

Striving for Efficiency in the German Health Care Sector:

Five Empirical Essays in Health Economics

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List of Abbreviations

A	excluded diagnosis (German: Ausschlussdiagnose)
AOK	German: Allgemeine Ortskrankenkassen
ATC	Anatomical therapeutical chemical
BKK	German: Betriebskrankenkasse
cf.	compare
CHC	chronic hepatitis C
CI	confidence interval
CVD	cardiovascular disease
DAA	direct acting antiviral
DRG	Diagnosis related group
EBM	German: Einheitlicher Bewertungsmaßstab
EHC	extrahepatic complication
EHM	extrahepatic manifestation
EU	European Union
F/U	follow-up (year)
G	confirmed diagnosis (German: Gesicherte Diagnose)
GP	general practitioner
GT	genotype
HC	hepatitis C
HCV	hepatitis C virus
HIV	human immunodeficiency virus
ICD-10-GM	International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification
IFN	interferon
J00	ICD-10-GM code „acute rhinopharyngitis“
J00-J06	ICD-10-GM code „acute infection of the upper respiratory system“
LKK	German: Landwirtschaftliche Krankenkasse
m	million
M2Q	at least two quarters (German: Mindestens zwei (2) Quartale)
N	number
No.	number
Obs	observables
OPS	German: Operationen- und Prozedurenschlüssel

OLS ordinary least squares
OR odds ratio
OTC over the counter
PPPY per patient per year
Q quarter
RKI Robert Koch Institute
RNA ribonucleic acid
S.B. standardized bias
SD standard deviation
SHI social health insurance
SVR sustained viralological response
SVR24 sustained viralological response rate after 24 weeks
T2DM Type 2 diabetes mellitus
Unobs unobservables
V suspected diagnosis (German: Verdachtsdiagnose)
WHO World Health Organization
Z (asymptomatic) condition after a diagnosis (German: (Symptomloser) Zustand nach einer Diagnose)

1. Introduction

1.1 Context and scope

Over the last decades, health care expenditures in Germany have been constantly on the rise. This holds for overall expenditures, but also for the share of health care expenditures among the gross domestic product and for per capita expenditures (Federal Health Monitoring, 2019). The latter is the more relevant number, due to an increase in the German population density over time (Federal Statistical Office, 2019). Rising health care expenditures can also be observed for the statutory health insurance (SHI) system which bears the biggest load with respect to health care expenditures in Germany (Federal Health Monitoring, 2019). For example, between 1992 and 2017, per capita health care expenditures paid for by the SHI have more than doubled (Federal Health Monitoring, 2019).

In Germany, a statutory and a private health insurance scheme coexist. While everybody is bound to insure themselves, not everyone can decide between the two systems. Only high earners¹, self-employed, and civil servants can (but do not have to) choose private health insurance. If they opt for the SHI, they are referred to as voluntarily insured while the rest below pension age are mostly compulsorily insured. Sickness funds have to accept all applicants, irrespective of their health status or income. The contribution to the SHI depends on the insurance member's gross wage only, not on the individual's age, gender, or health status. Dependent children and non-working spouses can be co-insured free of charge. Insured persons are free to choose their favorite provider, regardless of the sickness fund they are insured with. Most benefits are identical for all sickness funds and are provided as benefits-in-kind. In addition, sickness funds can offer supplementary benefits which may vary between sickness funds but which represent only a small part of all medical services (Thönnes, 2019).

In 2017, approximately 72.2 m individuals (87% of the German population) were insured in the SHI while approximately 8.8 m individuals (11%) were privately insured (Association of Supplementary Health Insurance Funds, 2019). Within the system of the SHI, there were 110 sickness funds in 2018 (Federal Health Monitoring, 2019). There are five types of sickness funds: The so-called general local health insurance

¹ The exact annual gross salary needed is adjusted each year. In 2011, e.g., it was at least 49,500.01 euros.

funds (*Allgemeine Ortskrankenkassen*² (AOK)), company health insurance funds (*Betriebskrankenkassen* (BKK)), guild health insurance funds (*Innungskrankenkassen* (IKK)), supplementary health insurance funds (*Ersatzkrankenkassen*), the agricultural sickness fund (*Landwirtschaftliche Krankenkasse* (LKK)), and the German pension fund Knappschaft-Bahn-See (*Deutsche Rentenversicherung Knappschaft-Bahn-See*). Thus, company health insurance funds – which will be of relevance later in this thesis – are part of the German SHI. In 2018, there were 85 company health insurance funds (Federal Health Monitoring, 2019), and 10.9 m individuals were insured via company health insurance funds (Association of Supplementary Health Insurance Funds, 2019).

Due to the high share of individuals statutorily insured, in this thesis the focus will be on the SHI. However, findings can also be relevant for decision makers in the private health insurance because also there, premiums have been increasing (Private Medical Insurance, 2019). Rising health care expenditures in the SHI are critical because they lead to higher contributions in order to finance these costs.³ Besides a tax-financed subsidy from the German state (*Bundesbeteiligung*), the SHI is mainly financed through contributions paid by the individuals insured in SHI. A further rise in contributions is undesired, because for the individual the burden due to the sum of taxes and social contributions is getting larger. Besides income tax and SHI contribution, statutorily insured employees are also obligated to pay social contributions to compulsory long term care insurance, statutory pension insurance, unemployment insurance, solidary tax⁴, and – if applicable – church tax. If the sum of these transfers is too high, employment becomes too expensive which has negative consequences for the economy.

Several drivers of health care costs have been identified. First of all, the demographic change in Germany leads to a shrinking portion of younger or working-age individuals and a rising share of older individuals. It is caused by a low number of children per woman of childbearing age, in combination with a rise in life expectancy (Federal Health Monitoring, 2019). Although the number of children per woman of childbearing age has been rising lately, it is still too low to guarantee population stability (e.g., 1.565

² Here and in the following, German terms are indicated by using italic letters.

³ Another reason for the rise of contributions is a slower increase in wages than in expenditures.

⁴ In August 2019, the German government decided that from 2021 on, the solidary tax will be abolished for 90% of the current payers (Tagesschau, 2019).

in 2017; Federal Statistical Office, 2019). As a consequence, contributions to the SHI have to be borne by a shrinking group of working-age individuals for a growing group of old-age individuals that do not only contribute less to the SHI (because pension is usually lower than income during working life) but instead cause high costs due to old-age sickness.

Another cost driver is technological progress. The development of improved therapy options and methods to diagnose diseases is a major requirement. However, newer techniques are frequently costlier than the old standard procedures. To name only one example, the pharmaceutical manufacturer Gilead Sciences developed the substance sofosbuvir which is being sold in Europe since 2014 as Sovaldi® (European Medicines Agency, 2019). It is used to treat hepatitis C which is a widely spread disease. The medication is taken orally (instead of by injection, like the former standard therapy), it is better tolerable to the patient compared to earlier therapy options, treatment is shorter and more simple, and it has high chances of cure (up to 90%) (Banerjee and Reddy, 2016; World Health Organization, 2016). However, each pill which has to be taken daily for (depending on the concrete patient) 12 or 24 weeks (European Medicines Agency, 2019) costs about 700 euros⁵ (Korzilius, 2014), so one treatment cycle amounts to nearly 60,000 or 120,000 euros, respectively. Given that there are approximately 249,000 to 415,000 hepatitis C patients in Germany⁶, the question of how much a new therapy is allowed to cost, and what costs can be borne by the SHI community, arises.

Thirdly, unnecessary costs arise because of inefficiencies in the health care sector, mainly due to undesirable behavior of patients or doctors. For patients, ex-ante moral hazard and ex-post moral hazard can be observed (Breyer et al., 2012). Ex-ante moral hazard means that because individuals know they are insured, they take less care in preventing damage to their health. This can include unhealthy behavior like smoking or drinking, e.g. In contrast, ex-post moral hazard means that once individuals are ill, they make use of too much treatment. This means they also choose treatments with no

⁵ In 2015, the National Association of Statutory Health Insurance Funds (*GKV-Spitzenverband*) and the pharmaceutical manufacturer agreed on a price reduction. The new price was 480 euros per pill (Kahle, 2015). In addition, discount contracts (*Rabattverträge*) have been negotiated between single sickness funds and the pharmaceutical manufacturer. As a result, costs per pill sank by the time, but treatment with Sovaldi is still costly.

⁶ Own estimation from 83 m inhabitants (Federal Statistical Office, 2019) and a prevalence rate of 0.3% to 0.5% (Poethko-Müller et al., 2013; Bruggmann et al., 2014; Robert Koch Institute, 2015).

or only a small additional value. For both ex-ante as well as ex-post moral hazard it has been found that co-payments can be a device to tackle these sources of inefficiency (Breyer et al., 2012). Furthermore, doctors may have incentives to conduct examinations or treatments that are dispensable or that are too expensive, just because the bill is not paid by the patients but by their insurance, and doctors may induce demand for their services (Breyer et al., 2012). This can happen because of the information asymmetry that usually exists between doctors and patients. In addition to misbehavior due to undesirable incentives, doctors may treat patients inefficiently, just because they do not have the knowledge about the most efficient way of examination or treatment, or because the treatment of one patient by several doctors is not well coordinated. Therefore, further research is needed to find the most efficient ways in order to help clinical decision makers improve their work. Finally, further knowledge about the prevalence or incidence of diseases is important.⁷ Only then resources can be used tactically instead of only reactively, and then they can be allocated in an efficiently.

Since the 1970s, several major reforms in the SHI intended to mitigate the rising of costs (Knieps and Reiners, 2015). However, although these reforms were certainly helpful, costs tend to rise further. Therefore, it is interesting and relevant from a policy point of view to search for ways of how costs can be hampered in rising further. While it is neither possible to simply stop demographic change nor wanted to impede technological progress, identifying inefficiencies – or striving for efficiency – in the health care sector is one promising approach. Striving for efficiency is necessary because the resources are finite, even though it is frequently said that health is the supreme good in life. It is inefficient if a given output costs too much, or if with a given budget a better output could be achieved. In this thesis, I deal with both aspects of inefficiency, although the focus is on costs. Direct and indirect costs can be differentiated, and I start by looking at direct costs. In Chapter 2, I investigate whether premium refunds, a special type of co-payment, can help to reduce ex-post moral hazard behavior among individuals that are insured via SHI. I hypothesize that this form of co-payment can make patients handle resources in a more parsimonious way. Chapters 3 to 5 use the disease hepatitis C as an exemplary illness for the analyses. Chapter 3 starts by estimating the number of prevalent and incident patients. In a next

⁷ Prevalence includes all patients that are ill at a given point of time, while incidence includes only those who are newly ill. Consequently, prevalence includes those that have been ill before as well as those that are newly ill.

step, Chapters 4 and 5 show that it is efficient to treat patients, and to treat them in an early phase of the disease, because this can reduce health care costs. If patients are not treated or not treated early enough, hepatitis C leads to hepatic as well as extrahepatic complications which cause further health care costs. As a side aspect, we also search for ways of how a given budget can achieve better outcomes. To be concrete, we find that treating hepatitis C (early) does not only reduce costs but due to reduced complications also leads to better non-financial outcomes like a better quality of life. Finally, Chapter 6 looks at indirect costs, namely sickness absence. Sickness absence does not only cause direct costs because the sickness fund has to pay sickness benefits after six weeks of sickness absence⁸; it also causes indirect costs because it leads to output losses. In this chapter we identify channels which make diseases appear more frequently. If these channels are known, decision makers can react accordingly so that (preventable) diseases and the associated sickness absence costs can be reduced.

Next, I will describe the data that were used in this thesis. Afterwards, I will provide some information on hepatitis C – the disease which serves as the basis for parts of the analyses in this thesis – and give a summary of the five following chapters.

1.2 Data

The data which were used in all studies of this dissertation are retrospective individual-level panel data obtained from several German company health insurance funds. Depending on the concrete study, data from one or more sickness funds were used. Therefore, data volume – or the number of individuals in the respective study – can be very different. However, the general structure of these data is identical. The longitudinal database allows the evaluation of patterns of healthcare and healthcare resource utilization on up to 5.2 million insured individuals in Germany and covers the years 2004 to 2014 at most. Depending on when the study was carried out, the available data may end in earlier years or begin in later years. All patient level data are anonymized and comply with German data regulations. All sickness funds of which

⁸ In case of sickness absence, insured persons receive their full wage by the employer. Only from day 43 of sickness absence (due to the same diagnosis) onwards, the sickness fund pays a sickness benefit which is limited to 70% of the latest gross salary (but no more than 90% of the net wage) and is paid for 78 weeks within three years at most.

data are used were informed about the projects and approved the use of their data for the study purposes.

The available data include full billing information of utilized health services in hospitals, at practitioners, on pharmaceuticals, sick leave, as well as a long list of so-called other costs. In addition, core data of the insured individuals are disposable. In all data sets, there is an anonymized identifier by which data sets can be merged.

In the following, the data will be described in more detail. However, data description is limited to aspects relevant for the studies in this thesis.

The data on hospital treatment report the date of admission and discharge to/from hospital and whether a treatment took place inpatient or outpatient. For every hospital visit we find up to three main diagnoses and for each main diagnosis up to ten concomitant diagnoses. Diagnoses are coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification (ICD-10-GM). In addition, the data contain information on up to 30 OPS codes (*Operationen- und Prozedurenschlüssel*; German classification for operations and procedures conducted in hospital or at practitioners) with the respective date of treatment. Finally, the data provide information on billed diagnosis-related groups (DRGs, German classification) and related costs.

Next, the data on practitioners inform about the date of treatment, the diagnoses, and the status of certainty for each diagnosis. Diagnoses (ICD-10-GM coded) are available on a quarterly basis only. The status of certainty differentiates between confirmed (G: “*Gesicherte Diagnose*”), suspected (V: “*Verdachtsdiagnose*”), excluded (A: “*Ausschlussdiagnose*”), or (asymptomatic) condition after a diagnosis (Z: “*(Symptomloser) Zustand nach einer Diagnose*”). In most cases, one would consider diagnoses marked by G or Z only because suspected and excluded diagnoses are not of interest for most research questions. In addition, the data allow to differentiate between general practitioners and specialists. Finally, the data contain the billed fee schedule items (*Gebührenordnungsnummern*) according to EBM (*Einheitlicher Bewertungsmaßstab*, German system of medical remuneration for outpatient services) as well as related costs.

The data on drug prescriptions inform about the date of prescription, the anatomical therapeutical chemical (ATC) code of prescribed medications, and related costs. The ATC code identifies the active substance within the respective medication.

Sick leave data report the first and last day of sickness absence, the main reason for sickness absence (ICD-10-GM coded), as well as the amount of sickness benefit paid by the sickness fund.

Next, there is a very heterogeneous group of data which is called other costs. These data contain remedies (e.g., occupational therapy, physiotherapy, logopedics); aids (e.g., glasses, hearing aids, prostheses); rehabilitation (outpatient, inpatient); grants for participation in certified prevention courses, in bonus programs, or in optional tariffs; transportation expenses; and many more.

Finally, the core data of the insured person comprise information on gender, age (in years), and the start and end date an individual was insured with a specific sickness fund. While this information is available for all individuals insured, there are some aspects that are only known for insurance members, not for co-insured family members. This applies, e.g., to the social security category (*Versichertensatus*), level of education, the profession, or the establishment identification number (*Betriebsstättennummer*). The latter shows which individuals work at the same establishment, although it remains unknown which company the insured actually works for.

Using an anonymized personal identifier, individuals can be observed across all areas of service and over time as long as they are insured with one of the observed sickness funds.

This data base is unique because it covers all fields but dentists that are relevant for the SHI, as well as a considerable number of individuals. Compared to other data bases used in the field of health economics, a volume of up to 5.2 million individuals is remarkable. In addition, these individuals can be tracked for up to 11 years⁹ which is substantial.

The representativeness of the data used for the total SHI was exemplarily analyzed with respect to age and gender in Chapter 2 (Table A1). It becomes apparent that while in the sample the share of women is lower than in the SHI (45% vs. 50%), overall differences are only small.

Despite the advantages of the data depicted above, there are important limitations which should be kept in mind when interpreting the results. First of all, it would be

⁹ The highest number of years which was used in one of the five studies was 10 years in Chapter 3.

desirable to have information on health related behavior (sports, drinking, smoking) or attitudes.

One shortcoming of data on practitioners is that diagnoses are available on a quarterly basis only and that these diagnoses cannot be assigned to the corresponding billed fee schedule items for which the date exists. Therefore, it is not always clear which treatment was made because of which diagnosis. Furthermore, due to lump sum billing, not every visit to the doctor is actually in the data. If a quarterly lump sum was billed, a follow-up doctor visit is only recorded if it contains a treatment which does not count to the lump sum. As a result, the number of doctor visits will be underestimated. While some lump sums had existed already before, there was a major reform in Germany called SHI competition reinforcement law (*GKV-Wettbewerbsstärkungsgesetz*) that led to even more lump sum billing from 2008 onwards. Therefore, the data are affected accordingly.

