



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer's code:** 00009848

**Reviewer's country:** United States

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-01-31 15:40

**Reviewer performed review:** 2019-02-08 01:50

**Review time:** 7 Days and 10 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Many studies have demonstrated that achieving SVR in CHC patients can improve the long-term outcomes in many aspects in these patients. This MS systemically reviewed the importance of curing HCV from clinical, economic, social, and patient's perspectives in China, a timely topic. It shares some interesting data on HCV in China that are not



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well known to worldwide hepatology society. It is also important to promote DAA treatment in China and Asian Countries. This reviewer will have the following comments:

1. The current title is “Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China”. As this MS emphasize the value of DAA, the title may need to include “DAA”, like Curing hepatitis C with DAAs....”
2. The authors mentioned there are 10 million CHC patients and many physicians are still using PR for HCV treatment. To better address the value of DAA treatment, it is essential to define the current related issues in China, such as current society guidelines on HCV treatment (ie the standard of treatment), the resource, availability and accessibility of DAA for most CHC patients (eg, CFDA approved, not approved, but accessible to the patients), the treatment costs, providers’ knowledge and experiences, and other barriers to promote DAA treatment in China.
3. It is also important to introduce all DAA treatment trial data in China in the text (not just listed in Table 1).
4. The MS emphasizes the important value of DAA, but focus mainly on Sof-based regimen, making the MS imbalanced to other non-Sof DAA regimens.
5. This seems a MS drafted by the medical writers funded by Gilead. In Author contributions’ statement, they declare all the authors “contributed equally”. It is important to detail the role of each individual author, especially those Gilead’s employees. Did all coauthors participate in MS drafting, or by medical writers?
6. The MS spends a great deal of time talking about cost-effectiveness by comparing Sof-based vs PR regimen. However, did not even mention another available pan-genotypic regimen, which could be even more cost-effective.
7. The MS spends too much time to compare PR data with DAA data, but PR regimens are considered the retired regimens, no longer used in many countries.



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8. Some portion is presented based on speculation, rather data driven (at least no references included). Such as “The resulting healthcare expenditures, as well as reduction in quality of life and loss of work productivity among the Chinese CHC population, are expected to have wide-ranging economic and societal implications.”, in page 6. Ref 17 is not accessible?

9. HCV-related EHMs can be divided to “related and possibly related”. The MS described all them so detailed, but indifferently. It is also important to include data on which EHSs are more commonly seen in CHC patients in China or Asia. Additional most references are based PR, but not DAA.

10. The MS mentioned harm reduction so briefly. It is valuable if this is further discussed to prevent recurrent HCV infection

11. As this MS focuses on The Clinical, Economic, Societal, and Patient Value of DAA treatment, it is valuable to statistically predict the exact changes or values after DAA application

12. Needs assessment in China in this field.

13. For all figures referenced in literature, a permit of use should to be obtained and stated in the legends.

Minor comments:

14. In China, the first DAA regimens were approved in 2017; however, as of 2018, PR “therapy is still used extensively in many areas[5].” These needs to be more detailed, especially why PR is still used, MS education, DAA availability, or funding coverage issue?

15. “systemic nature of CHC”, should be “besides liver, HCV infection may involve other organ system”.

16. “25.5 percentage points” should be “25.5%” in p9?

17. “Considering these data, it is reasonable to anticipate that a national roll-out of DAA



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treatment in China would significantly alleviate HCV-related disease burden by averting hundreds of thousands of cases of cirrhosis, HCC, and death.” should be “a national application of DAA” in p10?

18. “(vs no SVR, OR 0.44, 95% CI [0.28, 0.67])” should be “(vs no SVR, OR 0.44, 95% CI [0.28-0.67]),” in p 11?

19. “China sees substantial regional variation in risk factors for HCV infection” should be “Substantial regional variation in risk factors for HCV infection exists in China”, in p12?

20. The authors stated “In China, studies on PROs in HCV patients have been scarce.” But use discussed too much related issue by referencing non-Asian data.

21. “this papers.” should be this paper.” In p 25

22. Suggest move the ref list in table 1 from left to most right. Table 1 data should be well included to the text to make the MS balanced.

