

## From guidelines to personalised medicine

Nicola Natale

National Councilor of Federazione delle Società Medico-scientifiche Italiane (FISM)

To deal with this question, I have to point out the definitions, because too often there is confusion between the terms and their new judicial value requires preciseness in terminology.

*Guidelines:* recommendations for clinical conduct, drawn up through a systematic review of the literature and expert opinions, with the aim of helping doctors and patients decide on the most appropriate care procedures in specific clinical situations.

*Protocols:* pre-defined and binding rules of conduct during trials.

*Treatment profiles or diagnostic-therapeutic pathways:* adaptations of guidelines to local situations, with their specific organisational and management characteristics.

When applying the guidelines, we expect some of the results to be:

- for users: the opportunity to be informed and made aware of the scientific rationale supporting the treatments received;
- for health authorities: the opportunity to define and optimise the care processes and to plan investments;
- for institutions (State, Region, Local): the opportunity to reduce inequalities in service allocation and to facilitate the monitoring and assessment of the quality of the services delivered;
- for professionals: implementation of continual education, improvement in the relationship with patients and protection against medical litigations.

The scientific societies are the most qualified bodies to disseminate the guidelines and achieve the set objectives, given that they have the necessary human, scientific and technological resources for this task. In addition, the scientific societies operate right across the country and so are able to assess the influence of local variables on the guideline implementation process.

So, is it expedient to adopt guidelines?

Yes, because they define shared, clinically valid criteria verified over time by Scientific Societies.

Yes, because they help to optimise diagnostic-therapeutic-rehabilitative appropriateness.

Yes, because they are provided for by Presidential Decree of January 14, 1997.

Yes, because they are provided for by regional regulation (for example, Tuscany Regulation 61/R of December

24, 2010 and Liguria Regional Law 20 of July 30, 1999). Yes, because they are provided for by Balduzzi Decree Law 158 of September 13, 2012.

On the other hand, there is resistance to accepting them:

- if they are not the expression of accredited scientific societies;
- because there is a fear that they could inhibit the health structure's organisation;
- because there are extremely differentiated clinical situations, which require personalised treatments;
- because they require resources for widespread implementation.

The Scientific Societies have the duty to define and update the minimum organisational, structural and professional levels regarding the clinical impact of healthcare performance.

The sharing at national level of minimum accreditation criteria contributes to respect for the Constitution (art. 32) and the protection of patient's health uniformly throughout the country.

Doctors are called on to know, comply with and ensure compliance with the minimum accreditation requirements to protect the patient and their own professional activity.

There is large evidence in the literature suggesting that the lack of attention paid to the implementation phase is largely responsible for the poor impact of many guidelines.

The implementation process should also be assessed to check whether the guideline is capable of changing the knowledge and behaviour of practitioners and to identify any factors and obstacles that could contribute to the failure to adopt the guideline.

The production and updating of guidelines should be a priority for all the Medical-Scientific Societies, which are also responsible for constant updates on the evolution of scientific evidence, and should take place, in any case, at least every two-three years. They should be produced using the same methodology manual, so that their layout is also uniform. It should be remembered, in particular, that the National Guidelines System (SNLG) produced a manual in 2002 that is still topical today.

This manual (*How to produce, disseminate and update recommendations for clinical practice*) reports that the guidelines for a correct methodology must:

- to report the quality of the information (levels of evidence);
- to report the strength of the recommendations (graduation);
- to give a systematic review of the topic;
- to operate multidisciplinary involvement;
- to offer an indication of alternatives and their strength of recommendation;
- to consider the monitoring indicators;
- to report continual updates;
- to use plain language;
- to assess its reproducibility.

The production of guidelines is in itself worthless if they are not disseminated, implemented, used and continually updated as regards the specific reference issues.

Nothing is perfect and guidelines also have critical issues.

The first critical issue regarding the guidelines currently in force is the lack of consideration given to sex differences. This is accompanied by the need to stay aware of the precise personalisation that holistic medicine tends to offer, in other words medicine designed to treat the person and having a global vision, combining mind, body, living environment and society. Health research should hence targeted at the person and not just at the disease, at the cause and not at the symptoms and at the individual systems and/or organs.

Gender medicine, however, is based on scientific data that vouch for interpersonal diversity using the traditional methodology, whilst the second (the holistic medicine) is more reflective of a new philosophy, of a new way of treating human beings not only in terms of their fragmented organs and systems but in terms of their overall complexity.

However, even though holistic medicine is more person-friendly, it does involve a risk of diagnostic and therapeutic anarchy that reduces the opportunities for comparable conduct and contrasts medicine based on scientific evidence with medicine based on the individual. Both methods emphasise the individuality of the person and his/her personal characteristics.

There's still a whole world to explore.

After an in-depth analysis of the clinical aspects correlated with the guidelines we must also assess their medical-legal aspects to a greater or lesser degree which none of us can ignore.

The "old" medical-legal system has been updated with a recent law (March 8, 2017, n. 24) entitled: "Provisions concerning the safety of treatments and the person treated, as well as concerning the professional liability of practitioners in the healthcare professions". At article 5, paragraph 1, it states that "healthcare practitioners... adhere, subject to the specific nature of the concrete case, to the recommendations specified in the guidelines published in accordance with paragraph 3 and drawn up by public and private entities and institutions as well as by the scientific societies and technical-scientific associa-

tions of the healthcare professions..." and paragraph 3 of the same article states: "The guidelines and updates... are incorporated in the National System for the guidelines (SNLG)... The *Istituto Superiore di Sanità* publishes the guidelines and updates on its website..."

In addition, art 6 paragraph 1 advises that: "if the adverse event has been caused by negligence, culpability is excluded when the recommendations stated in the guidelines as defined and published are followed... or, in their absence, by good clinical and healthcare practice, provided that the recommendations stated in the aforesaid guidelines are adequate for the specific nature of the concrete case".

The "judicial" value of the guidelines cannot be underestimated even if the law explicitly stresses the "relative value" of the recommendations contained in the individual guidelines when one moves from an "ideal patient" to an individual "real patient", who is "specifically" different from other patients affected by the same clinical problem.

So, this reiterates the freedom to depart from the guidelines to the extent that these are contraindicated in the specific case.

But there are still "critical issues"; for example, article 5 paragraph 3 states that the guidelines are to be "... drawn up by public and private entities and institutions as well as by the scientific societies and technical-scientific associations of the healthcare professions", introducing a group of entities with the capacity to draw up the guidelines without coordinating them in order to avoid different or even contrasting guidelines.

So much so that the president of the Court of Cassation's penal section IV has asked the joint divisions to express an opinion on medical negligence in the light of the two laws (Balduzzi and Gelli-Bianco) which appear to be partly contradictory.

The fact that doctors must always demonstrate that they have acted with diligence remains valid and it is not up to patients or their families to prove otherwise.

To conclude, we should remind ourselves that:

- our patient is not just an illness or a syndrome;
- sex has a not insignificant influence on frequency and symptomology as well as a different reaction to drugs;
- correctly constructed guidelines are an important aid; but they are not insurmountable obstacles to the way we act.

And... we are waiting to know the direction the magistrature intends to take when judging their role.

Correspondence to

Nicola Natale

FISM - Federazione delle Società Medico-Scientifiche Italiane

Istituto Villa Marelli

Viale Zara 81

20159 Milano, Italy

email: nicolanatale@yahoo.it