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Can we predict how much government investments on health reduce households incurring catastrophic out-of-pocket health expenditure? A systematic review and longitudinal data analysis of 72 low- and middle-income countries

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An abstract of
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Abstract

Can we predict how much government investments on health reduce households incurring catastrophic out-of-pocket health expenditure? A systematic review and longitudinal data analysis of 72 low- and middle-income countries

By Taketo Tanaka

Reducing households incurring catastrophic out-of-pocket health expenditure (CHE) in low- and middle-income countries (LMICs) is a key measurement with respect to moving towards universal health coverage (UHC). It is not well-known how much governments should mobilize their budgets to the health sector to reduce the proportion of households with CHE. We examined the association between general government health expenditure (GGHE) and the incidence of CHE in LMICs. Our outcome, the incidence of CHE, was defined as any out-of-pocket (OOP) health payments exceeding 40% of household non-subsistence expenditure. We searched the following databases in June 2016: CENTRAL; MEDLINE; EMBASE; SCI-Expanded; SSCI; A&HCI; CCR-Expanded; and IC. We included studies that ensure national-level representation in the estimated incidences of CHE. Our exposure was GGHE as a share of gross domestic product (GDP). We extracted data of the exposure and potential confounders from the following databases: World Health Organization (WHO) Global Health Expenditure Database (GHED), WHO Global Health Observatory (GHO), and World Bank Open Data. We collected 39 articles that estimated 142 incidences of CHE and data of 18 potential covariates. We fit linear mixed effect models and general estimating equation (GEE) models to estimate coefficients of the incidence of CHE adjusted for six confounders. There were significant declines of the incidence of CHE associated with the increase of GGHE as a share of GDP in the mixed effect model (coefficient: -0.250, standard error (SE) 0.118, p-value: 0.037) and the GEE model (coefficient: -0.346, SE 0.102, p-value: 0.001). Although non-random selection of countries and mismeasurement of CHE may cause biases, the estimated coefficient will potentially be able to predict percent reduction in the incidence of CHE depending on the amount of GGHE in LMICs.

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First of all, the corresponding author would like to express my gratitude to Dr. Deborah A. McFarland, my thesis advisor and an Associate Professor at the Hubert Department of Global Health, Rollins School of Public Health, Emory University for her cordial assistance in my academic life. The authors acknowledge Dr. David Kleinbaum, a professor at the Department of Epidemiology, Rollins School of Public Health, Emory University for his teaching and valuable advice about statistical analysis. We appreciate Dr. Momoe Takeuchi, a team leader of Health Systems Development at the WHO Representative Office in Cambodia, for her insights to develop our research question. We also thank to Mr. Eijiro Murakoshi, a former consultant at the WHO Representative Office in Cambodia, for his inputs of knowledge about health financing in LMICs. Lastly, we would like to say thank you to all the original investigators who ever made great efforts to estimate the incidences of CHE in their respective countries.

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Chapter 1: Introduction

Rationale

The Sustainable Development Goals (SDGs) were adopted at the United Nations Sustainable Development Summit on September 25th, 2015. As described in Target 3.8 of the SDGs, more than 150 countries agreed to move their health systems towards universal health coverage (UHC) (United Nations, 2015). One of the main objectives of UHC is to protect people from financial burden due to use of health services. In order to monitor how health system effectively prevent people's health related financial difficulties in each country, the World Health Organization (WHO) and World Bank (WB) introduced an indicator called *catastrophic out-of-pocket health expenditure (CHE)* (World Health Organization & World Bank Group, 2015). The countries that signed the SDGs are responsible for tracking the incidence of CHE for the next 15 years and transforming health systems to reduce the proportion of households incurring CHE in their countries.

For the purpose of moving towards UHC, many low- and middle-income countries (LMICs) are expected to mobilize an increase in government budgets for the health sector. However, the adequate amount of investment needed is not well-known or documented. The previous agreements such as the Abuja Declaration encourage LMICs to allocate a higher proportion of their domestic government budgets for health but did not specify the target proportion of their domestic budgets (Organization of African Unity, 2001). The World Health Report 2010 also emphasized that governments of LMICs should optimize their shares of total government expenditure on health but did not mention what the ideal budget allocation was (World Health Organization, 2010). Thus, those governments do not know how many households are protected from CHE if the governments spend more money on health.

Therefore, it will be helpful for policy makers in LMICs if there is evidence to predict the relationship between government health expenditures and CHE in a given country and whether an increase in government health expenditure reduces the incidence of CHE in a given country.

Aims and objectives

The aim of this research is to quantify the association between general government health expenditure (GGHE) as a share of gross domestic product (GDP) and the fraction of households facing CHE in LMICs. In order to achieve this aim, there are several objectives:

1. To identify original studies that presented the incidence of CHE systematically;
2. To identify covariates to estimate an unbiased effect between the incidence of CHE and GGHE as percentage of GDP;
3. To examine the magnitude of the association between GGHE as GDP and the proportion of households incurring CHE in LMICs, adjusting for confounders;
4. To examine if there is heterogeneity of the estimated effects across countries.

In the previous literature, Xu and colleagues used total health expenditure (THE) as a share of GDP as the predictor variable and fit a linear regression model to estimate the association with the proportion of households with CHE. However, they used it as a proxy of health services utilization because THE would increase if out-of-pocket (OOP) payments increases in a given country (Xu et al., 2003). Instead of THE as a share of GDP, we will use GGHE as a share of GDP to fit statistical models. Xu and colleagues also showed a scatterplot

between the incidences of CHE and GGHE as percentage of GDP in another paper (Xu et al., 2010). However, they did not seem to fit any models between these two variables, which we will intend to do in our study.

This research will not be able to guarantee causal relationship between CHE and CCHE because this is an observational study. However, the evidence from our analysis might provide support for policy makers to forecast costs of reducing number of people that experience financial burden due to health services. Policy makers will be able to develop more reasonable budgets and have a strong case for advocacy with key stakeholders.

Definition of terms

In this research, universal health coverage (UHC) is defined as ensuring access to adequate health services for all the population in a given country without any financial hardship of people. Out-of-pocket (OOP) payment is defined as direct payments to health care providers by patients at the time they utilize health services. Catastrophic out-of-pocket health expenditure (CHE) is defined as any OOP health payments that exceed a given fraction of a household expenditure (World Health Organization & World Bank Group, 2015). More details of these terms and related issues are discussed in Chapter 2.

Chapter 2: Literature Review

Sustainable Development Goals and universal health coverage

Following the success of the Millennium Development Goals (MDGs), the 17 Sustainable Development Goals (SDGs) in the 2030 Agenda for Sustainable Development were adopted at the United Nations Sustainable Development Summit on September 25th, 2015. More than 150 countries will plan and execute actions to promote economic, social, and environmental development by following these 17 goals with 169 targets over the next 15 years. As reflected in Goal 3, Target 3.8, of the SDGs, transforming health systems towards universal health coverage (UHC) has now become one of the top global priorities.

"Achieve universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality and affordable essential medicines and vaccines for all" (United Nations, 2015)

UHC is defined as providing sufficient and quality health services to all the population without fiscal hardship of people. The health services here include not only diagnosis and treatment of illness but also health promotion, personal preventive services, rehabilitation and palliative care (World Health Organization & World Bank Group, 2015). This concept drew global attention when it was introduced in the World Health Report 2010, entitled "Health systems financing: the path to universal coverage" (World Health Organization, 2010). Additionally, on December 12th of 2012, the United Nations adopted a resolution to encourage countries moving forward to UHC during its General Assembly (United Nations, 2012). The SDGs fundamentally adhered to this resolution.

The form of UHC substantially differs among countries depending on epidemiological, demographic, and socioeconomic circumstances. However, there is a common concept called the "three dimensions" of coverage cube, which was initially emphasized in the World Health Report 2010 (Figure 1). The first dimension is population coverage, which indicates the proportion of the population in a country to be covered by health systems. The second dimension is service coverage, which denotes the range of services to be covered by health systems. The last dimension is financial coverage, which describes the fraction of total health care costs to be compensated by health systems. The box located at the center of the three dimensions is labeled "current pooled funds," which represents that the current coverage is maintained by pooled money (World Health Organization, 2010). Overall, a health system is expected to insure more people, cover more services, and draw from pooled money instead of charging people large out-of-pocket (OOP) payments.

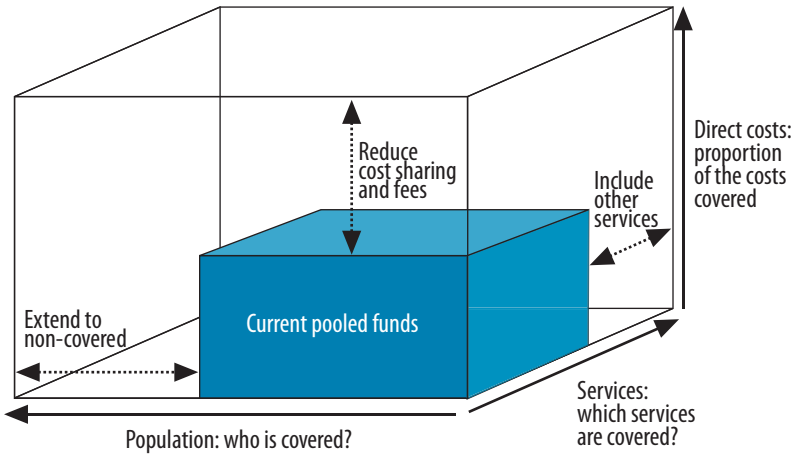

Figure 1: Three dimensions to consider when moving towards universal coverage. Reprinted from *The World health report: health systems financing: the path to universal coverage* (p. 12), by World Health Organization, 2010, Geneva: WHO Press.

