Expert Opinion

InforMatrix as an alternative tool in rational and transparent drug-decision making

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InforMatrix is a decision matrix technique by means of which a group of experts on a subject (health condition) determine, on the basis of agreed criteria, an order of merit for the various available treatment options for that condition. The goal of the InforMatrix program is to make a rational selection of first-choice medications or drugs following the evaluation of the clinical value of available therapeutic agents. This paper describes the InforMatrix methodology, and also provides an explanation of the various selection criteria that are used by the InforMatrix technique of drug selection.

Keywords: drug selection, evidence based medicine, InforMatrix, matrix models

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1. Introduction

In the previous articles of this 'Matrix Models' supplement [1,2], the SOJA method (System of Objectified Judgement Analysis) was described as a tool for rational decision making in pharmacotherapy. This manuscript deals with an alternative matrix model: InforMatrix.

InforMatrix is an interactive matrix model in which pharmacotherapeutic strategies are supported in a rational manner by means of a transparent selection methodology. This is achieved by means of interactive workshops, in which participants are facilitated in the determination of their own preference.

The InforMatrix method was developed in the early 1990s [3]. The criteria of the InforMatrix method are based on the healthcare process, and not so much on the properties of drugs as is the case in SOJA. Both methods are based on decision analysis models such as those used in economy and management, for example the Multiattribute Utility Technique (MAUT) method and matrix cognition and Full Criteria Analysis Method (FCAM) [4,5].

The treatment of many diseases is continually being modified as a result of the development of new treatment options, new insights into the pathophysiology of the disease in question or new evidence from clinical trials. The goal of the InforMatrix program is to make a rational selection of first-choice medications possible. It is important to describe the selection process and to make this process transparent. The InforMatrix methodology is a tool to achieve this aim, in which selection criteria are described; tested against the available literature and the various therapeutic alternatives evaluated as to their clinical value.

This paper provides a short description of the InforMatrix methodology and a description of the various selection criteria involved.

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Box 1. Fixed criteria and potential sub-criteria of InforMatrix.

Effectiveness

Clinical efficacy

Documented effects on clinically relevant end points

Quality of life

Safety

Rare, hazardous side effects

Documentation

Tolerance

Frequent, yet non-hazardous side effects

Ease of use

Dosing frequency

User-friendly administration form

Applicability

Availability of various administration forms

Drug interactions

Approved indications

Containdications

Use in children and the elderly

Use in case of kidney and liver function disturbances

Use in case of pregnancy and lactation

Special warnings and precautions

Costs

Acquisition cost

Pharmacoeconomic evaluations

2. InforMatrix methodology

InforMatrix is a so-called decision matrix technique wherein a group of experts in the subject area determine, on the basis of agreed criteria, for that specific category, an order of merit for the various available treatment options. Within this order of merit, different weightings are applied to each criterion by the expert group. Next, the various options per criterion are compared to each other. Data are necessary for this, both from the literature as well as from clinical experience. The literature is evaluated by a panel of authors for clinical value and evaluated per criterion.

The InforMatrix technique comprises six selection criteria. In most cases, a list of subcriteria is defined, dependent on the area being assessed. An example of an extended list of those subcriteria is presented in **Box 1**.

There are six criteria, which are listed below.

- Efficacy (the actualisation of positive outcomes and treatment goals).
- Safety (the avoidance of negative outcomes, such as hazardous side effects).
- Tolerance (the interruption of the care process due to less hazardous, generally transitory, side effects).
- Ease of use (ease for the patient, for example, dosing frequency).
- Applicability (what is the scope of the treatment freedom [drug interactions and such] and the ease for the care provider to initiate and monitor the treatment).
- Costs (price per day, month or year).

The InforMatrix technique takes place in the following steps: i) operationalisation of the six criteria; ii) literature synthesis; iii) relative weighting of the six criteria; iv) evaluation of the various treatment options on the basis of the literature and own knowledge and experience; and v) synthesis of the weightings and evaluations in the selection matrix: calculation of order of merit.

A group of experts in the field are requested to test the operationalisation of the above six selection criteria for relevance, for example, in the healthcare process of the treatment of serious rheumatoid arthritis. Following these selection aspects, the authors execute a literature synthesis. This results in a report, in which these aspects are evaluated on the basis of the selection criteria by a panel of experts in the field. In this overview, the report is evaluated in terms of its value in enabling rational consideration of the treatment options available.

