Diagnostic and therapeutic care pathway for fibromyalgia

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ABSTRACT

Early diagnosis and timely and appropriate treatments positively influence the history of fibromyalgia syndrome (FM), with favourable repercussions at clinical, psychological, social and economic levels. Notwithstanding, there are still significant problems with timeliness of diagnosis, access to pharmacological therapies – particularly to innovative ones – and appropriate and effective taking in charge of patients. All the aforementioned factors have a great impact on FM patients' quality of life. Indeed, even though the World Health Organisation recognised FM as a chronic condition in the International Classification of Diseases 10th edition (ICD-10), many countries still fail to recognise the syndrome, and this negatively influences the capability to appropriately protect and care for patients. This is the case in several European Countries. In Italy, a few Regions have started to put in place precise indications for people suffering from FM, aiming at the implementation of diagnostic-therapeutic pathways. The Diagnostic-Therapeutic Care Pathway (DTCP) provides an important tool to meet the needs of patients suffering from chronic diseases. They present the organisation of an integrated assistance network. This includes a seamless path for disease prevention, diagnosis and treatment, by means of cooperation among physicians and other healthcare professionals.

The Diagnostic-Therapeutic Care Pathway (DTCP): what is it?

"Active care" represents one of the newest models of healthcare delivery. In particular, the Chronic Care Model (1) is based on an effective and productive interaction between patients, physicians, nurses and other healthcare professionals. Patients are empowered through appropriate training and educational programmes, activation and inclusion in an enhanced participation community. The Expanded Chronic Care Model extends this vision by directing additional efforts to support patients and communities in the prevention of disease and the promotion of health. From this perspective, active care aims at both preventing and improving chronic disease management at every stage. Therefore, it involves all levels of the healthcare system, with positive effects expected both for the health of citizens and for the sustainability of the system.

Due to the increasing burden of chronic diseases worldwide (2), there is a growing pressure to use all possible governance tools in order to respond to the patients needs, promoting accessibility to quality care throughout the territory of countries and geopolitical communities, such as the European Union. The Diagnostic-Therapeutic Care Pathway (DTCP) emerges as an essential tool towards these goals (3). In fact, DTCPs draw an interdisciplinary care plan designed to respond to the citizen's complex health needs through the promotion of continuity of care, integration between operators, reducing clinical variability, spreading evidence-based medicine and using resources efficiently. In particular, DTCPs effectively respond to the organisational fragmentation of health services, especially at the hospital-territory interface: DTCPs reduce the risks associated with the passage of the patient from the hospital to territorial and general practice services. Moreover, DTCPs avoid duplication of health services and contain unjustified health expenditure while offering the patient an organised and simplified care pathway.

Through multi-professional and multidisciplinary collaboration, DTCPs seek to (4):

- identify care pathway players and their specific roles;
- effectively exchange information among the care pathway players;
- reduce the costs of health care;
- standardise the methodology, the effectiveness of care and follow-up monitoring modalities and indicators;
- give patients the opportunity of treatment at an early stage of the disease;
- reduce procedure activation times and eliminate waiting lists.

DTCP for fibromyalgia syndrome: why?

Fibromyalgia (FM) syndrome affects about 2-8% of the population worldwide (5, 6). The prevalence is estimated to be 2.22% (95% CI 1.36-3.19) in Italy (7), 5.8% in Germany, 4.0% in Spain, 2.2% in France and 3.7% in Portugal (8). Most patients with FM are between 45 and 64 years of age: *i.e.* they are in the midst of their active working life, which is greatly impaired by the pain and fatigue of FM. About one-third of all FM patients are disabled (9), and about one-third of the patients change their occupation to maintain their income. FM is, to date, one of the main causes of absences from work and of disability. All the aforementioned factors have a great impact on the quality of life of people with FM. Thus, the socioeconomic burden and work consequences of FM syndrome are far greater than the costs incurred to treat it (10, 11). Early diagnosis and timely and appropriate treatments positively influence the history of the syndrome, with favourable repercussions at clinical, psychological, social and economic levels (12, 13). Notwithstanding, there are still significant problems with timeliness of diagnosis, access to therapies - particularly to innovative ones – and coordinating appropriate care of these patients (13). These observations highlight the need for a DTCP for FM, aiming at the promotion of shared care pathways that are able to:

- guarantee early diagnosis;
- carry out multidimensional assessments of health needs;
- integrate the multiplicity of interventions, and ensure that patient care is not jeopardised by fragmentation of the path;
- guarantee optimal service;
- improve quality of care;
- correctly manage the condition and reduce its complications;
- guarantee fair access to treatments on an (inter)national basis;
- reinforcing the sustainability of National Health Systems;
- reduce socioeconomic costs.