Data on sickness absence may be incomplete for the first three days. This is because German law obligates employees to show a sick certificate (which has to be issued and signed by a doctor) on the fourth day of sickness absence at the latest. However, some (but not all) employers demand such a sick certificate earlier, sometimes from the first day of sickness absence onwards. Another threat to completeness of sickness absence data is that employees are supposed to hand in the sick certificate to their sickness fund. In case of minor illnesses, though, for which it is clear that they will not continue for six weeks or longer, the employee might decide not to hand it in – just because of convenience – as he faces no disadvantage in this case. In addition, the data only include cases that are closed at the time of data retrieval. This means, if data end on December 31, 2014, for example, a sickness absence spell that lasts until later than December 31, 2014 will not be in the data (but in the updated version that may be retrieved a year later, e.g.). The same applies to hospital visits that are not over yet.

Another shortcoming of data on hospital visits is that they only contain total costs per visit. However, in most cases patients have a multitude of diagnoses and treatments. Then, it is not possible to decide which part of the costs belongs to which diagnosis or treatment, and the full costs have to be used which results in an overestimation of disease-specific costs.

Generally, the data include only information that are relevant for remuneration of health care resource use between the sickness fund and the service provider. For

example, it contains the information whether some test was conducted but not the test result. Likewise, it does not contain information on medical services paid for by the patient, or on OTC (over the counter) drugs.

Finally, the representativeness of the data used with respect to sickness absence was exemplarily analyzed in Chapter 6 (Table 20). It firstly shows that for individuals insured with company health insurance funds the share of employees who are sick on the first day of each month is smaller than that for individuals in the total SHI; and secondly, that individuals insured in the sickness fund that was utilized in Chapter 6 are even less frequently on sickness absence on the first day of a month compared to individuals insured in any company health insurance fund. Although one single company health insurance fund is not representative of the entirety of company health insurance funds, and although one can think of a long list of other measures to check the representativeness of the data, the findings indicate that individuals insured in company health insurance funds may be healthier than those insured in other parts of the SHI. After all, one could think of even more aspects where it is not clear a priori whether the data used are representative of the SHI.

Only in Chapter 6 the described data were merged with another source of information, namely with quarterly unemployment rates by profession and gender. The data were provided by the Institute for Employment Research (IAB) (2012) and cover the period Q1/2005 until Q2/2011 (26 quarters).

1.3 Hepatitis C

In the following, it is explained why hepatitis C is a suitable disease to demonstrate how direct costs can be reduced. In addition, I provide some basic information on the disease and its treatment. First of all, hepatitis C is a major global health problem with over 80 m individuals infected worldwide (Gower et al., 2014), thereof approximately 14 m individuals chronically infected in the WHO European region (World Health Organization, 2017a) and around 2.6 m individuals infected with viremic¹⁰ HCV in Western Europe. In Germany, a substantial number of individuals is affected as well. Depending on how exactly infection is measured, the prevalence is estimated to be around 0.3% to 0.5% (Poethko-Müller et al., 2013; Bruggmann et al., 2014; Robert

¹⁰ I.e., the virus can be proved in blood samples.

Koch Institute, 2015) although Robert Koch Institute (RKI) (2018) admits that the actual prevalence is presumably higher because individuals living in treatment and nursing homes, hospitals, or prisons, as well as individuals that consume drugs by injection, that are homeless, or migrants from countries with higher HCV prevalence rates are usually underrepresented in German studies. Although the disease is relevant in both sexes, more than twice as many of the new infections pertain to men rather than to women. The highest share of new infections is observed in men and women both aged 30 to 39 years (Robert Koch Institute, 2018).

Hepatitis C virus (HCV) infection is a systemic disease with hepatic as well as extrahepatic complications (Younossi et al., 2016). Hepatic complications include cirrhosis, hepatocellular carcinoma, and liver failure (Younossi et al., 2017). HCV-related liver diseases do not only cause substantial health care costs (Nevens et al., 2012), but also lead to a remarkable number of individuals dying each year (World Health Organization, 2017a). In addition, HCV is associated with a variety of extrahepatic complication (EHCs) including major health burdens like type 2 diabetes, for example, but also a long list of other diseases (Cacoub et al., 2016). While the economic impact of HCV infection has been studied (see, e.g., Stahmeyer et al., 2014), the burden of hepatitis C-related extrahepatic manifestations is not fully understood for Germany (Kraus et al., 2018a).

Until 2011, the standard therapy option was to combine pegylated interferon alpha and ribavirin. Then, there were two major improvements in therapy options for hepatitis C. In 2011, the first direct-acting antiviral (DAA) therapies were introduced (telaprevir, boceprevir) that were used in combination with pegylated interferon alpha and ribavirin. Although causing higher therapy costs than the former standard therapy, they came with the advantage of a better sustained viral response (SVR) rate, i.e., a higher chance to cure the disease, and shorter treatment duration was necessary. Unfortunately, it was also accompanied by new side effects (Hofmann et al., 2012) and, because it had to be combined with interferon, was still poorly tolerable (Rosenthal and Graham, 2016). Then, in 2014, second-generation DAs were introduced which was a milestone change. They have a much higher efficacy, better safety, shorter treatment duration, and can be interferon-free which makes them more tolerable for patients than earlier treatment options (Banerjee and Reddy, 2016; Sarrazin et al., 2014; World Health Organization, 2016). Therefore, during the period studied (2007

to 2013 or 2014, respectively), therapy options changed dramatically and effects of treatment measured in the studies are a mixture of the various treatment types.

There is one big drawback of the disease for study purposes. Acute HCV infection is typically asymptomatic and is therefore often undiagnosed. The estimated diagnosis rate of HCV is 57% (Razavi et al., 2014). Other studies estimate that even 75% of the infected patients remain undiagnosed for a long time (Robert Koch Institute, 2018). Without being treated, up to 85% of the acute hepatitis C infections will become chronic (Robert Koch Institute, 2018). Chronic hepatitis C (CHC) is defined as an originally acute hepatitis C infection that persists for more than six months (Maier, 2002). However, one has to assume that in many cases diagnosis follows only years after the actual infection. Therefore, it might not always be clear whether a newly diagnosed HCV infection is actually acute or already chronic.

1.4 Summary of the five studies

In the following, I summarize the findings of the five studies and also highlight methodical issues. Due to diverse research questions, different micro-econometric methods were employed in the individual chapters of this thesis.

In Chapter 2 (“**Ex-Post Moral Hazard in the Health Insurance Market: Empirical Evidence from German Data**”) I analyze whether premium refunds, a special type of co-payment, are a suitable device to reduce ex-post moral hazard behavior among individuals insured in the SHI. Broadly speaking, if individuals who chose a tariff including premium refunds do not make use of the health insurance for one year, they will be rewarded by cash. Thus, premium refunds pursue the same goal as deductibles but they do not comprise any risk of loss for the insured. In this study, I use individual-level panel data from two German company health insurance funds that cover the years 2006 to 2010. I measure the effect of participation in 2010 on a variety of health resource use measures in 2010. Thereby, I want to find out whether participation in the premium refund tariff reduces health care resource use, especially in case of a minor ailment. Because participation in the tariff is voluntary, self-selection is a severe issue. To account for this, I use a large set of control variables including socioeconomic variables, lagged measures of medical demand, and some diagnoses, and combine propensity score matching with regression adjustment. Including lagged outcomes as control variables is supposed to account for any remaining unobserved

heterogeneity that cannot be accounted for explicitly because the necessary variables do not exist. I find that choosing the premium refund tariff is associated with a significant reduction in the probability of visiting a general practitioner. Furthermore, the probability of visiting a doctor due to a trivial ailment such as a common cold is reduced. Effects are mainly driven by younger (and therefore healthier) individuals, and they are stronger for men than for women. Medical expenditures for doctor visits are also reduced. I conclude that there is evidence that premium refunds are associated with a reduction in ex-post moral hazard. Robustness checks support these findings. Yet, by using observable characteristics for matching and regression, it is never possible to completely eliminate a potentially remaining selection bias and results may not be interpreted in a causal manner.

Chapters 3 to 5 have in common that they use the disease (chronic) hepatitis C as the basis of the analyses. Chapter 3 (“**The Number of Patients with Chronic Hepatitis C in Times of New Therapy Options: A Retrospective Observational Study on German Health Insurance Funds Data**”, joint work with Heiko Friedel and Heike Fröhlich) begins by estimating prevalence and incidence rates of patients that are affected by chronic hepatitis C (CHC). Furthermore, the study estimates the number of prevalent and incident patients among the SHI. We use data on 3.2 m individuals from the years 2004 to 2013 and estimate quarterly and annual prevalence and incidence rates for 2007 to 2013. Besides the absolute numbers, we were interested in whether the introduction of new promising therapy options (namely telaprevir and boceprevir) in 2011 was associated with an increase in diagnosing (new) patients. We hypothesized that better therapy options could encourage doctors to engage harder in identifying infected patients. It is challenging that only about 4.7% of the CHC patients receive treatment associated with doctor visits which is the only way to identify patients. Therefore, we assume that individuals suffer from CHC also in quarters with no diagnosis if we have already found one in any of the previous and additionally in any of the subsequent quarters. As a result, prevalence and incidence rates in the middle of 2007 to 2013 (especially 2009 to 2011) will be more reliable than at the left or right end of the timeline. To differentiate incident from prevalent patients, we search for an earlier diagnosis in the 12 quarters prior to each diagnosis. If we do not find one, we consider the patient being incident. A retrospect of 12 quarters, associated with the requirement that the patient must be fully insured during this time, is reasonably long to find an earlier diagnosis if it exists, but it has the disadvantage of

losing especially younger and healthier insureds because these tend to change the sickness fund more often and thus may not be fully insured during the retrospect. Using regression adjusted matching (1:n), we tested for a potential selection bias. Although results are statistically significant, they are very small in magnitude and we conclude that selection is not a problem here. We find a prevalence rate of approximately 0.2% which is slightly lower than in the literature (0.3-0.5%) and which corresponds to about 120,000 to 135,000 patients in the SHI. Surprisingly, there was no increase but rather a minimal decrease of patients in 2011. For the incidence rates we find a general declining trend over time with the sharpest drop between 2010 and 2011 (from 0.2% to 0.15%). This corresponds to around 14,000 and 10,000 newly diagnosed patients in the SHI per year, respectively. All in all, we conclude that there was no increase in CHC diagnoses. Although the new treatment had a higher efficacy and shorter treatment duration, it had a complex application algorithm and was still poorly tolerable for the patients. These drawbacks may have led doctors to a hesitant behavior in treating CHC.

Chapters 4 and 5 have in common that they result from the same research project. In the end, analyses were so diverse that we were asked to split them into two separate papers. They both use data on 5.2 m individuals from the years 2007 to 2014. While in Chapter 3 the focus is on CHC itself, Chapters 4 and 5 examine hepatic and extrahepatic complications (EHCs). Specifically, Chapter 4 (“**Clinical and Economic Burden of Hepatic and Extrahepatic Complications from Chronic Hepatitis C: A Retrospective Analysis of German Sickness Fund Data**”, joint work with Michael R. Kraus, Henning Kleine, Marc Pignot, and Yuri Sanchez Gonzalez) focuses on the clinical burden of EHCs that result from CHC, and on the economic burden of hepatic and extra-hepatic complications. EHCs include extrahepatic manifestations (EHMs) for which a documented clinical pathway with CHC is described in the literature, as well as other diseases that were found to be prevalent in our patient population. The list of EHCs contains type 2 diabetes, cardiovascular disease, Parkinson’s disease, mental and behavioral disorders (due to use of opioids, or due to multiple drug use and use of other psychoactive substances), fatigue, renal impairment, and malignancies, amongst others. In the first part, Chapter 4 looks at the clinical burden and assesses whether the risk of EHCs is higher for CHC patients than for individuals not affected by hepatitis C. It does so by estimating the prevalence of the various EHCs in follow-up years 1 and 5 as well as the cumulative four-year-

incidence. In addition, using logistic models, odds ratios and p-values are calculated to show how big differences actually are and to test whether differences are statistically significant. For this purpose, CHC patients are identified and matched to individuals not affected by CHC throughout the whole study period. For CHC patients, the index quarter is the first quarter for which we find a relevant diagnosis; for controls, a random index quarter is assigned. Matching is done 1:1 on the index quarter, age, gender, and the previous year's health care costs (all in categories). We find that prevalence and incidence of any EHC is higher in the CHC cohort than in the no-CHC cohort. This is mainly driven by mental and behavioral disorders. In the second part, Chapter 4 looks at the economic burden of hepatic and extrahepatic complications. Therefore, costs are measured from the index quarter until the end of follow-up (which is of variable length) and standardized to one year. CHC- and EHC-related costs are identified using relevant ICD-10-GM, EBM, DRG, OPS, and ATC codes. Then, costs are adjusted to reflect 2016 Euro exchange rates and compared between CHC patients and matched (1:5) no-CHC patients, using adjusted OLS regression models. The study looks at various cost categories: total costs (hospital, practitioner, sickness benefits, pharmacy costs), total costs but pharmacy costs, hepatic-complications related costs, EHC-related costs, CHC-related pharmacy costs, and non-CHC-related pharmacy costs. All types of costs are significantly higher in the CHC-cohort than in the no-CHC cohort, EHC-related costs being a major driver of this difference.

Chapter 5 (“**Improvement of Hepatic and Extrahepatic Complications from Chronic Hepatitis C after Antiviral Treatment: A Retrospective Analysis of German Sickness Fund Data**”, joint work with Michael R. Kraus, Henning Kleine, Marc Pignot, and Yuri Sanchez Gonzalez) applies similar methods as Chapter 4, but instead of comparing costs for CHC and no-CHC patients, it compares costs for incident CHC patients a) under treatment vs. not under treatment, and b) if they started treatment at an early stage (i.e., without having developed cirrhosis) vs. at a late stage of CHC. Time under treatment is measured from the quarter of treatment initiation until the end of follow-up. Untreated time is measured from the quarter of identification until the end of follow-up or until initiation of treatment, whichever comes first. As a result, the same patient may contribute time to both cohorts. To identify whether treatment starts at an early or late stage, we search for a diagnosis of cirrhosis during four quarters prior to treatment initiation. One difference to Chapter 4 is that in Chapter 5 cohorts are not matched. Instead, due to small cohort sizes, only

regression methods are used to adjust for differences between the groups. For the comparison, the same cost categories are used as in Chapter 4. We find that the economic burden from CHC-related hepatic and extrahepatic complications is reduced after initiating treatment. The savings for costs attributable to EHCs are primarily driven by mental and behavioral disorders. Total costs are lower during treated than during untreated time, too, if pharmacy costs are excluded. Only CHC-related pharmacy costs are substantially higher during treated than during untreated time which leads to higher total costs for this cohort. However, this does not mean that the observed additional costs may not be more than offset by savings in the long run (which has to be analyzed in further research). Finally, for nearly all cost categories, adjusted cost differences are in favor of early treatment beginning. This also holds for total costs, albeit without statistical significance. Here, the savings in costs attributable to EHCs primarily stem from malignancies.

We conclude from Chapters 4 and 5 that chronic hepatitis C is significantly associated with clinical and economic burden which can be attributed to hepatic and extrahepatic complications. Treating CHC (earlier) may help avoiding costs that are caused by the emergence of those complications. The results of the two chapters may help guide clinical decision making and thereby lead to significant cost savings for the SHI.