In the next phase, the report is given to user panels as background material in preparation for an interactive group evaluation and discussion of both the selection criteria and treatment options. In the first stage of these sessions, the participant has to divide 30 points over these six criteria, depending on the perception of their relative importance, with a maximum of 10 points per criterion. If all criteria are judged to be of equal importance, all criteria will yield 5 points. In reality, this is not the case, and the criteria relating to efficacy and safety will be awarded higher weightings than the other criteria. In the majority of cases, 16 – 20 points are assigned to efficacy and safety. In the following phase, the users must judge the value of each treatment option for each criterion on a scale of 0 – 10 points.

In the final calculation, the weighted score per criterion is determined by multiplying the assigned report grades by the weighting factor. In order to determine the final score of a drug, the weighted scores for all the criteria are totalled.

InforMatrix is therefore a blank matrix, which has to be completed entirely by the user.

All criteria that are used in InforMatrix (and SOJA) are relative criteria. Only those drugs that possess the properties essential to be regarded as potential options are included. Thus, drugs that are very effective and cheap, but that have an unacceptable incidence of adverse reactions, will not be included.

Box 2. Available InforMatrix programs.

- Angiotensin II blockers
- Anticoagulation in orthopedic surgery
- Antidepressant drugs
- Antidiabetic drugs, combinations
- Antiemetics in oncology
- Antiemetics in surgery
- Antipsychotics in schizophrenia
- Biologicals in rheumatoid arthritis
- Bronchodilators, long acting
- Calcium antagonists in hypertension
- Cholesterol target values
- Chronic obstructive pulmonary disorder (COPD) maintenance treatment
- Combinations of bronchodilators and corticosteroids
- Community acquired pneumonia
- COPD exacerbations
- HIV backbones
- Inhaled corticosteroids
- Interferons in multiple sclerosis
- Low molecular weight heparins
- Nasal corticosteroids
- Pain
- Reflux oesophagitis
- Statins
- Triptans

The InforMatrix programs are available on www.informatrix.nl. Literature on the InforMatrix technique can be found in the literature listed [3-5].

3. Discussion

A list of available interactive InforMatrix programs is presented in **Box 2**.

3.1 Editorial process

The aim of the InforMatrix method, as with SOJA, is to rationalise the selection process in pharmacotherapy. The authors of each manuscript should be as independent as possible. It will be obvious that it is not easy to define 'independent'. Almost all experts on a certain subject will have or have had contacts with many pharmaceutical companies and have received honoraria for lectures or other services. If 'independent' would be defined as never having had contacts of any kind with the pharmaceutical industry, it would simply be impossible to find an expert panel. Some conflict of interest cannot be avoided in most cases.

Therefore, a highly standardised procedure is used in the creation of a new manuscript to reduce potentially biased influences from the pharmaceutical industry. This process involves literature searches on Embase, the Cochrane database and for review articles for relevant publications as well as consultation of literature from sources such as the European Medicines Evaluation Agency (EMEA) scientific reports, the National Institute for Clinical Excellence (NICE) guidelines and so on.

On the basis of such sources, the most relevant publications are obtained.

The contents of these papers are critically reviewed but 'opinion' is minimised as much as possible. When it is obvious that drug 'A' is more effective than drug 'B', this is also included in the manuscripts, but terms such as 'much better' or 'superior' are avoided, as are phrases like 'major differences in acquisition cost'. All these aspects should be judged by the users of the interactive program.

The first draft is written by Rob Janknegt, in order to obtain a standardised judgement of the available literature. A panel of experts, with specific knowledge on the topic in question, judges the first draft of the manuscript on scientific correctness and completeness with respect to questions such as the following: are all relevant double-blind studies included; are the conclusions justified; are major limitations of the studies discussed; is relevant information on the subject in question missing?

In order to minimise potential bias, all final manuscripts are sent to experts on the topic in question, the organisation of general practitioners, an editorial board, and to all pharmaceutical companies active in that field, for a check on scientific correctness and completeness of the presented data.

As the last step, a panel of general practitioners and pharmacists judges each manuscript for its usefulness in drug selection.

The whole process from the start to the final manuscript takes, on average, ~ 1 year. **Figure 1** and **Table 1** illustrate the results from scoring according to an InforMatrix program; as an example, various antipsychotics for the management of schizophrenia have been used.

