

For a program of eradication of hepatitis C in the populations at risk (drug users and convicts)

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Summary. Injection drugs are the greater source for HCV infection. About 60% of drug users and about 20-30% of convicts are infected with HCV. HCV infection is often associated with behavioral disorders and drug use. At present, few subjects with HCV belonging to risk groups have been treated with Direct-Acting Antivirals (DAAs). SerDs and prisons should implement the screening for HCV. HCV populations at risk can be successfully treated with DAAs. The primary objective of the linkage to care is the holistic and integrated treatment, and the prevention of reinfections is a priority and essential part of the treatment goals. The removal of the barriers to treatment is a primary goal of the linkage-to-care models and integrated systems; the main action to be undertaken for the linkage to care of the HCV population at risk are screening, referral, treatment and prevention of reinfection. All HCV RNA+ patients may be eligible for treatment, and those with the clinical criteria for starting treatment should be treated with DAAs. All patients should receive a structured harm-reduction program (with skill training). The prevention of the infection is of paramount importance in the linkage to care of the HCV population at risk and is an element which should always be associated with the drug treatment. (www.actabiomedica.it)

Key words: HCV, drug users, direct-acting antivirals (DAAs)

Introduction

Data recently published in the scientific literature identify in the drug use (particularly if intravenous) the most important risk factor for the transmission of HCV, also highlighting how addicts are the most important source of the disease. Another population at risk is the convicts, especially because most of them (34.1% in Italy) have a history of drug use (1).

From the epidemiological point of view, the United Nations estimated that at global level there are about 12 million drug abusers, who inject drugs intravenous-

ly (the so-called PWIDs – People Who Inject Drugs) (2). Of these, about 6,000,000 are HCV+, while 80% of HIV+ PWIDs are co-infected with HCV (2).

European data show that 67% of PWIDs – that is, approximately 3 million people – are anti-HCV+ (3). The data also indicate that in Europe 49% of infected PWIDs are not diagnosed (4).

Injection drug use is therefore the most important risk factor for the transmission of the infection. Reports issued by the authority in charge of the protection of the world's health also show that injection drug use is responsible for 23% of the new infections (5)

and that each PWID with HCV infection can infect at least 20 other consumers, within the first 3 years of the start of the infection (6). These data therefore document how PWIDs currently represent the major reservoir of the disease and the main source of infection.

In 2016, the SerDs (*Servizi per le dipendenze* – “Addiction Services”) took charge of 143,271 users (2), while it is estimated that about twice as many are the users who are not cared by the Services, but would need a treatment anyway. In other words, in Italy there would be at least 450,000 high-risk consumers, i.e. subjects who, as a result of their problematic use of drugs, could suffer from serious negative consequences (also in infectiological terms) for their health. The data from the Annual Report to Parliament 2017 show that, out of the approximately 150,000 subjects cared by the SerDs, at least 27% are PWIDs (a probably underestimated data), and more than 70% are poly-consumers.

The exact prevalence of HCV in drug users in Italy is unknown. A recent epidemiological study conducted on 21 Italian SerDs which involved 543 drug users showed that 63.9% of users are anti-HCV+ (7). According to this data, it can be assumed that in Italy among the 150,000 users already in treatment in the SerDs, at least 90,000 are HCV+. This figure could go up to 270,000 subjects, when one considers that about 300,000 are the users still not treated by the SerDs and who may require being managed.

Similarly, there are no reliable data on the prevalence of hepatitis C in convicts, but certainly among them the behavior at greater risk for contagion of infection is drug consumption (particularly intravenously), followed by the practices of tattoos and unprotected sex (8). The official figures from the Department of Penitentiary Administration indicate that, in the course of 2016, 101,995 people were restricted to the 190 Italian Penitentiary Institutes, with daily presences oscillating between 53,000 and 55,000. A review of the literature on the prevalence of HCV in prisons quantified the prevalence of infection in a percentage between 22.4% and 38% of the entire prison population (8). These data indicate that it is likely that in the Italian prisons up to 30-35,000 anti-HCV+ subjects may transit each year.

