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Source / Izvornik: **Collegium Antropologicum, 2008, 32, 1283 - 1290**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:996779

Coll. Antropol. **32** (2008) 4: 1283–1290
Review

Clinical Guidelines Development and Usage: A Critical Insight and Literature Review: Thyroid Disease Diagnostic Algorithms

Jure Murgić, Daniela Salopek, Marin Prpić, Tomislav Jukić and Zvonko Kusić

Department of Oncology and Nuclear Medicine, University Hospital »Sestre milosrdnice«, Zagreb, Croatia

A B S T R A C T

Clinical guidelines have been increasingly used in medicine. They represent a system of recommendations for the conduction of specific procedures used in fields from public health to different diagnostic and therapeutic procedures in clinical medicine. Guidelines are designed to facilitate to medical practitioners the adoption, evaluation and application of an increasing body of evidence and arising number of expert opinions regarding the presently best treatment and to help in delivering proper decision for the management of a patient or condition. Clinical guidelines represent a part of complementar activity by which research is implemented into praxis, standards are defined and clinical excelence is promoted in all health care fields. There are specific conditions which quality guidelines should meet. First of all, they need to be founded on comprehensive literature review, apart from clinical studies and trials in the target field. Also, there are more systems for analyzing and grading the strenght of clinical evidence and the level of recommendation emerging from it. Algorithms are used to organize and summarize guidelines. The algorithm itself has a form of an informatic record and a logical flow. Algorithms, especially in case of clinical uncertainty, must be used for the improvement of health care, increasing it's availability and integration of the newest scientific knowledge. They should have an important role in the health care rationalisation, fight against non-rational diagnostics manifested as diagnostic procedures with no clinical indications, it's unnecesary repetition and wrong sequence. Several diagnostic algorithms used in the field of thyroid diseases are presented, since they have been prooved to be of great use.

Key words: *clinical guidelines, algorithms, thyroid disease, diagnostics, evidence-based medicine*

Guideline and Algorithm Concept

The concept of guideline means a recommendation for a certain procedure. Guidelines have to be based on relevant criteria, which means that they must relay on literature evidence, have to be useful for the whole community, and they must be efficient. Their main aim is scientific evaluation of a particular subject. Although many people use the term »algorithm«, the meaning of that world is often unknown.

Algorithms are composed of cells with questions followed by two possible answers. Arrows coming from the question cell point to the answers »yes« or »no« (Figure 1)[1].

The algorithm branching depends on the answers offered for the appointed question. The arrows can point to the »answer box«or finish on the »terminal node«.

As we can see in the offered example, algorithms have a shape of a diagram which helps to direct the decision making process in a logical order. In this way the specially selected criteria can be implicated with the purpose of recognizing and sorting out the nominated problem[2].

Guidelines and Algorithms in Medicine

Guidelines

Clinical guidelines can be defined as »systematically developed statements to assist practitioner and patient decision about appropriate healthcare for specific clinical circumstances«[3]. Their main purpose is to ease the assessment, use and implementation of the rising number