Relying on OOP payments to access health services is discouraged in terms of

financial protection, especially for poor households. OOP payment is defined as direct payment to health care providers by patients at the time they utilize health services. If people without financial protection sought care, they could be impoverished by large OOP spending that they must pay. Although the rich can pay by cash, the poor might sell their assets such as lands or livestock, essential for them to earn livings. Moreover, poorer people may avoid seeking care when they are ill, which could lead to worse health outcomes such as higher morbidity and mortality in a country (World Health Organization, 2000). Unfortunately, OOP payment is still the main source of financing health systems in many low- and middle-income countries. A report from the WHO indicates that 48 countries from Latin America, the Middle East, and South East Asia have at least 45% of OOP expenditure as a share of total health expenditure (THE). This report also reveals that the average percentage of OOP payments of countries in the South East Asian region accounted for 50% of THE in 2013 (World Health Organization & World Bank Group, 2015).

The primary focus of financial protection in the context of UHC is to reduce large OOP payment from people when they receive health services so that they can avoid impoverishment. The previous literature suggests that prepayment mechanisms to fund health systems, either social health insurance or tax-based systems, should be applied to every country with high OOP health expenditure (Xu et al., 2007). The term *prepayment* indicates that financial contributions for illness should be collected and pooled prospectively. The pooled funds are usually comprised of money from general government budgets, employers, or individuals.

Catastrophic out-of-pocket health expenditure

The key measurement to anticipate how OOP payments cause financial hardship of

people in a country is called catastrophic health expenditure (CHE). The term *catastrophic* health expenditure was initially introduced in the World Health Report 2000. Dr. Brundtland, the then Director-General of the WHO, emphasized that fairness of financial contribution was a key to construct equitable health systems as it referred to protecting people against extensive costs of illness (World Health Organization, 2000). Any OOP payments related to healthcare can be called "catastrophic" if they exceed a given fraction of a household's expenditure (Kawabata, Xu, & Carrin, 2002). The proportion of households in a country facing CHE should be calculated and followed to benchmark the performance of health systems. The framework to monitor progress towards UHC jointly created by the WHO and the World Bank stated that financial protection in terms of CHE should be achieved for all the population (World Health Organization & World Bank Group, 2014).

One issue related to CHE is that the definition of CHE varies. Indicators calculated by different methods are not comparable, which makes it difficult to conduct cross-country analyses. There are two methodologies that are commonly used in many peer-reviewed journals. The most common definition of CHE is the fraction of households for which health-related spending exceeds 40% of their capacity-to-pay (CTP) in a country. The CTP is defined as a household's non-subsistence spending, which is usually calculated by subtracting household food expenditure from total household expenditure. This definition was introduced in the working paper from the Evidence and Information of Policy (EIP) cluster of the Department of Health System Financing, WHO in 2005 (Xu, 2005). As a result, it was the most frequently used definition found in our literature review.

The second most common definition is the proportion of households in a country for which health-related spending exceeds 25% of their total household expenditure. The strength of

this method is its ease of calculation compared with the former definition. This definition is expected to become popular because the World Bank has used it in recent papers to track the progress of UHC (Wagstaff, Cotlear, Eozenou, & Buisman, 2016). However, some literature reported the incidence of CHE by using different benchmarks such as 10%, 15%, 20% of total household expenditure, which made them impossible to compare with each other (World Health Organization & World Bank Group, 2015).

Furthermore, the proportion of households facing CHE is primarily reported by using population representative samples of nationwide household surveys, which means one proportion for one country each year. However, some researchers used survey data that only included patients with specific illnesses or socioeconomic characteristics in order to estimate the incidence of CHE. For example, Che and colleagues calculated the incidence of CHE for those infected with Hepatitis B (Che et al., 2016). Karami and colleagues estimated the fraction of households with CHE for those living in eastern Iran, which was underserved as well as rural (Karami, Najafi, & Karami Matin, 2009). Unfortunately, these studies were not comparable with each other.

The determinants of CHE have been assessed in many previous journal articles. Saksena et al demonstrated that the following variables, not only at household-level but also country-level, were associated with the lower incidence of CHE: 1) households with heads with a higher level of education; 2) households living in urban areas; 3) households without children under 5 years of age or elderly members; 4) lower OOP health expenditure as a share of THE; 5) less income inequality (Saksena, Xu, & Durairaj, 2010). There is conflicting evidence if the gender of household heads influences the likelihood of experiencing CHE. The studies published by Adisa, Akinkugbe et al, Dyer et al, Tran, and Ukwajua et al suggested that female-headed

households were less likely to suffer CHE, whereas the studies by Jan (2015) and Negin et al showed an opposite result (Adisa, 2015; Akinkugbe, Chama-Chiliba, & Tlotlego, 2012; Dyer, Sherwood, McIntyre, & Ataguba, 2013; Jan, Kimman, Peters, & Woodward, 2015; Negin et al., 2016; Tran et al., 2013; Ukwaja, Alobu, Abimbola, & Hopewell, 2013). There are also conflicting results whether enrolling in a kind of financial protective scheme, mostly social or community-based health insurance, demonstrates the lower probability of facing CHE. Although the majority of the articles concluded that people covered by health insurance were less likely to experience CHE than people not covered, some articles written by Goepel et al., Lu et al., Ma et al., Tripathi et al., Wang et al., and Yang et al. revealed that such schemes had no significant impact to protect people from CHE (Goeppel, Frenz, Grabenhenrich, Keil, & Tinnemann, 2016; Lu et al., 2012; Ma, Xu, Zhang, & Wang, 2016; Tripathi, Saini, & Prinja, 2014; Wang, Li, & Chen, 2015; Yang et al., 2016). This difference may be caused by the design and range of the coverage of each financial protection scheme.

Utilization of health services is significantly associated with higher risk of incurring CHE. The focus of the cause of OOP health spending differs across the respective researchers. For instance, Engelgau et al. argued that noncommunicable diseases (NCDs) such as cardiovascular diseases, cancers, or traffic injuries were associated with the higher incidence of CHE than communicable diseases, while Thuan et al. asserted that communicable diseases affected the incidence of CHE more than NCDs (Engelgau, Karan, & Mahal, 2012; Thuan, Lofgren, Chuc, Janlert, & Lindholm, 2006). Bareness et al. and Werapong et al. pointed out that indirect costs of seeking care such as transportation were more influential than direct payments for healthcare (Barennes, Frichittavong, Gripenberg, & Koffi, 2015; Weraphong, Pannarunothai, Luxananun, Junsri, & Deesawatsripetch, 2013). In addition, many researchers such as Yang et al.

claimed that hospitalized patients had a higher likelihood of facing CHE than patients only receiving outpatient care (Yang et al., 2016). There were also some researchers such as Ukwaja and colleagues who argued that seeking care at private health facilities was more likely to lead financial catastrophe rather than seeking care at public facilities (Ukwaja et al., 2013).

How CHE became important with respect to the SDGs

After the SDGs and their targets were formally approved, CHE is becoming more important to measure the progress of UHC. There are two indicators to monitor Target 3.8. The indicator 3.8.1 serves for service coverage, and the indicator 3.8.2 serves for financial protection. Initially, measuring "number of people covered by health insurance or a public health system per 1,000 population" was suggested as the indicator 3.8.2 (United Nations, 2016). However, the WHO and World Bank proposed an amendment to this indicator because it was insufficient to track how high health spending affects people's livelihood (World Health Organization, 2016). For example, only insuring people does not mean reducing their financial burden from health spending. If they are forced to pay high OOP spending, they may still face the financial burden. In addition, illness, diagnostic strategies, and treatment options will change over time. If a health insurance plan does not change its coverage simultaneously with the transition of standard care, insured people will have to pay high OOP spending for uncovered treatment options.

The newly proposed indicator is "proportion of the population with large household expenditures on health as a share of total household expenditure or income," which is equivalent to the incidence of CHE. This replacement of the indicator 3.8.2 was also supported by the representatives of civil society in the Inter-agency and Expert Group on Sustainable Development Goal Indicators (IAEG-SDGs) (Kamal-Yanni, 2016). Finally, this amendment was

approved at the fourth meeting of the IAEG-SDGs held from 17th until 18th of November 2016 in Geneva (United Nations, 2016). Consequently, the incidence of CHE especially in low- and middle-income countries has become an essential indicator to evaluate the progress of the SDGs within the next 15 years.

A case study in Thailand

With respect to fiscal protection, there are good examples how UHC can be achieved in low- and middle-income countries (LMICs). Thailand achieved UHC in 2012. Before that, there were several financial schemes to protect specific labor groups from large OOP spending for health care services. For example, the Civil Servant Medical Benefit Scheme (CSMBS), established in the 1960s, covered public sector employees and their dependents, and pensioners. The coverage accounted for 9% of total population in 2002. There is also another payer, the Social Health Insurance (SHI), established in the 1980s. The SHI insured private sector employees but not their dependents (Tangcharoensathien et al., 2015). This institution covered 16% of the total population in 2002. However, 18.5 million people out of a population of 62 million were uninsured before the early 2000s (Towse, Mills, & Tangcharoensathien, 2004).

The health sector reform to achieve UHC in Thailand was prepared in the 1990s and the National Health Security Act was passed in 2002 to establish the Universal Coverage Scheme (UCS) (Towse et al., 2004). The UCS was responsible for insuring the remaining population who were not covered by the former two schemes. The UCS was financed by the general government budget. Initially, there was a co-payment of 30 baht (about US$ 0.70) per visit or admission but it was replaced by no co-payment in November 2006 (Sathāban Wičhai Rabop Sāthāranasuk, 2012). The UCS required beneficiaries to register for certain public healthcare providers. The

UCS pays providers' service fees by capitation for outpatient care and case-based payment for inpatient care.

