

# **Ermete: A Decision Support System for an Innovative Management of Knowledge and Prescription in Laboratory Medicine: A Trial of Two Italian Local Health Authorities**

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**Abstract:** Laboratory tests play an important role in the diagnostic process. Unfortunately, their utility is at present affected by a significant rate of inappropriate prescriptions. The current strategies to solve the problem are not adequate. The aim of this study is to propose a structural solution through the Health Information Technology. Between the years 2008 and 2010, a methodology to prescribe laboratory tests with the aid of a Decision Support System (DSS), denominated Ermete, has been tested in collaboration with General Practitioners of Local Health Authorities of Rovigo and Mirano. The DSS, during the process of prescription, showed indications of appropriateness in real time and the general practitioner might or might not accept the indication. The number of prescriptions processed with DSS was compared with the number of prescriptions issued by the same physicians, in the same period of the previous year, without the assistance of the DSS. Results showed a decrease of the total number of prescriptions when the DSS was used. The reduction rate was 37.2% in Rovigo and 26.1% in Mirano. The achieved results showed that it is possible to perform the governance of prescriptions without political and administrative actions. The DSS was effective in reducing inappropriateness and in managing knowledge.

**Keywords:** Decision Support System, Inappropriateness, Health Information Technology, Knowledge Management

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## **1. Introduction**

Diagnosis (δία-γνωσις from ancient Greek: “δία” through the, “γνωσις” knowledge) allows identifying the nature and location of a disease through the awareness of symptoms and signs. A diagnosis should be the result produced by listening,

observing and studying the patient. This process utilizes devices such as history and semiotics, which are flanked by laboratory tests that, as other techniques such as medical imaging, can be considered the technological extension of the senses of the physician. Knowledge is the faculty that allows conscious decisions within the diagnostic process and that leads the subsequent actions on the patient [1, 2]. Laboratory

tests have taken a leading role as diagnostic decision aids, having been estimated that the Laboratory Medicine influences 60-70% the diagnosis [3]. This leading role is confirmed, for example, by the data of the Veneto Region (about 5 million inhabitants), showing that in public health structures more than 70 million tests/year, for a value of about 322 million euros, are carried out [2]. The budget of Laboratory Medicine in Italy is only 2% of the total health care cost, which is anyway relevant. On the other hand, the utility of diagnostic tests is affected by a significant proportion of inappropriateness [5]. A literature estimates the phenomenon of over-and underutilization between 10-50% of the total demand [6-21].

Despite the difficulty to evaluate objectively the appropriateness [22], the feeling of its relevance among professionals is, in any case, widespread, especially with regard to the excessive demand, even if there are data that prove an underestimation of the potentialities of the laboratory [23]. The source of the problem may essentially come from three causes: a) the low cost of laboratory tests (account as "little ticket technologies") could lead physicians to think that these benefits cannot be denied to the patient. This fact together with the facility of access (usually without reservation and waiting times), may contribute to make the laboratory performance too easily available; b) defensive medicine may persuade the physician to prescribe tests in order to avoid the charge of not doing everything possible; c) slow response time to the innovation mainly due to the difficulty of transmission and consolidation of knowledge. In fact, even decades can pass from the evidence of the usefulness or uselessness of a test to the concrete change in the prescriptive act [24-27].

This is a critical issue not only in the diffusion of new knowledge, but also in the use of tests that may be defined historical [28]. The knowledge is the intellectual tool of decision that manages not only the quality of the tests (usefulness of tests, strategies proposed by prescriptive guidelines, sensitivity, specificity, predictive value, technical features, legislation, and costs), but also and above all, the quantity of needed tests. The main critical issue that affects the knowledge lies in the fact that if the first edition of Merck's Manual of 1899 [29] listed 13 tests easily memorized, the tests available today are more than 500 and therefore over the human cognitive ability [30]. In this paper we present an innovative informatics solution, integrated to clinical processes, in order to change the clinical approach to laboratory tests and, that can be a tool for improving knowledge. The percentages of inappropriateness mentioned above, are the main indicators of lack of efficacy of the strategies used up to now (guidelines, protocols and flow charts, conventions, treaties, consensus conferences, agreements between colleagues). The same have also proved not to be adequate to affect permanently and quickly on behavioral change. We think crucial to apply structural instruments for the transmission of scientific information in order to allow: a) the continuing education in order to decrease the response time to innovation, b) the consolidation

