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Pharmaceutical policy: cost containment and its impact

Pricing pharmaceuticals

Generic medicines: savings to health care systems?

Innovation and regulation in the pharmaceutical sector

Orphan drugs: challenges for economic evaluation • Public-private partnerships for health and development
Pharmaceutical pricing in France • Parallel trade and cost control • Access to medicines in sub-Saharan Africa

COMMENTARY

Ensuring affordability, safeguarding innovation

Health care systems are under continuous pressure to deliver high quality services that meet ever higher public expectations. They are also acutely aware of the need to contain costs. The direction of pharmaceutical policy is one challenge; for instance what pricing mechanisms help facilitate greater value for money? As Thomas Ceuni and Jim Attridge note in respective articles in this issue of *Eurohealth*, the benefits of pharmaceutical innovation to Europe are substantial; but in the prevailing economic climate how can Europe protect and nourish these industries and safeguard innovation? Moreover, to what extent should restrictions be imposed on access to new medications?

Thus it is to these complex issues that we devote this issue of *Eurohealth*, bringing together perspectives first aired at last year's European Health Forum Gastein. One approach to cost containment is value based pricing (VBP) where price is dependent on the effectiveness of medications in everyday practice. Although effective, as Philippe Sauvage points out, the impacts on overall health care costs in France are negligible. Alistair McGuire et al also note that while VBP may help reduce excessive profits for industry, this may also reduce future research investment or imply that it this is concentrated in areas where the greatest health gains can be predicted.

Such a policy might without careful consideration be short sighted and detrimental to investment in areas such as drugs for rare diseases. Michael Drummond argues here that conventional approaches to cost effectiveness analysis will mean that such drugs, even if developed, are unlikely to be reimbursed. New approaches that capture their social value are required. The parallel trade in drugs can generate a modest downward impact on costs in recipient countries, as Panos Kanavos and Stacey Kowal illustrate, but it can also have an adverse impact on access to medications in exporting countries. Yet at the same time Elisabeth Seeley and Panos Kanavos indicate that across the EU governments continue to pay too much for generic drugs. Clearly, there is much for health systems and the pharmaceutical industry alike to digest.

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Contents

Eurohealth
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Pharmaceutical Policy

- 1 Editorial – Cost containment: impact and consequences
Melinda Hanisch and Panos Kanavos
- 3 Pricing pharmaceuticals: value based pricing in what sense?
Alistair McGuire, Maria Raikou and Panos Kanavos
- 6 Pharmaceutical pricing in France: a critique
Philippe Sauvage
- 8 Can Europe afford innovation?
Thomas B Cueni
- 11 Innovation and regulation in the biopharmaceuticals sector
Jim Attridge
- 16 Challenges in the economic evaluation of orphan drugs
Michael F Drummond
- 18 Generic medicines from a societal perspective: savings for health care systems?
Elizabeth Seeley and Panos Kanavos
- 22 Does pharmaceutical parallel trade serve the objectives of cost control?
Panos Kanavos and Stacey Kowal

European Snapshots

- 27 When will it happen? Paving the way for risk adjustment in Slovakia
Lucia Kossarova

Health and Development

- 29 The 'Price is Right'? Promoting local production for ARVs in Sub-Saharan Africa
Kinsley Wilson, Jillian Cohen-Köhler and Alan Whiteside
- 33 Public-private sector partnerships as a means of development in Africa, in the context of HIV/AIDS
Gavin George and Tim Quinlan

Evidence-informed Decision Making

- 37 "Myth Busters" We can improve quality one doctor at a time
- 39 "Bandolier" On limitations

Monitor

42 Publications

43 Web Watch

44 News from around Europe

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Editorial:

Cost containment: impact and consequences

Melinda Hanisch and Panos Kanavos

Pharmaceutical cost control measures are becoming more widespread and complex as national health systems are under continuous pressure due to ageing populations, increasing incidence of chronic disease, persistent inequalities, and rising citizen expectations of what their health systems should deliver. Often unpredictable pricing and reimbursement controls are employed at the national and, increasingly, regional levels in the name of achieving value for money.

Yet, current approaches to pharmaceutical cost-containment may not achieve long-term health care cost savings. In fact, by discouraging health care innovation and inhibiting access to innovative treatments for patients who need them, they may have a negative impact on long-term costs, health outcomes, and the availability of new medical innovations. Articles in this issue, based on presentations made at the 2007 European Health Forum Gastein, provide evidence and argumentation that cost containment policies should be assessed in terms of their long-term effect on budgets, health benefits and access to care. They highlight the need for health care systems to continuously monitor policy implementation and evaluate performance of individual policy measures in a transparent and robust manner.

Ambiguous budget impact

With regards to their primary objective – lowering costs – it is hard to argue that on a short term basis some supply and demand measures such as volume or profit controls, rebates or paybacks, can achieve some degree of annual savings. However,

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these are often used in an unpredictable manner and their actual budgetary significance may be limited. For instance, Philippe Sauvage in this issue notes that in the case of France, rebates account for only about 1–2% of total annual pharmaceutical expenditure.¹ Consequently, while such measures may allow governments to redirect resources, they may not deliver huge savings.

Ironically, some cost containment policies may result in not more but less efficient use of limited health care resources. A prime example is reference pricing, which rewards generics with higher prices than they would have under competitive market conditions. Seeley and Kanavos in this issue demonstrate that in some European countries reference pricing produces relatively low levels of competition in the generics sector and higher than average prices for payers.² In Germany, France, Italy and Spain, prices for generics cluster around the reference price, and decline more slowly over time than in countries where generics operate in more competitive environments. As a result, governments that promote the use of generics in an effort to achieve savings in their pharmaceutical budget may actually spend more than they might if free pricing were allowed in that segment of the market. Thus fewer resources are available for payers to spend on innovative treatments.

There is a substantial body of evidence on the favourable long-term economic benefits of innovative medicines and treatments, which often offer the potential to more efficiently manage disease. The use of new medicines has been associated with significant reductions in mortality, lost work days, and other health care costs, resulting in a net reduction in the cost of treating a given condition.^{3–5} Other research has also confirmed that advances in medical science and technology were instrumental in the reduction of avoidable mortality in industrialised countries in the

latter part of the twentieth century.⁶ Restricting access to new medicines solely on the basis of containing static costs, then, represents a short-termist perspective both from an economic and a public health standpoint.

Reduced patient access

In the broader context, varying and complex pricing and reimbursement policies in Europe can cause both significant overall delays in access to new medicines across the region, and also large disparities in access between citizens of individual countries. Despite its limitations, the most recent European Federation of Pharmaceutical Industries and Associations WAIT (Waiting to Access Innovative Therapies) Indicator Report showed that patients in some Member States may wait more than a year longer than those elsewhere for access to the same medicine.⁷ This is in conflict with EU Member State commitments to address health inequalities.

In a similar vein, the current trend toward the use of health technology assessment (HTA) in pricing and reimbursement decisions highlights the conflict between cost effectiveness and societal values. Among others, the case of orphan drugs demonstrates that cost-effectiveness alone cannot determine when a new medicine provides value for money.⁸ Using HTA to make decisions about access to treatment for patients with unmet medical needs implies a trade-off between cost-effectiveness and societal values which may or may not coincide with citizen expectations.

Of course, from a financial standpoint the effect of this *de facto* restriction in patient access to innovative treatments would be to reduce the potential health gains such treatments might bestow, and the accompanying economic benefit. Therefore, any short term budget savings would be negated in the long term by increased health care costs.

A damper on future medicines

The aggregate effect of national cost containment policies in Europe may be to reduce the future availability of new medicines by failing to properly recognise the value of new products and reward the risks of pharmaceutical innovation.

As Jim Attridge notes in this issue, innovative pharmaceutical companies operate in a field of intense and increasing competition, and must simultaneously deliver value for money to their customers and sufficient levels of return to investors.⁹ Research and discovery is not an entrepreneurial activity but a long-term sustained process performed in the context of a portfolio of similar scientific efforts. Innovation occurs in increments rather than breakthrough events, and it is this incremental innovation which drives the discovery process, builds scientific knowledge and leads eventually to new waves of medical technology. Accordingly, company decisions regarding the scope and direction of pharmaceutical research are also necessarily long term in nature. This translates into huge risks if for some reason research outputs are not able to earn an appropriate return on investment.

Cost containment policies can increase this risk significantly. For example, therapeutic ('jumbo group') reference pricing, by grouping together patented and off-patent medicines, and by not distinguishing between the first and subsequent entrants in a therapeutic class, as a rule does not recognise the value of any existing incremental innovation and calls into question the benefits of new products. As a result, the incentive for companies to continue other related avenues of research is reduced. For instance, past major advances in medical technology which have been the product of incremental innovation, such as the immunosuppressant cyclosporine, might not have been available to patients if incremental innovation had not been rewarded.¹⁰ Similarly, HTA as it is currently applied to determine market access in several countries, has added to the atmosphere of uncertainty for new medicines in that HTA processes may not be sufficiently transparent, and that HTA methodologies cannot accurately measure the true value of a new medicine before it reaches the market.

The economic regulation of pharmaceuticals also directly contradicts current efforts to stimulate economic competitiveness in Europe in the spirit of the Lisbon Agenda. As Jim Attridge points

out, "the EU courts life sciences research through the Innovative Medicines Initiative and other national programmes with one hand, and with the other hand punishes the very products of this research."⁹ In the global competition for attracting high-technology investment, it is almost self-explanatory that Europe can hardly afford this paradox.

In short, economic regulation of medicines as it is pursued in Europe today often sends the wrong signals to companies engaged in the high risk endeavour of research and development of new medicines. As a result of the unpredictability and complexity of many pharmaceutical cost containment measures, companies must bring new products to market without definitive knowledge of the pricing and reimbursement environment. The uncertainty of return on investment in turn has a negative impact on decisions concerning the development of new treatments.

Concluding remarks

That pharmaceutical cost containment achieves its central mission – containing the rate of growth of health care costs – is questionable. Individual policies, such as price freezes or price cuts, or broader strategies such as generic policies, may have only a small and temporary impact on budgets. Health insurers may in fact incur higher costs than needed – either by overpaying for generics, or by being 'penny wise and pound foolish' in the way they allow disease to be prevented or managed. Market or competition-based pricing policies often seem to allow greater headroom for innovative medicines, allowing society to reap the benefits of advances in medical technology.

Further, cost-containment often restricts patient access to new treatments and creates significant disparities in access across Europe. This not only deeply conflicts with Member States' commitment to equity and solidarity and addressing inequalities in access to health care, but also denies society the long-term economic benefits of medical innovation. Lastly, by focusing on short term cost savings at the expense of long term savings and health gains, and by denying recognition and reward for innovation and its associated risks, cost containment policies discourage investment in and development of new medicines which can fulfil unmet medical need and curb health care cost.

While the use of cost containment policies appears to be inevitable and unavoidable,

arguments presented in this issue suggest the need for additional consideration on the intended and unintended impact of policies, and for continued efforts to strike a balance between financial sustainability, public health and continued investment in innovation. Importantly, they also highlight the role payers can play in assessing the short and long-term effectiveness and performance of their policies, strategically (re-)deploying resources where they are most needed and, as the Commission also points out, treating health care as a wealth-enhancing investment¹¹ rather than an unavoidably rising cost.

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Pricing pharmaceuticals: Value based pricing in what sense?

Alistair McGuire, Maria Raikou and Panos Kanavos

Summary: Reimbursement of pharmaceuticals ought to provide both incentives for and reward innovation, as well as set a price which reflects the market value of the product. In other words reimbursement must reward both dynamic and static efficiency in the pharmaceutical sector. Within the UK a debate has emerged concerning whether the Pharmaceutical Pricing and Reimbursement Scheme, a profits based regulatory scheme, should be replaced with a value based pricing scheme. This article defines these competing reimbursement schemes and outlines their relative costs and benefits.

Keywords: Pharmaceutical Pricing, PPRS, Value Based Pricing, UK

The continuing debate over the pricing of pharmaceuticals has emphasised the relationship of pricing to value. The recent UK Office of Fair Trading report on pricing within the UK¹ recommends the replacement of the Pharmaceutical Pricing Reimbursement Scheme (PPRS), essentially regulation through profit control supplemented with ad hoc intervention on prices through the imposition of price cuts if deemed necessary with a specific system of value-based pricing (VBP). It begins by defining the objectives of the regulatory environment and follows with a discussion of the PPRS and proposed VBP structure, with accompanying critical appraisal at both the conceptual and practical levels.

The aim here is neither to support, nor reject either system, but rather to provide a critical overview of both. In assessing the replacement of the PPRS with VBP a considered evaluation of the costs and benefits must be undertaken. Importantly, two aspects of efficiency must be considered: static efficiency, which relates to the pricing of a product about to enter or already on the market, and dynamic efficiency which relates to product inno-

vation as applied to future market conditions. Given the tensions in securing static and dynamic efficiency simultaneously there may be an optimal trade-off in the pursuit of both goals.

Background

The value derived from regulated products should reflect societal value. This is normally presented as the aggregate of producer and consumer surplus, defined as the welfare gain from consumers purchasing products at the lowest possible market price and producer gain in terms of the fair market return achieved on sales. Given the nature of pharmaceutical products and their reliance on high costs concentrated in the research and development (R&D) process, there is an argued tendency towards monopoly production, as these costs tend to prohibit entry into the market.

Monopoly is associated with the exploitation of consumer surplus through control over prices, with a monopolist gaining a higher return (profit) through selling reduced quantity at higher price. Conversely, monopoly power could be associated with higher levels of innovation, given the potential use of profits to protect future market status. With an estimated ten thousand molecules to be screened for every product developed for the market, it takes on average around £350 million (€443 million) to produce a pharmaceutical product.

Indeed, patent protection is given as an incentive to invest in such high R&D costs, thus protecting producer profits. While such protection is offered against molecule structure rather than specific products, patent protection can co-exist with product competition. Moreover, it can be noted that pure monopoly is never really consistent with investment in R&D. If monopoly protection exists there is little incentive to invest; investment in R&D is only pursued if there is potential future competition in the market, which leads to current competitive strategies that manifest themselves in investments in R&D processes.

PPRS

Of course regulation can also reduce consumer surplus if it distorts the rate at which products bestowing health benefits to individuals flow onto the market. The existing form of regulation within the UK is based on the PPRS which couples rate of return control with price control. The scheme imposes profit controls, through setting maximum and minimum achievable profit levels for individual company sales to the National Health Service (NHS), coupled with price controls which allow initial price setting freedom on launch but then impose restrictions on subsequent price increases. Increasingly there have also been price cuts on existing products when the PPRS has been renegotiated every five years or so. Finally, price modulation is allowed through firms altering prices within their product portfolio as

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long as expected volume-weighted revenue remains constant. The price cutting aspects of the scheme are arbitrary and open to gaming; higher price setting in anticipation of cuts.

The PPRS is often portrayed as being dominated by the profit controlled element, although it has been argued this has increasingly become less and less true as the profit rebate associated with PPRS is implemented with less and less frequency.² It is well known that the rate of return regulation that characterises the PPRS tends to over-capitalisation. Interpretation of the PPRS in this form could lead to an argument that it supports possible subsidisation of R&D capital. However, this is unlikely within the specific form of the PPRS as individual companies are unlikely to over-estimate costs, thus protecting profits, as costs are subject to a form of benchmarking.

Of course, given the multinational dominance of the industry, internal cost shifting remains a possibility. Indeed the lack of payback within the PPRS over recent years is consistent, as the OFT pointed out, with transfer pricing across different geographical areas, leading to the PPRS being ineffective. Moreover, even if Towse³ is correct in suggesting that, as the PPRS is a profit regulation rather than a regulation of economic return, with R&D merely being an expenditure, it remains the case that the allowance of relatively high rates of return in the pharmaceutical industry *may* lead to an over-investment in R&D facilities coupled with high producer surplus.

The “*may*” is emphasised to highlight the uncertainty that surrounds this issue. The optimal degree of investment is of course determined by the return in terms of social value. This depends on the combined value of consumer and producer surplus. Producers may acquire consumer surplus through price differentiation with little impact on total surplus value. They may also achieve excessive profits through abuse of monopoly power and therefore reduce total surplus or may influence future producer and consumer surplus through investment decisions. The first two possibilities are associated with static considerations, the later with dynamic considerations. There may also be equity concerns over who should realise any surplus value; what share of the value inherent in the R&D process should be returned to consumers and producers? The motivation to move to a VBP regulation appears to be that the current reim-

bursement of pharmaceutical products in the UK has tended to support delivery of producer surplus rather than protection of consumer welfare. The balance between dynamic and static efficiency has tended towards a regulatory environment that has supported producers rather than consumers.

This conclusion is consistent with the view that the PPRS does appear to provide healthy incentives for R&D investment through a profits allowance accompanied with pricing freedom for individual products within the given profit level, albeit moderated by the possibility of imposed price cuts. These price cuts are somewhat inefficient as they are implemented across the board and possibly with some time lag, depending on when the product is launched and PPRS negotiations take place. A tentative conclusion is that the PPRS provides incentives aimed at securing dynamic efficiency, indeed some argue that such incentives are provided by a scheme that featherbeds individual firms’ dynamic efficiency, while at the same time allowing considerable latitude with respect to static efficiency.

The role of NICE

PPRS regulation of price is currently complemented, although by no means comprehensively, by the cost-effectiveness analysis of specific interventions undertaken by the National Institute for Health and Clinical Evidence (NICE) in England, Wales and Northern Ireland. While obviously this is not a regulatory authority dealing with pricing mechanisms *per se*, for those drugs which are assessed it does imply some additional pricing constraints if the product is going to be purchased by the NHS. In circumstances where a product is assessed by NICE, this weakens the ability of companies to modulate prices across products in their portfolios. The complementary role of other regulators on the operation of the PPRS therefore ought not to be overlooked.

The existing system, combining patent protection with the PPRS and occasional NICE cost-effectiveness evaluations, could operate to underpin static and dynamic efficiency within the UK with respect to pharmaceutical products. Patent protection relates to molecule structure and not product protection; for example, a number of statins remain under patent protection competing with each other for market share. The operation of the PPRS allows free pricing within a profits

constraint across different products within a firm’s portfolio. The cost-effectiveness evaluation of some interventions then ensures an implicit control on price, if not across the board, then at least through threat. The role of NICE could, of course, be extended to further augment the PPRS without replacement.

Value Based Pricing

VBP regulation has been suggested as a replacement for PPRS in the OFT report.¹ This would establish a maximum price for a pharmaceutical based on an *ex ante* evaluation for new products and a rolling *ex post* evaluation of existing products. This might be supplemented by risk sharing contracts if there was insufficient evidence to allow a full *ex ante* appraisal, with the price being contingent on the realisation of treatment benefits. There would be non-linear pricing arrangements for different indications and sub-group applications, with generic pricing once off-patent if a generic was available. The evaluation would be based on the existing NICE type cost-effectiveness evaluations. In other words VBP would appear to be an extension of the type of evaluation already conducted as part of the valuation of a range of therapies that NICE deems to be cost-effective within the existing system. The proposed system would retain patent protection and combine this with a widened role for cost-effectiveness in pricing to pursue VBP. The emphasis therefore moves towards static efficiency, with the emphasis on value for money at launch, and away from dynamic efficiency.

A number of problems exist in using cost-effectiveness analysis, pertinent to both its existing use and future role in establishing VBP. One major issue relates to the use of clinical trial data to establish effectiveness. The objectives of such trials are normally to establish safety, tolerability and efficacy within a tightly controlled population. Such trials are normally short-term and therefore do not establish the long-term health effects required for a comprehensive cost-effectiveness analysis. The results from such trials are currently aimed at a different set of regulatory bodies than those concerned with pricing and reimbursement. Modelling, based on increasingly accepted methods, must therefore be undertaken not only for this reason but also as health economic data on endpoints and resource use are not routinely incorporated within clinical trial studies. For example, if Quality Adjusted Life Year (QALYs), the preferred outcome measure

for NICE, are to reflect outcomes over which the surplus is to be evaluated, then most products will have to transform clinical trial outcome measures into QALYs. Given that pricing and reimbursement is required on launch, the *ex ante* fast track appraisal method envisaged by the OFT will place heavy demands on evaluation data. This is not impossible to achieve, but it is open to uncertainty; hence the combination of *ex ante* and *ex post* evaluations.

Currently, NICE uses the Single Technology Appraisal Process (STAs) as a means of assessing comparator products within a limited time period.⁴ If used as the basis for VBP, as envisaged by the OFT, the data would have to be available quickly. This would, in principle, require head-to-head studies or indirect comparisons through some form of meta-analysis of a new product with existing comparator therapies. It is unlikely that this information would be readily available in all situations or clinical trials, increasingly designed with a global perspective, tapered to fulfil regulatory criteria in one market for pricing purposes. There may, in any case, be different standard comparator therapies in different geographical markets. Data limitations will therefore be inevitable, as within the current STA assessments, where there is already great pressure given the objective of realising a market price to ensure access to the product under evaluation. NICE however, currently lives within these data constraints, so it may not be impossible for VBP to tolerate such constraints.

NICE allows a considerable threshold of between £20,000 (€25,000) and £30,000 (€37,500) per QALY gained for acceptable treatment up-take. If this form of analysis is to be used for VBP a stricter threshold value, based on the changing opportunity cost of new treatments, will be required.⁵ This would only not be the case if sub-group analysis and non-linear pricing, as proposed in the OFT report, were permissible. While this could lead to a more flexible regulatory pricing mechanism, and in the extreme giving perfect pricing discrimination with all surplus being acquired by the company, in most circumstance this is very unlikely given the data required to substantiate such claims under the proposed VBP system. Even substantiating claims across a small number of sub-groups would be highly data intensive. Moreover, if VBP is attached to a risk-sharing analysis, as allowed in the OFT

report, given circumstances where there is a lack of data available to perform an *ex ante* analysis (for example, with chronic disease treatments), sub-group analysis will be even more unlikely as the risk transfer to companies increases with an increasing number of sub-groups. It can also be noted that such risk sharing schemes erode patent protection in any case as the length of time required to establish regulatory worth is increased.

Challenges

It is clear that both the PPRS and the envisaged VBP schemes have drawbacks. The efficiency of their implementation is largely concerned with the relative costs of implementation. VBP essentially drops the PPRS and considers an extended role for NICE type evaluations. This is supplemented with sub-group and risk-sharing analysis. Data availability is the major constraint. *Ex post* risk-sharing is only envisaged as a means of supporting situations where there is not enough available data for an *ex ante* consideration. The lag time for the implementation of *ex post* risk-sharing is of obvious interest. Too short a lag will not overcome data constraints and will not provide much incentive to participate; too long could lead to distortion of the perceived gains in static efficiency with firms gaining undue producer surplus.

Non-linear pricing within a VBP environment relies on the greater availability of data and a greater willingness of companies to accept risky pricing strategies. It is unlikely that non-linear pricing could result in perfect price discrimination,⁵ given the data requirements on sub-groups which would necessarily have to support pursuit of such a policy. Indeed, given that VBP is premised on an incentive with respect to dynamic efficiency that is meant to persuade firms to invest in those areas where health benefit is greatest, it is not clear that non-linear pricing will necessarily work towards this objective.

Long lead time mitigates against a firm *ex ante* considering non-linear pricing as a strategy, unless pursuing from the beginning of their investment a very sophisticated data collection and pricing strategy. As investment progresses the firm would have to pursue evidence on sub-groups and a range of indications, assuming that it had the foresight to see the aggregate rewards early in the investment cycle. Alternatively if a firm became aware of potential benefits of market segmen-

tation, it would have to start collecting data at a late stage of development.

While such data constraints are not insurmountable, they are substantial and have to be faced as an additional investment to secure value for money pricing. It would seem of doubtful regulatory efficiency to allow firms to pursue extensive *ex post* evaluations or risk-sharing agreements on the basis of non-linear pricing proposals.

Investment in R&D

Most of the discussion above relates to issues of static efficiency. The impact of VBP has been less discussed with respect to dynamic efficiency. The envisaged regulatory environment is one where companies would pursue investment over a long time frame, given that there is a chance of reward based on a product price set in accordance with achieved health benefit. It is envisaged that firms will have an incentive to invest in areas where achievable health benefits are greatest. Areas of high disease prevalence where there is unmet need are obvious areas for high returns. However, investment in R&D may be mitigated if these are also areas characterised by a long lag between research and product development or by high risks to individual firms. Firms may place a lower value on R&D projects than society in some areas leading to general under-investment.

Even if VBP leads to a firm adopting a concentration of investment in those areas where there is perceived to be greatest health gain, this may result over time in a narrowing of the general R&D base, with subsequent loss in the external economies of scale which tend to characterise larger R&D establishments. A narrow based focus may tend to cause risk-avoidance within firms, without the broad base to spread risk, which may lead to a lower valuation of research projects, in the absence of external economies, than in society at large. Large R&D programmes in the pharmaceutical sector may have inherent advantages through economies of scale and scope that are difficult to identify but are nonetheless present.⁶

The size of a firm may itself encourage innovation and a wide range of potential products. In this sense VBP seems consistent with a narrowing of firms' technological capacities as they become more specialised in those areas with the greatest potential health gain for their investment portfolio. This seems to undermine one aspect of a productive R&D capability; the

ability to maintain a broad technological base which would otherwise provide a form of insurance against inevitable research dead-ends. Within the context of VBP this occurs not only within but also potentially across companies as they will have an incentive to compete for areas of highest health gain.

Conclusion

The design of optimal regulation is not straightforward. The current discussion of how to regulate pharmaceutical prices in the UK highlights this. The existing UK regulatory environment has been voluntary and has allowed high rates of return as an incentive to motivate R&D. The proposed system emphasises that the presumed high prices consistent with these returns have eroded consumer surplus. Such a debate brings a clear perspective to the tensions associated with the pursuit of static and dynamic efficiency concerns. With either regulation there is a trade-off; with the PPRS the trade-off is that static efficiency concerns are relaxed to allow the pursuit of dynamic efficiency through the provision of incentives for R&D investments and, hopefully, a quick rate of market launch of beneficial products. Under the proposed VBM the trade-off would be to tighten static efficiency concerns against the cost of potentially reduced incentives for R&D. The actual judgement regarding which is, of course, an empirical one.