Finally, in Chapter 6 (“**Sickness Absence and Unemployment Revisited**”, joint work with Stefan Pichler), the focus moves from direct to indirect costs. Sickness absence is costly, even if no sick benefits are paid, because of output losses. We use data from 2005 to mid-2011 on 0.2 m individuals to estimate the relationship between sickness absence and unemployment. We hypothesize that the frequently observed pattern of higher sickness absence during economic booms (“procyclical sickness absence”) can be partly explained by incentives that change over the business cycle. To be concrete, we argue that there are two types of workers. On the one hand, there are workers whose sickness absence is procyclical, most likely because they fear job loss during recessions when they engage in presenteeism. We identify these workers in our data as those that do not change jobs during the study period. On the other hand, there are workers whose sickness absence is countercyclical, i.e., it is higher during recessions – most likely because during booms these workers engage in presenteeism: they want to make use of career (or bonus payment) opportunities, they have a leading position and cannot afford to be absent, or they just receive pressure through the employer who faces full order books. We identify these workers, for whom we assume

that they are not afraid of losing their job, as those that have changed jobs during the study period. In addition to the type of worker, the type of disease presumably plays a role. Therefore, we look at detailed health diagnoses. While the arguments above hold for non-contagious diseases, for contagious diseases literature has found that the procyclical relationship is largely driven by infections. Third, we differentiate between short and long sickness absence to account for the severity of the disease. We argue that for larger health shocks sickness absence is (almost) unavoidable and that it is not subject to the decision of the worker. Our theoretical model captures these three aspects. We only include working individuals aged 16 to 65, and only those where we find more than one worker per establishment in our data. Since we observe that our sample is healthier than the SHI, we partly take care of this selection by using the profession specific unemployment rate (rather than the overall unemployment rate) in order to capture the movement of the business cycle. For the empirical analyses, our main outcome variable is sickness absence, aggregated to quarterly data, while our main explanatory variable is the lagged quarterly profession specific unemployment rate provided by Institute for Employment Research (IAB) (2012). The lag is used because it is hard to imagine that the average unemployment rate over a full quarter influences sickness absence, particularly at the beginning of the quarter, and because it avoids endogeneity due to reverse causality. We estimate standard fixed effects models and – due to the nature of our dependent variable – count data models with fixed effects. The empirical results are in line with our theoretical model. We do not find that large health shocks vary with the business cycle, but short contagious diseases seem to drive procyclical sickness absence. Furthermore, among workers that do not change jobs, sickness absence due to non-contagious diseases is procyclical while for contagious diseases we find a negative but insignificant relationship. Finally, for workers changing jobs we find procyclical sickness absence for contagious diseases and countercyclical sickness absence for non-contagious diseases. We conclude that the relationship between sickness absence and the business cycle can be explained by different incentives of workers as well as different dynamics of contagious diseases over the business cycle. The overall procyclical sickness absence is driven by sickness absence due to contagious diseases. Since contagious diseases spread mainly during booms, firms who want to reduce procyclical sickness absence should incentivize workers to be absent when they are subject to a contagious disease.

2. Ex-Post Moral Hazard in the Health Insurance Market: Empirical Evidence from German Data¹¹

2.1 Introduction

In many developed countries, health insurance systems suffer from increasing expenditures (OECD, 2015) which is a financing challenge. The increase in expenditures is mainly driven by technological progress, demographic change, and inefficiencies in the health care system, one of them being moral hazard (Schmitz, 2012).

Generally, co-payment can be a device to reduce moral hazard. It may reduce demand for health care services by increasing the price paid by the consumer at the time of consumption (Arrow, 1963; Pauly, 1968). The magnitude of the effect depends on the price elasticity of demand. Imposed on price-elastic health care services, co-payment may be shown to reduce the demand.

Indeed, there is empirical evidence that co-payment – independent from the exact design – can reduce demand in the health insurance market. In the RAND Health Insurance Experiment, medical demand becomes smaller as the level of cost-sharing increases (Manning et al., 1987). Similarly, in the Oregon Health Insurance Experiment, randomly extending insurance coverage increases the use of health care services (Health Policy Brief, 2015).

Furthermore, there is non-experimental literature on compulsory co-payments. A rise in co-payments for doctor visits and drug prescriptions among retired public employees in the US reduces both kinds of medical utilization (Chandra et al., 2010). Likewise, for Switzerland it has been found that in contrast to cost-sharing full insurance coverage increases health care costs and decreases the probability of having zero health care expenditure (Boes and Gerfin, 2016). In 2004, the German statutory health insurance (SHI) introduced a co-payment that had to be paid for every first doctor visit in each quarter. According to Farbmacher and Winter (2013) it leads to a significant reduction in the probability of visiting a doctor by 4 to 8 percentage points. Effects are higher for younger than for older adults. The authors find for young male adults that the co-payment reduces the number of doctor visits by 0.2 to 0.3 visits per quarter, while young women do not seem to be affected. Also in a subsequent study

¹¹ See Thönnes (2019) for a published version of this chapter.

Farbmacher et al. (2017) estimate a significant increase in the probability of not visiting a doctor, while the subgroup of elderly women with more severe diagnoses and a higher level of drug consumption is rarely affected. In contrast, Kunz and Winkelmann (2017) use a different methodology and do not find any effect of this co-payment.

Finally, there is literature on settings in which individuals are free to choose more or less insurance coverage. Schmitz (2012) concludes that with less insurance coverage, the probability of visiting a doctor is reduced for insured individuals with previously few doctor visits, while individuals with previously many doctor visits are not affected. At last, optional deductibles are found to reduce the number of doctor visits and the probability of visiting a specialist. Medical expenditures are decreased, also in the medium term. The effect is stronger for higher deductibles (Felder and Werblow, 2008; Hemken et al., 2012; Pütz and Hagist, 2006).

All in all, the literature suggests that deductibles – be they compulsory or optional – can reduce demand for health care services. Interestingly, the design of the cost-sharing scheme plays an important role. Hayen et al. (2018) find that with a deductible scheme individuals react nearly twice as strongly compared to with a premium refund scheme. However, the authors use data from the Netherlands where insurance contracts are shaped differently from Germany. One crucial difference is that deductibles (premium refunds) increase (decrease) by one euro with every euro that is caused as costs to the sickness fund, until some threshold value is reached. Therefore, results cannot be generalized to the German system where any health care resource use (apart from some exceptions) cuts the premium refund to zero (see below). Furthermore, the German system differs from the Dutch system with respect to the type of exceptions that do not cut the premium refund.

Premium refunds are rather new to the German SHI and will be analyzed in this paper. They work differently from deductibles but pursue the same goal. Besides being optional, they are known for not comprising any risk of loss for the insured. Broadly speaking, if individuals who chose a tariff including premium refunds do not make use of the health insurance for one year, they will be rewarded by cash. There is no risk of paying more than a person that stays in the default (“full insurance”)¹² tariff, only the chance of missing the reward. Since individuals are often risk-averse, this may be a

¹² I call the default tariff in the German SHI “full insurance” although it exhibits some kinds of co-payment as well, e.g., for drug prescriptions or hospital stays. However, these are identical for individuals in both tariffs.

fitting solution when facing the incentives of deductibles without having the risk of paying more than in the default tariff. Insured persons are exempt from the premium refund as soon as they make use of their health insurance, so the reward scheme is highly nonlinear. Nonlinear schemes are of high policy relevance and credible evidence on their impact was found earlier (Farbmacher et al., 2017; Gerfin et al., 2015; Aaron-Dine et al., 2015). Yet, it could be a further improvement to look at specific diagnoses when analyzing moral hazard behavior.

My research question is whether premium refunds are a device to reduce ex-post moral hazard as well. Individuals that have opted for such a tariff will make use of the health insurance only if their utility from treatment is at least as high as their utility from forgoing treatment and receiving the premium. Due to information asymmetry, hospital treatment, drug prescriptions, and follow-up doctor visits are primarily decided on by the doctor. In contrast, the decision to visit a practitioner for the first time in the respective year often lies with the patient. This applies especially to general practitioners (GPs) and only to a lesser extent to specialists.

Moreover, one could imagine that participants of the premium refund tariff have an incentive to avoid visiting a doctor in the case of a trivial disease that can also be cured by means of self-medication, e.g., a common cold. Then, demand is supposed to be price-elastic. Assuming that nearly everybody gets a common cold once in a while, everybody is affected by this sickness in a similar way. If individuals visit a doctor due to a common cold, this does not mean that they are sicker than individuals with a common cold who do not visit a doctor. Instead, it reveals their behavior.

I use administrative data from two German sickness funds which both offer a premium refund tariff. I estimate the effect of choosing this tariff (in contrast to staying in the default tariff) in the year 2010 on the probability of visiting a GP or a specialist as well as on the probability of visiting a doctor due to a common cold in the same year. I am aware of the likely selection bias and use regression adjusted propensity score matching as well as a rich set of control variables. Selection is likely to result from the voluntary nature of the tariff. Younger and healthier individuals are especially more likely to opt for such an insurance scheme. Although multiple efforts are undertaken to reduce the selection bias, it is never possible to completely eliminate it using only matching on observables and OLS regression analysis. Therefore, results may not be interpreted in a causal manner. However, to support my findings, I carry out many robustness checks and I assess the level of remaining unobserved heterogeneity by

applying a method proposed by Altonji et al. (2005) and Oster (2016). Since this paper is motivated by increasing expenditures in the health care sector, I additionally estimate the effect on the sickness funds' medical expenditures for practitioners (GPs and specialists), although one has to keep in mind that due to information asymmetry in most cases, the patient cannot fully decide on the type and extent of treatment.

The literature suggests that the degree of moral hazard varies across individuals, e.g., by the extent of demand and the health status prior to the introduction (or removal) of any cost-sharing (Schmitz, 2012; Gerfin et al., 2015), or by the type of disease the individual is suffering from (Koç, 2011). Therefore, I repeat the analysis for subgroups to find out whether the effects are heterogeneous.

The contribution of this paper to the existing literature is first that by identifying relevant ICD-10-GM¹³ diagnoses, it is possible to directly test whether a reduction in medical demand is due to reduced ex-post moral hazard. This is not always clear if medical expenditures or doctor visits are analyzed. Second, to the best of my knowledge, this is the first study that analyzes the effect of premium refunds among the German SHI on moral hazard behavior.

The paper is organized as follows. Section 2.2 gives some background information on the legal regulations, while Section 2.3 discusses the identification and estimation strategy. In Section 2.4, the data are described. Results are shown in Section 2.5, and Section 2.6 discusses the results and concludes.

2.2 Background

The German health insurance system is characterized by the coexistence of a statutory and a private health insurance system. The vast majority of the population in Germany (85.34% in 2010) is covered by SHI (Federal Health Monitoring, 2019; Federal Statistical Office, 2019). Everybody is obligated to insure themselves. However, not everyone can decide between the two systems. Only high earners, self-employed, and civil servants can (but do not have to) choose private health insurance. If they opt for the SHI, they are referred to as voluntarily insured, while the rest below pension age are mostly compulsorily insured. Within the system of the SHI, there were 169 sickness

¹³ ICD-10-GM refers to "International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification".

funds in 2010 (National Association of Statutory Health Insurance Funds, 2019). Sickness funds have to accept all applicants, irrespective of their health status or income. The contribution to the SHI depends on the insurance member's gross wage only, not on the individual's health status. Dependent children and non-working spouses can be co-insured free of charge ("co-insured family members"). Insured persons are free to choose their favorite provider, regardless of the sickness fund they are insured with. Most benefits¹⁴ are identical for all sickness funds and are provided as benefits-in-kind. In addition, sickness funds can offer supplementary benefits which may vary between sickness funds but which represent only a small part of all medical services.

Premium refunds are rather new to the SHI. After some pilot projects (Malin and Schmidt, 1995), they were introduced to the whole system in 2007. In 2010, there were 152,571 individuals enrolled in the tariff (Federal Health Monitoring, 2019) which corresponds to 0.2% of all statutorily insured persons. It can but does not have to be offered by the sickness fund. If the insurance company installs the tariff, it is offered to all members that have been insured with the sickness fund for at least three months. Enrollment in the tariff is voluntary and may start any time of the year. Insurance members decide whether they want to participate in the tariff, co-insured family members have to follow accordingly. If a person enrolls during the year, some sickness funds allow for retrospective enrollment (i.e., enrollment applies to the whole calendar year), while others restrict enrollment to the remainder of the year. Given an insurance member and the co-insured family members do not cause expenditures within one calendar year, the insurance member receives a refund of 1/12 of his annual insurance contribution.¹⁵ Otherwise, the refund is cut to zero. Thus, the plan is highly nonlinear.

¹⁴ These benefits are recorded in the Code of Social Law Book V ("Sozialgesetzbuch V").

¹⁵ Each sickness fund has its own contribution rate which applies to both individuals in the default tariff as well as those in the premium refund tariff, and which is identical for both. As a contribution, 7.3% of the employee's gross income is paid by the employer, the rest by the employee. For example, if the total contribution rate is 15.5% the insured pays 8.2%. If they earn 2,000 euros gross per month, they pay a contribution of 164 euros each month. This is the amount a participant of the premium refund tariff may get back at the end of the year. For individuals in the default tariff, there is no premium refund at all.

The only treatment allowed where the refund is not lost is for the under-18s, early diagnosis examinations, and prevention.¹⁶

If individuals choose the premium refund tariff, they are bound to the respective sickness fund for one year which is one reason why not everyone wants to enroll. Another reason for the relatively small share of enrollees is that sickness funds do not promote this tariff very strongly.¹⁷ Furthermore, especially women in their childbearing years will not choose this tariff if they plan to collect a prescription for contraception every (second) quarter. Likewise, those under permanent medication do not have a reason to register for this tariff. Finally, for many individuals it is more attractive to choose another tariff which is often offered by sickness funds besides the premium refund tariff, the so-called deductible tariff. Here, individuals pay a lower premium to their sickness fund, but in the event of a sickness, they bear the risk of paying more than the premium of the default tariff. The advantage of the deductible tariff is that even if individuals visit a doctor for a minor issue, they might only pay a small deductible so that all in all, they are better off compared to the default tariff. Since insured individuals are not allowed to combine the premium refund tariff and the deductible tariff, many of those who are willing to choose any non-default tariff will select the deductible tariff.¹⁸

If sickness funds offer the premium refund tariff, they must prove to their respective supervision every three years that the tariff pays for itself, i.e., cross-subsidization is not allowed. This is supposed to prevent the rise of insurance contributions due to this tariff.

In addition, sickness funds are allowed to offer other tariffs. In so-called bonus programs, the insured are rewarded if they can prove a healthy lifestyle and preventive actions. Again, participation is voluntary.

¹⁶ For individuals that have been less than 365 days insured, the refund tariff works analogously: These individuals paid less insurance contribution in this year (e.g., only for 11 months) but they can still get a premium refund of 1/12 of their annual insurance contribution, i.e., the absolute value of the potential premium refund is lower.

¹⁷ Both sickness funds offer information on the premium refund tariff on their website. However, there was no additional information sent to the insured via newsletter.

¹⁸ In fact, in 2010 there were twice as many individuals enrolled in the deductible tariff compared to the premium refund tariff (Federal Health Monitoring, 2019).

2.3 Identification and estimation

I observe two groups. The treatment group consists of individuals that participate in the premium refund tariff, whereas the control group does not. Treatment takes place during the whole year of 2010 (cf. Figure 1). Outcomes, a group of various measures of medical demand, are quantified at the end of 2010 for the duration of the year, i.e., January 1, 2010, to December 31, 2010.

Figure 1: Timeline

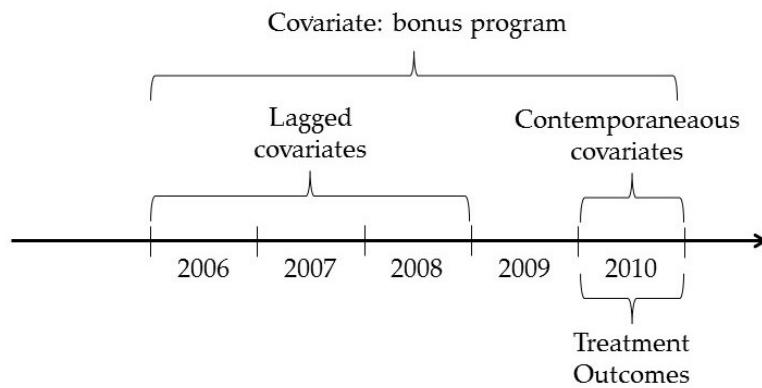


Figure 1 shows in which years the treatment variable, outcomes, and the different covariates are measured.

I am interested in the average treatment effect on the treated (ATT), which is the difference in demand for medical treatment between persons in the treatment group that have been treated on the one hand and persons in the treatment group had they not been treated on the other hand:

$$\tau_{ATT} = E[Y(1) | D = 1] - E[Y(0) | D = 1] \quad (1)$$

where $D = 1$ indicates that an individual belongs to the group that will choose the tariff. $Y(1)$ is the demand of individuals that actually chose the tariff, whereas $Y(0)$ is the demand of these individuals had they not chosen it.

Naturally, the counterfactual $E[Y(0) | D = 1]$ is not known. Since participation is voluntary, individuals opting for the tariff differ from persons who do not, even if there was no treatment (selection bias). Therefore, I use the large group of non-participants to find individuals that are similar to the participants in all relevant (pre-treatment) characteristics.

