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A prelude to the Matrix Models Supplement

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This paper introduces the concept of matrix models: a new project to ensure that there is clinically effective, safe and economic prescribing of medicines in an integrated manner, in both primary and secondary care, in Northern Ireland.

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1. Introduction

The steady rise in the cost of healthcare (in general) and medicines (in particular), combined with the expected increasing number of elderly citizens, has led to concern as to whether or not high-quality, safe and effective pharmacotherapy can still be provided in the future.

This supplement describes a new project to ensure that there is clinically effective, safe and economic prescribing of medicines in an integrated manner, in both primary and secondary care, in Northern Ireland. In this process, the quality of prescribing is improved with resultant patient benefit, whilst costs are decreased, thereby maximising healthcare resource utilisation.

The idea behind the project is that medicine selection must fundamentally be based on clinically relevant criteria, such as efficacy, safety, documented effects on clinical end points, ease of administration and so on. This quality hurdle must be passed first in order to ensure that the most safe and efficacious products are identified prior to carrying out a budget impact analysis.

The medicine selection process is complex, and the decisions made by prescribers or policy makers may have consequences for others who will have to accept the choices that have been made. Therefore, it is essential that the selection process is fully transparent and that all key stakeholders are involved in the selection process. This makes it imperative that the selection process is reproducible, with guaranteed quality.

Although everyone would agree that medicine selection should be a rational process ('evidence based medicine'), based on criteria such as clinical efficacy, documented effects on clinically relevant end points, safety, tolerability, experience, medicine interactions, dosage frequency and cost, the reality is that many other factors play a part in the prescribing decision.

2. Factors influencing medicine decision making

2.1 Practitioner experience

Previous experience with the use of a medicine is very important for all prescribers. This is an entirely logical approach which is based on the desired outcomes of therapy being attained with a particular agent, and this approach can work against the use of a new (perhaps more beneficial) agent for a specific condition. Thus, there is a balance to be struck between the use of a tried and trusted agent as compared with the adoption of a new product. The prescriber, therefore, needs criteria to devise his own set of medicines.

Personal experience with a certain severe side effects (e.g., bone marrow depression, severe anaphylactic reaction or convulsions) will have a much greater impact on an individual prescriber than a very thoroughly written review demonstrating that such reactions occur only rarely with the medicine in question. The 'experience criterion' is therefore not unequivocal, as one bad experience does not compensate for a good experience with the same medicine of another prescriber.

2.2 Pharmaceutical companies

Relationship is a powerful element of influence in a generic sense, and this concept is used very efficiently by the pharmaceutical industry.

Personal relationships with a given company clearly influence the medicine-decision making process. A negative experience with a company may have a long-lasting effect, even on a newly introduced product that may offer an advantage in therapy in that area. It has also been clearly demonstrated that requests by physicians that a medicine be added to a hospital formulary are strongly and specifically associated with the physician's interactions with the companies manufacturing the medicines. This is not surprising, given the comprehensive detailing provided by pharmaceutical company representatives in relation to products, and is often entirely appropriate. Pharmaceutical companies often invite clinicians and pharmacists to medical or pharmaceutical congresses. This is not only to allow them to participate actively in the congress and update their knowledge on a certain topic, but also to improve their relationships with the clinicians and pharmacists. If the sales representative has a good relationship with the individual clinicians and pharmacists, this will significantly lower the 'approach threshold' after the congress, or indeed, on other occasions. It is therefore necessary to develop guidelines for pharmaceutical industry support of congresses, meetings, lunches, postgraduate education and other such means of support.

The newly developed European guidelines, allowing the pharmaceutical industry to invite only active participants to the congress and prohibiting the invitation of the husband or wife of the attendee, are to be considered as a positive development.

Cultural differences between countries may also be important for medicine selection; for example, a patient with low blood pressure might be told by his German general practitioner that medicines are necessary to increase his blood pressure, whereas a British general practitioner would perhaps tell the patient to exercise more and to consume more salt, and an American general practitioner may write a letter to the patient's insurance company in order to get a discount on his premium because of the lower risk of cardiovascular complications.

2.3 Personal financial criteria

Personal financial criteria may also play a role (sometimes a very important one) in the medicine selection process, although it is difficult, if not impossible, to gain insight into this criterion. Several years ago, a new macrolide (clarithromycin) was introduced onto the Dutch market, which rapidly yielded a significant part of the 'market', despite comments in Dutch medical journals that the medicine was only a modest advance, if any, in anti-infective therapy. An investigation led to the conclusion that the company that introduced this product paid each general practitioner for every prescription, provided they correctly filled in a very short postmarketing surveillance record form. This has also been part of UK practice.