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Pharmaceutical pricing in France: a critique

Philippe Sauvage

Summary: In France, pharmaceutical pricing relies on an ex ante evaluation of the medical value of drugs. Prices are negotiated on the basis of an industry-wide contract between drug manufacturers and the Health Products Pricing Committee (Comité Economique des Produits de Santé). Together the Committee and the drug companies sign a number of contractual agreements, which give the national health system a variety of flexible means to monitor prices and drug use, also ensuring that public resources are properly allocated. Some drugs have different levels of therapeutic value, depending on who takes them. These products in particular need close monitoring. Rebate policies are one of the tools available to control such spending. The economic efficiency of such rebates should not be overestimated; in practice they do not significantly decrease spending.

Keywords: Pharmaceutical Policy, Reimbursement, Rebates, Evaluation, Added Therapeutic Value

A few words on pricing and reimbursement

Pricing and reimbursement decisions in France are taken on a step by step basis. Firstly there is the market authorisation of a drug at a national or European level. The product is then evaluated by an independent scientific committee, prior to price negotiations. This Transparency Committee, named after the European Transparency Directive, assesses the therapeutic value, or clinical benefits of a drug, and proceeds to compare it with existing therapies. Drugs are evaluated against two sets of complex criteria: their therapeutic value (*service médical rendu*) and added therapeutic value (*amélioration du service médical rendu*).

Therapeutic value takes into account the severity of the illness and the efficacy of

the drug. Although a drug's therapeutic value does not impact on pricing, it helps determine its reimbursement rate. The added therapeutic value of a drug is a relative notion, as it is measured through a comparison with the clinical benefits of existing drugs or therapies. Thus, it represents the 'added health gain' or the 'relative effectiveness' of a drug, compared to its alternatives. The main problem in assessing this added therapeutic value is the time it takes, as well as the lack of proper clinical trials against alternative products on the market.

Nonetheless, such evaluations are necessary and need to take place prior to any decision on reimbursement. They should also fit within the timeframe (normally ninety days) to reach a decision on reimbursement set out in the 1989 Transparency Directive (Directive 89/105/EEC). The duration of such evaluations have in fact decreased in recent years and now meet this requirement, while fast track procedures were also introduced to help assess those drugs of great significance.

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There are five levels of added therapeutic value (ATV) that may be assigned to a drug after comparison assessing the degree of improvement against existing therapies:

- I – major improvement;
- II – significant improvement;
- III – moderate improvement;
- IV – minor improvement; and
- V – no improvement.

ATV is the most influential factor in drug pricing. It is re-evaluated every five years or earlier, if the committee chooses. In most cases, a re-evaluation includes additional assessment of the drug's therapeutic value under real life conditions.

It should also be noted that evaluation and price negotiation is carried out before any reimbursement schemes are devised. In most cases this is before the drug is launched in the market. There are also specific procedures that allow a drug to be put on a temporary reimbursement list in the case of interventions for life threatening diseases. These procedures are however used prudently, reflecting the fact that once an individual is placed on a course of therapy it then becomes very difficult to interrupt such treatment. Thus without care these procedures might provide pharmaceutical companies with considerable leverage in subsequent negotiations on the longer term use of a drug.

General agreements and rules

Following the determination of added therapeutic value, the Health Product Pricing Committee negotiates with the drug manufacturer. The Committee follows a number of guidelines defined either by law or by general agreement with the pharmaceutical industry. All negotiations are contractual and may include provisions regarding volume limitations, rebates and price re-evaluations.

There are, however, two main rules: (1) ATV level V drugs can only be added to the reimbursement list if they allow savings for the social security system; and (2) prices of drugs which offer considerable improvement over existing therapies (levels I to III) must remain stable for the subsequent five years, and in line with other major European markets.

The agreement between the pharmaceutical industry and the Pricing Committee also includes a general payback procedure. Every year, parliament votes to approve a prospective budget for the public health insurance system, defining target increase-

rates (so called "k-rates") for each category of expenditure. When the increase in pharmaceutical expenditure exceeds the respective k-rate, the manufacturer must contribute via a rebate scheme.

Rebates are calculated for each company on the basis of how innovative their products are, i.e. their ATV levels and their share of the increase in expenditure (orphan drugs are exempt). Rates are subdivided by category and homogenous groups of products within each category, for example, statins. The pharmaceutical industry contribution can represent a large part of the excess, often 40% or more. 65% of rebate payments are proportional to turnover and 35% to growth.

The rationale for rebates

In recent years, the pharmaceutical industry has undergone great change. Manufacturers now tend to develop more complex products, targeted at very specific sub-groups of the population, or sometimes even sub-groups of a specific disease. Now that the most simple of ailments can be cured by drugs that are becoming ever cheaper (for example, generic drugs), companies need to find new, often biotech-oriented solutions, in order to address more complex medical conditions.

One consequence is that the characteristics of the target populations of many important drugs are becoming ever more similar to those for orphan drugs. The sheer cost of many of these drugs makes it crucial for the public health authorities to ensure that they are prescribed only to those who can benefit from their use. Physicians, of course, play a crucial role when it comes to ensuring that these new drugs are prescribed correctly. France has devised a number of schemes to encourage appropriate prescribing practices. Yet drug manufacturers also play a large part in how their products will be used. That is why the agreements they conclude with the Pricing Committee can include provisions on the volume of prescriptions, dosages and advertising campaigns. Companies are also held accountable for the correct use of their products.

Interestingly, French physicians tend to be heavier prescribers of drugs than most of their European counterparts. France's pharmaceutical history and culture, as well as the comparatively low price of many widely used drugs (i.e. aspirin and paracetamol), have led to a situation where 90% of doctor-patient appointments end with a prescription. It is critical therefore that all

products are used by their intended targeted populations.

Take a product that was recently included in the reimbursement list. It provides a very high level of improvement for a small population (population A). Its market authorisation is also valid for a much larger population (population B), even though it does not provide them with any health gain, compared to existing, very cheap therapies. It would obviously have been wrong to ban access to this product for population B. But why should the health care system pay a premium on a product that does not give most people any added medical value?

There are two options. One can either devise a reimbursement scheme for everyone, defining a 'median price' between the innovative part and the ordinary part of a product, or one could limit drastically the use of this product beyond the small target population. Nevertheless, both options call for scrupulous monitoring. Depending on market share and prices, rebate rates can be adjusted according to the terms of contracts. Furthermore, rebates are expected when a manufacturer's advertising campaign is not in line with a product's characteristics.

The rebate scheme for drugs has recently grown more complex. Increased access to hospital drugs has been granted through the creation of an 'additional list'. It registers expensive and innovative hospital drugs that may be reimbursed by hospitals, on top of diagnostic-related group payments. The reason for this scheme is that it is necessary to provide general access to expensive drugs. Yet such drugs may be used for very different purposes from one hospital to the other, depending on the nature of patients being treated. For example, a world-renowned cancer specialist may need to resort to more expensive drugs for complex cases, compared with an oncologist in a less specialised hospital. If both hospitals receive the same level of funding the more difficult cases will not necessarily get what they need. And if both hospitals are given the same access to expensive drugs, they will not have incentives to control their costs.

To go back to the earlier example, if a given drug is more expensive than its competitor in the B market, so much so that its competitor does not feature in the additional list, hospitals would have an

incentive to use the drug in both A and B markets, since they do not need to pay for it. Resources, in such a case, are not efficiently allocated. The solution is to restrict access to the additional list as much as possible, and monitor the use of the product.

Let us complicate things a bit further and consider that one such drug shares the A market with another expensive drug. If both drugs are authorised for the whole target population, they will spill into the B market without their manufacturers having to face any rebates. This is the reason why it was recently made possible to limit use to a given volume of products.

Conclusion

These examples demonstrate that rebate schemes are necessary to limit price increases in France and to monitor drug use. However, their impact should not be overestimated. Prices are essential in any regulated market to send the right message. Many factors in the system may lead to spontaneous price adjustments without the need to resort to rebates.

All in all, rebates in France do not account for more than 1% or 2 % of the total expenditure on pharmaceutical products in any given year. This is somewhere in the range of €500 million per annum, a sum which seems considerable in its own right. But it is still small, compared with the €25 billion that France spends on drugs every year. Such a modest share in the total health care budget means that one cannot accuse rebate schemes of distorting prices. Yet rebates still represent a crucial tool to control the use of very specific products. In some cases, the fact that they potentially may be used is more important than their actual use. They allow the public health care system to monitor marketing, advertising and use.

In conclusion, rebates do play a part in the correct allocation of health-insurance resources. The general rebate also helps to devise a more accurate estimate of annual pharmaceutical expenditures. An emphasis should be placed on the importance of the ex ante evaluation of any drug: it provides the health care system with a large number of tactics to control drug spending. Moreover, it also facilitates access to very innovative drugs by those patients in most need.

Can Europe afford innovation?

Thomas B Cueni

Summary: Finding a balance between reward for innovation, improved patient access to innovative medicines and controlling budgets remains a challenge for decision-makers, patients and industry in Europe. The industry has a clear preference for market-based pricing, yet, the predominance of administered pricing in most European countries, given, alternatives need to be explored. Today, Europe sees health care innovation too much as a cost rather than an asset. There is a need for constructive dialogue on what constitutes the value of new medicines and how added therapeutic value should be rewarded.

Keywords: Innovation, Value Based Pricing, Pricing, Reimbursement, Added Therapeutic Value

Pricing – an unpredictable lottery?

Finding a consensus among different stakeholders on what constitutes ‘value of innovation’ is almost like squaring a circle. From an industry perspective, it appears that payers are primarily interested in controlling costs, are unwilling to grant premiums for innovative new medicines and are delaying patient access to therapeutic advances. From a payer perspective, it may look as if pharmaceutical companies expect to recoup their investments into research and development (R&D), irrespective of added therapeutic value, want to meet or better exceed shareholder expectations for hefty profits, and are not concerned about escalating health care costs.

The truth may be somewhere in the middle and the problem for companies is less the requirement to justify higher prices with added value than the lack of predictability and erratic changes in national pricing and reimbursement systems. This is reflected in the World Health Organization’s report on Priority Medicines for Europe and the World: “at present, reimbursed prices are determined

by each country, often in a black box fashion where country reimbursement authorities set prices to ensure access and control costs. This results in an unpredictable lottery for companies who have brought a product to market through a series of regulatory hurdles and still do not know what the final reimbursed price will be.”¹ Now, the question of what constitutes a “just price” has been debated since Saint Augustine but it is interesting to note a statement from Vice-President Verheugen, Commissioner in charge of DG Enterprise, who said, “to begin with, the pricing for innovative products in Europe...needs to be improved.”²

Innovation – driver of economic growth

The underlying problem is that the European health care debate focuses too much on regarding innovation as a cost factor. Medical progress is seen as burden rather than an asset, and the concern is often about the high cost of new medicines rather than about the burden of disease. Such an approach is short sighted. In modern economies, innovation, i.e. technological progress, is the most important driver of competitiveness and economic growth. The effect of R&D activities on economic growth and productivity gains has been proven by numerous empirical studies. The main difference between the success story of market economies and all other economic systems “is free-market pressures that force firms into a continuing process of innovation, because it becomes a matter of life and death for many of

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them...It seems indisputable that innovation accounts for much of this enviable growth record," is how William J Baumol, the eminent US economist, put it.³

We live longer and in better health

The crux of today's health care debate is that pharmaceutical innovation focuses on the needs of the patients whereas the health policy debate is dominated by numbers and cost containment. Today, we can expect to live thirty years longer than one hundred years ago. Huge reductions in mortality (for example, in HIV/AIDS, many cancers or cardiovascular diseases) and a significant progress in the quality of life are the results of some big and many small steps in biomedical research. Contrary to common belief, higher life expectancy does not inevitably lead to degenerative disease and ever longer stays in nursing homes because we cannot only expect to live longer but we get older in better health. Higher blood pressure and cardiovascular disease can be controlled with antihypertensive drugs and cholesterol-lowering drugs, knee or hip replacements keep us from wheelchairs, and some cancers can be controlled or even cured thanks to newer targeted medicines. Yet, there remain huge challenges in areas such as Alzheimer's disease, multiple sclerosis, many cancers or orphan diseases.

Cost containment, however, dominates the debate in a majority of countries. Reference pricing, budget ceilings, tough generics policies and price cuts are the most widely used cost containment measures. Often, new policy measures are initiated before the success or failures of their predecessors are evaluated. Indeed, Jaime Espin and Joan Rovira recently concluded that it was difficult to assess the effectiveness of many of these policies since the (positive) impact on budgets has to be weighed against the (negative) impact on patient access to innovative treatments.⁴

Nonetheless, it would be unfair to state that the picture is all bleak. Many governments are trying to square the circle between rewarding innovation and improving patient access while maintaining budget control. In a number of European countries such as Ireland, France and the UK, framework agreements between the government and industry have been signed, and the EU Commission's agenda has generally been driven by an attempt to find a good balance between health policy and industrial policy objectives. Although some

people from industry are impatient with the slow process of implementation of the recommendations of the G10 Medicines High Level Group⁵ or the Pharmaceutical Forum, legislative measures such as the Supplementary Protection Certificate (SPC) restoring lost patent term, the setting up of an efficient European market approval system with the European Medicines Agency (EMA), improved regulations for data exclusivity, incentives for research into orphan diseases, better incentives for research into paediatric medicines as well as the most recent Innovative Medicines Initiative (IMI) all aim to make Europe more innovation-friendly for patients and industry alike. However, the predominance of Member States' more serious concerns about health care budgets has limited the positive impact of some of these EU-driven industrial policy initiatives, which explains why the EU was unable to regain relative attractiveness for pharmaceutical R&D investments over the past decade.

No progress on pricing and reimbursement

Whereas progress in the regulatory area is undeniable, the main issue impacting the economics of the industry has not been addressed. In many instances, pricing and reimbursement still remains an "unpredictable lottery". The debate on an industrial policy for the pharmaceutical industry in Europe has led to a broad agreement that inadequate reward for innovation and significant delays in patient access to new medicines play a major role in Europe's declining competitiveness as a location for pharmaceutical R&D. However, it is obvious that progress will only be possible if a balance can be struck between the objectives of rewarding innovation, improving patient access to innovative medicines and controlling health care budgets.

The first issue is how to put value to a new medicine? In principle, *market-based pricing* is the most efficient way to allocate resources and reward innovation. However, where there is a single government payer, there is no functioning market. Thus, alternatives to market-based pricing are needed. To an economist the recurrent theme of *cost-based pricing* is amazing. Critics of the industry ask how can we put a price on a product if one does not know the cost of manufacturing, or the cost of research and development? Cost-plus pricing was used historically in a number of countries such as Spain, Italy

and Japan. This method not only creates controversies about the measurement of costs but is neither efficient, nor effective. Cost-based pricing rewards input (investments) rather than outcomes (better cures). Whereas market-based pricing rewards the successful innovator handsomely and penalises failure, cost-plus pricing inherently favours risk-averse research and can lead to perverse results.

Other methods to value new medicines include therapeutic comparison (*value based pricing*), where clinical relevance and cost effectiveness are taken into consideration, or *country baskets* (price comparison with certain reference countries). Such country baskets are primarily driven by political considerations, since a comparison with prices in other countries is always a comparison of different pricing and reimbursement policies based on the concern that a country does not want to pay more than a neighbour or an economically comparable country. Companies naturally adjust to pricing signals. If they know, for example, that rich countries are unlikely to accept a higher price than poor countries, they will adjust their European price bands accordingly. This also leaves open the question of how to determine prices in the 'first' Member States that will serve later as the reference point.

Accepting the reality of administered pricing in most European countries, value-based pricing, i.e. reimbursement on the basis of comparative effectiveness is certainly the most interesting and politically relevant approach. Criteria which should be considered when assessing value include:

- Does the innovation address a high unmet medical need?
- Does it reflect a major, important or moderate clinical improvement?
- Is there an alternative treatment available and if so, is the superiority of the new treatment plausibly demonstrated?
- Is there sufficient choice to allow all patients to be treated?
- Is there a favourable cost-benefit ratio?
- What is the impact on public health?
- What is the broader societal benefit and cost?

Added value merits reward

The pharmaceutical industry has to accept that it can only receive a higher price for better value. Whereas a patent, by defi-

tion, equals an innovation from a technical perspective, a patent is not necessarily equivalent for added therapeutic value. A consequence of therapeutic comparison and value-based pricing is that major reward will be limited to significant innovation. However, the industry concern today is probably less the reward for breakthrough innovation which tends to receive a market price within a fairly narrow global band but the unwillingness in some countries to acknowledge incremental innovation. Medical progress rarely occurs in big leaps, small steps are the norm rather than the exception. Whereas the immunosuppressant Cyclosporine was a historic breakthrough for transplant surgery, the tremendous progress in transplant surgery since the first application of cyclosporine in 1978, was the result of many small steps in surgery as well as pharmaceutical research.

Without the acceptance of reward for incremental innovations, patients might not have received the benefits of step-by-step medical progress so important in many disease categories. However, negative examples of how innovation is valued in Europe today include the mixing of patented and off-patent products under reference price systems ('Jumbo' groups in Germany) which by definition pull up the price of generics and penalise patented medicines. Furthermore, in some cases health technology assessment is not used to identify value but to put up new hurdles. And in some countries with arbitrary budget thresholds or payback mechanisms, the pharmaceutical industry is often seen as the lender of last resort.

Huge differences in patient access

Valuing and rewarding innovation does not mean much if patients have no access to innovative medicines. In reality, not only costs vary from country to country, but also access to new drugs is subject to substantial differences. For example, the Karolinska report⁶ shows that the uptake of new cancer drugs is above average in Switzerland, Spain, Austria, and, more recently also in France, but is below average in countries such as UK, Norway or Poland. The IMS/EFPIA Patients W.A.I.T. Indicator⁷ shows that patients in some countries have to wait more than a year longer than patients in other European countries before they have access to new medicines. Do such differences matter given that there are critics from epidemiology who challenge the statistical approach of the Karolinska

study? It may be a subjective view but if I were a patient, I would not want to wait until somebody has proven the Karolinska study with epidemiological and statistical data beyond doubt. Personally, I believe that the Eurocare data on cancer survival⁸ do show significant differences in survival rates across European countries. There may be multiple factors but access to innovative treatments is most likely one of them.

Guiding principles – a fair balance

Industry is aware that finding solutions to the questions of value and affordability of innovation needs a willingness for dialogue from all stakeholders. While emphasising the need for reward and patient access to innovation, the budgetary implications and constraints cannot be ignored. The Pricing Working Group of the High Level Pharmaceutical Forum has worked out a set of guiding principles which demonstrate that dialogue between Commission, Member States and multiple stakeholders is possible. These guiding principles attempt a fair balance trying to meet the needs of patients, payers and industry alike. In particular, the principles recognise the need to not only reward breakthrough innovation but to also reward incremental innovation. The problem of uncertainty at the time of market approval is acknowledged and patient-friendly solutions are advocated. Furthermore, the paper contains an important conclusion regarding national pricing policies. In short, it states that national price controls are not meant to have an extraterritorial impact and that affordable prices for different countries in Europe should allow differentiation. The consensus on the 'guiding principles' was only possible because participants in the dialogue knew that they had to look for a fair balance between the potentially conflicting objectives of reward for innovation, improved patient access and the need for sustainable funding. More of this kind of dialogue is needed, in particular at Member States' level, to find new solutions to old problems.

Innovation is crucial to Europe and its economy. Pharmaceutical innovation brings benefits to patients and wealth to society. A balance between industrial policy and health policy needs to be maintained. In this respect, pricing is an indicator of society's willingness to pay for health benefits. Dialogue, openness and more flexible arrangements are required from governments and industry when it

comes to pricing decisions. Value-based pricing means a significant reward for breakthrough innovation and an incremental reward for incremental innovation. A common understanding of what constitutes value will remain a challenge. However, it was a comforting experience for an industry participant in the High Level Pharmaceutical Forum's Pricing Working Group that agreement on fairly broad "characteristics of innovation" was reached without much controversy.

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Innovation and regulation in the biopharmaceuticals sector

Jim Attridge

Summary: The innovative performance of the biopharmaceutical sector has weakened over recent years, most noticeably in Europe. This article summarises research on models of the innovation process and uses them to analyse the impact of various forms of regulation and incentives on this performance.

Keywords: biopharmaceuticals, innovation, regulation, Europe

This paper addresses two questions. How does biopharmaceutical innovation work? How do changes in EU market regulation impact upon the processes involved?

Innovation processes

Investment in, and the output of the biopharmaceutical sector is a function of three areas of decision-making: (1) individual product life cycle economics; (2) market and Research and Development (R&D) product portfolio risk and return assessments; and (3) sustainable business investment models.

Individual product life cycle models

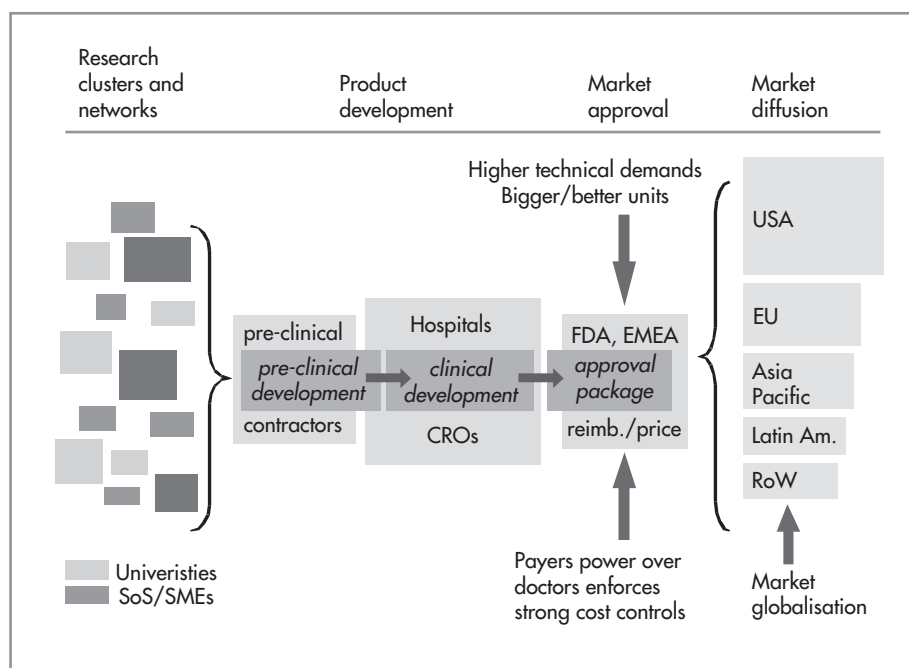
Basic models of product innovation propose a coupling process between two forces: ‘technology push’ based upon the creation of new scientific knowledge and ‘market pull’, based upon a societal need or opportunity.¹ Pharmaceutical innovation has been dominated by ‘technology push’, involving waves of parallel, incremental innovations in physiology, medicine, diagnostic techniques and drug therapies, underpinned by advances in biology, chemistry and other basic sciences. Up until recently the existence of a strong ‘market pull’ force, in the form of demand for better treatments has been largely taken for granted.^{2,3}

This model has four sequential components as shown in Figure 1:³

1. Bioscience and medical knowledge creation, ranging from fundamental advances in our understanding of molecular and cellular structures and processes in living organisms, through to improved clinical knowledge of disease aetiology.
2. Discovery of molecular entities, which in principle can disrupt or block these disease processes, and can be patented as inventions.
3. Product development processes, which through laboratory and clinical work translate the molecular entity into a product, culminating in a market license to sell it.
4. The innovation diffusion process, whereby patients benefit from improved therapy and companies achieve a return on their investment.

The term ‘innovation’ is best defined as a process. Sustainable innovation is one in which incentives exist for it to be continuously repeated in a cyclical manner. Commonly, individual products are called innovations if they have passed through the complete process and have been widely adopted in clinical practice.

Figure 1: A linear model for an individual new medicine



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Experience shows that it takes a new medicine five to ten years and costs many hundreds of millions of euros to meet the high, legally enforced standards for efficacy, safety and quality.⁴ This feature of the medicines innovation process distinguishes it from most other high technology sectors. Thus a classical economic model of innovation suggests that the first innovator to bring a new type of product gets a substantial 'first mover' advantage over any following competitors in the same field of innovation. However those that follow after the first entrant with incremental improvements will probably have the advantage of lower risks and lower development costs. In the biopharmaceutical sector, because of the dominant concern with safety, incremental followers in a class of medicines must perform exactly the same tests and trials required by the regulators for all medicines, incurring essentially the same costs and requiring much the same timescale.⁵

Over the past decade, two significant changes have occurred. At the front end of the process, more complex geographical clusters of academic centres, research institutes, 'spin-off' companies (SoS), small and medium sized enterprises (SMEs) and global pharma research centres have emerged, which create and trade knowledge. At the back end, there is increasing competition between large companies, whose core capabilities are their efficient parallel development processes and their 'global reach' – the ability to achieve timely market diffusion across developed countries.

In general innovation theory, it has proved useful to distinguish between major, or radical innovations and small, or incremental ones. At first sight, for biopharmaceuticals this can be interpreted as the first of a new class of medicines, based upon new understanding of disease processes and a new mode of action (a radical innovation) and follow-on products, which act in a similar way (incremental ones). However, closer inspection of the processes outlined in Figure 1, which lead to the sequential evolution of new product classes, suggests that the reality is more complex and variable.⁶

Biopharmaceuticals innovation at the product level consists of a sequence of three competitive races: (a) The 'research race' to translate original knowledge with useful potential applications into patents; (b) The 'development race' to convert the patented molecules or bio-entities into

technically approvable products; and (c) The 'commercial race' to achieve rapid international uptake of the product for the benefit of patients and to reward the innovator.

