September 2009 – SUPPORT Summary of a systematic review

Do pharmaceutical reference and index pricing policies have effects on drug use, health care utilisation, health outcomes and costs?

Pharmaceutical pricing and purchasing policies are used to determine or affect the prices that are paid for drugs. Examples are price controls, maximum prices, price negotiations, reference pricing, index pricing and volume-based pricing policies. This review found evidence for reference pricing and index pricing. In reference drug pricing, which is a reimbursment tool, a reference drug is chosen amongst drugs that are considered as therapeutically similar, and the price of the reference drug is reimbursed. For drugs that are more expensive than the reference drug, the patient has to pay the expenses above the reference price. An index price is the maximum refundable price to pharmacies for drugs within an index group. An index group consists of therapeutically interchangeable drugs. The price is refunded independent of which drug is dispensed.

Key messages

- **The use of reference pricing policies made by governments, non-government organisations or private insurers compared to not setting such pricing policies:**
  - Can reduce third party drug expenditures by inducing a shift in drug use towards less expensive drugs
  - produces no adverse effects on health
- **Reference pricing may not lead to any difference in total use of drugs and drug expenditures**
- **It is not known whether reference pricing affects drug prices, health care utilisation and any of the health outcomes measured.**
- **Index pricing may slightly reduce the price of the generic drug compared with no intervention and may not lead to any difference on the price of the brand drug.**
- **Some other factors must be considered when assessing whether the intervention effects are likely to be transferable to other settings because all of the studies included were developed in high-income countries.**

Who is this summary for?

People making decisions concerning use of pharmaceutical pricing and purchasing policies.

This summary includes:

- **Key findings** from research based on a systematic review
- **Considerations about the relevance of this research** for low- and middle-income countries

Not included:

- Recommendations
- Additional evidence not included in the systematic review
- Detailed descriptions of interventions or their implementation

This summary is based on the following systematic review:

Aaserud M, Dahlgren AT, Kösters JP, Oxman AD, Ramsay C, Sturm H. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD005979. DOI: 10.1002/14651858.CD005979.

What is a systematic review?

A summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise the relevant research, and to collect and analyse data from the included studies.

SUPPORT – an international collaboration funded by the EU 6th Framework Programme to support the use of policy relevant reviews and trials to inform decisions about maternal and child health in low- and middle-income countries.
www.support-collaboration.org

Glossary of terms used in this report:
www.support-collaboration.org/summaries/explanations.htm

Background references on this topic:
See back page.

Background

Large amounts of health care money are spent on drugs and these amounts are increasing. These increases put pressure on policy makers and insurers to control drug expenditures and to do so without causing adverse effects on health or increasing health care utilisation or other costs. Pharmaceutical pricing and purchasing policies intend to determine or affect the prices that are paid for drugs. They can be targeted at different components of drug prices – such as wholesale prices, retail prices, drug taxes and reimbursement prices. These policies can have an impact on drug expenditures in two main ways – directly, through price changes, and indirectly, through drug use changes related to the price changes. This summary shows evidence related with reference pricing and index pricing.

How this summary was prepared

After searching widely for systematic reviews that can help inform decisions about health systems, we have selected ones that provide information that is relevant to low- and middle-income countries. The methods used to assess the quality of the review and to make judgements about its relevance are described here: www.support-collaboration.org/summaries/methods.htm

Knowing what's not known is important

A good quality review might not find any studies from low- and middle-income countries or might not find any well-designed studies. Although that is disappointing, it is important to know what is not known as well as what is known.

About the systematic review underlying this summary

Review objective: To determine the effects of pharmaceutical pricing and purchasing policies on drug use, healthcare utilisation, health outcomes and costs (expenditures).

	What the review authors searched for	What the review authors found
Interventions	Randomised controlled trials (RCT), non-randomised controlled trials (CCT), controlled repeated measures studies (CRM), interrupted time series analyses (ITS) and controlled before-after studies (CBA) of policies on price and purchasing that determine or are intended to affect the price that is paid for drugs.	11 studies were found. Some of them had more than one design i.e. different designs for different outcomes 7 ITS 1 ITS/CBA/CRM 1 CRM/RM 2 CBA/RM This review found evidence for reference pricing (10 studies) and index pricing (1 study).
Participants	Health care consumers and providers	In all the Canadian studies the patients were Pharmacare beneficiaries: senior citizens aged 65 years and older. The other studies included all beneficiaries of national drug insurance plans, including vulnerable groups of people from all ages.
Settings	Large jurisdiction or system of care. Jurisdictions could be regional, national or international. Studies within organisations, such as health maintenance organisations were included if the organisation was multi-sited and served a large population.	The reference pricing studies: Canada (6), USA (1), Australia (1), Germany (1) and Sweden (1). The index pricing study was from Norway (1)
Outcomes	Drug use (prescribed, dispensed or actually used), Healthcare utilisation, Health outcomes, Costs (expenditures), including drug costs and prices, other health care costs and policy administration costs.	Seven studies reported a single effect measure (one outcome) and four did not specify a primary outcome. None of the studies presented data on all outcomes and none reported administration costs.