The consequence of this healthcare reform was notable. For example, there was a significant increase of health service utilization. The outpatient visits per member per year rose from 2.45 in 2003 to 3.22 in 2010. The hospital admissions per member per year also rose from 0.094 in 2003 to 0.116 in 2010. From the macroeconomic perspective, the THE as percentage of GDP has remained stable, between 3% and 4%. On the other hand, the OOP spending by households, which accounted for 33% of the THE in 2001, significantly decreased to 15% in 2008. 6.1% of Thai households experienced CHE in 1996, which was defined as spending on health that exceeded 10% of total household consumption, whereas it declined to around 3% in 2009 (Sathāban Wičhai Rabop Sāthāranasuk, 2012). Until now, Thailand is recognized as one of the most successful cases of UHC from middle-income countries.

A case study in Mexico

Mexico achieved UHC in 2012 (Knaul et al., 2012). Before the early 2000s, several payers covered certain populations. For instance, the Mexican Institute for Social Security (IMSS), which was established in 1943, insured private sector workers and their families (Frenk, González-Pier, Gómez-Dantés, Lezana, & Knaul, 2006). The coverage by the IMSS accounted for about 40% of the total population in 2000. There is also another payer called the Institute for Social Security and Services for Civil Servants (ISSSTE) (Frenk et al., 2006). It was established in 1959 and covered the federal public workers and their families, which accounted for about 7% of the total Mexican population in 2000. Only 3-4% of the total population was covered by private insurance companies in the same year. Both the IMSS and the ISSSTE were financed by

the federal government's budget and employers as well as the premium deducted from the employees' payroll. Meanwhile, about 50% of Mexican population remained uninsured.

The Mexican government started reforming the health system to achieve UHC and a new law to establish the System of Social Protection in Health (SSPH) was legislated in 2003 (Knaul et al., 2012). The SSPH aimed at insuring self-employed, unemployed, and fatherless families that were previously not covered by any other financial protection schemes from health risk. Since most of the beneficiaries did not have employers, the SSPH was co-financed by the federal and state governments (Gomez-Dantes, 2009). Although beneficiaries had to pay the premium, the poorest 20% of households were exempt from any contribution. Within the SSPH, there were several risk pooling mechanisms depending on different health needs. For example, the Fund for Personal Health Services (FPHS) was responsible for covering the basic and essential health services, which was called "Seguro Popular" in Spanish (Knaul et al., 2012). The Fund for Protection against Catastrophic Health Expenditures (FPCHE) covered designated high-cost and specialized services. Additionally, there was another fund named the Medical Insurance for New Generation (MING), which covered children and newborns care (Knaul et al., 2012).

By the end of April 2012, the SSPH successfully insured 52.6 million Mexicans who were previously not eligible for health insurance (Knaul et al., 2012). As a result, 98% of Mexican residents, about 110 million people, were covered by one of the financial protection schemes. From the macroeconomic perspective, THE as percentage of GDP gradually grew from 4.4% in 1990 to 5.1% in 2000, and 6.3% in 2010 (Gomez-Dantes, 2009). Health expenditure per person (US$ purchasing power parity (PPP)) also rose from 508 US$ in 2000 to 959 US$ in 2010. Catastrophic and impoverishing health expenditure dropped from 3.1% and 3.3% of

households in 2000 to 2% and 0.8% in 2010, respectively. However, OOP spending as % of THE did not decline much, from 50.9% in 2000 to 47.1% in 2010 (Knaul et al., 2012).

Chapter 3: Manuscript

Title

Can we predict how much government investments on health reduce households incurring catastrophic out-of-pocket health expenditure? A systematic review and longitudinal data analysis of 72 low- and middle-income countries

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Key words

Catastrophic out-of-pocket health expenditure, low- and middle-income countries, out-of-pocket health payments, Sustainable Development Goals, universal health coverage

Key messages

- The incidence of catastrophic out-of-pocket health expenditure (CHE) is a key indicator to track the progress of how countries move towards universal health coverage (UHC).
- There is a significant decline of the incidence of CHE associated with the increase of general

government health expenditure (GGHE) as percentage of gross domestic product (GDP) in low- and middle-income countries, even though after adjusting for confounders.

- The availability in data of the incidences of CHE as well as indicators showing socioeconomic and demographic status and performances of health systems in LMICs made it difficult to analyze unbiased estimates of the association between the incidence of CHE and GGHE as a share of GDP.

Acknowledgments

The authors acknowledge Dr. David Kleinbaum, a professor at the Department of Epidemiology, Rollins School of Public Health, Emory University for his teaching and valuable advice about statistical analysis. We appreciate Dr. Momoe Takeuchi, a team leader of Health Systems Development at the WHO Representative Office in Cambodia, for her insights to develop our research question. We also thank to Mr. Eijiro Murakoshi, a former consultant at the WHO Representative Office in Cambodia, for his inputs of knowledge about health financing in LMICs. Lastly, we would like to say thank you to all the original investigators who ever made great efforts to estimate the incidences of CHE in their respective countries.

Abstract

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Introduction

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Relying on OOP payments to access health services is discouraged in terms of financial protection, especially for poor households. OOP payment is defined as direct payment to health care providers by patients at the time they utilize health services. If people without financial protection sought care, they could be impoverished by large OOP spending that they must pay. Although the rich can pay by cash, the poor might sell their assets such as lands or livestock, essential for their livelihood. Moreover, poorer people will avoid seeking care when they are sick, which could lead to worse health outcomes such as higher morbidity and mortality in a country (World Health Organization, 2000). Unfortunately, OOP payment is still the main source of financing health systems in many low- and middle-income countries. A report from the WHO indicated that 48 countries from Latin America, the Middle East, and South East Asia had at least 45% of OOP expenditure as a share of total health expenditure (THE). This report also revealed that the average percentage of OOP payments of the countries in the South East Asian region accounted for 50% of THE in 2013 (World Health Organization & World Bank Group, 2015).

The primary focus of financial protection in the context of UHC is to reduce large OOP payment from people when they receive health services so that they can avoid impoverishment. The previous literature suggested that prepayment mechanism to fund health systems, either social health insurance or tax-based systems, should be applied to every country with high OOP health expenditure (Xu et al., 2007). The term *prepayment* indicates that financial contributions for illness should be collected and pooled prospectively. The pooled funds are usually comprised of money from general government budgets, employers, or individuals.

The key measurement to anticipate how OOP payment causes financial hardship of people in a country is called catastrophic health expenditure (CHE). The term *catastrophic* health

expenditure was initially introduced in the World Health Report 2000. Dr. Brundtland, the then Director-General of the WHO, emphasized that fairness of financial contribution was a key to construct equitable health systems as it referred to protecting people against extensive costs of illness (World Health Organization, 2000). Any OOP payments related to healthcare can be called "catastrophic" if they exceed a given fraction of a household's expenditure (Kawabata et al., 2002). The proportion of households in a country facing CHE should be calculated and followed to benchmark the performance of health systems. The framework to monitor progress towards UHC jointly created by the WHO and the World Bank stated that financial protection in terms of CHE should be achieved for all the population (World Health Organization & World Bank Group, 2014).

One issue related to CHE is that the definition of CHE varies. Indicators calculated by different methods are not comparable, which makes it difficult to conduct cross-country analyses. There are two methodologies that are commonly used in many peer-reviewed journals. The most common definition of CHE is the fraction of households for which health-related spending exceeds 40% of their capacity-to-pay (CTP) in a country. The CTP is defined as a household's non-subsistence spending, which is usually calculated by subtracting household food expenditure from total household expenditure. This definition was introduced in the working paper from the Evidence and Information of Policy (EIP) cluster of the Department of Health System Financing, WHO in 2005 (Xu, 2005). As a result, it was the most frequently used definition found in our literature review.

The second most common definition is the proportion of households in a country for which health-related spending exceeds 25% of their total household expenditure. The strength of this method is its ease of calculation compared with the former definition. This definition is

expected to become popular because the World Bank has used it in recent papers to track the progress of UHC (Wagstaff et al., 2016). Nevertheless, some literature reported the incidence of CHE by using different benchmarks such as 10%, 15%, 20% of total household expenditure, which made them impossible to compare with each other (World Health Organization & World Bank Group, 2015).

Furthermore, the proportion of households facing CHE is primarily reported by using population representative samples of nationwide household surveys, which means one proportion for one country each year. However, some researchers used survey data that only included patients with specific illnesses or socioeconomic characteristics in order to estimate the incidence of CHE. For example, Che et al. calculated the incidence of CHE for those infected with Hepatitis B (Che et al., 2016). Karami et al. estimated the fraction of households with CHE for those living in eastern Iran, which was underserved as well as rural (Karami et al., 2009). Unfortunately, these studies are not comparable with one another.

