

The Value of Diagnostic Information in Personalised Healthcare: A Comprehensive Concept to Facilitate Bringing This Technology into Healthcare Systems

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Keywords

Access to healthcare · Decision-making · Diagnostics information · EU policy · Healthcare services · Health economics · Personalized medicine

Abstract

Health systems around the world seek to address patients' unmet health needs for a range of acute and chronic diseases. Simultaneously, governments strive to keep healthcare spending sustainable, while providing equal access to high-quality care. This has fuelled debate around what constitutes a valuable healthcare intervention in a health system and the corollary consideration of what governments are willing to pay for a certain health intervention. Until recently, the value

of information in general, and the value of diagnostic information (VODI) specifically, was not part of the discussion. However, investment in diagnostic information can be a key development as information may guide more effective and efficient healthcare and help maintain an affordable health system. This paper therefore explores ways to best define, evaluate, and reward the value created from diagnostics in healthcare and how to include these value considerations in decision-making processes for diagnostics. The authors ultimately call for a holistic VODI framework that accounts for the full range of potential benefits of diagnostic testing, beyond the traditional clinical and health economic domains, and that is essential to recognise, measure, and fully leverage the benefits of diagnostics for patients, health systems, and society.

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Introduction

It is recognized that patients can live healthier and longer lives when disease progression is prevented or delayed or when patients recover through timely diagnosis, followed by appropriate clinical management [1]. Diagnostics deliver information that can benefit patients by enabling the selection of the right treatment, helping health professionals to choose appropriate preventive interventions and providing vital prognostic data that can optimise care pathways and management [2–4]. Diagnostic information may also enable informed choices regarding, for example, reproduction, nutrition, and changes in lifestyle. Furthermore, diagnostic information may help to avoid or shorten hospitalisation, decrease inappropriate medication use, or shorten the length of sick leave, thereby bringing economic value in terms of cost-containment as well as fostering improved health outcomes, ultimately leading to more efficient use of resources.

Unlike therapeutics, for which direct clinical effects can often be straightforwardly demonstrated, diagnostics provide information that indirectly influences patient management as well as the economic efficiency of healthcare systems. It is often more difficult to generate evidence to demonstrate the full potential of diagnostic information, as compared to generating such evidence for therapeutics, and may require a different approach. We introduce the value of diagnostic information (VODI), which goes beyond conventional cost-effectiveness metrics by including the “value of knowing” as well as quality of life improvements arising from this knowledge gain. Diagnostic information is valued across multiple dimensions with each dimension being weighted differently by different stakeholders. This might explain why diagnostics are generally considered only in the context of a specific treatment or circumstance, while the broader VODI is frequently overlooked.

A holistic framework for VODI that accounts for the full range of potential benefits of diagnostic testing, beyond the traditional clinical and health economic domains, is essential to recognise, measure, and fully leverage the benefits of diagnostics for patients, health systems, and society.

This paper is the result of an international multi-stakeholder dialogue aimed at recognising, building, and advancing the role of VODI in all its dimensions. The aim is to contribute to a broader debate about the best way to define, evaluate, and reward the value created from diagnostics in healthcare more generally, and how to include these value considerations in decision-making processes for diagnostics.

A Comprehensive Concept of Value for Diagnostics

A healthcare “value chain” is triggered when screening, or the suspicion of disease, leads to the application of a diagnostic test. The information obtained from the test may provide more certainty about the best course of action and thus improve patient management (i.e., intrinsic value of information). The information obtained may lead to further testing or, on the contrary, to no further action [5, 6]. It may also lead to treatment, or to a better choice of the most (cost-)effective treatment for a specific patient, thereby potentially avoiding the use of an ineffective treatment. Diagnostic information may also support decisions about family planning, future plans, or end-of-life patient care. These actions all refer to different dimensions of VODI and may be valued differently from the different perspectives of the relevant stakeholders [7]. For example, improved patient management resulting in better clinical outcomes may be one dimension of the VODI concept (e.g., the “clinical utility” of the test-treatment combination). Other dimensions could include patient empowerment through greater knowledge of their condition, the improvement of the effectiveness of other interventions (e.g., personalized medicine) after the test is applied, and guidance towards population risk stratification and the best use of resources. As shown in Figure 1, the perspective from which the value is evaluated predefines the set of dimensions that are likely to be included in an analysis of VODI.