of the state of the art, c) the improvement of the transmission of knowledge, in order to overcome the criticality of clinical staff turnover, d) the homogeneity of behavior. We believe that such targets could be achieved through a *strategic communication* [31] using a Decision Support System (DSS), to promote virtuous behavior of physicians in the act of prescription. The indications provided were collected in a handbook for the correct prescription of both traditional and innovative tests and particularly in the fields of molecular biology, genomics, proteomics and epigenetics. The Health Information Technology (HIT) makes it possible to test solutions that will make the information accredited, updated and available on the point of care, so that prescribers can adopt the most appropriate, synthetic, and cost effective choices [32- 36]. On the other hand, the literature shows that the use of a DSS improves significantly the performance of the physician and besides that, the attitude of General Practitioners (GPs) in respect of a DSS is good [37]. As regards the economic issue, the same in only a few studies has been exhaustively analyzed [38 - 41]. The way ahead is to adopt the indications generated by a consensus among peers and in agreement with the guidelines. Finally the idea has been to provide physicians with a list of indications updatable in real time and extensible progressively to most laboratory tests. The continuous updating through the information network would solve one of the main problems in the management of appropriateness. In fact, the judgment of appropriateness is often not a final choice, but is a developmental continuity linked to technological progress and scientific knowledge, and also to the cost/benefit. Connectivity should be the tool to define an explicit hierarchy and updated solutions, in which context the responsibility of prescribers might develop [42]. The aim of this paper is to illustrate the characteristics of a DSS and to present the results of two trials conducted in two Italian Health Care Authorities (Veneto Region). The objective of the trials was twofold: a) assessment of the technical feasibility of the software tool in terms of ease of use, while checking if the same software presented some sort of conflicts with the application programs of the General Practitioners (GPs); b) determining whether the use of the DSS could induce a change in prescribing behavior.

## 2. Materials and Methods

### 2.1. The DSS

The DSS, denominated Ermete, has been designed by one of the authors [43-44], and then applied to General Practitioners Electronic Medical Record (GP-EMR). The DSS interacts in real time with GP-EMR through a third software program linked to the first two, allowing a real time alert. In practice, the physician, in the action of prescription, when enters a test that the DSS has stated, a pop-up appears, where a summary of the suggestions established by Board are explained. Examples of prescribing indications listed on DSS are shown in Table 1.

**Table 1.** Examples of prescribing indications listed on DSS.

TEST	INDICATION
Ammonium	1. Useful in the evaluation high-grade hepatic insufficiency (2 <sup>nd</sup> level test).
Haptoglobin	1. Specific test for hemolytic anemia. Not suggested for evaluation of inflammation.
AST	1. Not recommended for screening and evaluation of liver disease.
Bence Jones	1. Suggested in patients with serum monoclonal components and diagnosis of micro-molecular myeloma (2 <sup>nd</sup> level test).
C3 Complement	1. Useful evaluation of the decrease in diseases by increased consumption. Not suggested for evaluation of inflammation.
Ca 15.3	1. Not suggested for the initial diagnosis of cancer. Useful for the evaluation of extension, response to treatment, early detection of progression, monitoring of therapy for metastatic disease.
CA 125	1. Useful to the differential diagnosis of benign disease, restricted to adenocarcinoma of the ovary. Useful for the evaluation of extension, response to treatment, early detection of progression, monitoring therapy for metastatic disease. 2. Useful in the diagnosis of endometriosis
OGTT	1. Useful in the evaluation of hyperglycemia in patients with fasting plasma glucose higher than 104 and less than 125 mg/dL.
D Dimer	1. Useful to the exclusion of deep vein thrombosis and pulmonary embolism. Recommended performing it in Hospital. 2. Useful in the diagnosis of DIC. Recommended performing it in Hospital.
Protein electrophoresis electrophoresis	1. Useful in the detection and monitoring of Monoclonal Components
ENA	1. Suggested after the determination of ANA or if there is a clinical suspicion of Systemic Autoimmune Disease (SAID) (2 <sup>nd</sup> level test).
Ferritin	1. Useful in evaluating microcytic anemia. (2 <sup>nd</sup> level test) 2. Useful in the evaluation of iron stores. (2 <sup>nd</sup> level test) 3. Useful in the diagnosis of hemochromatosis. (2 <sup>nd</sup> level test)
fT3	1. Not suggested for the initial evaluation and screening of thyroid diseases (TSH useful). (2 <sup>nd</sup> level test)
Homocysteine	1. Not suggested among the general population for the evaluation of cardiovascular risk.