In Northern Ireland, a combination of Informatrix and SOJA has been implemented within the Safe Therapeutic Economic Pharmaceutical Selection (STEPS) programme. This is discussed in detail in the article specifically related to this process [6]. As is the case for SOJA, all InforMatrix programs are continuously kept up-to-date to be able to provide a state-of-the-art overview of the existing data.

3.2 Differences between SOJA and InforMatrix

The most important differences between SOJA and InforMatrix are summarised in **Table 2**.

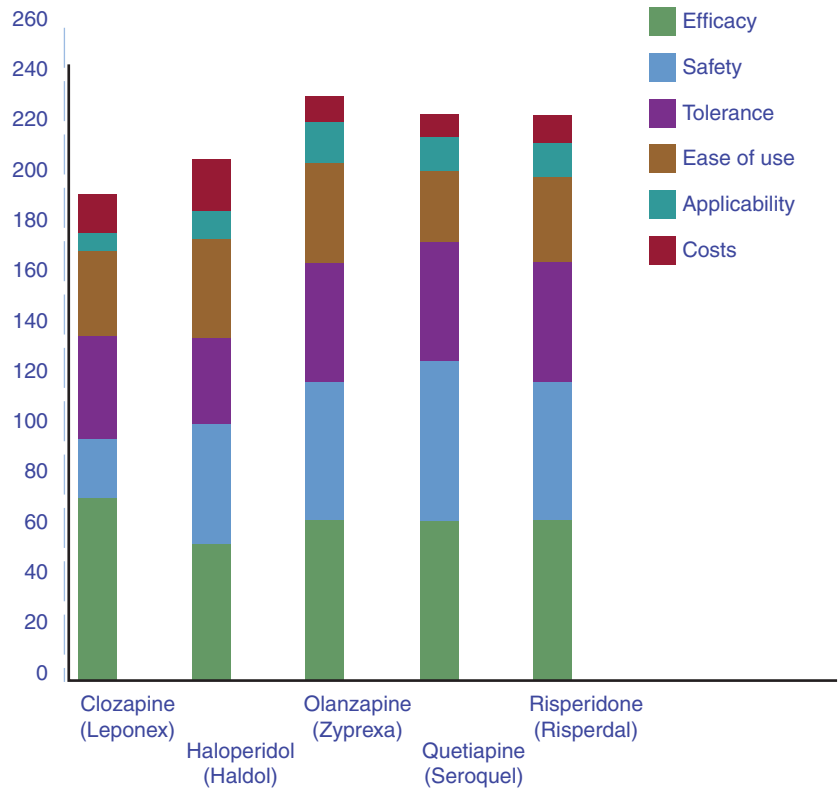

Figure 1. A graph depicting the ratings (resulting from an InforMatrix session) of five antipsychotics for the treatment of schizophrenia.
InforMatrix Schizophrenia – May 2005.

Table 1. A table depicting the ratings (resulting from an InforMatrix session) of five antipsychotics for the treatment of schizophrenia.

	Efficacy	Safety	Tolerance	Ease of use	Applicability	Costs	Total
Informatrix Schizophrenia – May 2005							
RWF	8	7	6	5	2	2	30
Clozapine (Leponex)	8	3	6	6	3	7	171
Haloperidol (Haldol)	6	6	5	7	5	9	183
Olanzapine (Zyprexa)	7	7	7	7	7	5	206
Quetiapine (Seroquel)	7	8	7	5	6	4	199
Risperidone (Risperdal)	7	7	7	6	6	5	199

RWF: Relative weighting factor.

The most important difference between both methods is that in an InforMatrix article, virtually no 'scaled judgements' are included. In a SOJA article, the panel of experts compares each drug with a hypothetical 'ideal' agent and assigns a percentage of that ideal value to each treatment option per criterion. This is not done in an InforMatrix manuscript. The InforMatrix manuscript is as neutral as possible and describes the present state of knowledge on each criterion, without directive comments. When it is obvious that drug 'A' is more effective than drug 'B', this is stated as such, without giving a weighting to either agent. The weighting is done by the participants in an interactive session, in which the InforMatrix manuscript is used as background input. During that session, the participants have to judge both the importance of the selection criteria and the relative properties of each treatment option per criterion. The judgement will be made on the basis of the underlying manuscript, but also on the clinical experience and opinions of the participants.

Table 2. SOJA-method and InforMatrix-method: differences and similarities.