Although the importance of the different dimensions of VODI may vary according to the perspective considered, the value assessment needs to be comprehensive, covering a time horizon long enough to account for all the outcomes and total costs during the expected healthcare pathway (which could be a lifelong time horizon in many cases). The assessment of the various dimensions might require different methodological approaches [7]. For example, patient satisfaction can be assessed with interviews or questionnaires, whereas assessing lifelong health benefits and costs often requires simulation modelling.

We now outline the benefits of VODI for each of the stakeholders represented in Figure 1.

VODI for Healthcare Professionals

Diagnostic information provides value to healthcare professionals by directly guiding appropriate care decisions and related clinical behaviour. Diagnostics generate data (e.g., a blood glucose level, the presence of infection,

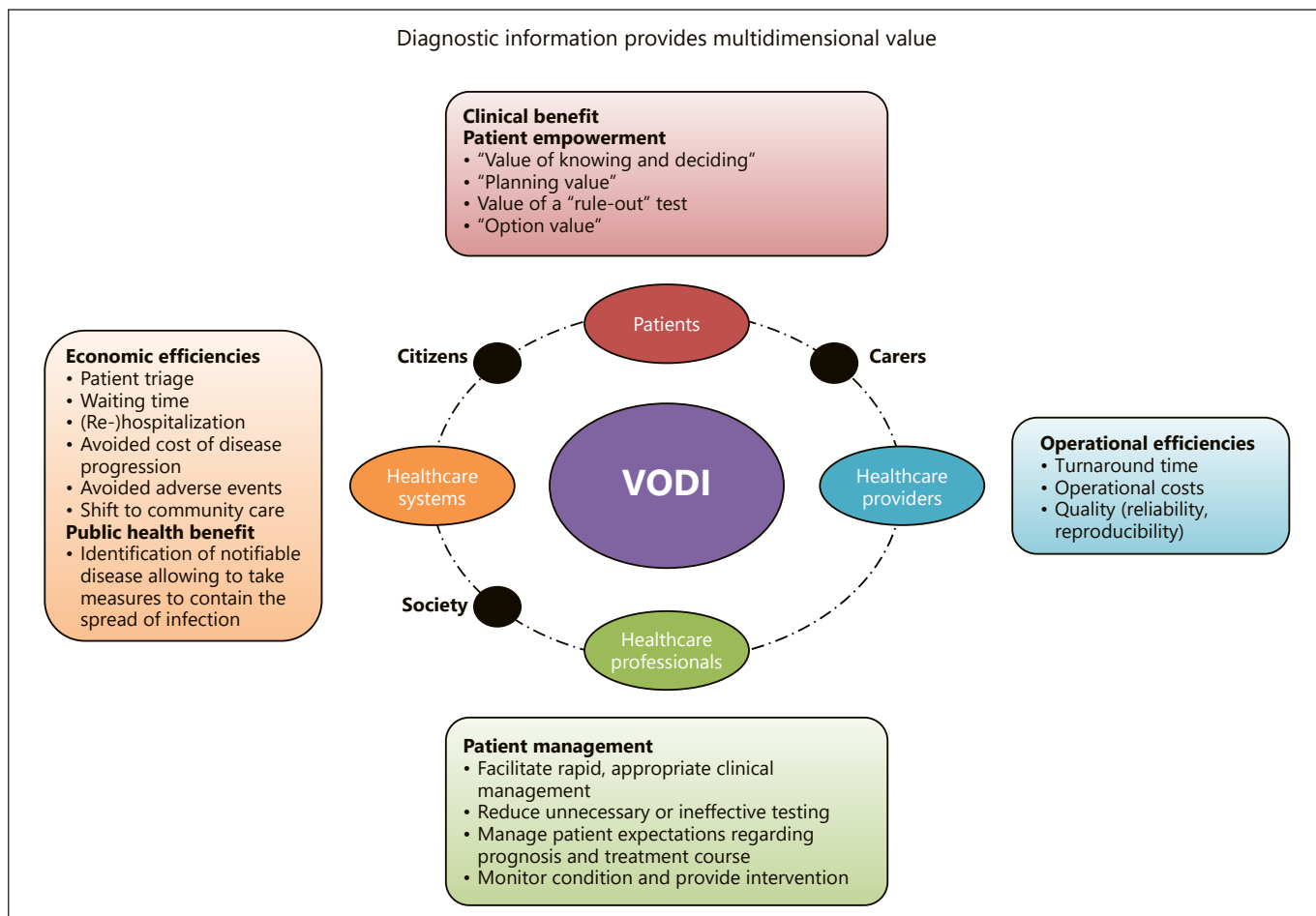


Fig. 1. VODI and its different dimensions.

or a cardiac or oncology marker at genetic level) that can be transformed into knowledge (information), thereby supporting clinical decisions. For example, blood glucose levels (derived from a laboratory or point-of-care test, or blood glucose meter) can be stored and shared in real time with healthcare providers who advise on the appropriate therapeutic action to take (e.g., modify insulin therapy). This may not only result in the desired health outcome for the patient, it may also avoid the need for subsequent or more invasive tests, the occurrence of adverse events, and/or delays in implementing the best possible therapy.

Efficiency gains can also be obtained from well-informed decisions: by selecting the group of patients most likely to benefit from a specific therapy. Another example is rapid detection of the presence of a marker of acute coronary heart disease allowing a prompt indication of the patient’s risk, followed by rapid diagnostic workup and, if needed, initiation of life-saving interventions.

Example: Value for Healthcare Professionals of Deciding with Greater Certainty

Healthcare professionals receiving rapid diagnostic information that rules out a bacterial infection can change their original decision to administer antibiotics. That means that sometimes a costly hospital admission for intravenous antibiotic treatment can be avoided and that overall, fewer antibiotics will be prescribed. Which then may lead to less antibiotic resistance. This type of diagnostic-driven decision-making brings value to healthcare systems in general by making better use of resources (e.g., avoiding unnecessary inpatient care).

VODI for Patients, Families, and Caregivers

From the patient and family perspective, diagnostic information has value both by promoting clinical benefit and through the “value of knowing.”