2.4 Unconscious criteria

All general practitioners and specialists use a so-called 'evoked set': this means that only a limited number of angiotensin converting enzyme (ACE) inhibitors, β-blockers or antidepressants are routinely prescribed by the individual doctor. Whenever he or she decides to prescribe an ACE inhibitor, one or two names 'automatically pop up'. The pharmaceutical industry uses its marketing apparatus to try to influence the decision-making process, and to have its product in this evoked set. That is why the desks of medical doctors and pharmacists are usually covered with noteblocks, pencils and pens, calculators and other similar items, each bearing the trade name of the product in question. Mailings, which are often not very informative, but in which the trade name of the product is prominently visible, have the same goal.

Furthermore, the choice of name is an important factor, as you might expect that the first medicine listed in a pull-down alphabetically arranged menu has a greater chance of being selected than one at the end.

2.5 Other factors

In addition to these factors, the decision-making process of the physician is also influenced by other factors, such as:

- colleague/specialist/pharmacist
- literature
- consensus meetings/national guidelines
- government/health insurance companies
- the patient.

Some of these factors are described below.

- Colleague/specialist/pharmacist
  The impact of the opinion of a colleague/specialist or pharmacist is very much relationship driven. If the relationship is good, they will try to reach consensus on the issues of medicine selection and other pharmacological items. On the other hand, pharmacotherapy is sometimes used as a tool to highlight the differences between physicians when the relationship is poor.
- Literature (information power)
  Several good sources of information are available for the physician, such as the British National Formulary (BNF).

However, it should be borne in mind that truly independent and objective information does not exist because any conclusion drawn by authors is by definition subjective and depends on the perspective from which these conclusions are drawn.

- Consensus meetings/national guidelines
  Consensus meetings and national guidelines for pharmacotherapy do play an important role in the decision-making process of general practitioners and medical specialists. However, a disadvantage of consensus meetings and national guidelines is that the vast majority of individual prescribers will not be involved in the decision-making process. This usually results in low compliance with such guidelines in clinical practice, demonstrating once again that it is fundamental to have all stakeholders involved in any selection process.

  Many guidelines focus primarily on clinical efficacy and documented effects on clinically relevant criteria. Therefore, practical aspects concerning applicability, tolerability and patient compliance are sometimes overlooked.
- Government/health insurance companies
  Some doctors feel that the government is no longer a serious negotiating partner, as they only focus on one criterion: cost. In fact, a reverse reaction is seen more often because of the huge impact of cost in all plans of governments, many prescibers are disinterested in the financial aspects of pharmacotherapy.

3. Matrix models

In the last 20 years, two different matrix models have been developed in the Netherlands: the System of Objectified Judgement Analysis (SOJA) and InforMatrix. These matrix models use only clinically relevant, rational criteria in the decision-making process of drug selection. Both methods also offer the opportunity for the user to fill in their personal scores, thereby increasing the acceptance of clinicians and pharmacists.

Therefore, matrix models are used for initial screening of medicines within a certain pharmaceutical class. In these methods, the user of the interactive program may assign his own personal weight to each selection criterion. In SOJA, the properties of each individual medicine per selection criterion are judged by a panel of experts, thereby allowing the user to make his own personal medicine selection within that class of medicines. InforMatrix is a blank matrix, in which the user has to judge both the weighting of the criteria as well as the properties of the medicines on each criterion.

Both methods have been used extensively in the Netherlands and are well accepted because of their transparency. The methodology of both tools is described in this supplement, and an application of both methods is presented as well: triptans, using the SOJA method and HIV backbones using the InforMatrix method [1,2].

Both methods offer various options concerning interactive medicine selection. This can be done in an interactive session moderated by an expert on the medicine class in question. Prescribers and pharmacists can go directly to the websites to fill in their own personal weightings, and a variety of other interactive internet options are available as well, including e-sessions. This is described in the paper of Brenninkmeijer *et al.* [3].

4. STEPS project

In Northern Ireland, the Safe Therapeutic Economic Pharmaceutical Selection method (STEPS) was developed. In this programme, matrix models were used in the first step to identify the most clinically efficacious products within a pharmaceutical class. In the next step of the STEPS process, the packaging of the products selected in the first step is judged in a prospective manner using a standard regionally agreed template. This is then followed by a third and final step incorporating both procurement and a budget impact analysis. Finally, only the top medicines (usually two or three) will be chosen as the preferred medicines (and supplier) in Northern Ireland. The process is described in the paper of Scott *et al.* [4].