The determinants of CHE have been assessed in many previous journal articles. Saksena and colleagues demonstrated that the following variables, not only at household-level but also country-level, were associated with the lower incidence of CHE: 1) households with heads with a higher level of education; 2) households living in urban areas; 3) households without children under 5 years of age or elderly members; 4) lower OOP health expenditure as a share of THE; 5) less income inequality (Saksena et al., 2010). There is conflicting evidence if the gender of household heads influences the likelihood of experiencing CHE. The studies published by Adisa, Akinkugbe et al., Dyer et al., Tran, and Ukwajua et al. suggested that female-headed households were less likely to suffer CHE, whereas the studies by Jan and Negin et al. showed an opposite result (Adisa, 2015; Akinkugbe et al., 2012; Dyer et al., 2013; Jan et al.,

2015; Negin et al., 2016; Tran et al., 2013; Ukwaja et al., 2013). There are also conflicting results whether enrolling in a kind of financial protective scheme, mostly social or community-based health insurance, demonstrates the lower probability of facing CHE. Although the majority of the articles concluded that people covered by health insurance were less likely to experience CHE than people not covered, some articles written by Goepel et al., Lu et al., Ma et al., Tripathi et al., Wang et al., and Yang et al. revealed that such schemes had no significant impact to protect people from CHE (Goeppel et al., 2016; Lu et al., 2012; Ma et al., 2016; Tripathi et al., 2014; Wang et al., 2015; Yang et al., 2016). This difference may be caused by the design and range of the coverage of each financial protection scheme.

Utilization of health services is associated with higher risk of incurring CHE. However, the focus of the cause of OOP health spending differs across the respective researchers. For instance, Engelgau et al. argued that noncommunicable diseases (NCDs) such as cardiovascular diseases, cancers, or traffic injuries were associated with the higher incidence of CHE than communicable diseases, while Thuan et al. asserted that communicable diseases increase the incidence CHE more than NCDs (Engelgau et al., 2012; Thuan et al., 2006). Bareness et al. and Werapong et al. pointed out that the indirect costs of seeking care such as transportation were more influential than direct payment for healthcare (Barennes et al., 2015; Weraphong et al., 2013). In addition, many researchers such as Yang et al. claimed that hospitalized patients had a higher likelihood of facing CHE than patients only receiving outpatient care (Yang et al., 2016). There were also some researchers such as Ukwaja and colleagues who argued that seeking care at private health facilities was more likely to lead financial catastrophe than seeking care at public facilities (Ukwaja et al., 2013).

After the SDGs and their targets were formally approved, CHE is becoming more

important to measure the progress of UHC. There are two indicators to monitor Target 3.8. The indicator 3.8.1 serves for service coverage, and the indicator 3.8.2 serves for financial protection. Initially, measuring "number of people covered by health insurance or a public health system per 1,000 population" was suggested as the indicator 3.8.2 (United Nations, 2016). However, the WHO and World Bank proposed an amendment to this indicator because it was insufficient to track how high health spending affects people's livelihood (World Health Organization, 2016). For example, only insuring people does not mean reducing their financial burden from health spending. If they are still forced to pay high OOP spending, they may still face the financial burden. In addition, illness, diagnostic strategies, and treatment options will change over time. If a health insurance plan does not change its coverage simultaneously with the transition of standard care, insured people will have to pay high OOP spending for uncovered treatment options.

The newly proposed indicator is "proportion of the population with large household expenditures on health as a share of total household expenditure or income," which is equivalent to the incidence of CHE. This replacement of the indicator 3.8.2 was also supported by the representatives of civil society in the Inter-agency and Expert Group on Sustainable Development Goal Indicators (IAEG-SDGs) (Kamal-Yanni, 2016). Finally, this amendment was approved at the fourth meeting of the IAEG-SDGs held from 17th until 18th of November 2016 in Geneva (United Nations, 2016). Consequently, the incidence of CHE especially in low- and middle-income countries had become an essential indicator to evaluate the progress of the SDGs within the next 15 years.

The reduction of the incidence of CHE through UHC will be achieved through mobilizing government budgets more for the health sector. However, the adequate amount of

investment needed is not well-known or documented. The previous agreements such as the Abuja Declaration in 2001 did not specify the target proportion of the countries' domestic budgets that should be allocated for health (Organization of African Unity, 2001). The World Health Report 2010 also emphasized that governments of LMICs should optimize their shares of total government expenditure on health but did not mention what the ideal budget allocation was (World Health Organization, 2010).

Therefore, we determined to create evidence to predict the relationship between government health expenditures and CHE and whether an increase in government health expenditure reduces the incidence of CHE in a given country. In the previous literature, Xu and colleagues used total health expenditure (THE) as a share of gross domestic product (GDP) as an independent variable to fit a linear regression model to estimate an association with the proportion of households with CHE. However, THE as percentage of GDP was used as a proxy of health services utilization since THE would increase if OOP health payments increase in a given country (Xu et al., 2003). We determined to use general government health expenditure (GGHE) as a share of GDP as an independent variable of our interest. We fit a statistical model to quantify the association between GGHE as a share of GDP and the incidence of CHE. This study cannot guarantee the causality because it is an observational study. Nevertheless, the evidence from our study might provide support for policy makers in LMICs to forecast costs of reducing people who experienced financial burden due to health services.

Methods

Criteria for considering studies for this review

The outcome of interest was the proportion of households in a country that incurred

CHE in a given year. We included original studies or reviews of original studies that estimated the incidences of CHE in low- and middle-income countries (LMICs) between 2000 and 2016. We used the World Bank's classifications by income-level to specify LMICs (World Bank Group, 2017). In addition, we only included studies using nationally representative household surveys or applying any appropriate sampling strategies to ensure nationwide representation. We also included studies that used the dataset from the World Health Survey (WHS) (World Health Organization, 2017b). We excluded studies that could not ensure national-level representativeness. For instance, any studies that only estimated the incidence of CHE of specific geographic areas in a country were excluded. We also excluded studies that targeted particular households such as those with the elderly as household members. Additionally, we excluded studies if authors were only interested in expenses derived from particular diseases such as HIV or specific types of health services such as inpatient care.

To ensure the methodological consistency to calculate CHE, we included studies applying the method proposed by the EIP cluster of the WHO in 2005 to calculate the incidence of CHE, which was described as OOP payments for healthcare that exceed 40% of a household CTP or non-food expenditure (Xu, 2005). Thus, we excluded studies applying different thresholds such as 10% or 25% or different denominators such as total household expenditure since the incidences of CHE calculated by different methods were not comparable with one another.

Search methods for identification of studies

We searched the following databases: CENTRAL (the Cochrane Library 2016 Issue 11); MEDLINE (1950 to December 2016); EMBASE (1980 to December 2016); Science

Citation Index Expanded (1955 to December 2016); Social Sciences Citation Index (1956 to December 2016); Arts & Humanities Citation Index (1975 to December 2016); Current Chemical Reactions (1986 to December 2016); Index Chemicus (1996 to December 2016). The original search was performed in June 2016. We did not apply any language restriction. We also attempted to search gray literature by Google and Google Scholar (December 2016).

Data collection and management

We imported all the retrieved literature on Zotero (version 4.0.29.15, Center for History and New Media, George Mason University) and eliminated duplicates. One author screened all the references to include in the review, extracted data and entered the data into Microsoft Excel as a data collection form. Since we did not intend to collect data from the respective household surveys and re-calculate the incidence of CHE, we did not contact corresponding authors of the studies retrieved. The following variables were entered into the data set: Country name/code; Incidence of CHE; Year survey data collected. While extracting data, we assessed the internal validity of selected papers by checking nationwide representation of the study population and use of the proper methodology in accordance with the WHO's working paper (Xu, 2005).

In case we observed more than two incidences of CHE in the same country as well as the same year from different studies, we preserved the lowest value and eliminated the others so that we could output our results based on the most conservative estimates of the effects. As the incidences of CHE were not calculated on regular basis in every country, a substantial amount of missing data was anticipated. However, we did not contact the original investigators since we assumed that they would not calculate the incidences of CHE in years where the data were

missing. We discuss any possible influences of the missing data that might cause selection bias in the discussion section.

Identification of exposure and predictors

Our exposure of interest was the general government health expenditure (GGHE) as percentage of GDP. We defined GGHE as spending from both central and local government budgets and social health insurance funds. We did not include any external loans and donations from international agencies and non-governmental organizations (NGOs). The health expenditure includes the provision of preventive and health services such as family planning, nutritional interventions, and emergency care but excludes the provision of water and sanitation. This definition is the same as that of the WHO and the WB. We searched and extracted the data from the WHO Global Health Expenditure Database (GHED) as a Microsoft Excel file (World Health Organization, 2014).

Table 1 shows the list of potential covariates and data sources. We applied directed acyclic graphs (DAGs), which were widely used for causal inference in the field of epidemiology, to identify confounding pathways and potential confounders that were needed to adjust (Pearce & Lawlor, 2016). The data sources included the WHO GHED, Global Health Observatory (GHO) data, and WB Open Data (World Bank Group, 2016; World Health Organization, 2014, 2017a). For GDP per capita, poverty gap, and poverty headcounts ratio, we used data converted into 2011 International $ (I$) by using PPP conversion factor to facilitate cross-country comparisons. We downloaded either Microsoft Excel files or comma-separated value (CSV) files containing the covariates from the web-based databases, imported them to Stata version 14.2 (StataCorp), and merged them into a single dataset by matching country codes and years. Finally,

the longitudinal dataset of the incidences of CHE in different years, which were clustered by countries, and corresponding covariates were created.