Clinical benefit comes from decisions about patient management made after testing. These management decisions affect patients' health outcomes. Hence, diagnostic information can provide clinical utility and medical benefit. This will depend on contextual factors in the healthcare pathway, including the availability of treatment after the diagnostic information, the effectiveness of treatments and management strategies for the diagnosed condition, standards of care, prevalence and other specific disease characteristics, and the experience of the person who interprets and uses the information. Assessing the clinical utility of diagnostic tests requires an integrated approach that considers all the contextual factors and multiple outcomes, including interactions with, and impact on, subsequent interventions, along the treatment pathway. This may require the use of mathematical or simulation modelling of these relationships [8].

With respect to the value of knowing, patients may, for example, have greater peace of mind knowing that they do or do not have a condition and may benefit from a treatment if it exists [9–11]. Patients or parents of young patients can derive value from information on their (child's) health status, disease, or prognosis regardless of whether that information would affect a treatment decision [9]. Furthermore, knowing the risk or chances of having a disease may enable informed decision-making.

Example: Value of Knowing for Patients

Beneficial effects on mental health and well-being are reported, with benefits including a sense of personal control, from patients receiving results of a genetic test for Huntington disease. The well-being value comes from the reassurance or the sense of self-control provided by knowing. Research suggests that the dimension of "knowledge and understanding" is the most cited reason for taking the test (38%), followed by life planning (17%) [12].

Families and caregivers may benefit from early access to diagnostic information. For example, an early and rapid diagnosis of a condition such as diabetes can help avoid or delay the progression of the disease and thus lessen or avoid a family's emotional and/or financial burden. Or the diagnosis of a genetic condition or predisposition (e.g., a cancer with a genetic component) might be very important for the prevention, surveillance, or early management of disease in relatives, including their reproductive planning and adequate clinical management. Caregivers may benefit from home or point-of-care monitoring of disease (e.g., coagulation or glucose monitoring) as most of the patient care may be provided at home or in the commu-

nity. This may lessen or avoid interference with activities of daily living both to patient and caregivers (e.g., they can go back to work, study) as fewer visits to the hospital or clinic would be needed when most of the management can be readily done near patients' homes.