Received for publication April 10, 2008

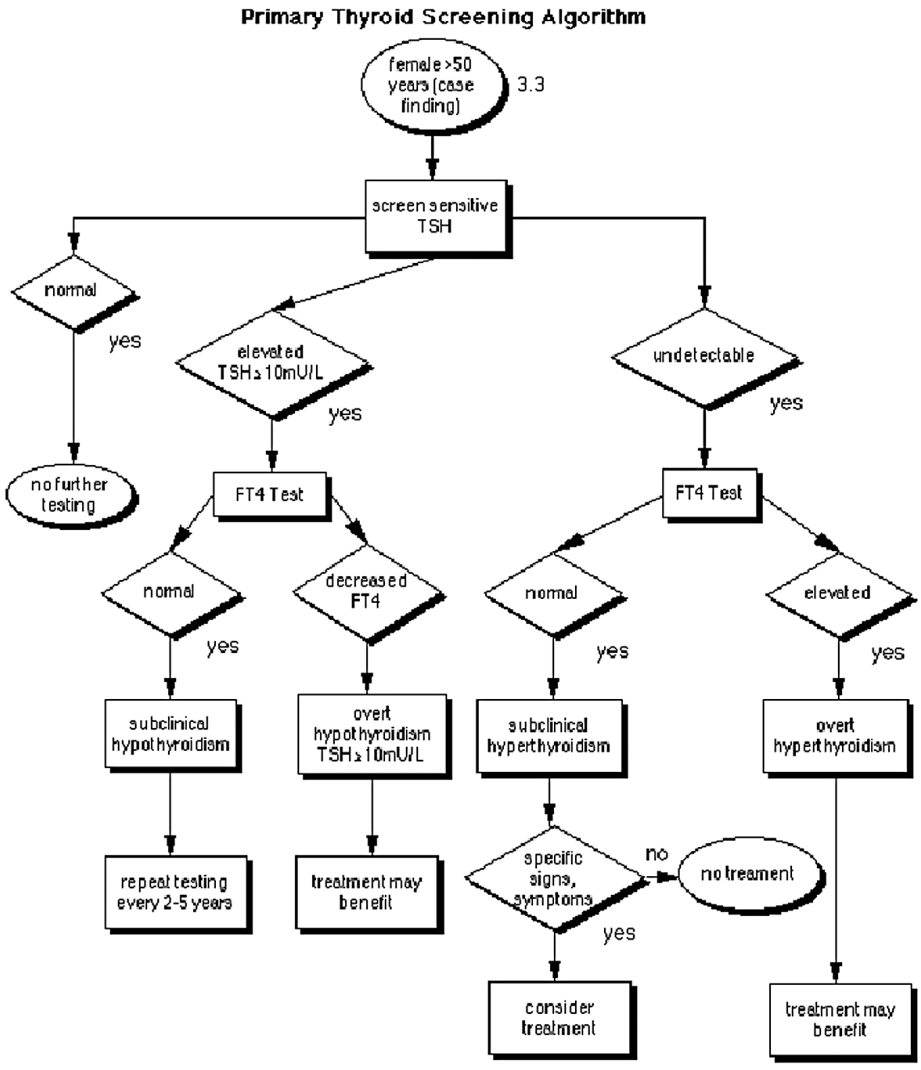

Fig. 1. Primary Thyroid Screening Algorithm[1].

of scientific material and expert prejudice on which would be the best existing procedure in a particular case. In this way the most suitable and efficient procedure or treatment can be picked. They are neither protocols nor precise directions, nor manuals. However, they are an important step in carrying the research into practice. Clinical guidelines help to obtain a high standard of patient care, but they are not on their own enough to assure it. The quality of the guidelines can be assessed according to the follow characteristics: validity, reproducibility, reliability, clinical applicability, flexibility, favorable cost--benefit relation, clarity, multidisciplinary approach, articulated tables and suitable documentation[3]. The role of guidelines is also to unify scientific opinion and tradition with clinical practice.

Guidelines are scientifically proved recommendations, needed to obtain an optimal and rational approach to the patient as an individual human person. They are created by different medical experts who discussed the matter together. There are several types of guidelines with regard on the way they are formed: guidelines based on expert opinion, based on formal consensus, based on evidence and based on the combination of consensus and evidence. They can relate to only one discipline or they can unify more disciplines, and they can deal with a particular problem or summarize the whole field of interest[3,4].

Guidelines based on expert opinion

Guidelines that have been used in the past were mostly based on the principles established by the major and leading expert in the particular field, and on the recommendations for medical care in a definite medicine domain according to these attitudes. The advantage of these proceedings is its cheapness, but the objection is that the leading expert's standpoints don't mean that they are based on quality evidence. A hidden conflict of interest can also be present. Associations of different experts are becoming more and more engaged in guidelines

formation. In the majority of cases the used methodology is negotiable. An article published in Lancet in the year 2000 presented 431 clinical guidelines formed by different specialists associations in the time span of ten years[5]. Guidelines were evaluated according weather they offered and listed the group of experts incorporated in their formation process, methods which served to identify evidence and if they ranked the recommendations according to the evidence. They found out that all the three criteria were stated in only 5% of cases. This result requests a formation of explicit criteria to improve standards for guideline creation and performance.

Guidelines based on formal consensus

In the process of creating these guidelines, formal consensus means conferences and nominal groups which are formed with the purpose to unify their opinions. The main aim of these groups is to define the degree of agreement in medical fields where evidence needed to form recommendations is to scarce. The problem is that their results can depend on the way that the problem is presented, variety of participating experts, form of instructions and methods used in uniting individual evaluations.