The conditional independence assumption (CIA) will be violated if there are differences between participants and non-participants with respect to their risk, i.e., their health status, and with respect to their risk aversion (Cutler et al., 2008). Individuals maximize their expected utility. Therefore, if individuals expect high expenses in the future, they will prefer more coverage. The health status in the past is associated with the health status and the demand for health services, both in the future, and, therefore, also with the tariff choice. I use lagged values of health care claims and certain diagnoses as a proxy for the health status previous to the year 2010 (cf. Figure 1, “Lagged covariates”).¹⁹

Furthermore, risk-averse individuals might avoid co-payments of any kind and may, therefore, be less likely to choose the premium refund tariff. Simultaneously, they might show higher preventive effort (Schmitz, 2012). As a proxy for the risk attitude toward health, I use the information of whether the individual participated in the sickness fund’s bonus program in any of the years 2006 to 2010 (cf. Figure 1, “Covariate: bonus program”). Individuals that participate in a bonus program are more concerned with their health status and are, therefore, suspected of being risk-averse. Also, Cutler et al. (2008) assess the “receipt of preventive health care as a behavior that likely captures individual risk aversion”. Since bonus programs primarily consist of preventive health activities, this is a useful proxy. I assume that risk attitude is stable over a period of five years, and that it is a valid signal if the individual participated in the bonus program in any of these years. The bonus program existed years before the premium refund tariff was implemented. Therefore, it is unlikely that choosing the premium refund tariff would affect participation in the bonus program. One limitation of this proxy is that the underlying risk aversion is presumably continuously distributed while participation in the bonus program is a dichotomous measure. Therefore, it is useful to also match on pre-treatment outcomes (cf. Figure 1, “Lagged covariates”). This approach accounts for historical factors that cause current differences in the dependent variable that are difficult to account for in other ways (Wooldridge, 2015) and has frequently been used in applied research (see, e.g., García-Gómez, 2011; García Gómez and López Nicolás, 2006; Hagan et al., 2009) to control for individual-specific unobserved heterogeneity. Being a rather unspecific approach,

¹⁹ To condition on lagged outcomes and on some lagged covariates, I use the average of the years 2006 to 2008. Observations of the year 2009 are not used as control variables because individuals could anticipate their participation in 2010 and choose to antedate medical demands. This behavior was shown by Chandra et al. (2010).

using lagged dependent variables as proxy variables may also help to account for other sources of unobserved heterogeneity such as genetic factors or lifestyle factors.

I use socioeconomic information measured in 2010 to further adjust the two groups (cf. Figure 1, “Contemporaneous covariates”). Besides age and gender, I control for insurance status and education as well as being insured with one of the two sickness funds.

While I chose some covariates due to economic theory, others were selected by an algorithm proposed by Imbens (2015)²⁰. In addition, the algorithm selected a large set of interaction terms which makes the model more flexible.

To take the CIA as given, it would be necessary to also consider the possibility of selection on moral hazard (Einav et al., 2013). When opting for or against more insurance coverage,²¹ individuals take into account how strongly they will react to an increase in insurance coverage. According to Finkelstein et al. (2015), if deductibles are optional, those who are less responsive than average to consumer cost-sharing are more likely to choose deductibles. Individuals with higher price sensitivity would rather not choose deductibles. Although premium refunds and deductibles are not the same, they set similar incentives. Therefore, the estimated effects will resemble a lower bound and effects may even be up to two or three times higher (Finkelstein et al., 2015) if participation was mandatory.

I use the Epanechnikov kernel estimator for the propensity score-based matching procedure.²² Propensity score matching has the advantage of condensing the information of numerous matching variables into a one-dimensional measure. The Epanechnikov kernel estimator is appropriate for this application because it takes many controls into consideration for every treated and gives more weight to rather

²⁰ Imbens proposes pre-selecting variables that are assessed as being important according to economic theory. In addition, a set of variables is selected where it is not clear whether they should be included in the model. Each of these variables is tested by comparing a logistic regression of the treatment dummy on pre-selected variables with a logistic regression of the treatment dummy on pre-selected variables plus one of the variables that are to be tested. The variable where the likelihood ratio test statistic is the highest is included in the model. This procedure is repeated until the test statistic falls below some threshold. In line with Imbens (2015), I use 1.00 as threshold value for linear terms and 2.71 for quadratic/interaction terms.

²¹ With an increasing degree of cost-sharing, insurance coverage becomes smaller because the sickness fund only pays for a smaller part of the costs.

²² For the estimation, I use the psmatch2 Stata command.

similar than to rather different controls. Using a probit model, the propensity score is estimated as follows:

$$participation = \alpha_0 + X'\delta + u \quad (2)$$

where X represents the vector of covariates (cf. Table 1, plus a long list of interaction terms), and u is the error term. As a result, treated individuals are matched to controls that have a similar but not identical propensity score. There may still be discrepancies between the covariates of the two groups, even though differences have already been reduced by the matching procedure. Hence, the estimator may still be biased. One can attempt to reduce this (residuary) bias by using regression methods (Imbens and Wooldridge, 2009). Therefore, I combine matching with regression adjustment.²³ Using the matched sample, I regress each outcome on participation in the premium refund tariff and on all control variables that have also been used for the matching procedure. The regression model is

$$Y = \beta_0 + \beta_1 participation + X'\gamma + \varepsilon \quad (3)$$

where Y is one of the outcomes (cf. Table 1), X again represents the vector of covariates, and ε is the error term. In addition, the weights which result from the matching procedure are used in the regressions. In line with Schmitz and Westphal (2015), in the OLS regressions I employ robust standard errors because they are easier to compute even though they are slightly more conservative than bootstrapped standard errors (Marcus, 2014).

The insured may be allowed to enroll retrospectively in the premium refund tariff, at the latest until the end of the calendar year. This leads to the problem that new participants are not necessarily affected by the tariff. Instead, one has to assume that a considerable share enrolls in the tariff by the end of the year if they discover they did not cause any insurance claims. I aim at removing this effect by eliminating all new participants of the year 2010 from the sample if they did not already participate in 2009.

The effect of more (or less) insurance coverage on medical demand consists of two parts (Finkelstein et al., 2015): The substitution effect is the moral hazard response

²³ Another advantage of combining propensity score matching and regression is that by comparing the distribution of propensity scores between the two groups participants with no or very few controls can be excluded from the analysis (i.e., the data are trimmed). Thereby, the two groups can be made more similar.

and therefore the effect I am interested in. In addition, there may be an income effect, i.e., individuals with more insurance coverage can afford treatment which would be too expensive for them if they had less coverage. Here, the latter presumably does not exist. At the time of treatment, individuals paid the same insurance contribution as if they had stayed in the default tariff. In both tariffs they have access to the same portfolio of benefits. The only difference is that at the end of the year, participants of the premium refund tariff lose a financial reward if they made demands for medical services. At the time of treatment, however, there should be no income effect. Therefore, what I will find is the substitution effect, i.e., the moral hazard response.

Whether the CIA is fulfilled cannot be directly tested. However, the assumption is supported if one does not find an effect of the treatment on a pseudo outcome, i.e., an outcome that is known to be unaffected by the treatment (Imbens and Wooldridge, 2009). I repeat the analysis illustrated above, replacing outcomes with the pseudo outcome “probability of visiting a hospital in 2010”. Treatment in hospital is mostly associated with severe illnesses. Therefore, the demand should be price-inelastic and the effect is expected to be zero.

Finally, to get a better idea of how strong the omitted variable bias may still be, I apply a method that was proposed by Altonji et al. (2005) and further developed by Oster (2016). They had the idea that the degree of selection on observables is a guide to the degree of selection on unobservables. Using the Stata command psacalc, I estimate the treatment effect for the various outcomes under three different assumptions: selection on unobservables is half as big as/as big as/twice as big as selection on observables.

2.4 Data

The panel data cover the years 2006 to 2010 and result from the billing processes of two German sickness funds. They cover the annual costs per insurance member, including co-insured family members but excluding under-18s. Costs contain expenditures for hospitalization, doctor visits, drugs, sickness payments, as well as so-called other costs.²⁴ Thereby, all relevant fields that are covered by the SHI, except for

²⁴ “Other costs” comprise all remaining types of costs and are therefore very heterogeneous. They contain payments for rehabilitation, prevention courses, and home healthcare products, amongst others. When constructing the sum of “other costs” that occur in the sickness fund, I exclude premiums that were paid out to the insured for participating in the premium refund tariff or in a bonus program.

information on visits to the dentist, are included. Annual costs (and count variables, e.g., the number of doctor visits) are standardized (averaged) according to the number of members of the specific family²⁵ as well as the number of days the family was insured with this fund in the respective year. The sample is limited to individuals who were insured for at least 150 days in the year 2010 as well as 150 days in sum of the years 2006 to 2008. This was done because observing individuals for a few days only may lead to biased results. Furthermore, participants of the year 2010 that had not participated in the 2009 tariff were excluded from the sample.²⁶

Beyond costs, information on the date and the ICD-10-GM diagnosis for any contact with the health care system is available. To identify doctor visits due to a common cold, I use two different measures – the ICD-10-GM codes J00 (acute rhinopharyngitis) and J00-J06 (acute infection of the upper respiratory system). I identify treatment of the common cold in the data on practitioners and at hospitals' outpatient departments. The data on practitioners differentiate between GPs and specialists.²⁷ For indicator variables (e.g., on diagnoses), the maximum per family is considered. Moreover, some socioeconomic information on the insured person is available. Finally, it is known whether the person participated in the bonus program. Table 1 provides an overview of all variables used in this paper and explains what they measure.

²⁵ Here, a family consists of the insurance member and his or her co-insured family members. If there are no co-insured family members, the data remain at the individual level. Otherwise, they are condensed to the family level. If both spouses are insurance members (instead of one being the insurance member and one being co-insured), they are recorded separately in the data and not as one family.

²⁶ See section 2.3 (Identification and estimation) for the motivation of this approach.

²⁷ This information has only been available since July 2008 and can therefore not be used for the matching process.

Table 1: Variable description

Variable	Definition/Further description	Measured in year(s)
<i>Dependent variables (Outcomes)</i>		
Doctor visit	= 1 if at least one doctor visit	2010
Doctor visit (GP)	= 1 if at least one visit to the GP	2010
Doctor visit (specialist)	= 1 if at least one visit to a specialist	2010
No. of doctor visits	Number of doctor visits	2010
No. of doctor visits (GP)	Number of visits to the GP	2010
No. of doctor visits (specialist)	Number of visits to a specialist	2010
Common cold (J00)	= 1 if at least one diagnosis J00	2010
Common cold (J00-J06)	= 1 if at least one diagnosis of J00 to J06	2010
Expenditures on doctor visits	Expenditures on doctor visits, measured in euros	2010
Expenditures on doctor visits (GP)	Expenditures on visits to the GP, measured in euros	2010
Expenditures on doctor visits (specialist)	Expenditures on visits to a specialist, measured in euros	2010
<i>Explanatory variables</i>		
Age	Measured in years	2010
Male	= 1 if male	2010
Bonus program in 2006 to 2010	= 1 if participated in bonus program in any of the years 2006 to 2010	2006 to 2010
Sickness fund 2	= 1 if individual is a member of sickness fund 2	2010
Compulsorily insured	= 1 if individual is compulsorily insured	2010
Voluntarily insured	= 1 if individual is voluntarily insured	2010
Unemployed	= 1 if individual is unemployed	2010
Pensioner	= 1 if individual is a pensioner	2010

Variable	Definition/Further description	Measured in year(s)
Educational category 1	= 1 if no apprenticeship and no university-entrance diploma	2010
Educational category 2	= 1 if apprenticeship but no university-entrance diploma	2010
Educational category 3	= 1 if no apprenticeship but university-entrance diploma	2010
Educational category 4	= 1 if apprenticeship and university-entrance diploma	2010
Educational category 5	= 1 if degree of university of applied science	2010
Educational category 6	= 1 if university degree	2010
Positive expenditures total, before	= 1 if total expenditures > 0 euro in any of the years 2006 to 2008	2006 to 2008
Expenditures total, before	Measured in euros; average per year	2006 to 2008
Doctor visit, before	= 1 if at least one doctor visit in any of the years 2006 to 2008	2006 to 2008
Expenditures on doctor visits, before	Measured in euros; average per year	2006 to 2008
No. of doctor visits, before	Average per year	2006 to 2008
Hospital visit, before	= 1 if at least one hospital visit in any of the years 2006 to 2008	2006 to 2008
Expenditures on hospital visits, before	Measured in euros; average per year	2006 to 2008
Drug prescription, before	= 1 if at least one drug prescription in any of the years 2006 to 2008	2006 to 2008
No. of drug prescriptions, before	Average per year	2006 to 2008
Sickness absence, before	= 1 if at least one sickness absence in any of the years 2006 to 2008	2006 to 2008
Expenditures on sickness benefit, before	Measured in euros; average per year	2006 to 2008
No. of times on sickness absence, before	Average per year	2006 to 2008
No. of days on sickness absence, before	Average per year	2006 to 2008
Other costs, before	Measured in euros; average per year	2006 to 2008
Common cold (J00), before	= 1 if at least one diagnosis J00 in any of the years 2006 to 2008	2006 to 2008
Common cold (J00-J06), before	= 1 if at least one diagnosis of J00 to J06 in any of the years 2006 to 2008	2006 to 2008

Variable	Definition/Further description	Measured in year(s)
<i>Pseudo outcome</i>		
Hospital visit (2010)	= 1 if at least one hospital visit during 2010	2010

GP = general practitioner. No. = Number.

All in all, the insurance members' structure in the sample is similar to that in the SHI with respect to gender and age (cf. Table A 1 in the appendix). For 2010, the raw sample contains 751,687 insurance members. After applying the above-mentioned inclusion criteria, the sample contains 439,143 insurance members whereof 13,187 participated in the premium refund tariff. Thereof, 1,492 members received a premium refund.²⁸ Once individuals chose the tariff, they often stayed with it for many years. Of the 13,187 participants in 2010, 12,120 and 10,072 individuals had already participated in 2008 and 2007, respectively.

This study analyzes the effect of premium refunds on a variety of outcomes. Table 2 shows mean values and standard deviations and reveals how these outcomes are influenced by the data processing. It is noticeable that individuals that participate in the premium refund tariff have lower medical demand compared to non-participants with respect to nearly all measures. Furthermore, it can be seen that trimming the data (column 2 vs. column 1) primarily affects the treatment group while matching (column 3 vs. column 2) mainly has an influence on the control group.

²⁸ Among participants who received a premium refund, the average value of the premium refund is 294.44 euros (minimum 22.38 euros, at most 744.60 euros).

Table 2: Descriptive statistics: Mean values of outcomes in 2010

Outcome	(1)		(2)		(3)	
	Untrimmed sample		Trimmed sample		Trimmed and matched sample	
	Treatment group	Control group	Treatment group	Control group	Treatment group	Control group
Doctor visit	0.85 (0.35)	0.89 (0.31)	0.87 (0.34)	0.89 (0.31)	0.87 (0.34)	0.88 (0.32)
Doctor visit (GP)	0.76 (0.43)	0.82 (0.39)	0.78 (0.41)	0.82 (0.39)	0.78 (0.41)	0.81 (0.39)
Doctor visit (specialist)	0.72 (0.45)	0.76 (0.43)	0.73 (0.44)	0.76 (0.43)	0.73 (0.44)	0.74 (0.44)
No. of doctor visits	8.23 (9.07)	12.24 (14.29)	9.39 (10.15)	11.91 (13.38)	9.39 (10.15)	9.88 (10.98)
No. of doctor visits (GP)	3.40 (3.85)	5.16 (6.57)	3.86 (4.28)	4.99 (6.01)	3.86 (4.28)	4.16 (4.72)
No. of doctor visits (specialist)	4.45 (6.42)	6.61 (9.80)	5.15 (7.23)	6.50 (9.31)	5.14 (7.23)	5.32 (7.73)
Common cold (J00)	0.01 (0.12)	0.02 (0.15)	0.02 (0.13)	0.02 (0.16)	0.02 (0.13)	0.02 (0.15)
Common cold (J00-J06)	0.22 (0.42)	0.28 (0.45)	0.26 (0.44)	0.28 (0.45)	0.26 (0.44)	0.28 (0.45)
Expenditures on doctor visits	241.87 (314.96)	352.41 (633.88)	275.02 (352.67)	341.29 (512.27)	275.02 (352.67)	288.16 (418.64)
Expenditures on doctor visits (GP)	90.49 (96.16)	128.49 (159.66)	100.07 (104.74)	124.94 (155.97)	100.07 (104.74)	107.23 (118.83)
Expenditures on doctor visits (specialist)	147.13 (266.00)	214.91 (522.78)	170.00 (299.62)	208.98 (430.65)	170.00 (299.62)	174.70 (338.67)
N	13,091	380,996	5,090	360,251	5,090	5,069

GP = general practitioner. No. = Number. Standard deviation in parentheses. Table 2 shows values before and after trimming the data as well as after matching the two groups. Due to missings in the data, number of doctor visits of GP and specialist do not add to the overall number. The same applies to expenditures on doctor visits and (in a modified manner) to the share of individuals with at least one doctor visit ("Doctor visit", first panel of Table 2).

2.5 Results

2.5.1 Matching quality

After trimming the data, participants of the tariff still differ in some dimensions from unmatched non-participants (cf. Table 3). This becomes obvious through the standardized bias which lies far above 5% for most of the variables. Both groups are nearly of the same age and have a similar probability of participating in the bonus program. The distribution of the insurance status and education is similar between the two groups. This also holds for all probabilities of medical utilization (e.g., the probability of visiting a doctor due to a common cold). However, on average, the share of men is higher in the treatment group. Non-participants, on average, cause higher costs. This holds for all kinds of costs. Moreover, the number of times they make use of the health care system (e.g., the number of drug prescriptions) is higher than for participants.

