August 2016 – SUPPORT Summary of a systematic review

What are the effects of reference pricing and other pharmaceutical pricing and purchasing policies?

Pharmaceutical pricing and purchasing policies are used to determine or affect the prices that are paid for drugs. This review found evidence for reference pricing, index pricing, and maximum prices. In reference pricing a reference drug is chosen amongst identical or similar medicines or therapeutically equivalent and the price of the reference drug is reimbursed for all the drugs in that group of drugs. For drugs that are more expensive than the reference drug, the patient has to pay the cost above the reference price. An index price is the maximum refundable price to pharmacies for drugs within an index group of therapeutically interchangeable drugs. A maximum price is a fixed price that attempts to secure pharmaceutical prices that are considered 'reasonable' for a given health system.

Key messages

- **Reference pricing may reduce insurers' cumulative drug expenditures by shifting drug use from cost share drugs to reference drugs.**
- **Index pricing may increase the use of generic drugs, reduce the use of brand drugs, slightly reduce the price of generic drugs, and have little or no effect on the price of brand drugs.**
- **It is uncertain whether maximum pricing affects drug expenditures.**
- **The effects of these policies on healthcare utilisation or health outcomes is uncertain.**
- **None of the included studies were conducted in a low-income country.**
- **The effects of other pharmaceutical pricing and purchasing policies are uncertain.**

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-income countries

X 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:

Acosta A, Ciapponi A, Aaserud M, et al. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: 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 was an international project to support the use of policy relevant reviews and trials to inform decisions about maternal and child health in low- and middle-income countries, funded by the European Commission (FP6) and the Canadian Institutes of Health Research.

Glossary of terms used in this report: www.supportsummaries.org/glossary-of-terms

Background references on this topic: See back page

Background

Large amounts of healthcare money are spent on drugs and these amounts are increasing. These increases put pressure on policymakers and insurers to control drug expenditures and to do so without causing adverse effects on health or increasing healthcare utilisation or other costs. Pharmaceutical pricing and purchasing policies are used as cost-containment measures to determine or affect the prices that are paid for drugs. Reference prices can be established based on external prices (from other countries) or, more frequently, internal prices (within a country). Reference pricing establishes a benchmark or reference price within a country which is the maximum level of reimbursement for a group of drugs. Other policies include price controls, maximum prices, index pricing, price negotiations, and volume-based pricing. 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.

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-income countries. The methods used to assess the reliability of the review and to make judgements about its relevance are described here: www.supportsummaries.org/how-support-summaries-are-prepared/

Knowing what's not known is important

A reliable review might not find any studies from low-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.

A lack of evidence does not mean a lack of effects. It means the effects are uncertain. When there is a lack of evidence, consideration should be given to monitoring and evaluating the effects of the intervention, if it is used.

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).

Types of	What the review authors searched for	What the review authors found
Study designs & Interventions	Randomized trials, non-randomized trials, controlled repeated measures studies (CRM), interrupted time series (ITS) studies and controlled before-after (CBA) studies of pharmaceutical pricing and purchasing policies	18 studies were included. Some used more than one design: 14 ITS, 1 ITS/CBA/CRM, 1 CRM/RM and 2 CBA/RM studies. 17 studies evaluated reference pricing, one of which also assessed maximum prices, and 1 study evaluated index pricing.
Participants	Healthcare users and providers	In 8 Canadian studies, the patients were Pharmacare beneficiaries in British Columbia: 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. One German and one Spanish study did not provide information about the participants.
Settings	Large jurisdictions or systems 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.	Canada (8), USA (2), Spain (2), Germany (2), Norway (2), Australia (1) and Sweden (1)
Outcomes	Drug use, healthcare utilisation, health outcomes, costs (expenditures), including drug costs and prices, other healthcare costs and administration costs	Drug use (10), third party (insurance) drug expenditures (9), drug prices (4), drug expenditures savings (5), and patient costs
Date of most recent search: December 2012		
Limitations: This is well-conducted systematic review with only minor limitations.		

Acosta A, Ciapponi A, Aaserud M, et al. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD005979.

Summary of findings

This review included 18 studies evaluating the effects of pharmaceutical pricing and purchasing policies.

1) Reference pricing

17 studies included in the review evaluated the effect of internal reference pricing on reference drugs (drugs that determine the reference price level, which are fully reimbursed) and cost share drugs (more expensive drugs in the same group as the reference drugs, which patients have to pay the difference between reference price drugs and the price of these drugs).
Three studies reported these outcomes one year after the transition period for insurers' cumulative drug expenditures; four studies for insurer's drug expenditures at specific time points, four studies for drug use, and no studies reported healthcare utilisation or health outcomes.

➔ **Reference pricing may reduce insurers' drug expenditures by shifting drug use from cost share drugs to reference drugs. The certainty of this evidence is low.**

About the certainty of the evidence (GRADE) *

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This is sometimes referred to as 'quality of evidence' or 'confidence in the estimate'.

† Substantially different = a large enough difference that it might affect a decision

See last page for more information.