SerDs must implement the activities of screening and diagnosis of HCV infection. The data from

the Annual Report to Parliament 2017 indicate that in 2016 the SerDs tested for HCV only 20.5% of their users; 9% of these were positive.

The test for hepatitis C is available in all Italian prisons, but few of them actually manage to test a significant proportion of prisoners. As with the SerDs, the most important reasons limiting the systematic screening of prison inmates are logistical and organizational.

Direct-Acting Antivirals (DAAs) for the treatment of HCV infection represent a huge opportunity to implement the linkage to care of drug users and to improve treatment outcomes (9). More generally, the availability of therapeutic tools capable of eliminating the HCV infection in the patient could allow to develop integrated models of treatment able to implement the screening, prevent reinfections through the increase of harm-reduction actions and improve the quality of life of patients (10). In high risk populations, such as drug users and detainees, DAAs may also be a therapeutic tool that can offer a potential value also as a disease prevention measure (11,12).

Populations at risk, such as drug users and prisoners with HCV infection, can be successfully treated with DAAs. Today, data in the literature indicate that in PWIDs the Sustained Virologic Response (SVR) rate with DAAs is entirely comparable with the general population infected (13), i.e. higher than 98%.

Today in Italy, access to care is ensured to all persons with HCV, regardless of the degree of disease severity (14).

However, at present it is still difficult to reach many of those infected with high-risk behavior – precisely those subjects who, in terms of public health, should be the primary target for the treatment of the disease – and to enable the achievement of the important goal of the eradication of the infection starting from 2030, as suggested by WHO.

Several clinical experiences have shown that drug users, along with the subjects with psychiatric problems, are at a higher risk of developing HCV infection (15). At the same time, there is also evidence showing that people with HCV have a higher chance of developing psychiatric problems (especially depression) and drug use (15,16). More generally, the evidence shows that (16):

- psychiatric co-morbidity and drug use are more prevalent in patients with HCV infection, rather than in the general population
- psychiatric co-morbidity and drug use are associated with a greater risk of contracting HCV infection
- some psychiatric symptoms (eg. depression, neuropsychological deficits) and the use of substances (eg. alcohol) are most frequently associated with HCV infection
- chronic HCV infection can lead to severe psychological “distress” (stigma, anxiety, decreased quality of life)
- chronic HCV infection has significant effects on the neurotransmission at central level, through inflammation mediators
- HCV can penetrate the brain and replicate.

The primary objective for the linkage to care of the subjects belonging to the population at risk, with HCV infection, is the development of a holistic and integrated treatment model able, among other things, also to facilitate access to treatment (17).

Evidence suggests that the development of an “intense” relationship between therapist and patient can produce an appreciable increase in the adherence to treatment (18). The literature and clinical experience have shown that integrated models capable of developing a strong synergy between specialists, through the production and implementation of common procedures and guidelines, can facilitate the access to care for populations at risk (19). Then again, there are many evidences showing that the treatment for hepatitis C in populations at risk can both facilitate the effectiveness of the linkage to care and enhance lifestyles, thus reducing risk behaviors, such as the consumption of substances, and also the commission of crimes (20).

One of the most critical aspects of the treatment of hepatitis C in the populations at risk could be the topic of reinfection. Studies conducted during the interferon era estimated that the risk of reinfection in PWIDs is low, and corresponds to a rate of 2.4 per 100 subject-years (21). In this regard, studies have also shown that the lowest rates are precisely in the North European Countries, where harm-reduction measures are most common and better applied (21). In this regard, harm-reduction measures have been shown to

minimize the likelihood of reinfection in the population at risk (22).

The current situation in Italy emphasizes the significant and critical barriers that currently prevent at-risk populations from accessing the treatment for hepatitis C. The most important of these barriers are those which regard: the low screening rate in the population at risk; the systemic lack of an interdisciplinary integrated organization for the linkage to care of patients with HCV, consisting of SerD specialists, prison doctors and hepatologists and infectivologists; the concern about the risk of reinfection (23).