Date of most recent search: October 2005.

Limitations: This review has minor limitations.

Aaserud M, Dahlgren AT, Kösters JP, Oxman AD, Ramsay C, Sturm H. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD005979. DOI: 10.1002/14651858.CD005979

Summary of findings

This review includes 11 studies evaluating the effects of pharmaceutical pricing and purchasing policies. All of them were done in developed countries (Canada, USA, Australia, Germany, Sweden and Norway). None of the studies presented data on all outcomes. The studies provided data on drug use (7 studies), drug expenditures from a drug insurer's perspective (5), drug prices (3), health outcomes (2), and health care utilisation (4). None of the studies reported effects on patient drug expenditures or other costs (either intervention costs or those in other parts of the health service).

1) Reference pricing

Ten out of the 11 studies in the review evaluated this intervention.

- **Reference pricing may increase the use of reference drugs and decrease the use of cost share drug compared with no intervention.**
- **Reference pricing may not lead to any difference in total use drugs and drug expenditures**
- **It is not known whether reference pricing affects drug prices, health care utilisation and any of the health outcomes measured**

About the quality of evidence (GRADE)

⊕⊕⊕⊕
High: Further research is very unlikely to change our confidence in the estimate of effect.

⊕⊕⊕◯
Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

⊕⊕◯◯
Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

⊕◯◯◯
Very low: We are very uncertain about the estimate.

For more information, see last page

Outcomes	Impact	Number of participants (studies)	Quality of the evidence (GRADE)
Drug use: Reference Drug	Use of reference drug increased by 60 to 196% immediately after a transition period following the introduction of the policy. At follow up (6 months to a year) the relative increase of the drug was larger in one study and smaller in two.	(4 studies)	⊕⊕⊕◯ Moderate
Drug use: Cost share drug	Use of cost share drug decreased immediately by 19 to 42%. In 1 out of 3 studies that provided data at 6 months, a larger reduction was observed.	(4 studies)	⊕⊕⊕◯ Moderate
Total use of drugs	The effect was smaller and not consistent (-9% to +11%)	(2 studies)	⊕⊕◯◯ Low
Drug expenditures	There was a trend towards an immediate reduction in expenditures for the drug in the reference group targeted (ranging from -5% to 50%)	(4 studies)	⊕⊕◯◯ Low
Drug prices	A reduction in drug prices was shown ranging from 11% to 26% for different reference drug groups.	(2 studies)	⊕◯◯◯ Very low
Health outcomes and health care utilisation	There were no significant differences in any of the health outcomes and health care utilisation measured.	(4 studies)	⊕◯◯◯ Very low

p: p-value GRADE: GRADE Working Group grades of evidence (see above and last page)

2) Index pricing

This review identified one study from Norway evaluating this intervention.

➔ **Index pricing may reduce the use of brand drug and increase the use of a generic drug compared with no intervention**

➔ **Index pricing may slightly reduce the price of the generic drug compared with no intervention and may not lead to any difference on the price of the brand drug**

Index pricing

Patients or population: No specific information provided
Settings: Norway, national public drug insurance
Intervention: Index pricing on six groups of active substances
Comparison: No index pricing

Outcomes	Impact	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Drug use: Reference Drug	Use of generic drug increased by 114% (immediate) and 55% (six months) after a transition period following the introduction of the index pricing system.	(1 study)	⨁⨁◯◯ Low	The effects on use of drugs in the index pricing groups were not analyzed appropriately in the study´s report. Results from reanalysis by reviewers
Drug use: Brand drug	Use of brand drug decreased, relatively, by 29 % (immediate) and 43% (after six months)			
Drug prices	Generic and brand drug prices were both reduced but the latter was not statically significant. Generic drug prices were reduced more (relatively) than the brand drugs. Long-term effects were slightly larger than the short-term effects (-5.3% vs. -4.0% for generic drugs; -1.1% vs. -0.8% for brand drugs)	(1 study)	⨁⨁◯◯ Low	The reduction in brand drug prices was not statistically significant

p: p-value GRADE: GRADE Working Group grades of evidence (see above and last page)

