RESEARCH ARTICLE

The effects of patient cost sharing on inpatient utilization, cost, and outcome

Yuan Xu1,2, Ning Li1 *, Mingshan Lu2,3, Elijah Dixon2,4, Robert P. Myers2,5, Rachel J. Jelley2, Hude Quan2

1 Beijing YouAn Hospital, Capital Medical University, Beijing, China, 2 Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada, 3 Department of Economics, University of Calgary, Calgary, Alberta, Canada, 4 Division of General Surgery, Department of Medicine, University of Calgary, Calgary, Alberta, Canada, 5 Liver Unit, Division of Gastroenterology and Hepatology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada

* liningya@ccmu.edu.cn

Abstract

Background

Health insurance and provider payment reforms all over the world beg a key empirical question: what are the potential impacts of patient cost-sharing on health care utilization, cost and outcomes? The unique health insurance system and rich electronic medical record (EMR) data in China provides us a unique opportunity to study this topic.

Methods

Four years (2010 to 2014) of EMR data from one medical center in China were utilized, including 10,858 adult patients with liver diseases. We measured patient cost-sharing using actual reimbursement ratio (RR) which is allowed us to better capture financial incentive than using type of health insurance. A rigorous risk adjustment method was employed with both comorbidities and disease severity measures acting as risk adjustors. Associations between RR and health use, costs and outcome were analyzed by multivariate analyses.

Results

After risk adjustment, patients with more generous health insurance coverage (higher RR) were found to have longer hospital stay, higher total cost, higher medication cost, and higher ratio of medication to total cost, as well as higher number and likelihood that specific procedures were performed.

Conclusion

Our study implied that patient cost-sharing affects health care services use and cost. This reflects how patients and physicians respond to financial incentives in the current healthcare system in China, and the responses could be a joint effect of both demand and supply side moral hazard. In order to contain cost and improve efficiency in the system, reforming provide payment and insurance scheme is urgently needed.
Introduction

With health care expenditures growing at an increasing speed worldwide, many health care systems are looking into health insurance reforms to contain costs [1–3]. One main cost containment strategy is to rely on patient cost-sharing (patients pay a portion of health care costs not covered by health insurance). It has been argued that the demand of health services could vary with the level of patient cost-sharing: patients with higher health insurance coverage tend to overuse health services, and patients with lower insurance coverage may underuse necessary and otherwise unaffordable care—i.e., the moral hazard effect [4, 5]. On the supply side, health insurance coverage may also influence physicians’ decision-making on health services use: physicians may tend to over-treat patients with more generous health insurance coverage, and under-treat those with poor health insurance coverage—i.e., the supply induced demand effect [1, 6].

In practice, treatment decision is likely made by patient and health care provider jointly. The final treatment decision, therefore, is subject to both demand side moral hazard and supplier-induced demand effects. However, it is difficult to segregate one from the other. Taking China’s health system as an example, patient cost-sharing reflects financial incentives not only for patients but also for health providers (hospitals and physicians), as hospitals are allowed to retain any surplus gained and use this to pay for instance, staff bonuses, which is a large proportion of their incomes [7]. Therefore, the overall effect of patient cost-sharing on health use and cost would reflect a joint effect of health providers’ and patients’ reactions to financial incentives.

For the purpose of evidence-based policy making in health care insurance reform, a key empirical question is: what are the impacts of patient cost-sharing on health care utilization, cost, and patient outcome? In spite of the large number of health economics studies assessing this question [8–12], most of these studies have limitations. Being the only randomized control trial on this topic, the RAND health insurance experiment (HIE) is a classic investigation that provided solid evidence on price elasticity of health care demand [13]. However, the HIE participants were assigned to different insurance plans which failed to count the individual patient’s actual cost-sharing [13, 14]. Many other studies in the literature have had to use data from non-experimental settings, suffering from selection bias. For example, in health insurance markets such as the U.S. there are variations in terms of health insurance coverage (patient cost-sharing), as patients may choose to enroll in different health insurance plans based on their health and expected demand of health services. While in other health insurance markets such as Canada, under universal health insurance coverage there is no variation in cost-sharing for services included in the public health insurance. Finally, it is a common limitation in most of these studies that detailed information on patient comorbidities and disease severity is not available to have proper risk adjustment.

The Chinese healthcare system and its electronic medical record (EMR) data provide us a unique opportunity to contribute to the existing literature and shed light on the above question. Through several large-scale health care reforms in the past decades, China has established a universal health care system in which there are large variations in actual coverage/reimbursement not only among but also within various health insurances [7, 15, 16]. Unlike the private health insurance market in which people choose to enroll in different private insurance plans, most Chinese are covered by different public health insurance plans based on their eligibility (which is determined by occupation, residence, etc.). In other words, there are large cost-sharing variations that can be studied with limited selection bias in the Chinese system. Furthermore, the EMR in China has been rapidly growing since 2006, and now most hospitals in
China are using EMRs. Chinese EMRs contain not only rich clinical (including diagnostic and
treatment procedure) information but also detailed and itemized billing data.

In this study, we examined the impacts of patient cost-sharing on hospitalization cost, med-
ication cost, treatment/procedures, and in-hospital mortality. Unlike most existing studies
using data that measures patient cost-sharing by type of health insurance, we used actual reim-
bursement ratio (RR, defined as percentage of reimbursed cost in total treatment cost), which
was derived using detailed financial information in our EMR data. Given the large variations
in RR both among and within different health insurances in China, using RR estimate has
allowed us to better capture financial incentive than if using type of health insurance. In addi-
tion, the rich clinical information in our EMR data has also allowed us to employ a risk adjust-
ment methodology with a wide range of risk factors to adjust for disease severity and
comorbidities.

Method

Study setting

Liver diseases in China. Liver disease, including viral hepatitis (e.g., Hepatitis B virus,
HBV), cirrhosis and primary liver cancer (PLC), is regarded as a large contributor to burden
of disease worldwide. Such disease burden is especially high for the Chinese population [17].
In China, about 97 million people are HBV carriers [18]; and at least 20 million patients have
chronic HBV infection with or without cirrhosis and/or PLC [17, 18]. This has resulted in high
volumes of hospitalized patients with liver disease. Between 2006 and 2010, about 1.2% of
inpatients were admitted due to cirrhosis (mainly hepatitis cirrhosis) in hospitals in Beijing
[19].