Guidelines based on evidence

These guidelines are based on systematic analysis of provided evidence, which demands knowledge and skill to recognize genuine evidence. This has been improved by internet use. However, it is important to differentiate high quality from low quality evidence while transferring the founded evidence unto recommendation. This type of guidelines is most advantageous in fields where there is present a high number of high quality evidence, as for example in the field of malignant disease treatment. However, they are of less importance in fields where proper evidence is scarce, which is the case with mental illnesses. This kind of investigation and results presentation is called »evidence-based medicine«. All recommendations in the field of scientific research, diagnostics, therapy and public health are supposed to be formed this way[6]. The relationship between guidelines and evidence has to be clear, scientifically based and it is important to know that evidence proved in clinical praxis is always more relevant that someone's opinion, even if it is an expert opinion. The best guidelines are those written by different physicians societies such as American College of Physicians (ACP), American College of Cardiologists (ACC), American Heart Association (AHA) because they are detailed, based on a strict evidence analysis, they are transparent and already accepted as a standard in providing medical care[7]. In reality, the major number of clinical guidelines consists of elements of both, evidence and consensus, which joined form useful and quality guidelines. The methodology used in the process of creating these guidelines has to be open and transparent in such a way to enable the user to evaluate their validity and usefulness according to the necessities in his field of work.

The strength of the recommendation differs with regard to the evidence used to create a certain recommendation. The strength of his recommendation based on available evidence designed by the U.S. Preventive Services Task Force is shown in Table 1[8].

Also, it is present another form grading entitled SIGN' grading system, shown in Table 2[9]. SIGN was founded in the year 1993 by the Academy of Royal Colleges and their Faculties in Scotland. Their main aim is to develop evidence-based clinical guidelines for the National Health Service (NHS) in Scotland[10].

Because the need of combining guidelines and evidence which support them, SIGN introduced the term of »considered judgment«. Groups engaged in guideline de-

TABLE 1
STRENGTH OF PANELISTS' RECOMMENDATIONS BASED ON AVAILABLE EVIDENCE[8]

Rating	Definition
A	Strongly recommends. The recommendation is based on good evidence that the service or intervention can improve important health outcomes. Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.
B	Recommends. The recommendation is based on fair evidence that the service or intervention can improve important health outcomes. The evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes.
C	Recommends. The recommendation is based on expert opinion.
D	Recommends against. The recommendation is based on expert opinion.
E	Recommends against. The recommendation is based on fair evidence that the service or intervention does not improve important health outcomes or that harms outweigh benefits.
F	Strongly recommends against. The recommendation is based on good evidence that the service or intervention does not improve important health outcomes or that harms outweigh benefits.
I	Recommends neither for nor against. The panel concludes that the evidence is insufficient to recommend for or against providing the service or intervention because evidence is lacking that the service or intervention improves important health outcomes, the evidence is of poor quality, or the evidence is conflicting. As a result, the balance of benefits and harms cannot be determined.

TABLE 2
SIGN'S GRADING SYSTEM[9]

Level of evidence	
1++	High-quality meta-analyses, systematic reviews of RCTs (randomized controled trials), or RCTs with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding bias, or chance, and a high probability that the relationship is causal.
2+	Well conducted case-control or cohort studies with a low risk of confounding bias, or chance, and a moderate probability that the relationship is causal.
2–	Case-control or cohort studies with a high risk of confounding bias, or chance, and a significant risk that the relationship is not causal.
3	Non-analytic studies, e.g. case reports, case series.
4	Expert opinion.
Grades of recommendation	
A	At least one meta-analysis, systematic review of RCT, or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisiting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consisitency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consisitency of results; or extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consisitency of results; or extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+.

RCT: randomized controled trial

velopment unify their opinions and views of the total evidence material presented in each table. This survey should comprehend the following views:

- Quality, quantity and consistency of evidence
- Possibility to generalize the research results
- Possibility of direct application of the particular guideline to the aimed population
- Clinical impact (for example to evaluate the impact on the particular patient group, and the necessary resources for their treatment)
- Conductibility of guidelines

One other way to assess recommendations is according to the Agency for Health Care Policy and Research, 1992 (AHCPR), used for the UK Guidelines in the Thyroid Function Test[11] (Tables 3 and 4).

The process that SIGN uses in creating guidelines follows the order: selection of guideline matter → formation of the group supposed to create the particular guideline → comprehensive literature review → guideline creation → consultations and peer review → publication and diffusion → local implementation → assessment.