Table 3: Descriptive statistics: Mean values of covariates

Covariate	Treatment	Unmatched control		Matched control	
	group	group	S.B.	group	S.B.
	Mean	Mean		Mean	
Age	41.86 (11.40)	41.40 (12.32)	2.4	41.57 (11.36)	0.9
Male	0.71 (0.46)	0.59 (0.49)	25.1	0.70 (0.46)	0.3
Bonus program in 2006 to 2010	0.07 (0.26)	0.06 (0.24)	4.4	0.06 (0.25)	3.2
Sickness fund 2	0.12 (0.35)	0.72 (0.45)	-153.4	0.13 (0.34)	-2.1
Compulsorily insured	0.89 (0.31)	0.86 (0.35)	8.6	0.87 (0.33)	4.6
Voluntarily insured	0.08 (0.27)	0.08 (0.27)	-1.0	0.09 (0.28)	-4.0
Unemployed	0.00 (0.04)	0.02 (0.14)	-17.3	0.00 (0.06)	-1.1
Pensioner	0.02 (0.14)	0.03 (0.17)	-6.4	0.02 (0.14)	-0.0
Educational category 1	0.06 (0.24)	0.11 (0.32)	-17.6	0.07 (0.25)	-2.4
Educational category 2	0.71 (0.46)	0.63 (0.48)	16.6	0.71 (0.46)	-0.2
Educational category 3	0.05 (0.21)	0.07 (0.25)	-9.3	0.04 (0.20)	2.1
Educational category 4	0.08 (0.26)	0.08 (0.26)	-0.1	0.07 (0.26)	0.7
Educational category 5	0.04 (0.21)	0.04 (0.19)	2.7	0.04 (0.21)	-0.1
Educational category 6	0.06 (0.24)	0.08 (0.26)	-4.6	0.06 (0.24)	0.4
Positive expenditures total, before	0.94 (0.24)	0.93 (0.25)	3.8	0.95 (0.22)	-2.3
Expenditures total, before	492.79 (1,103.19)	694.63 (1,536.11)	-15.1	494.41 (1,149.67)	-0.1
Doctor visit, before	0.94 (0.24)	0.93 (0.26)	5.0	0.95 (0.23)	-2.9
Expenditures on doctor visits, before	194.63 (212.99)	246.00 (281.47)	-20.6	194.33 (211.76)	0.1
No. of doctor visits, before	7.50 (7.01)	9.53 (8.94)	-25.3	7.55 (6.92)	-0.7
Hospital visit, before	0.20 (0.40)	0.23 (0.42)	-8.3	0.20 (0.40)	0.5
Expenditures on hospital visits, before	170.79 (606.26)	246.62 (828.58)	-10.4	173.52 (614.02)	-0.4
Drug prescription, before	0.85 (0.35)	0.85 (0.35)	-0.2	0.85 (0.35)	-0.2

Covariate	Treatment	Unmatched control		Matched control	
	group Mean	group Mean	S.B.	group Mean	S.B.
No. of drug prescriptions, before	2.56 (3.44)	3.66 (4.65)	-27.0	2.58 (3.27)	-0.6
Sickness absence, before	0.72 (0.45)	0.69 (0.46)	6.9	0.72 (0.45)	0.3
Expenditures on sickness benefit, before	59.03 (426.77)	81.72 (488.07)	-4.7	57.06 (402.95)	0.4
No. of times on sickness absence, before	0.77 (0.90)	0.91 (1.16)	-13.2	0.78 (0.90)	-0.9
No. of days on sickness absence, before	7.79 (15.67)	10.23 (20.47)	-13.4	7.87 (14.93)	-0.4
Other costs, before	113.82 (260.01)	95.53 (322.54)	6.2	107.19 (298.64)	2.3
Common cold (J00), Before	0.05 (0.21)	0.05 (0.22)	-2.0	0.04 (0.21)	1.0
Common cold (J00-J06), before	0.48 (0.50)	0.50 (0.50)	-3.3	0.48 (0.50)	-0.3
N	5,090	360,251		5,069	

S.B. = standardized bias. No. = Number. Standard deviation in parentheses. Educational category 1: No apprenticeship, no university-entrance diploma. Educational category 2: Apprenticeship, no university-entrance diploma. Educational category 3: No apprenticeship, university-entrance diploma. Educational category 4: Apprenticeship, university-entrance diploma. Educational category 5: Degree of university of applied science. Educational category 6: University degree. The data presented have already been trimmed. In addition to the variables presented here, numerous quadratic and interaction terms are used as covariates. Covariates concerning diagnoses, costs, or other measures of medical utilization are measured during the years 2006 to 2008. Socioeconomic covariates are measured in 2010.

After the matching procedure, the average value of all covariates has converged between the treatment and the matched control group (cf. Table 3). The standardized bias is less than 5% for all variables that were used for matching. Thus, the matching procedure is successful (Caliendo and Kopeinig, 2008). Common support exists after having carried out trimming procedures.²⁹

²⁹ Treatment and control group were rather different with respect to the propensity score. Figure A 1 in the appendix shows the distribution of the untrimmed propensity score for the treatment and control group. Therefore, the data had to be trimmed relatively strongly. Figure A 1 suggests trimming the data at propensity score = 0.1 because there are few observations in the control group with a propensity score higher than 0.1. Thereby, 8,001 participants and 20,745 non-participants were excluded from the analysis. Since other authors may have decided differently on the trimming threshold, I will vary this threshold in the robustness checks.

2.5.2 Estimation results

Estimation results are presented in Table 4.³⁰ The probability of visiting a GP is significantly reduced by 2.6 percentage points. In contrast, the effect on the probability of visiting a specialist is smaller and only marginally significant. These findings are in line with theory. Likewise, the number of visits to the GP is significantly reduced by 0.3 visits (-7.4%), while there is only a smaller reduction of visits to a specialist (-0.2 visits or -3.5%, respectively). Moreover, I find that participants have a 0.7 or 2.1 percentage-point lower probability of visiting a doctor due to a common cold (depending on the definition of the ailment). This is a further indication that ex-post moral hazard behavior has been reduced. As expected, individuals avoid visiting a doctor due to trivial ailment such as a common cold. With a magnitude of 8 or 35%, respectively, this reduction is substantial.

³⁰ Table 4 only shows the coefficients of interest, i.e., the treatment coefficient of each of the regressions run. Additional results are shown in the appendix in Table A 2 (linear coefficients of the propensity score estimation) and Table A 3 Fehler! Verweisquelle konnte nicht gefunden werden. (linear coefficients of the various regressions run in the main specification).

Table 4: Estimation results (main specification)

Outcome	Kernel matching plus regression
Doctor visit	-0.018*** (0.004)
Doctor visit (GP)	-0.026*** (0.005)
Doctor visit (specialist)	-0.011* (0.006)
No. of doctor visits	-0.479*** (0.121)
No. of doctor visits (GP)	-0.284*** (0.051)
No. of doctor visits (specialist)	-0.181** (0.091)
Common cold (J00)	-0.007*** (0.002)
Common cold (J00-J06)	-0.021*** (0.006)
Expenditures on doctor visits	-13.227*** (4.443)
Expenditures on doctor visits (GP)	-6.883*** (1.236)
Expenditures on doctor visits (specialist)	-5.060 (3.920)
N treated	5,090
N controls	360,251
N controls (weighted)	5,069

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each line contains the coefficient of treatment in separate regressions, i.e., for different outcomes. Bandwidth = 0.005, trimming at 0.1.

Furthermore, I find a significant reduction in the medical expenditures for visits to the GP of 7 euros while there is no significant reduction in expenditures for specialists. Although 7 euros does not seem to be much, it corresponds to a decrease of 7%, which is substantial.

2.5.3 Sensitivity analysis

I test whether results are stable and I carry out numerous robustness checks. First of all, in order to find support so that the CIA is fulfilled, I run regressions for the pseudo outcome (cf. Table 5). As expected, there is no significant effect of participating in the premium refund tariff in 2010 on the probability of visiting a hospital in the same year, and the coefficient is close to zero. Since the CIA cannot be directly tested, this is not a proof, but it supports the assumption. It implies that the treated observations are not distinct from the controls in that the distribution of $Y(0)$ for the treated units is comparable to the distribution of $Y(0)$ for the controls.

Table 5: Robustness checks I

Outcome	Kernel matching plus regression
Hospital visit (2010)	-0.006 (0.004)
N treated	5,090
N controls	360,251
N controls (weighted)	5,069

Robust standard errors in parentheses. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.10$. Table 5 contains the coefficient of treatment for the pseudo outcome. Bandwidth = 0.005, trimming at 0.1. Covariates are measured in the same years as in the main specification.

Next, I vary the trimming procedure since there is some area of discretion. For most outcomes, this does not lead to considerable differences (cf. Table 6, columns 1 and 2) and results are qualitatively robust to the exact cutoff for the trimming procedure although they tend to become slightly smaller. It is noticeable that the probability of visiting a specialist becomes insignificant, and an effect should not be assumed. Furthermore, I vary the bandwidth from kernel matching. Exemplarily, results are shown for a bandwidth of 0.01 (cf. column 3). They are essentially the same as those in the main specification.

I also try other matching estimators that rely on the propensity score. For nearest neighbor matching (1:30, cf. column 4), results are qualitatively similar to those in the main specification, only slightly smaller. For radius matching combined with regression, results are virtually the same as those in the main specification (cf. column 5). Moreover, I extend the minimum days an individual can be observed in the data from 150 to 365 (cf. column 6). This does not affect the results. Subsequently, instead

of pooling the years 2006 to 2008 to create the lagged covariates and instead of leaving out 2009, I match treated and controls in the years 2006 to 2009 separately (cf. column 7). It is noticeable that the results are qualitatively the same as in the main specification, even if slightly smaller. Finally, I refrain from matching and trimming the data. Instead, I use OLS. The advantage of matching the two groups and trimming the data is that the common support can be ensured and groups can be made more similar. However, I want to assess its effect on the estimation. OLS results (cf. column 8) are weaker in magnitude but qualitatively similar to the main specification. All in all, results are stable over this variety of robustness checks.

Table 6: Robustness checks II

Outcome	(1) Kernel matching plus regression (modified trimming 1)	(2) Kernel matching plus regression (modified trimming 2)	(3) Kernel matching plus regression (modified bandwidth)	(4) Nearest neighbor Matching (1:30)
Doctor visit	-0.017*** (0.004)	-0.013*** (0.004)	-0.018*** (0.004)	-0.011** (0.005)
Doctor visit (GP)	-0.024*** (0.005)	-0.021*** (0.005)	-0.027*** (0.005)	-0.019*** (0.006)
Doctor visit (specialist)	-0.007 (0.006)	-0.006 (0.005)	-0.011* (0.006)	-0.001 (0.007)
No. of doctor visits	-0.450*** (0.112)	-0.351*** (0.110)	-0.487*** (0.120)	-0.327** (0.150)
No. of doctor visits (GP)	-0.238*** (0.049)	-0.222*** (0.047)	-0.288*** (0.051)	-0.242*** (0.063)
No. of doctor visits (specialist)	-0.202** (0.083)	-0.123 (0.083)	-0.186** (0.091)	-0.079 (0.107)
Common cold (J00)	-0.007*** (0.002)	-0.007*** (0.002)	-0.007*** (0.002)	-0.007*** (0.002)
Common cold (J00-J06)	-0.020*** (0.006)	-0.016*** (0.005)	-0.021*** (0.006)	-0.017*** (0.006)
Expenditures on doctor visits	-12.587*** (4.153)	-9.327** (4.083)	-13.404*** (4.437)	-7.899 (5.292)
Expenditures on doctor visits (GP)	-5.694*** (1.180)	-5.199*** (1.139)	-6.935*** (1.238)	-5.728*** (1.562)
Expenditures on doctor visits (specialist)	-5.343 (3.604)	-2.327 (3.553)	-5.147 (3.915)	-1.369 (4.482)
N treated	5,787	6,205	5,090	5,090
N controls	366,246	369,199	360,251	360,251
N controls (weighted)	5,768	6,197	5,069	---

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each line contains the coefficient of treatment in separate regressions, i.e., for different outcomes. Ad (1): Similar to the main specification but modified trimming; bandwidth = 0.005, trimming at 0.12. Ad (2): Similar to the main specification but modified trimming; bandwidth = 0.005, trimming at 0.14. Ad (3): Similar to the main specification but modified bandwidth; bandwidth = 0.01, trimming at 0.1. Ad (4): Nearest neighbor matching based on the propensity score.

Table 6: Robustness checks II (continued)

Outcome	(5) Radius matching plus regression	(6) Kernel matching plus regression (at least 365 days insured)	(7) Kernel matching plus regression (lagged covariates not pooled)	(8) OLS
Doctor visit	-0.018*** (0.004)	-0.018*** (0.004)	-0.015*** (0.004)	-0.003 (0.003)
Doctor visit (GP)	-0.027*** (0.005)	-0.026*** (0.005)	-0.025*** (0.005)	-0.015*** (0.004)
Doctor visit (specialist)	-0.011* (0.006)	-0.010* (0.006)	-0.006 (0.006)	-0.005 (0.004)
No. of doctor visits	-0.484*** (0.121)	-0.436*** (0.122)	-0.342*** (0.113)	-0.358*** (0.078)
No. of doctor visits (GP)	-0.287*** (0.051)	-0.275*** (0.052)	-0.198*** (0.050)	-0.212*** (0.036)
No. of doctor visits (specialist)	-0.184** (0.091)	-0.149 (0.092)	-0.141 (0.087)	-0.163*** (0.059)
Common cold (J00)	-0.007*** (0.002)	-0.007*** (0.002)	-0.006*** (0.002)	-0.005*** (0.001)
Common cold (J00-J06)	-0.021*** (0.006)	-0.021*** (0.006)	-0.014** (0.006)	-0.017*** (0.004)
Expenditures on doc- tor visits	-13.322*** (4.446)	-11.641** (4.496)	-10.751** (4.375)	-3.776 (3.408)
Expenditures on doc- tor visits (GP)	-9.911*** (1.237)	-6.841*** (1.233)	-4.754*** (1.229)	-8.087*** (0.990)
Expenditures on doc- tor visits (specialist)	-5.121 (3.923)	-3.528 (3.980)	-4.297 (3.915)	1.365 (3.078)
N treated	5,090	5,019	4,585	13,091
N controls	360,251	332,481	317,522	380,996
N controls (weighted)	5,090	5,000	4,563	---

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each line contains the coefficient of treatment in separate regressions, i.e., for different outcomes. Ad (5): radius = 0.005, trimming at 0.1. Ad (6): bandwidth = 0.005, trimming at 0.1. Instead of limiting the sample to individuals that are at least 150 days insured in 2010 and in 2006 to 2008, here, this threshold is extended to 365 days. Ad (7): bandwidth= 0.01, trimming at 0.1. Instead of using the average of 2006 to 2008 for lagged covariates, here, lagged covariates are measured in 2006, 2007, 2008, and 2009 separately. Ad (8): Data are untrimmed. Regressions are unweighted.

Finally, to get a better idea of how strong the omitted variable bias still is, I apply Oster's (2016) method as already described above. Columns 1 and 2 in Table 7 show that, for the trimmed and matched data, the use of control variables in the regression is not important. Columns 3 to 5 make different assumptions concerning the degree of selection on unobservables relative to selection on observables. It becomes obvious that no matter whether selection on unobservables is smaller than (column 3), equal to (column 4), or bigger (column 5) than selection on observables, results are very stable, which is another reassuring result indicating that selection on unobservables is not strong in this application.

Table 7: Robustness checks III

	(1)	(2)	(3)	(4)	(5)
Tests according to Oster (2016)					
Outcome	Uncontrolled	Controlled	$Selection_{Unobs} < Selection_{Obs}$	$Selection_{Unobs} = Selection_{Obs}$	$Selection_{Unobs} > Selection_{Obs}$
Doctor visit	-0.018	-0.018	-0.017	-0.017	-0.017
Doctor visit (GP)	-0.027	-0.026	-0.026	-0.026	-0.026
Doctor visit (specialist)	-0.009	-0.011	-0.013	-0.014	-0.016
No. of doctor visits	-0.488	-0.479	-0.470	-0.463	-0.453
No. of doctor visits (GP)	-0.301	-0.284	-0.267	-0.254	-0.236
No. of doctor visits (specialist)	-0.177	-0.181	-0.188	-0.193	-0.199
Common cold (J00)	-0.007	-0.007	-0.008	-0.008	-0.008
Common cold (J00-J06)	-0.021	-0.021	-0.020	-0.020	-0.020
Expenditures on doctor visits	-13.141	-13.227	-13.353	-13.439	-13.548
Expenditures on doctor visits (GP)	-7.162	-6.883	-6.594	-6.374	-6.061
Expenditures on doctor visits (specialist)	-4.706	-5.060	-5.756	-6.167	-6.632
N treated			5,090		
N controls			360,251		
N controls (weighted)			5,069		

GP = general practitioner. No. = Number. Robust standard errors in parentheses. Each line contains the coefficient of treatment in separate regressions, i.e., for different outcomes. Significance is not shown in this table. Ad (1): Main specification without control variables. Ad (2): Main specification. Ad (3) to (5): Tests according to Oster (2016). The coefficients shown are estimated using different assumptions. Ad (3): Assumption that selection on unobservables is half as big as selection on observables. Ad (4): Assumption that selection on unobservables is as big as selection on observables. Ad (5): Assumption that selection on unobservables is twice as big as selection on observables.

