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International experience in controlling pharmaceutical expenditure: influencing patients and providers and regulating industry – a systematic review

Iyn-Hyang Lee[1], Karen Bloor[2], Catherine Hewitt[3] and Alan Maynard[4]

Abstract

Objective: To review international policies to control expenditure on pharmaceuticals by influencing the behaviour of patients and providers and regulating the pharmaceutical industry.

Method: Systematic review of experimental and quasi-experimental studies. Published studies were identified with an electronic search strategy using MEDLINE and EMBASE from 1980 to May 2012. Studies were eligible if they assessed the effect of policies aimed at influencing the behaviour of patients and providers, and regulating the pharmaceutical industry. Outcome measures included pharmaceutical expenditure, prices or utilization; other resource use relating to pharmaceuticals; and health outcomes and patients' or providers' behaviour relating to pharmaceutical use. Quality assessment criteria for each study design were developed based on the standard criteria recommended by the Cochrane Effective Practice and Organisation of Care (EPOC) group.

The review includes studies based on randomized controlled trials and rigorous quasi-experimental designs (interrupted time-series and controlled before-and-after studies). Studies were excluded if they were conducted within a single hospital or practice; related to pharmaceutical care services or disease management; had less than 6 months of follow-up period (or less than 12 months overall for interrupted time series); if data in controlled before-and-after studies were not collected contemporaneously or if no rationale was stated for the choice of control group; or if relevant and interpretable data were not presented.

Results: A total of 255 studies met the inclusion criteria for this review. The majority of the studies relating to patients evaluated cost sharing interventions such as user charges (52 studies). User charges do reduce utilization of pharmaceuticals, and reduce public expenditure by shifting costs to patients. But they reduce the use of essential as well as non-essential drugs, and without adequate exemptions they affect vulnerable groups disproportionately.

The majority of studies relating to doctors evaluated the effects of educational approaches (78 studies), reimbursement restrictions (48 studies) and incentive systems (22 studies). Evidence on these policies is of mixed quality. It appears possible to influence prescribing modestly, through various means, but it is essential that messages to prescribers are based on good evidence of effectiveness and cost-effectiveness.

Twenty-nine studies related to industry regulation, and they were of mixed quality. Evidence from studies of reference pricing suggests that this may result in cost savings. These are, however, achieved not by companies reducing or restraining prices, or by reductions in the overall volume of prescriptions, but by some shifts in use and shifting costs to patients, with consequent adverse effects on the equity of access to medicines. Other price and profit controls remain almost completely lacking in evaluative evidence.

Conclusions: It may be that the undesirable consequences of policies influencing patients, particularly user charges, can outweigh the benefits. To influence demand for pharmaceuticals, it is more appropriate to influence prescribing doctors and although interventions to improve prescribing practice have been developed, they often achieve relatively modest

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benefits and sometimes at high cost. Good evaluative evidence related to industry regulation is scarce despite its policy importance.

Keywords
Pharmaceutical policy, prescribing, user charges, pharmaceutical industry, systematic review

Introduction

Expenditure on pharmaceuticals has increased in real terms and as a proportion of overall expenditure in many health care systems in the developed world over recent decades.[1] Governments have adopted a variety of supply and demand side policies to control pharmaceutical costs. Our aim was to review international policies which seek to control expenditure on pharmaceuticals and/or improve the efficiency of pharmaceutical use (making best use of resources to maximize health). On the demand side of this market, we review studies assessing the effect of policies aimed at influencing the behaviour of both patients and prescribers. On the supply side, we review studies assessing the effect of policies aimed at regulating the behaviour of the pharmaceutical industry, particularly governments' control of licensing, reimbursement, prices and profit.

Methods

Search strategy

Published studies were identified with an electronic search strategy carried out by one of the authors (IL) in consultation with a specialist librarian, using MEDLINE and EMBASE from 1980 to May 2012. The search was conducted in July 2008 and repeated in June 2012. Search strategies are in online Appendix 1 and detailed methods of the review are available from the authors on request. No language restrictions were applied. Reference lists of all potentially relevant reviews were scrutinized. The search strategy combined terms about the targets of potential policies (industry, doctors and patients) with terms to indicate pharmaceutical use and prescribing, and terms to identify rigorous study designs.