	SOJA (System of Objectified Judgement Analysis)	InforMatrix
Weighting	During a session, the weighting for each criterion is assigned by the participants. The properties of each drug have been judged by a panel of experts	During sessions, the weighting for each criterion and the judgement of the properties of each drug are assigned by the participants
Description of criteria	Drug related (e.g., pharmacokinetics)	Disease-process related (e.g., applicability)
Target group	Formulary committees in hospitals, general practitioners, community pharmacists	Expert groups, formulary committees in hospitals
Complexity	Very easy to perform. Once the members are familiar with the program, decisions can be made within 10 min in an interactive session Participants require no specialised knowledge	More time-consuming, as the participants have to judge both the criteria and the judgement of each individual drug on each criterion Specific knowledge on the pharmaceutical group in question is necessary Important advantage: local acquisition cost in each hospital can be used instead of official acquisition cost

This means that an InforMatrix session will take more time than an interactive SOJA session. Whereas a SOJA evaluation can be done in 10 min, if so desired, an InforMatrix session will take at least 60 – 90 min. The major advantage of InforMatrix is that there is a much more in-depth discussion during the session than is the case with SOJA. The role of the moderator is to facilitate the discussion by probing the participants about their weighting of the criteria and the properties of the treatment options.

3.3 Advantages of InforMatrix

The advantages of matrix models, as such, have been described in detail in the article on SOJA, earlier in the supplement. The reader is referred to the arguments stated in the discussion section of that article [1].

An advantage of InforMatrix is that the method is still applicable when there is insufficient data to set up a clinically sound SOJA score. If there are none or virtually no comparative studies between the drugs in a certain therapeutic class, it is very difficult (if not impossible) to make a scaled judgement on their relative efficacy and safety. In that case, it will not be possible to produce a SOJA score. However, an InforMatrix evaluation is still possible in such cases, as the available data on each individual treatment option is presented as such, and the judgement is left to the participants in an interactive session (rather than by intuition or trial and error). Hence, InforMatrix programs are available, for example, on interferons in multiple sclerosis, antibiotics in severe community acquired pneumonia and biologicals in rheumatoid arthritis, whereas there is no SOJA equivalent for these programs.

Another advantage of InforMatrix above SOJA is that when the method is used in a hospital, the actual acquisition cost of that hospital can be used for calculation of the score in stead of the 'official' listed acquisition price. Similarly, with regards to antibiotics, local resistance patterns can be utilised in the discussion rather than regional or national rates, thereby increasing the validity of the outcome.

3.4 Why both methods?

A limitation of the SOJA method is that the outcome of the program is heavily dependent on the judgement of the panel of experts. The users do not have to agree with their judgement on the relative performance of each drug per criterion. When the users feel overly constrained by the judgement of the panel of experts, InforMatrix, as a blank matrix, might be an alternative. In that case, InforMatrix is the answer to this disadvantage of SOJA.

On the other hand, users of InforMatrix have to fill in the entire blank matrix. In order to do this properly, they need expertise on the topic in question, or else, they are dependent on the underlying document, which is again written by a similar panel of experts. Most general practitioners and community pharmacists feel unable to score the entire InforMatrix in a realistic manner. This is, in fact, the reason why SOJA was developed. In this case, SOJA is the answer to this disadvantage of InforMatrix. In Northern Ireland, as previously stated, a combination of both methods is used.

During many sessions in the Netherlands, it has been shown that the average outcomes of SOJA and InforMatrix sessions are quite similar, provided that both methods are available, and the judgements are sufficiently objectified. The results of SOJA sessions were highly predictable, as all users give high weightings to efficacy, documented effects on clinical end points, safety and dosage frequency. Because there is no variability in the judgement of the panel of experts, the outcome of most sessions is not

very variable. In fact, this makes SOJA a suitable tool for formulary selection. If there was a large variability, the tool would not be useful. The outcome of an InforMatrix session is more variable, given its more user-specific methodology, but in general, is also predictable. Almost all users assign > 50% of the total weight to the criteria efficacy and safety. In that, there is no difference between SOJA and InforMatrix. Because the participants in a session also have to judge the properties of the drugs, there will be more variability among the other criteria.

4. Conclusions

InforMatrix is an alternative matrix model that can be used in combination with or in stead of SOJA. InforMatrix is more suitable in hospital care, whereas SOJA is more practical in primary care. However, the use of both systems in a combined process in Northern Ireland has proved successful and perhaps does offer a different, but equally effective manner of operation, particularly with regard to achieving ownership by primary care doctors and pharmacists.

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