EMR development in China. Researchers worldwide have recognized the potential value
of EMR and tremendous efforts are underway to advance EMR research [20–22]. EMRs are
greatly advantageous in that they provide large geographical coverage and are easily accessible,
as well as providing rich and timely longitudinal clinical data for research purposes [23, 24]. In
China, developing EMRs has been identified as a primary focus in on-going health care
reforms, and the implementation of EMRs has been rapidly growing since 2006 [23]. The cov-
erage, functionality, and interoperability of EMRs will continue to be greatly improved as
these developments take place. Currently, most hospitals in China use EMRs; and these EMR
systems continue to collect massive amounts of individual clinical and billing information [23,
25].

Healthcare system in China. Through recent health reforms, China has established
nearly universal health insurance coverage for its population. Under the current public health
insurance system, there are three main components: Urban Employee Basic Medical Insurance
(UEBMI) which was launched in 1998, New Cooperative Medical Scheme (NCMS) launched
in 2003, and Urban Resident Basic Medical Insurance (URBMI) launched in 2007 [26].
Although the health insurance is predominantly public, patients do not have options to choose
which public health insurance she/he enrolls. A citizen’s public health insurance type is deter-
moved by residency (urban or rural) and employment status (employed or unemployed).
However, the insurance policies and coverage, including deductibles, limits, and reimburse-
ment rates for different drugs and services, vary widely not only within but also among the
insurance schemas by age, length of employment, and working sectors. Therefore, RR may not
be an exogenous variable, but we believe the selection effect of the variation of RR is less in
China compared with that in western countries with different arrangements in both insurance
and labor markets. Our study adopts similar methodology as that in several previous studies to
address the impacts of health insurance (measured by RR) on health care services utilization and cost in China [27–29].

Although China’s public hospitals deliver more than 90% of the country’s health service output [26], since the late 1980s, the government has made large cut backs to its financial input to public hospitals. After the large financial input cut, China’s public hospitals were permitted to retain surplus from drug or services sales [30, 31]. In China prescription drugs are predominantly distributed and sold in hospitals, which accounts for over 70% of all drugs sold and distributed [32], as well, the hospitals are allowed to mark-up drug price (usually 15% margin on drugs) [28] to gain profit for operating costs and retaining surplus. Hospitals pay bonuses to their chief executive officers (CEOs) as well as physicians using the retained surplus. In China, public hospital CEOs’ and physicians’ income consists of a salary and bonuses. Their salary levels are set very low with bonuses accounting for the majority of their income.

Under the current system, there are strong financial incentives for hospitals to become profit-driven to maximize their incomes. Methods to over-value service costs include increasing medication prescriptions or medical material use, as physician workload-related services such as visits and work hours have relatively low-value in terms of cost [26, 30, 31]. For example, transcatheter arterial chemoembolization (TACE) is a common micro-invasive treatment for patients with liver cancer or cirrhosis and can act as an alternative treatment for patients who are not suitable or refused for liver surgery [33]. However, TACE is not a curable method for liver cancer or cirrhosis and is often repeatedly performed upon disease reoccurrence [34]. The catheter material cost is the main contributing factor to the overall cost of TACE. Because pricing policies including over-valuing material costs allow physicians and hospitals to retain a certain margin of the catheter cost, and this impacts physician income. Thus, there are financial incentives for physicians to suggest patients with liver cancer or cirrhosis to choose TACE as a first treatment and to undergo more TACE procedures when the disease reoccurs.

Data and analysis method

Data and sample selection. This study was approved by the YouAn Hospital Research Board of Ethics and the Health Research Ethics Board at University of Calgary (Ethic committee’s reference number: REB14-0815). The EMR data used in this study was derived from Beijing YouAn hospital, which is one of the leading teaching hospitals specializing in liver diseases in China, treating over 300,000 patients from all-over China annually. In 2008, the EMR system was officially implemented in YouAn hospital. EMR data are inputted by physicians and regularly audited by the medical records department in the hospital, as its quality is a part of the physicians’ monthly performance evaluations.

The EMR financial data is directly drawn from the hospital billing system and reflected in the patient’s actual total and out-of-pocket expenses of hospitalization, which includes itemized costs that occur in hospital, such as fees for bed occupation, medication, and surgery or procedures.

For our study sample, we included in-patients with common liver diseases including cirrhosis, PLC, viral hepatitis, alcoholic hepatitis or fatty liver, who were admitted to Beijing YouAn hospital between January 1st, 2010 and September 30th, 2014, 18 years old or older, and consented to use their EMRs for research. We had no access to any patient identifying information as part of the study. In our previous study, we developed and validated a data extraction method for a Chinese EMR, and we defined 40 liver disease severity and comorbidity variables using this extraction method [35].

Using the financial information in our EMRs, we constructed the actual reimbursement ratio (RR) and used this as a measure of actual patient cost-sharing [27]. RR was defined as the
ratio of the risk-pooling fund paid costs to total hospital costs: \( RR = \frac{(TC - OOP)}{TC} \times 100\% \), where TC denotes total hospital cost, and OOP denotes out-of-pocket cost. When \( RR = 0\% \), this indicates that the total hospital cost is completely self-paid, and when \( RR = 100\% \), this indicates that the total hospital cost is fully reimbursed.

Reimbursement ratio in our data ranged between 0 and 1. Because public health insurance is not portable in China, patients from other provinces have to first pay the hospital costs completely out-of-pocket (\( RR = 0 \) in our billing data). To avoid mixing patients who did not have any insurance with those who required reimbursement in their resident provinces/cities (\( RR = 0 \) for both cases), we excluded patients with \( RR = 0 \) from our sample. This resulted in 10,858 adult patients with liver disease in our study sample.

**Analysis method.** We estimated the impacts of patient cost-sharing using the following model specifications:

\[
Y_i = \alpha + \beta RR_i + \gamma Procedure_i + \delta L_i + \gamma X_i + \epsilon
\]

where \( Y_i \) indicates cost, health care utilization, and patient outcome. Cost measures included total hospital cost (TC, log transformed), medication cost (MC, log transformed), and ratio of medication cost to total cost (RMT, log transformed). As discussed earlier, our hypothesis is that patients with a higher \( RR \) have higher hospital costs, i.e. higher TC, MC and RMT. All cost values were inflated to 2010 RMB.

Health care utilization was measured using hospital length of stay (LOS, log transformed), TACE use (TACE = 1 if TACE was used, TACE = 0 if TACE not used), and number of TACE procedures (nTACE, 1 for having one TACE, 2 for having two times TACE, 3 for having 3 times TACE, and so forth). As discussed earlier, our hypothesis is that patients with higher \( RR \) will have both a higher likelihood of undergoing TACE and increased number of TACE procedures, as well as a longer hospital LOS. Finally, outcome was measured using in-hospital mortality (1 for yes, 0 for no).

