Slow Medicine
Measured Respectful Equitable

CHOOSING WISELY ITALY
Doing more does not mean doing better

Tests, treatments and procedures at risk of inappropriateness in Italy

that Physicians and Patients should talk about.

Five Recommendations from the Italian Society of Human Genetics (SIGU)- 2nd List

1	**Do not perform genetic testing for polymorphisms in genes involved in detoxification processes for the diagnosis of Multiple Chemical Sensitivity (MCS)**
	Multiple Chemical Sensitivity Syndrome (MCS) or Idiopathic Environmental Intolerance to Chemical Agents (IIAAC) is a chronic disorder, affecting multiple organs and systems, with a response to exposure to chemicals at lower levels than those generally tolerated by the general population. To date, there are no solid benchmarks for the diagnosis of this pathology, there is also a lack of functional tests able to explain signs and symptoms. Epidemiological studies conducted on the correlation between MCS syndrome and genetic polymorphisms involved in the detoxification process are still insufficient in number but, above all, conflicting with each other also with regard to the importance of the component of genetic variability rather than epigenetic or expression. Therefore, taking into account the international scientific literature, to make the diagnosis of MCS, there is insufficient evidence for the use of genetic tests aimed at typing metabolic polymorphisms P450 (CYP) 2E1, glutathione S-transferase (GST) M1, GSTT1, GSTP1). Good practice: inform patients about the unreliability of the correlation between the above polymorphisms and MCS.
2	**Do not perform genetic testing for Y chromosome microdeletions as a screening test for all male patients with reproductive problems**.
	Microdeletions of the Y chromosome are long arm submicroscopic alterations that cause the loss of different genes for the control of spermatogenesis. These microdeletions, "de novo" in most cases, can cause alterations in spermatogenesis ranging from complete azoospermia to severe oligozoospermia. The detection rate (DR) of this type of test is about 10% when performed on selected patients, so when the test is used with "diagnostic" value. Conversely, if the test is used as a "screening" test for all male patients with reproductive problems, the DR drops below 2%. Good practice: do not require the test for the detection of Y microdeletions in normospermic patients, with mild oligozoospermia (sperm count >15ML/ml) or with obstructive azoospermia, even if initiated to a path of Medically Assisted Reproduction (MAP), and in any case before having excluded the presence of karyotype abnormalities or non-genetic causes of sterility.
3	**Do not include Glucose 6 Phosphate Dehydrogenase (G6PD) in the tests required for Medically Assisted Reproduction (MAP)**
	In the context of Medically Assisted Reproduction (MAP), especially in the absence of a positive family or personal history for the condition, testing for the G6PD enzyme should not be recommended. In the literature, in fact, there is no evidence to confirm that this deficit may explain infertility in couples. The available studies evaluating such associations are few, very dated, inconclusive and unconfirmed. It has also been confirmed that the G6PD deficit does not increase the susceptibility of sperm to oxidative stress. The role of G6PD in placental cells has been demonstrated in mouse models, but has not been confirmed in humans. Good practice: Do not require G6PD testing every PMA pathway.
4	**Do not perform prenatal testing that can be performed on circulating fetal free fetal DNA (cfDNA) by non-invasive prenatal testing (NIPT) without first informing women about the limitations and accuracy of the different prenatal investigations that can be performed**
	Non-invasive prenatal testing (NIPT) is one of the most popular approaches in prenatal diagnosis today and its use is constantly increasing. Considering that the insertion of the technique on free circulating fetal DNA (cfDNA) in clinical practice is relatively recent, scientific evidence allows to attribute high sensitivity and specificity to the test for the study of the main aneuploidies (13,18,21,X,Y). On the other hand, there are lesser data, although growing, for the study of rare aneuploidies, which are analyzed by many laboratories, while there is currently no evidence considered sufficient for other applications (study of microdeletions/microduplications, large genomic imbalances and pathogenetic variants in disease genes); in addition, the use for these reasons not supported by sufficient scientific results leads to an increase in the use of invasive prenatal diagnoses that risk being unjustified. Good practice: considering the need to provide correct information about the possibilities and limitations of different types of prenatal tests on cfDNA, it is essential that these are offered as part of a pre and post-test genetic counseling process during which correct and comprehensive information about the limits and accuracy of the tests is provided.
5	**Do not perform test investigating genes associated with food metabolism and food intolerances (genetic testing for nutrition) to define a dietary path**
	Many tests used for nutritional purposes are not to be considered informative as they consider only a subset of the genetic component associated with multifactorial traits, such as food intolerances and individual metabolic characteristics. The genetic tests currently available in this area should therefore be considered as an additional tool in the hands of the professional (geneticist, endocrinologist, nutritionist, dietician, etc.) to better understand the characteristics of each individual and consequently better define a dietary path and/or a series of nutritional advice. For example, it makes no sense to perform these genetic tests in the absence of 1) precise information on the general state of health of each individual, 2) instrumental and laboratory data (e.g. weight, height, Body Mass Index (BMI), lean/fat mass, biochemical parameters, etc.), 3) type and amount of physical activity performed weekly, 4) nutritional diary. Good practice: correctly inform that the variants found are polymorphisms also present in the normal population, that the test has an exclusive predictive value and that by itself does not define a dietary path. It is recommended to consult your medical geneticist or branch specialist. Genetic counseling allows you to understand the test and its possible implications.