2.5.4 Effect heterogeneity

Furthermore, I analyze how the effects are composed, i.e., whether subgroups are affected differently. I differentiate individuals by gender and age group. According to Table 8 (column 1), the subgroup of men reacts more strongly to the tariff's incentives than the whole sample. For women (column 2) it is noticeable that I do not find a significant negative effect on the probability of visiting a GP. Some effects found in the overall sample become insignificant for women. Obviously, men react stronger to the premium refund tariff's incentives than women.

Table 8: Estimation results by subgroups

Outcome	(1) Men	(2) Women	(3) Aged 34 and younger	(4) Aged 35 to 49	(5) Aged 50 and older
Doctor visit	-0.032*** (0.006)	0.015*** (0.006)	-0.022** (0.009)	-0.018*** (0.007)	-0.005 (0.007)
Doctor visit (GP)	-0.032*** (0.007)	-0.011 (0.009)	-0.038*** (0.011)	-0.025*** (0.008)	-0.004 (0.008)
Doctor visit (specialist)	-0.027*** (0.008)	0.024*** (0.008)	-0.024** (0.011)	-0.010 (0.009)	0.005 (0.010)
No. of doctor visits	-0.528*** (0.133)	-0.299 (0.257)	-0.608*** (0.176)	-0.589*** (0.183)	-0.012 (0.275)
No. of doctor visits (GP)	-0.244*** (0.061)	-0.285*** (0.096)	-0.362*** (0.066)	-0.283*** (0.078)	-0.004 (0.127)
No. of doctor visits (specialist)	-0.271*** (0.094)	-0.025 (0.207)	-0.240* (0.145)	-0.266* (0.137)	-0.037 (0.189)
Common cold (J00)	-0.008*** (0.002)	-0.005 (0.004)	-0.006* (0.004)	-0.009*** (0.003)	-0.004 (0.003)
Common cold (J00-J06)	-0.019*** (0.007)	-0.026** (0.011)	-0.027** (0.011)	-0.020** (0.009)	-0.015 (0.011)
Expenditures on doctor visits	-15.640*** (4.793)	-9.219 (9.622)	-19.567*** (6.068)	-13.786** (6.932)	1.457 (10.213)
Expenditures on doctor visits (GP)	-6.697*** (1.463)	-6.745*** (2.336)	-8.485*** (1.575)	-7.464*** (1.879)	-0.386 (2.980)
Expenditures on doctor visits (specialist)	-7.587* (4.085)	-1.947 (8.817)	-9.792* (5.478)	-4.857 (6.129)	1.909 (8.875)
N treated	3,551	1,479	1,550	2,137	1,323
N controls	210,197	144,134	118,007	129,920	86,176
N controls (weighted)	3,540	1,476	1,545	2,132	1,306

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each line contains the coefficient of treatment in separate regressions, i.e., for different outcomes. Ad (1): bandwidth = 0.005, trimming at 0.1. Ad (2): bandwidth = 0.001, trimming at 0.1, standardized bias slightly too high (7.9 at most). Ad (3): bandwidth = 0.005, trimming at 0.1. Ad (4): bandwidth = 0.01, trimming at 0.1. Ad (5): bandwidth = 0.005, trimming at 0.1.

Although there are three age groups that were analyzed, results show that they could be condensed into two groups. Individuals aged 34 and younger³¹ (column 3) and those aged 35 to 49 (column 4) react very similarly. Results are qualitatively the same as in the whole sample but effects are slightly stronger. In contrast, individuals aged 50 and older³² (column 5) do not react to participation in the tariff at all. All coefficients are insignificant and they are mostly close to zero.

2.6 Discussion

This paper examines whether premium refunds are a suitable instrument to reduce ex-post moral hazard in the health insurance market. I use panel data covering the years 2006 to 2010 which result from the billing processes of two German sickness funds. I analyze the effect of participating in the premium refund tariff in 2010 on several health measures in the same year by combining propensity score matching and regression.

I find that participating in the premium refund tariff is associated with a significant reduction in the probability of visiting a GP (-2.6 percentage points). This is in contrast to Felder and Werblow (2008) but in line with Farbmacher and Winter (2013) and Health Policy Brief (2015) although they report a higher reduction. However, this is not unexpected: since potential selection on moral hazard (Einav et al., 2013) was not accounted for in the present study, the estimated effects in this paper resemble a lower bound (Finkelstein et al., 2015) and true effects may be higher. Like Farbmacher and Winter (2013), I also find that effects are higher for younger than for older individuals and that men are more strongly affected than women. The number by which doctor visits are reduced in this study is of a similar magnitude as in Farbmacher and Winter (2013) and the effect goes in the same direction as in Chandra et al. (2010). In addition, I find that the probability of visiting a doctor due to a common cold is decreased by 0.7 (or 2.1) percentage points. Both findings can be interpreted as evidence of reduced ex-post moral hazard. Obviously, the amount of the premium refund is high enough to encourage individuals to forgo unnecessary doctor visits.

Effects differ among subgroups. They are mainly driven by individuals aged 49 and under, and men have a stronger reaction than women. By contrast, individuals aged 50

³¹ The youngest participant is 20 years old.

³² The oldest participant is 71 years old.

and over do not react to the tariff's incentives at all. A reason why women have a weaker reaction to these incentives might be that they are, in general, more risk-averse than men (Borghans et al., 2009). Probably, most women prefer a doctor's opinion even in rather harmless situations. Individuals aged 50 and over do, on average, suffer from more severe illnesses compared to younger individuals. For these illnesses, demand is less price-elastic. This explains why they generally do not react to the premium refund's incentives, and is in line with previous research. Schmitz (2012) finds that individuals that had high medical demands in the past – presumably ill individuals – do not react to the expansion of insurance coverage. Likewise, Gerfin et al. (2015) observe that healthy individuals react much more strongly to incentives.

Even though I use lagged outcomes as proxy variables for unobserved heterogeneity, one possible weakness of this study is that relevant characteristics cannot be explicitly controlled for (e.g., lifestyle factors). Another limitation is that the data only comprise individuals from two sickness funds which may not be completely representative of all sickness funds in Germany.

This study focuses on contemporaneous effects. Further research is needed to truly identify causal effects, to consider more strongly the nonlinear nature of this scheme, and to find out about the long-term consequences of the tariff's incentives.

2.7 Appendix

Table A 1: Comparison of the sample and the SHI population in 2010

Age groups	Sample: Share in %		SHI: Share in %	
	Men	Women	Men	Women
14 and younger	0.22	0.18	0.13	0.12
15 - 19	1.89	1.27	0.78	0.57
20 - 24	4.15	3.15	2.85	2.62
25 - 29	4.42	3.35	3.88	3.65
30 - 34	3.92	3.01	3.78	3.36
35 - 39	4.06	2.95	3.69	3.18
40 - 44	5.44	4.05	4.92	4.27
45 - 49	5.79	4.23	5.39	4.73
50 - 54	4.89	3.62	4.69	4.19
55 - 59	3.99	2.91	4.01	3.61
60 - 64	3.32	2.60	3.42	3.22
65 - 69	3.32	2.91	3.37	3.80
70 - 74	3.92	3.54	3.85	4.54
75 - 79	2.83	2.76	2.47	3.20
80 and older	2.89	4.50	2.43	5.29
Total	54.97	45.03	49.65	50.35

Source: Federal Health Monitoring, 2019, and own calculations.

Table A 2: Linear coefficients of propensity score estimation in main specification

Covariate	
Age	0.096*** (0.006)
Male	0.679*** (0.062)
Bonus program in 2006 to 2010	0.819*** (0.130)
Sickness fund 2	-1.504*** (0.016)
Compulsorily insured	0.719*** (0.166)
Voluntarily insured	1.114*** (0.171)
Unemployed	0.802 (0.581)
Pensioner	-0.484*** (0.151)
Educational category 2	0.388*** (0.060)
Educational category 3	-0.600*** (0.220)
Educational category 4	0.544*** (0.123)
Educational category 5	0.460*** (0.074)
Educational category 6	0.117*** (0.031)
Positive expenditures total, before	0.403 (0.256)
Expenditures total, before	-0.000 (0.000)
Doctor visit, before	1.593*** (0.169)
Expenditures on doctor visits, before	-0.001*** (0.000)
No. of doctor visits, before	-0.006*** (0.002)
Hospital visit, before	-0.441 (0.360)
Expenditures on hospital visits, before	0.000 (0.000)
Drug prescription, before	0.046 (0.246)

Covariate	
No. of drug prescriptions, before	0.051** (0.025)
Sickness absence, before	0.323*** (0.122)
Expenditures on sickness benefit, before	-0.000 (0.000)
No. of times on sickness absence, before	0.013 (0.115)
No. of days on sickness absence, before	-0.005** (0.002)
Other costs, before	0.000 (0.000)
Common cold (J00), before	0.016 (0.043)
Common cold (J00-J06), before	-0.076*** (0.013)
N treated	13,157
N controls	409,750

Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Table A 2 shows the coefficients in the propensity score matching for all linear matching variables in the main specification. Beyond that, a long list of quadratic and interaction terms was used for the matching as well. These coefficients are available upon request from the author. Covariates concerning diagnoses, costs, or other measures of medical utilization are measured during the years 2006 to 2008. Socioeconomic covariates are measured in 2010.

Table A 3: Detailed results for the main specification

Coefficient	(1) Doctor visit	(2) Doctor visit (GP)	(3) Doctor visit (specialist)	(4) No. of doctor visits	(5) No. of doctor visits (GP)	(6) No. of doctor visits (specialist)
Premium refund tariff	-0.018*** (0.004)	-0.026*** (0.005)	-0.011* (0.006)	-0.479*** (0.121)	-0.284*** (0.051)	-0.181** (0.091)
Age	0.005* (0.003)	0.003 (0.003)	0.009*** (0.003)	0.002 (0.063)	-0.009 (0.026)	0.032 (0.046)
Male	-0.136*** (0.038)	-0.022 (0.036)	-0.205*** (0.038)	-2.236*** (0.717)	-0.104 (0.184)	-2.058*** (0.641)
Bonus program in 2006 to 2010	0.081 (0.091)	0.072 (0.094)	0.097 (0.089)	-0.381 (2.033)	0.936 (0.817)	-0.978 (1.617)
Sickness fund 2	-0.041*** (0.010)	-0.054*** (0.012)	-0.042*** (0.012)	-0.299 (0.213)	-0.056 (0.092)	-0.153 (0.163)
Compulsorily insured	0.506*** (0.074)	0.449*** (0.072)	0.375*** (0.080)	3.431** (1.654)	1.415** (0.655)	1.998* (1.178)
Voluntarily insured	0.220** (0.088)	0.176** (0.088)	0.153 (0.096)	0.437 (2.078)	0.437 (0.803)	-0.049 (1.564)
Unemployed	0.439** (0.185)	0.161 (0.233)	0.346* (0.201)	2.270 (2.740)	-0.632 (2.110)	2.618* (1.573)
Pensioner	0.013 (0.103)	0.008 (0.104)	-0.056 (0.100)	0.827 (1.757)	-0.735 (0.589)	1.516 (1.257)
Educational category 2	-0.103 (0.028)	-0.022 (0.034)	-0.077** (0.035)	-1.434* (0.792)	-0.645** (0.303)	-0.789 (0.661)
Educational category 3	0.051 (0.118)	-0.013 (0.112)	0.025 (0.130)	1.300 (3.442)	-1.175* (0.621)	2.285 (2.929)
Educational category 4	0.051 (0.064)	0.002 (0.073)	0.047 (0.069)	-0.283 (1.389)	0.000 (0.466)	-0.359 (1.187)

Coefficient	(1) Doctor visit	(2) Doctor visit (GP)	(3) Doctor visit (specialist)	(4) No. of doctor visits	(5) No. of doctor visits (GP)	(6) No. of doctor visits (specialist)
Educational category 5	-0.025 (0.054)	0.008 (0.055)	0.007 (0.053)	0.031 (0.701)	-0.132 (0.273)	0.186 (0.553)
Educational category 6	-0.025 (0.018)	-0.063*** (0.021)	-0.007 (0.021)	-0.774 (0.762)	-0.591*** (0.156)	-0.216 (0.763)
Positive expenditures	-0.304** (0.142)	-0.390*** (0.120)	-0.202 (0.134)	-0.586 (1.724)	-1.223* (0.698)	0.885 (1.015)
Expenditures	0.000** (0.000)	0.000** (0.000)	0.000 (0.000)	0.001 (0.001)	0.000 (0.000)	0.000 (0.001)
Doctor visit, before	-0.060 (0.117)	-0.095 (0.117)	-0.047 (0.115)	0.527 (1.717)	0.059 (0.750)	0.648 (1.215)
Expenditures on doctor visits, before	0.000*** (0.000)	0.000*** (0.000)	0.000** (0.000)	0.001 (0.005)	-0.001 (0.001)	0.002 (0.004)
No. of doctor visits, before	0.003*** (0.001)	0.005*** (0.001)	0.008*** (0.001)	0.422*** (0.033)	0.153*** (0.012)	0.259*** (0.030)
Hospital visit, before	-0.000 (0.106)	0.107 (0.100)	-0.076 (0.099)	-1.725 (1.544)	-0.881 (0.831)	-0.612 (0.832)
Expenditures on hospital visits, before	0.000 (0.000)	-0.000 (0.000)	-0.000* (0.000)	-0.002** (0.001)	-0.000 (0.000)	-0.002** (0.001)
Drug prescription, before	0.390** (0.127)	0.418*** (0.110)	0.291** (0.127)	1.165 (1.667)	0.697 (0.721)	0.001 (0.884)
No. of drug prescriptions, before	0.021 (0.024)	0.024 (0.023)	0.048* (0.025)	-0.128 (0.352)	-0.222* (0.118)	0.095 (0.282)
Sickness absence, before	-0.139** (0.070)	-0.077 (0.068)	-0.103 (0.072)	-1.368 (1.177)	-0.100 (0.712)	-1.264* (0.685)
Expenditures on sickness benefit, before	0.000** (0.000)	0.000 (0.000)	0.000** (0.000)	-0.003*** (0.001)	-0.001*** (0.000)	-0.002** (0.001)

Coefficient	(1) Doctor visit	(2) Doctor visit (GP)	(3) Doctor visit (specialist)	(4) No. of doctor visits	(5) No. of doctor visits (GP)	(6) No. of doctor visits (specialist)
No. of times on sickness absence, before	-0.136*** (0.037)	-0.108*** (0.034)	-0.082** (0.037)	-1.087* (0.630)	-0.855** (0.401)	-0.272 (0.310)
No. of days on sickness absence, before	-0.002** (0.001)	-0.002* (0.001)	-0.001 (0.001)	-0.059** (0.028)	-0.017 (0.012)	-0.041* (0.022)
Other costs, before	-0.000** (0.000)	-0.000* (0.000)	-0.000** (0.000)	-0.002 (0.001)	-0.001 (0.001)	-0.001 (0.001)
Common cold (J00), before	0.027 (0.017)	0.045** (0.020)	0.046* (0.024)	-0.410 (0.445)	-0.327* (0.194)	-0.071 (0.325)
Common cold (J00-J06), before	0.027*** (0.006)	0.042*** (0.007)	0.035*** (0.008)	0.417*** (0.147)	0.082 (0.063)	0.320*** (0.111)
N treated				5,090		
N controls				360,251		
N controls (weighted)				5,069		

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each column contains the coefficients of one regression. To all regressions applies: bandwidth = 0.005, trimming at 0.1. Table A 3 shows the coefficients in the regression adjustment for all linear covariates in the main specification. Beyond that, a long list of quadratic and interaction terms was used in the regressions as well. These coefficients are available upon request from the author. Covariates concerning diagnoses, costs, or other measures of medical utilization are measured during the years 2006 to 2008. Socioeconomic covariates and all outcomes are measured in 2010.