The STEPS approach is well accepted by both prescribers and pharmacists because of the fact that product selection is based on quality aspects, such as efficacy, documented effects on end-points, safety, tolerability and ease of use. Also, individual physicians and pharmacists can easily fill in their own personal score, which usually will be quite similar to the one used in the STEPS process, because almost all users will assign a high weight to the criteria described above and a lower weight to other criteria. This process has resulted in savings being generated, which can be re-invested in healthcare for further patient benefit and demonstrates that safety and efficacy does drive economy.

The key elements of the STEPS approach are summarised below:

- STEP I – clinical evaluation
  Evaluation and continuous updating of all available evidence relating to efficacy, evidence, safety, tolerability, ease of use, medical interactions and experience is carried out. Application of this information in matrix models to support the pre-selection of medicines within a therapeutic class is purely based on clinical criteria.
- STEP II – risk assessment
  This phase focuses on factors that could impact upon the safe use of the various products during routine use by patients. This risk assessment is aimed at the packaging and instructions, to minimise difficulties for patients and help them safely and optimally use their medicines.

- STEP III – budgetary impact analysis
  This phase entails looking at the impact of the use of the agents in a therapeutic class on the complete healthcare economy, in both primary and secondary care. Reduced medicine costs are the result of the fact that, of all the products that meet the evidence and safety as outlined, the most cost effective are selected to deliver the desired outcomes at minimised cost to the health service.
- STEP IV – final procurement selection
  The new procurement model also allows for a radical redesign of the medicine tariff based upon safety, efficacy and economy. Flexibility is built into the process as it does not demand 100% compliance with the product selections, but rather, only requires a reasonable percentage compliance (70 – 80% depending on the group).

5. Matrix models: implementation and supporting infrastructure

5.1 Integrated medicines management

This system is now the regional model in Northern Ireland in terms of optimising pharmacy input into patient care. This facilitates the optimising of patients' medication in secondary care, including switching of products. A full suite of standard operating procedures are available for this, together with switching protocols. The two systems greatly assist in ensuring optimal use of medicines and enhanced integration between the sectors.

In addition, an electronic system for pharmacist interventions can also be made available as part of the management, as it aids clinical pharmacists to ensure optimal medicines management, and also records data for analysis linked to medicines, demographics and diagnosis. The negotiation of a new community pharmacy contract will consolidate this process to ensure full continuity of medicines use in recognising the role of the community pharmacist as a medicines expert . The new contract will contain a focus on remuneration based on clinical expertise, rather than the current emphasis on reimbursement based on a medicines supply service.

5.2 Interactive matrix models

Two different matrix models (SOJA and InforMatrix) are available in interactive workshop formats, and web/internet tools exist to allow organisation of interactive sessions, or online sessions on the internet to maximally involve all prescribers and pharmacist in the pre-selection process [3].

5.3 Guidelines

Evidence-based guidelines and prescribing policies on the use of medicines indicated in specific disease states are developed by secondary and primary care experts. These are agreed and disseminated on a regional basis. Integration of prescribing between primary and secondary care is enhanced to reduce the present lack of standardisation to overcome an additional risk factor for patient care.

The guidelines will be available to healthcare practitioners in Northern Ireland in both a paper and electronic web-based format. The web site will initially be hosted on the Department of Health and Social Services and Public Safety (DHSSPS) web site (www.dhsspsni.gov.uk). They will be available following completion of the specific guidelines and regional authorisation by both the Chief Medical Officer and Chief Pharmaceutical Officer and will be updated as required by the relevant expert group.

6. Outcomes

In healthcare, there are significant savings to be in the drug-decision and distribution process. These savings, if made, can then be re-invested into other treatments or infrastructure needs, to further improve patient care. In Northern Ireland, (population 1.7 million), the expected savings to be made on the application of matrix models (with respect to five specific therapeutic groups), according to the authors' estimates, are specified below:

- statins – £7.7 million
- proton pump inhibitors – £5.5 million
- selective serotonin re-uptake inhibitors – £2.0 million
- angiotensin converting enzyme inhibitors – £0.7 million
- angiotensin receptor blockers – £1.5 million

This adds up to an annual cost reduction of ~ £10 per capita.

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