THE COST-EFFECTIVE LABORATORY: IMPLEMENTATION OF ECONOMIC EVALUATION OF LABORATORY TESTING

TROŠKOVNO ISPLATIVA LABORATORIJA: IMPLEMENTACIJA EKONOMSKE PROCENE LABORATORIJSKIH TESTOVA

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Summary

Laboratory testing as a part of laboratory *in vitro* diagnostic (IVD) has become required tool in clinical practice for diagnosing, monitoring and prognosis of diseases, as well as for prediction of treatment response. The number of IVD tests available in laboratory practice has increased over the past decades and is likely to further increase in the future. Consequently, there is growing concern about the overutilization of laboratory tests and rising costs for laboratory testing. It is estimated that IVD accounts for between 1.4 and 2.3% of total healthcare expenditure and less than 5% of total hospital cost (Lewin Group report). These costs are rather low when compared to pharmaceuticals and medical aids which account for 15 and 5%, respectively. On the other hand, IVD tests play an important role in clinical practice, as they influence from 60% to 70% of clinical decision-making. Unfortunately, constant increases in healthcare spending are not directly related to healthcare benefit. Since healthcare resources are limited, health payers are interested whether the benefits of IVD tests are actually worth their cost. Many articles have introduced frameworks to assess the economic value of IVD tests. The most appropriate tool for quantitative assessment of their economic value is cost-effectiveness (CEA) and cost-utility (CUA) analysis. The both analysis determine cost in terms of effectiveness or utilities (combine quantity and quality of life) of new laboratory test against its alternative. On the other hand, some investigators recommended calculation of laboratory test value as product of two ratios: Laboratory test value = (Technical accuracy/Turnaround time) ×

Kratak sadržaj

Laboratorijska ispitivanja, kao deo *in vitro* dijagnostike (IVD), neophodan su alat u kliničkoj praksi za dijagnostiku, praćenje i prognozu bolesti, kao i za predviđanje odgovora na terapiju. Tokom proteklih nekoliko decenija broj dostupnih IVD testova rastao je postepeno i verovatno će se takav trend nastaviti i u budućnosti. Postoji zabrinutost zbog povećanog i neracionalnog korišćenja laboratorijskih testova i shodno tome, porasta troškova za laboratorijsko testiranje. Međutim, na osnovu izveštaja Levin Groupe procenjuje se da IVD testovi čine manje od 2% troškova ukupne zdravstvene zaštite (ZZ) i manje od 5% bolničkih troškova. Ovi troškovi su prilično mali u poređenju sa izdacima za lekove (15%) i medicinska pomagala (5%). S druge strane, laboratorijska ispitivanja igraju važnu ulogu u kliničkoj praksi, jer omogućavaju donošenje 60% do 70% kliničkih odluka. Na žalost, konstantan porast izdataka u ZZ nije u relaciji sa porastom zdravstvene koristi. Pošto su resursi za ZZ ograničeni, finansijere u zdravstvu (fondove zdravstvenih osiguranja) interesuje da li troškovi laboratorijskih testova (posebno novih testova) opravdavaju dobijenu korist. Preporučeni su okviri za procenu ekonomske vrijednosti laboratorijskih testova. Najpogodniji instrumenti za kvantitativno procenu njihove ekonomske vrednosti su analiza troškovne isplativosti (CEA) i analiza korisnosti troškova (CUA). Obe analize procenjuju troškove u odnosu na efektivnost (CEA) ili u odnosu na korist (kombinuje kvantitet i kvalitet života – CUA) laboratorijskog testa poređenjem sa alternativom. S druge strane, neki istraživači preporučuju izračunavanje vrednosti laboratorijskog testa iz proizvoda dva količnika: vrednost laboratorijskog testa =

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(Utility/Costs). Recently, some researches used multicriteria decision analysis which allows comparison of diagnostic strategies in terms of benefits, opportunities, costs and risks. All analyses are constructed to identify laboratory test that produce the greatest healthcare benefit with the resources available. Without solid evidence that certain laboratory tests are cost-effective, laboratory services cannot be improved. Consequently, simple policy measures such as cost cutting may be imposed upon many laboratories while patients will have limited access to laboratory service.

Keywords: laboratory tests, cost-effectiveness, cost-utility, multicriteria decision analysis

(tačnost / TAT) × (klinička korist / troškovi). Poslednjih nekoliko godina preporučuje se i analiza višekriterijumskog donošenja odluka koja omogućava poređenje dijagnostičkih strategija u smislu korisnosti, mogućnosti, troškova i rizika. Ove analize mogu da identifikuju laboratorijski test koji ima najveću zdravstvenu korist za raspoloživa sredstva. Bez dokaza da su laboratorijski testovi isplativi u smislu efekata i troškova, korišćenje laboratorijskih usluga ne može se unaprediti. Posledično, mogu biti primenjene mere kao što su smanjeno finansiranje laboratorija, a pacijenti će imati ograničen pristup laboratorijskim uslugama.