Relevance of the review for low- and middle-income countries

➔ Findings	▷ Interpretation*
APPLICABILITY	
➔ The target population were vulnerable groups covered by national insurance plans. The studies included a reduced group of drugs. ➔All of the 11 studies included were developed in high-income countries. Thus there is uncertainty regarding the transferability of the results to low and middle-income country settings and other drug classes.	▷ *Applicability of these interventions to low and middle-income country settings depends on several factors such as:* – *Availability of adequate incentives for patients, physicians, pharmacists and pharmaceutical companies to comply with the reference price system* – *There should be significant price differences between the drugs in a reference group before the reference price system is introduced, with relatively high prices on the drugs most used.* – *Provision of clinical and managerial information support for users the availability and access to drugs.* – *The quality of generics drugs should be considered.* *The existence of a regulatory framework which allows generic substitution and/or prescribing by International Non-Proprietary Name (INN) could be important for a better system perform .*
EQUITY	
➔ Overall, the targeted population was the beneficiaries of national health insurance plans. However the included studies provided little data regarding differential effects of the interventions for disadvantaged populations within the studied beneficiaries.	▷ *Some interventions relied on technologies such as pharmaceutical drugs, may not always be appropriate when attempting to contact low income households. Implementation of pricing reference in such settings may exacerbate health inequities in population without health care access* ▷ *Doctors should be directly asked to recomend the less expensive medicine included in the reference or index pricing policy to the underserved population.*
ECONOMIC CONSIDERATIONS	
➔ Some of the findings summarised here are based on two- level measures: inmediate and short-term effects after the interventions. The review did not address the long-term effects and how support should best be provided. ➔ Price levels could modify the effects of reference drug pricing. ➔ Reasonable mechanisms for exemptions for patients that need it for medical reasons. ➔ None of the studies provided a full analysis of cost-effectiveness.	▷ *It is not clear if the effects on drug prices would be mantained in the long term. Studies with short-term follow up showed different trends on the effect on prices.* ▷ *To achieve savings there should be significant price differences between the drugs in a reference group before the reference price system is introduced, with relatively high prices on the drugs most used.* ▷ *Too limited exemptions could lead to higher co-payments of the most effective drugs and incentive the prescription of less effective drugs by physicians. Too generous exemptions could reduce the savings, by not shifting the drug use towards cheaper drugs.*
MONITORING & EVALUATION	
➔ Evaluations in the majority of included studies focus on relatively short term outcomes	▷ *Longer-term analyses would provide important supplementary evidence although the risk for bias related to other confounding interventions could increase with the length of the observation period.* ▷ *Availability of pharmaceutical bioequivalence studies are needed to implement safe policies.* ▷ *It is important to have a clear legal provision of what are generics in each country.*

*Judgements made by the authors of this summary, not necessarily those of the review authors, based on the findings of the review and consultation with researchers and policymakers in low- and middle-income countries. For additional details about how these judgements were made see: http://www.support-collaboration.org/summaries/methods.htm

Additional information

Related literature

Austvoll-Dahlgren A, Aaserud M, Vist G, Ramsay C, Oxman AD, Sturm H, Kösters JP, Vernby , Å. Pharmaceutical policies: effects of cap and co-payment on rational drug use. Cochrane Database of Systematic Reviews: Reviews 2008 Issue 1

Sturm Heidrun, Austvoll-Dahlgren Astrid AA, Aaserud Morten, Oxman Andrew D, Ramsay Craig, Vernby Åsa, Kösters Jan Peter. Pharmaceutical policies: effects of financial incentives for prescribers. Cochrane Database of Systematic Reviews: Reviews 2007 Issue 3

Aaserud M, Dahlgren AT, Sturm H, Kösters JP, Hill S, Furberg CD, Grilli R, Henry DA, Oxman AD, Ramsay C, Ross-Degnan D, Soumerai SB. Pharmaceutical policies: effects on rational drug use, an overview of 13 reviews (protocol). Cochrane Database of Systematic Reviews: 2006 Issue 2

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Conflict of interest

None declared. For details, see: www.support-collaboration.org/summaries/coi.htm

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Keywords

All Summaries: evidence-informed health policy, evidence-based, systematic review, health systems research, health care, low- and middle-income countries, developing countries, primary health care.

About quality of evidence (GRADE)

The quality of the evidence is a judgement about the extent to which we can be confident that the estimates of effect are correct. These judgements are made using the GRADE system, and are provided for each outcome. The judgements are based on the type of study design (randomised trials versus observational studies), the risk of bias, the consistency of the results across studies, and the precision of the overall estimate across studies. For each outcome, the quality of the evidence is rated as high, moderate, low or very low using the definitions on page 3.

For more information about GRADE:
www.support-collaboration.org/summaries/grade.htm

SUPPORT collaborators:

The Alliance for Health Policy and Systems Research (HPSR) is an international collaboration aiming to promote the generation and use of health policy and systems research as a means to improve the health systems of developing countries. www.who.int/alliance-hpsr

The Cochrane Effective Practice and Organisation of Care Group (EPOC) is a Collaborative Review Group of the Cochrane Collaboration: an international organisation that aims to help people make well informed decisions about health care by preparing, maintaining and ensuring the accessibility of systematic reviews of the effects of health care interventions.
www.epocoslo.cochrane.org

The Evidence-Informed Policy Network (EVIPNet) is an initiative to promote the use of health research in policymaking. Focusing on low- and middle-income countries, EVIPNet promotes partnerships at the country level between policy-makers, researchers and civil society in order to facilitate both policy development and policy implementation through the use of the best scientific evidence available. www.evipnet.org

For more information:
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