The control variables in our regression models included the following: \( RR_i \), which was the reimbursement ratio of patient \( i \) and key variable of interest of our analyses; Procedure\(_i\), which

| Table 1. Outcomes, the corresponding explanatory variables and the regression models. |
|-----------------|-------------------------------|-----------------|
| **Dependent Variable** | **Independent Variable** | **Regression** |
| LOS | RR, age, sex, admission status, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (PLC, cirrhosis, viral hepatitis, alcoholic hepatitis, and fatty liver) | Generalized linear |
| TACE (yes/no) | RR, age, sex, admission status, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (viral hepatitis, alcoholic hepatitis, and fatty liver) | Logistic |
| nTACE | RR, age, sex, admission status, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (viral hepatitis, alcoholic hepatitis, and fatty liver) | Generalized linear |
| TC | RR, age, sex, admission status, LOS, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (PLC, cirrhosis, viral hepatitis, alcoholic hepatitis, and fatty liver) | Generalized linear |
| MC | RR, age, sex, admission status, LOS, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (PLC, cirrhosis, viral hepatitis, alcoholic hepatitis, and fatty liver) | Generalized linear |
| RMT | RR, age, sex, admission status, LOS, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (PLC, cirrhosis, viral hepatitis, alcoholic hepatitis, and fatty liver) | Generalized linear |
| Mortality | RR, age, sex, admission status, Elixhauser comorbidities, MELDNa, major procedure/surgery (hepatectomy and TACE), liver disease categories (PLC, cirrhosis, viral hepatitis, alcoholic hepatitis, and fatty liver) | Logistic |

LOS: length of stay at hospital; RR: reimbursement ratio; MELDNa: model for end-stage liver disease and sodium; TACE: transcatheter arterial chemoembolization; PLC: primary liver cancer; nTACE: number of TACE; TC: total cost; MC: medication cost; RMT: ratio of medication cost to total cost; RMT: ratio of medication to total hospital cost.

https://doi.org/10.1371/journal.pone.0187096.t001
Table 2. Main characteristics of patients with liver disease.

| Variable | Definition | Mean (SE) |
|----------|------------|-----------|
| RR | Numerical variable, RR = reimbursement divide by total hospital cost, therefore it was between 0 and 1. | 0.68 (0.19) |
| Age | Numerical variable, the unit was year. The minimum age was 18 years. | 45.9 (15.5) |
| MELDNa score | Numerical variable ranged from 6.43 to 40; MELDNa = MELD + (140—Na)(1−0.025*MELD); MELD = 3.8 ln(total bilirubin) + 11.2 ln(INR) + 9.6 ln(creatinine) + 6.43; the units for serum level of total bilirubin, creatinine, and INR are mg/dL, mg/dL and 1, respectively. | 11.5 (4.9) |
| LOS | Numerical variable, it was calculated by subtracting discharge date by admission date, the unit was day. | 19.94 (21.0) |
| Total cost | Numerical variable, the unit was Yuan, RMB. | 28908.3 (44249.2) |
| RMT | Numerical variable, RMT was calculated by dividing total hospital cost by medication cost and was between 0 and 1. | 0.49 (0.19) |
| Medication cost | Numerical variable, the unit was Yuan, RMB | 17035.1 (27259) |
| Death | Dummy variable = 1 if patient was dead in hospital, 0 otherwise | 0.055 (0.002) |
| Sex | Dummy variable = 1 if patient was male, 0 female | 0.489 (0.005) |
| Admission status | Dummy variable = 1 if patient was urgently admitted, 0 otherwise | 0.139 (0.003) |
| Hepatectomy | Dummy variable = 1 if patient underwent hepatectomy in hospital, 0 otherwise | 0.008 (0.001) |
| TACE | Dummy variable = 1 if patient underwent TACE in hospital, 0 otherwise | 0.040 (0.002) |
| Primary liver cancer | Dummy variable = 1 if patient was diagnosed as primary liver cancer, 0 otherwise | 0.204 (0.004) |
| Cirrhosis | Dummy variable = 1 if patient was diagnosed as cirrhosis, 0 otherwise | 0.344 (0.005) |
| Hepatitis B | Dummy variable = 1 if patient was diagnosed as hepatitis B, 0 otherwise | 0.583 (0.005) |
| Hepatitis C | Dummy variable = 1 if patient was diagnosed as hepatitis C, 0 otherwise | 0.032 (0.002) |
| Alcoholic hepatitis | Dummy variable = 1 if patient was diagnosed as alcoholic hepatitis, 0 otherwise | 0.079 (0.003) |
| Congestive heart failure | Dummy variable = 1 if patient was diagnosed as congestive heart failure, 0 otherwise | 0.002 (0.000) |
| Peripheral vascular disease | Dummy variable = 1 if patient was diagnosed as peripheral vascular disease, 0 otherwise | 0.001 (0.000) |
| Dementia | Dummy variable = 1 if patient was diagnosed as dementia, 0 otherwise | 0.001 (0.000) |
| Chronic obstructive pulmonary disease | Dummy variable = 1 if patient was diagnosed as chronic obstructive pulmonary disease, 0 otherwise | 0.014 (0.001) |
| Rheumatologic disease | Dummy variable = 1 if patient was diagnosed as rheumatologic disease, 0 otherwise | 0.004 (0.001) |
| Peptic ulcer disease | Dummy variable = 1 if patient was diagnosed as peptic ulcer disease, 0 otherwise | 0.073 (0.002) |
| Diabetes complicated | Dummy variable = 1 if patient was diagnosed as diabetes complicated, 0 otherwise | 0.011 (0.001) |
| Diabetes uncomplicated | Dummy variable = 1 if patient was diagnosed as diabetes uncomplicated, 0 otherwise | 0.294 (0.004) |
| Hemiplegia or paraplegia | Dummy variable = 1 if patient was diagnosed as hemiplegia or paraplegia, 0 otherwise | 0.001 (0.000) |

(Continued)
indicated whether the patient \(i\) underwent a major procedure (i.e., hepatectomy or TACE); \(L_i\), which referred to the common types of liver disease including hepatitis B and C, alcoholic hepatitis, fatty liver, cirrhosis, and PLC (all were included as separate dummy variables); as well as \(X_i\), a vector of patient-level risk adjustors.

Based on our earlier study comparing the performance of various risk adjustment models for liver disease using the same data set, the model combining the liver disease severity score (i.e., the model for end-stage liver disease and sodium (MELDNa)) and comorbidity index (i.e., Elixhauser comorbidity index) as risk adjustors showed the best prediction performance [36]. Therefore, we used the following patient-level risk adjustors \((X_i)\) in our model: patient-level demographic information (age, sex, and admission status), the MELDNa score and Elixhauser comorbidity index.