At the core of the concept is the need to define, organise and streamline the most appropriate sequence of events and actions to ensure that the patients' health concerns are effectively addressed. The communication between physician and patient is of utmost importance in this process. Indeed, even if the path is defined by the National Health System, the doctor cannot set up a therapeutic procedure without taking into account the patient's habits and needs, and the patient cannot ignore the limits of the health intervention and the need to comply with agreed procedures. Moreover, multi-professional and multidisciplinary interventions become often necessary, addressing different physical, psychical and social issues.

To conclude, DTCP is a tool of *Clinical Governance* which, by means of stepwise processes,

1) defines objectives, roles and areas of intervention;
2) guarantees clarity of information to the patient and clarity of tasks to the operators;
3) helps improve quality, consistency, reproducibility and uniformity of services provided;
4) helps predicting and reducing risks and complications;
5) facilitates flexibility by integrating activities and interventions in a context in which different specialties, professions and areas of action are involved.

DTCP for fibromyalgia syndrome: how?

It is widely accepted that management of people with FM, and in general of the chronic disease patient, needs an integrated approach (14). It comprises the general practitioner (GP), the reference specialists (rheumatologists/algologists) as well as other health care professionals who come into play at different moments of the care pathway. The effective organisation of the system requires three essential components: a DTCP that defines specific roles and tasks for each caretaker;

1) effective communication among the various caretakers (GPs / specialists/ health care professionals);
2) a patient who is motivated, informed and educated about his/her illness management.

The first point will be the subject of this paper. For points 2 and 3, local initiatives are hoped for (see Box 1). They could be framed by local healthcare agencies involved in the implementation of the DTCP document.

DTCP actors

1) *General practitioner (GP)*

The GP is the mainstay of primary care. He or she is usually the first contact person of the patient with the healthcare system and establishes a continuous relationship with the patients, proving easy access to consultations. The GP is responsible for the identification of any risk factors, signs and symptoms related to FM syndrome and for deciding whether in-depth diagnostic investigations or referral to second and third level specialists are warranted. The GP can, therefore, have a decisive contribution to avoid diagnostic delays, disease complications, improper use of resources and inadequate prescription of therapy. Furthermore, the GP also has an essential role in empowering patients and family members, by providing information on the disease, its evolution and on the effectiveness and tolerability of available treatments. Furthermore, the GP plans and activates home assistance for patients who need it, in collaboration with other health professionals (nurse, physiotherapist, social assistant, psychologist, etc). All these tasks can and should be accomplished in close collaboration with the physicians and departments providing secondary or tertiary support.

2) *Specialised physician of the secondary and tertiary care*

Herein, by "specialised physician" we mean the rheumatologist or algologist. The choice of either the two depends on patient's preferences and the local context. Their role is to make a diagnosis in case of doubts or laboratory exams alterations, to establish a therapeutic programme and assess its effectiveness over time, to perform follow-up visits and to prescribe second-level investigations when needed. The main roles of the specialist are summarised in Table I.

3). *Allied health professionals (nurse, psychologist, physiatrist, physiotherapist, etc.)*

They will support the patient in any other aspect of his or her disease. They have a major role for the psychologic, rehabilitation and occupational issues of FM patients (see below: DTCP phases – 2nd phase). The need of a consultation with one of these Health professionals is evaluated by the GP and/or by the specialised secondary or tertiary care physician, who draw the individualised therapeutic programme. Table II shows a summary of the role of the other health professionals involved in the DTCP for FM.

Table I. The main roles of the specialised physician in the context of the DTCP, in relation with the general practitioner.

GP	Specialist (rheumatologist/algologist)
Prescription of first-level exams	Comprehensive evaluation
Diagnosis of fibromyalgia syndrome	Diagnosis of fibromyalgia syndrome, differential diagnosis
Possible referral to specialist	Second-level investigations
First therapeutic indications and patient and family education	Definition of a therapeutic program
Assessment of efficacy and tolerability of the therapy over time	Regular follow-up visits and assessment of therapeutic effectiveness
Access to DTCP	DTCP continuation
Communication with the specialist	Communication with the GP

DTCP: diagnostic-therapeutic care pathway; GP: general practitioner.