For the most part as a consequence of the patent disclosure system and largely transparent clinical research methods, competition in development is conducted in a remarkably open manner at all stages compared to other industrial sectors. In biopharmaceuticals there is little scope for gaining competitive advantage by maintaining high levels of secrecy. Insofar that a 'break-through' or radical step can be identified, it comes at the invention or patent stage and many academic and industrial individuals and centres may claim to have made a contribution to it. The patent system provides the currency through which inventors can sell their knowledge and get rewarded for their contribution.

Over the past decade, a shift in the balance of the technology base of the sector has occurred – from chemical to biological – largely led by the USA. This is a long and complex transition, which has been underway for over twenty years and is still continuing today. Its significance lies in a change in the first phase of the innovation processes in the form of a more profound understanding of disease processes in terms of molecular biology and genetic processes. This has created a dramatic increase in novel bio-markers or bio-targets; new starting points from which research can begin to find molecular entities that can interfere with disease processes in quite new ways. The molecular agents that are emerging from this new era of research may be small molecules, proteins, or biological entities such as monoclonal antibodies. As with all step changes in technology, although opening up new vistas for research, it is in itself highly disruptive of the entire process of development and the economics of innovation. It continues to offer previously unimaginable opportunities to create new therapies to address unmet medical need in some of the most intractable diseases. Some evidence suggests that the very wide scope of new options that have opened up at this early stage, with little experience as to which avenues of research might be most attractive, has of itself contributed to the lower productivity of R&D in recent years.

It has led to the emergence of specialised, biotechnology based companies, a few of which have grown entrepreneurially into

major players, albeit operating in limited disease segments. In response, leading companies have adapted both their strategies and organisational forms and currently are competing to collaborate with or acquire biotech-based SME companies that have sound patent positions.⁶

Efficiency in the development race benefits from highly competitive investment and the organisational capabilities of large companies. The lead in the race to market for a new class of medicines may change hands many times. Also there is little correlation between the order of market entry and the combination of benefit and risk attributes that individual products offer. Thus in the light of mature experience in deploying a new therapeutic class of products, it may be the third, fourth, or fifth entrant which offers the best treatment for a typical patient.⁶ However, others may offer the optimal treatment for more precisely defined patient sub-sets. The order of market entry, often seen as a sign of priority or leadership in achieving success in innovation to the casual observer, is as likely to be a consequence of relative competitiveness in the development race, as a measure of inventiveness or inherent originality of the product active ingredient *per se*.

Therefore simple classifications of new medicines within a class as either 'break-through' or 'me-too',⁸ based upon the order of market entry is inconsistent with numerous studies of the clinical value of individual products.^{9,10} Hence, also the distinction between radical and incremental innovation can be potentially misleading when applied to this sector, where it might be best to reserve the term 'radical' for the class as a whole and to regard *all* products within it as incremental alternatives.

Market and R&D portfolio models

Creating and sustaining a portfolio of R&D projects, which will feed through into a market product portfolio, is a crucial issue in sustaining innovation as a routine, industrial process as opposed to a discontinuous, entrepreneurial one.¹¹ The overall R&D strategy defines the allocation of investments to disease areas. These strategic decisions are long-term because building the necessary capabilities to compete effectively in a given disease sector takes many years. It requires teams with diverse scientific skills, facilities and external relationships, which cannot easily

be replicated or transferred.

Companies continuously review the scientific, medical and commercial viability of a portfolio of around fifty to one hundred projects and must select those that go forward and those that are terminated. Some of these are high-risk, with a low probability of commercial success, while others offer more immediate prospects of a return. Some projects will be in the earliest stages of the six to ten year time-line from early research to market approval, while others will be closer to market entry. Managing the balance of this portfolio over time requires a sophisticated mix of project evaluation techniques, experience and risk-taking judgements. As a very broad generalisation, there is a direct correlation between the risk of failure in translating a project into a clinically approvable and saleable product and its innovativeness, i.e. the more original the potential product concept, the greater the risk of failure.

For leading companies at any given point in time 70–80% of total revenue comes from no more than three to five patented products and correspondingly the prospects for new products emerging from R&D into the market over the next five years will also depend upon no more than three to five key late stage development projects. Hence the rapid failure of just one major late stage development project or an important in-market product can seriously destabilise the business of the company concerned.

Sustainable business models

Biopharmaceutical companies are private sector entities which have a responsibility to provide both value for money to their customers and a level of return to their investors commensurate with the associated risks of loss. Investors constantly switch their investments between industrial sectors based on their prospects. For higher risk, higher return, technology-based industries there is a strong emphasis on evaluating the long-term sustainability of each sectors' business models. For biopharmaceuticals, the contents of R&D pipelines, flows of innovative new products into the market, and the decline and effective 'death' of established products at patent expiry are all scrutinised in sophisticated models.¹¹

Recent work by Porter¹² shows that over the period 1992–2006 major US pharmaceuticals ranked fourth amongst industry sectors in terms of profitability (return on invested capital). On average European

pharmaceutical companies are less profitable than their US counterparts.

The spread of cheap generics across world markets has greatly reduced life cycle revenues over the past decade. A combination of improved cost efficiency through mergers and acquisitions and partial restoration of revenues by global expansion has stabilised the biopharmaceutical business model in the face of this challenge. But, currently revenues are coming under renewed pressure due to a combination of lower prices for both off- and on-patent products and the sustained period of low R&D productivity.¹³ Projections over the next five years¹¹ suggest that if this trend continues, when taken in conjunction with a series of major product patent expiries, it will require companies to radically re-think their business models, reducing costs further to sustain acceptable returns to investors.

The value of innovative medicines and how it is shared

Innovation creates social and economic value which is shared between stakeholders. Teece¹⁴ observed that over the long run, four parties share the value generated by innovations: customers, the innovator, imitators and other suppliers. In practice, defining value and estimating shares is very difficult.

However, recent studies suggest that the share of value created which accrues to medicines innovators may be lower than is commonly believed. In a 25 year retrospective analysis of the use of innovative classes of medicines in the USA for HIV/AIDS, Philipson and Jena¹⁵ assessed a societal benefit of US\$ 1,330 billion compared to only US\$ 63 billion for innovative companies. This is rather less than 5% of the estimated societal gain. They conclude, "despite the high annual costs of these drugs to patients, the low share of social surplus going to innovators raises concerns about advocating cost-effectiveness criteria that would further reduce this share, and hence reduce incentives for innovation".

Similar, recent research by Garrison *et al.*¹⁶ on trastuzumab for breast cancer, and Parvinen¹⁷ on schizophrenia medicines, broadly support this thesis.

Changing patterns of regulation in Europe and their impact on innovation processes

The 'three sequential races' model, outlined above has limitations, notably it

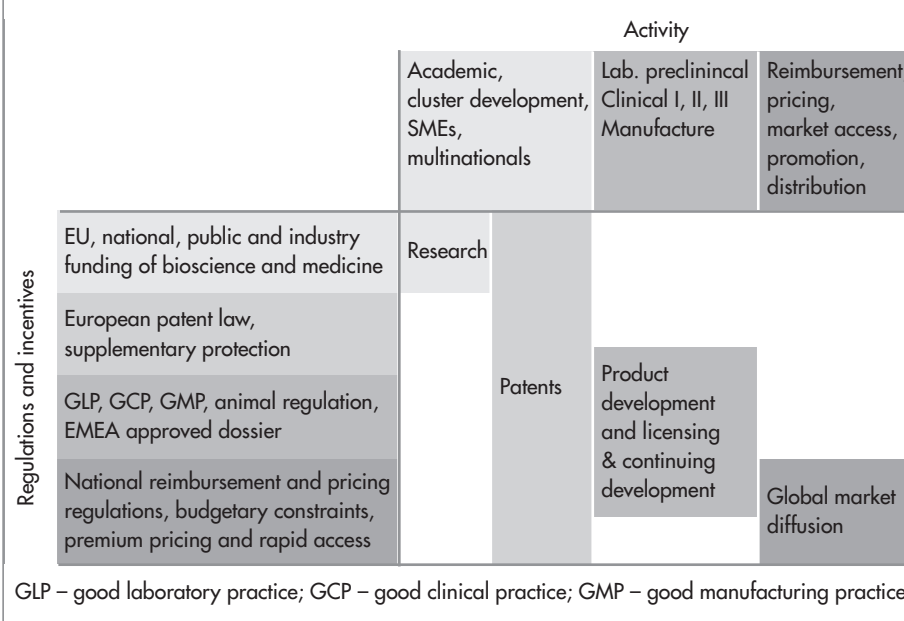
overlooks the fact that product development costs and risks continue at a high level into the market diffusion phase. However, it offers a useful framework within which to assess the impact of changing patterns of technical and market regulation in EU countries.

Recent studies^{18,19} indicate that as part of the change to a biological basis for R&D two important new patterns are emerging in the innovation process. Firstly, the more promising bio-targets are resulting in new medicines that may prove useful over a more diverse range of diseases than in the past. This represents a greater challenge in deciding which of many options to pursue into the expensive clinical phases. Secondly this multiplicity of possible uses is pushing an even higher proportion of the clinical work to explore them in the period after the products launch for its first indication. This latter trend further exacerbates the serious problem now faced in the EU in the use of *ex-ante* health technology assessment (HTA) methods to assess the added value of new products as a basis for determining prices and reimbursed access to national markets. It appears likely that in future the full therapeutic potential of many new products will not be realised or assessable with any degree of accuracy until many years after they first enter the market.

Figure 2 juxtaposes the three phases of innovative activity with the four main areas of government regulation and incentives, which affect each of them, i.e. science and medicines public policy and funding, patent law and exclusivity regulations, EMEA (European Medicines Agency) development regulations, and member state market regulations. We now consider these combinations.

In the race to create new knowledge and invent patentable biologics or chemical entities, global investment continues apace driven by government public sector faith that bioscience will deliver both health and other social benefits and an industrial platform for competitive economic growth. The EU Commission funding through its framework research programmes for bioscience continues to grow and a new 'government-industry' collaboration, the Innovative Medicines Initiative (IMI), has been approved, which will give further impetus to 'academic-industry' collaborations across the EU. However, similar levels of investments by countries as diverse as Australia, South Korea, China and Brazil indicate the

Figure 2: The interplay of regulation and innovative processes



growing intensity of global competition by governments to achieve a stake in these high-tech industry sectors, but overall the prospects for the EU in this area look good.²⁰

In the field of European patent and data exclusivity law, the cornerstone of the incentive system for investment and reward in this sector, useful progress has been made in harmonising and codifying exclusivity criteria and terms.

In the race to develop products, there has been a high profile debate as to whether the multiple requirements of agencies, such as the US FDA (Food and Drug Administration) and EMEA, were stifling innovation because they were too demanding or whether in the light of some late failures of new products in the market phase, that they were too lax and should be strengthened, regardless of the cost and time implications for innovators. An EU sponsored study in 2004¹³ took the optimistic view that if one examined the progression of projects through the development phases, there were grounds for optimism that ‘a bulge’ of successful projects was working its way down pipelines and would restore the output of products entering the market to former levels. More recent assessments of FDA and EMEA product approvals suggest that although this has not happened yet, neither has there been any further decline in product output and it can be argued that the quality, or added value of products now coming to the market is higher than in the recent past. However, sceptics

suggest that the potential of biologics has been much overestimated.^{21,22}

Currently, a joint FDA-EMEA review process is underway aimed at further unifying and streamlining the development requirements. Obviously the incentive to invest in R&D will improve if this can result in lower costs and shorter development time. It may also improve EU competitiveness and limit the haemorrhaging away of development activities to low cost Asian markets.

In the final phase of the innovation process – market diffusion – the race to achieve reimbursement at mutually acceptable prices and acceptance by doctors and patients the situation also looks less promising. Over recent years, many initiatives have been taken by Member States to contain annual expenditure growth in medicines to ‘affordable’ levels. Many of these have just cut prices on all products on a *force majeure* basis. Others have sought to improve the static efficiency of markets through engendering more competition between suppliers.²³ By far the most damaging to the innovative sector has been the initiative pioneered in Germany, therapeutic reference pricing which in effect cuts the prices of all innovative patented products in a class to the level of the cheapest generic in that class.⁵

The National Institute for Health and Clinical Excellence (NICE) operating in England and Wales, has led what is the latest popular approach based upon HTA in some EU markets. This in principle this holds out some prospect to innovators of

discrimination in favour of innovative products in allocating scarce funding. However, the close linkage of decision making to vague notions of health system affordability, which has led to the introduction of an upper limit cost per quality adjusted life year (Qaly) threshold for access to reimbursement, suggest that contrary to this aim, it may well discriminate against the most innovative leading edge advances.²⁴

Regardless of the mechanism, the inescapable consequence of many such initiatives, across the twenty-seven Member States, has been to achieve short-term cost savings for the health systems and reduce revenues for suppliers of innovative products. This, by definition, reduces the dynamic efficiency of the markets and the incentives to invest in R&D. The rationale for such policies is rooted in a belief that the need for health services to contain costs is very great and the innovative industry is robust and can easily sustain its *modus operandi*, despite the cumulative impact of such interventions. The analysis in this paper suggests that, certainly for some EU companies, this premiss will not hold good for much longer.

Conclusions

To summarise, there is good growth in research funding and incentives to invest at the front end of the innovation process, but market opportunities for innovative new products are ever more severely constrained in EU countries at the other end of the process. While the downward pressures on off-patent sectors through generic competition is a perfectly valid approach, the current trend to then use market regulation to formally link these low generic prices to the prices of innovative patented products, forcing them down to close to generic levels is simply incompatible with sustaining a viable EU innovative sector over the long-term. The tension between these two conflicting forces is at the heart of the stress, if not distress, observed in phases II and III of clinical development decision-making where many projects are now terminated.

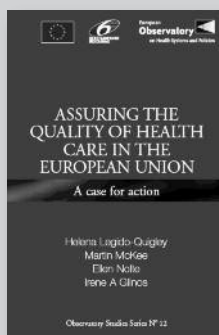
The new HTA methods offer some scope for customers and suppliers to go forward together in a rational manner, but recent English and German experience indicates that the application of ‘thresholds’, reducing to just another cost containment tool appears to be proving irresistible. In the light of this analysis of the innovation

process, the incentive for innovation is only likely to be restored, if short-term, budget driven ex-ante assessments are abandoned and the emphasis placed upon a judgemental approach to giving innovative products the 'benefit of the doubt' at launch, by allowing rapid access to reimbursement at a reasonable price, followed by a rigorous assessment three to five years later with a re-negotiation of prices and, if necessary, the terms for reimbursement.

From a global industry and consumer perspective generally, the fact that only circa 25% of industry revenues come from the EU, whereas around 45% comes from the USA may offer a degree of comfort that the latter will continue to provide the bulwark for sustaining industry business models and innovative output. However, the continuation of such a situation does not augur well for EU industrial policy aspirations to be a world class competitor in this sector in the future.

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Challenges in the economic evaluation of orphan drugs

Michael F Drummond

Summary: Increasing pressures on health care budgets have led to a growing interest in the use of economic evaluation in reimbursement decisions for drugs and other health technologies. Although economic evaluation methods are becoming more established internationally, doubts have been raised about their use in drugs for rare diseases (often known as 'orphan drugs'). This paper discusses the potential deviation between social value and cost-effectiveness, the impact of rarity on the estimation of the cost-effectiveness ratio and the key questions surrounding the economics of orphan drugs.

Keywords: cost-effectiveness analysis, health policy, resource allocation.

Increasing pressures on health care budgets have led to a growing interest in the use of economic evaluation in reimbursement decisions for drugs and other health technologies. Under this approach, an assessment of value for money is undertaken by comparing the incremental costs of the new technology (with respect to relevant existing technologies) with the incremental benefits. The incremental benefits are normally defined in terms of health gain, either by use of a generic measure such as the quality-adjusted life-year (QALY), or by use of a relevant clinical outcome for the disease area concerned.

The economic evaluations do not, of themselves, determine whether a given health technology gives good value for money. This has to be judged against an external standard, such as the cost-effectiveness of interventions that are already funded in the health care system, or an explicit benchmark (or threshold) of willingness-to-pay for a unit of health gain. For example, in England and Wales, the National Institute for Health and Clinical Excellence (NICE) operates a threshold range of £20,000–£30,000 per QALY

gained.¹ Health technologies with an incremental ratio of less than £20,000 per QALY gained are highly likely to be reimbursed; those with a ratio in excess of £30,000 would require other arguments in order for them to be funded.

NICE is unusual in being so specific about its decision-making threshold. Most reimbursement agencies do not reveal their thresholds and, in the case of agencies not using a generic measure like the QALY, such thresholds would be hard to infer.

Although economic evaluation methods are becoming more established internationally,² doubts have been raised about their use in drugs for rare diseases. Most of the orphan drugs appraised to date have cost-effectiveness thresholds well in excess of the 'accepted' level and would not be reimbursed according to conventional criteria. McCabe *et al*^{3,4} argue that this is not an argument for treating orphan drugs any differently from pharmaceuticals in general and question whether there should be any premium for rarity. On the other hand, Drummond *et al*⁵ argue that there may be more to assessing the social value of health technologies than the estimation of the incremental cost-effectiveness ratio. Therefore this paper discusses (i) the potential deviation between social value and cost-effectiveness (ii) the impact of rarity on the estimation of the cost-effectiveness ratio and (iii) the key questions surrounding the economics of orphan drugs.

Potential deviation between social value and cost-effectiveness

As mentioned above, the denominator in the cost-effectiveness ratio is usually a measure of health gain, typically the QALY. In addition, QALYs in the calculation are normally equally weighted; that is, a gain of one QALY is considered to be the same no matter to whom it accrues.

However, an analysis of decisions by the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia⁶ showed that, while decisions followed a general cost-effectiveness logic, it was clear that other factors were taken into account. George *et al* give several reasons for the apparent deviation from the cost-effectiveness criterion. These include the lack or inadequacy of alternative treatments for the disease concerned, perceived need in the community, seriousness of the patient's condition, pursuit of equity, the rule of rescue, as well as access and affordability from the patient perspective and financial implications for the government.

The extent to which these factors do, or should, impact on health care decision-making is a matter for discussion and debate. However, it is clear that most orphan drugs are for serious conditions, for which other treatments may not be available. Orphan drugs also tend to be expensive on a per patient basis, but have limited impact on the health care budget as a whole, as there are so few patients with these health conditions.

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Rarity and the cost-effectiveness ratio

The most obvious impact of rarity on cost is that, because the patient population for most orphan drugs is very small, the costs of research and development (R&D) need to be recovered by charging a much higher cost per patient than for drugs with large sales potential. Although there is some evidence of a relationship between the size of the population and annual treatment cost,⁷ the pricing of all drugs (including orphan drugs) is rather opaque.⁴ Therefore, it is not surprising that decision-makers have some doubts about prices charged. The only audited public statement about the costs of R&D of an orphan drug, in the annual accounts of the Genzyme Corporation, suggests that development costs are substantial, although a little lower than the cost of a mainstream pharmaceutical (mainly because the clinical development programme involves smaller patient numbers).

The main impact of rarity on the estimation of effectiveness is that, given the small patient population, it is difficult to enrol sufficient numbers of patients in clinical studies. Also, because of small numbers, the epidemiology of rare diseases is less well understood, making the projections of long-term benefit, beyond the end of the trial, or from surrogate markers to final clinical outcomes, more speculative. This greatly increases the uncertainty facing the decision-maker when considering orphan medicines.

Key questions surrounding the economics of orphan drugs

How much efficiency is the public willing to trade for access to orphan drugs?

Given their lack of cost-effectiveness, the funding of orphan drugs can only be justified if the public is willing to give up some of the overall health gain produced by the health care system, because access to treatments for rare diseases is perceived to be a socially valuable objective. More exploration of this issue is required, either by surveying members of the public, or by using the 'person trade-off' (PTO) approach to estimating QALYs. This approach,⁸ estimates QALYs by asking respondents how many individuals, with a given disease receiving treatment, would be equivalent to saving one healthy life.

How can social value best be introduced into the technology assessment process?

If there is, indeed, more to the assessment of social value than cost-effectiveness,

these additional elements would need to be incorporated into the assessment process. A different way of weighting QALYs, either by use of the PTO approach or another set of equity weights, would be one option. The other main approach would be a structured discussion, whereby the various identified factors (for example, condition seriousness) would be discussed alongside data on cost-effectiveness.

The latter approach is already used to some extent by NICE.¹ More research is required on the pros and cons of the different approaches to introducing the consideration of social value into the technology assessment process.

How can we ensure that the returns from investment in orphan drug development are reasonable?

The European Union, the USA and Japan have offered incentives (such as tax rebates and market exclusivity) to companies willing to invest in clinical research into treatments for rare diseases. However, these incentives are meaningless if the drugs, once developed, are not reimbursed. Therefore, there is an urgent need to harmonise incentives for research with the potential for market access. In many ways, offering incentives for R&D is like putting the cart before the horse. The appropriate way to tackle the problem is to be clearer on what, if anything, society is willing to pay for these treatments. Then manufacturers would then be able to assess whether levels of reimbursement offered provide adequate incentives for investment in the research required.

How can we ensure that funds devoted to the reimbursement of orphan drugs are used appropriately?

It was pointed out that, because of the small number of people with rare diseases, there is often more uncertainty about the clinical benefits from treatment. The best way to deal with this uncertainty is to collect more long-term data on the clinical outcomes for patients receiving treatment, through the establishment of registries. Given the small number of patients in individual countries, there would be a role for international collaboration, through organisations like the EU.

Another step towards securing value for money would be to target therapy to patients achieving substantial clinical benefit. Therefore, it may be necessary to establish stopping rules for patients failing to respond to therapy. In some cases, such

stopping rules have been combined with risk-sharing schemes, whereby the manufacturer gives the payer a rebate in cases where the patient's therapeutic response does not reach a pre-defined level. However, such schemes are not simple to devise or monitor. They do not represent a 'magic bullet' for payers concerned about the high cost of orphan drugs.

Conclusions

Orphan drugs present several challenges, both in the assessment of cost-effectiveness and in the development of appropriate funding mechanisms. As illustrated in this article, manufacturers and policy makers might adopt new ways of working together in order to tackle these challenges.

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Generic medicines from a societal perspective: Savings for health care systems?

Elizabeth Seeley, Panos Kanavos

Summary: Despite the emphasis placed on generic policies, as a means of creating savings to health insurance budgets, there seems to be a lack of robust evidence on their effectiveness. By studying generic policies in seven OECD countries (USA, UK, Germany, France, Italy, Spain, Canada) and for a number of drugs, we find that generic penetration varies significantly among them and could be enhanced further, particularly in France and Italy, but also Spain and Canada. We also find that generic price decline post patent expiry is variable and that countries regulating generic prices, e.g. through price capping or reference pricing, display significantly lower price declines over time compared with countries that do not. As generic savings are influenced by the combined effect of genericisation and price reduction post-patent expiry, we conclude that significant additional savings to health insurance can be realised – up to 43% of current generic sales – if generic purchasing and genericisation improve further.

Keywords: Generic medicines, pharmaceutical policy, competition, efficiency

Background and conventional thinking

Given the intense debate surrounding health care cost containment and efficiency in health care resource allocation, it is not surprising that generic policy has received much attention in Organisation of Economic Co-operation and Development (OECD) countries. Generic medicines are both chemically equivalent and bioequivalent to their branded equivalents, but can be significantly cheaper since they do not have to recoup large R&D costs and are protected by a patent. In general, originator drug prices may not decline significantly after patent expiry, but rather pursue a market harvesting strategy that focuses on the brand loyal, price insensitive portion of the market, leaving their lower priced generic equivalents to compete for the more price sensitive

consumers.^{1,2} As a result, health insurers, both public and private, have been eager to promote generic drug use, with a view to reducing off-patent drug costs. Failure to do so implies that health insurance will continue to pay premium prices for products whose patents have expired.

There are significant differences in regulatory frameworks for generic medicines across OECD countries and North America. In France, Italy and Spain, for instance, regulators have implemented reference pricing for generics as well as generic substitution, in addition to promoting generic prescribing. In other countries, generic prescribing and dispensing have been key features of pharmaceutical policy for decades (for example, the USA and the UK). Table 1 provides an overview of supply and demand side generic policies across the EU-G5 (UK, Germany, France, Italy, Spain), the USA and Canada. These policies may help to improve generic substitution as well as spur generic price competition. To the extent that generic savings are achieved, policy makers may then have more

resources to invest in new treatments, creating headroom for innovation.

Despite the emphasis on generic policies,³ there is a lack of robust evidence on their actual effectiveness in different environments, whether they indeed result in high rates of generic penetration, and whether they encourage sustainable price reductions. In this article we briefly address three questions:

How does generic penetration compare across countries?

Are generic prices influenced downwards by the entry of new competitors?

How do price regulation and market structure affect generic competition and savings to health insurance?