We assessed the effect of RR on the hospital LOS, TC, MC, and RMT through applying a generalized linear regression model. We estimated the effect of RR on the likelihood of using TACE among cirrhosis and PLC patients using a logistic model, and the number of TACE procedures among patients who underwent at least one TACE during the study period using a

### Table 2. (Continued)

| Variable                  | Definition                                                                 | Mean (SE)   |
|---------------------------|-----------------------------------------------------------------------------|-------------|
| Renal disease             | Dummy variable = 1 if patient was diagnosed as renal disease, 0 otherwise   | 0.089 (0.003) |
| Metastatic solid tumor    | Dummy variable = 1 if patient was diagnosed as metastatic solid tumor, 0 otherwise | 0.020 (0.001) |
| AIDS                      | Dummy variable = 1 if patient was diagnosed as AIDS, 0 otherwise            | 0.005 (0.001) |
| Cardiac arrhythmias       | Dummy variable = 1 if patient was diagnosed as cardiac arrhythmias, 0 otherwise | 0.034 (0.002) |
| Valvular disease          | Dummy variable = 1 if patient was diagnosed as valvular disease, 0 otherwise | 0.002 (0.000) |
| Hypothyroidism            | Dummy variable = 1 if patient was diagnosed as hypothyroidism, 0 otherwise  | 0.007 (0.001) |
| Lymphoma                  | Dummy variable = 1 if patient was diagnosed as lymphoma, 0 otherwise        | 0.002 (0.000) |
| Blood loss anemia         | Dummy variable = 1 if patient was diagnosed as blood loss anemia, 0 otherwise | 0.141 (0.003) |
| Deficiency anemia         | Dummy variable = 1 if patient was diagnosed as deficiency anemia, 0 otherwise | 0.123 (0.003) |
| Depression                | Dummy variable = 1 if patient was diagnosed as depression, 0 otherwise      | 0.005 (0.001) |
| Psychoses                 | Dummy variable = 1 if patient was diagnosed as psychoses, 0 otherwise       | 0.002 (0.000) |
| Renal failure             | Dummy variable = 1 if patient was diagnosed as renal failure, 0 otherwise   | 0.022 (0.001) |
| solid tumor               | Dummy variable = 1 if patient was diagnosed as solid tumor, 0 otherwise     | 0.217 (0.004) |
| Hypertension uncomplicated| Dummy variable = 1 if patient was diagnosed as hypertension uncomplicated, 0 otherwise | 0.176 (0.004) |
| Hypertension complicated  | Dummy variable = 1 if patient was diagnosed as hypertension complicated, 0 otherwise | 0.101 (0.003) |
| Alcohol abuse             | Dummy variable = 1 if patient was diagnosed as alcohol abuse, 0 otherwise   | 0.177 (0.004) |

SE: standard error; RR: reimbursement ratio, RMT: ratio of medication cost to total hospital cost; LOS: length of stay at hospital; MELDNa: model for end-stage liver disease and sodium; AIDS: acquired immune deficiency syndrome; TACE: transcatheter arterial chemoembolization.

https://doi.org/10.1371/journal.pone.0187096.t002
Table 3. Effect of RR (coefficient and standard error) on hospital utilization.

| Parameter                          | LOS N = 10,102 | TACE use or not N = 4,736 | Number of TACE N = 434 |
|------------------------------------|----------------|---------------------------|------------------------|
| Intercept                          | 1.051*** (0.019) | -1.604*** (0.482) | -0.534 (1.131) |
| RR                                 | 0.131*** (0.017) | 2.330*** (0.519) | 1.511*** (0.676) |
| Age                                | 0.004*** (0.000) | 0.010** (0.005) | 0.009 (0.008) |
| Sex                                | -0.177*** (0.007) | -0.686*** (0.134) | -0.321 (0.198) |
| Admission status                   | -0.126*** (0.008) | -1.477*** (0.319) | -0.230 (0.502) |
| MELDNa score                       | -0.005*** (0.001) | -0.290*** (0.022) | -0.100*** (0.035) |
| Primary liver cancer               | 0.014* (0.008) | - | - |
| Cirrhosis                          | 0.104*** (0.007) | - | - |
| Hepatitis B                        | -0.094*** (0.008) | 0.474*** (0.146) | 0.373 (0.250) |
| Hepatitis C                        | -0.068*** (0.017) | -0.001 (0.288) | 0.114 (0.443) |
| Alcoholic hepatitis                | -0.031 (0.019) | -1.706*** (0.464) | 0.219 (0.719) |
| Combined hepatitis (B, C or alcoholic) | 0.013 (0.015) | -0.191 (0.280) | 1.399*** (0.444) |
| Chronic obstructive pulmonary disease | -0.003 (0.023) | 0.049 (0.360) | -0.466 (0.517) |
| Rheumatologic disease              | 0.004 (0.042) | 0.467* (0.702) | -1.215 (1.053) |
| Peptic ulcer disease               | 0.081*** (0.011) | -0.412** (0.170) | -0.101 (0.261) |
| Diabetes complicated               | -0.038 (0.028) | -0.881 (0.552) | -0.078 (0.878) |
| Diabetes uncomplicated              | 0.032*** (0.007) | 0.183 (0.114) | 0.424** (0.166) |
| Renal disease                       | 0.040*** (0.012) | 0.175 (0.196) | 0.134 (0.305) |
| Metastatic solid tumor             | -0.005 (0.020) | -0.553 (0.451) | -0.376 (0.700) |
| Cardiac arrhythmias                | 0.001 (0.015) | -0.283 (0.267) | -0.028 (0.404) |
| Hypothyroidism                     | 0.073** (0.032) | -0.356 (0.630) | 2.546*** (0.958) |
| Blood loss anemia                  | 0.040** (0.019) | -0.091 (0.364) | 0.339 (0.601) |
| Deficiency anemia                  | -0.015 (0.020) | -0.617 (0.435) | -0.802 (0.715) |
| Depression                         | 0.024 (0.040) | -0.361 (0.754) | 0.152 (1.274) |
| Renal failure                      | 0.005 (0.021) | 0.886*** (0.332) | -0.163 (0.477) |
| Solid tumor                         | -0.003 (0.008) | 1.002** (0.404) | -0.204 (0.536) |

(Continued)
negative binomial regression model. The effect of RR on the hospital mortality was analyzed using a logistic regression model (Table 1).

