

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Clinical Outcomes and Resource Utilization in Medicare Patients with Chronic Liver Disease: A Historical Cohort Study
AUTHORS	Younossi, Zobair; Zheng, Li; Stepanova, Maria; Venkatesan, Chapy; Mishra, Alita

VERSION 1 - REVIEW

REVIEWER	John Lake University of Minnesota Medical School USA
REVIEW RETURNED	19-Nov-2013

GENERAL COMMENTS	<p>The results are just not very interesting and when presented in isolation, it is difficult to know what they mean. Why it is not interesting:</p> <ol style="list-style-type: none">1. This only relates to Medicare recipients and thus, is of little interest to those on other counties and even tells an incomplete story of what is going on in the US.2. Some of the diagnoses to define the outpatients are marginal indicators of CLD, e.g. abnormal liver enzymes or abnormal imaging.3. The after-discharge death reporting seems flawed. Everyone is going to die and Medicare beneficiaries at an accelerated rate based on age. Only deaths related to liver disease would be of interest.
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REVIEWER	John W Ward Centers for Disease control and prevention Atlanta, Georgia, USA
REVIEW RETURNED	19-Dec-2013

GENERAL COMMENTS	<p>In the discussion, the authors should include the new CDC/USPSTF recommendations for HCV testing of persons born 1945-1965 which includes some of the Medicare population. the discussion should highlight the large proportion attributed to HCV.</p> <p>Introduction; Add growing burden of HCV related CLD in the population of or approaching Medicare age over this time period. Note that the national strategy is for viral hepatitis related CLD.</p>
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REVIEWER	Lesley H Curtis Duke Clinical Research Institute
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GENERAL COMMENTS

Using Medicare claims data, the authors examine trends in Medicare spending for chronic liver disease from 2005-2010. While the topic is important, there are major flaws in the approach that limit the usefulness and validity of the manuscript.

o The coding algorithm includes codes that have the potential to capture patients that do not have chronic liver disease. Examples include 790.4, 790.5 that are used for nonspecific abnormal serum enzymes levels. A patient may present with abnormal liver function tests from an acute etiology such as Tylenol overdose or drug-induced liver injury. Such a patient, if hospitalized with ICU admission and ultimately transplantation, would require a significant amount of resources but not truly represent the cohort of interest. Another example is the use of primary liver cancer which will capture a number of patients with cirrhosis and subsequent HCC but may also include patients with cholangiocarcinoma or HCC in the absence of chronic liver disease. For these reasons, the use of a validated algorithm that more accurately identifies patients with chronic liver disease and minimizes false positives and negatives is paramount to achieving reliable results.

o A second major issue of methodology is the means of selecting "CLD-related claims" by only choosing those claims with a given primary ICD-9 diagnosis code. While primary diagnosis has specific meaning in inpatient claims ("the condition established after study to be chiefly responsible for the admission"), the first-listed diagnosis on an outpatient claim may not carry specific meaning. Arguably, a liver diagnosis anywhere on the claim likely contributes to the patient's medical condition and may contribute to clinical outcomes and resource utilization given the systemic effects of chronic liver disease. Examples include cirrhotic patients who are hospitalized for an unrelated procedure such as a hip replacement but experience decompensation and complications in the setting of surgery that changes a routine procedure to a prolonged hospitalization. The primary diagnosis may be DJD with hip replacement but if the provider includes the liver disease in the secondary diagnoses under the current algorithm this patient would be missed but actually provides relevant information to the analysis.

o The rationale for removing cases with LOS > 60 days was unclear as they may have high utilization and important clinical outcomes as outliers. The authors should provide a clear rationale for their exclusion

o No rationale is provided for presenting hospital charges which generally carry little meaning. For a Medicare claims analysis, a Medicare perspective on resource use can be achieved by focusing on Medicare payment amounts. Beneficiary payments may be of interest but, as the author notes, supplementary insurance may reduce or eliminate those out-of-pocket expenditures

o Please explain the rationale for using 10 diagnoses and 6 procedure codes in the outpatient files. Is this how it is provided or was there a consistent way that these were chosen?

o Based on the results of small decrease in LOS, increase in total payments, decrease in inpatient mortality but increase in outpatient mortality, a more concise discussion that ties these things together and offers an explanation of the trends is critical. What is the clinical significance of the small drop in LOS and increase in Charlson score? Based on the construct of your cohort, it is difficult to really understand how ESRD or ethnicity can help target resources for the future, for example.