Study selection criteria

Randomized controlled trials and rigorous quasi-experimental designs (interrupted time-series and controlled before-and-after studies) were eligible for inclusion. Outcome measures include pharmaceutical expenditure, prices or utilization; other resource use relating to pharmaceuticals; and health outcomes and patients' or providers' behaviour relating to pharmaceutical use. Studies were excluded if: they were conducted within a single hospital or practice; related to pharmaceutical care services or disease management; had less than six months of follow-up period (or less than 12 months overall for interrupted time series); data in controlled before-and-after studies were not collected contemporaneously or if no rationale was stated for the choice of control group; or relevant and interpretable data were not presented. Information on the participants, interventions, study setting, main outcomes, study duration, results for the main outcome measures and sponsors of the study was extracted from included studies by one author (IL), consulting other contributors (KB and CH) when there was any uncertainty, using a data extraction form designed for the reviews. Quality assessment criteria (online Appendix 2) for each study design were developed based on the standard criteria recommended by the Cochrane EPOC group.[2] The list of all included studies is in online Appendix 3.

Results

Overview of included studies

From the search for evaluative studies of policies influencing patients, 494 studies were identified, and 74 met the inclusion criteria (see online Appendix 4). The majority of the studies relating to patients evaluated cost sharing interventions, including user charges (52 studies), tiered copayments (12 studies) and prescription caps (6 studies). Single studies evaluated the effect of an educational intervention, an over-the-counter switch programme and a savings account plan.

From the search for evaluative studies of policies influencing prescribers, 1147 studies were identified and 152 met the inclusion criteria (online Appendix 5). The majority of studies relating to doctors evaluated the effects of educational approaches (78 studies), reimbursement restrictions (48 studies) and incentive systems (22 studies). Four studies evaluated the effect of free drug samples and single studies evaluated the effect of generic substitution, the effect of a repeat prescribing programme and the separation of prescribing and dispensing of drugs.

From the search for evaluative studies of industry regulation, 526 studies were identified and 29 met the inclusion criteria (online Appendix 6). The majority of studies relating to industry evaluated price control

interventions, particularly reference pricing policies. Three studies explored the effects of market authorization procedures (providing cost-effectiveness information on reimbursement decisions or setting drug-review deadlines on approvals), two studies examined patent expiry and a single study evaluated profit control.

Influencing patients

Cost sharing schemes. User charges, tiered copayments and prescription caps were the most frequently evaluated interventions aimed at influencing patients (online Appendix 7). Such cost-sharing schemes require patients to pay a flat rate copayment ('deductible') (as in England), a proportion of the cost of the prescription ('coinsurance') or a different (tiered) copayment depending on the category of medicine (e.g. generic or brand-name drugs; formulary and non-formulary products). Cost sharing systems are often combined with safety net exemptions. For example, in England less than 10% of prescriptions are actually subject to a prescription charge.[3]

Overall, evidence about the effect of user charges and coinsurance demonstrates that cost sharing reduces payer expenditure on pharmaceuticals, but this is achieved by reducing utilization of drugs and by shifting costs to patients. Although use of less essential drugs decreases at a greater rate, it is clear that user charges can also reduce the use of essential drugs. Predictably, the greater the cost-share, the larger the reduction in utilization. Some evidence suggests that patients who were newly diagnosed were more likely to give up their medication.[4] The effect of user charges on vulnerable populations (elderly, sick, low income) depends on the presence of safety net exemptions.[5]