**Results**

As shown in Table 2, the mean age of our study sample was 46 years old, and 49.0% (5,313) of the study population was male. Urgently admitted patients account for 13.9% (1,508). 4.9% (527) patients underwent hepatectomy or TACE. RR ranged from 0.1 to 1.0, and the average RR of the patients was 0.68 (SD 0.19). Among the 10,858 liver disease patients, 20.4% (2,219) had PLC, 34.4% (3,734) had cirrhosis, and 83.8% (9,094) had hepatitis. Among the 4,736 cirrhosis and/or PLC patients, 434 underwent TACE. The five most common comorbidities were: diabetes (with or without complications) 30.5% (3,212), hypertension (complicated or uncomplicated) 27.8% (3,015), anemia (blood loss or deficient) 26.4% (2,861), solid tumors 21.7% (2,357), and alcohol abuse 17.7% (1,926). The mean MELDNa score of the liver disease patients was 11.5 (SD 4.9). The overall in-hospital mortality was 5.5% (600), the mean LOS was 20 days (SD 21 days), the average total cost was 28,908.3 (SD 44,249.2) RMB, the mean medication cost was 17,035.1 (SD 27,259.0) RMB and the mean RMT was 0.49 (SD 0.19).

As shown in Table 3, after adjusting for liver disease severities, comorbidities and major procedures, the RR was found to be significantly correlated with LOS (1.051, p < 0.0001): patients with higher RR (i.e., more generous insurance coverage) were found to stay longer in hospital. Specifically, every 10% increase of RR was related to a 3% increase of LOS. We analyzed the effect of RR on the use of TACE among patients with PLC and/or cirrhosis including two outcomes: use or not and number of TACE. As presented in Table 4, our results showed that after adjusting for demographics and case mix, patients with a higher RR were significantly more likely to undergo TACE than patients with a lower RR (2.330, p < 0.0001), and also tended to have higher number of TACE (1.511, p = 0.025). This means that every 10% increase of RR is associated with a 0.15 increase in the number of TACE and a 30% increase of

Table 3. (Continued)

| Parameter                  | LOS | TACE use or not | Number of TACE |
|----------------------------|-----|-----------------|----------------|
| N = 10,102                 |     |                 |                |
| Hypertension uncomplicated | 0.018* (0.011) | 0.060 (0.169) | 0.177 (0.245) |
| Hypertension complicated   | -0.012 (0.013) | 0.021 (0.205) | 0.136 (0.289) |
| Alcohol abuse              | -0.061*** (0.015) | 0.201* (0.299) | -1.068*** (0.453) |
| Hepatectomy                | 0.120*** (0.031) | -1.351*** (0.474) | -0.980 (0.736) |
| TACE                       | 0.097*** (0.015) | - | - |

c-statistic = 0.809

SE: standard error; RR: reimbursement ratio, RMT: ratio of medication cost to total hospital cost; LOS: length of stay at hospital; MELDNa: model for end-stage liver disease and sodium; AIDS: acquired immune deficiency syndrome; TACE: transcatheter arterial.

^ TACE is only for primary liver cancer and cirrhosis patients, so the primary liver cancer and cirrhosis are excluded when modeling the TACE use and the number of TACE

*** indicates that coefficient is significant at 1% level
** indicates that coefficient is significant at 5% level; and
* indicates that coefficient is significant at 10% level.

https://doi.org/10.1371/journal.pone.0187096.t003
Table 4. Effect of RR (coefficient and standard error) on hospital cost.

| Parameter                               | Total cost         | Medication cost    | MTratio         |
|-----------------------------------------|--------------------|--------------------|-----------------|
| **N = 10858**                           | **N = 10858**      | **N = 10858**      |                 |
| Intercept                               | 3.655*** (0.019)  | 2.815*** (0.044)  | -0.773*** (0.025) |
| RR                                      | 0.049*** (0.017)  | 0.566*** (0.038)  | 0.439*** (0.022)  |
| Age                                     | 0.004*** (0.001)  | 0.003*** (0.001)  | -0.001** (0.000)  |
| Sex                                     | -0.096*** (0.007) | -0.099*** (0.016) | -0.016 (0.009)   |
| Admission status                        | 0.020** (0.009)   | 0.065*** (0.02)   | 0.036*** (0.011)  |
| Primary liver cancer                    | 0.224*** (0.009)  | 0.237*** (0.077)  | 0.030** (0.012)  |
| Cirrhosis                               | 0.159*** (0.008)  | 0.055 (0.037)     | 0.073*** (0.010)  |
| Hepatitis B                             | -0.008 (0.009)    | 0.006 (0.02)      | 0.004 (0.011)    |
| Hepatitis C                             | -0.030* (0.018)   | -0.036 (0.041)    | -0.014 (0.023)   |
| Alcoholic hepatitis                     | 0.001 (0.021)     | 0.011 (0.046)     | -0.004 (0.026)   |
| Combined hepatitis (B, C or alcoholic)  | -0.006 (0.016)    | -0.011 (0.035)    | -0.015 (0.020)   |
| Hepatectomy                             | 0.249*** (0.034)  | 0.240*** (0.017)  | -0.016 (0.044)   |
| MELDNa score                            | -0.001* (0.001)   | 1.030*** (0.307)  | -0.001 (0.001)   |
| Chronic obstructive pulmonary disease   | 0.024 (0.025)     | 0.06 (0.056)      | 0.031 (0.032)    |
| Rheumatologic disease                   | 0.029 (0.046)     | -0.084 (0.104)    | -0.064 (0.059)   |
| Peptic ulcer disease                    | 0.087*** (0.012)  | 0.121*** (0.027)  | 0.034*** (0.015)  |
| Diabetes complicated                    | -0.062** (0.029)  | -0.125* (0.066)   | -0.056 (0.038)   |
| Diabetes uncomplicated                  | 0.084*** (0.007)  | 0.128*** (0.016)  | 0.036*** (0.009)  |
| Renal disease                           | 0.070*** (0.012)  | 0.061** (0.028)   | -0.010 (0.016)   |
| Metastatic solid tumor                  | 0.02 (0.021)      | 0.083* (0.048)    | 0.053* (0.027)   |
| Cardiac arrhythmias                     | -0.001 (0.017)    | 0.004 (0.037)     | 0.000 (0.021)    |
| Hypothyroidism                          | 0.036 (0.035)     | 0.068 (0.078)     | 0.030 (0.045)    |
| Blood loss anemia                       | 0.206*** (0.02)   | 0.265*** (0.046)  | 0.056** (0.026)  |
| Deficiency anemia                       | -0.035 (0.022)    | 0.002 (0.049)     | 0.026 (0.028)    |
| Depression                              | 0.025 (0.041)     | 0.052 (0.094)     | 0.019 (0.053)    |
| Renal failure                           | 0.033 (0.023)     | -0.015 (0.051)    | -0.046 (0.029)   |

(Continued)
the odds of undergoing TACE. Our results show that in-hospital utilization for liver disease patients, with both demographics and case mix adjusted for, is consistently and significantly higher for patients with more generous insurance coverage.