Table A3: Detailed results for the main specification (continued)

Coefficient	(7)	(8)	(9)	(10)	(11)
	Common cold (J00)	Common cold (J00-J06)	Expenditures on doctor visits	Expenditures on doctor visits (GP)	Expenditures on doctor visits (specialist)
Premium refund tariff	-0.007*** (0.002)	-0.021*** (0.006)	-13.227*** (4.443)	-6.883*** (1.236)	-5.060 (3.920)
Age	-0.001 (0.001)	0.001 (0.003)	2.443 (2.474)	-0.875 (0.661)	3.530 (2.204)
Male	-0.002 (0.004)	-0.061** (0.027)	-87.778** (36.688)	-2.955 (5.436)	-84.763** (35.860)
Bonus program in 2006 to 2010	-0.004 (0.019)	-0.124 (0.080)	60.404 (75.907)	23.294 (21.555)	50.642 (69.783)
Sickness fund 2	0.002 (0.003)	-0.022** (0.010)	-10.413 (8.112)	-1.344 (2.414)	-8.411 (7.150)
Compulsorily insured	0.020 (0.017)	0.167** (0.067)	127.631** (63.574)	45.791*** (15.457)	83.107 (56.683)
Voluntarily insured	0.006 (0.021)	-0.071 (0.083)	31.150 (79.622)	29.337 (20.141)	-2.643 (71.955)
Unemployed	0.005 (0.023)	0.177 (0.150)	200.895** (98.282)	11.209 (42.168)	187.600* (104.063)
Pensioner	-0.000 (0.012)	0.003 (0.031)	12.459 (61.658)	-22.715 (20.333)	34.617 (45.507)
Educational category 2	-0.003 (0.009)	0.016 (0.037)	-41.735 (29.777)	-10.067 (7.386)	-32.055 (27.761)
Educational category 3	-0.024 (0.026)	0.092 (0.129)	88.857 (145.950)	-16.943 (16.588)	107.143 (140.128)
Educational category 4	-0.000 (0.019)	0.087 (0.066)	-45.562 (61.758)	4.350 (12.211)	-47.671 (58.702)

Coefficient	(7)	(8)	(9)	(10)	(11)
	Common cold (J00)	Common cold (J00-J06)	Expenditures on doctor visits	Expenditures on doctor visits (GP)	Expenditures on doctor visits (specialist)
Educational category 5	-0.007 (0.005)	-0.042 (0.032)	-3.451 (25.118)	-0.237 (7.462)	1.546 (22.417)
Educational category 6	-0.000 (0.004)	-0.006 (0.019)	-42.699 (41.939)	-13.683*** (3.885)	-25.674 (42.498)
Positive expenditures	0.004 total, before (0.007)	0.045 (0.080)	-26.399 (52.936)	-44.655** (18.703)	25.480 (39.944)
Expenditures	0.000* total, before (0.000)	0.000 (0.000)	-0.008 (0.028)	0.007 (0.009)	-0.014 (0.026)
Doctor visit, before	-0.012 (0.011)	-0.065 (0.079)	60.901 (73.308)	-3.581 (23.102)	64.405 (62.979)
Expenditures on doctor visits, before	0.000 (0.000)	0.000* (0.000)	0.153 (0.250)	0.018 (0.037)	0.133 (0.256)
No. of doctor visits, before	-0.000 (0.000)	0.001 (0.001)	4.542*** (1.514)	2.196*** (0.330)	2.346 (1.569)
Hospital visit, before	-0.017** (0.007)	-0.076 (0.080)	-41.845 (47.883)	-14.292 (23.395)	-21.344 (35.876)
Expenditures on hospital visits, before	-0.000 (0.000)	-0.000 (0.000)	-0.040 (0.033)	0.004 (0.013)	-0.0447 (0.028)
Drug prescription, before	-0.011* (0.006)	-0.058 (0.071)	33.998 (47.637)	28.700 (19.572)	-3.482 (32.435)
No. of drug prescriptions, before	0.003 (0.004)	0.037** (0.019)	-8.459 (13.420)	-2.727 (3.126)	-5.218 (12.469)
Sickness absence, before	-0.002 (0.011)	-0.051 (0.050)	-21.293 (43.760)	6.357 (23.591)	-26.512 (31.038)
Expenditures on sickness benefit, before	-0.000 (0.000)	0.000 (0.000)	-0.065 (0.041)	-0.025* (0.014)	-0.044 (0.035)

Coefficient	(7)	(8)	(9)	(10)	(11)
	Common cold (J00)	Common cold (J00-J06)	Expenditures on doctor visits	Expenditures on doctor visits (GP)	Expenditures on doctor visits (specialist)
No. of times on sickness absence, before	-0.007* (0.004)	-0.048* (0.025)	-36.302* (21.771)	-24.238* (13.731)	-13.801 (12.039)
No. of days on sickness absence, before	0.000 (0.000)	-0.004*** (0.001)	-1.855 (1.244)	-0.590* (0.327)	-1.344 (1.146)
Other costs, before	-0.000 (0.000)	-0.000 (0.000)	-0.065 (0.053)	-0.043** (0.019)	-0.032 (0.043)
Common cold (J00), before	0.051*** (0.012)	0.021 (0.027)	-15.176 (17.233)	-2.349 (5.152)	-11.190 (14.642)
Common cold (J00-J06), before	0.008*** (0.003)	0.119*** (0.008)	18.886*** (5.584)	2.177 (1.538)	16.571*** (5.008)
N treated			5,090		
N controls			360,251		
N controls (weighted)			5,069		

GP = general practitioner. No. = Number. Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.10. Each column contains the coefficients of one regression. To all regressions applies: bandwidth = 0.005, trimming at 0.1. Table A 3 shows the coefficients in the regression adjustment for all linear covariates. Beyond that, a long list of quadratic and interaction terms was used in the regressions as well. These coefficients are available upon request from the author. Covariates concerning diagnoses, costs, or other measures of medical utilization are measured during the years 2006 to 2008. Socioeconomic covariates and all outcomes are measured in 2010.

Figure A 1: Untrimmed propensity score

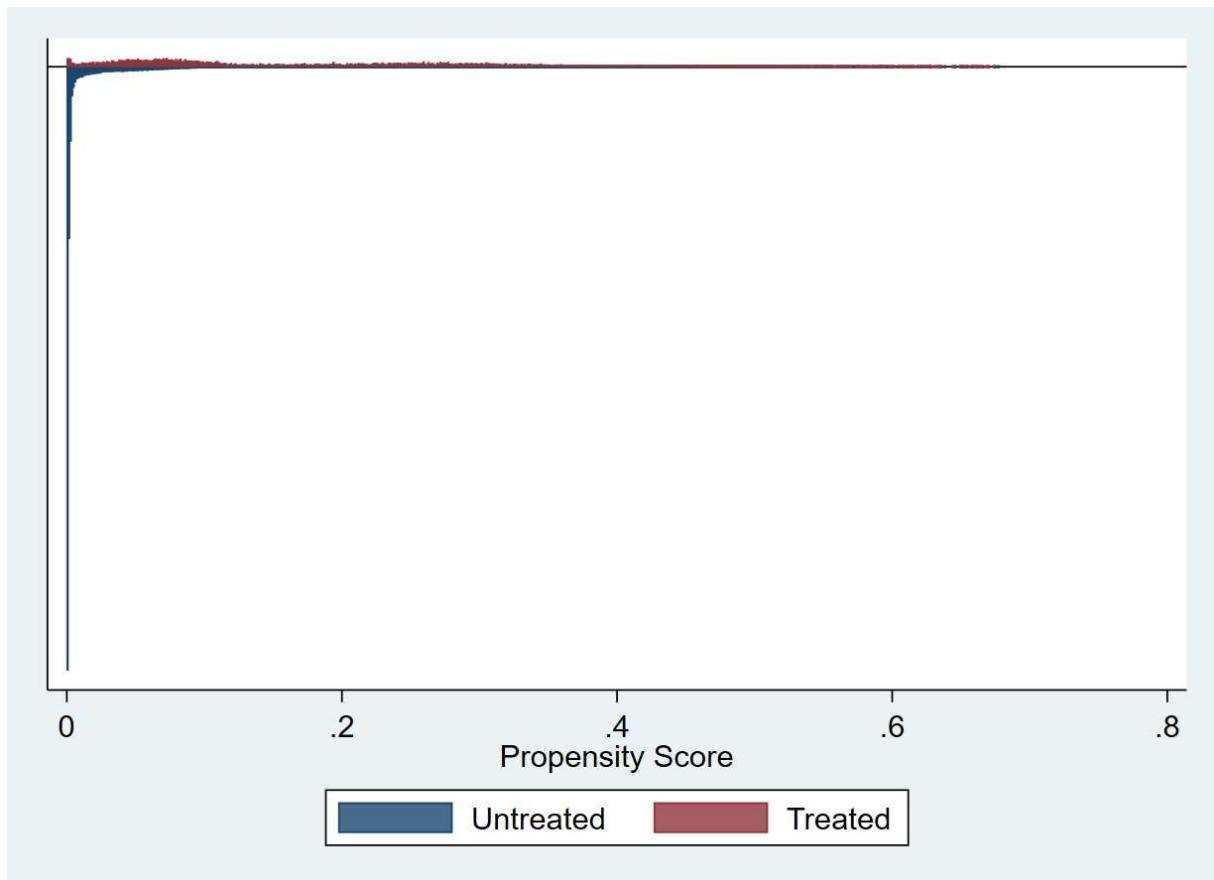


Figure A 1 shows the distribution of the untrimmed propensity score for the treatment and control group.

3. The Number of Patients with Chronic Hepatitis C in Times of New Therapy Options: A Retrospective Observational Study on German Health Insurance Funds Data³³

3.1 Introduction

Chronic hepatitis C (CHC) is a worldwide health problem. It is estimated that 85% of the acute hepatitis C (HC) infections will become chronic (Robert Koch Institute, 2011; Robert Koch Institute, 2015). A national study carried out in 2011, the German Health Interview and Examination Survey for Adults, estimated the HCV antibody-positive prevalence to be 0.3% (0.1–0.5%) (Poethko-Müller et al., 2013). This study suggested a null prevalence among individuals under the age of 40 years, which is refuted by data from the Robert Koch Institute (RKI) reporting 5,817 new cases (acute and chronic) in 2014, with the highest number among individuals younger than 40 years of age (Robert Koch Institute, 2015).

Estimates focusing on antibody-positive prevalence show a prevalence of 0.5% (0.3–0.9%), but for a laboratory-confirmed diagnosis of HCV (viremic prevalence), the prevalence is 0.3% (0.2–0.6%) (Bruggmann et al., 2014). Furthermore, Bruggmann et al. (2014) also reported a treatment rate for 2011 of 12,700 patients in Germany. The majority of the CHC patients have genotype (GT) 1 (63%) (Hüppe et al., 2008).

The first new therapies were the NS3/4A-protease inhibitors boceprevir and telaprevir launched in Germany in July and September 2011, respectively (Hofmann et al., 2012). Both were used as triple therapies with pegylated interferon (IFN)-α and ribavirin and replaced the dual therapy with pegylated IFN-α and ribavirin as the standard regimen for the treatment of patients with CHC of GT 1 (Hofmann et al., 2012). The main difference between dual and triple therapy is not only in annual treatment costs but also in the sustained virological response (SVR) rate. While for the dual therapy, the SVR rate after 24 weeks (SVR24) in treatment-naïve patients is 38–44%, for GT 1, with costs of 7,709–34,692 EUR, the SVR rate for the triple therapy in treatment-naïve patients is 63–75%, with costs of 34,143–60,990 EUR (Stahmeyer et al., 2014; Sarrazin et al., 2012). There was no improvement in safety endpoints.

³³ This study is joint work with Heiko Friedel and Heike Fröhlich. See Thönnies et al. (2017) for a published version of this chapter.

The aims of this study were first to contribute toward the literature on epidemiological measures of CHC, which is still affected by uncertainty, and estimate the prevalence and incidence (absolute number and rates) of diagnosed CHC patients in the total population of the German Statutory Health Insurance (SHI). Second, we aimed to assess whether and how the introduction of boceprevir and telaprevir as the first direct-acting antiviral (DAA) therapies for CHC in 2011 could have affected the incidence and prevalence of CHC of GT 1. The latter was done because it was assumed that the knowledge of the better SVR rates of both breakthrough therapies (telaprevir and boceprevir) for CHC GT 1 may have led to an increase in new diagnoses.

3.2 Patients and methods

An anonymized representative panel of 3.2 million patients from several German company health insurance funds³⁴ was analyzed for the years 2004–2013. These claims data include sociodemographic characteristics (age, sex, insurance status), insurance time, diagnoses from inpatient and outpatient care, as well as sickness notifications. The analyzed sample was not restricted with respect to any dimension. Because of a unique identifier, it was possible to follow an individual over time. Analyses were carried out using SAS, version 9.4 (SAS Institute, Cary, North Carolina, USA). Sickness funds' approval for data evaluation exists.

The sample was sufficiently representative of the German SHI. The comparison of insured individuals with respect to age and sex was exemplarily carried out for 2013.

We calculated the quarterly and annual number of prevalent and incident patients with CHC for the period 2007–2013.

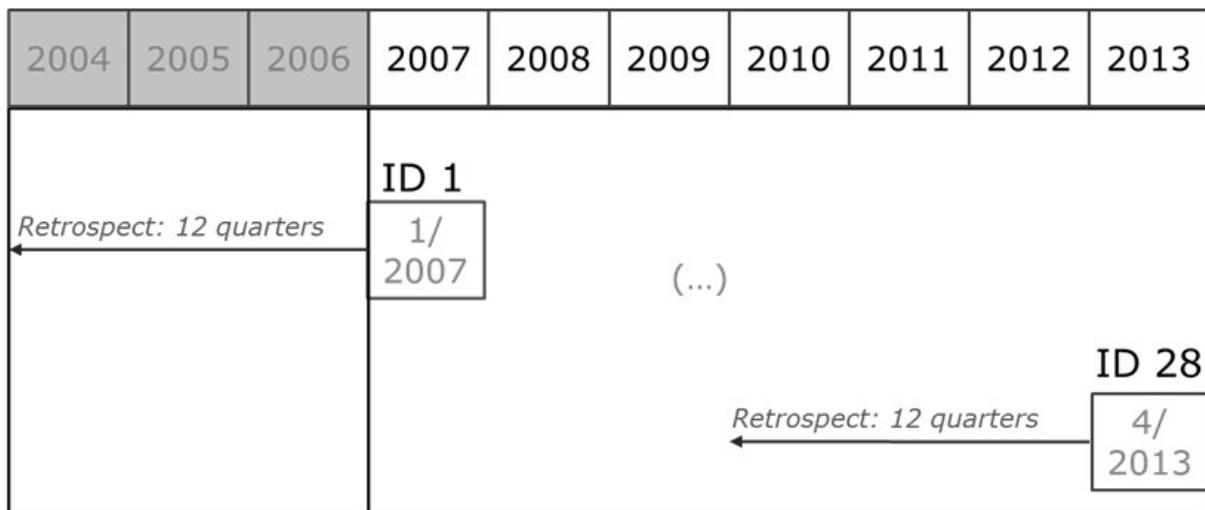
Selection criteria for (prevalent) patients were at least one outpatient or inpatient diagnosis for acute or CHC (ICD-10-GM³⁵ B17.1 or B18.2) or an equivalent sickness notification between the first quarter of 2007 and the fourth quarter of 2013 (Figure 2). We also used the ICD-10-GM code B17.1 (acute hepatitis C) because chronic patients are in practice frequently coded as acute (Tomeczkowski and Cornberg, 2015). For outpatient care, we accepted only confirmed diagnoses (marked by the supplement „G“

³⁴ Betriebskrankenkassen (BKK).

³⁵ ICD-10-GM refers to „International Statistical Classification of Diseases, 10th revision, German Modification“.

or „Z“).³⁶ In data on inpatient care, we searched in primary and secondary diagnoses. In case of at least one diagnosis in a specific quarter, individuals were defined as CHC patients.

Figure 2: Study design



Although we believe that this is the most pragmatic approach for our estimation, it may have led to an underestimation as we cannot exclude that a diagnosis was made before the year 2004 and because approximately only 4.7% of the CHC patients do receive treatment associated with doctor visits (Hardtke and Wedemeyer, 2015), which is how we can identify patients. Therefore, we also imputed diagnoses and marked individuals as suffering from HC in quarters where we do not find a diagnosis if we have already found one in any of the previous quarters (starting in January 2004) and additionally in any of the subsequent quarters (ending in December 2013). We argue that an individual has not been healed if the diagnosis recurs at a later point of time. In contrast, we assume that an individual has been cured if the diagnosis does not recur at a later point of time. Because of the low treatment rate mentioned above, we did not expect any additional information from medication and therefore did not include information on medication to identify patients. Finally, we set the diagnosis to missing if the number of days that the individual was insured in the respective quarter was less than 60. This is done to avoid an under-reporting of diagnoses: if a quarter is observed

³⁶ In 2006, the data lacked information on this supplement. Therefore, in 2006, we treated any diagnosis as confirmed. Year 2006 served as part of the preobservation period for some of the identification quarters (see below).

for only a few days, it is unlikely to observe a coded diagnosis even if the patient has the respective disease. For the same reason, the sample is limited to individuals who have been insured for at least 60 days in the quarter of identification.