Diagnostic information may also allow patients to understand their prognosis and plan their lives accordingly, including, in the case of genetic disease, making reproductive decisions. This "planning value" [10] or ability to inform patients about choices on disease surveillance (for "at risk" individuals), reproduction, work, retirement, and long-term health is another important domain of VODI.

Example: "Planning Value" for Patients – Behavioural Change

The patient receiving diagnostic information about the presence of a chronic condition (e.g., high cholesterol, diabetes) may attempt to pursue a healthier lifestyle. This may in turn promote better health and socioeconomic outcomes, avoiding disease progression, and fostering active and healthy ageing while decreasing the use of chronic medications, thereby lowering the cost of care.

By labelling their condition, patients may become able to seek specific care and avoid ineffective palliation of symptoms. Patients can feel empowered and in control of their care if they themselves have access to this diagnostic information. This might lead to better adherence and thus better self-management of chronic conditions (e.g., diabetes), which can lead to better health outcomes [13].

Non-medical services such as education and social care may be more difficult to secure without diagnostic information as they often need a medical indication. Furthermore, diagnostic information on their condition allows patients and families to seek peer support from others with the same condition.

Patients might also assign value to being reassured about the absence of disease (i.e., the value of a "rule-out" test [6]). Another domain is the possible future value ("option value" [10, 14]) assigned by the patient to the information provided by the test (i.e., knowing disease status now may enable leverage of a specific management strategy that becomes available in the future).

Examples of Relevant Patient Outcomes Facilitated by Diagnostic Information

- Reported relevant outcomes to patients including clinical benefit of more favourable treatment or management strategy.
- Knowing health status or prognosis empowers patients' choices about their own health status, and on reproduction, work, retirement, long-term health, and end-of-life management ("value of knowing and deciding").

- Reassurance regarding the absence of disease (“rule-out” value).
- Empowerment and an increased sense of well-being and satisfaction due to being in charge of their health.
- Future usefulness from current information (“option value”).
- Improved adherence to treatment and care.
- Positive behavioural change.
- Connecting with others with the same condition for peer support.
- Seeking education and social care.

VODI for Health Systems and Healthcare Institutions

The information provided by diagnostic technologies can have important implications for health systems and healthcare institutions. Diagnostic information can support cost containment by identifying patients in the early stages of chronic disease or at risk of disease onset (e.g., diabetes, cancer). Timely preventive and therapeutic interventions can then be implemented, reducing the risk and speed of disease progression and the long-term costs of chronic disease management and disability. Diagnostic information can also result in earlier diagnosis of acute conditions such as heart attack and consequently reduce lives lost and sequelae with disability.

Examples of VODI for Health Systems

- Reduce costs related to in-hospital stay and outpatient visits, through early identification and prevention.
- Improve the efficiency of care delivery by better targeting of treatment and monitoring of “at risk” individuals.
- Decrease hospital and medication-related adverse event costs.
- Decreasing or increasing overtreatment costs.
- Decreasing the costs of treating disease complications.
- Maximising the cost-effectiveness of available treatments by selecting the population that will most likely respond and be less likely to experience adverse events.

VODI also plays an important role in the performance of healthcare institutions such as hospitals, outpatient clinics, laboratory facilities, and pathology units. Diagnostic information may prevent resources waste in healthcare delivery by improving patient triage and freeing beds in high-complexity and costly inpatient care units. For example, rapid ruling out of acute coronary artery disease may avoid hospital admissions and facilitate a shift from hospital care to community-based patient management, avoiding potential future costs of hospital-related adverse events such as nosocomial infections. The use of unnecessary, non-personalised, non-efficacious high-cost medicines can be decreased by testing cancer patients for specific markers related to treatment response [8].

At the laboratory and pathology facility level, economic efficiency can be achieved with diagnostics. These diagnostics enable accurate and reliable detection of critical biomarkers in a fraction of the usual time, or even detect multiple markers from multiple patients at the same time. These technologies improve turnaround time, which should decrease operational costs and waiting time. Reliable and reproducible tests reduce the need for re-testing of tissue samples and potentially the collection of additional tissue (e.g., re-biopsy) or blood samples. As another example, the rapid rule-out of acute cardiac disease together with knowledge on patient characteristics (e.g., disease history, age, other risk factors) may improve patient flow in the emergency room, freeing healthcare professionals and beds and reducing waiting times.