Ključne reči: laboratorijski testovi, analiza troškovne isplativosti, analiza korisnosti troškova, analiza višekriterijumskog donošenja odluka

Introduction

Laboratory *in vitro* diagnostic (IVD) tests, two- and three-dimensional imaging and various types of endoscopy are examples of diagnostic technologies. They form an integral part of effective healthcare systems by providing essential information for medical decision-making, from personalised cancer treatment to treatment of infections by the appropriate antibiotic selection (1). IVD tests use samples for example blood, urine and tissue that have been taken from the human body in order to assess the potential risk of developing a disease, monitor disease progression, treatment response, efficacy of therapy and to medicate patients with specific drugs and therapies (2). The demand for quicker and more accurate medical diagnostics, including IVD tests, is rising. Improving the accuracy and efficiency of testing provides a substantial contribution to healthcare resource saving. As a consequence, the number of IVD tests available in laboratory practice has increased over the past decades and is likely to further increase in the future.

It is estimated that IVD accounts for between 1.4 and 2.3% of total healthcare expenditure (3, 4) and less than 5% of total hospital cost (Lewin Group report) (5). These costs are rather low when compared to pharmaceuticals and medical aids which account for 15 and 5%, respectively (6). According to Serbian Health Insurance Fund data, in 2016 IVD tests, consumables and medical supplies accounted for 10% and drugs, pharmaceuticals and medical aids accounted 21% of total healthcare expenditure, respectively (7). Despite the fact that laboratory tests form a very small part of total healthcare expenditure they exert a great influence on medical decisions (8).

Unfortunately, constant increases in healthcare spending are not directly related to healthcare benefit. There is a great deal of evidence to suggest that costs due to over-utilization (9), errors (10), unnecessary or inappropriate test utilization and unnecessary test repetition (11) accounted for expenses much higher than those due to the direct costs of appropriate laboratory tests (12). In addition, a British study has estimated that eliminating inappropriate testing could save the National Health Service up to £1 billion in test costs alone (13). On the other hand, the growing number of laboratory tests in recent years has created challenges for physicians and laboratory professionals to determine the best strategy to diagnose disease, monitor disease progression and monitor treatment response. In many cases laboratory professionals make choices between two or more laboratory tests with similar diagnostic importance but with different associated costs without supporting data from comparative research studies. An apparently expensive test might turn out to be cost-saving if it averts costly procedures and/or therapy. Since healthcare resources are limited, health payers are interested whether the benefits of IVD tests are actually worth their cost.

Problems in implementing economic evaluation of laboratory testing

For many years in the European Union only the CE label was required for diagnostic test registration. However, in the light of financial constraints third-party payers need to be sure that CE-labelled diagnostic tests have realistic pricing and/or add true value to society's healthcare (14).

Many articles have introduced frameworks to assess the economic value of IVD tests. The most appropriate tool for quantitative assessment of their economic value is cost-effectiveness (CEA) and cost-utility (CUA) analysis. Both analyses compare the costs and effectiveness/utility of two or more health interventions, for example IVD tests (15). Potential usefulness from IVD testing is early and accurate diagnosis, appropriate patient selection for therapy and consequently increasing patients' life expectancy and quality of life. Therefore, utility in CUA is frequently expressed as quality-adjusted life-years (QALY) (15). Unfortunately, this value is rarely available for IDV tests. In cross-sectional or cohort studies test accuracy is the most accessible value. However,

Table I Multi-criteria decision table.

		Alternative $_1$	Alternative $_2$	Alternative $_f$
Weight$_1$	Criterion $_1$	S$_{11}$	/	S$_{1f}$
Weight$_2$	Criterion $_2$	/	/	/
Weight$_\varepsilon$	Criterion $_t$	S$_{i1}$	/	S$_{1f}$
		OWF$_1$	OWF$_2$	OWFn

Criterion$_1$ – Criterioni (rows) and Alternative 1 – Alternative $_f$ (columns) represent the criteria and alternatives, respectively. The score S$_{if}$ describes the performance of Alternative$_f$ against Criteria$_t$. A higher score value means a better performance. Weight$_1$ – Weight $_\varepsilon$ reflect the relative importance of Criteria $_t$ to the decision. The overall weighted scores (OWF) are the final ranking values of the alternatives. The alternative with the highest OWF value is the best of the alternatives.

this value is a surrogate for patient-important outcomes, as studies often provide low quality evidence for IVD test utility (16). In addition, decision makers face problems in interpreting diagnostic accuracy. It is necessary to present and interpret the results so that clinicians, policy makers, consumers and other researchers can perfectly understand them. In such situations, Van den Bruel and colleagues recommended an investigation into the test's influence on physicians' opinions about diagnosis (17). Such evidence may be used for CEA of IVD tests in an early stage of an investigation. On the other hand, utility value should also be determined by expert elicitations (18).