Box 1. Communication among DTCP actors

FM syndrome requires a complex treatment that must be continuously monitored and adapted over time. The aim is both to better control the illness and to monitor treatment, in order to prevent side effects. This requires a constant collaboration and communication between the specialist and the GP, which can be served by summaries, written by both of them, of the diagnosis, the prescribed therapy, its tolerability and patient's compliance, and the follow-up tests performed. The specialist has the role of defining the diagnosis, establishing the therapeutic program and assessing its effectiveness over time. Cooperation is expected from the general practitioner in the continue support of the patient and family, and regular assessment of the efficacy and tolerability of the therapy through periodic assessments and scheduled treatment changes.

DTCP phases

1st phase: diagnosis

Although diagnostic criteria for FM have been refined over the last ten years, the diagnosis of FM syndrome continues to raise challenges to physicians. The latest American College of Rheumatology (ACR) criteria (2010/2011 and 2016 revision) abandoned the assessment of tender points, which was at the basis of the 1990 ACR criteria (15-18). They defined FM as a multi-symptom disorder, considering fundamental the presence of ancillary symptoms of chronic widespread pain, sleep disturbances, fatigue, and cognitive dysfunction. Subsequently, the ACTTION-APS Pain Taxonomy diagnostic criteria published in 2018 (19) highlighted the concept of generalised pain and created the "core" criteria for FM, which are generalised pain, chronic fatigue and sleep disturbances. The diagnosis of FM syndrome remains essentially clinical as a diagnostic biomarker is not currently available. A complete medical (including drug) history and complete physical examination is mandatory in the evaluation of a patient with chronic widespread pain in order to consolidate the diagnosis of FM syndrome or identify features that may suggest other conditions with similar clinical presentation (Table III). Since many other diseases are similar, experience is of undoubtable value for a correct diagnosis. The GP can either diagnose FM syndrome, or if in doubt promptly refer the patient to the specialist for confirming diagnosis, so that multimodal therapies can be started as soon as possible, in order to try to change the evolution of the disease. Table IV lists the symptoms and findings that give a rational for referral to a specialist.

Laboratory and imaging tests must be tailored to the individual case in order to confirm or deny the suspected diagnosis. These tests are listed in Table V, divided as first and second level exams.

2nd phase: the integrative GP/specialist/nurse relationship for FM treatment

– The GP

The GP can refer the patient to a specialist mainly when diagnosis is in doubt or later if inadequate response to treatment occurs. Once the diagnosis is confirmed, either by GP or specialist, the GP can start patient education in order to stimulate the patient to change his/her lifestyle and to take an active role in managing the disease. He or she also takes part in the drawing of the therapeutic programme, communicating with the Secondary/Tertiary care physician, and considers referring the patient to other Health professionals when needed.

– The Secondary/Tertiary care physician (rheumatologist/algologist)

After completion of a full diagnostic workup for FM diagnosis, the specialist will draw the therapeutic programme for FM patients, will continue managing the most complex and severe cases and the patients with relevant comorbidities with more frequent follow-up visits,

and will refer for other specialistic care if necessary, in cooperation with the GP. It is the obligation of rheumatologists and algologists to ensure that they maintain state-of-the-art knowledge and competency in the investigation and management of FM syndrome.

– Nursing care

The correct organisation of adequately customised care paths is essential to reach the highest care quality. The "case manager" nurse is the best positioned professional to guarantee the organisation and management of these paths. An adequately trained nurse can carry out numerous activities - such as clinimetric evaluation, counselling and patient education, and emotional support. Of no less importance is the organisation of the care path, *i.e.* managing of appointments, helping in achieving compliance with drug administration, updating of clinical documentation and planning of hospitalisation and related workloads. In addition, the nurse can organise, in collaboration with the specialist, the activities that may become necessary if adverse events appear during treatment with different drugs.

– Therapeutic strategy

Treatment should consistently pursue the following goals are: (i) minimise pain, (ii) improve sleep, (iii) treat mood disorders, (iv) mitigate fatigue (21). For FM syndrome a multimodal approach is mandatory, in which different pharmacological and non-pharmacological interventions, addressing different symptoms, are combined, following EULAR 2016 recommendations (22) (Fig. 1).

a) *Pharmacologic treatment*

A comprehensive review of pharmacologic treatment is beyond the scope of this article. Herein, we provide a short summary of the drugs which are mostly used for FM syndrome, keeping in mind that at present, in Europe, there are currently no drugs approved by the European Medicines Agency (EMA) for FM syndrome.