After adjusting for patient characteristics and case mix, RR is also significantly associated with total inpatient cost: patients with higher RR had a higher total hospital cost versus patients with a lower RR ($0.049, p < 0.0001$) (Table 4). In addition, patients with a higher RR were found to incur significantly higher medication costs ($0.566, p < 0.0001$). For patients with a higher RR, percentage of medication cost in their total inpatient cost (RMT) was also significantly higher ($0.439, p < 0.0001$) after adjusting for other factors. In other words, when RR increases 0.1 (e.g., from 0.1 to 0.2), the total hospital cost, medication cost, and percentage of medication cost of total cost increases 1.0%, 10.0%, and 10.0%, respectively.

After adjusting for the disease severity, comorbidities and major procedures (such as hepatectomy and TACE), RR was not found to be significantly associated with patient outcome, measured by in-hospital mortality ($p = 0.08$, OR $1.87$, 95% CI: $0.92–3.81$) (See Table 5). Patient cost sharing did not seem to have led to significant differences in outcome among patients with different insurance coverage, as measured by in-hospital mortality. This result indicates that financial incentives may not impact the life-threatening outcomes (such as death) given that mortality is mainly related to clinical factors and health providers and patients reactions to financial incentives do not aim to and are not able to change such a disease outcome.

### Discussion

Using rich EMR data with detailed clinical and financial information from China on inpatients with liver disease, our results showed that after controlling for patient characteristics and case mix, patients with more generous health insurance coverage were found to have significantly higher LOS, higher total hospital cost, higher medication cost, higher ratio of medication cost, higher likelihood of having TACE performed and a higher number of TACE performed.

Addressing some of the limitations in former studies, our study contributes to the existing
| Parameter                                      | Estimate (SE)     | Odds Ratio (95% CI)  |
|-----------------------------------------------|-------------------|---------------------|
| Intercept                                     | -8.964*** (0.387) | 1.872 (0.92–3.808)  |
| RR                                            | 0.627** (0.362)   | 1.46 (1.038–1.055)  |
| Age                                           | 0.045*** (0.004)  | 1.046 (1.038–1.055) |
| Male                                          | -0.476*** (0.121) | 0.621 (0.49–0.788)  |
| Admission status                              | 0.33*** (0.126)   | 1.391 (1.087–1.779) |
| Hepatitis B                                   | -0.087 (0.130)    | 0.917 (0.711–1.183) |
| Hepatitis C                                   | -0.218 (0.286)    | 0.804 (0.459–1.409) |
| Alcoholic hepatitis                           | -0.858** (0.352)  | 0.424 (0.213–0.846) |
| Combined hepatitis (B,C or alcoholic)         | -1.057*** (0.296) | 0.348 (0.195–0.621) |
| MELDNa score                                  | 0.184*** (0.010)  | 1.202 (1.179–1.226) |
| Cirrhosis                                     | 0.254** (0.111)   | 1.29 (1.038–1.603)  |
| Primary liver cancer                          | 1.422*** (0.111)  | 4.147 (3.334–5.159) |
| Chronic obstructive pulmonary disease         | -0.219 (0.306)    | 0.803 (0.441–1.464) |
| Rheumatologic disease                         | -0.919 (0.684)    | 0.399 (0.104–1.524) |
| Peptic ulcer disease                          | -0.148 (0.159)    | 0.862 (0.631–1.178) |
| Diabetes uncomplicated                        | -0.932** (0.407)  | 0.394 (0.177–0.875) |
| Diabetes complicated                          | 0.398*** (0.104)  | 1.489 (1.215–1.824) |
| Renal disease                                 | 0.657*** (0.132)  | 1.928 (1.488–2.499) |
| Metastatic solid tumor                        | 0.211 (0.316)     | 1.234 (0.665–2.292) |
| Cardiac arrhythmias                           | 0.247 (0.19)      | 1.281 (0.882–1.858) |
| Hypothyroidism                                | 0.857*** (0.410)  | 2.357 (1.055–5.267) |
| Blood loss anemia                             | 1.266*** (0.201)  | 3.546 (2.392–5.257) |
| Deficiency anemia                             | -0.795*** (0.227) | 0.452 (0.289–0.705) |
| Depression                                    | -0.182 (0.580)    | 0.833 (0.268–2.594) |
| Renal failure                                 | 0.346* (0.201)    | 1.414 (0.954–2.097) |
| Solid tumor                                   | 0.376 (0.443)     | 1.456 (0.612–3.468) |
| Hypertension uncomplicated                    | -0.041 (0.166)    | 0.959 (0.693–1.328) |

(Continued)
literature by providing clear empirical evidence for the potential impact of patient cost-sharing on health care utilization, cost and outcome.

The current health system in China provides strong financial incentives for physicians to make decisions based not only on patient health status (i.e., with or without insurance) but also the generosity of patient health insurance coverage. Our findings are consistent with the Rand Health Insurance Experiment (HIE) which demonstrated the effect of patient cost-sharing on the use of health care, except that the observed effect of patient cost-sharing on health care utilization and cost in our study may be explained by a joint effect of not only demand but also supply side moral hazard.

The unique health insurance system in China has allowed us to study the impact of patient cost-sharing in a setting where there are large variations in insurance coverage and limited selection bias in insurance plan choice. The validity of this study was also greatly enhanced by the use of actual reimbursement ratio and through employing a robust risk adjustment method which was validated in our previous study [36]. This risk adjustment method considered the important risk factors for health care utilization, cost and outcome including patient disease severity and comprehensive comorbidities.