The literature and clinical experience indicate that the main actions to remove the obstacles that prevent the treatment of HCV infection in PWIDs are the following (24):

- develop integrated health and social interventions
- create multidisciplinary interventions, which contain elements of prevention, protection of the patient and the community and fight against the stigma
- facilitate access to treatment, through the development of proximity interventions
- implement the creation of local care networks (connected with the hospitals), such as to facilitate linkage to care and access for people at all levels of health needs, including substitution treatment
- implement programs of individual interventions, focused on the person.

In this regard, the integrated linkage to care of the subject at risk for HCV infection could be a major challenge for modern health care systems, as well as a strong paradigm of integration between hospital and territory, such as to allow an equity of access to health care among all subjects infected with HCV but, above all, to allow the achievement of the important public health goal of eradication of the disease by 2030.

The linkage-to-care structural elements

Clinical experience and evidence from the literature indicate that the main actions to be undertaken for the linkage to care of the HCV population at risk are:

- screening

- referral
- treatment
- prevention of reinfection (through harm-reduction actions).

In this sense, according to the various indications provided by the literature and clinical experience, it seems a priority to propose algorithms for the linkage to care of the HCV population at risk, in order to facilitate the implementation on the territory of networks and effective and efficient organizational models.

Algorithms for the linkage to care of the HCV population at risk

The screening phase (Fig. 1) must be characterized by the following essential elements, that facilitate the execution of the test on the part of the patient, and which consist in the ability by SerDs and Prisons to:

- perform blood samplings for the conventional

diagnosis of the disease, possibly with the use of rapid tests also

- inform about the disease, the treatments and the mode of infection (through brochures, websites, public information campaigns, also on social networks)
- provide the user with psycho-educational and motivational counseling, able to optimize the patient's adherence to the test
- offer organizational systems able to ensure to the users the access to and the execution of the test, both at the beginning and then periodically during the linkage to care, so as to be able to intercept in the therapeutic context also any new infections or reinfections.
- Screening for HCV should be **offered to all drug/substance users**
- The screening proposal should be **accompanied by a psycho-educational and motivational counseling**