Twelve studies of moderate to high quality evaluated the effect of tiered copayments, all from the US. Tiered copayments usually comprise a cost structure where patients face lower charges for cheaper (often generic) products. The evidence demonstrated that they tend to lower public drug expenditure both by reducing utilization, particularly of non-formulary products, but also by shifting costs to patients. Six studies examined the effects of prescription capping, where payers reimburse a fixed number of prescriptions per month, five from US Medicaid or low income senior populations and one from the Netherlands. It was found that prescription caps lower drug expenditure by reducing utilization, but they have been demonstrated to reduce the use of essential drugs in vulnerable populations, and in some populations to substantially increase non-drug expenditure.[6] In the Netherlands, the savings from the cap were lessened by prescribers increasing the volume of prescriptions.[7]

Other interventions. One study in Spain[8] used a cluster randomized design to evaluate the effect of an educational approach targeted at patients (online Appendix 8). The intervention increased the use of generics by around 2.5 times, compared with the control group, but with limited reductions in expenditure. A US study evaluating over-the-counter switch and drug utilization using an interrupted time series design[9] found that prescription rates for drugs that were switched to over-the-counter dropped to zero after six months, and prescriptions for prescription-only substitute products also declined. Three studies studying the effects of direct-to-consumer advertising in North America showed that it was associated with an increase in utilization or costs of target products. One study from the USA reported that a savings account plan reduced pharmacy expenditures by about 30%, compared with traditional plans.[10]

Influencing prescribers

Educational interventions. Four groups of studies were identified that evaluated educational interventions with the aim of improving prescribing (online Appendix 9). Interventions consisted of general or specific prescribing guidelines (for example, NICE guidelines in England); group level or individualized prescribing feedback (for example, Prescribing Analysis and Cost (PACT) data in the NHS); drug utilization review, which informs prescribers of patients' medication histories and/or prescribing recommendations and educational interventions employing computerized support. Evaluative studies were identified in a wide variety of settings. Some interventions were national (e.g. PACT data and NICE guidance), but most were at regional or multi-institutional level. Most interventions were voluntary, and thus results from 'enthusiasts' may not be representative of the general population of practitioners. Evidence from the studies suggests that educational interventions can lower pharmaceutical utilization and expenditure when the focus of the intervention is on cost-effectiveness information, but that changes are likely to be modest. Multi-faceted and collaborative approaches tend to achieve better outcomes, but these approaches may have significant costs. One English study of prescribing guidelines in general practice[11] included the costs of implementing the guidance in the overall estimation of cost-effectiveness, finding that these additional costs can in some situations outweigh the savings made from reducing prescribing.

Reimbursement restrictions. Forty-eight studies were identified that evaluated the effect of reimbursement restrictions, all but three from North America (with one in

Spain, one in Norway and one in Australia) (online Appendix 10). Reimbursement policies stipulate that payers prioritize publicly funded drugs, which are intended to make prescribers prescribe drugs that are fully subsidized away from those where reimbursement is limited. Under these regulations, some products are ruled out from reimbursement (delisting or negative lists) or preferred (positive lists, formularies or preferred drug lists). Providers must undergo pre-requisite procedures (prior-authorization) or treatments (step-therapy). Studies were of mixed quality, but little association was found between quality rating and the direction or strength of results. Evidence from these studies suggests that such policies can lower spending on drugs and switch use between categories, such as increasing generics use, but some studies revealed potential unintended consequences. Simple withdrawal of reimbursement without other interventions such as guidance on alternatives can mean that prescribers switch to even more undesirable options.