Table 1. Potential Covariates Considered to estimate Magnitude of Association between Incidence of CHE and GGHE as % of GDP

Potential Covariates	Data Sources
Economic Indicator	
GDP per capita[a]	WB Open Data
Poverty headcount ratio at $1.90 a day (%)[a]	WB Open Data
Poverty gap at $1.90 a day (%)[a]	WB Open Data
GINI Index	WB Open Data
Demographic Indicator	
Fertility rate	WB Open Data
Population aged 65 or older (%)	WB Open Data
Urban population (%)	WB Open Data
Primary school completion rate (% of relevant age group)	WB Open Data
Health Financing Indicator	
GGHE as % of GDP	WHO GHED
OOP as % of THE	WHO GHED
Health Service Indicator	
Pregnant women received ANC at least once (%)	WB Open Data
Births attended by skilled health staff (%)	WHO GHO
DPT vaccination coverage (% of children ages 12-23 months)	WB Open Data
Tuberculosis treatment success rate (% of new cases)	WHO GHO
Improved water source (% of population with access)	WHO GHO
Improved sanitation facilities (% of population with access)	WHO GHO
Health Infrastructure Indicator	
Hospital beds per 1,000 people	WB Open Data
Health Workforce Indicator	
Physicians density per 1,000 population	WHO GHO

Abbreviation: ANC, antenatal care; CHE, catastrophic out-of-pocket health expenditure; DPT, diphtheria, pertussis, and tetanus; GDP, gross domestic product; GGHE, general government health expenditure; GHED, Global Health Expenditure Database; OOP, out-of-pocket; PPP, purchasing power parity; THE, total health expenditure; WB, World Bank; WHO, World Health Organization

[a] The economic indicators are constant to 2011 International $, converted by PPP conversion factor.

Statistical analysis

We designed a longitudinal data analysis to predict the magnitude of the association between the proportion of households incurring CHE and GGHE as a share of GDP. We fit two

models by using different statistical techniques to estimate the beta coefficients and p-values of GGHE as percentage of GDP associated with the incidence of CHE. First, we used a two-level linear mixed model of the form:

$$\ln CHEij = \beta 0 + \beta 1 * GGHEij + \sum_{n=1}^{6} \gamma n * Vnij + uj + \varepsilon ij$$

Where CHE_{ij} is the outcome variable of year i in a jth country, $GGHE_{ij}$ is the predictor variable, β_0 and u_j are the intercepts of the fixed effect and the random effect for countries, respectively, β_1 and γ_n are the coefficients of $GGHE_{ij}$ and nth confounder adjusting $GGHE_{ij}$ on, respectively, and ε_{ij} indicates residuals. We transformed our outcome variable, CHE_{ij}, by natural logarithm to satisfy the linearity and normality assumption. We dropped the random coefficient for countries from the above model since it was not statistically significant. We applied a restricted maximum likelihood (REML) method for log-likelihood calculations. We used Kenward and Roger method to approximate the denominator degree of freedom (DDF) as the dataset was a relatively small and unbalanced (Kenward & Roger, 1997). We chose an autoregressive (AR1) structure as residuals correlation. We determined not to fit a generalized linear mixed model (GLMM) because the statistical software did not allow us to specify the correlation structure except *independent* in GLMMs. We believed that independent correlation structure would be inappropriate for our analysis since the dataset was longitudinal.

Our alternative approach is to use a GEE model of the form:

$$\ln\{E(CHEij)\} = \beta 0 + \beta 1 * GGHEij + \sum_{n=1}^{6} \gamma n * Vnij\,, \qquad CHEij \sim Gamma$$

This model does not output any cluster-specific effects but a population-averaged effect. We chose a Gamma distribution as the distributional family rather than Gaussian since the

quasi-likelihoods under the independence model criterion (QICs) were always lower when we compare Gamma and Gaussian models regressed on the same covariates. We chose *exchangeable* as the correlation structure since we could not specify some working correlation structures such as AR1, stationary, or unstructured due to insufficient observations as well as unbalances of the dataset. We used robust variance estimations to address the potential misspecifications of correlation structure.

In accordance with our DAG, we included the following seven covariates in our full model, which were: 1) OOP as percentage of THE; 2) Tuberculosis treatment success rate (percentage of new cases); 3) Improved water source (percentage of population with access); 4) Improved sanitation facilities (percentage of population with access); 5) Urban population (percentage); 6) Aging rate (percentage of population aged 65 years or older); and 7) GDP per capita (2011 I$, PPP). All the interaction terms between the exposure variable and these covariates were not statistically significant, which resulted in being dropped from the full model. There was no significant multicollinearity across the variables in the full model. We eliminated the third covariate, which was a percentage of population with access to improved sanitation facilities, from the full model and selected the other six covariates as confounders that should be included in our final model. Keeping access to improved sanitation facilities was not meaningful because its implication overlapped with access to water source as well as it was not statistically significant. Based on our DAG, which we assumed it might be correct, we were able to control for all the confounding pathways using the selected six covariates. OOP as percentage of THE indicated how effectively a country's health system protected people from financial burden. Tuberculosis treatment success rate and access to an improved water source were proxies of how effectively the health system delivered services in terms of curative and preventive services,

respectively. Both urban population and aging rate influenced demand for health services. GDP per capita was not a perfect but obtainable proxy of a country's median household income (Nolan, Roser, & Thewissen, 2016). We did not regress on other potential covariates such as primary school completion rate (percentage of relevant age group) or GINI index due to insufficient observations, which caused significant random errors.

Sensitivity analysis

We conducted a sensitivity analysis by using the alternative dataset that eliminated any countries if the countries contained only one observation. We assumed that a more balanced dataset, including any clusters that had at least two observations, might allow more precise estimates although we would lose some observations and countries. We fit the same models as shown above. We used Stata version 14.2 (StataCorp) as a statistical software.

Results

Result of search

Figure 2 describes the articles included in our systematic review. The original systematic search of databases found 334 articles (duplicates excluded). From these, we excluded 154 articles that did not meet the eligibility criteria, English-written original studies or reviews of original studies that calculate the incidence of CHE in LMICs, by reading the titles and abstracts. In addition, we found 15 additional articles, which were searched by Google and Google Scholar that met our criteria. These articles include non-peer-reviewed literature such as health financing reports from international organizations or governments of LMICs. From these, we excluded 156 studies in accordance with the exclusion criteria. Almost 80 percent of the excluded studies did

not have the national-level representativeness to estimate the proportion of households that incur CHE. In these studies, the investigators conducted cross sectional surveys targeting specific areas in a country or populations with specific health conditions. As a result, the estimated incidences of CHE appeared to be higher than those calculated by using national-representative surveys. The rest of the excluded studies did not apply the WHO definition for CHE but used the World Bank definition to calculate the CHE. At the end, 39 articles were selected for further data analysis.

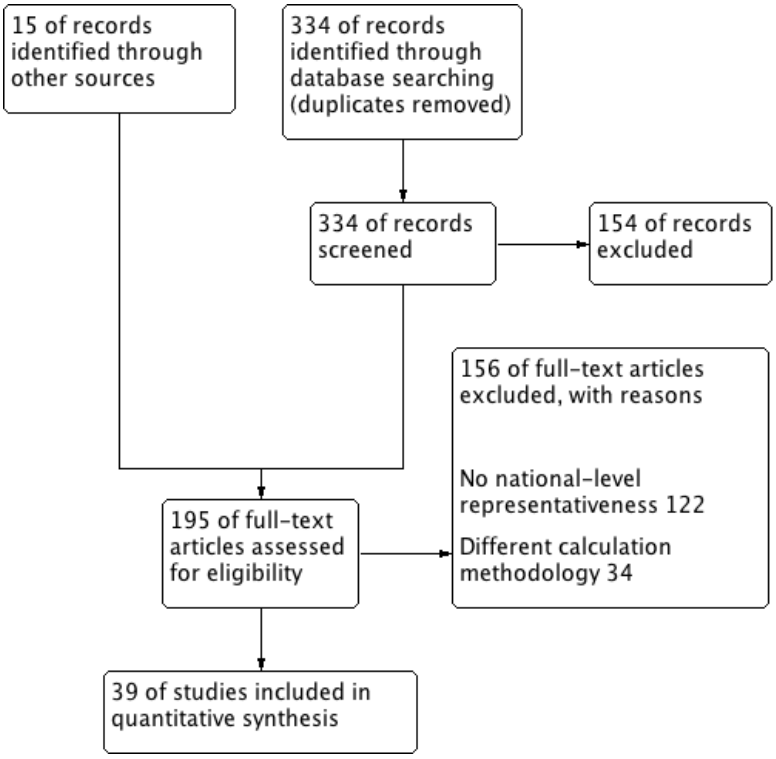

Figure 2. Study flow chart

Country characteristics

Table 2 summarizes the economic, demographic and health related characteristics of the countries that have data of the outcome variable (i.e. the incidence of CHE). The number of

non-missing values, its proportion to total number of observations, means, and standard deviations (SDs) of variables are shown, respectively. From the 39 selected articles, we extracted 142 point estimates of the incidence of CHE from 71 countries. The mean incidence of CHE was 7.4% with standard deviation (SD) of 7.5%. Besides the incidence of CHE, the numbers of missing values largely vary across the covariates. For instance, we obtained complete data of some SDG indicators such as "the percent of population with access to improved water source" or "the percent of population with access to improved sanitation facilities." However, some indicators such as "the percent of pregnant women who received antenatal care (ANC) at least once" had nearly 70 percent of missing values.