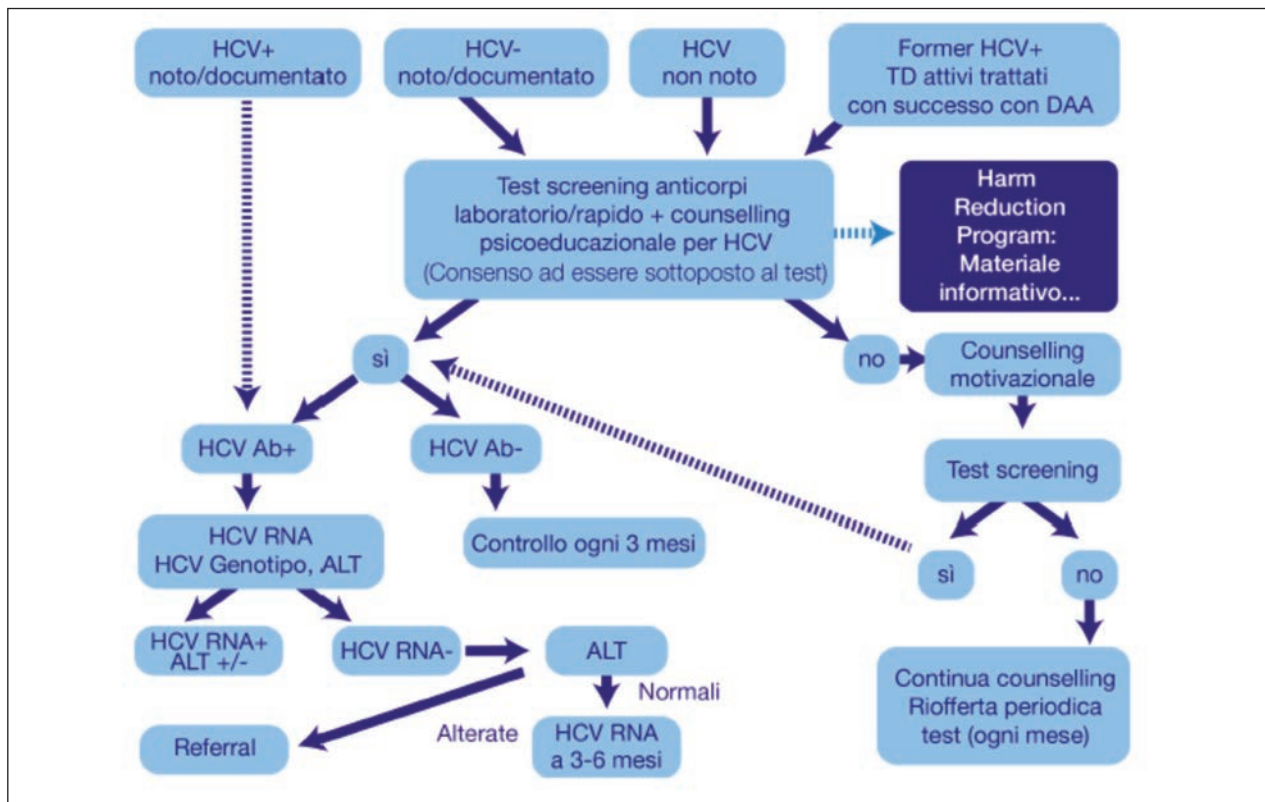


Figure 1.

- The screening proposal should be **associated with the spreading of information about the disease, the treatment and the modes of contagion**
- The screening, **if negative, should be reposed periodically (at least every three months)**
- The screening, **if refused, should be reposed periodically, combined with a motivational counseling (at least monthly)**
- **The screening should be proposed to active consumers successfully treated with DAAs for the early detection of reinfection (at least every 3 months)**

The referral phase (Fig. 2) is characterized by the following essential elements, that are intended to motivate the patients to the treatment and to facilitate their contact with the hepatologist-infectious disease specialist; these elements are:

- the patient's motivation to treatment, through motivational interviewing techniques

- the transfer to the patient of basic harm-reduction principles (in order to limit the consequences of the disease, both for themselves and for the community, also in terms of prevention of reinfection)
- the development of organizational models that include the referral, preferably in the same place of the user's linkage to care (SerD or Prison)
- the referral of the patient to a specialist only when "ready" for the treatment from a motivational point of view (while the patient who is still "not ready" should be kept linked to the Service through motivational interviewing techniques aimed at the information and the development of the relationship)
- the periodic proposal of being referred to a specialist for the patients who refuse treatment.
- **All patients eligible for treatment should be referred to the specialist** (infectivologist/hepatologist)