Please note that these items are provided only for information and are not intended as a substitute for consultation with a clinician. Patients with any specific questions about the items on this list or their individual situation should consult their clinician.

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How this list was created

The SIGU Board of Directors (CD) during the Annual Congress 2017 has spread among members and members the survey, proposed by Choosing Wisely Italy, on the survey of satisfaction and appreciation of practices of inappropriateness, previously elaborated (February 2015). The aim was to assess whether within the society, the 5 recommendations that must be at the center of the medical patient dialogue are known and applied or if there are difficulties in their application. The results were very positive. At the same time, the campaign began to collect proposals for new recommendations on practices at risk of inappropriateness, both directly from the participants of the 2017 Congress and through the collaboration of the coordinators of the SIGU Working Groups and their members. The CD has thus collected further proposals from which the 5 recommendations listed here have been selected and developed. For their drafting, a review of the guidelines of the scientific societies, where available, and of the current literature has been carried out.

Sources

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Slow Medicine, an Italian movement of health professionals, patients and citizens promoting a Measured, Respectful and Equitable Medicine, launched the campaign **"Doing more does not mean doing better- Choosing Wisely Italy"** in Italy at the end of 2012, similar to Choosing Wisely in the USA. The campaign aims to help physicians, other health professionals, patients and citizens engage in conversations about tests, treatments and procedures at risk of inappropriateness in Italy, for informed and shared choices. The campaign is part of the Choosing Wisely International movement. Partners of the campaign are the National Federation of Medical Doctors' and Dentists' Orders (FNOMCeO), that of Registered Nurses' Orders (FNOPI), the Academy of Nursing Sciences (ASI), National Union of Radiologists (SNR), Tuscany regional health agency, PartecipaSalute, Altroconsumo, the Federation for Social Services and Healthcare of Aut. Prov. of Bolzano, Zadig. www.choosingwiselyitaly.org; www.slowmedicine.it

The **Italian Society of Human Genetics (SIGU**) brings together professionals in Italy dealing with Human Genetics and Medical Genetics. This discipline plays quite a relevant role within the National Health System. Indeed services of Medical Genetics (including more than 500 centers of Clinical Genetics and Genetics Laboratory) are engaged in the diagnosis and investigation of all the diseases due to genetic alterations (more than 7000), which may be due to individual genes (monogenic diseases) or up to whole chromosomes (chromosome disorders). More than 1000 members SIGU are active in all Italian regions, two thirds of whom are under the age of 50, most women (73%), including profiles of biologist and medical doctor that are represented as 73 % and 12%, respectively.
For more details: www.sigu.net