Table 2. Economic, Demographic, and Health Related Characteristics of Countries that Estimated Incidences of CHE between 2000-2016

Characteristics	n (%)	mean (SD)
Economic Indicator		
GDP per capita[a]	140 (98.6)	6875 (5299)
Poverty headcount ratio at $1.90 a day (%)[a]	83 (58.5)	15.1 (18.5)
Poverty gap at $1.90 a day (%)[a]	83 (58.5)	5.0 (7.3)
GINI Index	83 (58.5)	41.1 (8.0)
Demographic Indicator		
Fertility rate	142 (100.0)	3.2 (1.5)
Population aged 65 or older (%)	142 (100.0)	6.1 (3.9)
Urban population (%)	142 (100.0)	45.5 (20.6)
Primary school completion rate (% of relevant age group)	101 (71.1)	86.8 (18.1)
Health Financing Indicator		
Incidence of CHE	142 (100.0)	7.4 (7.5)
GGHE as % of GDP	138 (97.2)	2.7 (1.3)
OOP as % of THE	139 (97.9)	42.8 (18.0)
Health Service Indicator		
Pregnant women received ANC at least once (%)	42 (29.6)	87.1 (14.9)
Births attended by skilled health staff (%)	66 (46.5)	83.7 (22.1)
DPT vaccination coverage (% of children ages 12-23 months)	139 (97.9)	86.0 (13.7)
Tuberculosis treatment success rate (% of new cases)	138 (97.2)	80.0 (11.9)
Improved water source (% of population with access)	142 (100.0)	82.2 (15.2)
Improved sanitation facilities (% of population with access)	142 (100.0)	62.5 (27.9)
Health Infrastructure Indicator		

Hospital beds per 1,000 people	63 (44.4)	3.3 (2.7)
Health Workforce Indicator		
Physicians density per 1,000 population	57 (40.1)	1.2 (1.1)
Total	142 (100.0)	

Abbreviation: ANC, antenatal care; CHE, catastrophic out-of-pocket health expenditure; DPT, diphtheria, pertussis, and tetanus; GDP, gross domestic product; GGHE, general government health expenditure; OOP, out-of-pocket; PPP, purchasing power parity; THE, total health expenditure.

[a] The economic indicators are constant to 2011 International $ and converted by using PPP for cross country comparison.

Table 3 describes the distributions of observations and countries (i.e., clusters) classified by World Bank income and geographical region. More than half of the countries had only one observation since there was only one estimate of the incidence of CHE in those countries. In addition, more than 20 percent of the countries only had two incidences of CHE observed. There were only three countries that tracked the incidence of CHE more than seven years. As a result, the final dataset became considerably unbalanced.

Table 3. Distributions of Observations and Countries that estimated Incidences of CHE between 2000-2016

Characteristics	**Observation**	**Country**
	n (%)	**n (%)**
Number of observations within a country		
1	38 (26.8)	38 (53.5)
2	32 (22.5)	16 (22.5)
3	27 (19.0)	9 (12.7)
4	12 (8.5)	3 (4.2)
5	10 (7.0)	2 (2.8)
7	7 (4.9)	1 (1.4)
8	16 (11.3)	2 (2.8)
World Bank Income Classification		
Low income country	55 (38.7)	28 (39.4)
Lower middle income country	61 (43.0)	29 (40.9)
Upper middle income country	26 (18.3)	14 (19.7)
World Bank Region		
East Asia & Pacific	34 (23.9)	10 (14.1)
Europe & Central Asia	32 (22.5)	16 (22.5)
Latin America & Caribbean	16 11.3)	11 (15.5)

Middle East & North Africa	14 (9.9)	5 (7.0)
South Asia	11 (7.8)	5 (7.0)
Sub-Saharan Africa	35 (24.7)	24 (33.8)
Total	142 (100)	71 (100)

Abbreviation: CHE, catastrophic out-of-pocket health expenditure

Figure 3 shows the data points of the incidence of CHE in given years across the World Bank regions. The number of observations of the estimated incidence of CHE was the largest in 2003 since the World Health Survey (WHS) 2003, which was initiated by the EIP cluster of the WHO, was conducted in the year. In contrast, only two countries calculated the proportion of households that incur CHE in 2001, 2013, or 2014 as monitoring CHE was not mandatory for the LMICs.

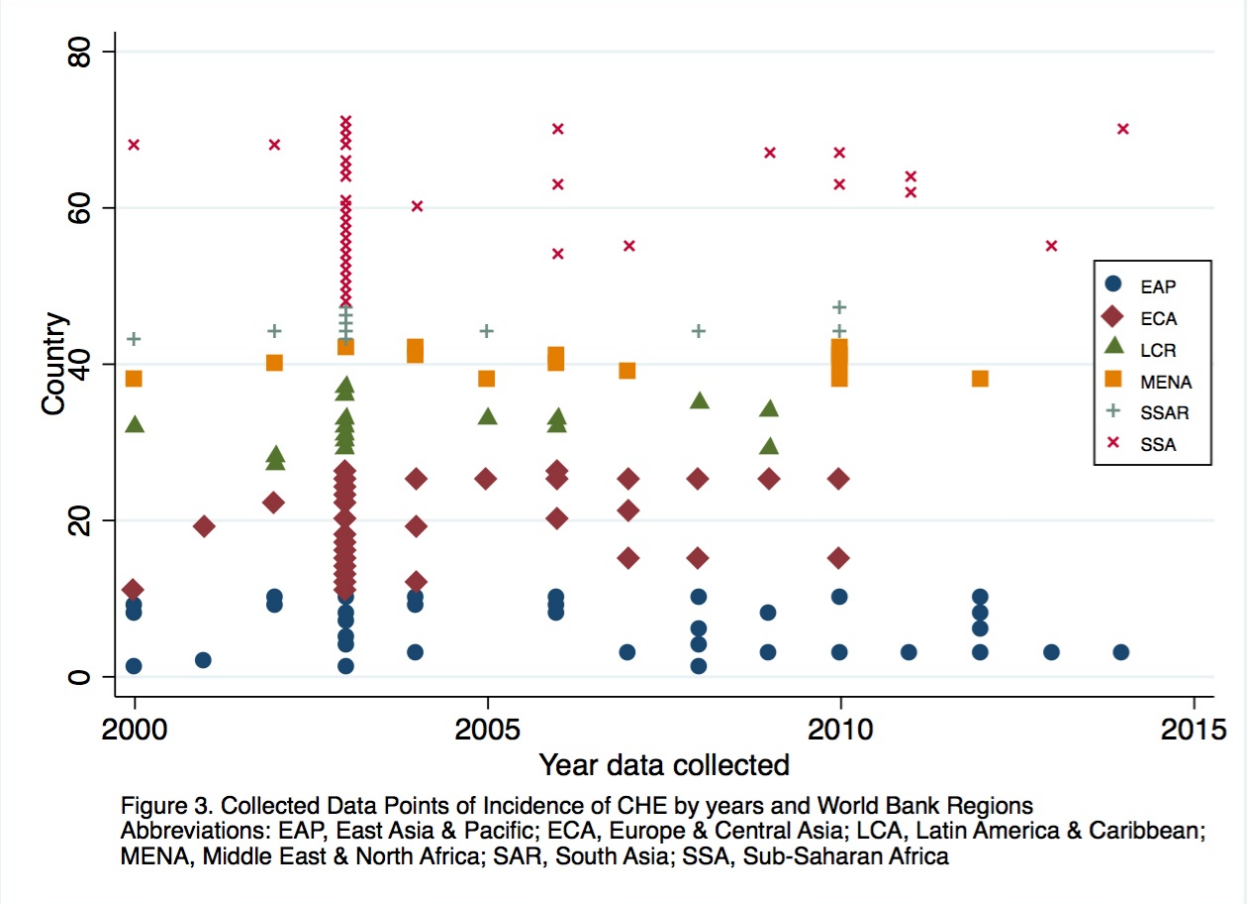

Figure 3. Collected Data Points of Incidence of CHE by years and World Bank Regions
Abbreviations: EAP, East Asia & Pacific; ECA, Europe & Central Asia; LCA, Latin America & Caribbean; MENA, Middle East & North Africa; SAR, South Asia; SSA, Sub-Saharan Africa

Figure 3. Collected data points of incidence of CHE by years and World Bank regions

Result of statistical analysis

Table 4 presents the results of analyzing the crude and adjusted effects of the incidence of CHE associated with GGHE as a share of GDP. Overall, the decline of the proportion of households incurring CHE was associated with the increase in GGHE as a share of GDP. The crude effects estimated by the mixed effect model (coefficient: -0.333, standard error (SE): 0.076, p-value: <0.001) and by the GEE model (coefficient: -0.321, SE 0.070, p-value: <0.001) were similar. For both model, the standard errors (SEs) were inflated by adjusting on confounders, although the effects were still significant. However, the magnitude of the adjusted effect estimated by the mixed model (coefficient: -0.250, SE 0.118, p-value: 0.037) became smaller than that estimated by the GEE model (coefficient: -0.346, SE 0.102, p-value: 0.001).

Table 4. Crude and Adjusted Beta Coefficients, Standard Errors (SEs), P-value of Incidence of CHE by GGHE as % of GDP, estimated by Log Linear Mixed Effect Model and General Estimating Equation (GEE) Model by using Full Dataset.

		Mixed Effect Model[a]		GEE Model[b]	
Characteristics	**No. of Observations (No. of Countries)**	**Coefficient (SE)**	**p-value**	**Coefficient (SE)**	**p-value**
Crude Effect	138 (69)	-0.333 (0.076)	<0.001	-0.321 (0.070)	<0.001
Adjusted Effect[c]	133 (66)	-0.250 (0.118)	0.037	-0.346 (0.102)	0.001

Abbreviation: CHE, catastrophic out-of-pocket health expenditure; GDP, gross domestic products; GEE, General Estimating Equation; GGHE, general government health expenditure; OOP, out-of-pocket; SE, Standard Error; THE, total health expenditure

[a] Log-transformed incidence of CHE was regressed by accounting countries for a random effect.

[b] Log-gamma models, country-level clustering was applied for GEEs.

[c] Results were adjusted by GDP per capita (2011 Int$, PPP), urban population (%), and aging rate (% of population aged 65 years or older), OOP as % of THE, tuberculosis treatment success rate (% of new cases), Improved water source (% of population with access).