Various resources can be used in the introduction of the first guideline version into a community: internet, messages, leaflet etc. After the period of time provided for discussion is over, the version becomes final; the guidelines become accepted, valid and obligatory for all experts in the covered field.

The primary role of guidelines is to identify patients which could possibly benefit from a particular procedure (diagnostic or therapeutic) or would not benefit from it[3].

Finding the right guidelines

Because of the increase in internet accessibility and use, it has become easier to find guidelines used in different countries. Many guideline creators, such as SIGN, give their guideline available online, usually free of charge, and there are available many sites which classify them. For example the National Guidelines Clearinghouse from the USA contains information upon more than 1700 guidelines[12]. G-I-N (Guidelines International Network), is a data base where different guidelines from all over the world are collected together with the supporting evidence. The G-I-N database is available on subscription and more detail information can be found on the Web[13].

Other worthy and informative sources which help to trace guidelines to be used in clinical practice are: Embase, MEDLINE, Cochrane Library, Canadian Practice Guidelines InfoBase, UK Health Technology Assessment Programme, US Agency for Health Care Research and Quality[14,15,16,17,18,19].

Every professional who uses guidelines has to evaluate their favor and benefit in his own field of work. Some of the key questions to be used in that assessment are: are they answering questions relevant for my population? Do the questions appointed refer to the technology used in my field of work? Are they up to date or has the

TABLE 3
TYPE OF EVIDENCE[11]

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomized controlled trials.
Ib	Evidence obtained from at least one randomized controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomization.
IIb	Evidence obtained from at least one other type of well-designed quasiexperimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

TABLE 4
GRADING OF RECOMMENDATIONS[11]

Grade	Evidence levels	Description
A	Ia, Ib	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B	IIa, IIb, III	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation.
C	IV	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

theory changed drastically since they were written? Is there some kind of barrier, cultural or some other, preventing me to use them? If the guidelines are developed and used according to these principles they provide order and systematization and allow the freedom of choice in the medical procedure.

Algorithms

Algorithms have been in use in the health care system for many years. They are often of great help to doctors and other medical professionals in clinical diagnostic procedure. Algorithms are systems for classification and identification which enable the clinician to approach their patients with specific problems in an effective and efficient way. Diagnostic is only one form of classification and identification. A simple diagnostic algorithm is presented in Figure 2[20].

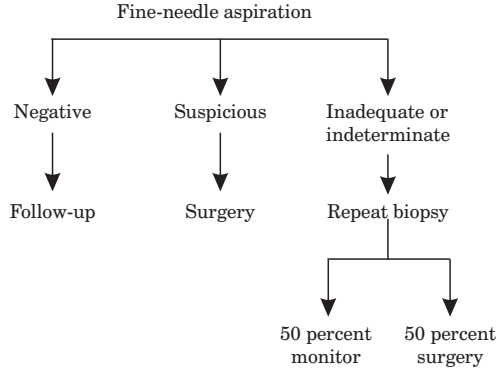

Fig. 2. Algorithm for fine-needle aspiration of a thyroid nodule[20]. Reproduced with permission from Thyroid Nodules from the February 1, 2003 issue of American Family Physician. Copyright © 2003 American Academy of Family Physicians. All Rights Reserved.

The shape of algorithms enables application of the recommendations according to the guidelines for the quality assessment while considering the most adequate care. There are many different types of algorithms, those simple and more complicated, with one ore with more key points and accents[4,21,22].

There is a difference between a simple diagnostic algorithm and a management algorithm. A simple diagnostic algorithm does not require any user action except his observation, which in the case of clinical practice means patient examination and notion of the observed results. This kind of algorithm is imperfect because the clinicians not only observe but also provide therapy. This means that diagnostics and therapy are always joined together with the management strategy. Algorithms containing both, diagnostic and therapeutic modalities, are called management algorithms (Figure 3)[23].

This kind of algorithms consists of boxes (nodes) where instruction is written. Also, they classify patients into separated subgroups, according to their needs. Considering this, algorithm construction can never be simple. Algorithms, especially in case of clinical uncertainty, have the role to improve and rationalize clinical care and add new scientific knowledge. The advantages of algorithm usage are[2,24]:

– They differentiate patients which are, or are not covered by these recommendations, as well as directing decisions and proposed strategies. They sort out the guidelines and enable the user to see the whole picture.