Generic penetration and price competition in off-patent markets

We empirically examined aspects of competition in the market for relatively established drugs in seven OECD countries (USA, EU-G5 and Canada) and used a panel of twelve products (shown on

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Table 1: Generic policies in EU-G5, USA and Canada

Measure	UK	Germany	France	Italy	Spain	USA	Canada
Proxy demand-side							
Promoting generic prescribing		√	√		√	√	√
Compulsory generic prescribing	√						
Generic substitution		√	√	√	√	√	√
Flat or regressive margin		√	√	√	√		
Discounting allowed officially	√		√			√	√
Clawback	√						
Demand-side							
Differential co-payments						√	
Supply-side							
Price cap	√		√	√	√		
Reference Pricing		√	√	√	√		√

Source: Kanavos, Costa-Font, Seeley⁴

Figure 1: Generic sales as a proportion of total sales, 2005, twelve molecules

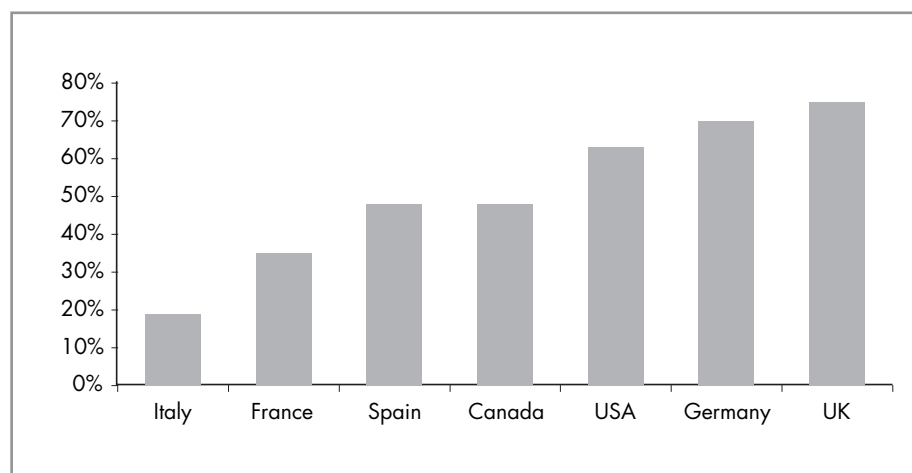


Table 2) subjected to generic competition post-patent expiry, and accounting for 19% of the off-patent market by value in these countries.

We find that generic penetration varies significantly among countries and that it could be enhanced further in most countries, especially in France and Italy, which appear to have the lowest generic penetration. Spain and Canada exhibit average levels of generic penetration, while the US, Germany and the UK exhibit the highest levels of generic penetration for these products (Figure 1).

While generic penetration may be a necessary condition for the creation of savings to health care systems, it is not sufficient, as savings are greatly affected by price levels and in particular, the price differential between originator and generic drug, as well as the speed with which generic prices decline. It is therefore necessary to take a closer look at generic prices in order to better evaluate the degree of savings national generic policies are achieving. Our study shows that there is significant variability in generic prices which sometimes result in a fifteen-fold

difference between countries for the same molecule. In addition to comparing prices at one point in time, the evolution of prices over time must also be compared across countries. Figure 2 shows that, in general, US and UK generic prices decline faster post-patent expiry than other countries, while French, Canadian and Italian generic prices are the most rigid downwards.

In looking at Figure 3, we see that prices range very little among generics in countries with reference pricing, (such as Germany, France and Italy) suggesting a lack of price competition in reference pricing countries. This is not surprising. Under a reference price scheme, patients are made to pay the difference between the reference price and the price of the product in the form of a co-payment. Moreover, reference prices are usually pegged to some of the lowest generic prices in the market. As a result, if companies were to price above the reference price, they would likely experience a collapse in market share, whereas if they were to price below the reference price, this would further drive down the reference price itself, forcing other companies to follow suit or health insurance to adjust reference prices downwards. The result is a clustering of prices around the reference price, rather

Figure 2: Generic price evolution over time (2000–2005)

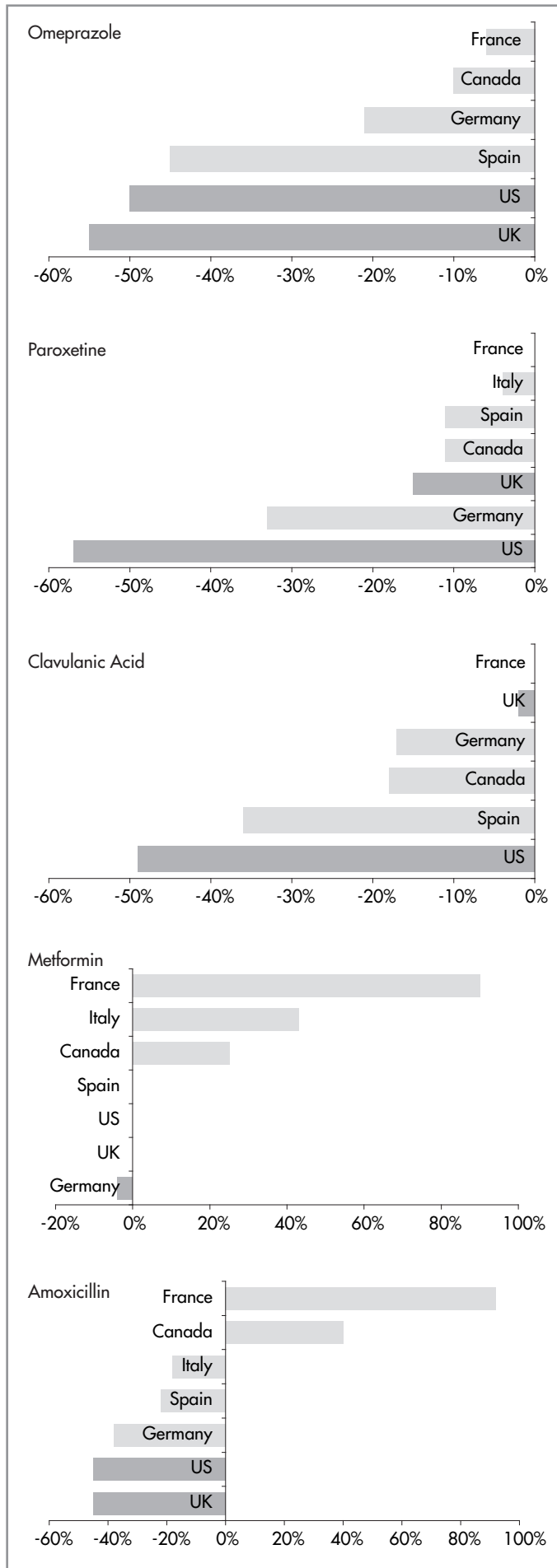


Figure 3: Impact of reference pricing on generic prices and competition, 2005 (prices in Euros per pack)

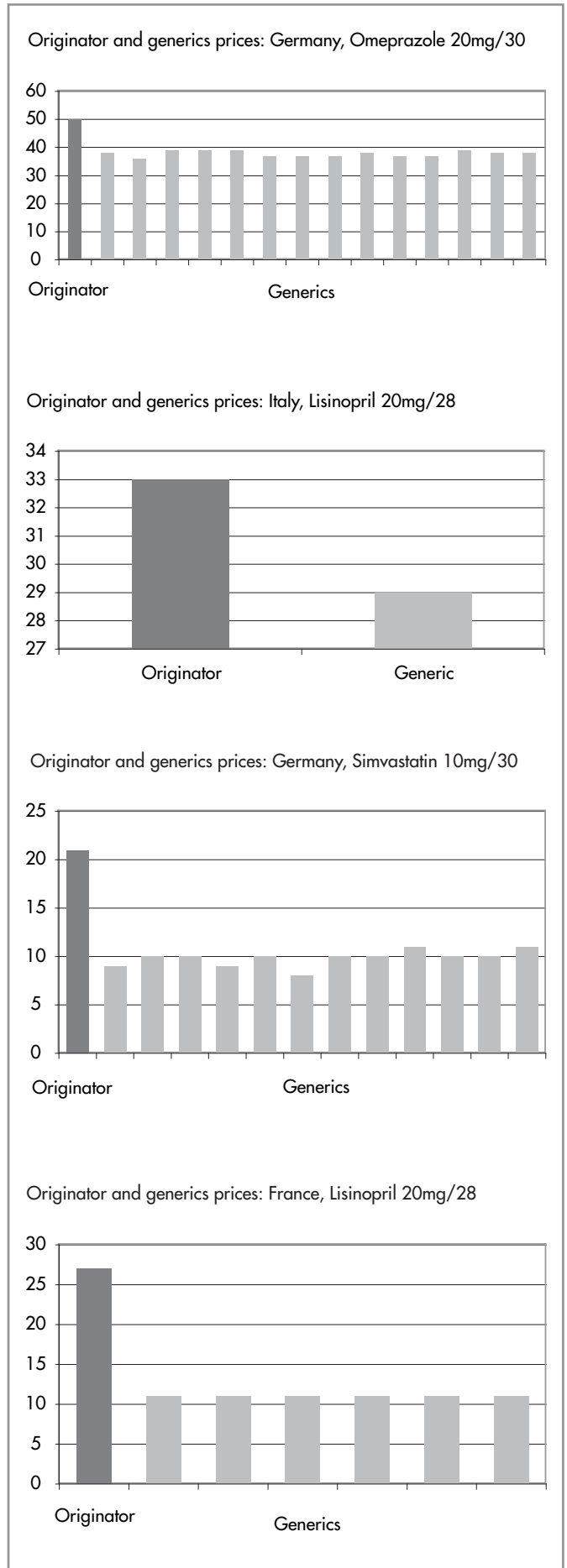


Table 2: Proliferation of generic firms in European Countries, 2004

Molecule	Germany	Italy	France	UK	Spain	Total EU-5	Canada	USA
Amoxicillin	45	41	17	15	64	182	11	48
Clavulanic Acid	16	6	10	4	20	56	3	7
Hydrochlorothiazine	60	6	8	9	28	111	15	80
Iron ferrous	126	34	31	30	22	243	48	144
Lisinopril	24	1	7	3	13	48	1	16
Mesalazine	19	16	3	5	3	46	5	6
Metformin	49	10	16	7	2	84	17	25
Methylphenidate	4	0	1	4	2	11	5	19
Omeprazole	24	0	14	6	44	88	1	6
Paroxetine	24	5	7	4	15	55	8	7
Salbutamol	27	6	6	13	5	57	13	52
Simvastatin	33	1	N/A	5	27	66	10	N/A

than price reductions over time, as would be expected in a price competitive market.

Generic prices seem to remain relatively stable in countries with reference pricing and decline slowly, whereas a significant reduction in prices is seen in countries without reference pricing, such as the USA and the UK.

Finally, it is important to understand the effect that the number of generic firms (i.e. generic entry) has on generic price competition. In a competitive market, price premiums should attract new competitors, which should, in turn, result in price competition that leads to lower prices. The analysis of competition patterns within the generic segment suggests that the number of generic entrants is not a predictor of lower generic prices in most study countries. For example, Table 2 shows that for many products, Germany and the USA have the largest number of generic competitors, despite Germany exhibiting slow price reduction and the USA relatively faster price reduction over time. Thus, the effect of the number of generic firms on price competition seems muted in Germany, as the reference price incentives discussed above would predict.

Meanwhile, the UK has relatively few generic competitors, despite showing signs of relatively fast price declines. This suggests that the off-patent market displays non-linearities such that the addition of a new firm to those already

existing may not be linked directly to price reductions. For prices to be impacted by generic entry, there may need to be a significant increase in the number of generic entrants. It seems, therefore, that entry by generic producers is in itself a necessary but not sufficient condition for a sustainable reduction in generic drug prices for payers and that (generic) price regulation may have an adverse effect on generic price reduction irrespective of the number of players entering the market.

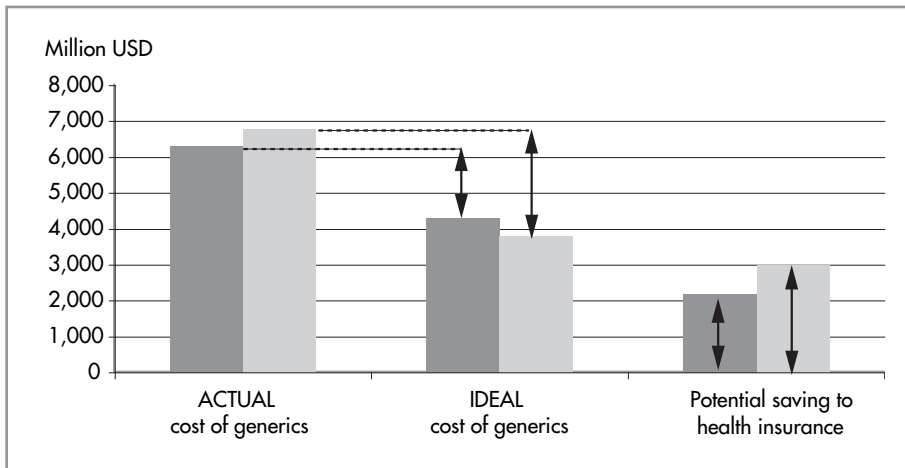
In summary, competition in the off-patent market seems to be variable and country-dependent. The countries showing little evidence of downward price trends within the generic segment following generic entry are France, Italy, Spain and Canada, whereas in Germany generic prices respond to generic entry weakly. Whilst the results were expected for France, Italy and Spain, three countries that have only in recent years introduced measures to promote generic drug use and have smaller generic penetration levels and high generics prices, they were not in Germany, given its overall market size (in monetary terms), the level of generic penetration (in terms of generic market share for patent expired molecules) and depth (in terms of the number of generic firms active on each product market). In short, current regulatory frameworks may encourage high prices for generics and limit potential savings for health insurers.

Savings for payers

As a result of the above it looks as though governments, particularly in Europe, may not be realising the full benefits of genericisation and are even wasting resources by overpaying for generic products. The potential savings to health care systems could improve significantly, provided generic penetration increases through improved generic prescribing and dispensing practices and provided generics are available at competitive prices. This requires greater competition in this segment. In total, we estimate potential savings to be in the vicinity of \$3 billion, or 43% of current sales of generic medicines in our sample, as depicted in Figure 4. These foregone savings, if realised, could be invested in novel treatments that improve quality of life and offer significant health gains.

To achieve more efficient generic purchasing, countries need to revise some of their generic policies. For example, in order to reduce price rigidity where it exists and achieve greater price responsiveness to competitive forces, it may be necessary to introduce policy changes that would promote the latter; potential options could include the abolition of reference pricing as a factor that stifles price competition over time, or introducing 'managed competition' through gradual stepwise price reductions by payers once off-patent product markets mature further. In order to encourage

Figure 4: Total effect of efficient generic purchasing in EU-G5, Canada and USA



greater generic penetration, generic prescribing should be encouraged further through financial and non-financial incentives that target physicians, and cost sharing strategies that target patients, such as co-payments. Finally, in terms of further encouraging generic entry, regulatory

hurdles such as price setting and capping should be eliminated, so that the generics market can acquire depth. Where eliminating regulations appears difficult for several reasons a system of 'managed competition' could help to achieve price reductions over time.

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Does pharmaceutical parallel trade serve the objectives of cost control?

Panos Kanavos and Stacey Kowal

Summary: The extent to which pharmaceutical parallel trade can contain pharmaceutical costs has been debated intensely. Although parallel import penetration is significant in many EU countries, parallel trade generates at best moderate savings to health insurance, is not necessarily associated with sustainable long-term price competition and can lead to product shortages in exporting countries and, recently, a higher probability of counterfeiting. Parallel distributors emerge as the key beneficiaries from this practice. The high transaction costs associated with parallel trade, the lack of sustainable long-term price competition and the lack of tangible benefits to patients make this practice an inefficient means of containing costs.

Keywords: pharmaceutical parallel trade, efficiency, cost containment, single market

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Background

Parallel trade refers to the "legal importation of a patented product from one country where it is legally marketed into a second country where the patent holder also markets that product but without authorisation of the patent holder".¹ Therefore, it

constitutes a form of arbitrage, or the purchase and sale of identical products from different markets for the purpose of gaining a profit from unequal prices.² While parallel trade is illegal in many parts of the world, it is legal within the European Union (EU) after the move to a single market for phar-

Table 1: Policies to promote the use of parallel imported drugs in key importing countries in the European Union (2004)

Policy to promote use of parallel imported drugs	Denmark	Germany	Netherlands	Norway	Sweden	United Kingdom
Pharmacy required to inform patient of availability of parallel imported products	X	X			X	
Pharmacy quota on parallel import dispensing rates		X				
Financial incentives for pharmacy to dispense parallel imported drugs			X	X		X
Financial incentives for dispensing lower-price drugs in general, including parallel imported drugs				X	X	

Source: Kanavos P, Gross D, Taylor D, 2005.¹³

maceuticals. Within the single market, key changes in the harmonisation of regulation under the EU's mutual recognition procedure, and Articles 28–30 governing the free movement of goods have fostered an environment where parallel trade can capitalise on pharmaceutical price differences across countries.^{3,4}

“Views on the impact of parallel trade in the EU are highly polarised”

Parallel trade comprises a growing share of the pharmaceutical retail market and a significant share of pharmaceutical expenditure. Its presence is the result of differential country regulation and weak control over the pharmaceutical distribution chain.⁵ Community exhaustion within the EU dictates that a drug approved for human use in one EU member state must be granted authorisation in all other member states unless the concerned member state objects through a formal process. However, drug companies must still negotiate with individual countries over pricing and reimbursement.

Parallel trade in the EU is further fuelled by the structure of the distribution chain (wholesale and retail). The large number of players in the pharmaceutical distribution chain prevents total vertical control by any one stakeholder.⁴ In the presence of pharmaceutical price differences across countries, parallel distributors, who are

themselves registered wholesalers, increase their profit potential by acquiring products from low priced countries and selling such goods to pharmacies in countries with higher drug prices.

Views on the impact of parallel trade in the EU are highly polarised. Proponents claim that parallel trade offers savings to health insurers and patients by increasing the affordability of high priced drugs.⁶ They also claim that affordability may be further increased by manufacturer responses to parallel trade, suggesting that the threat of parallel trade may cause manufacturers to lower prices.⁷ Conversely, opponents claim parallel trade will have long term negative implications in discouraging research and development, thus potentially reducing product quality and impairing future research.⁸

How are individual stakeholders affected?

The implications of parallel trade, however, are contingent upon the viewpoints of the stakeholders involved, namely health insurers, pharmacy, parallel distributors, patients and the pharmaceutical industry.

Health insurance has the potential to benefit from parallel trade if the retail prices of parallel traded drugs are lower than the locally sourced identical products.⁹ In order to increase savings, it is in the interest of health insurance to encourage pharmacies to dispense parallel imported medicines. Given this perception of potential savings, many health insurance organisations have been either directly or indirectly promoting the use of parallel

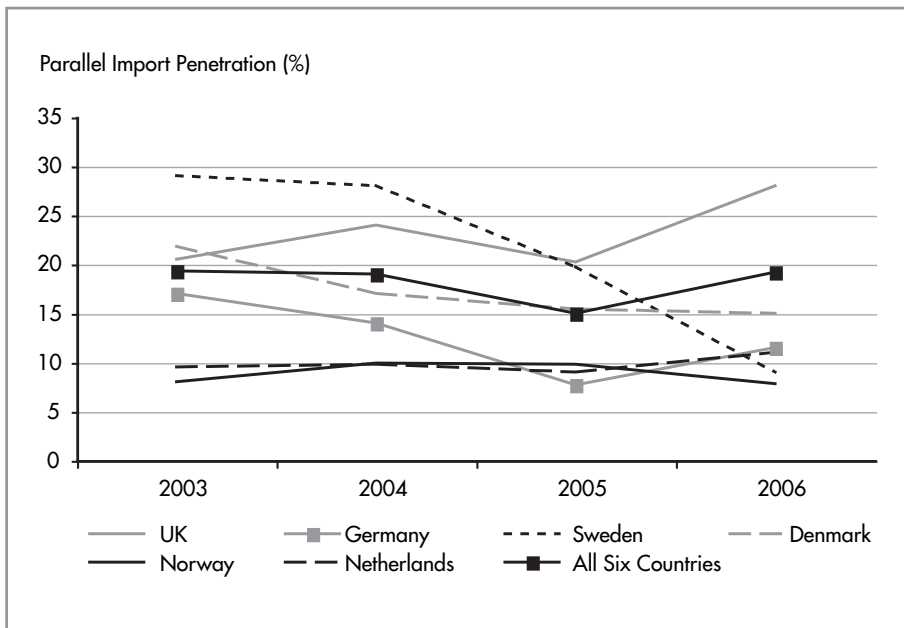
traded goods. Table 1 outlines policies used to promote the use of parallel imported drugs in key destination countries. The table illustrates that most countries aim at influencing the behaviour of pharmacies to some degree.

Despite the proliferation of policies promoting the use of parallel imported medicines, empirical work suggests that these savings are very small in relation to the size of the pharmaceutical market and disproportionately small in relation to the penetration of parallel imports in individual countries and product markets. Ganslandt *et al* empirically demonstrated that parallel imports were associated with a reduction in prices for the top fifty selling drugs in Sweden.² Kanavos *et al* discuss the potential savings to health insurance but empirically find that little savings were gained by health insurance for nineteen high volume, high cost drugs in Germany, Sweden, Norway, Denmark, the UK and the Netherlands between 1997 and 2002.¹

In addition to incentives from health insurance, pharmacists may have reimbursement related incentives that promote the use of parallel imported goods. Many pharmacies are reimbursed on a fixed margin, which offers no additional incentives to dispense parallel traded goods. However, policies rewarding the use of lower priced drugs may lead to benefits for pharmacists for the dispensing of parallel traded goods where parallel imports are less costly than locally sourced products.

Several countries offer explicit incentives, such as sharing the savings from the price

Figure 1: Parallel trade penetration in destination countries



Source: The authors from IMS.

difference between the locally sourced and parallel traded goods with pharmacies. In Norway savings are split equally between health insurance and pharmacies and the Netherlands offers a similar practice but with a 66-33 split.¹ Finally, some countries may penalise pharmacists if parallel import quotas are not met. While these incentives may encourage the use of parallel traded products, the continued use of a fixed margin for reimbursement may not translate into the use of cheaper drugs and subsequent savings to health insurance.

Parallel distributors, as licensed wholesalers, are profit maximisers and are interested in acquiring drugs at the lowest possible prices and selling them at the highest price in the importation country. Given increasing product homogeneity under the harmonisation of EU drug regulations and allowances for the sale of parallel imported goods in packaging from the source country, it is suggested that many of the potential barriers to moving products across countries are negligible. However, a pervasive concern is the sustainability of supply for parallel distributors. In order to maintain purchasing relationships with pharmacies, parallel distributors must ensure a sustainable supply of parallel imported goods.

Sustainability is complicated as parallel distributors are reliant on locating sufficient supplies of desired products in low priced countries. This has often led to product shortages in source countries, such as Spain and Greece, as available quantities to service the local market are siphoned off for exportation.

The effects of pharmaceutical parallel trade on patients are contingent upon a country's co-payment structure and extent of exemptions. In many countries, universal coverage shields patients from the full cost of pharmaceuticals. In the UK and the Netherlands, co-payments are not related to the cost of the dispensed medicine and therefore patients do not gain direct benefits from price differences between the cost of the parallel import and the locally sourced product.

Germany uses a structured payment system which blends co-insurance with a pre-determined minimum and maximum range for patient contribution, creating the potential for benefits to patients within the co-insurance range, although this may be limited. Finally, Denmark, Norway, and Sweden have, among others, co-insurance for out-patient pharmaceuticals up to a maximum ceiling, which theoretically enables patients to gain a marginal benefit

from using lower priced parallel imports. However, price differences between parallel imports and locally sourced drugs in destination countries are generally very small, suggesting that, even in those cases, savings to patients are negligible.^{1,2}

For the pharmaceutical industry, the growing presence of parallel trade presents a challenge as it reduces potential profits and mitigates the ability of manufacturers to recoup research and development costs.⁴ Parallel trade is most pervasive in the on-patent market given limited competitors and high drug prices. However, manufacturers rely on the market exclusivity granted under patents to recoup their research and development costs.¹⁰ The movement of parallel imported goods from low price countries to high price countries causes a reduction in manufacturer profits as the volume of higher priced products in destination countries decreases. Pharmaceutical manufacturers have taken steps to reduce the potential for parallel trade by working to improve control over the distribution chain.³ However, these efforts require additional resources which may also reduce profits.

Is parallel trade an effective method of pharmaceutical cost control?

When addressing the question of whether pharmaceutical parallel trade is an effective method of cost control one needs to consider (a) entry and penetration, (b) competition in markets characterised by parallel imports, (c) savings to payers, and (d) safety and quality of parallel imported medicines.

Entry and penetration

Eighteen products across six therapeutic categories* were used to investigate the overall penetration of pharmaceutical parallel trade in key importing countries (UK, Germany, Sweden, Denmark, Norway and the Netherlands) and, in particular, to identify the benefits accruing to health insurance from this practice over the period from 2003–2006. This builds on previous work conducted in this area, up to 2002.¹

The penetration of parallel imports in the six destination countries under investigation is depicted in Figure 1. The overall

*Namely, statins (atorvastatin, pravastatin, simvastatin), ACE (angiotensin-converting enzyme) I inhibitors (captopril, enalapril, quinapril, ramipril), ACE II inhibitors (losartan, valsartan), atypical antipsychotics (clozapine, olanzapine, risperidone), proton pump inhibitors (lansoprazole, omeprazole, pantoprazole), and selective serotonin reuptake inhibitors (SSRIs) – citalopram, paroxetine, and sertraline.

Table 2 Competition in parallel trade markets (Number of parallel importers and price differentials)

	Number of parallel importers	Price of locally sourced drug 2002 (€)	Highest parallel import price 2002 (€)	Lowest parallel import price 2002 (€)
Germany				
Simvastatin	11	223.4	221.7	212.6
Olanzapine	9	175.4	157.8	155.6
Fluoxetine	5	182.7	1282.1	119.8
Netherlands				
Simvastatin	11	50.4	50.2	45.3
Olanzapine	4	74.2	66.5	62.5
Fluoxetine	8	47.1	40.0	39.5
United Kingdom				
Simvastatin	n/a	55.6	55.4	49.9
Olanzapine	n/a	81.8	73.4	68.9
Fluoxetine	n/a	51.9	44.1	43.5

Source: Adapted and amended from Kanavos P, Costa-Font J, 2005.¹

market share of parallel imports in Europe (as approximated by the six destination countries) remained relatively stable, changing from 18.44% in 2003 to 18.40% in 2006. The most marked changes were observed in Germany and Sweden. In Germany, the percentage of parallel import penetration in the market fell from 17.62% in 2003 to 11.22% in 2006. Conversely, Sweden demonstrated an increase in the parallel trade retail market share, growing from 8.40% in 2003 to 26.66% in 2006. Slight increases were also observed in Denmark and the UK while slight decreases were present in the Netherlands.