At this moment the prescriber may choose whether to join or not the suggestions. The software does not use a top-down logic, but the one of memory assistant, leaving the physician free will. In fact, the DSS requires four reasons for non-adherence to the indication proposed. The reasons have been designed so as to be always the same, regardless of the selected test (table 2).

**Table 2.** Reasons for non-adherence.

Clinical situation not provided for indication.
Specialist prescription.
Disagreement on the indication.
Other reasons.

The only condition subsistent is to motivate the choice, indicating one of four different reasons. The acceptance of

indication occurs by a click that automatically inserts the test in the recipe. The choices of prescription are logged by generating an Excel file that records the number of times the test was prescribed according to the proposed indication and how many times was chosen the non-adherence and why. The tests are available with two ways: a) search for a single test; b) search into pathology folders, represented by logical groups related to certain diseases (liver, thyroid, check-ups, etc.) or in subfolders (e.g. weeks of gestation). The pathology folder offers the advantage of being able to display the test useful within a given pathology scope and in the case of a test with more indications, presenting only the indication relevant to the scope of the folder (Table 3).

Example is represented by the test Prothrombin Time in Table 3.

**Table 3.** Example of the test Prothrombin Time.

The single test has three indications: Useful in assessing the risk of bleeding or a hemorrhagic event. Useful in monitoring oral anticoagulant therapy Evaluation of hepatic insufficiency and malabsorption. The same test prompted in the folder "liver disease" shows only indication 3: Possible use in the evaluation of liver disease and malabsorption.
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Moreover, the references used to build up the indication can be displayed for each test. The program is customizable so that it can display information such as the place of execution, information for patient (diet, exercise, posture, etc.), collection methodology (urine twenty-four hour, urinary cytology, etc.), mandatory indications (niche tests, pregnancy, etc.), number of tests that may be prescribed in each recipe.

## 2.2. Design of DSS

The idea comes from a paper by Karl Raimund Popper in which the epistemologist wondered: "how to act in circumstances where the available information are incomplete" [45]. The logic of construction of the DSS and of indications of prescribing departs from the studies of cognitive science [46-50]. According to them the decision with little time available, both in the relational life (economic investments, rentals, purchase of goods) and professional (prescriptive act) is entrusted mainly on intuition or, more simply on the good sense, to guide us through countless shortcuts to solve rapidly complex problems, when information are lacking. As exemplification it might be used as hyperbolic image, the one of the hunter: which hunter, facing a wild lion, with pen and paper would calculate the trajectory of the bullet? No one would, having to take the action more possible and faster. This is the mindset that we daily use and that is unconsciously the main source of our mistakes. The example shown may help to understand the building logic of the DSS, in fact the physician too, in the prescriptive act, is facing a "wild lion", represented by the patient with his medical needs and anxieties, by the limited time available, by bureaucracy, by ranks of the patients out door, by difficulties in finding information hic et nunc (here and now), by the inadequacy of memory and reasoning biases

[51]. The DSS has been designed on Theories of Bounded Rationality of Herbert Simon (Nobel Prize in Economics, 1978) in order to provide the physician with the minimum number of elements for deciding, that is to say the rescribing indications" were able to restrict the information needed for right choice tests. The prescribing indications are the aid to the physician in the practice, synthesizing and making available an, otherwise, not manageable number of information and guiding the same physician in the context of the wide range of possibilities, in order to find the main road in the intricate Babel of scientific knowledge, regulations and economic contingency. Indeed, no clinician can fully know and correctly use the array of tests available. It's obvious that the indications are not built to exhaust all existing diagnostic possibilities or to conclude the cognitive process, or crystallize the complexity in canned recipes within a schema, but they should have the function of establishing a backup point, updated in real time over the network, where the evidence is given by the revision index. This is the reason why a test can be accepted in disagreement with the proposed indication. This means providing a wide range of freedom and autonomy. Therefore, the indication acts as an advice, as a guide on the route to be taken and also as a tool for governance of knowledge in its original etymological meaning. The only prerequisite required by the DSS is the reason of choice, free from sanctioning issues (ticket not refundable, inspections etc.)