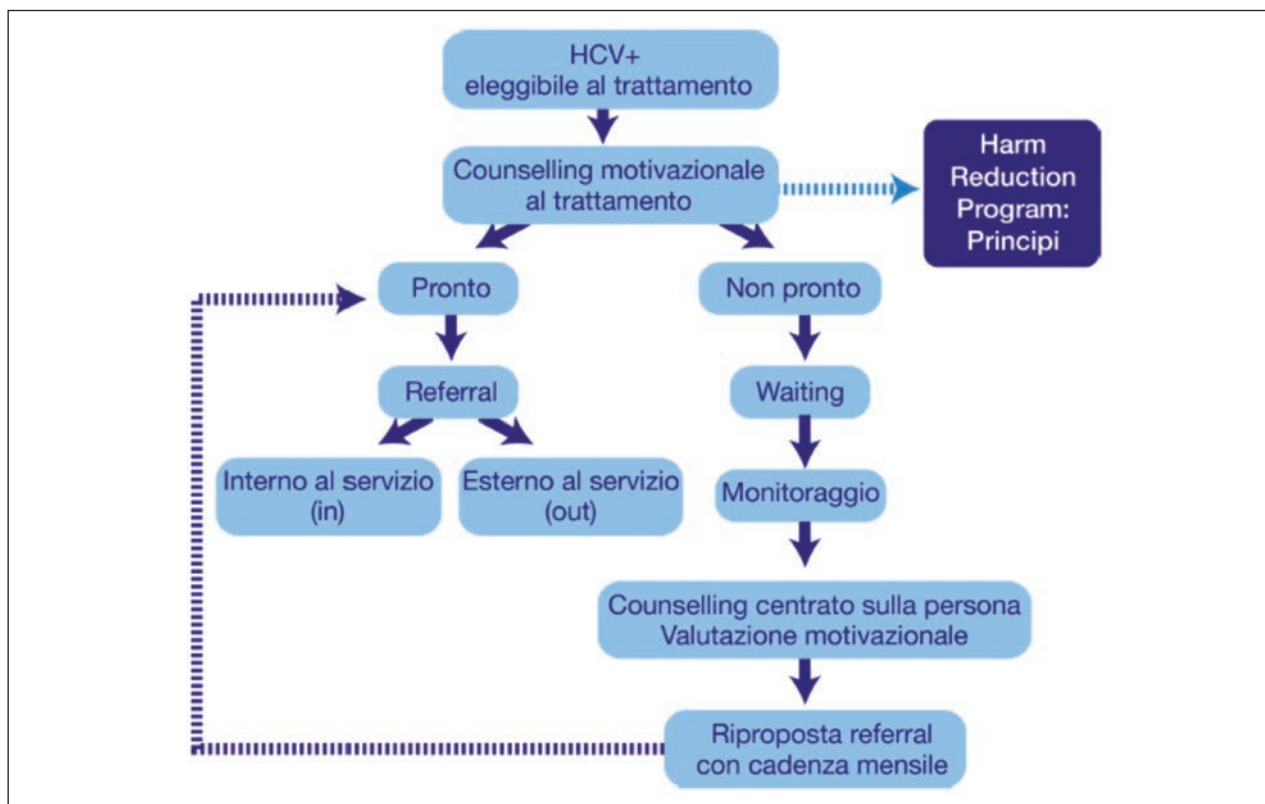


Figure 2.

- **The referral** should be accompanied by a **motivational counseling**
- **All patients who are referred to a specialist** (infectivologist/hepatologist) for treatment should receive a **structured harm-reduction program** (knowledge of the principles and measures, as indicated by WHO)

The treatment phase (Fig. 3) is characterized by the following essential elements, that have the aim of appropriately treating the patient through:

- a complete clinical evaluation carried out by the hepatologists-infectivologists, aimed at the start of treatment (preferably where the linkage to care took place)
- close monitoring (by both specialists) of the compliance with the treatment, based on the therapeutic relationship and the motivational support
- a periodic follow-up assessment (at 3 and 6 months from the start of treatment) by the specialists (individually and/or jointly) for the objectives of virologic and toxicological response and the evaluation of the quality of life
- an offer of harm-reduction programs, aimed

at reducing risk behaviors, through the development of skill training in the management of harm-reduction actions and the provision of harm-reduction kits

- a verification of the patient's ability to use the harm-reduction measures
- **All HCV RNA+ patients** may be eligible for treatment
- **All patients with the clinical criteria** for starting treatment **should be treated with DAAs**
- **All patients should receive a structured harm-reduction program** (with skill training)
- **The monitoring of the treatment** should provide for the **evaluation of the adherence to therapy and the assessment of the achievement of the infectivological, toxicological and behavioral outcomes**
- The **end of treatment** should be followed by an **infectivological follow-up** and by an **evaluation on the ability to use harm-reduction measures**
- **All patients being treated with the DAAs should receive a harm-reduction kit**

