

The risks of therapeutic drug substitution policies

With the aim of controlling health care spending, public authorities in several countries increasingly are regulating the prescription, use and reimbursement of drugs, as in the case of therapeutic substitution policies applied in various forms in Germany, the United Kingdom, New Zealand or Canada. Facing the high cost of certain products, they put doctors and patients under pressure to replace them with cheaper drugs, even if their chemical composition is different, their effectiveness weaker or their side effects stronger.

Although a policy of therapeutic substitution can reduce some pharmaceutical spending, this involves a bureaucratisation of drug use that presents risks for the health of the insured and a potential increase in health care costs. The "market test" and freedom of choice of insured patients remain the sole criteria to determine if therapeutic categories are clearly defined and, in addition, if insurance policies based on these categories provide added value in their view. It is worrying to see – in contrast to the possible adoption of such strategies by insurance companies in competitive situation – that these criteria are missing in the context of the legal monopoly of public health insurance systems.

Bureaucratic substitution

To avoid ambiguity, it is essential to distinguish between generic substitution and therapeutic substitution.

In the former case, patients and doctors are encouraged to replace an original drug whose patent has expired with generic versions that are bio-equivalent and contain the same active ingredients. Such policies are found in several public health insurance systems.

With therapeutic substitution, on the other hand, doctors and patients are urged to replace certain drugs with other patented (but less expensive) drugs or with generic drugs that are not bio-equivalent to the drug that is replaced. In brief, this involves substituting drugs with others that have different chemical compositions and different active molecules.

Accordingly, the health insurance system puts certain drugs together in the same category because they supposedly treat the same conditions. Public authorities view some drugs as interchangeable although they may actually be different even from a medical standpoint (see Figure 1). Specialists characterise such substitutability among drugs as bureaucratic.(1)

There are many reasons that two drugs – even if the public health insurance system sees them as therapeutic substitutes – may nonetheless have different medical effects on patients.

There may be differences in their composition, in their power and dosage, in their speed of absorption, in their bio-availability (fast or slow action, with or without delayed effects), or in their contra-indications or side effects.(2) If a therapeutic substitution policy is however applied, it is fundamental for insured persons to have a choice in terms of medical insurance – and for doctors in terms of prescription – rather than having to endure the bureaucratic decisions of a monopoly.

Substitution encouraged by arbitrary coverage

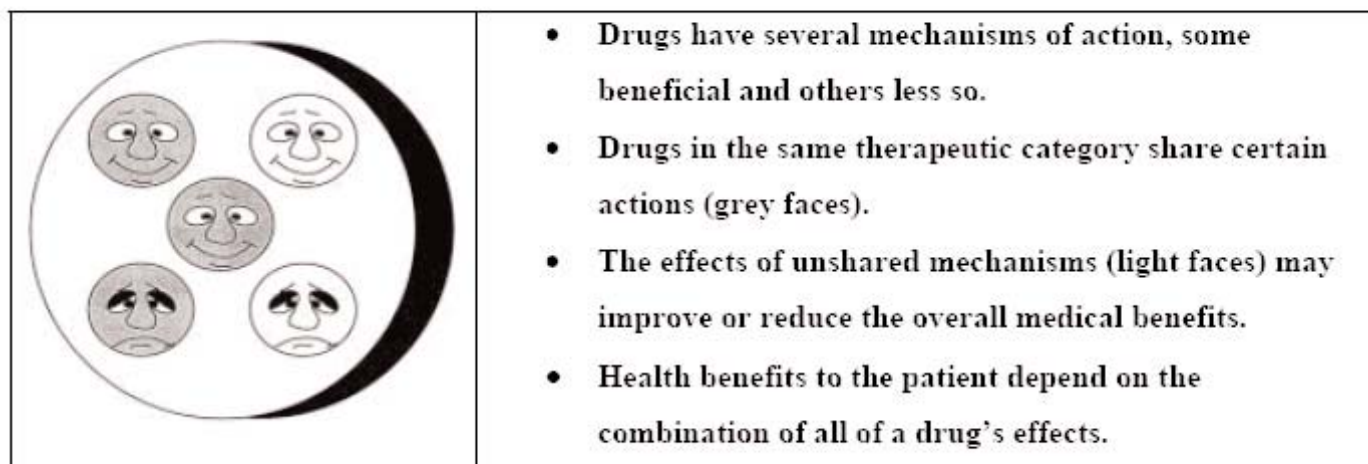
Therapeutic substitution policy goes beyond merely putting different drugs in the same category. It also consists of applying highly specific coverage policies that cause patients to change therapy.

For instance, the health insurance system may decide not to cover drugs in the same category if they are priced higher than another drug chosen as a reference – often among the least

1. See J. Zammit-Lucia and R. Dasgupta, "Reference pricing. The European experience," *Health Policy Review*, Paper No. 10, St. Mary's Hospital Medical School, 1995, cited in Guillem Lopez-Casasnovas and Jaume Puig-Junoy, "Review of the literature on reference pricing," *Working paper*, April 2000, p. 12, available at: <http://www.econ.upf.edu/docs/papers/downloads/362.pdf>.