The drugs that have proved most effective in treating FM are centrally acting medications, particularly antidepressants and anticonvulsants (6). They exert their action by increasing the presence of pain-inhibitory neurotransmitters or decreasing systemic hyperexcitability. Opioids are burdened by severe side effects and are not effective for FM pain, therefore their use should be avoided (23). Tramadol is the only analgesic drug that may be effective in reducing FM pain (22), and this is due to a combination opioid agonist action with inhibition of serotonin and partly noradrenaline reuptake. Antidepressants (24) include mainly duloxetine and milnacipran, both Food and Drug Administration (FDA)-approved for FM, since they had good results in terms of efficacy and tolerability in patients with FM. Nonetheless, side effects may lead to withdrawal of medication. Among the anticonvulsants (25), recent meta-analyses underlined that pregabalin is, in fact, effective and safe for FM (26-28), and it is so far the only FDA-approved anticonvulsant for FM. Myorelaxants, such as cyclobenzaprine, can also be considered for FM treatment (29), and cannabis has also been recently proposed as an interesting phytotherapeutic compound (30-32).

Table II. The role of other Health Professionals in the management of fibromyalgia (*e.g.* physiotherapist, nurse, psychologist).

GP	Other specialist
Comorbidity management and referral of difficult-to-manage comorbidities	Therapeutic indications (pharmacologic treatment, physical therapies, rehabilitative interventions, psychological interventions, etc.)
Clinical surveillance, therapy side effect surveillance	Periodical follow-ups
Patient education	Patient education
Communication with the Health Professional	Communication with GP

Table III. Main fibromyalgia differential diagnoses.

Main fibromyalgia differential diagnoses
Statin-induced myalgias
Hypothyroidism
Inflammatory/rheumatic conditions
Various types of neuropathies
Sleep apnea syndrome
Anxiety/depression/somatoform diseases
Viral illnesses

Adapted from (13) Häuser W *et al.*: *Clin Exp Rheumatol* 2019; 37 (Suppl. 116): S90-7.

Table IV. Criteria for referral to rheumatologist/algologist for the purpose of differential diagnosis ("Red flags") and/or to identify co-existent diseases that need treatment of specialist.

Criteria to be considered for referral to the specialist
Fever
Photosensitivity, rash, aphthae, alopecia, Raynaud's phenomenon, xerophthalmia, purpura
Joint swelling, redness, heat
Lab test abnormalities
Neurologic signs and symptoms
Pain refractory to common analgesics

Adapted from (20) Arnold LM *et al.*: *Mayo Clin Proc* 2011; 86: 457-64.

Table V. I and II level tests in the diagnostic workup for fibromyalgia syndrome .

I level	II level
Complete blood count	ANA, ENA
C-reactive protein, erythrocyte sedimentation rate, protein electrophoresis	Rheumatoid factor
AST, ALT, creatinine	Anti-CCP
CPK	Electromyography
TSH, fT4, fT3	Joint ultrasound
Vitamin D	Magnetic resonance imaging
Iron, electrolytes	

Adapted from (13) Häuser W *et al.*: *Clin Exp Rheumatol* 2019; 37 (Suppl. 116): S90-7.