	<ul style="list-style-type: none"> o The third paragraph of the introduction (discussion of Medicare) seems out of place and does not tie intro to methods well and should be moved. o The exclusion of 2008 data is poorly justified and, therefore problematic. Why were data missing from standard Medicare files? o The rationale for inflation adjustment is odd; the issue is that inflation makes 2005 Medicare payments not directly comparable to 2010. The authors should consider using medical component of the CPI. o Trends over time is the focus of the manuscript, so trends should be displayed in Table 1. It does not make sense to show a p-value for a test for trend without showing the data. o The use of the phrase “estimated cost” is inaccurate. Should be “Medicare payments” o Please clarify over what prior period baseline characteristics were ascertained.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Q1. This only relates to Medicare recipients and thus, is of little interest to those on other counties and even tells an incomplete story of what is going on in the US.

A1. Although the reviewer is correct and the Medicare population is unique for the U.S., spending policies set by private insurers in the U.S. usually follow those previously set by Medicare including fee-per-service charges. Medicare population is also the largest consumer of healthcare-related spending in the U.S. With ageing of baby-boomers, the cohort with the greatest number of hepatitis C infected individuals; most of them are about to become Medicare-eligible in the coming years, so understanding the factors that are associated with CLD-related spending is becoming even more important. Thus, although we totally agree that Medicare population is anything but representative of the U.S. population, we believe our results can be used to appreciate CLD spending predictors and trends in those in the entire U.S. for the next years. Furthermore, the U.S. pattern of health care is certainly of interest, not only to readers in the U.S. but also to those outside the U.S. In fact, European model of health care, including those by countries such as Britain and Canada have of intense interests by the U.S. consumers. We believe the reverse is also true.

Q2. Some of the diagnoses to define the outpatients are marginal indicators of CLD, e.g. abnormal liver enzymes or abnormal imaging.

A2. We excluded diagnoses that can be associated with conditions other than CLD from the study; see the updated Methods section. In fact, we have re-run the entire analysis after these exclusions.

Q3. The after-discharge death reporting seems flawed. Everyone is going to die and Medicare beneficiaries at an accelerated rate based on age. Only deaths related to liver disease would be of interest.

A3. The cause of death is not available in the Medicare claims data, which limited the mortality analysis to all-cause mortality. We updated the presentation mortality follow-up data which was reported as of March following the year of claim, and now refer to it as “short-term post-discharge mortality”.

Reviewer: 2

Q1 .In the discussion, the authors should include the new CDc/USPSTF recommendations for HCV testing of persons born 1945-1965 which includes some of the Medicare population. the discussion should highlight the large proportion attributed to HCV.

A1. We agree and have added to the introduction and discussion.

Q2. Introduction; Add growing burden of HCV related CLD in the population of or approaching Medicare age over this time period. Note that the national strategy is for viral hepatitis related CLD.

A2. We updated the Introduction accordingly.

Reviewer: 3

Q1. The coding algorithm includes codes that have the potential to capture patients that do not have chronic liver disease. Examples include 790.4, 790.5 that are used for nonspecific abnormal serum enzymes levels. A patient may present with abnormal liver function tests from an acute etiology such as Tylenol overdose or drug-induced liver injury. Such a patient, if hospitalized with ICU admission and ultimately transplantation, would require a significant amount of resources but not truly represent the cohort of interest. Another example is the use of primary liver cancer which will capture a number of patients with cirrhosis and subsequent HCC but may also include patients with cholangiocarcinoma or HCC in the absence of chronic liver disease. For these reasons, the use of a validated algorithm that more accurately identifies patients with chronic liver disease and minimizes false positives and negatives is paramount to achieving reliable results.

A1. We excluded diagnoses that may be associated with conditions other than CLD from the study; see the updated Methods section, and updated all the related information in the Results, Discussion, as well as the tables.