**2.3. The Board**

A scientific board has been set up in order to build the prescribing indications and ensure scientific authority, continuous updating and sharing with GPs. The board in both trials consisted of a group of permanent members, formed by the Inventor of the software, by Directors of Laboratory Medicine, Hospital General Medicine, Health and Social Care and by a delegation of the GPs. Whenever it has been necessary to have specialized information (e.g. nephrology, gynecology, hepatology, rheumatology, etc.), the Board involved professionals, accredited in the specific discipline. The six rules on which the Board based its building the "indications" are shown in Table 4. The reference sources in the building the indications have been intentionally limited, due to the fact that at that stage it was matter of priority checking the feasibility and efficacy of the tool. For this purpose as references the latest edition of Harrison's [52], some guidelines of Scientific Societies and the Clinical experience of the participants to the Board were taken. So, the "indications" had purpose to be the compendium of the observation of the events that clinicians every day face and attempt to turn into a permanent features, from which obtaining defined rules and verbal formulations. The verbal formulation, as known in linguistics, is all the more effective the higher its shortness, clarity and density of statement [53]. The final choice was that to adopt short statements in which focusing complex processes and a "method" of choice of performances, the latter divided into levels, according with nosology and costs (table 5).

Principles for building rules in Table 4 e Table 5.

**Table 4. Principles for building rules.**

1	Tending toward a process of synthesis of scientific knowledge, reporting the essential specialized knowledge through short, unambiguous and easy to understand sentences.
2	Building information tools useful in the prescribing at the precise time of need, that is to say "in front of the patient," when the physician has limited time and trouble to consult scientific sources. Highlighting the elements needed during the prescription by removing the information useful for the only interpretation of results. e.g. ACE (Angiotensin Converting Enzyme): the DSS submits only the indication "Useful for diagnosis and monitoring of sarcoidosis."
3	There are not knowingly information useful for the interpretation of a result out of the reference values, but that does not justify a prescription for a diagnosis of diabetes, primary biliary cirrhosis, myeloma, chronic lung disease, hyperthyroidism, amyloidosis, situations in which the literature reports this enzyme increasing. Identifying right application area for some laboratory tests and, defining consequently the clinical situations in which their use is a priori inappropriate. e.g. Markers of Cancer: it is possible to establish for many of them the inappropriate prescription for diagnostic purposes. Even if it is not possible to define a priori the sure inappropriateness for other tests, it is possible to identify the <i>rational</i> limits of use. It will then be possible to suggest the right clinical environment of some tests and to exclude instead others.
4	e.g. AST: it is not rational to propose its prescription for suspicion of early liver disease. Establishing priority levels of prescription for some tests (1 <sup>st</sup> and 2 <sup>nd</sup> level tests).
5	e.g. Ammonium: it is a 2 <sup>nd</sup> level test, which is useful in the evaluation of stated high-grade hepatic insufficiency.

**Table 5. Example of building rules.**

Rule	Useful in evaluating macrocytic anemia. 2 <sup>nd</sup> level test
<b>FOLIC ACID</b>	
The short sentence is the following: before prescribing the determination of folic acid it is appropriate to have the evidence of macrocytic anemia, that is to say, a complete blood count with hemoglobin less than the reference values and increased MCV.	

For the purposes of the trial, indications for only 110 tests and only 10 Pathology folders have intentionally been formulated and structured.

**2.4. Detailed Rules of Trial**

On the basis of the above solutions, two trials were carried out using the DSS, the first, lasted six months, at Local Health Care Authority of Rovigo in 2008, involving 23 voluntary GPs, the second, lasted seven months, at the Local Health Authority of Mirano in 2010 involving all 196 local GPs. In both trials, the data of prescriptions processed with the use of the DSS were compared with the data of prescriptions dispensed by the same physicians, in the same months of the previous year. In the trial of Rovigo it was used as control group, data (provided by the Management Control) from all other GPs who did not use DSS. In the trial of Mirano, having all GPs participated in the trial, it was used as a control group data relating to 671 GPs of Veneto Region

(non-user DSS), extrapolating the data from management programs used by GPs. The training was made up of a learning event on themes of appropriateness and on explanation of the logic of DSS. The operating characteristics of the software were provided when the DSS was installed, by means of a synthetic and specific operating procedure.