2. See Guillem Lopez-Casasnovas and Jaume Puig-Junoy, *Op. cit.*, p. 12. See also Valentin Petkantchin, "Economic effects of Germany's reference pricing policy for drugs," *Research paper*, Institut économique Molinari/CNE, 2006, pp. 26-27, available at: <http://www.institutmolinari.org/pubs/germanreferencepricing.pdf>.

Figure 1: Drugs in the same category that are medically different for patients



Source: Curt D. Furberg and Bruce M. Psaty, "Should Evidence-Based Proof of Drug Efficacy Be Extrapolated to a 'Class of Agents'?", *Circulation*, Journal of the American Heart Association, 2003; 108: 2608-2610, available at <http://circ.ahajournals.org/cgi/reprint/108/21/2608>.

expensive in the category (under a reference pricing system that sets a ceiling for coverage in each product group). Insured persons who must pay on their own for a more expensive drug – as is the case in countries including Germany, New Zealand and the Netherlands – have a powerful incentive to change to a less expensive but more broadly covered therapy. In Germany, for example, after the anti-cholesterol drug atorvastatin came under this type of system in 2005, those insured by the public system were pressured in massive numbers into substituting a generic drug – simvastatin – that is chemically different but cheaper since it is available in a generic version.

Health insurance systems may also decide to cover only one drug in a given category. Pressure is exerted on doctors to prescribe these drugs, and there is an even stronger incentive for patients to use them: other than the drug in question, no drugs at all are covered.

Such policies have been instituted, for example, in the Canadian province of British Columbia where officials running a public insurance program, Pharmacare, decided in 2003 to cover only a single anti-ulcer drug in the proton pump inhibitor category. Patients following other therapies had to change and opt for the drug designated by the public authorities if they wanted to be covered.⁽³⁾ Doctors had to prescribe this drug automatically to new patients.

In the United Kingdom, doctors have had financial incentives since 2004 to change therapies on a broad scale, abandoning prescriptions for the anti-cholesterol drug atorvastatin in favour of another molecule, simvastatin. It is expected that other drug categories will be subjected to the same therapeutic substitution policy, although it is being challenged in the courts.⁽⁴⁾

Incentives to change therapy for a cheaper drug become all the stronger in that the main source of information for patients comes from the public health insurance systems. There are risks of bias due to their monopoly position and the priority given to cost controls.

Substitution that restrains doctors and poses risks for patients

To begin with, the existence of several drugs to treat the same conditions offers advantages. Each patient reacts differently to drugs. The existence of different active substances for the same illness, giving doctors a choice based on each patient's individual case, allows for treatment to be personalized. A policy of therapeutic substitution goes against this logic: doctors and patients are encouraged to be part of a massive shift, adopting the same therapy determined by public authorities.

Second, such substitution in favour of cheaper drugs, conducted on a broad scale and

3. See the document from the Canadian Society of Intestinal Research titled "Stemming Rising Drug Costs & Providing Quality Patient Care: A Delicate Balance - Therapeutic Substitution of Proton Pump Inhibitors (PPIs) - The BC PharmaCare Experience," January 2005, p. 4, available at: http://www.badgut.com/pdf/csir_ppi_impact_statement.pdf.

4. See the article "Government faces legal challenge on drug switching," *Pulse*, 5 July 2007, available at: <http://www.pulsetoday.co.uk/story.asp?storycode=4113265>.

involving a significant proportion of insured persons, may produce its own risks. A change in therapy could result in less effective drugs being administered, with more side effects and different interactions with other drugs taken by individual patients.

A number of examples illustrate the existence of such risks (see Table 1).

Insured persons in New Zealand were thus pressured in the late 1990s to replace their anti-cholesterol therapy with a less expensive drug

cardio-vascular incidents, conducted by a cardiology specialist at the North Staffordshire University Hospital. This drug switching from atorvastatin to simvastatin was associated with a mortality rate more than three times higher and an increase in the patient cardiac readmission rate at the hospital (44% compared to 33% for patients to whom atorvastatin was prescribed). According to the study, “wholesale change from an effective treatment to one less efficacious might adversely affect patients' morbidity and mortality.”(8)

Table 1: Illustration of risks related to drug therapy switching

Country	Drug category	Consequences of change in therapy
New Zealand	Statins	Rises in cholesterol levels and higher risk of cardio-vascular incidents
British Columbia, Canada	Proton pump inhibitors	Ineffectiveness in 25% of patients
United Kingdom	Statins	Mortality rate up from 5% to 17% Readmission rate up from 33% to 44%