Competition

Much of the debate on pharmaceutical parallel trade has focused on the extent to which it creates sustainable price competition over the longer term. By examining competition patterns in three high selling products across three countries, it is shown that in the majority of cases, the difference between the highest and lowest parallel distributors' price does not exceed 7%, with the sole exception of simvastatin in the Netherlands, where the spread between highest and lowest imported price is 11% (Table 2).

In the majority of cases, the distributors with the largest market share are those with prices towards the lower end of the spectrum, or those with the lowest price in the range. Prices of locally sourced equiv-

alent products have nevertheless increased over time in the three countries, despite seeing their domestic market share declining in the presence of parallel imports.

Small price differences between locally sourced and parallel imported drugs, combined with the significantly lower acquisition prices by parallel distributors suggest that there may be little price competition in products subjected to intensive parallel distribution. In addition, the uncertainty of a sustainable single source of product acquisition by parallel distributors is unlikely to fuel sustainable downward price competition over the longer term.

Pecuniary benefits to stakeholders and savings to health insurance

Existing evidence points at modest to moderate savings to health insurance from parallel importation of medicines.^{1,9,11} More recent evidence updating previous analysis also confirms this.¹⁴ Overall, the savings to health insurance in imported countries range between 0.4% and 2.2% of the retail prescription drug market. Other stakeholders also benefit from this practice, as discussed previously. For instance, the benefits to pharmacy were approximately 0.09% of the pharmaceutical retail market costs.^{1,14}

By contrast, exporting countries may be

faced with shortages of parallel trade products. The larger the market for a particular product, the greater the probability it will be traded intensely and, thus, the greater the likelihood it will result in shortages in export countries. The rents accruing to parallel distributors, however, are a multiple of the rent accruing as saving to health insurance. Evidence suggests^{1,14} that parallel distributor rents were between 2.5 and twenty times higher than savings to health insurance. While it is true that more than one distributor may be involved in the movement of medicines across countries, the fact remains that all distributor parties benefit from this practice.

Safety and quality of parallel imported medicines

Until recently, the arguments surrounding the safety and quality of parallel traded medicines were unproven. The theoretical risk existed that so long as parallel traded medicines could be re-packaged and re-boxed, this could lead to counterfeiting. Yet, parallel distributors are obliged to notify the regulatory authorities as well as the manufacturer of any changes made to the product concerned, thus, making themselves liable in case counterfeit medicines enter the distribution chain from this source.

In 2007, however, there were several recalls of counterfeit medicines that had entered

the UK supply chain via a parallel distributor. Several thousand packs of three medicines were seized or recalled by the UK Medicines and Health Care Products Regulatory Agency (MHRA). The counterfeit medicines, made in China and shipped to Singapore, entered the EU in Luxembourg, where they were re-sold without being checked to UK and Belgian wholesalers. This situation raises concerns about the safety and quality of medicines entering the EU and raises further questions about re-packaging and re-boxing.

Shortages in exporting countries

Whereas the pricing structure and the distribution system in exporting countries favour parallel exportation, an important question arises as to what happens to the availability of medicines to patients in exporting countries. Evidence suggests that the end result can be shortages in drugs that are exported intensively. This has been documented in Greece and Spain, both of which have explicitly raised questions of shortages. This is reflected in recent regulatory interventions by the two respective national governments, essentially placing a requirement on wholesalers to declare the destination of the product they acquire from manufacturers. One would of course argue that drug manufacturers should increase production in exporting countries to meet need, but, this does not provide a long-term solution to the problem.

Overall welfare effects

Given a range of complex stakeholder considerations and the current brevity of empirical evidence on welfare implications, the overall welfare effects for parallel trade are at best ambiguous.^{2,11} Perceived short term benefits in increasing affordability may support possible welfare increases but such gains are arguably at the expense of potentially negative long-term implications. Furthermore, despite the perceived benefits from increased affordability claimed by proponents of parallel trade, current and previous empirical work found that parallel trade did not lead to aggregate and sustainable price reductions in key destination countries.¹

In regards to long term implications, it is argued that short term gains in potential savings will be erased by the long term implications of a reduction in product quality from losses to research and development.^{4,12} Furthermore, it has been suggested that parallel trade reduces global welfare by creating an environment where

manufacturers have no incentive to choose to serve countries with lower drug prices.¹³

Conclusions

Pharmaceutical parallel trade has been a controversial practice enabled by the European single market. Much of the debate surrounding parallel trade in pharmaceuticals has focused on the economic impact it has on stakeholders and whether it facilitates patient access to medicines. While proponents and opponents to the practice may disagree on the precise pecuniary effects of parallel trade on individual stakeholders, the fact remains that, overall, its impact on health insurance budgets in importing countries is very small and the effect on patients negligible. By contrast, patients in exporting countries may be faced with significant shortages and access problems. Those who perform the practice also gain significantly from it. Importantly, however, it is likely that parallel trade results in misallocation of resources and may have a significant long-term welfare effect in terms of investment in innovation.

"Savings from parallel trade are very small relative to the size of the pharmaceutical market"

Finally, in recent months, the ability of parallel trade to procure safe medicines has been called into question; the fact that re-packaging and re-boxing can take place, increases the probability of counterfeiting; on the other hand, the meticulous checking of all parallel traded packs of medicines increases transaction costs significantly and may result to poor allocation of resources. On balance, although the practice of parallel trade is still legal in Europe, it is associated with little actual pecuniary benefits and high transaction costs to health insurers, regulators and patients, in both importing and exporting countries, making it an undesirable cost containment tool.

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When will it happen?

Paving the way for risk adjustment in Slovakia

Lucia Kossarova

As the revenues of health insurance companies in Slovakia increase (Table 1), their role as effective spenders of resources and purchasers of high quality services for the population is becoming ever more important. However, the current incentive structure for health insurance companies (HICs) does not necessarily encourage this function. The risk adjustment* mechanism in place is based only on age and gender; it is coupled with a new amendment to the Health Insurance Act which obliges HICs to use any profits generated for health care services and also requires them to reduce administrative costs from 4% to 3.5% of total annual premium payments. This imperfect risk adjustment mechanism and a lack of options to compensate for losses may encourage the HICs to 'cheat' the system instead of becoming more efficient purchasers. They may 'cream skim' and select healthier patients or provide poor quality of care in order to compensate for high cost patients.

The case for risk adjustment

Individuals require a wide variety of health care services throughout their lifetimes, depending on their personal characteristics and behaviour, social, economic and physical environment. As a result, purchasers of health care services have to finance a range of health care expenditures. While for some individuals, these expenditures can to some extent be planned for (for example, patients with a chronic condition), for others they are more unpredictable. Therefore, in countries with plural systems of health care service purchasers, such as Slovakia, where premiums are set by law and HICs are not allowed to openly select their enrollees or

Table 1: Health care resources in Slovakia (Slovak Korunas billions)

	2005	2006 ^e	2007 ^p	2008 ^p	2009 ^p	2010 ^p
Revenues of health insurance companies	73.5	80.3	89.7	94.4	101.4	108.9
Ministry of Health (excluding the state's payment for its insurees)	3.0	3.1	2.9	2.6	2.6	2.6
Resources of cities, municipalities and regions	0.5	0.6	0.5	0.5	0.5	0.5
Eurofunds	0.0	0.0	0.3	1.5	1.5	1.5
Net financial expenditures of households	19.9	21.2	21.0	22.9	24.9	27.3
Total Resources	96.9	105.3	114.4	121.9	130.9	140.9
Public resources (% of GDP)	5.2	5.2	5.3	5.1	5.1	5.1
Private resources (% of GDP)	1.4	1.3	1.2	1.2	1.2	1.2
Total resources (% of GDP)	6.6	6.5	6.4	6.3	6.3	6.3

Source: 2007–2010 General Health Policy Framework²; e: estimation, p: projection

adjust their premium rates to accommodate for health care expenditure risks, there may be a motivation to engage in hidden selection to improve the health profile of the pool of the insured. In addition, undersupplying care to those patients who need it, and oversupplying it to healthier ones, or simply not treating those cases that are expensive, are ways that HICs can attempt to reduce high health care expenditures.

While the evidence from Slovakia is still scarce, there have been several instances which suggest that HICs may have been engaging in risk selection instead of focusing on improvements in quality and

efficiency. These include the recent revelations that individuals have been reinsured by HICs without their knowledge, while misleading advertisements have also been published, including offers of products that cannot be provided or products clearly targeted at the healthier part of the population.³ While not all of these activities can be directly attributed to risk selection, some clearly aim to attract the healthier element of the population into their insurance pools. Moreover, anecdotal evidence suggests that HICs may have been involved in selection activities for one group of patients who represent a substantial portion of annual health expenditures – people requiring renal dialysis.

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*Risk adjustment can be defined as the use of information to calculate the expected health expenditures of individual consumers over a fixed interval of time and set subsidies to consumers or health plans to improve efficiency and equity (see Folland S, Goodman AC, Stano M, 2001¹)

Table 2: Relative frequencies of dialysis in Slovak health insurance companies

Health insurance company (HIC)	A	B	C
Number of dialysis patients per 1,000	1.62	0.28	0.56
Number of dialysis sessions per 1,000	155.36	30.32	47.32
Number of dialysis sessions per N17–N19 diagnosis	19.66	3.92	7.73

Source: Sanigest Internacional, 2003⁴

While HICs may not be able to predict which patients will need dialysis, they may limit access, for example by contracting with a more limited number of dialysis providers. Available data⁴ bear this out; examination of three HICs suggests great variation in both the number of dialysis patients and dialysis treatment sessions provided (Table 2).

While regulatory measures and lawsuits against the HICs can to some extent control such activities, it is necessary that they be coupled with an appropriate risk adjustment and redistribution mechanism; one that will compensate for higher risks while at the same time not providing perverse incentives on cost-effectiveness and efficiency.

Current situation in Slovakia

Slovakia has a system of mandatory social health insurance where citizens can freely choose from six HICs, re-register once a year and are entitled to uniform benefits*. The insurance premium is set out in the law as a percentage of income to be paid by economically active citizens, self-payers, while the state contributes from general taxation for the economically inactive portion of the population.

In order to achieve a certain level of fairness in the system Slovakia has been developing its redistribution mechanism to compensate HICs for the potentially sicker and more costly patients. The risk adjustment mechanism has undergone numerous changes, evolving from a system where adjustment was only by age (two age groups) to the one implemented in 2005 where 85.5% of the premiums

collected by the HICs are redistributed using two parameters: age (seventeen age groups) and gender.⁵ The insured are divided into age groups by gender, where each group has a corresponding cost risk index, adjusted on a yearly basis, according to historical data. Thus those HICs who have enrolled a substantially higher number of more risky individuals, as determined by age and gender, are compensated by the remaining purchasers who have a less risky pool of citizens. This mechanism is overseen by the Health Care Surveillance Authority.

While risk adjustment based on demographic parameters is better than no risk adjustment at all, it does not take into account the health status of the population. A young male can be considered low risk yet he could be suffering from a disease which is extremely costly to treat. If the HICs cannot adjust their premiums and redistribution depends on age and gender only, the health plans will incur substantial predictable losses on their high-risk members as demographic models are weak predictors of individual expenditure and explain only up to 5% of overall variance.¹ Thus they will continue to be motivated to select low-risk members or take other measures, including poor quality of care or reduced access to care for high-risk individuals, to reduce their costs.

One of the main goals of the 2007–2010 General Health Policy Framework² is to improve the redistribution mechanism. The Framework proposes the establishment of (i) high risk pools which would help to cover catastrophic costs such as transplants or rare diseases; (ii) the

expansion of the current redistribution mechanism by health status parameters based on diagnosis, drugs, and presence of chronic disease or inclusion in a disease management program; or (iii) carve outs where some services or diseases that HICs are likely to select by would be managed separately.

One proposal⁶ to amend the 2004 Health Insurance Act (2004) sought the creation of a ‘high risk pool’ which would be used to compensate HICs for cases above a certain threshold. This proposal seemed to be a positive step towards establishing risk sharing, which is an ex-post tool where HICs are retrospectively reimbursed for part of their costs and could to some extent mitigate high cost individuals that the age-gender redistribution mechanism does not account for. Unfortunately, this proposal has not been approved.

Conclusion and recommendations

The absence of an appropriate redistribution mechanism coupled with a continued lack of progress on this front should worry both policy makers and patients. Morbidity, through the use of diagnosis, needs to be taken into consideration as a parameter for risk adjustment, or failing this some other form of risk sharing should be introduced**. Without this HICs are likely to improve their “risk selection skills” by providing lower quality services instead of improving efficiency. For example, they can decide not to contract physicians who have an excellent record of treating patients with chronic or expensive illnesses; the underlying aim being to reduce the number of such patients enrolled with their company. With the prevalence of chronic diseases in Slovakia (for whom costs are more predictable than acute episodes) now becoming similar to that seen in other parts of Europe, this is something that Slovakia needs to worry about.

Inappropriate incentives, a lack of understanding of the complexities of risk adjustment, implementation difficulties and data weaknesses are the main areas requiring the full attention of policy makers. The current system does not provide the right incentives for health care purchasers and recent changes in the law may have exacerbated the situation. While getting the incentives right is not an easy task, only once policy makers begin to understand the technicalities surrounding risk adjustment and its implications for access to quality care, can the necessary

* Some insurance companies started to offer additional benefits such as screenings, home visits, vaccinations etc. However, there continues to be almost no competition on the basis of benefits.

** (i) Proportional risk sharing; (ii) outlier risk sharing or (iii) risk sharing for high-risks.

changes be implemented. This has to go hand in hand with a focus on improving data quality and a gradual implementation of the more refined risk adjustment mechanism. Everyone involved in data collection and reporting needs to understand how data is to be used and how it can contribute to the better functioning of the system.

In addition, patients should also begin to share information on their experiences within the health care system, especially if in switching health plans, they have experienced problems accessing care or have been denied care altogether. Their inputs are essential. Finally, providers should clearly state to their patients if they cannot provide appropriate care as a result of inappropriate incentives from HICs. Disclosing all this information would help raise public awareness about the gravity and importance of these issues. It would also help encourage HICs to reduce their risk selection activities and facilitate demands on policy makers to implement an appropriate, fair and viable redistribution mechanism.

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The Price is Right?

Promoting local production for ARVs in Sub-Saharan Africa

Kinsley Wilson, Jillian Cohen-Köhler and Alan Whiteside

Summary: Affordability is a key concern of European donors who finance antiretroviral drugs (ARVs) to treat AIDS in Sub-Saharan African countries. In country manufacture of ARV drugs could favourably affect ARV access through increased affordability; however, generics are a volume based market, relying on economies of scale. The ability of Sub-Saharan African countries to reduce their prices below large-scale manufacturers in India is challenging. Additionally, these medicines must meet WHO prequalification standards. While the cost of second-line ARVs remains a concern, donors should focus resources on other components ARV access, such as the supply of human resources for health, health infrastructure and issues of sustainable financing.

Keywords: ARV drugs, Access to medicines, Developing countries, Generic manufacture, Donor financing

To increase access to antiretroviral drugs (ARVs) for treating AIDS in the developing world, donor countries and multilateral agencies have developed a variety of initiatives. In 2008, the European Commission and European countries provided over 60% (about €1.19 billion) of the Global Fund to Fight HIV/AIDS, Malaria and Tuberculosis budget. With these sustained pledges, Global Fund supported programmes project to treat 1.8 million HIV infected patients over a five year period.¹ To equitably access this treatment, the World Health Organization (WHO) emphasises a drug's rational selection and use, sustainable financing and affordable pricing, while also maintaining reliable health and supply systems.² For ARV treatment, a notable challenge has

been affordability. This is why the promotion of local production has the potential to address the critical issue of ensuring sustainable ARV supply.

One of the barriers to ARV price in high prevalence HIV/AIDS countries is the World Trade Organization's Agreement on the Trade Related Aspects of Intellectual Property (TRIPS). In exchange for international trade liberalisation, TRIPS requires twenty years of pharmaceutical patent protection. This provides a market monopoly for patent holding drug companies and enables them to set their prices freely. ARV prices are often out of reach for developing and least-developed countries. In 2000, when few generic drugs were available, the lowest price triple combination ARV treatment was US\$10,439 (€11,326).³

Since TRIPS took effect in 1995, international organisations, such as Médecins Sans Frontières (MSF), have encouraged both developing and the least-developed countries to exercise flexibilities in the agreement and subsequent Doha Declaration in order to increase ARV access. Compulsory licensing authorises government use of a patent under public

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health crises or a national emergency. A transition period allows developing and least-developed countries until 2006 and 2016, respectively, to implement pharmaceutical patents in domestic legislation. Both enable the domestic manufacture of generic ARVs.

Brazil and Thailand have been noteworthy in their efforts to reduce the prices of patent holding drug firms.³ In both countries, compulsory licensing threats initiated significant price negotiations with multinationals. This, along with generic production of ARVs that were not patented domestically prior to TRIPS, facilitated a more affordable scale up in treatment. India also made use of the TRIPS Agreement's 2006 developing country transition period. By waiting to enforce product patents in its domestic legislation, India fostered and expanded its generic drug industry. Following these initiatives, a number of Sub-Saharan African countries with substantial populations of infected people (South Africa, Zimbabwe, Zambia, Tanzania, Uganda, Kenya, and Ethiopia) are reported to be trying to manufacture ARVs domestically.

Generic production is able to lower the cost of drugs, since it does not have to carry the large research and development (R&D) costs of the drug discovery process. Within the WHO framework, local manufacture is assumed to predominantly have an impact on the affordability of drugs. This in turn improves the cost-effectiveness of ARV therapy; frees resources to increase treatment numbers; and strengthens other access components. The link between domestic production and access, however, relies on two conditions:

- that these medicines can be manufactured more cheaply than they can be imported; and
- they will meet WHO prequalification standards required for donor financing.

Donors have become involved in local production capacity-building. The development of local capacity has been assisted by the European Commission, which in 2003 established a health line grant for domestic drug manufacturing. The priority area specifically includes "technology transfer, leading to local production of affordable key pharmaceuticals and commodities in prevention, treatment and care of HIV/AIDS, malaria and tuberculosis" and offered to finance proposals of up to €5 million. At present, the authors are aware of only one example of this grant

accessed for ARV production. In November 2006, a German non-governmental organisation, Action Medeor, partnered with a Tanzanian manufacturer, Tanzania Pharmaceutical Industries, was successfully awarded this budget for the construction of a new ARV plant.

Arising from these efforts, the question is: can local ARV production increase treatment access cost-effectively? The European Commission grant may suggest that domestic production should deliver more affordable treatment, but this may not be the case, as the perennial debate of whether it is financially more attractive to 'make' or 'buy' still seems to rest on the latter. This article will discuss the ability of Sub-Saharan African countries to produce first-line ARV products at a competitive price and quality while considering some emerging issues concerning the production of second-line therapies.

Competitive pricing

With efforts from AIDS advocates and international organisations, such as the William J Clinton Foundation and MSF, India's generic firms paved the way for dramatic ARV price reduction and now act as the major suppliers for developing countries. This occurred concurrently with the development of domestic manufacture in Brazil and Thailand, while in South Africa, the excessive pricing complaint brought before the Competition Commission led to the first voluntary ARV licenses under reasonable royalty terms in a developing country.

Since 2000, first-line therapy prices have plummeted from over US\$10,000 (€6,700) per patient per year for patented products to under \$100 (€67) per patient per year for the leading triple therapy lamivudine, stavudine, and nevirapine (3TC+d4T+NVP).³ This price reduction coupled with increases in multilateral and bilateral aid enabled WHO's '3 by 5' initiative to scale up treatment numbers significantly. At the end of 2006, an estimated 1.3 million people in Sub-Saharan Africa were receiving ARVs, equalling 28% coverage, up from 100,000 individuals or 2% coverage at the launch of the 2003 initiative.⁴

While there is no doubt that generic competition stimulates the reduction of drug prices and increases affordability, the debate over domestic manufacturing in developing countries remains polarised. Advocates argue domestic production increases access to essential medicines;

strengthens long-term health security, self-sufficiency and employment while also saving foreign exchange.⁵ However, research contends that a local manufacturing industry is often not a viable alternative for developing countries and does not necessarily reduce prices compared to imported drugs.⁶

The South African National Economic Development and Labour Council found that 80% of a manufacturer's profits on a generic drug will be captured within eighteen months of the originator drug coming off patent.⁷ Therefore, unless a generic manufacturer is one of the first to enter, the ARV market essentially becomes commodity-based and price is the distinguishing factor among products. WHO recommends, and donors require, international competitive tenders to ensure the lowest cost ARVs are procured. Here, razor-thin margins and large volumes are required to remain competitive. The WHO promotes the 'rule-of-five' which states that five bids on a tender engage enough competition to ensure the lowest generic price.⁸ Competition facilitates greater affordability by pushing prices down to marginal costs, but it is difficult for new manufacturers to match the price of longstanding firms.

Currently, six generic manufacturers produce a leading WHO prequalified treatment regime 3TC+d4T+NVP. The most sophisticated generic drug industry in Sub-Saharan Africa is in South Africa. The country's leading ARV manufacturer, Aspen Pharmacare, currently produces its regime at a quoted price of US\$158 (€106) per person per year.⁹ A least-developing country manufacturer has yet to announce a price publicly. Comparatively, the listed median transaction price in 2007 was US\$92 (€62) and US\$91 (€61) per patient per year in low income and middle income countries, respectively.¹⁰ Even though tendered prices often differ from the estimated and listed prices, the disparity between Aspen's treatment cost and the median price is noteworthy.

Therefore, within the access framework, the question facing Sub-Saharan African countries is whether they can make ARVs inexpensively and justify their manufacture over their import. They have limited resources and manufacturers lack vertical integration which limits their capacity and keeps production costs high. The skilled labour necessary to develop and formulate ARVs is sparse in Sub-Saharan Africa compared to industrialised

countries (where drug discovery most commonly occurs) and the emerging economies of India and China (where the generic industry flourishes). As an example, researchers employed in R&D per million population amount to an average of 2,538 individuals across EU Member States, 708 individuals in China, 119 in India, 307 in South Africa, and less than 51 in any other reporting Sub-Saharan African country.¹¹ Therefore, the sheer size of China and India's skilled human resource population magnifies the industry's development potential and reduces labour costs compared to Sub-Saharan African countries, with the possible exception of South Africa.

Most crucial to ARV production is the level of manufacturing capacity. The capacity to synthesise or extract active pharmaceutical ingredients (APIs) needed to formulate ARVs is the key to drug costs: APIs are volume dependent and comprise 55% to 99% of the manufacturers' cost.¹² Without the technology to manufacture APIs, they must be imported from producing countries, such as India and China. As a result, the fight for market share is fierce as large and vertically integrated API producing generic firms are positioned with lower costs and greater economies of scale. In order to compete, a Sub-Saharan African manufacturer needs to be assured an expanded national and/or regional market to generate the larger volumes necessary to reduce the contracted price of APIs. This is difficult in the public tender system where quantities are generally determined once the tender is awarded, but pricing is required upfront.

Quality matters

At the end of 2007, programmes supported by the Global Fund reported that 1.1 million individuals in Sub-Saharan Africa were receiving treatment.⁴ These and other donors, especially European governments, the United States President's Emergency Plan for AIDS Relief (PEPFAR), and development agencies, play a critical role in ARV market entry as they largely finance procurement in Sub-Saharan Africa. With donor financing, ARVs must meet a minimum quality threshold in international competitive tenders: WHO prequalification.

The WHO prequalification programme was introduced in 2001 to assist developing countries without stringent drug regulatory authorities (DRAs) to assess the

quality of ARVs on the international market. The programme publishes a list of certified products and manufacturers that meet quality and safety standards to facilitate the public procurement process. Tenders financed with donor aid limit eligibility to WHO prequalified manufacturers and products. In Africa, only Aspen Pharmacare, has achieved WHO prequalification for a triple therapy regime.

Donors and developing countries alike appreciate WHO prequalification as it streamlines regulation and quality assurance where there are limited resources to assess ARVs independently. However, it has come under some scrutiny. DRAs striving to achieve national recognition for their capacity suggest that their ability and authority to evaluate product and manufacturer standards is undermined by the programme. For manufacturers, achieving WHO prequalification is a rigorous process requiring a large upfront investment and strong technical and development resources that are often lacking in Sub-Saharan Africa. The costs associated with the completion and submission of a product dossier can be over US\$200,000 (€134,000) and the review process can last up to twenty-four months. These upfront costs are difficult for a small local manufacturer to bear. As the eligibility criterion disqualifies local manufacturers from donor financed tenders, these products are unable to compete in most public tenders.

Without meeting WHO prequalification requirements, local industry can only compete in tenders supported by domestic financing where (unless specified by the tender board) only local DRA approval is required. This occurs, for example, within the Ministries of Health of countries like Brazil and Thailand where government financing procures ARVs from their state-owned enterprises. However, it is a challenge to convince Sub-Saharan African country governments who have much larger populations on ARVs and who rely heavily on donor aid to finance their own ARV procurement programmes entirely. This is particularly the case if there are questions of ARV price and quality.

The next generation

Currently, a significant number of first-line generics are on the market. Eleven WHO prequalified generic manufacturers produce a range of first-line ARV products. The issue of affordable supply, therefore, is now being directed toward second-line regimes. These ARV regimes

are crucial for HIV/AIDS patients who have failed or are resistant to first-line therapy. As with first-line ARVs, there is an opportunity for generic competition to reduce prices and increase affordability. Second-line regimes, however, change many of the ARV market characteristics as there is a smaller market size, higher development costs and less competition than their first-line counterparts.