The prevention of the infection is of paramount

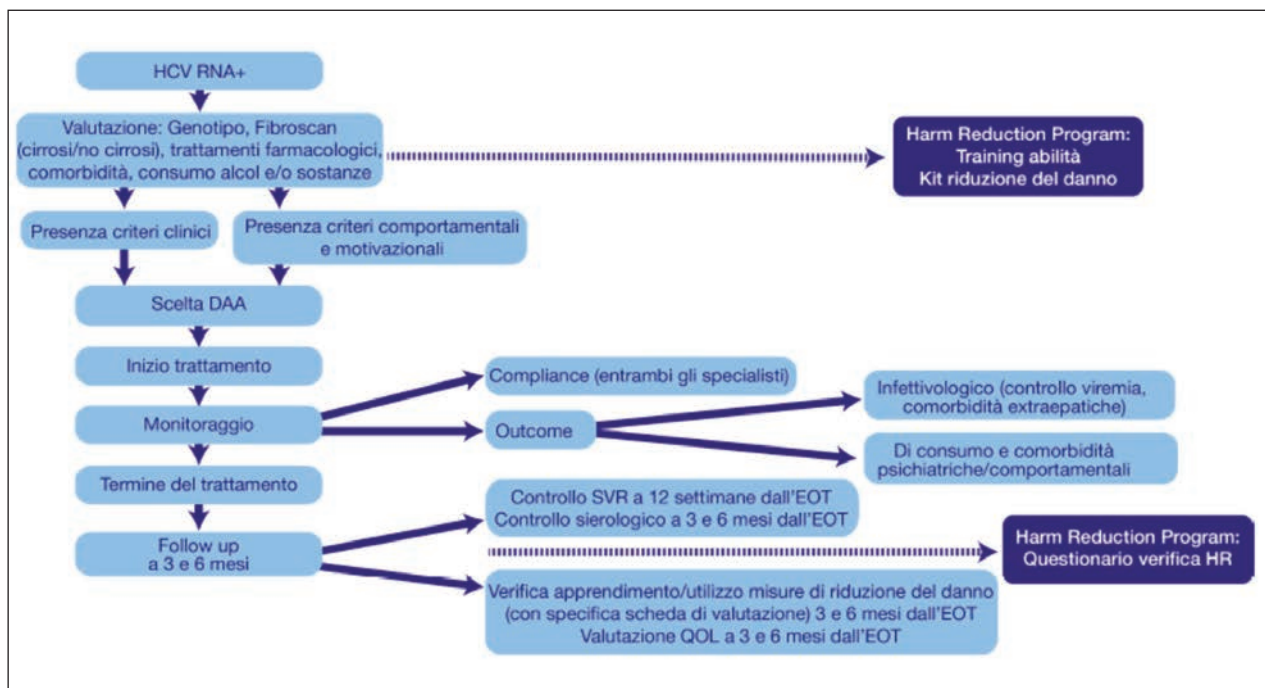


Figure 3.

importance in the linkage to care of the HCV population at risk and is an element which should always be associated with the drug treatment.

The prevention of the infection should occur through the harm-reduction actions, as identified by WHO.

In particular, harm-reduction measures include the use of:

- information and support materials (including online) (to be used on a priority basis in the screening stages)
- specific training on the basic harm-reduction principles (to be used on a priority basis in the referral stage)
- skills training on the harm-reduction actions (to be used on a priority basis in the treatment stages)
- harm-reduction kit, to be supplied to the population at risk (to be used on a priority basis in the treatment stages)
- processes for the verification of the acquisition/

use of harm-reduction measures (to be used on a priority basis in the follow-up stages).

Harm-reduction actions should articulate following all the phases of the linkage-to-care “chain” (Fig. 4), with the aim of strengthening the achievement of the objectives set by the individual phases, facilitating the access and the adherence to the treatment but, above all, reducing risk behaviors and minimizing the reinfection rate.