Q2. A second major issue of methodology is the means of selecting "CLD-related claims" by only choosing those claims with a given primary ICD-9 diagnosis code. While primary diagnosis has specific meaning in inpatient claims ("the condition established after study to be chiefly responsible for the admission"), the first-listed diagnosis on an outpatient claim may not carry specific meaning. Arguably, a liver diagnosis anywhere on the claim likely contributes to the patient's medical condition and may contribute to clinical outcomes and resource utilization given the systemic effects of chronic liver disease. Examples include cirrhotic patients who are hospitalized for an unrelated procedure such as a hip replacement but experience decompensation and complications in the setting of surgery that changes a routine procedure to a prolonged hospitalization. The primary diagnosis may be DJD with hip replacement but if the provider includes the liver disease in the secondary diagnoses under the current algorithm this patient would be missed but actually provides relevant information to the analysis.

A2. We updated the outpatient section so that it covers secondary diagnoses as well; see updated Results.

Q3. The rationale for removing cases with LOS > 60 days was unclear as they may have high utilization and important clinical outcomes as outliers. The authors should provide a clear rationale for their exclusion.

A3: In this study, we are trying to assess the demographic and clinical factors that affect patient's length of hospital stay. According to Medicare policy, Medicare payment differs between hospital

stays of 1-60 days and stays of over 60 days. Patients only pay a one-time hospital deductible with no coinsurance for hospital stay of 1–60 days, but need to pay coinsurance for longer stay. In 2013, patients pay \$296 per day for days 61 through 90, and more for longer stays. Therefore, hospital stays longer than 60 days were deleted from analysis in order to minimize the potential effect of various co-insurance on length of stay. In addition, there were very few inpatient visits with length of stay longer than 60 days (37 cases out of 25,294 chronic liver disease inpatient visits). The total proportion of claims with such length of stay was approximately 0.15% with maximum of 177 days. Excluding these cases is unlikely to affect the validity of the results.

Q4. No rationale is provided for presenting hospital charges which generally carry little meaning. For a Medicare claims analysis, a Medicare perspective on resource use can be achieved by focusing on Medicare payment amounts. Beneficiary payments may be of interest but, as the author notes, supplementary insurance may reduce or eliminate those out-of-pocket expenditures

A4. We agree that healthcare charges carry less meaning so we excluded this outcome from the study.

Q5. Please explain the rationale for using 10 diagnoses and 6 procedure codes in the outpatient files. Is this how it is provided or was there a consistent way that these were chosen?

A5. This is how Medicare billing data is provided to third party researchers. The total number of diagnoses, however, may exceed 10, but only 10 are given explicitly.

Q6. Based on the results of small decrease in LOS, increase in total payments, decrease in inpatient mortality but increase in outpatient mortality, a more concise discussion that ties these things together and offers an explanation of the trends is critical. What is the clinical significance of the small drop in LOS and increase in Charlson score? Based on the construct of your cohort, it is difficult to really understand how ESRD or ethnicity can help target resources for the future, for example.

A6. We agree and have addressed this in the discussion

Q7. The third paragraph of the introduction (discussion of Medicare) seems out of place and does not tie intro to methods well and should be moved.

A7. We fixed the logic of Introduction.

Q8. The exclusion of 2008 data is poorly justified and, therefore problematic. Why were data missing from standard Medicare files?

A8. The Medicare claims data that CMS released to us has missing data on patient's residence state in 2008. We put it back to summary tables but had to exclude most of the records from this year from multivariate analysis due to missing data.

Q9. The rationale for inflation adjustment is odd; the issue is that inflation makes 2005 Medicare payments not directly comparable to 2010. The authors should consider using medical component of the CPI.

A9. We changed the way of adjustment for inflation; now it is the medical component of CPI.

Q10. Trends over time is the focus of the manuscript, so trends should be displayed in Table 1. It does not make sense to show a p-value for a test for trend without showing the data.

A10. We included two years explicitly to compare the trends to Table 1. All six years are now included as supplementary material due to space limitations.

Q11. The use of the phrase "estimated cost" is inaccurate. Should be "Medicare payments"

A11. We changed the wording to "total payment" which includes Medicare payment, secondary insurance payment, and out-of-pocket expenses.

Q12. Please clarify over what prior period baseline characteristics were ascertained.

A12. Patient's baseline characteristics were from Medicare Denominator file which contains data on all Medicare beneficiaries enrolled in a given year. Those include demographics, residence, and Medicare eligibility category. The denominator file was provided for each of the study years separately.