Reference pricing policy compared to no reference pricing

People Beneficiaries drug insurance plans
Settings Canada, USA, Germany
Intervention Reference pricing
Comparison No Reference pricing

Outcomes	Impact: Median relative effect (Range)	Certainty of the evidence (GRADE)
Insurer's cumulative drug expenditures one year after the transition period	**Reference drug*:** Median relative reduction in cumulative drug expenditures of -18% (Range: from -36% to 3%)	⊕⊕◯◯ Low
	Reference drug + cost share drugs:† Relative reduction in cumulative drug expenditures of -1.54%	⊕◯◯◯ Very low
Insurer's drug expenditures one year after the transition period	**Reference drug:** Median relative reduction in drug expenditures of -10% (Range: from -53% to 4%)	⊕⊕◯◯ Low
Drug use one year after the transition period	**Reference drug:** Median relative increase in prescriptions of 15% (Range: from -14% to 166%)	⊕⊕◯◯ Low
	Cost share drugs:‡ Median relative decrease in prescriptions of -39% (Range: from -87% to -17%)	⊕⊕◯◯ Low
Healthcare utilisation	No studies met the inclusion criteria	-
Health outcomes	No studies met the inclusion criteria	-

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

*** Reference drugs:** drugs that determine the reference price level. There is no cost share by the patients for these drugs, which are fully reimbursed. The expectation is that reference pricing will lead to an increase in use of these drugs.
† Reference + cost share drugs: both the reference drugs and the cost share drugs. The expectation is that reference pricing will lead to little or no change in the overall use of these drugs.
‡ Cost share drugs: drugs in the same group as the reference drugs that cost more. Patients have to pay the difference between reference price drugs and the price of these drugs. The expectation is that reference pricing will lead to a decrease in use of these drugs.

2) Index pricing

The review included one study from Norway that evaluated index pricing.

➔ **Index pricing may increase the use of the generic drugs, reduce the use of brand drugs, slightly reduce the price of generic drugs, and have little or no effect on the price of brand drugs. The certainty of this evidence is low.**

Index pricing compared to no index pricing		
People	Beneficiaries of a national drug insurance plan taking one of the following drugs: citalopram (depression), omeprazol (anti-ulcer), cetirizin and loratadin (allergy), enalapril, amlodipin and lisinopril (hypertension), or simvastatin (high cholesterol)	
Settings	Norway	
Intervention	Introduction of index pricing	
Comparison	Prior to introduction of index pricing	
Outcomes	**Relative effect (95% confidence interval)**	Certainty of the evidence (GRADE)
Drug use at 6 months after policy start date	**Generic citalopram**: relative increase 55% (95% CI 11% to 98%) **Brand citalopram**: relative decrease -43% (95% CI -18% to -67%)	⨁⨁◯◯ Low
Drug prices 6 months after policy start date	**Generic drug prices**: -5.30 % (95% CI Not Availabe) **Brand drugs prices**: -1.1 % (95% CI Not Availabe)	⨁⨁◯◯ Low
Drug expenditures	No studies met the inclusion criteria.	-
Healthcare utilisation	No studies met the inclusion criteria.	-
Health outcomes	No studies met the inclusion criteria.	-
GRADE: GRADE Working Group grades of evidence (see above and last page)		

3) Maximum prices

The review included one study from Spain that evaluated maximum prices.

➔ **It is uncertain whether maximum prices affect drug expenditures because the certainty of this evidence is very low.**

Maximum pricing compared to no maximum pricing		
People	Patients taking statins	
Settings	Andalusia, Spain	
Intervention	Introduction of maximum prices	
Comparison	Prior to introduction maximum prices	
Outcomes	**Relative effect (95% confidence interval)**	Certainty of the evidence (GRADE)
Drug expenditure one year after the transition period	21.4% (19.0 to 23.7) increase in volume of sales for all statins.	⨁◯◯◯ Very low
Drug prices	No studies met the inclusion criteria.	-
Healthcare utilisation	No studies met the inclusion criteria.	-
Health outcomes	No studies met the inclusion criteria.	-
Drug use	No studies met the inclusion criteria.	-
GRADE: GRADE Working Group grades of evidence (see above and last page)		