Result of sensitivity analysis

We eliminated all the countries that consist of only one observation from the full

dataset. The reduced dataset for this sensitivity analysis was comprised of 104 observations divided into 33 countries. Table 5 presents the results of analyzing the crude and adjusted effects of the incidence of CHE associated with GGHE as a share of GDP. We applied the same models as described in Table 4 for estimating the effects. We found the similar results in the crude effects to our previous analysis. The crude effect estimated by the mixed effect model (coefficient: -0.331, SE: 0.095, p-value: 0.001) and that estimated by the GEE model (coefficient: -0.355, SE: 0.084, p-value: <0.001) indicated the negative association between the proportion of households that incur CHE and GGHE as a share of GDP. Contrary to the crude effects, the direct effects estimated by neither mixed model (coefficient: -0.098, SE: 0.151, p-value: 0.519) nor GEE model (coefficient: -0.232, SE -0.346, p-value 0.100) were statistically significant.

Table 5. Crude and Adjusted Beta Coefficients, Standard Errors (SEs), P-value of the Incidence of CHE by GGHE as % of GDP, estimated by Log Linear Mixed Effect Model and General Estimating Equation (GEE) Model by using Dataset eliminated Countries containing One Observation.

		Mixed Effect Model[a]		GEE Model[b]	
Characteristics	**No. of Observations (No. of Countries)**	**Coefficient (SE)**	**p-value**	**Coefficient (SE)**	**p-value**
Crude Effect	101 (32)	-0.331 (0.095)	0.001	-0.355 (0.084)	<0.001
Adjusted Effect[c]	99 (32)	-0.098 (0.151)	0.519	-0.232 (0.141)	0.100

Abbreviation: CHE, catastrophic out-of-pocket health expenditure; GDP, gross domestic products; GEE, General Estimating Equation; GGHE, general government health expenditure; OOP, out-of-pocket; SE, Standard Error; THE, total health expenditure

[a] Log-transformed incidence of CHE was regressed by accounting countries for a random effect.

[b] Log-gamma models, country-level clustering was applied for GEEs.

[c] Results were adjusted by GDP per capita (2011 Int$, PPP), urban population (%), and aging rate (% of population aged 65 years or older), OOP as % of THE, tuberculosis treatment success rate (% of new cases), Improved water source (% of population with access).

Discussion

We found 39 articles with 142 point estimates of the incidences of CHE from 71 LMICs. Our review revealed that there is a significant decline in the proportion of households

experiencing CHE associated with increasing GGHE as percentage of GDP after adjusting for health service delivery and financing indicators as well as sociodemographic indicators. We could not find significant heterogeneity of the estimated coefficients across countries with respect to the association between the incidence of CHE and GGHE as a share of GDP. The association between the incidence of CHE and GGHE as a share of GDP was not statistically significant when we conducted a sensitivity analysis by using the dataset that dropped countries with only one observation.

We applied two different modeling approaches, which were a linear mixed effect model and a GEE model. The fixed coefficients of the mixed models denoted the average of country-specific coefficients of all the countries in the population, while the fixed coefficients of the GEE models denoted the coefficients for the entire population. In non-linear models, like GEE, an average of cluster-specific coefficients and population average are usually not identical. With respect to the context of our research, we prefer to rely on the mixed effect model rather than the GEE model since it is reasonable to assume that each country has its own coefficient depending on its performance of health system.

Although someone might argue that our review is observational, the result of our review might be useful for the governments in LMICs to anticipate how much total domestic government investments in the health sector roughly reduce the incidences of CHE, as Xu and colleagues did in the most relevant previous study (Xu et al., 2003). Let us present Cambodia as an illustration of our results (Case study 1) (National Institute of Statistics/Cambodia, Directorate General for Health/Cambodia, & ICF International, 2015; World Bank Group, 2016; World Health Organization, 2014). If the Cambodian government could have increased its GGHE as a share of GDP one percent, from 1.3% to 2.3%, the proportion of households incurring CHE

would decline from 6.7% to 5.22%. This reduction of the incidence would roughly be equivalent to 49,000 households that were averted from CHE. In this scenario, the Cambodian government would have needed approximately 168 million US dollars as an additional investment.

Case study 1: How to approximate number of households averted from CHE by applying our study findings: A case study in Cambodia 2014

1. Collect demographic and economic data needed for calculation
   Estimated total population[a]: 15,328,136
   Mean size of households[b]: 4.6
   GDP (current US$)[a]: $16,777,820,330
   GGHE as a share of GDP[c]: 1.3%
   Incidence of CHE: 6.7%
2. Calculate total number of households in a country, by dividing total population by mean household size.
   $$15{,}328{,}136 \div 4.6 = 3{,}332{,}203$$
3. Calculate the incidence of CHE relative to an incremental change of GGHE as percentage of GDP, by indexing the fixed coefficient from Table 4
   $$e^{-0.250} = 0.7788$$
4. Estimate the incidence CHE after increasing GGHE as a share of GDP from 1.3% to 2.3% (i.e., one percent increase), by multiplying the incidence of CHE by the exponent value of the fixed coefficient
   $$6.7(\%) \times 0.7788 \cong 5.22(\%)$$
5. Estimate number of households averted from CHE
   $$3{,}332{,}203 \times (6.7 - 5.22)(\%) \div 100 \cong 49{,}000$$
6. Estimate an additional investment to reduce the given incidence of CHE
   $$16{,}777{,}820{,}330(US\$) \times 1(\%) \div 100 \cong 168\ million\ (US\$)$$

[a] Data was retrieved from the World Bank Open Data
[b] Data was retrieved from Cambodia Demographic and Health Survey 2014
[c] Data was retrieved from the WHO Global Health Expenditure Database

There is a limitation with respect to applying our results to the real world. Our analysis used the WHO methodology since more studies that we reviewed adopted the WHO definition. However, the SDGs adopted the World Bank methodology as the definition of CHE to track

financial hardship due to health services use. Subsequent analyses of CHE are likely to use the World Bank methodology. OOP health payments should be divided by household non-subsistence expenditure in the former definition, while OOP health payments should be divided by total household expenditure in the later definition. Therefore, the coefficients and SEs estimated from our analysis will not be applicable if any future research uses the World Bank approach. However, our analytical concepts are certainly applicable no matter which definitions will be utilized in the future research.

There are some other limitations in terms of internal validity of the retrieved data. First, we could not assess the accuracy of the estimated incidences of CHE. While reviewing the literature, we found some articles that showed different values of the incidence of CHE in the same countries and years even though they used the same household surveys (Reddy, Ross-Degnan, Zaslavsky, Soumerai, & Wagner, 2013; Saksena et al., 2010). This implies potential miscalculation of CHE by the original researchers. However, it was not possible for us to obtain the original data from household surveys that the authors utilized so we were unable to recalculate the proportion of households with CHE. Although we made the best effort to investigate the methodological consistency across the articles, the level of detail about the methodologies used is highly variable. Thus, we had no choice but to accept the analyses done by the original researchers.

Secondly, Lu and colleagues pointed out that the estimated values of the incidence of CHE were affected by the design of survey instruments. In general, any household surveys have several question items regarding household health spending within certain recall periods. However, a number of question items and length of recall period give fluctuations in the estimated household OOP expenses. For example, fewer question items in a survey gave a lower

estimate for average health spending. A shorter recall period yielded a larger estimate for average health spending than a longer recall period (Lu, 2009). There is no worldwide consensus on the appropriate number of question items and recall period, hence we cannot judge which survey design elicits the most unbiased estimate of household health spending. Consequently, Raban and colleagues found the estimated proportions of households that had CHE by using data from the WHS or the Study on Global Ageing and Adult Health (SAGE) were substantially higher than those by using data from the National Sample Surveys on Household Consumer Expenditure (NSSs), which were nationally representative surveys in India (Raban, Dandona, & Dandona, 2013). Thus, it may be a reasonable option for future researchers to exclude the incidences of CHE from analyses if they were derived from the WHS data. However, we determined to include all the studies regardless of which household survey the original investigators utilized in order to obtain adequate observations and avoid random errors.

Thirdly, although we were able to include data from all the eligible studies, non-randomness of the retrieved data might cause selection bias. For instance, Table 3 implies the incidence of CHE was assessed in roughly 90 percent of low-income countries because there were 31 low-income countries worldwide in 2016. In addition, the incidence of CHE was examined in more than half of the countries in South Asia and sub-Saharan Africa regions, whereas about 20 percent of the countries were assessed in other regions. These may result in overestimating the coefficients since those countries had higher incidences of CHE relative to lower GGHE as a share of GDP. However, we were unable to obtain sufficient observations to conduct either random sampling or sub-group analysis.

Fourthly, there were some possibly important covariates related to the socio-economic status that we could not include in the final model in order to avoid random errors. For instance,

Saksena and colleagues included the Gini coefficient in their model (Saksena et al., 2010). However, we were unable to include this variable because only 83 out of 142 observations were obtained when we matched the incidences of CHE by the same countries and years. Unfortunately, the WHO and World Bank's global databases from which we extracted the data contained a considerable amount of missing information. The previous literature demonstrated that low socio-economic status, such as income inequality, worsened health outcomes of people, hence it was rational to presume demand for health services would increase (Pickett & Wilkinson, 2015). We were concerned that our adjusted fixed effects shown in Table 4 were still somewhat biased since we could not control for such unmeasured confounders. However, we drew multiple causal diagrams to identify potential confounding pathways and were able to include one covariate on each confounding pathway in our final model. We also compared multiple models to examine statistical precision and goodness-of-fit before selecting the final model.

Lastly, we dropped a coefficient of the random effect in our final model because it was not statistically significant. The random intercept, which was significant, represented the country-level heterogeneity of the baseline incidence of CHE in each country. On the other hand, this random coefficient could have indicated country-level heterogeneity in terms of the percent difference in the incidence of CHE associated with the percent difference of GGHE as a share of GDP. These findings may contradict our assumption because it is rational to assume that different health systems possess different performances to reduce the economic burden of households on health. Despite the considerable effort of reviewing literature, the final dataset contained a substantial amount of missing values, which might cause random errors. Thus, if we could have had a larger dataset, we might be able to estimate more robust random effects.