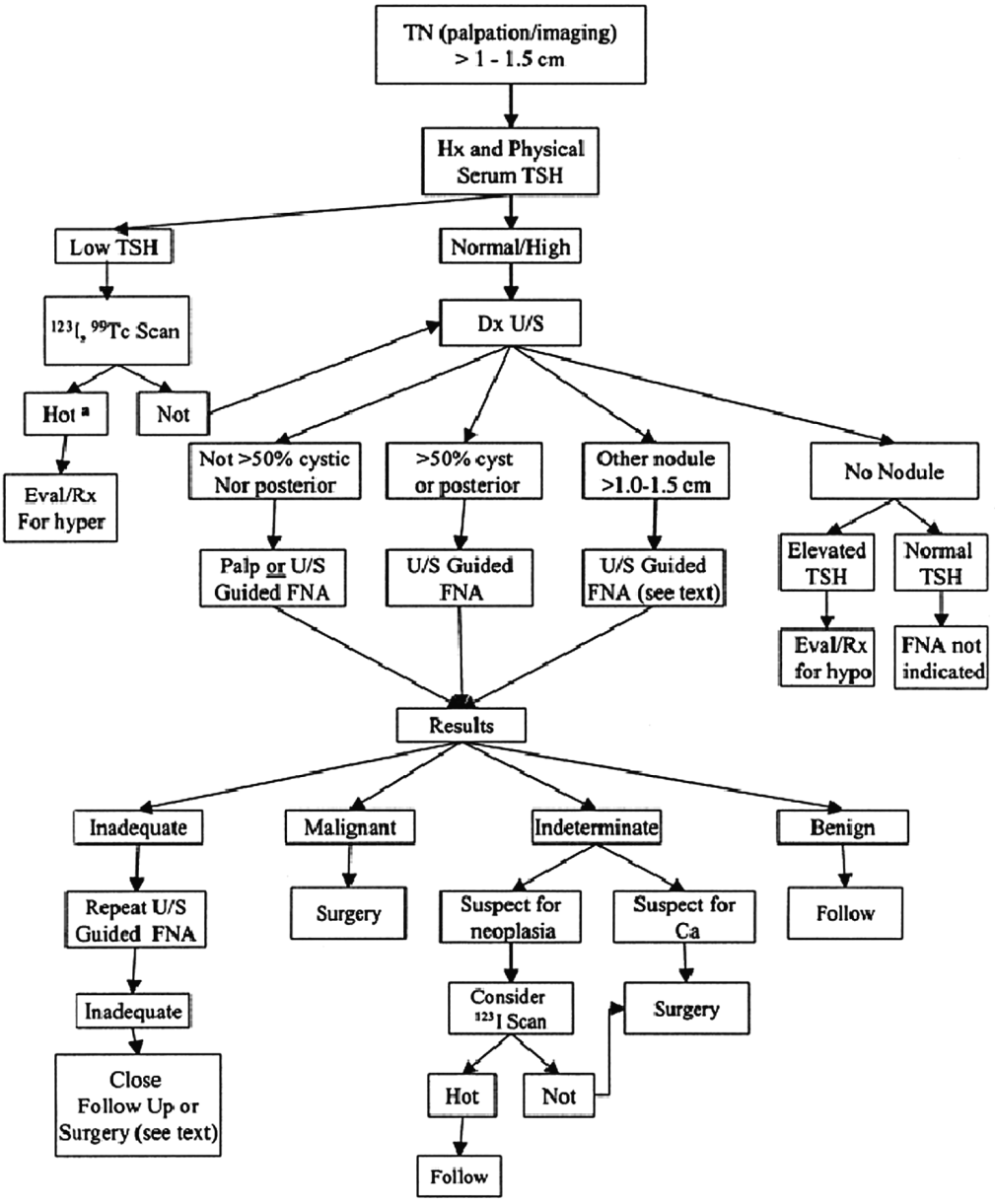

Fig. 3. Algorithm for the evaluation of patients with one or more thyroid nodules[23].

- The results are faster learning, better remembrance, and better compliance than in using the standard prose text.
- They detect cases in which further investigation is not needed. The testing are often carried out regardless the management strategy, but using the algorithms, the testing will be conducted only if the action presented in following box depends on that result.
- Algorithms which are properly designed help to the guidelines developers to assign adequate indications for a particular action strategy. Well formulated questions enable to the guidelines developers to define the type of patients who should or should not be taken into consideration for a particular intervention and who should or should not be treated in a particular way.
- They are easy to translate into a computerized format in order to use them and to assess them.
- They enable the assessment of result, cost and priority change with regard to the structure and guideline contents.