Incentive systems. Among the 22 studies exploring incentive systems, nine examined UK fundholding, mainly using controlled before and after designs. Incentive systems were also evaluated in Sweden, Switzerland, China, Taiwan and the USA, amongst other countries (online Appendix 11). All of the studies used prescriptions databases, either nationally or within an organization. Results from the studies were inconsistent, but suggested that if changes in pharmaceutical use did occur, they were likely to be small. All but two found reductions no greater than 5%, although one study from Taiwan indicated a 12% decrease in antihypertensives after introduction of a global budget.[12] One study evaluated the effect of a more recent system of incentives to improve primary care in the English NHS, the quality and outcomes framework.[13] This analysis found that prescriptions that were incentivized by the new system increased both before and after its introduction compared with those that were not incentivized. Existing prescribing trends were therefore rewarded and reinforced, rather than changed. Seven of the nine studies of GP fundholding in the NHS suggested savings, but these were largest in the first year of fundholding in all waves, and they declined over time. Dispensing fundholders were more affected than non-dispensing practices.[14] Rewards for generic prescribing in the USA did not influence prescribing[15] and bonuses to Dutch physicians in return for adhering to prescription guidelines created only small changes in prescribing practice in the target drugs.[16] Financial incentives for more prescriptions (e.g. fee-for-service payment) can nullify other cost containment strategies, as illustrated in Taiwan.[17,18] Selection bias is a potential problem in many of the studies in this category, and the study quality is moderate to low. Overall, incentives for prescribers have been demonstrated to achieve modest savings, but again there are transactions costs and rewards for prescribers that should be included in any estimate of the overall cost-effectiveness of these interventions.

Other interventions. Four studies evaluated the effect of distributing free samples (e.g. of generic products) but found minimal or no effect on physicians' prescribing (online Appendix 12). One study evaluated the effect of mandatory generic substitution in Sweden, finding a sharp decrease in both public and private expenditure on pharmaceuticals, which was maintained over the two-year follow-up.[19] One study explored the effect of an intervention transferring responsibility for repeat prescriptions to pharmacists in Britain, finding minimal effects on drug volume and expenditure, but some improvements in medication quality, for example by detecting combinations of drugs that could result in adverse reactions.[20]

Regulating industry

Price controls. Governments have attempted to regulate pharmaceutical prices for decades, by setting, agreeing and sometimes cutting prices of drugs[21] (online Appendix 13). In 1989, the German health system introduced a reference pricing scheme, which has since been adopted by many other countries. In reference price systems, a reimbursement price is set for a therapeutic category of products, and patients pay the difference between the cost of the product prescribed and the reference price. New and innovative pharmaceuticals are rarely covered by the scheme. There are different ways to set the reference price; it may be set as the average price of a category (Germany), or the highest price generic product (Portugal), or the lowest price product (Canada), or the lowest price product accounting for at least 20% of the market (Spain), or the lowest price plus a proportion (Sweden). While some companies can choose to price at the reference price, others may price higher and rely on patients' willingness to pay part of the cost.

This review identified studies evaluating the impact of reference pricing policies in Germany, Portugal, Sweden, Spain and parts of Canada and the USA (see Appendix 13, available online). Consistent with an earlier Cochrane review by Aaserud and colleagues,[22] we found that the majority of studies evaluated the effect of reference pricing introduced over the 1990s in Canada. Most of the Canadian studies were of moderate to high quality and involved elderly beneficiaries of the PharmaCare plan in British Columbia as an intervention population, with one evaluating a similar

policy in Ontario. Six studies, mostly published since the Aaserud review,[22] were conducted in Europe (Germany, Portugal, Sweden and Spain), and were rated of mixed quality. All but three studies used interrupted time series, with one using both interrupted time series and controlled before and after techniques. Three of the other studies used a controlled before and after design.

Evidence from these studies demonstrates that reference-pricing policies have little impact on overall use of pharmaceuticals, but they may reduce the volume of non-reference products while increasing the volume of reference products (see Appendix 13, available online). This may be linked to reductions in payers' expenditure, as concluded by Aaserud et al.'s review.[22] Reference pricing has minimal impact on pharmaceutical prices, but patients' out-of-pocket payments increase, implying consequent effects on equity of access to medicines. In addition, some studies found undesirable substitution effects, for example after applying reference pricing to non-steroidal anti-inflammatory drugs, and one study reported an increased in use of opiate medications.[23] Few of the studies overall explored unintended consequences or effects on patients' expenditure.[22]

Nine of the studies assessed the effect of other national or state-level price controls, using interrupted time series (six studies) or controlled before and after design (three studies). These studies were based in Maryland, USA; Iceland, Ireland, South Korea and Taiwan. Only one of these studies found any notable changes in expenditure resulting from the different price control systems that were implemented: in Ireland, consecutive reductions in the wholesale margin and pharmacy mark-up for four years curbed the increasing trend of pharmaceutical expenditure and created a downward trend between 2008 and 2010.[24]

