would be conducive to prompt

incorporation of intervention recommendations. Acceptance of recommendations provided via prescriber feedback requires recipients to approach future patient visits with the results in mind. However, the need to address more critical issues during office visits may prohibit incorporation of intervention recommendations, particularly if intervention effect does, in fact, decrease over time. Alternatively, physicians could retrospectively review their patient populations to determine specific individuals who may benefit from therapeutic adjustment. While thorough, the time-consuming nature of this task may dissuade physicians and therefore prohibit the potential impact of prescriber feedback. Our review indicated that prescriber feedback may be most useful in intervention involving antibiotics or medications with abuse potential.^{26,27,30} Overprescribing such agents is denounced by the medical community as well as much of the general population. This negative outlook may prompt physicians to reevaluate their prescribing habits if they appear to be elevated, particularly in comparison with their peers.

Other factors that may contribute to intervention success included identifying recipients based on prescribing habits rather than geographic location or participation in a health care network. Programs that mailed interventions to prescribers based solely on practice location typically had little to no impact.^{5,6,28,30,32,43-45} This is consistent with the findings by Figueiras et al. (2001), who concluded that interventions that were personalized to recipients were associated with a higher rate of success.³⁴ If costs permit, addition of pharmacists and/or patients as recipients may further improve intervention success. Additionally, interventions that consisted of educational materials alone rarely had an impact on prescribing practice.^{24,44,50,51}

The majority of programs offered recipients generalized recommendations that could be applied to the entire target population. Two programs reported successful results of interventions that provided patient-specific recommendations: Each enlisted a multidisciplinary team of practitioners to conduct case-by-case evaluations and formulate recommendations.^{15,47} While both methods were associated with positive results, providing generalized recommendations appeared to be a more timely and cost-effective approach. Furthermore, Meyer et al. found no difference between interventions that provided generalized and patient-specific recommendations.¹⁷ Whether a generalized or patient-specific manner is employed, recommendations supported by widely accepted guidelines or literature may be considered most acceptable to intervention recipients. Additionally, creating a focused, strongly supported intervention may be more effective than attempting to address multiple concerns.

The biggest study limitation cited by the majority of the authors is the use of claims data to describe prescription and medical histories. Data entry errors at the dispensing pharmacy can result in a multitude of inconsistencies with regard

to prescriber information, such as incorrect physician identification and incorrect/outdated prescriber addresses. Among interventions that provided a response form, between 9% and 23% of recipients indicated they had received an intervention letter regarding a patient that did not belong to them and/or a medication they did not prescribe.^{18,20,21,46,48} In addition to the potential for administrative errors, prescription claims histories assume dispensing of medications as surrogate markers for disease states and prescription use. Though such markers can certainly provide insight into a patient's therapeutic management, this method is subject to error, particularly if selection is based solely on a computerized analysis. While it is efficient to preselect patients based on surrogate markers, it cannot replace the clinical judgments of a pharmacist. Several programs sought to reduce this potential for error and conducted manual reviews of identified profiles to ensure correct patient selection.^{10,15,25} Despite these potential drawbacks, claims data remain a widely accepted method of measuring drug exposure.

Limitations

All publications were identified using a single search engine, and other methods were not used to identify unpublished works or reports from individual agencies. Nevertheless, the authors felt PubMed provided a reliable representation of the majority of the publications in this field. It should be noted that there may be a potential bias towards publication of positive results. In a retrospective evaluation of publication bias, Easterbrook et al. (1991) found studies with a positive impact were twice as likely to be published as compared with those shown to have no impact.⁵² A majority of the mailed intervention programs were funded by governmental agencies, many of which were developed in response to OBRA 90.¹ Mandates from federal legislation and/or drug utilization review boards may have resulted in methodological flaws that prohibited reports from being considered for publication. Additionally, selective reporting of the results may also have been guided by the funding source, as programs do not want to be targeted for wasting resources on failed initiatives.

As stated by Figueiras et al., organizational differences between health care systems and individual/cultural differences among prescribing practitioners may limit the generalizability of results.³⁴ This may be especially true for programs that were conducted in countries that offer universal health coverage, as recipients may have differing views of intervention providers (particularly if it is governmental in nature) or health care as a whole. This review did not account for the potential differences in objectives between governmental and commercialized mailed intervention programs. The level of heterogeneity between reviewed publications, particularly with regard to targeted populations, outcomes, and disease states, prohibits provision of definitive results. For this reason, the authors elected to describe reported findings and identify

general patterns associated with program success. In doing so, the authors acknowledge that it is likely external factors (i.e., seasonal variations, nature of disease state, patient population, and pharmaceutical marketing) may have contributed to observed changes in prescribing behavior.

Many of the reviewed publications reported outcomes from programs conducted in the 1990s to early 2000s. It is likely that prescriber attitude towards pharmacists and/or pharmacy benefits provider recommendations may have evolved since that time. Additionally, the majority of reports cited “physician” or “prescribers” as the primary intervention recipient and therefore may not have taken the expanding role of mid-level prescribers into account. Similarly, many reports did not specify if interventions were sent to primary care practitioners or specialists. For this reason, this review referred to all prescriber recipients as “prescribers.”

Both randomized controlled and nonrandomized controlled/observational reports were included in this review. Many of the reviewed publications followed a pre/post quasi-experimental design and therefore may be subject to regression to the mean.^{3,4,7-14,19,21,22,24,25,30,45,48,50,53} The authors recognize the potential drawbacks of including nonrandomized controlled trials; however, due to a lack of available literature, we elected to include all reports of mailed letter interventions. Even among the randomized controlled reports, methodological errors existed (i.e., short duration that does not account for seasonal variability in prescribing, unmatched baseline characteristics, or use of comparator rather than true control group). This is likely because mailed intervention programs are initiated (and funded) with the primary goal of changing prescribing patterns to all beneficiaries. Measuring impact of an intervention is often a secondary motive, and exclusion of beneficiaries to create a control group may be viewed unfavorably by funding entities. While inclusion of quasi-experimental and observational studies may impact internal validity, the authors hope this comprehensive review will prove beneficial in the development of future mailed intervention programs.

Conclusions

The results of this review indicate that a well-orchestrated letter intervention program has the potential to produce successful outcomes. Identifying recipients based on prescribing habits (as opposed to practice location), provision of recommendations that are supported by widely accepted clinical guidelines, inclusion of patient-identifying information, and addition of a second intervention recipient may have been associated with significant changes in prescribing behavior. Whether these changes translate into cost savings is unknown. Future research should focus on longer assessment periods, particularly for interventions that provide regular mailings over a period of months or years. Extended follow-up periods could also be used to determine if the impact of an intervention

does in fact decrease over time. Though the funding source of mailed intervention programs may prohibit the use of randomized controlled designs, improvements in methodology would certainly improve the validity of study results. Additionally, future projects may wish to identify factors that prohibit prescriber acceptance of intervention recommendations from translating into actual changes in therapy.

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DISCLOSURES

The authors reported no funding for this manuscript and no financial or other potential conflicts of interest related to the subject matter of this manuscript. At the time of submission, Dr. Ho was Clinical Assistant Professor of Pharmacy Practice and Director of Retrospective Drug Utilization Review Program and Dr. Venci was Clinical Pharmacist at Retrospective Drug Utilization Review Program, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, Buffalo, New York.

Concept and design, data collection, and data interpretation, writing, and revisions were performed by both authors. Portions of this manuscript were presented as a poster abstract at the American Pharmacist Association's Annual Meeting and Exposition in New Orleans, Louisiana on March 10, 2012.

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