Our study has a few limitations. First, generalizability of the study result may be a concern, given that we only used EMR data from one hospital. Moreover, in this retrospective observational study the variation of RR may not be entirely random and might contribute to potential selection bias. However, YouAn hospital is a well-known liver disease-specializing hospital treating patients from all regions of China. Such wide geographic coverage would mitigate any potential selection bias. Second, the EMR data contained large amounts of missing values in demographic and socioeconomic data such as income level, education and employment status. As a result, these potential confounding factors were not adjusted in our analyses. Third, using only one hospital’s data may not capture all the hospitalizations for one patient if the patient was admitted to other hospitals during the study period. This may affect the analysis on TACE use if the patient had undergone TACE in another hospital. However, this situation may not count for a large proportion among the sample, given that YouAn hospital is one of the leading liver disease centers with very high volume of TACE treatments and attracts a lot of liver diseases patients who are specifically seeking this treatment. Finally, our results indicated that patient cost-sharing did not lead to significant differences in patient outcomes. However, our

### Table 5. (Continued)

| Parameter              | Estimate (SE) | Odds Ratio (95% CI) |
|------------------------|---------------|---------------------|
| Hypertension complicated | -0.374*       | 0.688 (0.468–1.012) |
| Alcohol abuse          | 0.645**       | 1.906 (1.041–3.491) |
| Hepatectomy            | -1.451        | 0.234 (0.032–1.735) |
| TACE                   | -0.498**      | 0.607 (0.381–0.969) |
| Model diagnostics      | N = 10858     | c-statistic = 0.915 |

SE: standard error; CI: confidence interval; RR: reimbursement ratio, RMT: ratio of medication cost to total hospital cost, LOS: length of stay at hospital, MELDNa: model for end-stage liver disease and sodium, AIDS: acquired immune deficiency syndrome, TACE: transcatheater arterial.

*** indicates that coefficient is significant at 1% level;
** indicates that coefficient is significant at 5% level; and
* indicates that coefficient is significant at 10% level.

https://doi.org/10.1371/journal.pone.0187096.t005
outcome measure only included in-hospital mortality, which did not capture long term disease outcomes.

**Conclusion**

In summary, our study implied that patient cost-sharing affects health care use and cost. This reflects how patients and physicians respond to financial incentives in the current healthcare system in China, and could be a joint effect of both demand and supply side moral hazard. In order to contain cost and improve efficiency in the system, reforming provider payment and insurance coverage is urgently needed.

**Acknowledgments**

The authors thank Dr. Guanmin Chen from Alberta Health Service (AHS) and Libin Cardiovascular Institute of Alberta and Dr. Mingfu Liu from Alberta Health Service (AHS) for their supports on data mining and analysis.

**Author Contributions**

**Conceptualization:** Yuan Xu, Ning Li, Mingshan Lu, Elijah Dixon, Robert P. Myers, Rachel J. Jelley, Hude Quan.

**Data curation:** Yuan Xu, Mingshan Lu, Rachel J. Jelley, Hude Quan.

**Formal analysis:** Yuan Xu, Ning Li, Mingshan Lu, Elijah Dixon, Rachel J. Jelley, Hude Quan.

**Methodology:** Yuan Xu, Ning Li, Mingshan Lu, Elijah Dixon, Robert P. Myers, Rachel J. Jelley, Hude Quan.

**Project administration:** Yuan Xu.

**Supervision:** Ning Li, Mingshan Lu, Elijah Dixon, Robert P. Myers, Hude Quan.

**Validation:** Ning Li, Mingshan Lu, Elijah Dixon, Robert P. Myers, Rachel J. Jelley, Hude Quan.

**Writing – original draft:** Yuan Xu, Mingshan Lu, Rachel J. Jelley, Hude Quan.

**Writing – review & editing:** Yuan Xu, Ning Li, Mingshan Lu, Elijah Dixon, Robert P. Myers, Rachel J. Jelley, Hude Quan.

**References**

1. **Powell-Jackson T, Yip WC, Han W.** Realigning demand and supply side incentives to improve primary health care seeking in rural China. Health economics. 2015; 24(6):755–72. https://doi.org/10.1002/hec.3060 PMID: 24807650.

2. **Ginsburg PB.** Achieving health care cost containment through provider payment reform that engages patients and providers. Health affairs. 2013; 32(5):929–34. https://doi.org/10.1377/hlthaff.2012.1007 PMID: 23650327.

3. **Ginsburg PB.** Reforming provider payment—the price side of the equation. The New England journal of medicine. 2011; 365(14):1268–70. https://doi.org/10.1056/NEJMp1107019 PMID: 21991947.

4. **Van de Voorde C, Van Doorslaer E, Schokkaert E.** Effects of cost sharing on physician utilization under favourable conditions for supplier-induced demand. Health economics. 2001; 10(5):457–71. https://doi.org/10.1002/hec.631 PMID: 11466806.

5. **Culyer AJ NJ.** Handbook of health economics. 1st ed. Amsterdam; New York: Elsevier; 2000.

6. **Mort EA, Edwards JN, Emmons DW, Convery K, Blumenthal D.** Physician response to patient insurance status in ambulatory care clinical decision-making. Implications for quality of care. Medical care. 1996; 34(8):783–97. PMID: 8709660.
7. Ma J, Lu M, Quan H. From a national, centrally planned health system to a system based on the market: lessons from China. Health affairs. 2008; 27(4):937–48. https://doi.org/10.1377/hlthaff.27.4.937 PMID: 18607026.

8. Borah BJ, Burns ME, Shah ND. Assessing the impact of high deductible health plans on health-care utilization and cost: a changes-in-changes approach. Health economics. 2011; 20(9):1025–42. https://doi.org/10.1002/hec.1757 PMID: 21630375.

9. Winkelmann R. Co-payments for prescription drugs and the demand for doctor visits—evidence from a natural experiment. Health economics. 2004; 13(11):1081–9. https://doi.org/10.1002/hec.868 PMID: 15386685.

10. Chang GM, Cheng SH, Tung YC. Impact of cuts in reimbursement on outcome of acute myocardial infarction and use of percutaneous coronary intervention: a nationwide population-based study over the period 1997 to 2008. Medical care. 2011; 49(12):1054–61. https://doi.org/10.1097/MLR.0b013e318235382b PMID: 22009149.

11. Remler DK, Atherly AJ. Health status and heterogeneity of cost-sharing responsiveness: how do sick people respond to cost-sharing? Health economics. 2003; 12(4):269–80. https://doi.org/10.1002/hec.725 PMID: 12652514.

12. Devlin SS R.A. Do physician remuneration schemes matter? The case of Canadian family physicians. J. Health Econ., 2008; 27 (5), pp. 1168–1181. https://doi.org/10.1016/j.jhealeco.2008.05.006 PMID: 18563431.

13. Manning WG, Newhouse JP, Duan N, Keeler EB, Leibowitz A, Marquis MS. Health insurance and the demand for medical care: evidence from a randomized experiment. The American economic review. 1987; 77(3):251–77. PMID: 10284091.

14. Group NJaTIE. Free for all? Lessons from the Rand Health Insurance Experiment. Harvard University Press: Cambridge, MA, 1993.