Conclusion

The decline of the incidence of CHE seems to be associated with an incremental change in GGHE as percentage of GDP. Further research is needed to clarify how the strength of the health system in a given country differentiates the magnitude of the association. Future research will need efforts to obtain the original data derived from the nationally representative household surveys and re-estimate incidences of CHE to ensure consistency in calculation methodology. The methodology defined by the World Bank should be used since it is officially adopted as an SDG indicator which will be globally tracked in the next decades. The design of each survey instrument should be evaluated carefully to assess whether any differences in the design cause variation in estimated household OOP health spending or not. Future research will also need some extra efforts to create a larger and more balanced longitudinal dataset to reduce random error and secure internal validity.

Chapter 4: Conclusion and Recommendations

Public health implications

We found 39 articles with 142 point estimates of the incidences of CHE from 71 LMICs. Our review revealed that there was a significant decline in the proportion of households experiencing CHE associated with increasing GGHE as percentage of GDP after adjusting for health service delivery and financing indicators as well as sociodemographic indicators. We could not find significant heterogeneity of the estimated coefficients across countries with respect to the association between the incidence of CHE and GGHE as a share of GDP. The association between the incidence of CHE and GGHE as a share of GDP was not statistically significant when we conducted a sensitivity analysis by using the dataset that dropped countries with only one observation.

Although someone might argue that our review is observational, the result of our review might be useful for the governments in LMICs to anticipate how much total domestic government investments in the health sector roughly reduce the incidences of CHE, as Xu and colleagues did in the most relevant previous study (Xu et al., 2003). The estimated coefficients shown in table 4, such as -0.250, are the natural logarithm of the incidence of CHE associated with any incremental changes of GGHE as percentage of GDP in LMICs. Thus, if we index the coefficients, these numbers will indicate the incidence of CHE relative to percent changes of GGHE as a share of GDP. For instance, the exponent value of -0.250 is 0.7788.

Let us present Cambodia as an illustration of our results. The estimated total population was 15,328,136, the mean size of households was 4.6, GDP was US$16,777,820,330 (current US$), and GGHE as a share of GDP was 1.3% in Cambodia in 2014, respectively

(National Institute of Statistics/Cambodia et al., 2015; World Bank Group, 2016; World Health Organization, 2014). Thus, if we divide total population by mean household size, we can estimate the approximate number of households in Cambodia, which was 3,332,203 in 2014. If the Cambodian government could have increased its GGHE as a share of GDP one percent, from 1.3% to 2.3%, the proportion of households incurring CHE would decline from 6.7% to 5.22%, which was calculated by multiplying 6.7% by 0.7788. This reduction of the incidence would roughly be equivalent to 49,000 households that were averted from CHE. In this scenario, the Cambodian government would have needed approximately 168 million US dollars as an additional investment.

Study limitations

There is a limitation with respect to applying our results to the real world. As mentioned in the method section of Chapter 3, our analysis used the WHO methodology since more studies that we reviewed adopted the WHO definition than the World Bank definition. However, the SDGs adopted the WB methodology as the definition of CHE to track financial hardship due to health services, hence subsequent analyses of CHE are likely to use the World Bank methodology. The biggest difference between the World Bank's approach and WHO's approach in calculating CHE is its denominator. OOP health payments should be divided by total household expenditure in the former definition, while OOP health payments should be divided by household non-subsistence expenditure. Therefore, the coefficients and SEs estimated from our analysis will not be applicable if any future research uses the WB's approach. However, our analytical concepts are certainly applicable no matter which definitions will be utilized in the future research. Future investigators will be able to adapt our analytical methods to predict the

more robust association between the incidence of CHE and GGHE as percentage of GDP.

There are some other limitations in terms of internal validity of the retrieved data. First, we could not assess the accuracy of the estimated incidences of CHE. While reviewing the literature, we found some articles that showed different values of the incidence of CHE in the same countries and years even though they used the same household surveys (Reddy et al., 2013; Saksena et al., 2010). This implies potential miscalculation of CHE by the original researchers. However, it was not possible for us to obtain the original data from household surveys that the authors utilized so we were unable to recalculate the proportion of households with CHE. Although we made the best effort to investigate the methodological consistency across the articles, the level of detail about the methodologies used is highly variable. Thus, we had no choice but to accept the analyses done by the original researchers.

Secondly, Lu and colleagues pointed out that the estimated values of the incidence of CHE were affected by the design of survey instruments. In general, any household surveys had several question items regarding household health spending within certain recall periods. However, a number of question items and length of recall period give fluctuations in the estimated household OOP expenses. For example, fewer question items in a survey gave a lower estimate for average health spending. A shorter recall period yielded a larger estimate for average health spending than a longer recall period (Lu, 2009). There is no worldwide consensus on the appropriate number of question items and recall period, hence we cannot judge which survey design elicits the most unbiased estimate of household health spending. In addition, Raban and his colleague found the estimated proportions of households that had CHE by using data from the WHS or the Study on Global Ageing and Adult Health (SAGE) were substantially higher than those by using data from the National Sample Surveys on Household Consumer

Expenditure (NSSs), which were nationally representative surveys in India. The authors also mentioned that OOP health expenses for outpatient and inpatient care in the WHS and SAGE were two or three times higher than those in the NSSs (Raban et al., 2013). Thus, it may be a reasonable option for future researchers to exclude the incidences of CHE from analyses if they were derived from the WHS data. However, we determined to include all the studies regardless of which household survey the original investigators utilized in order to obtain an adequate number of observations and avoid random errors.

Thirdly, although we were able to include data from all the eligible studies, non-randomness of the retrieved data might cause selection bias. For instance, Table 3 implies the incidence of CHE was roughly assessed in 90 percent of low-income countries because there were 31 low-income countries worldwide in 2016. To be exact, this "90 percent" is incorrect since the number of countries in each World Bank classification varies every year. However, this probability still seems to be higher than those in other income groups. In addition, the incidence of CHE was examined in more than half of the countries in the South Asia and sub-Saharan Africa regions, whereas about 20 percent of the countries were assessed in other regions. These may result in overestimating the coefficients since those countries had higher incidences of CHE relative to lower GGHE as a share of GDP. However, we were unable to obtain sufficient observations to conduct either random sampling or sub-group analysis.

Fourthly, there were some possibly important covariates related to the socio-economic status that we could not include in the final model in order to avoid random errors. For instance, Saksena and colleagues included the Gini coefficient in their models (Saksena et al., 2010). However, we were unable to include this variable because only 83 out of 142 observations were obtained when we matched the incidences of CHE by the same countries and years.

Unfortunately, the WHO and World Bank's global databases from which we extracted the data contained a considerable amount of missing information, thus it hindered cross-country comparisons. The previous literature demonstrated that low socio-economic status, such as income inequality, worsened health outcomes of people, hence it was rational to presume demand for health services would increase (Pickett & Wilkinson, 2015). We were concerned that our adjusted fixed effects shown in Table 4 were still somewhat biased since we could not control for such unmeasured confounders. However, we drew multiple causal diagrams to identify potential confounding pathways and created a list of variables needed to be adjusted. We were able to include at least one covariate on each confounding pathway in our final model. We also compared different reduced models of all the possible combinations of covariates to examine statistical precision and goodness-of-fit before selecting the final model. We believe that our estimates are the most unbiased of all the statistical options that we examined.

Fifthly, we applied two different modeling approaches, which were a linear mixed effect model and a GEE model. The adjusted coefficients of the mixed effect models differed from that of the GEE models. The fixed coefficients of the mixed models denoted the average of country-specific coefficients of all the countries in the population, while the fixed coefficients of the GEE models denoted the coefficients for the entire population. In non-linear models, like GEE, an average of cluster-specific coefficients and population average are usually not identical. With respect to the context of our research, we prefer to rely on the mixed effect model rather than the GEE model since it is reasonable to assume that each country has its own coefficient depending on its performance of health system.

Lastly, we dropped a coefficient and kept an intercept of the random effect in our final model because the coefficient was not statistically significant. This random coefficient could

have indicated country-level heterogeneity in terms of the percent difference in the incidence of CHE associated with the percent difference of GGHE as a share of GDP. The random intercept, which was significant, represented the country-level heterogeneity of the baseline incidence of CHE in each country. The question is whether these study findings, particularly the non-significant random coefficient, supports the argument that there is no difference across LMICs in how much health systems of each country can reduce the incidences of CHE by increasing GGHE as a share of GDP. Despite the considerable effort of reviewing literature, the final dataset contained a substantial amount of missing values, which might cause random errors. As every country has different health systems, it is still rational to assume that efficiency of government investments to reduce the economic burden on health will also be differentiated. With a larger dataset, we might be able to calculate more robust estimates of random effects.

Future directions

The decline of the incidence of CHE seems to be associated with an incremental change in GGHE as percentage of GDP. Further research is needed to clarify how the strength of the health system in a given country differentiates the magnitude of the association. Future research will need efforts to obtain the original data derived from the nationally representative household surveys and re-estimate incidences of CHE to ensure consistency in calculation methodology. The methodology defined by the WB should be used since it is officially adopted as an SDG indicator which will be globally tracked in the next decades. The design of each survey instrument should be evaluated carefully to assess whether any differences in the design cause variation in estimated household OOP health spending or not. Future research will also need some extra efforts to create a larger and more balanced longitudinal dataset to reduce

random error and secure internal validity.

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