Sources: Evan Begg and al. (2003), *Op. cit.*; Canadian Society of Intestinal Research (2005), *Op. cit.*; Rob Butler and James Wainright (2007), *Op. cit.*

judged by bureaucrats to be perfectly substitutable. What happened later is that those who switched experienced substantial rises in their cholesterol levels, resulting in higher risk of cardio-vascular incidents.(5)

In British Columbia, six months after a therapeutic substitution policy was instituted for anti-ulcer drugs in July 2003, nearly 25% of patients who opted for the cheaper drug referred had to stop taking it because of its therapeutic ineffectiveness.(6) As stated by a Canadian specialist, "thousands of people went from being stabilized on a medication, to experiencing severe heartburn and side effects including diarrhea, vomiting, nausea, chest pain, and fatigue."(7)

In the United Kingdom, the risks from the change between two anti-cholesterol drugs were observed in a study on patients at high risk of

Substitutability between two products makes sense only if consumers appreciate it. Also, substitutability between two drugs goes beyond medical considerations and is justified only if it brings added value for patients. The policy of therapeutic substitution gives insured persons and their doctors no voice in the matter. In reality, this is a bureaucratic classification that patients cannot reject – if the risks and drawbacks exceed the advantages – by subscribing to a competing insurance provider.

A policy that is a potential source of added costs

An insurance provider in a competitive situation could have incentives to substitute cheaper drugs if it turned out they could in fact be substitutable in the eyes of insured customers and their doctors. These are the people who end

5. See among others Evan Begg, Andrew Sidwell, Sharon Gardiner, Gary Nicholls and Russell Scott, “The sorry saga of the statins in New Zealand - pharmacopolitics versus patient care,” *Journal of the New Zealand Medical Association*, 14 March 2003, Vol. 116 No. 1170, available at <http://www.nzma.org.nz/journal/116-1170/360/content.pdf>.

6. See the document from the Canadian Society of Intestinal Research, 2005, *Op. cit.*, p. 4; author's calculations.

7. See Gail Attara, “Does one size really fit all?,” *The Inside Tract*, Canadian Society of Intestinal Research, 158, November/December 2006, p. 13.

8. See Rob Butler and James Wainright, “Cholesterol lowering in patients with CHD and metabolic syndrome,” *The Lancet*, Volume 369, Number 9555, 6 January 2007, available at: <http://www.thelancet.com/journals/lancet/article/PIIS0140673607600257/fulltext>. See also Berkeley Phillips, Craig Roberts, Amy E. Rudolph, Steve Morant, Fayaz Aziz and Christopher P. O'Regan, “Switching Statins: The Impact on Patient Outcomes,” study presented to the Congress of the European Society of Cardiology, Vienna, 1-5 September 2007, available at http://online.wsj.com/media/WSJ070905_SwitchingStatinsTheImpacto.pdf.

up deciding and who, in case it proves to be a failure, will have grounds for changing to a competing insurance company. An insurance provider that engages in therapeutic substitution would thus have incentives to take account of all the effects of this policy in terms of expenses.

Public health insurance systems, on the other hand, have a captive customer base. With political pressure to cut pharmaceutical spending, they can apply measures that may achieve savings with respect to a drug or category of drugs, but add to the cost of other items elsewhere in the health care system.

A policy of substitution is far from unlikely to cause added costs and extra use of medical resources. Complications due to a wholesale change in therapy may necessitate extra spending because of the fact that more visits to the doctor will be required to check the performances of the new drug, along with more analyses and more tests. More resources are also needed in the event of poor interaction or poor acceptance of the new drug by the patient.

The report of the Canadian Society of Intestinal Research sums up the situation well in this regard in comments on the experience in British Columbia: "forced therapeutic substitution policy has resulted in increased health care costs due to increased doctors' visits, increased hospital utilisation, increased diagnostic testing, increased workload of doctors and pharmacists, and increased bureaucracy for health care and government officials."⁽⁹⁾

The rise in the hospital readmission rate – as with the English experience – may more than offset the savings connected to the therapeutic substitution of a drug that is less expensive but also less effective.

To these financial costs must obviously be added the non-monetary, but nonetheless very real, costs to patients in terms of lost time or suffering due to the policy of therapeutic substitution.

Conclusion

When a therapy, with the correct dosage and the right combination, has been found to be effective, the risks for a patient in changing therapy must be taken into account by health insurers. The notion of substitutability between two drugs ultimately is subject to evaluation by patients, assisted by their doctors. What counts is not only that bureaucrats consider two drugs to be substitutable but that this is also true in the eyes of patients, for their own personal cases.

Seeking to present certain lower-cost drugs as substitutable for patients may be a legitimate strategy for an insurance provider. However, for such a policy truly to benefit patients, and for its risks to be taken effectively into account, insurers must be submitted to competition and to the market test. Insured persons must have the choice of changing insurers if they feel that therapeutic substitution not only is inadequate and brings no added value in their view but that, on the contrary, it illegitimately increases risks to their health.



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9. See the document of the Canadian Society of Intestinal Research, *Op. cit.*, p. 2.