Relevance of the review for low-income countries

➔ Findings	▷ Interpretation*
APPLICABILITY	
➔All of the 18 included studies were in high-income countries.	▷ *The effectiveness of reference pricing in low-income countries may depend on factors such as:* – *Health systems financial arrangements, such as copayments, reimbursment, and cost sharing* – *Access to data sources for prices* – *Availability of adequate incentives for healthcare providers, patients, physicians, pharmacists and pharmaceutical companies to comply with the reference pricing policy* – *Significant price differences between the drugs in the intervention group before reference pricing is introduce* – *Clear information for managers, clinicians and patients* – *Availability and access to drugs in the reference group* – *A regulatory framework that allows generic substitution or prescribing by International Non-Proprietary Name (INN)* – *Appropriate exemptions (Exemptions that are too limited could lead to higher co-payments for appropriate use of more expensive drugs and incentives to use a less effective drug. Exemptions that are too broad could reduce savings by not shifting drug use towards appropriate use of less expensive drugs.)*
EQUITY	
➔ The included studies provided little data regarding differential effects of the interventions for disadvantaged populations.	▷ *Reference pricing might exacerbate health inequities if disadvantaged populations have less access to clear information or the reference drug, or if doctors do not recomend the less expensive drugs to those patients.*
ECONOMIC CONSIDERATIONS	
➔ Long-term effects of reference pricing are uncertain. **➔ No studies reported the cost-effectiveness of pricing policies.**	▷ *Administrative costs, costs associated with potential impacts on health service utilisation, patients' out-of-pocket costs, and long term impacts on costs should be considered if reference pricing is implemented.*
MONITORING & EVALUATION	
➔ Evaluations in the majority of included studies focus on relatively short term effects of reference pricing policies. **➔ Only one study was found that evaluated the effects of index pricing and, maximum prices.**	▷ *The long term effects of reference pricing are uncertain and should be montitored and evaluated, including impacts on health and healthcare utilisation.* ▷ *Index pricing, price controls, maximum prices, price negotiations, volume-based pricing and other pricing and purchasing policies should be rigoursly evaluated.* ▷ *Randomized trials or interrupted time series studies should be used to assess effects on health, overall expenditure, and cost effectiveness.*

*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-income countries. For additional details about how these judgements were made see: www.supportsummaries.org/methods

Additional information

Related literature

Systematic reviews of other pharmaceutical policies:

Luiza VL, Chaves LA, Silva RM, Emmerick ICM, Chaves GC, Fonseca de Araújo SC, Moraes EL, Oxman AD. Pharmaceutical policies: effects of cap and co-payment on rational use of medicines. Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD007017.

Rashidian A, Omidvari AH, Vali Y, Sturm H, Oxman AD. Pharmaceutical policies: effects of financial incentives for prescribers. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD006731.

Green CJ, Maclure M, Fortin PM, Ramsay CR, Aaserud M, Bardal S. Pharmaceutical policies: effects of restrictions on reimbursement. Cochrane Database of Systematic Reviews 2010, Issue 8. Art. No.: CD008654. DOI: 10.1002/14651858.CD008654.

Faden L, Vialle-Valentin C, Ross-Degnan D, Wagner A. Active pharmaceutical management strategies of health insurance systems to improve cost-effective use of medicines in low- and middle-income countries: a systematic review of current evidence. Health Policy 2011; 100:134-43.

Puig-Junoy J. Impact of European pharmaceutical price regulation on generic price competition: a review. Pharmacoeconomics 2010;28(8):649-63.

This summary was prepared by

Agustín Ciapponi, Instituto de Efectividad Clínica y Sanitaria, Buenos Aires, Argentina

Conflict of interest

None declared. For details, see: www.supportsummaries.org/coi

Acknowledgements

This summary has been peer reviewed by: Morten Aaserud, Andy Oxman, Sabine Vogler, Anban Pillay, Esperança Sevene, Alda do Rosário Elias Mariano, Julie Cliff, and Angela Acosta.

This review should be cited as

Acosta A, Ciapponi A, Aaserud M, et al. Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD005979.

The summary should be cited as

Ciapponi A. What are the effects of reference pricing and other pharmaceutical pricing and purchasing policies? A SUPPORT Summary of a systematic review. August 2016. www.supportsummaries.org

About certainty of the evidence (GRADE)

The "certainty of the evidence" is an assessment of how good an indication the research provides of the likely effect; i.e. the likelihood that the effect will be substantially different from what the research found. By "substantially different" we mean a large enough difference that it might affect a decision. These judgements are made using the GRADE system, and are provided for each outcome. The judgements are based on the study design (randomised trials versus observational studies), factors that reduce the certainty (risk of bias, inconsistency, indirectness, imprecision, and publication bias) and factors that increase the certainty (a large effect, a dose response relationship, and plausible confounding). For each outcome, the certainty of the evidence is rated as high, moderate, low or very low using the definitions on page 3.

For more information about GRADE:
www.supportsummaries.org/grade

SUPPORT collaborators:

The Cochrane Effective Practice and Organisation of Care Group (EPOC) is part of the Cochrane Collaboration. The Norwegian EPOC satellite supports the production of Cochrane reviews relevant to health systems in low- and middle-income countries .
www.epocoslo.cochrane.org

The Evidence-Informed Policy Network (EVIPNet) is an initiative to promote the use of health research in policymaking in low- and middle-income countries. www.evipnet.org

The Alliance for Health Policy and Systems Research (HPSR) is an international collaboration that promotes the generation and use of health policy and systems research in low- and middle-income countries.
www.who.int/alliance-hpsr

Norad, the Norwegian Agency for Development Cooperation, supports the Norwegian EPOC satellite and the production of SUPPORT Summaries.
www.norad.no

The Effective Health Care Research Consortium is an international partnership that prepares Cochrane reviews relevant to low-income countries. www.evidence4health.org

To receive e-mail notices of new SUPPORT summaries or provide feedback on this summary, go to:
www.supportsummaries.org/contact