Two major critics can be heard regarding the use of algorithms in clinical praxis. The one most often heard is that algorithms impose to the doctors some kind of rigidity, converting them into robots who can not think and

that the patients are to diverse and have diverse priorities in comparison to the way they are presented. What's more, the use of algorithms in practice is questionable in regard to the clinical justification. In order to overcome the lack of flexibility, during the process of evaluation and follow up »counseling and decision nodes« are used. This means that patients are offered with two or more options of clinically agreeable medical help (for example internal medicine and surgical care) and get acquainted with the expected outcome following each procedure. Counseling and decision nodes present a very important degree of clinical flexibility, and an insight into the conclusions made while reviewing the literature according to the guidelines. In the same time patients can choose which is the most appropriate option for them, according to their preferences and their values[4]. The question of validity of algorithms is solved by inserting a systematic literature review used in the process of creating and designing the guidelines. They are based on systemic notation for every point in the algorithm, wherever there is a special finding, characteristic or intervention described, which is related to the guideline text where that topic is discussed and where the used literature and citations are stated.

Conclusion

Evidence-based clinical guidelines provide to medical professionals a possibility to stay in touch with the current and the latest evidence and recommendations which derive from the mentioned evidence. The realization of quality guidelines for the clinical practice is a complex and serious process which demands firm collaboration of various experts. We can say that the algorithm construction is an art, even though within medicine, whose aim is to convert experience and observation into science. It is true that there are imperfections and deficiencies in guideline use in clinical practice and in algorithms deriving from them, but surely there are even more advantages from their usage, especially regarding the improvement of the standard of medical care, for both those who provide and those who are provided.

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J. Murgić

Department of Oncology and Nuclear Medicine, University Hospital »Sestre milosrdnice«, Vinogradska 29, 10000 Zagreb, Croatia
e-mail: juremurgic@inet.hr

RAZVOJ I PRIMJENA KLINIČKIH SMJERNICA – KRITIČKI OSVRT I PREGLED LITERATURE: STUDIJA DIJAGNOSTIČKIH ALGORITAMA ZA BOLESTI ŠTITNJAČE

S A Ž E T A K

Kliničke smjernice imaju sve veću upotrebu u kliničkoj medicini. One podrazumijevaju sustav preporuka za provođenje secifičnih postupaka kako u javnom zdravstvu tako i u dijagnostičkim i terapijskim procedurama u kliničkoj medicini. Smjernice su osmišljene kako bi olakšale praktičarima usvajanje, procjenu i primjenu sve veće količine dokaza i stručnih mišljenja o trenutno najboljem načinu liječenja određenog stanja i time pomogle u donošenju odgovarajuće odluke o načinu postupanja s pacijentom. Kliničke smjernice su dio komplementarnih aktivnosti kojima se istraživanja prevode u praksu, određuju standardi i promovira klinička izvrsnost u bilo kojoj grani zdravstvene djelatnosti. Postoje specifični uvjeti koje kvalitetne smjernice moraju zadovoljiti, prije svega moraju se temeljiti na sveobuhvatnoj reviziji literature, uz pregled kliničkih studija u ciljnom području. Postoji više sustava za analizu jačine kliničkog dokaza te stupnja preporuke koji iz toga proizlazi. Algoritmi pak služe kako bi organizirali i saželi te smjernice. Sam algoritam ima oblik informatičkog zapisa logičkog tijeka. Algoritmi, osobito u slučaju kliničke nesigurnosti, moraju služiti poboljšanju zdravstvene skrbi, dostupnosti i objedinjenju najnovijih znanstvenih spoznaja. Trebali bi imati ulogu u racionalizaciji zdravstvene zaštite (gospodarski učinak), tj. u borbi protiv neracionalne dijagnostike koja se očituje u dijagnostičkim postupcima bez kliničkih indikacija, nepotrebnom ponavljanju i pogrešnom slijedu dijagnostičkih postupaka. Prezentirano je nekoliko dijagnostičkih algoritama iz područja bolesti štitnjače, u kojima vlada potreba za uprabom algoritama te koje su zbog niza osobina zahvalno područje za uporabu algoritama.