Licensing and reimbursement. Licensing pharmaceutical products is 'ultimately the most powerful economic control as it can exclude products from the market'[25] (online Appendix 14). Licensing procedures around the world require evidence of efficacy, safety and manufacturing quality of new medicines. Increasing numbers of countries are requiring a 'fourth hurdle' of evidence of cost-effectiveness as part of their process of deciding whether or not new products will be reimbursed by health care systems. This requirement was led by pharmaceutical regulators in Ontario, Canada and in Australia during the early 1990s. The National Institute for Clinical Excellence (NICE) was created in 1999 in England and Wales, to assess the evidence of effectiveness and cost-effectiveness of new clinical interventions through technology appraisal, and to produce and promote clinical guidance. This introduced a 'fourth hurdle' reimbursement mechanism to the NHS. NICE has been criticized for creating delays in access to new medicines, and for prioritizing new products above existing interventions as a result of its high cost-per-QALY threshold.[26] Two studies of formal requirements for economic evidence in Canada, Finland and Sweden found that the new procedure including economic evidence tended to prolong the time lag before reimbursement decisions or to decrease the proportion of drugs listed. Reimbursement decision delay was observed only in the first year of implementation in Finland and Sweden.[27]

We found one study exploring changes in licensing policy; the Prescription Drug User Fee Act of the USA, which imposed deadlines for the completion of drug reviews. This study reported that rushed approvals might be associated with the higher post-marketing safety problems.[28]

Other regulatory mechanisms. The UK Pharmaceutical Price Regulation Scheme (PPRS) regulates pharmaceutical prices indirectly, by controlling company profits. Companies are allowed freedom of pricing but negotiate target profits from pharmaceutical sales to the NHS, with a target rate of return on historic capital of 21%.[29] Manufacturers earning excessive profits may be required to reduce prices of products sold to the NHS. One study explored the effect of changes in the rate of return cap and found little impact on pharmaceutical prices: a 1% per cent change in the maximum rate of return generated only a 0.15% change in the aggregate price index overall.[30]

Discussion

Principal findings

Interventions aiming to influence patients were mostly based on cost sharing, including user charges, tiered copayments and prescription caps. Overall, evidence showed that cost sharing reduces payer expenditure on pharmaceuticals by reducing utilization and shifting costs to patients. One study[8] evaluated patient educational interventions (encouraging use of generics) which may merit further research. Interventions aimed at improving the practice of prescribing were more varied and included educational interventions, reimbursement restrictions and incentive systems. These tended to have effects that were modest but largely positive. Evaluations of interventions aimed at regulating industry remain scant. Reference pricing has a demonstrable impact on payer expenditure but this is a result of shifting costs to patients rather than reducing prices. Studies of other price controls overall found no notable changes in expenditure.

Policies to influence demand for pharmaceuticals can be aimed at patients or at their prescribing physicians. A substantial evidence base exists to evaluate the effect of user charges on patient demand for pharmaceuticals, reinforcing the findings of an earlier review.[31] There exist many large, well-conducted experimental and quasi-experimental evaluative studies over varied settings. Lessons from these studies are remarkably consistent. User charges do reduce utilization of pharmaceuticals and reduce public expenditure by shifting costs to patients. But they can reduce the use of essential as well as non-essential drugs, and without adequate exemptions they affect vulnerable groups disproportionately.[5] User charges have been described as 'misguided and cynical attempts to tax the ill and/or drive up the total cost of health care while shifting some of the burden out of government budgets',[32] and contrary to the aims of public health systems.[33]

Evidence on the effect of policies aiming to influence physicians' prescribing practice has developed substantially since an earlier similar review,[34] although it is of mixed quality. It appears possible to influence prescribing through various means, but for this to be positive, it is essential that messages to prescribers are based on good evidence of effectiveness and cost-effectiveness and that prescribers are not overloaded with information. In addition, changes in prescribing from most of these interventions appear to be relatively modest, particularly if interventions rely simply on distributing information. The cost of achieving change, particularly if interventions are multi-faceted or involve physician rewards, should be incorporated in judgements about the value of such interventions.