Innovative diagnostic solutions in the laboratory, or in point-of-care testing, can be integrated with data from electronic healthcare records, registries, hospital claims, and other digital data. This information can be incorporated into clinical decision support systems and enable the measurement of health outcomes and improve healthcare quality while containing costs.

Examples of VODI for Healthcare Institutions

- Improvement in patient triage and/or accurate diagnostic information may result in lower waiting time for outcomes of the test, less testing, and less resource use.
- Early and accurate diagnostic and monitoring information can facilitate reduced inpatient hospital stays and a shift to community care.
- Improving the effectiveness of other interventions by enabling healthcare professionals to select the groups of patients who are most likely to benefit by receiving treatment at the right time in the clinical pathway. This avoids trial and error, reduces the costs of under- and overtreatment, and reduces patient adverse events associated with inappropriately targeted treatment.
- Efficiencies at the laboratory level, with improved turnaround time, as well as a decrease in operational costs and waiting time.
- Accurate and reliable information on a biomarker available in outpatient clinics may decrease hospital admissions, the use of more invasive testing, and unnecessary treatments.
- Streamlining with other sources of health data and integrating healthcare pathways may allow more efficient patient management, avoiding waste or duplication of resources.

VODI for Citizens and Society

From a socioeconomic perspective, screening and early or timely diagnosis can ultimately facilitate a faster return to normal daily activities (i.e., work, study, and lei-

sure), keeping people healthy, productive, and socially active. This may result in increased consumption of goods and services and require less support from social care, disability pensions, etc.

Also, shared knowledge among researchers, so-called “scientific spillover,” can expand research and innovation development opportunities, with important long-term implications for patients and society [11].

Examples of VODI for Citizens and Society

- Benefits of returning earlier to work (economic benefits for individual, family, and society; improvement in quality of life for individual and carers through sustaining independent living).
- Savings on welfare programs.
- Overall lowering the disease burden by early diagnosis through screening programs.

How the VODI Concept Could Account for Misdiagnosis and Overdiagnosis

The VODI concept depends, at least partly, on the validity of the diagnostic information and on how the information is being used. Tests may result in false-positive results, meaning that people who do not have the disease of interest still have a positive test result. On the other hand, people with the disease of interest may end up having a test result indicating that this is not the case (false negatives). The VODI concept needs to include both positive and negative consequences of testing and can help improve understanding of the impact of false-positive and false-negative results.

Patients and their caregivers may value the burden of a false-positive result differently from a false-negative result, depending on their respective consequences. For example, a false negative test result may result in benefits foregone if the subsequent targeted treatment is not given to the patient. This will have different clinical implications depending on whether the targeted treatment would have been given *in addition* to usual care or whether it would be the only treatment option. A false-positive test result may mean that patients receive the toxicity of the subsequent targeted treatment but for no additional benefit in terms of resolving their condition.

Furthermore, the burden perceived by patients and caregivers may differ from the burden perceived by healthcare professionals and institutions. False-negative results may lead to missed or delayed diagnoses, leading to increased morbidity and mortality. Individuals are of-

ten worried about those missed diagnoses, especially for lethal diseases. Society, healthcare institutions, and the health system may be more affected by the false-positive results, which may lead to overtreatment and overtesting. Depending on the absolute numbers of people being referred for (potentially unnecessary) further investigations or unnecessary treatment or even harmful treatment, this can put a large burden on the healthcare system and on society.

The VODI concept may provide a framework for dealing with these differences among stakeholders. A VODI concept that explicitly considers the possibility of false negatives and false positives and their consequences may also be able to identify tests or testing practices that are not valuable (anymore).