Currently, around 4% of adults and 1% of children are on second-line treatment in low and middle income countries, approximating to 180,000 individuals in 2008. With such small demand a large generic market does not yet exist for second-line treatments. As ARV resistance is estimated at a rate of 3% a year,¹³ alternative first and second-line regimes will become a larger portion of ARV procurement. Important to the second-line regime is a newer class of drugs, protease inhibitors, of which many are protected under patents (patents are currently pending in India for WHO's priority recommended lopinavir/ritonavir and atazanavir). As a result, these ARVs are procured primarily by patent holding pharmaceutical firms and can be priced ten to twenty times greater than first-line ARVs. Prices for the few generic second-line drugs available are also quite variable. Generic prices for second-line regimes are often greater than those of patented products with median prices ranging from US\$948 to US\$4,245 (€635 to €2,844) against US\$865 to US\$2,577 (€580 to €1,727), respectively.¹⁴ As these prices consume a substantial proportion of donor and government budgets, advocates call for these prices to be reduced further.

This is difficult with few second-line generics currently on the market. A few patent holding drug firms have contracted non-exclusive licenses for second-line ARVs to Indian and South African manufacturers (such as Bristol Myers Squibb's atazanavir to Emcure Pharmaceuticals and Aspen Pharmacare). Efforts are also underway in Thailand to import, as well as produce, generic versions of Abbott's lopinavir/ritonavir and Merck Sharpe and Dohme's alternative first-line ARV efavirenz under compulsory licenses issued in 2007 and 2006, respectively. However, both the European Commissioner for Trade and the Office of the United States Trade Representative (USTR) emphasised their deep concern over the process of compulsory licensing to the Thai Ministry of Commerce. As a result, Thailand was placed on the Priority

Watch List of the annual USTR Special 301 trade report. This international trade pressure to enforce patents stalls generic ARV market entry and contradicts the intention of the European Commission grant to support manufacture of generic ARVs. However, it is unlikely that this trend will stop as the imposition of TRIPS-plus standards on countries is now a core strategy of the research-based pharmaceutical industry, primarily through the imposition of new standards under bilateral and regional trade agreements.

Market entry also lags for many second-line products because of small volumes, pending patent status (in India), time for development, increased technological complexity and its associated costs, as well as DRA and WHO prequalification application processes and delays. What these licenses and other generic production efforts will mean for price reduction has yet to be determined. There is concern that the multiple voluntary licenses may make it increasingly difficult for advocates to suggest there is a lack of competition in the marketplace in order to negotiate further price reductions.

The issue of second-line ARVs, therefore, encourages least-developed countries to utilise their 2016 transition period and manufacture these drugs, such as current efforts underway in Tanzania. Yet, like first-line regimes, their ability to do so remains in question. In Tanzania, second-line drugs are not tendered publicly, but financed, procured, and supplied by PEPFAR. Market penetration is limited without US Food and Drug Administration approval or WHO Prequalification.

The way forward?

In order to maximise ARV treatment access through affordable pricing, tenders must seek the lowest cost quality drugs available. This is typically the system in place in Sub-Saharan African countries as donors stipulate international competitive tenders to procure ARVs. The success of local manufacturers then relies on the capacity of the firm to achieve two necessary components of donor financed tenders: international quality standards and economies of scale to lower price. The targeted financial support from the European Commission has resulted in only one grant of which we are aware and its position on the use of TRIPS safeguards to promote generic manufacturing appears contradictory. We believe that local manu-

facture in Sub-Saharan Africa, under current constraints, is difficult to achieve successfully. It is not presently in the interest of patients, the governments of their countries, donors or drug companies.

Consideration has and should be taken to develop regional cooperation among DRAs and manufacturers to shorten the time to market authorisation and to pool procurement volumes to increase economies of scale, respectively. Politically, however, an initiative of this type seems unlikely. Manufacturing is not solely an issue of access, but also economic development. It must address issues of financing, technology, employment, self-sufficiency, and revenue requiring policies that are difficult for a region to agree upon.

Additionally, of particular note to donor countries is that financing drug procurement and encouraging local production efforts fails to address many other critical components of the WHO access framework that prevent affordable medicines from reaching patients. Increased donor attention should address shortages of human resources, patient adherence and sustainability of pledged donor financing. While increasing the number of people receiving treatment is a short-term goal that provides impressive statistics, it neither addresses sustainability nor does it improve the fragmented health system and poor health infrastructure that limit the availability of treatment and basic care.

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Public-private sector partnerships as a means of development in Africa, in the context of HIV/AIDS

Gavin George and Tim Quinlan

Summary: Where and how the private sector can work in partnership with public agencies to improve human welfare is a wide ranging public debate. The broad issues, nonetheless, have been resolved; for example, the 'Millennium Development Goals' affirm the need for multi-sectoral, co-ordinated interventions and Corporate Social Responsibility is now an axiom of sound business practice. Indeed, private-public 'partnerships' are an accepted premiss for stimulating national development in the countries where there are HIV/AIDS epidemics. Where there is much debate, however, is over the details of where and how these partnerships can and do work effectively. Here, we focus on one 'big' question: how to promote development in the context of HIV/AIDS? We also focus on one set of issues, the role of the private sector in public health management in countries with HIV/AIDS epidemics.

Keywords: public-private partnerships, HIV/AIDS, treatment, health

"If health systems are to be considered the vehicle for the delivery of services and interventions to deal with HIV/AIDS, [the public health community] has over the last few years tended to neglect the vehicle". Much more attention has been paid to getting the passengers into the vehicle and determining where the vehicle is supposed to go, as opposed to trying to address the deficiencies of the vehicle itself." (McCoy)¹

The quote above by McCoy succinctly captures the widespread concerns, past and present, about the capability of public health services in Africa to confront the HIV/AIDS pandemic. A case in point is the ongoing, very public debate on the exodus of health professionals from Africa, their active recruitment by health services in the 'north', and subsequent government policy changes in some European and African countries to mitigate the problems created for the public health services in Africa.* Our contention is that McCoy's observation also applies to the current state

of private sector health-oriented interventions.

Today, there is little to contest over the capability of the private sector to play a critical role, particularly in developing countries, to reduce poverty and improve public health through independent and co-operative interventions.² Indeed, private-public 'partnerships' are an accepted premiss for stimulating national development in the countries where there are HIV/AIDS epidemics. The International Labour Organization (ILO), the Global Fund, and other partners are working together to support expanding public-private partnerships in the world of work.

This includes community outreach where the employer covers the costs of antiretroviral drugs for permanent employees and the Global Fund or other donors extend access to these drugs to the families, contractors and the local community.³

Here, however, we draw attention to practical challenges facing the private sector, which exist irrespective of arguments about where and how companies can contribute to the public good in rolling back the pandemic and whether they can do more than they are doing. In other words, we ask what precisely are a 'vehicle's deficiencies'? We discuss this question in relation to the global effort to expand anti-retroviral treatment (ART) programmes and, specifically, to the evolution of workplace 'wellness/health management' programmes in South Africa. Our purpose is to illustrate policy-relevant issues that lie beneath debates about the

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* South Africa, for instance, entered into an agreement with the United Kingdom in 2003 which made allowances for health professionals of one country to work in another for a specified period.

need for, and possible forms of private-public sector partnerships.

Core challenges

Large multi-national corporations are providing a lead in South Africa on the design and implementation of health management programmes. We refer here to the impetus towards comprehensive health services which include multiple interventions (for example, education and awareness programmes; voluntary counselling and testing[VCT]; access to, or direct provision of ART – and nutritional supplements – to staff in need; extension of these services to workers' spouses; and support of 'community-based interventions').⁴ These companies have an advantage over public health services on several grounds; for example, defined, concentrated populations and considerable financial resources to develop services. However, the results to date are disappointing: while many companies can boast high participation rates in education and awareness programmes and in VCT campaigns, few, if any can show high uptake rates of workers in ART programmes*.⁴ Furthermore, workers who do enrol for treatment usually do so when they are too sick to work, thereby negating the fundamental purpose of a workplace programme, which is to keep workers healthy and productive.

At root, private sector health initiatives encounter two core challenges which confront all health systems in countries where there are HIV/AIDS epidemics. One is the lack of precedents on how to contain and manage HIV/AIDS; hence, the imperative for innovation in health systems delivery. The second is the quantum leap involved in conceiving and implementing comprehensive programmes which are effective in both preventing the transmission of the virus and treating those who are infected. There is little resemblance between standard occupational health programmes and 'wellness' programmes. The latter invokes the concept of the 'continuum of care' which,

as we noted above, demands multiple interventions. Those interventions entail substantive investment in expertise either through 'in-house' employment of health professionals or payment to external service providers. The long term logic and scope of those investments inevitably raises consideration of collaboration with the public health sector, as at some point companies must confront issues such as drug procurement and enabling retrenched staff to migrate to public treatment programmes.

In turn, the lack of precedents demands experimentation which is reflected in South Africa, in the existence of different models of health care within the private sector. Likewise, there are standard protocols for health care in South Africa's public health service but, in practice, there is huge variation from the norm and between different provincial and local health service departments and, indeed, between different hospitals and clinics.**

Our central argument, therefore, is that debates about, and policy-making on, public-private sector partnerships all too easily focus on form and satisfy political and ideological interests at the expense of appreciating the necessity of experimentation and innovation.

The situation in South Africa

In 2003 the South African government announced that it would begin providing treatment through the public health service. However, the roll out has been extra-ordinarily slow even though the public programme added greatly to the number of people who were accessing treatment via non-governmental organisation and private sector services. In 2006, the estimated total number of people needing treatment was 711,000.⁵ By 2007, approximately 306,000 people were receiving treatment,⁶ having risen from 280,000 in 2006⁷ and from less than 50,000 in 2003.^{8,9} Currently (April 2008), South Africa's public media is broadcasting that '2%' of the population has tested for HIV.***

Even allowing for a sizeable margin of error, these statistics show that South Africa has yet to achieve substantive success with regard to containing HIV and AIDS. Numerous reasons are put forward for this failure, ranging from a prevailing culture of stigma and discrimination to lack of political will. We have no reason to doubt the explanations nor, indeed, the possibility of significant inroads into the epidemic within the next few years as the manifold small and large scale interventions begin to have direct and indirect effects. However, ambitions for co-ordinated intervention with attendant multiplier effects, based on private-public sector partnerships, will not be achieved without consideration of the core challenges.

In the first instance there are structural constraints to consider. Sengwana and Veenstra, for instance, recorded that managers at all levels of the public health services spoke more readily of limited capacity to deliver services in health care facilities, than management capacity deficiencies.⁹ As a result, health workers shortages came across as a more pressing issue than capacity deficiencies resulting more specifically from the decentralisation of management functions. The shortage of health care workers was moreover not related to the number of posts, but was rather attributed to the limited number of health care workers trained, inadequate recruitment procedures, poor human resource management impacting on retention, and increasing deaths among nurses as they succumbed to HIV/AIDS.¹⁰

Wadee and Khan highlighted the general shortage of health workers in South Africa.¹¹ Very recently, the government reaffirmed its approach to tackling this problem. In reply to a question in parliament, the Minister of Health reported that her department had, in the sixteen month period, since November 2006, appointed '507 doctors – predominantly from developing countries' to public sector posts (*Mercury* newspaper, 28th March 2008).

* A review of company websites will show that it is very difficult to find figures on actual numbers and proportion of staff on treatment and other success indicators such as treatment adherence rates and survival rates. This same is evident in the case of South Africa's public health services at national, provincial and local levels.

** As revealed in a HEARD project establishing the cost effectiveness of different models of antiretroviral treatment programmes across clinical sites in KwaZulu Natal in urban and rural settings.

*** In a country with approximately 40–44 million inhabitants, this percentage suggests that approximately eight to nine hundred thousand people know their status, thereby intimating that those who do get tested are predominantly those who are both HIV positive and have sought treatment.

Table 1: Medical practitioners by population for the private and public sectors

	Ratio medical practitioner to population	Medical practitioners per 100, 000 population
Public sector dependents	1 per 4219	23.7
Medical scheme beneficiaries	1 per 602	166.3

Source: Wadee H, Khan F, 2007.¹¹

The shortage is exacerbated by the uneven distribution of health workers between the public and private health sectors. Table 1 shows the number of medical practitioners available to those served by the public and private sector respectively. Additionally, the retention of health workers appointed to rural posts is difficult and rural areas tend to have a lower ratio of health workers to population than urban areas.¹²

What these figures also allude to is the existence in South Africa of distinct parallel health services that are not mutually supportive. Simply put, the public health services serve, however imperfectly, the majority of the population and primarily the sub-population of HIV infected people, while the private sector serves a small minority of the national population and primarily those who are not infected (as attested by their success with VCT campaigns).

Both sectors have limited reach. In the case of the public health services there are few facilities where individuals can get tested – the current government policy is for one facility per district. There are more facilities which provide treatment if necessary but they are not always the same as those which provide testing; hence people need to travel and make different arrangements to get access to treatment. Private sector employees access treatment through medical insurance or as a contract benefit if employed by companies that operate comprehensive workplace programmes. Furthermore stigma and discrimination are frequently cited by managers in both sectors and, indeed, by individuals as reasons for low levels of participation, be it for VCT or ART in any facility.⁴

Nonetheless, other more prosaic reasons are emerging. In the private sector, these include:¹³

- Lack of ‘buy-in’ from management; for example, when line managers and supervisors view interventions such as peer education and ‘know your status’

campaigns (VCT and company-wide sero-prevalence surveys) as factors that disrupt daily production demands and so they reluctantly support employee participation in them;

- Insufficient training, time or means given to peer educators to interact with employees;
- Disincentives such as when contract or casual employees see that they are entitled to VCT services but access to treatment is restricted to permanent employees;
- Workers not seeking treatment if they have not disclosed to their spouses and/or the latter do not have access to treatment.
- Interventions that ‘do not speak’ to the individual, taking into account factors such as age, gender, social circumstances and culture.

Yet, these problems along with those of stigma and discrimination are what stimulates innovation and experimentation by managers – in the public and private sector – to improve the reach and effectiveness of their HIV/AIDS services. In the public sector, the government began in 2004 to dismantle HIV/AIDS specific programmes and to integrate them into normal health service programmes and infrastructure. They also began to expand services such as looking for better ways to ensure adherence to treatment, establishing ‘youth-friendly’ clinics (where adolescents would not face moralistic injunctions from staff) and increasing the number of facilities that provide treatment.¹⁴

Changes to private sector workplace programmes in the mining industry and in the automotive industry illustrate the general direction of both the private and public sectors. Put schematically, the

history of workplace programmes since 2000 reveals that companies often start with education and awareness programmes, proceed towards provision of ART, incorporate supplementary services such as food supplements and then are driven to expand further through providing access to services for workers’ spouses and/or supporting HIV/AIDS ‘supply chain’ initiatives (assisting companies that supply them with components or other services). Less discernable but in the same vein are initiatives within the public sector. A conference on ART services included many reports by clinicians and managers of public health service facilities that outlined how they had or were changing protocols and procedures and creating opportunities to collaborate with surrounding communities and businesses and NGOs in a quest to improve the effectiveness of both their prevention and treatment programmes.* In some cases these innovations were being done with the approval of local health authorities (for example, Cape Town). In many cases, however, they were initiatives of frustrated clinic and hospital staff who were prepared to dispense with formally sanctioned protocols. These dynamics are significant for revealing not only the current experimentation within health programmes in South Africa but also for indicating the inevitable outcome: a diverse range of models, structures and partnerships; in short fragmented evolution of public and private health services.

Conclusion

We have outlined the expansion of health-related services in South Africa to illustrate the dynamic nature of private and public sector initiatives in contexts where there are rampant HIV/AIDS epidemics. Our purpose has been to qualify the long-standing interest in public-private sector partnerships as a means to combat HIV and AIDS and, more broadly, to enable development in the context of HIV/AIDS epidemics. Such partnerships may be desirable but, in practice, their form and content (hence the actual role of the private sector) cannot be prescribed in view of the experimentation and innovation that is occurring in the absence of effective solutions to curbing HIV/AIDS in developing countries. Nonetheless, we discern an opportunity in these circumstances for

* Roundtable on Health Systems and Antiretroviral Access, Bloemfontein, 22 and 23 October 2007.

policies that support the drive towards private-public sector partnerships. The private sector has proved capability to achieve an essential first step in containing the transmission of HIV: widespread participation in VCT campaigns. It has not achieved substantive success in expanding access to treatment. However, it has demonstrated capability to systemic innovation; in short greater flexibility and commitment than the public sector to act upon experience and evidence. These are characteristics which support greater funding support from international agencies to companies specifically. Inevitably, companies come up against the same challenges as the public health services such as drug procurement and lack of health-care infrastructure. Providing support on the basis of their capability to systemic innovation is a required step towards making public-private sector partnerships an effective option.

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Mythbusters

Myth: We can improve quality one doctor at a time

The solo doctor who embodies every process needed to ensure highest quality care is now nearly a myth. All physicians depend on systems, from the local ones in their private offices to the gargantuan ones of national health care.¹ Quality problems are pervasive. But poor quality is not a result of a series of individual mistakes.²

Individual doctors are often singled out as ‘bad apples’ when health care safety is lacking.³ In the same way, when it comes to achieving a high-quality health care system, doctors are frequently regarded as the system’s lone rangers, standing to improve quality of care one ‘first-rate’ doctor at a time.¹ But the performance of the health care system depends on the actions of many players: just imagine a rowing boat with a team of rowers pulling on the oars; one is a doctor and is rowing at a completely different rhythm from the rest of the team. Progress will be slow, frustrating for all, and with a great deal of splashing and bruising.

The belief that quality of health care rests solely on the shoulders of doctors has led to strategies focused on improving the quality of care offered by individual physicians through approaches such as clinical practice guidelines. Clinical guidelines have long been regarded as key to improving quality of care; this idea is based on the notion that if we gather the evidence on appropriate health care for specific circumstances and tailor this evidence to the needs of individual practitioners, we can improve professional practice and health outcomes.⁴ Unquestionably, guideline development is worthwhile, but doctors face a number of barriers — including those that are beyond their control — that serve to undermine guideline implementation.^{5–7} For example, physician adherence to clinical guidelines often relies on systems-level improvements such as acquisition of new resources, facilities, and enhanced staff support.^{5,8,9} One academic put it best when he said “there has been a preponderance of patient-level outcome studies within a biomedical paradigm which is incomplete without attention to the context within which patients receive their care.”¹⁰

There’s undeniably no ‘magic bullet’ when it

comes to improving clinical practice,¹¹ and the same is true for improving quality in health care.^{12,13} A more promising strategy would bear in mind not only the evidence on effective practice, but the evidence on how to transform the health care system at large.

No simple prescription

While the popular focus is on solo doctors, we know “no person acting alone is as effective as a team to drive best practices and outcomes.”¹⁴ And looking beyond the clinical level, a broader team exists. It is at the macro level, where managers and policy makers drive system-wide quality improvement initiatives, including greater use of information technology, performance measurement and reporting, and integration of services.

Few would dispute the significance of inter-professional collaboration in promoting safe, efficient, and quality health care.^{15,16} Teams are less prone to making mistakes than individuals, especially when team members are well aware of their own and their team members’ roles and responsibilities.^{17,18} And a health care system that supports effective teamwork can improve the quality of care through enhanced patient safety and reduction of workload issues causing burnout among health care professionals.¹⁹ Systematic reviews of collaboration and teamwork also show effectiveness across a range of chronic conditions — from cancer to mental health to geriatric care — ultimately leading to shorter hospital stays, reduced costs, and increased patient satisfaction.^{20–23} An additional benefit of teamwork is its ability to help with effective transfer of evidence to practice.⁸

Taking a systems approach

Another important contribution from research is to consider processes (such as information and patient flow)²⁴ and systems (suites of processes) for improving health care outcomes.²⁵

The ‘theory of continuous quality improvement’ (or CQI) counteracts the still-popular ‘theory of bad apples’^{1,3} and operates on the principle that, while health care providers aim to do their best, they are limited by faulty health care processes.^{1,25,26} With an emphasis on

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A series of essays by the Canadian Health Services Research Foundation on the evidence behind healthcare debates



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improving processes and systems for improving health care quality, CQI initiatives take the heat off individuals.

One example of CQI functioning at its best comes from the American Department of Veterans Affairs (VA), which initiated a “system-wide re-engineering” to improve its quality of care in the mid-1990s.²⁷ Taking a systematic approach to measure, manage, and be held accountable for quality, the VA saw a drastic upgrade in its overall performance, with statistically significant improvements for all quality indicators collected from 1994–95 through to 2000.²⁷ In addition to instituting routine quality indicators and performance measurements and introducing an electronic medical record system, the VA’s success relied on performance contracts and making performance data public, which served to make managers accountable for meeting quality improvement goals.²⁷

Conclusion

Physicians aim to provide quality health care for their patients, but they cannot achieve high-quality health care alone or without support. If we are to improve health care quality, we must focus our attention at the systems level – the ‘big picture’ – and involve multiple actors, from health care providers to managers and policy makers.

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On limitations

The thing about looking at evidence of any sort is that there are likely to be limitations to it. Trials may not be properly conducted, measure outcomes that are not useful, be conducted on patients not like ours, or present results in ways that we can easily comprehend; trials may have few events, when not much happens, but make much of not much, as it were. Observational studies, diagnostic studies, and health economic studies all have their own particular set of limitations, as well as the more pervasive sins of significance chasing, or finding evidence to support only preconceptions or *idées fixes*.

Perfection in terms of the overall quality and extent of evidence is never going to happen, if only because the ultimate question – whether this intervention will work in this patient and produce no adverse effects – cannot be answered. The average results we obtain from trials are difficult to extrapolate to individuals, and especially the patients in front of us.

Acknowledging limitations

Increasingly we have come to expect authors to make some comment about the limitations of their studies, even if it is a nod in the direction of acknowledging that there are some. This is not easy, because there is an element of subjectivity about this. Authors may also believe, with some reason, that spending too much time rubbishing their own results will result in rejection by journals, and rejection is not appreciated by pointy-heads.

Even so, the dearth of space given over to limitations of studies is worrying. A recent survey¹ that examined four hundred papers from 2005 in the six most cited research journals and two open-access journals showed that only 17% used at least one word denoting limitations in the context of the scientific work presented. Among the twenty-five most cited journals, only one (*JAMA*) asks for a comments section on study limitations, and most were silent.

Few events

It is an unspoken rule that to have a paper published it helps to have some measure that displays a statistically significant difference. This

leads to the phenomenon of significance chasing, in which data are analysed to death, and the aim is any test that shows significance at the paltry level of 5%. One issue arising is correcting for multiple statistical testing, something almost never done, as pointed out in *Bandolier* 153.

The more important question, not asked anything like often enough, is whether any statistical testing is appropriate. Put another way, when can we be sure that we have enough information to be sure of the result, using the mathematical perspective of sure, meaning the probability to a certain degree that we are not being mucked about by the random play of chance? This is not a trivial question, given that many results, especially concerning rare but serious harm, are driven by very few events.

A few older papers keep being forgotten. When looking at the strengths and weaknesses of smaller meta-analyses versus larger randomised trials, a group from McMaster² suggested that with fewer than two hundred outcome events research (meta-analyses in this case) may only be useful for summarising information and generating hypotheses for future research.

A different approach using simulations of clinical trials and meta-analyses³ arrived at pretty much the same conclusion, that with fewer than two hundred events the magnitude and direction of an effect becomes increasingly uncertain.

Just how many events are needed to be reasonably sure of a result when event rates are low (as in the case for rare but serious adverse events) was explored some while ago.⁴ Bandolier's best try at explaining lots of maths and tables appears in Table 1. This looks at a number of examples, varying event rates in experimental and control groups, using probability limits of 5% and a more stringent one of 1%, and with the power of 80% and 90% to detect an effect.

Higher power, greater stringency in probability values, lower event rates, and smaller differences in event rates between groups all militate towards needing more events and larger numbers of patients in trials. Once event rates fall to about 1% or so, and differences between experimental and control to less than 1%, the number of events needed approaches one hundred and the number of patients rises to tens of thousands.

Table 1: Examples of numbers of events and numbers of subjects required to be reasonably sure of the direction of a result at various levels of significance and power for rare events

Event rates (probabilities)		Mean event rate (%)	Power of 80%				Power of 90%			
Experimental	Control		p < 0.05		p < 0.01		p < 0.05		p < 0.01	
		Events	Total	Events	Total	Events	Total	Events	Total	
0.1	0.01	5.5	12	218	14	255	15	273	21	382
0.01	0.001	0.55	12	2,182	14	2,545	15	2,727	21	3,818
0.001	0.0001	0.055	12	21,818	14	25,455	15	27,273	21	38,182
0.1	0.05	7.5	67	893	> 75	> 1,000	> 75	> 1,000	> 75	> 1,000
0.01	0.005	0.75	67	8,933	> 75	> 10,000	> 75	> 10,000	> 75	> 10,000
0.001	0.0005	0.075	67	89,333	> 75	> 100,000	> 75	> 100,000	> 75	> 100,000
0.04	0.01	2.5	23	920	34	1,360	29	1,160	42	1,680
0.004	0.001	0.25	23	9,200	34	13,600	29	11,600	42	16,800
0.0004	0.0001	0.025	23	92,000	34	136,000	29	116,000	42	168,000
0.03	0.01	2	33	1,650	48	2,400	42	2,100	59	2,950
0.003	0.001	0.2	33	16,500	48	24,000	42	21,000	59	29,500
0.0003	0.0001	0.02	33	165,000	48	240,000	42	210,000	59	295,000
0.02	0.01	1.5	> 75	> 5,000	> 75	> 5,000	> 75	> 5,000	> 75	> 5,000
0.002	0.001	0.15	> 75	> 50,000	> 75	> 50,000	> 75	> 50,000	> 75	> 50,000
0.0002	0.0001	0.015	> 75	> 500,000	> 75	> 500,000	> 75	> 500,000	> 75	> 500,000

Subgroup analyses

One of the best examples of the dangers of subgroup analysis, due to unknown confounding, comes from a review article.⁵ It examined the thirty day outcome of death or myocardial infarction from a meta-analysis of platelet glycoprotein inhibitors. Analysis indicated different results for women and men (Figure 1), with benefits in men but not women. Statistically this was highly significant (p<0.0001).