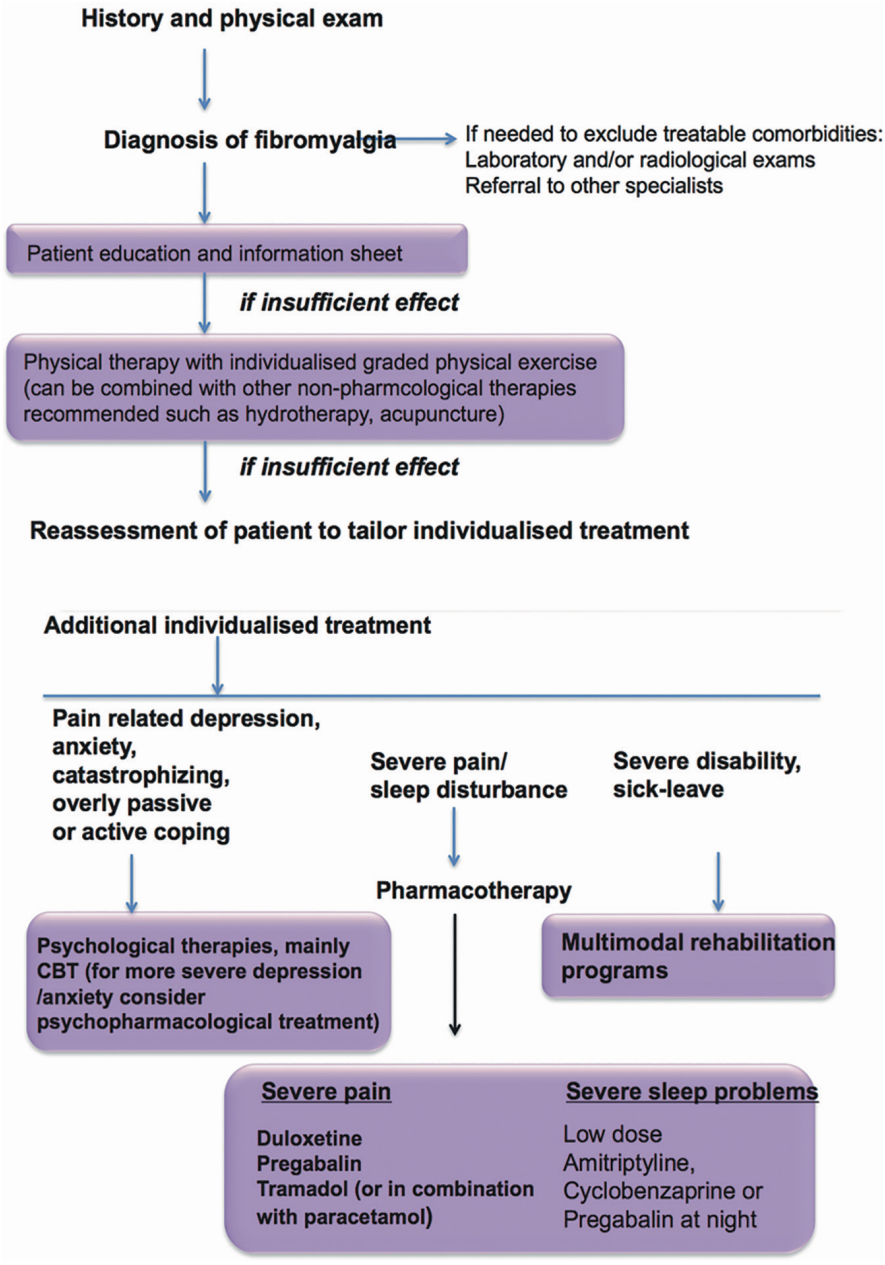

Fig. 1. Management of fibromyalgia following the latest EULAR recommendations.

Despite the better understanding of the pathogenetic mechanisms underlying this disease, and the increasing availability of molecules with central analgesic action, results obtained with pharmacological treatment alone are often unsatisfactory, and drug treatment should be part of a multidisciplinary therapeutic approach, which also includes non-pharmacological strategies (33).

b) *Non-pharmacologic treatment*

The first step consists in educating the patient and the family, reassuring them that FM is a "real" disease in order to legitimate patient's suffering. It should be also stated that FM, although an invalidating condition, is not progressive, and that the patient him/herself has a predominant role in disease management, introducing the concept of "self-management" (34, 35). The role of stress, mood disturbances and sleep disorders have to be recognised, and the patient should be elicited to learn relaxation techniques and start good sleep hygiene. FM patients should be also initiating a low-impact, gradual aerobic exercise, adapting it to individual physical resources and needs: physical activity must be regular, combined with periods of rest and recovery (22). Stretching is a valuable exercise to recover muscle elasticity. Exercise in thermal water has also been shown to be effective in some clinical studies. Movement meditation (36) (tai-chi, yoga, qigong) can be also very effective.

In association with exercise, cognitive behavioural therapy, meditation and mindfulness, that integrate mind and body, are important (37, 38). Numerous studies underlined their antalgic action also according to neuroimaging studies (39). As regards physical therapies (thermotherapy, massotherapy and cryotherapy), at present their use is based more on the opinion of expert panels than on irrefutable scientific evidence.