23. Conclusion is too long, usually one para.

24. Would suggest including a session on the current challenge and future research and commitment direction.

25. The MS seems too long, should be shorten dramatically (defer to staff editor).

## **INITIAL REVIEW OF THE MANUSCRIPT**

### ***Google Search:***

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[ Y ] No

### ***BPG Search:***



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer's code:** 02528812

**Reviewer's country:** Iran

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-02-10 05:45

**Reviewer performed review:** 2019-02-10 07:39

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This review summarizes the value of hepatitis C treatment in China from clinical, economic, societal, and patient experience perspective. The study is well written and organized. I have a few comments. Authors should include the following: 1) The emergence of HCV resistance-associated variants (RAVs), which occur naturally during



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the replication of the virus and select under the pressure of DAAs and finally results in treatment failure. 2) Strategic planning to avoid the emergence of RAVs. 3) A list of prophylactic vaccine candidates against HCV infection. 4) Mechanisms of vaccines failures: what we learned from failures. 5) Social and economic side of HCV elimination.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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##### ***BPG Search:***

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer's code:** 03475479

**Reviewer's country:** Japan

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-02-09 23:23

**Reviewer performed review:** 2019-02-12 06:35

**Review time:** 2 Days and 7 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Authors described about the clinical, economic, societal effect of anti-viral treatment for chronic HCV infection in China. This review is well-addressed and well-written, and informative for clinicians. In China, HBV-coinfection might be frequently found. Authors should mention about HBV-coinfection (e.g. prevalence, the effect or the caution



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in anti-viral treatment)

#### INITIAL REVIEW OF THE MANUSCRIPT

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##### *BPG Search:*

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- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer's code:** 00503849

**Reviewer's country:** Taiwan

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-02-11 11:56

**Reviewer performed review:** 2019-02-13 11:46

**Review time:** 1 Day and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The manuscript was well written which can provide useful information to the readers. I recommend publishing this manuscript.

**INITIAL REVIEW OF THE MANUSCRIPT**



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### *BPG Search:*

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Duplicate publication

Plagiarism

No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer’s code:** 03488192

**Reviewer’s country:** Mexico

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-02-12 15:33

**Reviewer performed review:** 2019-02-16 21:47

**Review time:** 4 Days and 6 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Interesting and valuable article by Xie Q et al., on the Clinical, Economic, Societal, and Patient consequences of HCV Cure in China. It presents a good introduction and extensive review on HCV cure-related topics in China. The burden of liver disease in China is an important subject of great interest both for the journal and for the



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international community of hepatologists-gastroenterologists. It follows a trend, with increasing numbers of articles, presenting and informing about the advances in the management of HCV infection in that great nation with an important number of patients with HCV infection representing 6.6 % of the HCV positive world population (Wang et al. Hepatology 2014). This reviewer has read and agrees with all the information presented. However, there are two important aspects that should be included and reviewed. An important point is that when writing about some predictive modeling in China, specifically refs. 52, 53 and 85, they cite abstracts which do not have all the information to read about the methodology, to check the results and get a thorough opinion. I suggest the authors obtain the full articles or substitute them with complete articles. Unfortunately the authors rely importantly on these type of sources. On the other hand, there is/are recent articles using some predictive models about the prevalence and mortality related to HCV infection in China which should be included (Wu...Li, et al, Hepatology 2018, e publication). In that respect I think that the authors could use that information to do the cost-analysis of treatment HCV with DDAs in terms of projected prevalence on the one hand and the benefits of DDAs treatment on reduced mortality on the other. Those results could also be included in Figure 2. An important part of the analysis of the value of using DAAs en HCV treatment which is also related to the treatment of advanced cirrhosis and HCC is transplantation, which is not included in the review but is a piece of information which will complete the analysis i.e. how many liver transplants will not be needed or performed after the general use of DDAs (to be included also in Figure 2). Finally, the word "Curing" in the title looks somehow peculiar although it can be used. A first attempt to find similar titles in PubMed, showed that it is not in the main key word descriptors list and I found it only as "HIV cure". I suggest changing the word for something which is more readily found with most search browsers.



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#### INITIAL REVIEW OF THE MANUSCRIPT

***Google Search:***

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- Duplicate publication
- Plagiarism
- No

***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 44669

**Title:** Curing Hepatitis C: The Clinical, Economic, Societal, and Patient Value for China

**Reviewer’s code:** 00503536

**Reviewer’s country:** Japan

**Science editor:** Li-Jun Cui

**Reviewer accepted review:** 2019-02-10 05:52

**Reviewer performed review:** 2019-02-17 09:27

**Review time:** 7 Days and 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The review written by Xie et al. summarizes the treatment efficacy for HCV infection with the economic and societal burden of chronic hepatitis C. The review is comprehensive and well written. However, there are some misspelling and a concern that need to be addressed. Minor point 1. The efficacy of DAA is different according to



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the genotype of HCV. Especially, the efficacy is lower in patients with HCV genotype 3 than those with genotype 1 or 2. Therefore, the data should be separated.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- [ ] Duplicate publication
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- [ Y ] No

##### ***BPG Search:***

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- [ ] Plagiarism
- [ Y ] No