In fact, it was found that men had higher levels of troponins (a marker of myocardial damage) than women, and when this was taken into account the difference between men and women is understandable, with more effect with greater myocardial damage; sex wasn't the source of the difference.

Trivial differences

It is worth remembering what relative risks tell us in terms of raw data (Table 2).

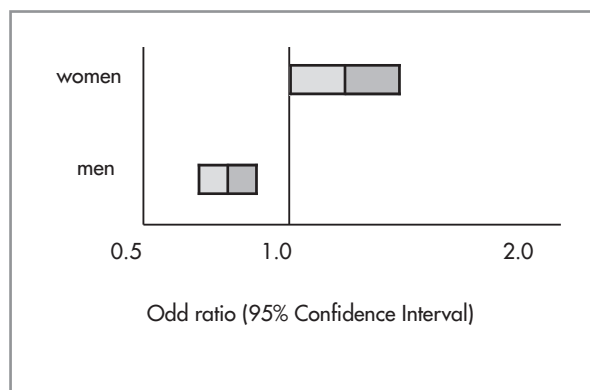


Figure 1: Subgroup analysis in women and men of death or myocardial infarction with platelet glycoprotein inhibitors (95% confidence interval)

Suppose we have a population in which one hundred events occur with our control intervention, whatever that is. If we have one hundred and fifty events with an experimental intervention, the relative risk is now 1.5. It may be statistically significant, but most events were those occurring anyway. If there were two hundred and fifty events, the relative risk would be 2.5, and now most events would occur because of the experimental

intervention.

Large relative risks may be important, even with more limited data. Small relative risks, probably below 2.0, and certainly below about 1.5 should be treated with caution, especially where the number of events is small, and even more especially outside the context of the randomised trial.

The importance of a relative risk of 2.0 has been accepted in US courts.⁶ “A relative

Table 2: What different levels of relative risk actually mean

Relative risk	What this means
< 1.0	The risk of an event is reduced for the experimental intervention compared with the control intervention
1.0	No increased or decreased risk for experimental versus control
1.0 – 2.0	Higher risk of events with experimental intervention, but most events occur because of underlying factors - like the patient population being studied
> 2.0	Higher risk of events with experimental intervention, and most events occur because of the experimental intervention

risk of 2.0 would permit an inference than an individual plaintiff's disease was more likely than not caused by the implicated agent. A substantial number of courts in a variety of toxic substance cases have accepted this reasoning.”

Confounding by indication etc.

Bias arises in observational studies when patients with the worst prognosis are allocated preferentially to a particular treatment. These patients are likely to be systematically different from those not treated, or treated with something else (paracetamol, rather than non steroidal anti-inflammatory drugs in asthma, for instance).

Confounding, by factors known or unknown, is potentially a big problem, because we do not know what we do not know, and the unknown could have big effects - like troponin above. When relative risks are small, say below about 1.3, potential bias created because of unknown confounding, or confounding by indication improperly adjusted, becomes so great that it makes any conclusion at best unreliable.

Comment – the uncertainty principle

These are just a few of the limitations Bandolier sees in papers and talks. There are more, obviously. Worst of all is an outcome failing to reach statistical significance at a trivial level like 5% despite multiple statistical comparisons, then being trumpeted as a 'result' and extrapolated to whole populations. If it is not statistically significant, it does not signify.

The trouble is that we live in an imperfect world, where we never have the truth, the whole truth, and nothing but the truth on which to work and build judgements. We have to make do with what we have and

try our best to exclude the rubbish. Some try a philosophical approach to calculate thresholds above which we can begin to believe,⁷ but that seems a bit too glib.

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New Health Systems in Transition Profile: Estonia



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Edited by Ewout van Ginneken

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This latest addition to series illustrates that Estonia has vigorously and quite successfully reformed its health system over the last decades. Whereas incremental changes are observed in the last five years, larger scale legislative reforms were implemented from the early 1990s. The current system is built on solidarity based health financing; a modern provider network based on family-medicine centred primary health care; modern hospital services and more attention for a public health. This has resulted in a steadily increasing life expectancy and continuously high population satisfaction rates with access and quality.

However, a number of challenges remain. They include reducing inequities in health status and health behaviour; improving control of and responding to the consequences of the high rates of HIV and related conditions; improving regulation of providers to ensure better public accountability; and, sustaining health expenditures and human resources on a level that ensures timely access and high quality of care. The last challenge is particularly important in the face of rising patient expectations and increased costs and volume of health care services. If solidarity and equity are to be maintained and guaranteed for the future, additional resources need to be found from public sources of revenue.

Sales growth of new pharmaceuticals across the globe: the role of regulatory regimes

Stefan Stremersch and Aurélie Lemmens



Rotterdam: Erasmus Research Institute of Management, 2008

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44 pages

Freely available online at:
<http://publishing.eur.nl/ir/repub/asset/12340/ERS-2008-026-MKT.pdf>

As part of the Erasmus Research Institute of Managements report series on Research in Management, this new publication examines the role of regulatory regimes in explaining the international sales growth of new pharmaceutical products. The publication analyses fifteen new molecules in thirty-four countries and endeavours to shed light on the effect regulatory regimes have on new drug sales across the globe.

The report examines several aspects of the regulatory environment on: manufacturer price, physician prescription budgets, patient co-payments, marketing efforts to physicians, and direct-to-consumer (DTC) advertising. Based on a time-varying coefficient model, the authors find that differences in regulation substantially contribute to cross-country variation in sales. Although manufacturer price controls had a positive effect on drug sales, the other forms of regulation, such as restrictions on physician prescription budgets and the prohibition of DTC

advertising, tend to hurt sales. Furthermore, regulations on physician prescription budgets and DTC advertising have a differential effect for newly launched and mature drugs. In addition to these regulatory effects, other mechanisms that affect drug sales include national culture, economic wealth, introduction timing, lagged sales and competition. These findings may be used by public policy administrators to compare drug sales across countries and to assess the role of regulatory regimes.

Contents:

Abstract
 Introduction
 Data
 Model specification
 Results
 Discussion
 References

Payment for Performance (P4P): international experience and a cautionary proposal for Estonia

Alan Maynard



Copenhagen: World Health Organization, 2008

26 pages

Freely available online at:
http://www.euro.who.int/Document/HSE/P4P_Estonia.pdf

This Health Financing Policy Paper published by the WHO Regional Office for Europe's Division of Country Health Systems looks at Payment for Performance (P4P) in health systems. Alan Maynard first reviews evidence of common provider problems in all health systems and their implications for introducing a P4P system. This is followed by a review of P4P reforms in England and the United States in particular. Throughout the analysis, he places an emphasis on gaps in the evidence base and the need for careful experimentation and evaluation to inform service reform.

The ultimate goal of P4P reforms is to promote evidence-based care and to ensure that in doing so process management is supplemented by patient-reported outcome measures. Maynard argues that focus should be on gradually and systematically shifting the policy processes from analysis of process to outcome measurement and management to inform decision-makers about whether health care expenditure actually leads to the desired patient outcomes.

With regards to Estonia, the organisational structure to finance and provide health care has been established with elements of contracting and provider payment systems, but additional incentives to enhance quality are desired. The recommended P4P reforms for providers and hospitals, Maynard notes, have to be carefully designed, implemented and evaluated.

Contents:

Executive summary
 Background
 Common problems confronting purchasers and providers
 Incentivising change in health care provision and purchasing
 Reinforcing the purchaser role: development of normative incentives
 Conclusions
 References

French EU Presidency 2008

<http://www.ue2008.fr/PFUE>

News and information from the French Presidency of the European Union

European Centre for Disease Control (ECDC)

<http://ecdc.europa.eu>

The European Centre for Disease Prevention and Control, based in Stockholm, was established in 2005. It is an EU agency with an aim to strengthen Europe's defences against infectious diseases. The web site provides information about the organisation's activities, publications for free download (scientific and technical papers, newsletters, the *Eurosurveillance* journal, and annual reports), events including conferences, calls for tender and news. There are special news sections on influenza and vaccines and immunisations. There is also a searchable list of health topics.

European Public Health Alliance

<http://www.ephia.org>

The Brussels based EPHA is an international non-profit association composed of organisations working on all aspects of public health. Its English language web site features: an 'Environment' section which provides news on a variety of topics including air and water, nuclear energy and road safety; a 'Europe' section which provides health related news from the European Institutions; a 'Food and Agriculture' section which provides news on this topic (including health related news on the Common Agriculture Policy (CAP), genetic modification and biotechnology and obesity and overweight); and a 'Society' section which provides news about civil society, governance issues, health rights, NGOs, public interest, patients, health inequalities, social policy, alcohol, drugs, tobacco, Global Health. There is also information about European health related publications and events and a newsletter.

The Commonwealth Fund

<http://www.commonwealthfund.org>

The Commonwealth Fund is a New York-based private foundation that supports independent research on health care issues and makes grants to improve health care practice and policy. Although predominantly US focused, it has an international programme in health policy designed to stimulate innovative policies and practices in the US and other industrialised countries. The English language web site provides publications, including *The Commonwealth Fund Digest* and an annual report; downloadable charts (mainly featuring US data); a US state scorecard; surveys, including results from international surveys; news about health systems innovations; and details about grants, programmes and fellowships.

European Federation of Pharmaceutical Industries and Associations (EFPIA)

<http://www.efpia.org>

EFPIA represents thirty-two national pharmaceutical industry associations and forty-three leading pharmaceutical companies operating in Europe. Its mission is to improve the competitiveness of the research-based pharmaceutical industry in Europe in a regulatory and political environment, which above all stimulates research and development and rewards innovation. The website contains a range of statistical information, including the patient WAIT indicator which provides data on the length of time patients have to wait for access to medications in different European countries. The publications section of the website contains a range of policy documentation as well as the 2008 edition of *The Pharmaceutical Industry in Figures*. Press releases, video presentations and information on forthcoming events are also available.

Improving Chronic Illness Care (ICIC)

<http://www.improvingchroniccare.org>

The web site of the Improving Chronic Illness Care Programme, an initiative of the Robert Wood Johnson Foundation, offers a range of resources and teaching tools designed for leading and managing improvement efforts in chronic diseases management within a variety of settings. It focuses mainly on the US but provides many resources that are also relevant to the European context, including: a compendium of tools for clinicians involved in changing chronic disease care for their patients; learning materials; surveys (including Spanish and Danish translations); ICIC reports; ICIC presentations with downloadable graphics; and evidence in the form of literature reviews (condition specific and related to the chronic care model).

EUROPEAN MONITOR

European ministers sign groundbreaking charter on health systems

Ministers of health from the fifty-three countries of the WHO European Region signed a new charter on health systems in Tallinn, Estonia on 27 June, committing themselves to concrete and measurable action on strengthening health systems that will allow both their own people and the international community to hold them to account.

All countries have pockets of people who miss out on quality health care. The charter stresses that strong health systems must be put in place to remove barriers such as insufficient access, costs and lack of information, to ensure coverage across the board. The charter declares that “today, it is unacceptable that people become poor as a result of ill-health. ... We, the Member States, commit ourselves to: promote shared values of solidarity, equity and participation through health policies, resource allocation and other actions, ensuring due attention is paid to the needs of the poor and other vulnerable groups.”

WHO estimates that, each year, health expenses cause 150 million people to suffer financial catastrophe and push 100 million below the poverty line.

“Health is the right of everyone and it has value in itself. It is in the interest of all governments to invest in the health of their populations, as improving the health of the population makes a material contribution to the wealth of the nation,” said Dr Marc Danzon, WHO Regional Director for Europe, at the charter signing ceremony.

“I am personally thrilled by the value system so clearly evident in the Tallinn charter,” said WHO Director-General, Dr Margaret Chan, addressing

the Conference. “As we now know, cash, commitment and commodities cannot boost adequate progress in the absence of delivery systems that reach those in great need, on an adequate scale, in time.”

The charter details the key actions needed to make health systems stronger, such as improving transparency and accountability for health spending and ensuring that spending is aligned to policy objectives. “Increasing investment in health will pay dividends only if it’s well spent,” said Dr Nata Menabde, Deputy Regional Director, WHO Regional Office for Europe. “There is no ‘right’ or ‘optimal’ size of budget that should be devoted to health. We do not want to give the impression that simply increasing the level of budget allocations to the health sector will solve all problems. The health system needs to increase and demonstrate its capacity to use the money in a prudent and transparent manner.”

As part of the preparations for the charter, WHO conducted studies that have produced evidence of the link between the health and wealth of the population, making the case for giving serious political attention to the performance of health systems. WHO’s research also indicates that in the past the importance of the health system to the general health of the population has been underestimated, as has the impact of better health on economic growth. Rather than being seen as a ‘necessary burden’, investment in effective health systems should be considered as an investment in the future well-being of the population.

Speakers at the Conference stressed that good health systems should not be a luxury that only rich countries can afford, but a fundamental part of the social and physical infrastructure that supports a country’s prosperity, cohesion,

and social well-being, underlining that the charter places particular emphasis on ensuring people are treated with dignity and respect when they come into contact with their health system.

The final text of the charter, together with material and recordings from all Conference sessions, including the charter signing ceremony, are available at <http://www.euro.who.int/healthsystems2008>

Commission adopts proposal for directive on patients' rights in cross-border health care

On 2 July the European Commission adopted a proposal for a directive to facilitate the application of European patients' rights in relation to cross-border health care, as well as a Communication on improving cooperation between Member States in this area. The move came following calls from both the European Parliament and the Council of Ministers for the Commission to propose a specific initiative on cross-border health care, in a way explicitly adapted to, and respecting, the unique nature of the health care sector. Previously it been excluded from the scope of Directive 2006/123/EC on services in the internal market.

Despite several consistent European Court of Justice rulings confirming that the EU Treaty gives individual patients the right to seek health care in other Member States and be reimbursed at home, uncertainty remains over how to apply the principles of this jurisprudence more generally. With this proposal the Commission aims to provide legal certainty on the issue. Prior public consultation conducted by the Commission reported that the majority of 280 respondents received favoured some form of Community action on health care, combining both legislative elements and practical support for cooperation between

European health systems.

Speaking of the proposed directive, European Health Commissioner Androulla Vassiliou said that it “aims to clarify how patients can exercise their rights to cross-border health care, while at the same time providing legal certainty for Member States and health care providers. It ensures that the quality and safety of health care will be guaranteed throughout the Union, and promotes cooperation between health systems to provide better access to specialised care.”

According to the Commission, the directive, if adopted by the Council and the European Parliament, will provide a clear framework for cross-border care. Under its major provisions patients would have the right to seek health care abroad and be reimbursed up to what they would have received at home. The directive will provide clarity over how these rights can be exercised, including the limits that Member States can place on such health care abroad, and the level of financial coverage that is provided for cross-border health care.

The directive will also facilitate European cooperation on health care. It will provide a basis to support the development of European reference networks, which will bring together, on a voluntary basis, specialised centres in different Member States. This collaboration potentially will bring benefits to patients through easier access to highly specialised care. It may also be useful to health systems as it would facilitate the efficient use of resources, for example by pooling resources to tackle rare conditions.

The initiative is also intended to help to reduce overlap and duplication of efforts in the field of health technology assessment and hence promote the effective and efficient use of resources. The directive will also put in place shared formats and standards for e-health technology that can be used between different systems and different countries. Information and communication technologies have enormous potential to improve the quality, safety and efficiency of health care.

‘Long row’ predicted

Enshrining the draft directive into legislation will be far from a smooth process. A stakeholder debate on the Commission’s proposal at the European Parliament on 15 July indicated the

strength of feeling in some quarters. Robert Madelin, Director General at DG Health and Consumers, predicted that early discussions on the draft directive signalled “the beginning of a long row” as he defended the proposal against hesitations over the legal workability of the system. Others in the debate pointed to the gap that the proposal could create between rich and poor.

“In a decade, we will look back and see how far we’ve got,” said Madelin, suggesting that discussions over the matter could take many years. The draft directive only “streamlines the rights that the Court has already delivered,” said the EU official. “It is not the end of the world as seen by health managers,” he added.

Irene Wittmann-Stahl, health attaché at the Permanent Representation of Germany to the EU, said a lot of questions remained to be answered before the Council was able to form its opinion on the draft directive. Among others these included issues of legal certainty; whether the European Court of Justice jurisdiction should be seen as the starting point for legislation or something stricter is required? Another issue is whether it should protect individual patients or health care systems which already have the obligation and need to guarantee equal access to treatment, moreover, at what stage the Directive should override Article 152 of the Treaty which ensures that competence for health matters remains a Member State responsibility?

Irish MEP Avril Doyle argued that the directive was “a charter for the wealthy to opt for care abroad,” as people need to pay for the care first themselves “which is not an option for the poor”. Therefore, she said, it would lead to more inequality than equality. Marc Schreiner from the German Hospital Federation also flagged up concerns over whether sufficiently comparable information was available to develop a reimbursement system that could function across the EU. He stated that “the core problem of this directive is that as national health systems are not comparable, the reimbursement system can’t work out and the directive would not help to initiate a cross-bordering supply of health services”. He also said that as proposal put forward by some commentators to create a basket of treatments to which all citizens have a right all over Europe, and the price of which

would be agreed upon “would clearly exceed the competence of the EU.”

The proposal has little chance of going through the co-decision procedure during the lifetime of the current Commission. There may be a first reading in the Parliament next spring, but the process will have to begin again after the June 2009 European Parliament elections.

The draft directive on the application of patients' rights in cross-border health care is available at http://ec.europa.eu/health/ph_overview/co_operation/health_care/cross-border_healthcare_en.htm and the results of the public consultation at http://ec.europa.eu/health/ph_overview/co_operation/healthcare/cross-border_healthcare_en.htm

Commission proposes to harmonise minimum taxes on tobacco prices

On 16 July the European Commission proposed harmonising minimum taxes on tobacco products to cut down on smuggling and eventually deter smoking through increased prices. The draft Directive foresees a gradual increase in the EU minimum taxation levels on cigarettes and fine cut tobacco up to 2014. It also updates the definitions of different types of tobacco products so as to remove loopholes which allow certain cigarettes or fine cut tobacco to be presented as cigars, cigarillos or pipe tobacco and therefore benefiting from a lower tax rate.

László Kovács, Commissioner for Taxation and Customs Union said the proposal will “help reduce illicit trade and cross-border shopping, which undermine the revenue and the health objectives of Member States which impose high taxes to deter smoking”. According to the Commission, the proposed Directive will also make taxation rules more transparent, thereby creating a level playing field for manufacturers and giving flexibility to Member States to set minimum taxes. It aims to contribute to reducing tobacco consumption by 10% within the next five years.

Taxation forms part of the EU’s overall strategy on the prevention and dissuasion of tobacco consumption. This strategy also includes other important measures such as non-price measures, protection from exposure to tobacco smoke, regulation of contents, and advertising

restrictions. However, according to the World Bank, price increases in tobacco products are the most effective single intervention in preventing smoking.

At present, there are considerable differences in taxation levels between the lowest and the highest taxing Member States. For cigarettes, the difference can be up to almost 600% of the excise burden expressed in Euros. Commission studies show, that in 2006 cigarettes were six to seven times more expensive in the UK than in Latvia and 13% of the tobacco consumed in the EU is not purchased in the country that is used. "4–5% of this comes from legitimate cross-border shopping and 8–9% from illicit trade," Kovács stated, adding that in some countries the share of illicit trade is as high as 20%.

Currently, excise duties levied on cigarettes must account for at least 57% of price, and must be at least €64 per 1,000 cigarettes, for products falling under the 'most popular price category' in that country.

The concept of the 'most popular price category' was designed more than thirty years ago, when national markets were dominated by one brand that was clearly 'most popular'. Nowadays, markets are more dynamic with several popular brands and regular price changes.

In order to create more transparency and to ensure a level playing field for manufacturers, the Commission proposes replacing the most popular price category with a weighted average price of all cigarettes for determining the tax base. In order to underscore health objectives it will be combined with a monetary minimum tax applicable to all cigarettes. The current percentage of 57% will be increased to 63% of the weighted average price and the rate of €64 will rise to €90 for all cigarettes by 2014, under the new proposal. It is estimated that this will contribute to a 10% decrease in tobacco consumption in most Member States within the next five years.

The Commission also proposes to give Member States more flexibility in tobacco taxation by abolishing the existing rule which forbids Member States levying a minimum excise tax higher than 100% of the total excise on the most popular price category. Furthermore, the Commission proposes to widen the band of the specific component of the excise duty from 5–55% to 10–75%.

Acknowledging the problems that the directive might pose for some of the new Member States Kovács indicated that these countries would be granted one or two years extra time to comply with the directive. The Commissioner hopes to see discussion on the proposal finalised by mid-2009 and the directive finally adopted by the end of 2009. The proposal is, however, likely to be subject to a heated debate as it needs to be adopted unanimously.

More information at http://ec.europa.eu/taxation_customs/taxation/excise_duties/tobacco_products/index_en.htm

Health priorities under the French presidency

The French EU Presidency's health priorities are five-fold: food safety, healthy ageing, cross-border health care, health determinants such as alcohol and tobacco, and pharmaceuticals, French Health Minister Roselyne Bachelot told the European Parliament. France wants to focus on the areas where the added value of EU-level action is undeniable, said Bachelot, speaking to Parliament's Environment, Public Health and Food Safety Committee on 15 July 2008.

We have ambitious objectives, acknowledged Bachelot, before listing the "five axes of work" on which the Presidency hopes to make a difference. The healthy ageing priority comprises working together to fight degenerative diseases such as Alzheimer's and the Presidency hopes to develop an EU Alzheimer's plan focusing on joint research efforts and improving the quality of life of people with this condition. A special conference on Alzheimer's will take place in Paris on 30–31 October.

Regarding the Commission's recent proposal on patients' rights in cross-border health care, Bachelot said work had already started and the dossier would be the subject of a special ministerial meeting to be held in Paris on 13–14 October. As for specific health determinants, Bachelot said particular focus would be placed on two lifestyle related determinants: alcohol and tobacco. The Presidency promised to kick-off work on a Commission Communication on smoke-free environments, expected to be adopted this autumn.

The Presidency also plans to make progress on the various pharmaceutical dossiers currently on the table as well as

the 'Pharmaceuticals Package', expected to be adopted by the Commission in November. The dossiers include work on pharmacovigilance, information for patients and counterfeit drugs.

She said counterfeiting would be one of the main issues discussed by an EU pharmaceutical ministerial forum to take place on 2 October. The forum will "take stock of the work done over the past three years" on the three topics of drugs pricing, their relative effectiveness and information for patients.

The Presidency Programme is available at http://www.ue2008.fr/webdav/site/PFUE/shared/ProgrammePFUE/Programme_EN.pdf

EMA accepts electronic-only marketing authorisations

Since 1 July 2008, the European Medicines Agency (EMA) has been accepting electronic-only marketing authorisation (MA) applications for medicinal products for human use in the centralised procedure. These electronic-only MA applications of the Common Technical Document (CTD) are now submitted without a corresponding paper-based application.

The CTD was developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use as a standard format for regulatory submissions in Europe, Japan and the USA. The eCTD is an electronic version of the CTD, with corresponding structure, folder and file names. In addition, it contains technical components which enable the management of the lifecycle of individual files in the application, and the lifecycle of the product itself.

The current plan is to phase out the paper-based and non-eCTD formats, the latter being any submission of electronic information to support an MA application that is formatted to a simple set of electronic files and folders. For a number of years, agencies have been accepting and processing non-eCTD electronic submissions in addition to paper-based submissions, but these are difficult to navigate and do not allow easy updates or status markers. Both the US and Europe are planning to accept eCTD applications only from 2009.

Europe's mental health in the spotlight

Commissioner for Health Androulla

Vassiliou launched the European Pact for Mental Health and Well-Being at a High Level Conference on Mental Health in Brussels on 13 June. This was the first conference to bring together ministers, experts, patients, health professionals, researchers and high profile personalities and other stakeholders to agree future joint actions to improve mental health in Europe.

The Pact is a call for partnership action. It was launched by the European Commission in collaboration with the Slovenian Presidency and the World Health Organization Regional Office for Europe. It is a follow up to the consultation on the Green Paper on Mental Health, which was presented by the Commission in autumn 2005. More than 230 written contributions, including a European Parliament Resolution, and a number of consultation meetings showed strong support for enhanced EU efforts to raise the visibility of mental health as a priority and to create opportunities for exchange and cooperation in tackling common mental health challenges.

It recognises the health, social and economic benefits of good mental health for all and the need to overcome the taboo and stigma still associated with mental illness. An estimated 11% of Europeans experience some form of mental illness each year. Such disorders are the leading cause of suicide; every nine minutes there is a suicide within the EU. Data from western and southern EU Member States indicate a lifetime prevalence of major depression in 9% of adult European men and 17% of adult European women. The economic costs of depression in the EU alone are substantial; being more than €2,000 for every European household. While the health system costs are high the majority of costs occur outside of the health sector, in particular through work absenteeism, work disability and early retirement. Many mental health problems can develop in the early years of life, while there is also a strong need to plan for good mental health in older age.

To address this problem and to benefit from shared experience, ministers and experts from across Europe pledged to work together and focus on five key areas: prevention of suicide and depression; promoting mental health in youth and education; mental health in workplace settings; the mental health of older people; and combating stigma and

social exclusion.

Speaking at the conference Commissioner Vassiliou said that “today, we in Europe, have raised our voices and spoken out about the devastating effect that mental illness has on society. This Pact is a symbol of our determination in Europe to take up the challenge and deliver action in our different areas of responsibility and across the health, education and labour sectors. We need to act in partnership because mental health concerns us all.”

Five consensus documents have been produced in cooperation with national ministries, practitioners and researchers from several sectors. They cover the five key priority areas previously outlined. Each of these consensus documents highlights the current data, policies and state of the art on the subject, and will support the implementation of the Pact and a series of thematic conference planned over the next two to three years.