Another phenomenon sometimes observed in testing is the shifting of the threshold value for test positivity. This has an impact on the percentages of false positives and false negatives but may also have an impact on the final diagnosis. Especially if a diagnostic is being used as part of the disease definition, shifting the threshold for test positivity to a more lenient definition may result in many more individuals suddenly fulfilling a disease definition, whereas previously they did not. These extra individuals may not necessarily benefit from treatment. This leads to a phenomenon called “overdiagnosis”: an increased number of individuals with a diagnosis who do not necessarily benefit from having that diagnosis and subsequent treatment. Having this diagnosis can also be harmful, as it stigmatizes the affected persons. The VODI concept should take this into account and may provide a tool to discuss the problem of overdiagnosis with stakeholders.

Challenges to Capturing the Value of Diagnostic Information and Possible Next Steps

In applying the concept of the VODI, it is important that the full range of consequences, including clinical and economic outcomes as well as negative effects of testing, is taken into consideration. Some important attributes related to VODI are difficult to measure or attach specific value (or weight). However, this does not mean they should be left unaccounted for. If positive attributes are not identified, measured, and valued appropriately, patients and health systems can be deprived of valuable innovative diagnostics and treatments. If, conversely, negative attributes are not appropriately accounted for, inefficient or suboptimal care may be provided.

The influence of testing on life expectancy, the number of cases of disease detected, health-related quality of life, and healthcare costs are commonly accounted for in traditional health economic evaluations (cost-effectiveness or cost-utility analyses). This is based on the importance of these attributes, the availability of systematic approaches to measure them, and guidance on their value to society (e.g., through a willingness-to-pay or cost-effectiveness threshold). However, some important attributes related to VODI may not be directly linked to health-related quality of life or costs and are therefore often not included in conventional health economic evaluations of tests.

As an example of a positive attribute, genetic information can be valuable for the whole family, but preference-based methods of measuring health state utility such as the quality-adjusted life year (QALY) generally exclude the impact on family members' utilities. Furthermore, non-health outcomes are also important for patients, including reduced waiting time for test results or a more convenient location for receiving care (home/near-patient testing), which are not generally captured in health state utilities. Key societal elements of value such as the burden of disease on families and caregivers, and increased tax revenue from active citizens, are also not captured using the traditional cost-per-QALY metric.

Examples of Challenges – What to Do with the Information if No Treatment Available?

In a less favourable context, although early diagnosis is often desirable, patients with Huntington's disease may prefer not to know that they will get the disease, as appropriate medical management options do not (yet) exist. Previous research has shown that predictive testing in Huntington's disease may increase the occurrence of chronic depression or the number of suicide attempts in affected individuals [15, 16].

The importance of incorporating broader aspects of value in health economic evaluations is increasingly being recognized. To illustrate this, consider for example a comprehensive study regarding a social cost-benefit analysis of regulatory policies to reduce alcohol use in the Netherlands. In this study, the feeling of well-being that consumers may experience from drinking alcohol has also been measured and expressed in monetary terms. The monetary benefits of alcohol have been subtracted from the costs of alcohol to arrive at the final estimate of net costs for society [17]. In a health economic context, the general challenge is therefore to measure, quantify, and express all relevant advantages and disadvantages of testing in monetary units or health impact. Alternatively,

health economic outcomes can be supplemented by non-health economic outcomes, to inform decision-making in a multi-criteria context [18].

Fit-for-purpose and tailored methodologies will be needed to define and measure the different domains or elements of value in a framework adaptable to the perspective of the various relevant stakeholders. These methodologies may also need to be flexible enough to consider (a) geographical or regional factors, for example, due to the heterogeneity of approaches that European countries use to value diagnostics, (b) the usual omission of a whole range of value elements beyond clinical domains, and (c) the lack of incentives for manufacturers to generate evidence of added value. Furthermore, since reimbursement for novel diagnostics in many developed economies is not based on value, the signals for innovation are distorted. To promote the development and effective incorporation of innovative tests into the health systems, a clear way to reward value creation is needed [19].

Conclusion

The value assessment of diagnostics as presented in Figure 1 constitutes an initial framework for improving informed decision-making in healthcare and having the intrinsic VODI recognised. VODI can be thought of as a compass for the multiple downstream consequences of testing. An accurate early diagnosis has the potential to maximise the efficiency of other health technologies that will be used after testing. The development of a pragmatic assessment framework, where evidence is considered in light of the complete spectrum of the value of diagnostics, is important so that high-value innovation may be recognised and evidence generation incentivised.

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