An additional problem in IVD economic evaluation by CEA and CUA is lack of an appropriate threshold value. An intervention is considered to be "cost-effective" if the cost effectiveness ratio is below the threshold (19). However, it is difficult to estimate the thresholds at which IVD tests are effective enough to justify funding. The UK National Institute for Health and Care Excellence (NICE) recently recommended cost-effectiveness threshold in a range from £20,000 to £30,000 per QALY for drugs (20). Unfortunately, this threshold massively exceeds the cost of conventional diagnostic testing (21). Alternatively, in low and middle income countries the World Health Organization (WHO) has recommended thresholds of 1 to 3 times the gross domestic product *per capita* (22). However, the consequence of threshold use, if it is an inappropriate measure of the health cost, is that thresholds are likely to reduce, rather than increase, population health. Up to now CEA and CUA have only been employed towards a limited number of diagnostics.

Additional recommendations for laboratory test economic evaluation

To avoid such a problem, calculation of laboratory test value as a product of two ratios, test performance and efficiency has been recommended by Equation:

Laboratory test value = (Technical accuracy/ Turnaround time) × (Utility/Costs)

Good test performance is associated with high accuracy and low turnaround time, while high efficiency is associated with a high percentage of clinical decisions made (clinical utility) over costs. In this case utility represents the most accurate conclusion given the available evidence for a diagnostic test (23).

In addition, healthcare decisions should be based on a broad range of variables that are not part of the CEA, CUA or laboratory test value model such as clinical accuracy, number of both false and true positive and negative values, priorities, accessibility and ease of use (24). In the laboratory/hospital context multiple criteria should be considered simultaneously when deciding whether or not to adopt a new laboratory test. Recently, some investigators have used multi-criteria decision analysis (MCDA) methodology. In MCDA each criterion is scored and weighted (25). Scores represent ranked alternatives for each criterion. Weights for each of the criteria reflect their relative importance to the decision. They represent the opinion of a single decision maker or combine opinions of a group of experts. A mathematical equation combines these two components and the result is overall weighted scores that provide an overall assessment of each alternative, *Table I* (25). MCDA distinguishes acceptable from unacceptable laboratory tests. It is a tool that goes beyond cost-effectiveness by allowing complex integration of more factors (26).

Examples of laboratory test economic evaluation

The goal of an effective and efficient laboratory is to identify laboratory tests that create the greatest healthcare benefit with the resources available. In addition, overuse, underuse and misuse of laboratory testing should be minimized. An example of cost-effective laboratory test selection was described by Petrovic and coworkers (27). They created the deci-

sion analytical model to describe different strategies for acute kidney injury diagnosis in children after cardiac surgery using monitoring of creatinine (standard monitoring) and new biomarkers [serum cystatin C (sCys C), urine neutrophil gelatinase-associated lipocalin (uNGAL) and urine liver fatty acid-binding protein (uL-FABP)]. Tests for uNGAL and sCys C were associated with higher costs and lower effectiveness compared to uL-FABP. The use of uL-FABP would likely represent an economically advantageous strategy for early diagnosis of child acute kidney injury after cardiac surgery. Another example of CEA application by laboratory professionals as a tool for avoiding inappropriate test utilization examined the cost-effectiveness of two different strategies for screening of deep vein thrombosis (DVT) with three different D-dimer assays (Innovance D-dimer, Hemosil D-dimer HS and Vidas D-dimer Exclusion II) (28). One strategy included assesment of clinical probability for DVT (PTP) and another strategy excluded PTP assessment. CEA indicated an advantage of D-dimer measurements in combination with PTP assessment over D-dimer measurements without PTP. For laboratories assessing high numbers of DVT patients, the best cost-effectiveness ratio was for the diagnostic strategy which employed the Vidas D-dimer Exclusion II assay. In contrast, the Hemosil D-dimer HS assay was the most cost effective strategy for laboratories with a small number of DVT patients.

Conclusion

In summary, IVD testing can reduce both direct and indirect healthcare costs if it results in more accurate and timely medical diagnoses. However, without solid evidence that certain laboratory tests are cost-effective, laboratory services cannot be improved. Harsh across-the-board cost cutting of laboratory services will limit the diagnoses of patients as a reduced number of tests will be available. Therefore, determining cost-effectiveness prior to cost cutting is much more logical but requires extensive education of both laboratory professionals and non-clinical laboratory staff in order to determine which tests will remain and which will be omitted from the laboratory test portfolio.

Conflict of interest statement

The authors stated that they have no conflicts of interest regarding the publication of this article.

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