More information on the conference and access to the Pact and Consensus Papers is available at http://ec.europa.eu/health/ph_determinants/life_style/mental/mental_health_en.htm

COUNTRY NEWS

France: New tax on health insurers

On 29 July the French government unveiled proposals for a tax on health insurers as part of a package of measures intended to help reduce the budget deficit for health which last year amounted to €4.6 billion. The proposed tax will be levied on the turnover of private health insurance companies and mutual insurance funds. It is expected to raise €1.6 billion per annum.

While the budget deficit has been decreasing in recent years, Finance Minister Eric Woerth, in an interview with *Le Parisien*, warned that without action it is set to increase by €2 billion per annum. Pointing to the challenges of an ageing population, long term care needs and the changing nature of illness, he stated that reforms were essential if the government is to meet its target of balancing the budget by 2011.

France spends approximately 11% of its GDP (€152 billion) on publicly funded health care per annum. Several measures to cut costs have been introduced in recent years, including higher

prescription charges and fees levied on individuals who consult direct with a specialist rather than first going to a primary care doctor. In looking at further efficiency measures, the new proposed tax may appear to be more palatable politically than simply increasing the costs of social insurance to employers and employees in a country that already has some of the highest labour costs in Europe. Opposition politicians claim that health insurers will simply raise their premiums to cover these taxes. However taxing these health insurance funds and mutuals direct will not affect the 8% of the population who do not purchase additional insurance.

In the same interview with *Le Parisien* Health Minister Roselyne Bachelot stated that this latest reform would build on the important reforms already in place to strengthen the role of primary care doctors, reduce the price of prescription medicines and reorganise and rationalise the hospital care. She also announced accounting reforms that avoid interest payments of more than €400 million per annum on current health system debts.

Another step in reducing costs will be to increase the amount of revenue raised by the health system when treating occupational injuries and accidents. Previously an independent expert commission reported that the level of compensation received by the health system from occupational insurance (€410 million per annum) is well below the costs to the health care system of treating these accidents.

These latest reform measures will be presented to Parliament in September and, if approved, should be implemented from the spring of 2009.

The interview with Ministers Woerth and Bachelot is available [in French] at <http://www.leparisien.fr/economie/le-patient-ne-doit-etre-en-aucun-cas-perdant-29-07-2008-105653.php>

Blueprint on future of the English NHS

On June 30 Health Minister Lord Darzi published a review entitled *High Quality Care For All* setting out plans for the next ten years of the English NHS. The review, which took twelve months to complete, was led by 2,000 clinicians and staff across the country and involved 60,000 patients, public and staff. It is intended to meet key future challenges: rising public expectations, demand driven

by an ageing population; the changing nature of disease and changing needs of the health system workforce. The changes will be driven not through top-down targets but by giving responsibility to the staff at local level.

Specific attention is placed on tackling variations in quality of care, it also further emphasises the need to personalise services and proposes that the concept of patient choice be enshrined as a right in a new NHS Constitution. Choice will be expanded further within primary care: catchment areas for general practitioner (GP) practices will be expanded, while patients will also be able to express a preference to be seen by a GP within specific practices. Patients with long term care problems will also receive individualised care plans and personal budgets, again promoting the notion that patients can be empowered to purchase services that best meet their needs.

Information on the quality of an NHS body's service will be published on the web and on clinical 'dashboards' in hospitals and GP surgeries. Moreover, all providers of NHS care will have to publish quality accounts each year. The report states that "a range of quality measures covering safety (including cleanliness and infection rates), clinical outcomes, patient experience and patient's views about the success of their treatment will be used."

Overall it is anticipated that quality-linked funding could make up between 3% and 4% of the average district general hospital's budget of around £250m within a few years.

Speaking at the launch of the review, Lord Darzi said that it "will enable frontline doctors, nurses and patients – who provide and use NHS services – to put into practice their visions for high quality care." He added that "by measuring this quality across the service and publishing that information for the first time, both staff and patients can work together to make better informed choices about their care."

The appraisal process used by the National Institute for Health and Clinical Excellence (NICE) is also to be reformed; the review recommends that the appraisal process should in future take a maximum of six months to complete. NICE will also be charged with setting and approving more

independent quality standards.

Giving the report a cautious welcome, chair of the British Medical Association (BMA), Hamish Meldrum said that "there is much here that could bring about improvement – if it can be delivered. That will depend on the details, and on the true engagement of NHS staff in implementing change." He warned however that "if they are sidelined, these are little more than fine words and we will not see the improvements the NHS desperately needs." The BMA also welcomed the intention to "move away from target-driven health policies and to focus instead on the quality of patient care." Peter Carter, General Secretary of the Royal College of Nursing (RCN), also welcomed the review stating that "the overwhelming majority of care provided by the NHS is safe, but the RCN believes the ambition now must be to drive up patients' experience from a 'safe' to a 'high quality' service." He added that "if fully implemented, these recommendations have the potential to achieve this ambition."

Health spokesman for the opposition Conservative Party, Andrew Lansley, was more critical, claiming that the plans would not reduce bureaucracy. He stated that it is "no good talking about focusing more on health outcomes if doctors and nurses continue to be micro-managed by bureaucrats in [central government] and their local strategic health authorities. What health professionals want and need is for politicians to stop interfering and to allow them to do the job they were trained to do."

A review of workforce planning, training and education was also published alongside the review. This proposes the establishment of NHS Medical Education England – an independent, advisory non-departmental body that will scrutinise workforce planning proposals for doctors and dentists, as well as bringing a coherent professional voice on matters relating to education and training. There will also be a new tariff-based system for education funding. This will mean for the first time that education funding will follow the trainee, which it is hoped will improve transparency, promote fairness and reward quality.

More information on the next stage review of the NHS in England and on workforce developments can be found at <http://www.ournhs.nhs.uk/>

UK: New checks to protect patient safety

Plans to improve patient safety and support professionals in sustaining their high standards were set out on 23 July by the Chief Medical Officer for England, Sir Liam Donaldson.

In proposals, outlined in the report *Medical Revalidation – Principles and Next Steps*, doctors will be required to renew their professional registration every five years, in order to provide assurance that they are practising to the standard that patients, the public and the profession itself expect. It will also play a part in putting quality at the heart of NHS care – a key element of the proposals outlined in Lord Darzi's report *High Quality Care for All*.

Patients will play an important role in this process. They will be asked for views on their doctor, including effective communication, including listening, informing and explaining; involving patients in treatment decisions; care coordination and support for self-care; and showing respect for patients and treating them with dignity.

Speaking on publication of the report, Sir Liam said that he was "confident that this process, agreed with doctors' representatives will help raise standards of medical practice and improve the quality of the patient experience. The involvement of patients and public in the process will help define what counts as good health care and in the rare cases where doctors are falling short, provide them, where possible, with the support needed to renew their registration."

The General Medical Council (GMC) will be establishing a programme board to support the development of revalidation processes as well as to consider the practical issues around implementation. The GMC, the Academy of Medical Royal Colleges and UK Health Departments have all committed to working together with patients, the profession, and employers.

Underlining the support which doctors themselves have given the proposals, President of the GMC, Sir Graeme Catto said that the "introduction of revalidation represents the biggest change to medical regulation in one hundred and fifty years. The GMC welcomes the opportunity to work with partners in health care organisations across the United Kingdom to develop a supportive process focussed on raising standards that will deliver benefits

to both patients and professionals.”

Members of the Academy of Medical Royal Colleges will have a central role in setting standards for recertification and designing the methods by which doctors will be evaluated against those standards. The revalidation and recertification process will be introduced in stages from spring 2009 following a series of pilots scheduled to begin at the start of the year. These arrangements will be supported by the introduction of Responsible Officers, senior doctors in each health care organisation who will take responsibility for collating the information needed to support a recommendation on revalidation.

The report, Medical Revalidation – Principles and Next Steps, can be downloaded at http://www.db.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_086430

Flooding in Eastern Europe

Heavy rains and rising flood waters in Ukraine, Romania and Moldova since 23 July have caused the loss of forty-two lives, and necessitated the evacuation of about 40,000 people (as of 1 August 2008). A large number of houses, bridges, roads, agricultural lands have been damaged.

In the Ukraine heavy rainfall has resulted in rising high waters of the Rivers Dniester and Prut and serious floods affected six oblasts (provinces) in Western Ukraine. Thirty-six people have died. 40,703 houses and 33,882 hectares of farm land have been flooded. The total losses in the western regions are estimated at \$650–870 million. As of 4 August the majority of the evacuated population has returned home. Areas most affected by floods were rural; urban areas remained intact. The government, at both national and local levels, various organisations, groups and individuals responded to the disaster in a prompt and efficient manner. Other countries have responded by launching initial humanitarian support, while the WHO responded by conducting a initial rapid assessment of most affected areas and supporting the coordination of response effort.

In Romania, more than 10,000 people have been evacuated due to the floods while more than 6,700 houses and agriculture have been damaged.

Meantime, the risk of flooding remained in Moldova and by August 1 more than 5,700 people had been evacuated while three people lost their lives in the capital, Chisinau.

Flooding can have profound consequences for human health. Drowning is the leading cause of death in case of flash floods and coastal floods while fatal injuries can occur during evacuation or clean-up activities. Other injuries typically include small lacerations or punctures due to the presence of glass debris and nails as well as electrical shocks.

In the short term, the impact of floods on the transmission of communicable diseases is limited, with outbreaks of communicable diseases rarely observed. However the impact on health infrastructures and all lifeline systems can be massive and can result in food shortages and the interruption of basic public health services such as the water supply.

Contamination by toxic chemicals during floods is theoretically possible but no verifiable correlation has been observed or measured so far. Mental health problems are frequently observed among flood victims. As well as having themselves experienced a traumatic event, the victims may also have to cope with the loss of family members, friends and property. In addition, there is a risk of physical and mental exhaustion during the clean-up phase.

More information at http://www.euro.who.int/emergencies/fieldwork/20080730_1

Ireland: First All-Island Census of the Traveller Population

Preparations are now underway for the first all-island Census of Traveller Population to be carried out from in the autumn. The Census, which will include information on accommodation, is part of the All-Ireland Traveller Health Status Study launched last year. Only Travellers who self ascribe will be included in the Census. This means that individuals who do not wish to be identified as Travellers will not be included.

Irish Travellers are a small indigenous minority with a unique shared history, culture, customs and language. Their distinctive lifestyle and culture, based on a nomadic tradition makes them an identifiable group, both to themselves and others. It is twenty years since Traveller health was examined in the

South of Ireland by the Health Research Board. Those findings highlighted that Travellers of all ages have much higher mortality rates than people in the general population, with differentials in life expectancy averaging eleven years less than the general population.

No national research has been conducted on Travellers since 1987 until now. The All Ireland Health Study has been commissioned by the Department of Health & Children (Ireland) and the Department of Health Social Services and Public Safety (Northern Ireland) and builds on the study of 1987 by the Health Research Board. It will be conducted by the School of Public Health and Population Science at University College Dublin (UCD). It is the first study of Travellers' health status and health needs that involves all Travellers living in the island of Ireland and will be completed in 2010.

The study will identify health needs as identified by Travellers and health services providers and measure the health status of Travellers. The findings from the study will provide a framework for policy development and practice in relation to Travellers.

For further information visit the UCD web site <http://www.UCD.ie/phps/research/trav.htm> or email: socialinclusion@HSE.ie

Tajikistan: Germany to finance €2 million TB Control Project

On July 28 Tajikistan's Ministry of Economic Development and Trade and the German Development Bank KfWEntwicklungsbank signed an agreement worth €2 million to finance a tuberculosis (TB) control project in Tajikistan. The project will include rehabilitating a TB hospital in the country's Vahdat district. According to Nusratullo Salimov, Tajikistan's Minister of Health, detection of TB in Tajikistan has improved, and the functioning of TB hospitals has become more transparent. Salimov added that an increase in the number of recorded TB cases “does not mean that TB has spread in Tajikistan” but might indicate that TB detection has improved. Salimov said that official figures provide an accurate estimate of the TB situation in the country.

Not enough debate in Finland on how climate change affects health

“Finland has been setting trends in many areas. I would, however, like to highlight one particular area where we need more debate than at present especially from the health perspective, that is, climate change and its health impacts”, said the Minister of Health and Social Services Paula Risikko in the joint press conference with the WHO Director-General Margaret Chan in Helsinki on 24 June.

“In recent years, heatwaves, drought, and floods have caused more and more havoc all over the world. Climate change and especially the effects of weather extremes are a serious threat to health. A concrete example of this is the morbidity and increased mortality during heatwaves. Risk groups include cardiac patients who get exhausted by heat and elderly people whose blood vascular system is no longer as effective as with young adults.”

Minister Risikko stated that the complex interconnection of climate change and diseases is visible also in Finland. “For example the tick, a vector for brain fever, has become more common and widespread, which may be a result of climate change. Another example of global warming is that the growing season is extending in Finland, which makes it more profitable to cultivate food, but at the same time the number of allergenic elements is growing and their season is getting longer,” said Minister Risikko.

“Climate change affects our health both directly and through the measures we use to control it. As we must adjust ourselves to direct global emission effects, we in Finland must take part in reducing global emissions in accordance with agreements,” Minister Risikko stressed.

“The development of broad-based health systems is of utmost importance also in future. We need the Health in All Policies approach even in dealing with climate issues. Changing the focus from corrective work to prevention and health promotion is a necessary step for ensuring our ability to take care of everyone even in future. We need great changes in our ways of thinking and acting, and I believe we can achieve that by working closely with WHO,” Minister Risikko concluded.

Sweden: Reforms in dental health care

The Swedish dental care system has been the subject of investigation by a

government commission over recent years. Reforms to the system were implemented on 1 July following commission recommendations, writes Anne Melke from the School of Public Administration at Gothenburg University. The Swedish dental care system has not been fully within the publicly funded health system and consequently, patient charges have been the subject of more minimal regulation and not covered by the general health care high-cost protection scheme.

While the July reforms do not change the institutional structure of the system, they do encourage the more frequent use of preventive dental health check ups through a reduction in out of pocket costs to patients.

First, a voucher worth 300 or 600 SEK (€30 or €65) will be allocated to all citizens every second year. The higher amount is targeted to those aged twenty to twenty-nine, as well as people over the age of seventy-five. The voucher is supposed to fully or partially cover the costs of a dental visit.

Second, a high-cost protection scheme is being introduced for those who need further treatment (though with restrictions on treatment content). 50% of all charges over 3,000 SEK (€325) will be covered by the public purse; for those expenses exceeding 15,000 SEK (€1,630) this figure will rise to 85%.

Patients will also be encouraged to take account of price differentials between dental surgeries when choosing which dentist to visit. In order to facilitate such comparisons, the national insurance agency will publish information on the fee schedules used by many private and public providers. Dentists must also provide prospective patients with written information on their treatment changes.

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Sweden: Costs of care could rise by 270% by 2040

The costs of care at Swedish hospitals have been projected to rise by 270% by the year 2040 due to an ageing population, according to a new research. As the generation born in the baby boom of the 1940s reach retirement age, more and more will require care while fewer will be working.

Anders Klevmarcken, professor emeritus at Uppsala University, and Björn

Lindgren from Lund University, writing about their research in a debate article published in *Dagens Nyheter* state that this will inevitably lead to higher taxes, unless there are savings made in other parts of the state budget or drastic changes are made to how health care is financed.

This increase in costs was estimated using a simulation model which estimated future demands on the health care system in a country where the number of people over sixty-five will have increased from 17% to 24% by 2040. The authors do however indicate that their model projects that if health improves for everyone over forty, and in particular for the oldest segment of the population, the increase in hospital costs may be limited to 65% rather than 270%. Moreover, they note that if, at the same time, a greater number older people stay in the workforce, this will increase incomes which contribute to financing health care, either through taxes or patient fees. Thus their research concludes by recommending a concerted effort to improve public health and conditions allowing older workers to stay in the job market.

Spain: New law on pricing of pharmaceuticals and devices.

Enacted on 26 July, the new law entitled Guarantees and the Rational Use of Medicinal Products and Medical Devices, establishes the general pricing framework for medicinal products for human use to be provided by the Spanish National Health System and to be dispensed within Spanish territory under an official prescription.

The law, along with a Royal Decree from 16 May, sets distribution and dispensing margins; enables the adjustment of these margins and deductions to the current economic situation; and allows the contributions of pharmacists and distributors to be adjusted to reflect profit volume.

The distribution margins are fixed at 7.6% of the distributor's sale price (excluding taxes) for products with a laboratory sale price of €91.63 or lower, and above this value the profit margin is 7.54% for each product. For pharmacy sales to the general public of products with a laboratory sale price of €91.63 or lower the margin is fixed at 27.9% of the retail price (excluding taxes), and above this value the margin for dispensing is 38.37% for each product.

Deductions are calculated on a monthly basis for the dispensing of products with official prescriptions and financed by public funds. The minimum external monthly sales are fixed at €32,336.12, which means that approximately 45% of Spanish pharmacists should not make any contributions. Also, pharmacists have the option of applying discounts of up to 10% of the retail price (taxes included) in the dispatching of over-the-counter products.

IMF loans 'fuelling TB deaths' in eastern Europe

The rapid spread of tuberculosis (TB) in eastern Europe and the former Soviet Union has been fuelled by the economic policies of the International Monetary Fund (IMF) according to a new study published in the July issue of the journal *Public Library of Science Medicine*.

Researchers from Cambridge and Yale universities looked at twenty-one countries in the WHO European region which had received IMF loans. Such loans are subject to conditions which demand that countries meet strict economic targets. Doctors have warned that these stipulations might lead to reduced government funding for health services such as hospitals and clinics, undermining the fight against diseases such as TB. This new study suggests that the loans programmes led to less being spent on health care and as a result increased the rate of TB.

Looking at the timing of rises in the TB rate and comparing them with the timing of IMF intervention, study authors David Stuckler, Lawrence King and Sanjay Basu claimed that a direct relationship could be observed; the start of the increases matched the starting point of IMF programmes and continued rising as the programme continued. This they claimed had led to a 16.6% increase in deaths across the twenty-one countries rather than an expected fall of 10% in deaths. They also reported a 13.9% annual increase in new cases of TB and a 13.3% increase in the number of people living with TB. Each 1% increase in IMF loans was associated with a 0.9% increase in mortality. Public spending, they noted, as a proportion of GDP averaged an 8% fall in government spending, while there was a 7% drop in the number of doctors per head of population and a fall in the principal method of TB treatment, 'directly observed therapy.

These adverse effects were not associated with the activities of other lenders, such as the European Bank for Reconstruction and Development, which invests in Eastern Europe. Nor did it vary in step with other factors such as HIV, conflict, or the rate at which people were put in prison, where much TB transmission takes place the region.

"This report suggests that the IMF has its priorities backwards," said Cambridge sociologist Stuckler. "If we really want to create sustainable economic growth, we need first to ensure that we have taken care of people's most basic health needs," he added. Co-author, Basu said that "despite the International Monetary Fund's good intentions to produce economic stability, their programmes could be destabilising public health and taking a toll in human lives."

In response the IMF criticised the study as being flawed, arguing that the "fundamental problem is that the study does not take properly into account that countries implement IMF-supported reforms in times of economic distress." They added that "any analysis that seeks to estimate the impact of IMF-supported programmes on economic or social outcomes should take into account the economic and political conditions that first led the country to agree to an IMF-supported programme. By not including these conditions, this study confuses the reasons for asking IMF assistance with the consequences of this assistance." They also claimed that the increase in expenditure on public health programmes was greater in countries that had received IMF assistance than in countries without such assistance.

In contrast, Paul Sommerfeld, from the UK based international charity TB Alert, said the findings were "unsurprising" claiming that "the surge of TB in ex-USSR countries through the nineties was an unforeseen and unwelcome result of the end of communism – because of the vast drop in public spending, including on public health, of which IMF policies are a contributory part." However, he said that an over-reliance on expensive "sanatoria" for TB patients was another reason for problems in Russia.

The study is available at <http://dx.doi.org/10.1371/journal.pmed.0050143>

Russia: Government backs tougher legislation on drink-driving

On 21 July the Presidium of the government of the Russian Federation approved a bill to increase the penalties faced by drunk-drivers. The bill, presented by Interior Minister Rashid Nurgaliyev, will increase the maximum penalty for drunk drivers responsible for the deaths of two or more people by two years to nine years in prison. Where just one fatality is involved the maximum penalty will increase to five years, with a increase to three years for non-fatal injuries.

Prime Minister Putin said that the legislation is "long overdue". According to Minister Nurgaliyev more than 11,700 people died in some 90,600 road accidents in the first six months of 2008. Another 111,500 were injured in road accidents during the same period. One in every fourteen accidents involves a drunk driver.

Nurgaliyev said the amendment was aimed at establishing an aggravated factor for drunk drivers who face criminal charges. The Criminal Code currently makes no distinction between drunk and sober drivers who cause road accidents. Drivers' rights advocates supported the bill, which must be passed in the State Duma and the Federation Council before being sent to the President to be signed into law.

However, the new bill comes just weeks after the end of Russia's zero-tolerance policy for alcohol while driving. Under a law that came into effect 1 July, the maximum legal blood-alcohol level for drivers increased from zero to 0.3g per litre of blood – roughly equal to a glass of wine, a half-litre of beer or 50g of vodka for a man weighing eighty kilogrammes. According to the Russian newspaper, *Novosti*, the new rules have been criticised by the country's Chief Medical Officer, Gennady Onishchenko. Speaking to reporters in Japan during the G8 summit he said that the decision was "a crime and a dangerous decision for our country."

News in Brief

Latest health statistics on-line

The WHO European Health for All database and European mortality database were updated on 25 July. With over six hundred indicators, plus mortality by sixty-seven causes, they provide fast and easy access in graphical form to a wide range of basic health statistics on the fifty-three countries of the WHO European Region.

The database can be accessed at <http://www.euro.who.int/hfad>

WHO calls for complete tobacco advertising ban

On May 30, the WHO urged governments to protect the world's 1.8 billion young people by imposing a ban on all tobacco advertising, promotion and sponsorship. The WHO call came on the eve of *World No Tobacco Day*. This year's campaign focuses on the multibillion dollar efforts of tobacco companies to attract young people to its addictive products through sophisticated marketing. Recent studies suggest the more young people are exposed to tobacco advertising, the more likely they are to start smoking. Despite this, only 5% of the world's population is covered by comprehensive bans on tobacco advertising, promotion and sponsorship. Tobacco companies continue targeting young people by associating the use of tobacco products with qualities such as glamour, energy and sex appeal. "In order to survive, the tobacco industry needs to replace those who quit or die with new young consumers. It does this by creating a complex 'tobacco marketing net' that ensnares millions of young people worldwide, with potentially devastating health consequences" said WHO Director-General Dr Margaret Chan.

More information on *World No Tobacco Day* at <http://www.who.int/tobacco/wntd/2008/en/index.html>

Netherlands: Smoke-free workplaces

On 1 July 2008 workplaces in the catering, sports and cultural sectors became smoke free. Employers in these sectors no longer have an exemption from the statutory duty to protect their employees from exposure to tobacco smoke. The ban in the catering sector applies to all establishments, both those with employees and those run by sole traders.

The ban is the latest restriction on smoking in the Netherlands. In 1990, under the Tobacco Act 1988, smoking was banned in government, education and health care buildings. In 2004 smoking was also banned on public transport and in most workplaces.

Further information on the new legislation is available at <http://www.minvws.nl/en/Overig/vgp/2008/information-on-the-smoke-free-workplace.asp>

Malta and Libya sign agreement on medical services and public health

On July 31 in Tripoli, Malta and Libya signed a memorandum of understanding on medical services and public health, aimed at developing collaborations to counteract public health threats. In a speech marking the agreement, Maltese Social Policy Minister John Dalli said the Mediterranean experiences of the health and epidemiological effects of irregular migration from sub-Saharan Africa are ample demonstrations of the need to enhance networking for surveillance of communicable disease around the Mediterranean. He stated that "Malta has set out its goals to develop the health sector into a European centre of excellence in the Mediterranean. One of the areas we are seeking to develop is international medical training. We therefore look forward to opportunities aimed at strengthening the links between our institutes responsible for training of health care professionals." He added that as trade and industry links between Malta and Libya continue to grow, it is important for both countries to gain a deeper mutual understanding of their health systems and to share ideas and experience on counteracting common challenges.

Mass gatherings and public health: the experience of the Athens 2004 Olympic Games

The Olympic Games are a very popular but vulnerable global event and thus intrinsically raise the expectations of the international community on all aspects of preparedness, including public health. A new publication, edited by Agis Tsouros and Panos Efstathiou, looks in depth at this experience. The book contains strategic, technical and scientific information about epidemiological

surveillance, environmental management, emergency and hospital care, preparedness for the potential deliberate use of explosives, biological and chemical agents or radio-nuclear material, disease prevention, as well as coordination and unified command. It also highlights that mass sports gatherings such as the Olympics can be powerful platforms for promoting health messages, especially physical activity and active living, healthy nutrition and avoidance of smoking. Finally, it synthesises conclusions and lessons learned and offers insights and strategic points for future organisers of mass gatherings.

The book can be freely downloaded at <http://www.euro.who.int/document/e90712.pdf>

Roma exclusion requires joint response, says EC report

Millions of Europeans of Roma origin are subject to persistent discrimination, both at individual and institutional level, and far-reaching social exclusion, says a European Commission report published on 2 July. The report is a response to a request by EU leaders in December 2007 to examine policies and instruments available at EU level to improve Roma inclusion. It concludes that there is a powerful framework of legislative, financial and policy coordination tools available and that these are increasingly used, but that there is still an implementation gap in the Member States. EU Structural Funds, including the European Social Fund, and pre-accession instruments are crucial to overcoming exclusion. The report examines instruments, legislation, cohesion policy and non-discrimination actions, as well as the most important policy areas for Roma inclusion: employment, social inclusion, education, public health, enlargement and gender equality.

The report is available at <http://ec.europa.eu/social/BlobServlet?docId=481&langId=en>

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