- **Harm-reduction** measures, as suggested by WHO, **should be applied to all drug users** (whether active and/or being treated with DAAs)
- **Harm-reduction** measures should accompany – with specific actions and modes – **all the stages of linkage to care of the drug/substance user with HCV infection** (screening – referral – treatment – follow-up)
- **Harm-reduction kits should be provided to all drug/substance users who are (or have been) in treatment with DAAs**

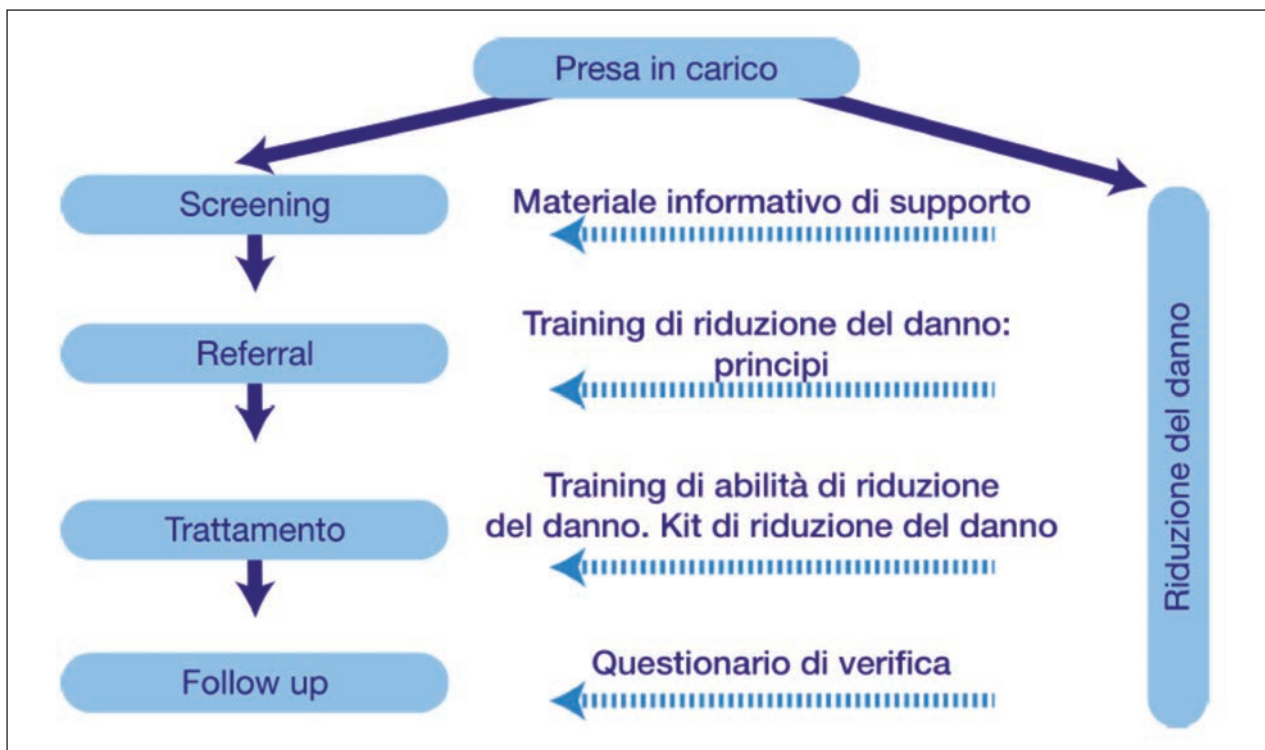


Figure 4.

The basic principles for the linkage to care of drug/substance users and convicts with HCV

- The treatment of the population at risk (drug users and prisoners) should become a priority for the health systems, in order both to ensure equity of access to care and to achieve the public health goal of the eradication of HCV
- Linkage-to-care programs should be integrated, flexible, multi-disciplinary, individual and of proximity
- Linkage-to-care programs should be based on scientific evidence, and should be distributed evenly throughout the national territory
- Linkage to care should be supported by procedures and guidelines which should include also harm-reduction measures, as suggested by WHO.

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