15. Yip W, Powell-Jackson T, Chen W, Hu M, Fe E, Hu M, et al. Capitation combined with pay-for-performance improves antibiotic prescribing practices in rural China. Health affairs. 2014; 33(3):502–10. https://doi.org/10.1377/hlthaff.2013.0702 PMID: 24572187.

16. Wang H, Zhang L, Yip W, Hsiao W. An experiment in payment reform for doctors in rural China reduced some unnecessary care but did not lower total costs. Health affairs. 2011; 30(12):2427–36. https://doi.org/10.1377/hlthaff.2010.0573 PMID: 22147872.

17. Huang H, Hu XF, Zhao FH, Garland SM, Bhatia N, Qiao YL. Estimation of Cancer Burden Attributable to Infection in Asia. Journal of epidemiology / Japan Epidemiological Association. 2015; 25(10):626–38. https://doi.org/10.2188/jea.JE20140215 PMID: 26399446; PubMed Central PMCID: PMC4626392.

18. Liang X, Bi S, Yang W, Wang L, Cui G, Cui F, et al. Epidemiological serosurvey of hepatitis B in China—declining HBV prevalence due to hepatitis B vaccination. Vaccine. 2009; 27(47):6550–7. https://doi.org/10.1016/j.vaccine.2009.08.048 PMID: 19729084.

19. Bao XY, Xu BB, Fang K, Li Y, Hu YH, Yu GP. Changing trends of hospitalisation of liver cirrhosis in Beijing, China. BMJ open gastroenterology. 2015; 2(1):e000051. https://doi.org/10.1136/bmjgast-2015-000051 PMID: 26629359; PubMed Central PMCID: PMC4650903.

20. Sada Y, Hou J, Richardson P, El-Serag H, Davila J. Validation of Case Finding Algorithms for Hepatocellular Cancer From Administrative Data and Electronic Health Records Using Natural Language Processing. Medical care. 2016; 54(2):e9–e14. https://doi.org/10.1097/MLR.0000000000000346 PMID: 23929403; PubMed Central PMCID: PMC3875602.

21. Williamson T, Green ME, Birtwhistle R, Khan S, Garies S, Wong ST, et al. Validating the 8 CPCSSN case definitions for chronic disease surveillance in a primary care database of electronic health records. Annals of family medicine. 2014; 12(4):367–72. https://doi.org/10.1370/afm.1644 PMID: 25024246; PubMed Central PMCID: PMC3985475.

22. Tian Z, Sun S, Equale T, Rochefort CM. Automated Extraction of VTE Events From Narrative Radiology Reports in Electronic Health Records: A Validation Study. Medical care. 2015. https://doi.org/10.1097/MLR.0000000000000346 PMID: 25924079.

23. Lei J, Sockolow P, Guan P, Meng Q, Zhang J. A comparison of electronic health records at two major Peking University Hospitals in China to United States meaningful use objectives. BMC medical informatics and decision making. 2013; 13:96. https://doi.org/10.1186/1472-6947-13-96 PMID: 23984797; PubMed Central PMCID: PMC3847100.

24. Xu Y, Wang Y, Liu T, Liu J, Fan Y, Qian Y, et al. Joint segmentation and named entity recognition using dual decomposition in Chinese discharge summaries. Journal of the American Medical Informatics Association: JAMIA. 2014; 21(e1):e84–92. https://doi.org/10.1136/amiajnl-2013-001806 PMID: 23934949; PubMed Central PMCID: PMC3957392.
25. Liu D, Wang X, Pan F, Yang P, Xu Y, Tang X, et al. Harmonization of health data at national level: a pilot study in China. International journal of medical informatics. 2010; 79(6):450–8. https://doi.org/10.1016/j.ijmedinf.2010.03.002 PMID: 20399139.

26. Yip WC, Hsiao WC, Chen W, Hu S, Ma J, Maynard A. Early appraisal of China’s huge and complex health-care reforms. Lancet. 2012; 379(9818):833–42. https://doi.org/10.1016/S0140-6736(11)61880-1 PMID: 22386036.

27. Yuan S, Liu Y, Li N, Zhang Y, Zhang Z, Tao J, et al. Impacts of health insurance benefit design on percutaneous coronary intervention use and inpatient costs among patients with acute myocardial infarction in Shanghai, China. PharmacoEconomics. 2014; 32(3):265–75. https://doi.org/10.1007/s40273-013-0079-9 PMID: 23975740.

28. Liu X, Liu Y, Lv Y, Li C, Cui Z, Ma J. Prevalence and temporal pattern of hospital readmissions for patients with type I and type II diabetes. BMJ open. 2015; 5(11):e007362. https://doi.org/10.1136/bmjopen-2014-007362 PMID: 26525716; PubMed Central PMCID: PMC4636613.

29. Zhao T, Cheng J, Chai J, Feng R, Liang H, Shen X, et al. Inpatient care burden due to cancers in Anhui, China: a cross-sectional household survey. BMC Public Health. 2016; 16(1):1471–2458;308. https://doi.org/10.1186/s12889-016-2995-z PMID: 27067524.

30. Yip W HW. China’s health care reform: a tentative assessment. China Econ Rev 2009; 20: 613–19.

31. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, Zhou M, et al. Rapid health transition in China, 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet. 2013; 381(9882):1987–2015. https://doi.org/10.1016/S0140-6736(13)61097-1 PMID: 23746901.

32. https://www.atkearney.com/documents/10192/265152/Chinas_Pharmaceutical_Distribution.pdf. Accessed on October 17, 2016.

33. Roayaie S. TACE vs. surgical resection for BCLC stage B HCC. Journal of hepatology. 2014; 61(1):3–4. https://doi.org/10.1016/j.jhep.2014.04.005 PMID: 24727122.

34. Farinati F, Giacomini A, Vanin Y, Giannini E, Trevisani F. TACE treatment in hepatocellular carcinoma: what should we do now? Journal of hepatology. 2012; 57(1):221–2. https://doi.org/10.1016/j.jhep.2011.12.022 PMID: 22286000.

35. Xu Y, Li N, Lu M, Myers RP, Dixon E, Walker R, et al. Development and validation of method for defining conditions using Chinese electronic medical record. BMC Med Inform Decis Mak. 2016; 16:110. https://doi.org/10.1186/s12911-016-0348-6 PMID: 27542973; PubMed Central PMCID: PMC4992264.

36. Xu Y, Li N, Lu M, Dixon E, Myers RP, Jolley RJ, et al. Comparison of risk adjustment methods in patients with liver disease using electronic medical record data. BMC gastroenterology. 2017; 17(1):5. https://doi.org/10.1186/s12876-016-0559-4 PMID: 28061757; PubMed Central PMCID: PMC5219741.