It is important to maintain an appropriate dietary and nutritional regime and correct any deficiencies (vitamin D, magnesium, phosphorus and calcium) to reduce the risk of comorbidities such as cardiovascular disease and osteoporosis. Other supportive therapies can also be used - such as acupuncture (40).

c) *Rehabilitation*

Rehabilitation is an important element in the management of FM (41). It is important to initiate it at an early stage, when, together with pharmacologic treatment, the aim is the prevention of pain aggravation and related limitations of daily activities and social engagement. Since the primary objective of rehabilitation is the functional protection of the person within a health strategy, as defined by the World Health Organisation, it is essential to carry out a health status evaluation and management (42). Therefore, a patient-tailored rehabilitation project must take into account his or her needs, preferences, current and potential impairments, residual and recoverable abilities, available resources, and, finally, environmental and social influences. A rehabilitation programme should be activated as soon as possible, fitting it to the stage of the disease and integrating it with other professional figures.

The dynamic interaction between physicians and other health care professionals, with the patient and his family members, places the person with his or her needs and expectations at the centre of the rehabilitation process.

d) *Psychological/psychiatric assistance*

FM is frequently comorbid with psychiatric disorders. These may be highly disturbing by themselves (43), but they also interfere with the severity and treatment of FM, for example by aggravating the affective component of pain, amplifying functional deficits or impairing therapeutic adherence (44). Psychiatric referral is suggested when a comorbid psychiatric disorder does not respond to prescribed FM drugs or shows severe and/or complex clinical manifestations, for example self-injury, psychotic symptoms or severe personality disorders. Anyhow, it is always desirable to advise patients on the importance of asking for psychological help, since FM is frequently accompanied by a state of psychological suffering and a preponderant negative affect; in addition, in a large majority of FM patients subthreshold forms of post-traumatic stress disorder have been found (45).

Table VI. Measurable DTCP quality indicators.

Process	Quality indicator
Access to the DTCP	If there is a diagnostic suspicion, diagnosis should be done within 3 months. *NUMERATOR: number of patients that are referred to the specialist in 3 months* *DENOMINATOR: number of patients that are referred to the specialist for the first time and receive a diagnosis of fibromyalgia*
Fibromyalgia definition/severity assessment	If the patient has a diagnosis of fibromyalgia, he or she has to have tested (at least) TSH, ANA, CRP, ESR and complete blood count within 3 months after the diagnosis.
Pharmacologic and non-pharmacologic treatment	If a patient has a new diagnosis of fibromyalgia, he or she should have prescriptions of: analgesics, antidepressants and/or anticonvulsants and/or cognitive-behavioral therapy and/or functional rehabilitation, with consequent assessment of work capability and disease activity.

In support of this, many studies demonstrated that cognitive-behavioural therapy is very effective in FM (46). The psychiatrist and/or psychologist identifies and carries out the most appropriate psychological or chemical interventions in relation to the patient's cognitive characteristics, deficits, psychological and environmental resources.

e) *Social and work reintegration and facilitations*

FM syndrome is one of the main causes of disability and loss of working capability (47). Both have a significant negative impact on the quality of life and financial status of the person, together with adverse effects on workplace (48). It is therefore important to implement an organised care network for work reintegration and job rehabilitation for FM patients, with the creation of working places and social frames that are able to accommodate patients abilities and needs to optimise the outcomes in terms of health, personal satisfaction and productivity (48).

3rd phase: feedback and follow-up

There is a wide variety of tools for the evaluation of people with FM but the best choices for the individual patient are not always clear (49). One of the main problems is the multifactorial nature of the syndrome which makes it necessary to evaluate primary and secondary outcomes in an integrated frame, *i.e.* one should consider not only pain as the primary outcome but also other symptoms such as sleep, fatigue or asthenia, and, not least, socio-relational signs. This assessment can be carried out using disease-specific clinimetric tests and scales (50), such as the FM Impact Questionnaire (51) and its revised version (52, 53) and the FM Assessment Status (54, 55), with its modified form (56). More specific tools may be considered to address individually relevant issues.

4th phase: evaluation of DTCP

A set of indicators for the monitoring of DTCPs (health care quality indicators) should be defined *a priori* on the basis of validity, reproducibility and feasibility criteria. They are registered in a database with the help of appropriate codes, identifying prevalent cases, new cases, drug prescriptions (new/old), check-ups and diagnostic tests (Table VI). Some processes are not currently measurable, raising the need for an upgrade of the current Information Technology (IT) system.

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