



What Is the Ethical Responsibility of a Provider When Prescribing the New Direct-Acting Antiviral Agents to Patients With Hepatitis C Infection?

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Treatment of chronic hepatitis C (CHC) has recently witnessed tremendous advances.¹ Development and approval of new direct-acting antiviral agents for treating hepatitis C virus (HCV) infection, has brought cure rates exceeding 95% with well-tolerated and simple regimens.¹ Furthermore, these regimens improve patient-reported outcomes such as fatigue and health-related quality of life.²⁻⁹ Additionally, these new anti-HCV regimens have been shown to meet the threshold for cost-effectiveness and have led to significant cost savings to the society by reducing the indirect costs associated with work productivity losses of patients infected with HCV.¹⁰⁻¹⁵ In fact, a recent analysis of quality-adjusted cost of care for the new anti-HCV regimens revealed that despite their higher costs, these new regimens are associated with higher long-term economic gains, leading to substantial savings for the society.¹⁴ Despite the mounting evidence for the superiority of these regimens, there is still a great deal of debate about the cost of these drugs and whether they should be provided to all patients infected with HCV, especially when we are faced with limited resources.

In the context of this debate, the clinician is faced with making treatment decisions based on potentially conflicting ethical perspectives. From the patient perspective, three ethical principles must guide the clinical decisions: 1) autonomy (the right to accept or refuse treatment), 2) beneficence (acting for and/or representing patients' best interests), and 3) nonmaleficence ("first, do no harm").¹⁶⁻²⁰ If one takes patients' perspective when making treatment decisions about HCV, challenges or requirements imposed on clinicians outside these key ethical principles may create a sense of "violating" the best interests of our patients. Therefore, from patients' perspective (beneficence and

autonomy), patients with CHC should be offered treatment acknowledging that most will accept the new treatment regimens (autonomy) and will benefit from achieving sustained virologic response or HCV cure. On the other hand, by not offering these treatment regimens (ie, choosing not to treat these patients or to treat them with the older regimens with their known side effects and negative impact on patients' well-being and work productivity), the clinician may actually harm the patient which is a violation of the ethical principle of "nonmaleficence".

In contrast to the patients' perspective, others have argued that caregivers have a responsibility to the society. In particular, they argue that societal ethical principles must be used as a guide for decision-making. Specifically, these societal principles are 1) stewardship (the duty to protect resources) and 2) parsimony (to choose the most economical treatment among similarly effective treatments whenever it is practical and feasible).¹⁶⁻²⁰ Furthermore, due to "limited resources", clinicians are also asked to consider the ethical principle of justice (fairness and equity in the distribution of health care resources regardless of socioeconomic status) when prescribing medications to treat patients with CHC. In this context, clinicians are asked to consider treatment strategies that are associated with lower short-term budgetary costs.^{10-14,21-24} It is also argued that many patients with CHC have limited resources or they currently receive care through government-sponsored health insurance (taxpayer supported). From this perspective, the limited budgetary resources available for healthcare utilization should be spent "justly" to treat a number of important chronic diseases benefiting a larger proportion of the society. Therefore, clinicians as "the stewards of societal resources and practitioners of the principle of justice", are asked

Abbreviations: CHC, chronic hepatitis C; HCV, hepatitis C virus

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to limit prescribing these drugs only to those with documented advanced stage of hepatic fibrosis. The proponents of this approach tend to rely on the economic analysis of these regimens (primarily budgetary impact analysis) and argue that we cannot “afford” to treat all patients with CHC regardless of their stage of liver disease.^{10-14,21-24} It is probably accurate that this strategy does provide the least costly approach in the short term from the budgetary standpoint, mostly benefiting the payers’ perspective.⁹⁻¹⁴ Although the strategy of treating only patients with advanced fibrosis appropriately provides treatment to those with the most urgent need for treatment, limiting treatment only to this group of patients is unlikely to provide the best value to the society in the long run.^{9-15,21} This is because CHC patients with earlier stages of liver disease can still suffer from hepatic and nonhepatic consequences of HCV, for which the society has to pay in the long term.^{9,22} In fact, the societal perspective in carrying out economic analysis requires a long-term horizon to establish or refute the cost-effectiveness of an intervention.^{9,15} Although most economic analyses have taken the life-time horizon, none have taken into account the total clinical and economic burden of HCV infection (hepatic, nonhepatic, work productivity losses) to the patients and to the society.^{10-15,21,24}

In this context, one can argue that the true burden of HCV infection should not only include liver disease but also the extrahepatic manifestations of HCV (eg, diabetes, chronic renal disease, depression) as well as HCV-related impairment of patients’ health-related quality of life, and the direct (healthcare spending) and indirect (lost worker productivity) costs to the individuals and to the society.^{2-14,22} Thus, being able to prescribe medications that offer a cure with few or no

side effects seems to be prudent and could potentially lessen the economic burden to the society in the long run.¹⁵ This view is supported by evidence demonstrating that obtaining a HCV cure (sustained virological response) is associated with a reduction in the rate of HCV-related cirrhosis, hepatocellular carcinoma, mortality, improvement of extrahepatic manifestations such as fatigue, and lower losses due to impairment in work productivity.^{2-8,10-15,21-24}

Therefore, deciding on a treatment regimen for CHC only through the “lens” of medication costs, and without considering all the available clinical, patient-related, and economic evidence, will lead clinicians and policy-makers to limit their decisions based on a narrow perspective that will not benefit the patients and the society. It is true that those with an immediate need for treatment (patients with advanced hepatic fibrosis) should be prioritized and treated urgently. Nevertheless, devising a strategy to treat all patients with CHC, regardless of their stage of fibrosis, will be ethical from patients and societal perspectives.

In summary, regardless of which ethical framework is applied (patients or societal), it is apparent that clinicians have an obligation to prescribe the intervention that would be most beneficial to the patient while serving the long-term ethical principles of the society. In other words, the intervention that improves the patients’ quantity and quality of life as well as their work productivity should be great for the patients and good for the society.

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