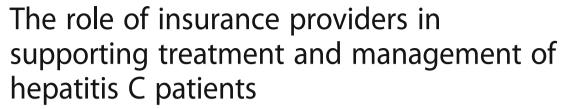
# **CORRESPONDENCE**

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### **Abstract**

Today, one of the most important global public health challenges is represented by hepatitis C virus (HCV), which imposes relevant costs. Globally speaking, the median cost of HCV-related complications ranges from \$280 for an uncomplicated hepatitis to \$139,070 for a liver transplantation. There are effective therapies for HCV patients worldwide, which has increased the hope of improving the process of managing and curing these patients. The adherence of patients to the pharmacological treatment and the use of effective drugs in the management of HCV disease are of crucial importance for health policy- and decision-makers. Studies show that, globally, insurance coverage for patients with HCV is not adequate in that still many patients are not covered by insurance programs. This issue as well as the economic conditions of countries are very serious challenges for ensuring an effective treatment. The most important and greatest help currently available to ensure HCV treatment is to implement plans to reduce costs and support patients. Some studies have shown that the expansion of coverage by private payers seems able to generate positive spillover benefits to public insures. Insurers, in addition to maintaining and increasing their own interests, are trying to increase their social status as a sponsor of patients. In conclusion, HCV disease requires serious policies and affordable insurance coverage.

Keywords: Hepatitis C virus, Treatment, Insurance, Policy

#### Main text

#### **HCV** epidemiology

Today, one of the most important global public health challenges is represented by hepatitis C virus (HCV), which imposes a dramatically relevant burden in terms of morbidity and mortality in many parts of the world. As such, the health sectors of the different countries have designed and implemented various programs for preventing, controlling and treating HCV [1]. According to the World Health Organization (WHO), 399,000 people die annually due to HCV and its complications, such as cirrhosis and liver cancer. This represents a major source of concern for health decision- and policy-makers [2].

There are effective therapies for HCV patients worldwide, which has increased the hope of improving the process of managing and curing these patients [3]. With the

# **HCV**-generated economic burden

HCV is responsible for a huge economic burden for the countries of the world [5]. Direct costs (related to medical expenses for hepatic and extra-hepatic complications of HCV) as well as indirect costs (incurring from impaired QOL, and the loss of work productivity due to inability) have become a real challenge worldwide [6, 7]. In particular [8], according to a recent systematic review and meta-analysis of 102 studies, extra-hepatic complications such as diabetes (occurring in 15% of patients) and depression (occurring in approximately 25% of patients) are the major drivers of such relevant economic burden. Due to financial constraints, the health systems of many countries, in many cases, are not able to cover

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emergence of new viral treatments such as direct-acting antivirals (DAAs), the health sectors of the different countries are working to provide treatment for these people in order to increase their quality of life (QOL) and prevent complications related to the disease [4].

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most of the costs generated by the treatment for these patients [7]. Direct, indirect, cumulative and lifetime costs generated by HCV vary according to the setting and the health system adopted; estimates computed for different countries are reported in Table 1 [9–19].

#### The role of insurance programs

Economic-financial crises, rising HCV infection incidence rates, the availability of new biomedical technologies, and increased staff costs are the main factors that have limited the allocation of funding for the health sector and, as such, healthcare decision- and policy-makers are not able to meet with all the population's health needs to properly satisfy them [20].

As a result, many patients face serious problems in having their disease properly managed and treated. This has prevented the establishment of a universal financial protection for these patients from the health sectors. In the meantime, increased out-of- pocket (OOP) expenditure has made it difficult for the poor people to meet their health-related needs [21].

The adherence of patients to the pharmacological treatment and the use of effective drugs in the management of HCV disease are of crucial importance for health decision-and policy-makers. Despite the effectiveness of DAAs [22], drug prices are high, and many patients are not able to pay for these costs. Therefore, many of them cannot use these medications and the treatment process is facing serious challenges [23].

The WHO reported in 2013 on trends in countries' policies and programs related to hepatitis. In this report, many countries have referred to drugs for the treatment of HCV patients for activities such as drug subsidies, but one of the things that should be considered by health decision- and policy-makers is the lack of insurance coverage for these patients. In developed and developing countries, insurers do not play, indeed, a major role in helping/assisting HCV patients [24].