### 3. Results

#### 3.1. Trial of Rovigo

Between years 2007 and 2008, the results showed a decrease by 37.2% of the tests (DSS listed) prescribed according to the proposed indication and a decrease by 13.5% of all prescribed tests, including those without indications (Table 6).

Results relating to the only tests with DSS VS without DSS in table 6

Table 6. Results relating to the only tests with DSS VS without DSS.

Without DSS - year 2007	DSS - year 2008	Nrs decWithrease	% decrease
29.703	18.660	11.043	37.2%
Results relating to all tests with and without DSS			
Without DSS - year 2007	With DSS - year 2008	Nrs decrease	% decrease
118.848	102.869	15.979	13,5%

In the control group of GPs without DSS, the tests were increased by 4%. Significant changes in the prescription of some single test were also measured (Table 7).

Trial of Rovigo with 23 GPs: changes of some tests without DSS (2007) and with DSS (2008) in table 7.

Table 7. Results relating to the only tests with DSS VS without DSS.

TEST	Year 2007	Year 2008	Nrs Change	% Change
Urea	2510	1010	1500	- 60%
AST	4601	1965	2636	- 57%
Lipase	101	52	49	- 49%
ft3	991	613	378	- 38%
Fibrinogen	391	222	168	- 43%
Protein Electrophoresis	1593	1078	515	- 32%
CA 125	173	127	46	- 27%
ALP	1008	696	312	-31%
Antithrombin	224	155	69	-31%
Iron	1369	959	410	-30%
Ferritin	944	673	271	-29%
CA 19.9	272	215	57	-21%
PSA	1720	1358	362	-21%
ft4	1684	1340	344	-20%
Direct Bilirubin	1519	1211	308	-20%

The medical experimenters, interviewed by telephone, judged DSS tool useful, practical and applicable in daily work.

#### 3.2. Trial of Mirano

Since DSS was provided to GPs without any specific training on program, it was not utilized on an ongoing basis,

as highlighted by evaluation of the results and by interviews with Prescribers (for example, during leave or sickness when Prescribers were replaced by colleagues who did not know the use of DSS). When the Prescribers continuously used the DSS, the test number decreased by 26.1% (Table 8). Significant changes in prescription of some single test were also measured (Table 9). Otherwise, in control group (DSS non-users) the tests increased by 4.1%.

Results relating to the only tests with DSS VS without DSS in table 8

Table 8. Results relating to the only tests with DSS VS without DSS.

Without DSS - year 2007	With DSS - year 2008	NRS decrease	% decrease
225.080	166.440	58.640	26,1%

Trial of Mirano with 196 GPs: changes of some tests without DSS (2009) and with DSS (2010) in Table 9.

Table 9. Trial of Mirano with 196 GPs: changes of some tests without DSS (2009) and with DSS (2010).

TEST	Year 2009	Year 2010	Nrs Change	% Change
Fructosemia	237	57	180	- 76%
5HT	40	19	21	- 52 %
Ca72.4	20	12	8	- 40%
AST	81.455	58.725	22.730	- 28%
ft3	16.700	12.520	4.180	- 25%
D-dimer	134	107	27	-20,00%
OGTT	155	125	30	- 19%
C-protein	939	783	156	- 17%
CYFRA 21.1	117	99	18	- 15%
Pseudocholinesterase	1.042	894	148	- 14%
ALP	17.407	15.382	2.025	- 12%
Reticulocyte test	908	796	112	- 12%
Urea	46.375	41.059	5.316	- 11%
Direct Bilirubin	16.098	14.614	1.484	- 9%
PSA	6.161	5.666	495	- 8%

During both trials, technical critical issues related to Information Technology, between DSS and GP- EMR did not occur. These features were of course key elements to assess the technical feasibility of applying software.