Like other incentive-based systems, GP fundholding in the UK NHS had some effect on prescribing but it was concentrated in the first year of its operation, change was small and transactions costs may have been high. The implementation of GP payment for performance under the quality and outcomes framework (QOF) has been difficult to evaluate due to the absence of 'before' data, but studies have demonstrated some improvements in prescribing and reduction in dispersion of performance.[35] There has also been some questioning of the targets,[36] possible payment for performance that was already being delivered[37] and some 'gaming' of the system.[38] Again any improvements may have been bought at a high price – for example, estimates of expenditure on the QOF are around £1 billion.[39]

Until relatively recently, international regulatory policies have focused on the safety and efficacy of pharmaceuticals. But following sharp increases in pharmaceutical expenditure over recent decades, efforts have been made to contain costs and control prices. Price-control mechanisms tend to be crude ways of controlling costs; to contain expenditure effectively requires regulation not just of pharmaceutical prices but also of the volume of prescribed medication. Price controls, unless they are linked with carefully monitored economic evaluation, may not necessarily promote efficiency in use of medicines.

Strengths and weaknesses of the study

The broad inclusion criteria for this review create both strengths and weaknesses. The overview of varied policies to influence prescribing costs and practice is useful and findings across different systems and regions are often surprisingly consistent. But the varied patient populations and settings, as well as heterogeneity in the interventions and outcome measures, make synthesis difficult. Including the three most robust study designs lessened the heterogeneity between well- and poorly designed studies and improved the reliability of review outcomes. Weaknesses of this review also include the reliance on electronic searching and hand searching of journals, which may have resulted in missed reports from 'grey' literature, and single data extraction. The first of these was minimized by contacting key authors in the field and the second by a second review of any papers where the main reviewer had any uncertainty about the findings.

Unanswered questions and future research

A number of areas remain under-researched. These include non-financial interventions to influence patients (e.g. educational interventions) and rigorous evaluations of policies aimed at industry. Good evaluative evidence is scarce in relation to regulating the pharmaceutical industry. Only 29 studies met the inclusion criteria for this review and the studies identified were of mixed quality. The only policy intervention where evidence has improved notably since our previous related review in 1996[40] is the use of reference pricing systems. Reference pricing policy has begun to move towards linking prices of pharmaceuticals with value, as a higher price is allowed only with evidence of therapeutic benefit. But evidence from the studies identified suggests that cost savings are achieved not by companies reducing or restraining prices, or by reductions in the overall volume of prescriptions, but by some shifts in use from non-reference to reference products, along with shifting costs to patients, with consequent adverse effects on the equity of access to medicines. Other price and profit controls remain almost completely lacking in evaluative evidence. Apparently, existing rigorous evidence is limited to a handful of settings, mostly enjoying high economic status. Given the low transferability of policy outcomes, there is a pressing

need for other types of settings to produce inherent evidence of each.

Conclusions

Following sharp increases in pharmaceutical expenditure over recent decades, efforts have been made to contain costs, including policy interventions to constrain demand for drugs and regulate their supply. Overall, it seems that the undesirable consequences of policies influencing patients, particularly user charges, may outweigh any benefits. To influence the demand for pharmaceuticals, it is necessary to influence prescribing doctors and although interventions have been developed and evaluated to improve prescribing practice, they often achieve relatively modest benefits and sometimes at high cost, a factor which is often omitted from evaluative studies. On the supply side of this market and in relation to industry regulation, it is also essential for future policies to be accompanied by rigorous evaluation to determine costs and effects, to ensure that unintended consequences are minimized and to develop the evidence base for policy in this area.

Declaration of Conflicting Interests

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Supplementary Material

The online appendices are available at http://hsr.sagepub.com/supplemental-data.

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