Studies show that, globally, insurance coverage for patients with HCV is not adequate in that still many patients are not covered by insurance programs. This issue and the economic conditions of countries

**Table 1** Direct, indirect, cumulative and lifetime costs generated by hepatitis C virus (HCV) infection

Country/ Reference	Direct costs	Indirect costs	Cumulative cost	Lifetime cost
USA [9]			\$6.5 (\$4.3–8.4) billion, increasing to \$9.1 (\$6.4–13.3) billion in 2024	\$64,490
Canada [10]	56–81% (due to cirrhosis and its complications)	19–44%		\$64,694
Germany [11]	Mean total cost <i>per</i> patient for hepatic complications €556–1425, for extra-hepatic complications €1921-3547, for chronic HCV €116–577, for non-chronic HCV-related pharmacy costs €1479–3719		Mean total cost <i>per</i> patient €5430-10,108	
Belgium [12]	€126 million (€30–257 million)		€1850 million	
France [13]	84% (47% due to liver cirrhosis, 18% to hepatocarcinoma and 19% to liver transplantation)	16%	€65,956,938	
Spain [14]	71.5%	28.5%	Mean total cost <i>per</i> patient €3198	
UK [15]				£97,555–125,359 for disability, £26,424– 32,235 for healthcare
Ireland [16]			Mean total cost <i>per</i> patient €38,286–62,457 (interferon-based regimen), €55,734–81,873 (interferon-free regimen)	
Italy [17]	39.4%	60.6%	€1.06 billion	
Iran [18]	Total annual cost <i>per</i> patient USD1625.50, USD6,117.2, and USD11,047.2 for chronic HCV, cirrhosis, and hepatocellular carcinoma			
Worldwide [19]	Median cost of liver transplantation \$139,070 (\$15,430-443,700), refractory ascites \$16,740 (\$8990-35,940), hepatocellular carcinoma \$15,310 (\$3370-84,710), decompensated cirrhosis \$14,660 (\$3810-48,360), variceal hemorrhage \$12,190 (\$3550-46,120), hepatic encephalopathy \$9180 (\$5370-50,120), diuretic sensitive ascites \$3400 (\$1320-7470), compensated cirrhosis \$820 (\$50–2890), and chronic hepatitis C \$280 (\$90–1860).			

represent very serious challenges for ensuring an effective treatment [25, 26].

Insurers have a very important role to play in supporting the health sector in creating financial resources and helping people to offset the financial catastrophe by offering support. Insurance should improve the process of treating HCV disease and play a more vibrant role in facilitating this process [27], ensuring, for instance, the continuity between HCV screening and healthcare (the so-called HCV screening and linkage-to-care or SLTC continuum or care cascade, which include different subsequent steps, namely: diagnosis, linkage to care, retention in care, prescription of antiretroviral therapy, and sustained virologic response/viral suppression) [28].

Medical expenses are causing poverty and financial catastrophe to patients and their families [29], and the payout increases from the OOP. Unfortunately, in patients with HCV, the increase in OOP has made the treatment problematic [30]. On the other hand, those who have been insured have been able to enjoy good antiviral treatment and, in addition to recovery, this will reduce the HCV-generated economic burden [31].

# The need for a consolidation and integration of the various insurance programs

There are diverse insurance providers, either public or commercial, offering a variety of programs and plans, such as government public programs for employees, or for urban and rural areas/settings, and government-provided catastrophic health insurance, or commercial health insurance programs. As such, creating an alliance for insurance managers is very important, to meet with different health needs, specific populations and curb costs, while, at the same time, delivering high-quality healthcare services. Consolidation and integration of payers and providers, leading to a "mosaic of insurance programs" can result in greater value and clinical safety in a sustainable way. "In a typical integrated network, the payers stipulate a framework whereby provider groups agree to care for a specific patient population with the goal of reaching or surpassing a predetermined set of quality and cost benchmarks. The integration model encourages healthcare organizations to deliver value to patients and reduce the overuse of treatments" [32].

Insurers should understand the conditions of the disease and the treatment of patients. Many insurance companies are unwilling to participate in the treatment of HCV patients due to their high costs. Meanwhile, some healthcare decision- and policy-makers seem to have overlooked the importance of treating these patients and are indifferent to them [33].

Due to the economic conditions of countries and the crises that every day affect the health system, negotiating with insurance managers is becoming more and more fundamental. If we want to achieve the goal of eliminating/eradicating HCV by the year 2030 [34], in addition to the Ministry of Health (MoH), other organizations, such as insurance companies, should be the main trustees that provide healthcare services to patients.

Treatment and adherence to patients are not complete unless the cost of treatment for them is lower and affordable and treatment provides these patients with better conditions for control and prevention. Reducing this disease, especially by increasing the use of injectable drugs, can be very effective in improving the overall health of the population [25].

# Obstacles and barriers for insurers in ensuring treatment access to HCV patients

There are different obstacles and barriers to ensure treatment access for HCV patients. For instance, there is a gap between health decision- and policy-makers and insurance managers/providers, and this could be a serious warning for the treatment of HCV patients. This gap can be due to different goals, aims, and perspectives (public health and societal point of view versus commercial purposes).

In order to cope with the high costs of the new DAA regimens, some insurers are restricting access to medications, establishing selective criteria for reimbursement. Gowda and collaborators [35] performed a prospective cohort study among American HCV patients. Authors found that absolute denials of DAA regimens by insurers have remained high and increased over time.