### 4. Discussion

It is mandatory in order to comment on results and assess the potentialities of software, to recall that in the experimental phase the indications knowingly regarded some of the more than 500 tests available, and that 10 pathology folders had only been structured. The overall decrease by 37.2% obtained in Rovigo may be in our opinion considered a good result, aligning this datum with the ones reported in the literature. But it is also true that a careful assessment of appropriateness would require during the trial the knowledge of the clinical questions that led the prescriptions, as well as knowing the outcome. In spite of these limitations, it seems reasonable to believe that the results shown could be considered a positive indicator of appropriateness. On the other hand, the DSS is chiefly a system of knowledge management, representing the appropriateness, the

epiphenomenon of its application. In addition to the datum of the overall decrease by 13.5% of prescribed tests can be positively interpreted as meaning that the use of DSS has probably changed the prescribing behavior, even for tests for which indications had not been provided. This is a present hypothesis, but the increase by 4% of prescriptions in the control group that did not use DSS, leads us to consider it likely. On the other hand Prescribers that joined on a voluntary basis to the research committed themselves to continuously utilize the DSS, prefiguring the possible results achievable by the use of the software in wide population of highly motivated Prescribers. The overall decrease of 26.1% in Mirano is a positive result considering the increase in the prescription of 4.1 in the control group, but probably affected by the use of DSS on non-voluntary basis, and by the lack of a structured training. The results achieved may be ascribed to the synthesis of several factors. The instant faculty of DSS to access the GP-EMR without needing to change or enter other applications played a crucial role. A further factor of compliance was the graphical intuitive feature of interface, as also pointed out by the experimenters. The probably most effective property was the freedom of prescription that DSS allows the physician. The act of freedom is particularly expressed in the sentence "non-adherence for other reasons", allowing the physician a choice of opportunities towards the patient. Opportunity is a different situation than appropriateness, regarding the first the world of values rather than the one of knowledge and expertise. For example, prescriptions pressed by the patient and relatives can be justified on the basis of a broader assessment such as the psychological wellness of the person or the family, but even the impossibility of the same patient to submit himself to tests at two different times, as the logic of DSS might propose (e.g. first and second level tests). Finally, a crucial element has been the recognition by Prescribers of the authoritativeness of Board members, whom a relationship between peers has been established, with so that a circular and bi-directional communication overcame, and that the same allowed the transmission of knowledge among organizational nodes (Prescribers, Local Health Authority, and Laboratory Medicine) [54]. A weak point in the building of DSS should be the simplification of information. Shortness and simplicity of the sentences has two precise reasons. Shortness is useful to support the action of the prescribing physician, but also to call to mind concepts that should already be baggage of his knowledge. On the other hand, simplicity is likewise useful to transmit to physician, by means of a phrase "ad hoc" (for this), information that instantly recalls the complexity of the clinical picture. A point of strength, instead, should be the logic of the DSS when, in addition to limiting the use of a test (for example the fT3, Table 1), proposes alternative performance (e.g. TSH), but also when, in case of cultural gap, the same DSS proposes bibliographic references, offering physicians prompt to deepen knowledge, that may be also later performed. In this case an undeniable authoritativeness of the Board is needed. With regard to defensive medicine, we believe that the

indications provided by DSS in association with risk management strategies, do not tout court safeguard the forensic immunity, but may represent a guarantee of good medical practice, as they contain the summary of medical knowledge, and of ethic behavior [55-58]. In this case too, an undeniable authoritativeness of the Board is needed. Even if it has not been possible to take out the share of tests induced by defensive behavior, the results obtained utilizing the DSS may be assessed as a contribution in decreasing number of tests prescribed for the benefit of physician and not of patient. Last but not least, the financial side. Appropriateness is one of the main tools for spending review, as well as for application of principles of morals and justice, according to which the limited financial resources should be devolved to useful health benefits. In this regard, the trials show the potential for governance of the prescription without resorting political and administrative actions (ticket, taxes, fixing a quota on reservations, etc.) that could lead to restrictions and inequalities induced by a spending review not guided by scientific criteria [59-60]. On the other hand, medical doctors have to ensure that computer solutions planned for management of knowledge are not misused as a means of control and inspection or restriction of prescriptive freedom. The DSS, in this regard, has been designed as a solution managed exclusively by physicians so that no one could consider it a "Deus ex machina". In fact, DSS has to work close to physicians as a tool modifiable and adaptable to new needs of knowledge, as well as a dynamic machine continuously rebuildable.

## 5. Conclusion

On the basis of the foregoing, we believe that DSS Ermete might be a tool able to manage demand for laboratory tests, inducing a change in prescribing behavior, allowing, at the same time, the physician full decisional freedom and autonomy. By improving the appropriateness it might be possible to handle the challenges in the future, offering to users prescriptions proper to their clinical needs, updated and consistent with scientific progress, as well as economically viable.

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