It should be emphasized that the health department is not a closed system and it has to use the high and effective potential of insurance programs. Insurers offering support to target and beneficiary groups can play a very valuable role in the treatment process. Health decisionand policy-makers can provide their support for HCV treatment by effectively communicating with insurers [36].

## Opportunities for insurers

The most important and greatest help currently available to guarantee HCV treatment is to implement plans to reduce costs and support patients. Of course, it should not be forgotten that insurers have a benefit in addition to their support for the health plan, which should also be addressed by policy- and decision-makers. Governments can give them concessions to obtain insurance, and provide insurance companies with incentives to support patients for further economic-financial coverage [26]. In the USA, Medicaid reimbursement [37] for therapeutics needed for the proper management and treatment of HCV infection has increased from \$723 million to \$2.35 billion in the period 2012–2015. Significant variations in the Medicaid reimbursement scheme for

DAAs between states in 2014 could be detected that became even more evident in 2015. Expansion states were characterized by a higher increase in reimbursement for DAAs per individual suffering from HCV infection with respect to non- or late-expansion states, adjusting for pre-expansion reimbursement. In conclusion, approximately a third of states contributed more than 5–15% of pharmacy reimbursements to DAAs. New healthcare policies are, therefore, urgently needed in order to ensure coverage for an increasing number of expensive drugs required for the effective treatment of a rising number of patients.

Furthermore, according to a mathematical model analysis [38], the pricing scheme of drugs for the management of HCV infection seems to follow a value-based model, with a rather steady ratio of costs *per* achieved sustained virologic response over a period of 25 years. This leads to the paradoxical *conundrum* that healthcare systems are challenged by the economic-financial issues arising by the high resource utilization of these new drugs despite their cost-effectiveness [39] and their short- and long-term benefits in terms of health. Therefore, a synergy among the different stakeholders (pharmaceutical industries, healthcare payers and insurance providers) should be sought and established in order to find innovative drug pricing schemes to manage all the HCV patients.

Treating all eligible Medicaid patients [40], regardless of fibrotic stage, was computed to result in significantly fewer liver transplants and cases of cirrhosis, hepatocellular carcinoma and HCV-related deaths, as well as in significantly additional life-years and quality-adjusted life-years *per* patient. Treating all Medicaid chronic HCV patients was projected to result in significant cost savings and total costs of care reduction. However, the "treat-all" strategy appears to be promising and cost-effective, if properly supported by new funding and payment schemes, such as cost-sharing mechanisms [41], like plan premiums, deductibles, co-payments, and coinsurance, among others [42].

#### The roles of the different insurance programs

The role of health insurance programs is recognized as a major contribution to the health sector and should be used to promote and improve health plans. Insurers can ensure pharmacological treatment and management to many poor people unable to receive health services, and governments can diversify their healthcare service packages. Insurers, in addition to maintaining and increasing their own interests, are trying to increase their social status as a sponsor of patients.

However, discrepancies between public and private/ commercial insurance providers do exist. Such discrepancies could be due to economic factors. For instance, Mukka et al. [26], in a retrospective study of 160 HCV patients, found that patients with private insurance were more likely to receive treatment compared to patients with public aid. Vu and colleagues [43] performed a multivariate regression analysis and found that predictors of fewer steps in the authorization cascade were having non-Medicaid insurance, and being HCV non genotype 2. At the survival analysis, non-Medicaid insurance and mid-range fibrosis were significantly associated with fewer days to the authorization approval.

On the other hand, the role of private/commercial insurance providers can be positive. Moreno and collaborators [44] have modeled the costs and spillover effects of private insurers' coverage and have found that, with expanded HCV treatment coverage, private payers may reduce medical expenditures, and, over a 20-year period, may experience even overall savings, also generating positive spillover effects to insures like Medicare.

#### **Conclusions**

In conclusion, HCV disease is a challenging public health issue, that requires serious policies and affordable insurance coverage. Patients need to receive drugs, and bad economic conditions can represent barriers to the treatment, leading to poor access to healthcare. Negotiations between health decision- and policy-makers and insurance managers, either public or private, should be taken seriously. Preventing a higher incidence of disease should be a major concern for them. With the increasing incidence of disease in recent years, support for ensuring treatment of patients is very important and everyone should feel the onus to try to reduce the disease. Financial support for patients with HCV is very important and patients should not be liable for their costs. Insurance is an effective leverage for the adherence of all patients to treatment.

### Abbreviations

DAAs: Direct-acting antivirals; HCV: Hepatitis C virus; MOH: Ministry of Health; OOP: Out-of- pocket; QOL: Quality of life; SLTC: Screening and linkage-to-care; WHO: World Health Organization

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# Author's contributions

All authors were involved in the development of the design of the study. All authors drafted the manuscript. All authors contributed to the drafting of the study and have read and approved the final manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

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The authors declare that they have no competing interests.

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