To differentiate between prevalent and incident patients, we used data of 2004–2013. For the annual or quarterly assessment of incidence, we focused on the years 2007 onwards, starting in the quarter of identification (which is between the first quarter in 2007 and the fourth quarter in 2013) and looking back 12 quarters to search for an earlier diagnosis (Figure 2). If we did not find one and patients had full insurance coverage during the 12 quarters retrospect, we counted the patient as incident. By using a relatively long period of 12 quarters, the probability of finding an earlier diagnosis is increased. However, it could also cause a potential selection bias because younger and on average healthier individuals could have decided more often to change the health insurance fund than older and sicker patients (Hoffmann and Icks, 2011). As a consequence, they might have not fulfilled the required insurance times and were excluded from the sample. In contrast, for the identification of prevalent patients, we did not request this 12-quarter restriction.

To calculate the prevalence or incidence rate, we divided the identified number of patients by the respective population under risk. For example, for incident patients (the numerator of the fraction), at least 60 days' insurance coverage in the quarter of identification, full insurance coverage in the previous 12 quarters of retrospection, as well as no previous HC diagnosis were required. Then, for the population under risk (the denominator of the fraction), the same restrictions were required.

In the results, we present quarterly and annual period prevalence as well as the prevalence at the cut-off date 1 July. Incidence is also presented on a quarterly and annual level.

The results were also corrected for differences between the analyzed sample and the SHI population in Germany with respect to age and sex to estimate the respective numbers for the total SHI.

Finally, sensitivity analyses were carried out to assess the probability of an overprediction of the incidence rate of CHC patients. If non-diagnosed patients have a lower probability of being thoroughly insured during the retrospect, they are excluded from the analysis too often. Then, the denominator of the incidence rate would be too small and the incidence rate would be overestimated. For this purpose, a comparison

between patients diagnosed with CHC and those who were not was carried out with respect to their insurance time in the retrospect. Only those patients were included who were at least 60 days insured during the quarter of identification. To adjust for systematic differences between CHC-diagnosed and non-CHC-diagnosed patients, a direct matching by age, sex, and insurance status, followed by ordinary least square regression („regression adjusted matching“), was performed. If there was more than one suitable control for one CHC patient, all suitable controls were used and their weight was divided by the number of controls used.

3.3 Results

After the exclusion of 264 patients because of less than 60 days' insurance coverage in the quarter of identification, a total of 10,379 CHC patients were identified for further analyses.

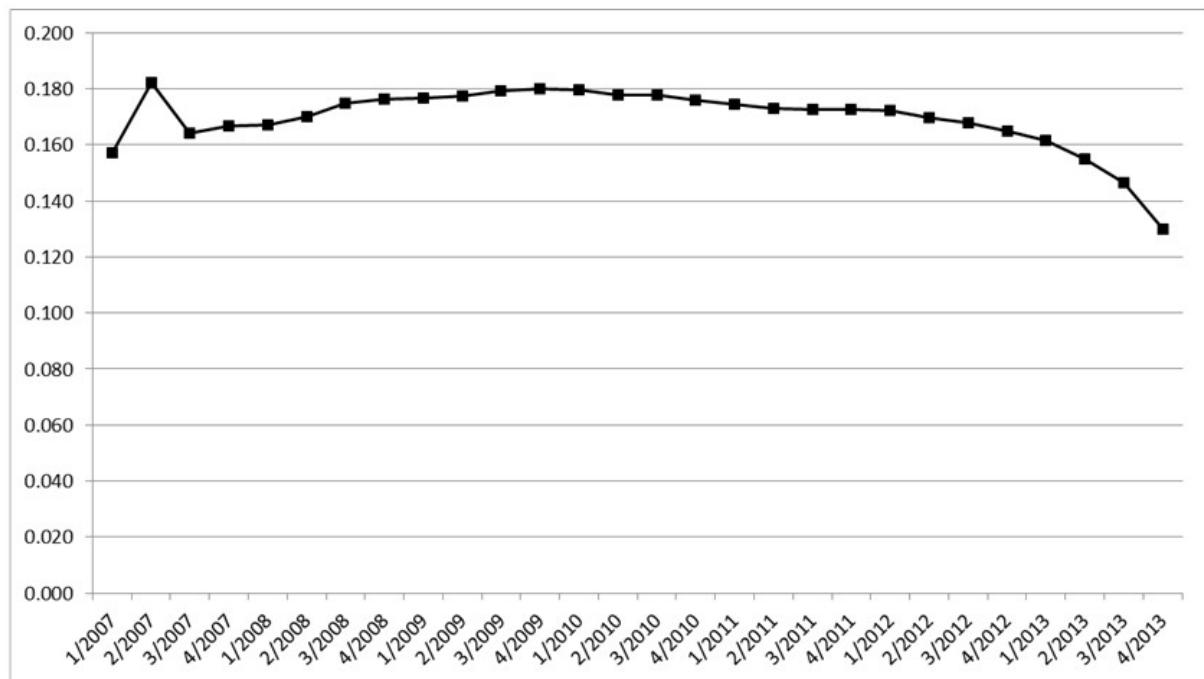
On 1 July 2013, 45.8% of the 10,379 patients had a HC diagnosis (acute or chronic) in this quarter (see Table A 4). The majority of patients were men (57%) and the patients were on average 53.5 years of age (± 15.7 years). The median age was 52 years (25th and 75th percentile: 42 and 63 years, respectively).

We found that the imputation approach (see above) for 2007–2008 and 2012–2013 was not reliable enough for an adequate estimation of the prevalence and incidence rate. Therefore, we focused in the following on the years 2009–2011.

For the calculation of prevalence, all 10,379 identified patients were used. Overall, we found slight differences in the prevalence between the annual and the quarterly approach. This is mainly because the quarterly approach requires a diagnosis in each specific quarter, whereas the annual approach requires only one diagnosis in any of the four quarters. The prevalence rate in the quarterly approach was quite constant, being around 0.18% between 2009 and 2011 (Figure 3)³⁷, although a slight decrease to 0.17% existed for the year 2011. On extrapolation to the total German SHI population, this would mean approximately between 120,000 and 125,000 patients with CHC.

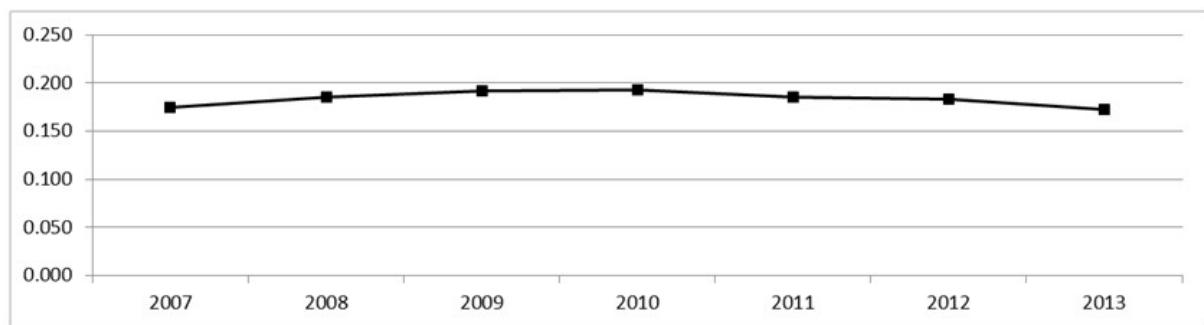
³⁷ The precise number of patients as well as the prevalence and incidence rates which are shown in Figure 3 to Figure 6 and Figure A 2 are presented in Table A 5 to Table A 9.

Figure 3: Quarterly period prevalence rate (in %)



When choosing the annual approach, the average prevalence rate was around 0.19%, with a small decrease for 2011 (Figure 4). On extrapolation to the total German SHI population, this would lead to approximately between 130,000 and 135,000 patients with CHC.

Figure 4: Annual period prevalence rate (in %)



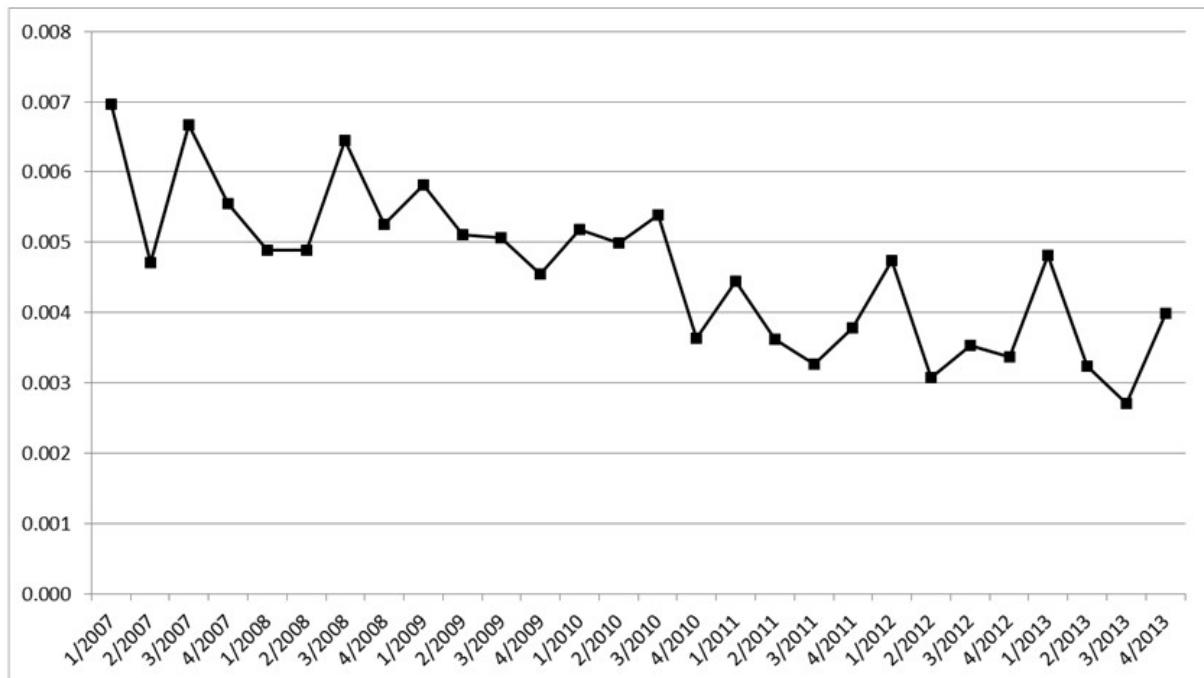
When adopting the cut-off date approach (1 July) to calculate the prevalence rate (see Figure A 2), the results were almost the same as the annual period prevalence rates.

The results by quarter as well as the annual analyses of the prevalence of CHC allow the assumption that the introduction of the first DAA therapies with boceprevir or telaprevir did not coincide with an increase in the number of diagnosed CHC patients.

For the calculation of the incidence rate, 2,821 (27.18%) of the 10,379 patients who were identified between 2007 and 2013 lacked sufficient insurance coverage in the 12 quarters before the quarter of identification; thus, only 7,558 patients were included for the analysis of incidence.

The analyses of incidence rates per quarter (see Figure 5) showed a general declining trend combined with an eye-catching seasonal pattern. Although the incidence rate was relatively stable at first with around 0.006% per quarter, there was a decline between 2009 and 2011 until around 0.004% per quarter. On extrapolation to the total German SHI population, this would mean around 4,000 newly diagnosed patients in each quarter before the predicted number of newly diagnosed patients per quarter decreased to 2,000–3,000 from 2009 onward.

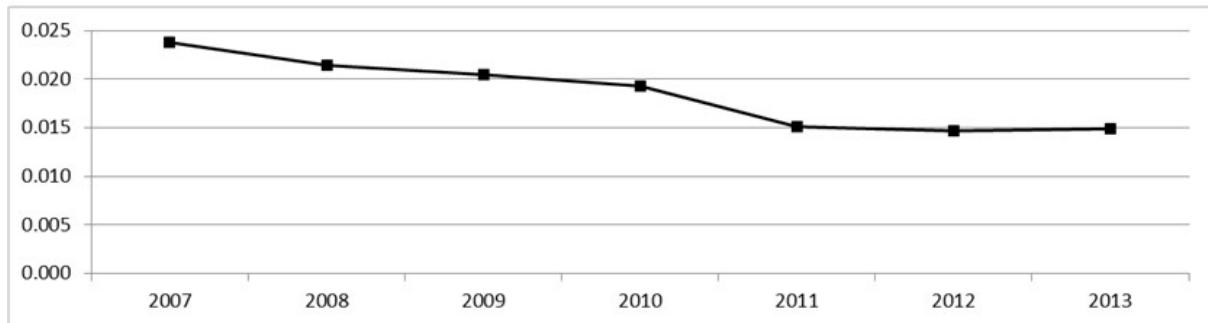
Figure 5: Quarterly incidence rate (in %)



The declining trend was also evident in the annual analysis (Figure 6). The sharpest decrease was from 2010 to 2011: the incidence rate decreased from 0.02 to 0.015%. On extrapolation to the total German SHI population, this would mean around 14,000

newly diagnosed patients each year until 2010. From 2011 onward, there would have been around 10,000 per year.

Figure 6: Annual incidence rate (in %)



Overall, both approaches on the incidence of CHC diagnosis showed that the introduction of the first DAA therapies with boceprevir or telaprevir did not coincide with an increase in the number of new diagnoses.

Finally, we carried out a sensitivity analysis for incidence rates to assess the strength of the selection bias by the 12-quarter-insurance coverage limitation. To evaluate the potential overprediction in the number of newly diagnosed CHC patients, a comparison between patients with or without diagnosis of CHC was carried out. We performed the sensitivity analyses exemplarily for the first quarter in 2013.

Overall, 5,283 CHC-diagnosed patients fulfilled the inclusion criteria, of whom 452 were excluded because of missing values. Table 9 shows the results of this analysis. Patients with a diagnosis of CHC had a 3-day longer insurance coverage than non-diagnosed insurants of the same age, sex, and insurance status (column 1). Although the difference was statistically significant, it was economically negligible when comparing 3 days with the reference time of 12 quarters (i.e., 1,096 days). We also found that patients with CHC diagnosis had a 0.1 percentage point higher probability of showing full insurance coverage compared with non-diagnosed patients (column 2). Although this effect was statistically significant, it was very small and therefore may not be relevant for our conclusions. However, there may still be a marginal chance of overestimating incidence rates by potentially excluding systematically more non-CHC-diagnosed insurants.

Table 9: Sensitivity analysis

	(1)	(2)
	Sum of days that a person was insured in the 12 quarters prior to 1/2013	Probability that a person was fully insured during the 12 quarters prior to 1/2013
Hepatitis C infection in 1/2013	3.017*** (0.190)	0.001** (0.000)
N patients	4,831	
N controls	2,269,424	

Standard errors in parentheses. * p < 0.10; ** p < 0.05; *** p < 0.01.

3.4 Discussion

This is the first study to estimate prevalence and incidence using SHI data with the aim of measuring the effect of the first DAA therapies for CHC – boceprevir and telaprevir – when entering the German market on the diagnosis rate of CHC until December 2013.

We found that the quarterly incidence rates showed a noticeable seasonal pattern. The peaks for new diagnoses and (possibly) treatment were in the first quarter and sometimes also in the third quarter of a year. The rationale for this could be that in the fourth quarter of a year, it may be too impractical to start an IFN-containing therapy because of its specific application, the possibility of unpredicted side effects, and the lack of HCV-RNA monitoring during and after Christmas holidays.

Overall, the results of the quarterly as well as the annual analysis approaches on incidence as well as on the prevalence of CHC diagnosis showed that the introduction of the first DAA therapies with boceprevir or telaprevir did not coincide with an increase in both rates. This is in agreement with data from Robert Koch Institute (2015), which showed that the major increase in incidence occurred in 2014/2015 with the introduction of the second-generation DAA, i.e., sofosbuvir, simeprevir, and daclatasvir as well as ombitasvir/paritaprevir/ritonavir plus dasabuvir (Robert Koch Institute, 2015). Unlike this study, RKI does not use routine data from sickness funds, but reports by physicians. In contrast to the second-generation DAA regimens, the treatment with boceprevir and telaprevir was not considered as a major improvement for CHC patients: although they had a higher efficacy and shorter treatment duration compared with previous IFN-based dual therapy options, the regimens were much more complex (stopping rules and application restrictions) and still poorly tolerable

because of the IFN combination. The milestone change in CHC treatment came with new second-generation DAA therapies because they have a much higher efficacy and better safety with shorter treatment rules than dual or triple therapies, and are IFN-free for many genotypes, especially when combined with each other (mix-and-match regimen) (Banerjee and Reddy, 2016; Sarrazin et al., 2014). This may have led to a more hesitant prescription of the dual and/or triple therapies and, because of this, also to a decrease in the number of new diagnoses.

In our analysis, at the cut-off date of 1 July 2013, a small majority of CHC patients were men (57.4 vs. 42.6%), which is in accordance with latest RKI statistics (Robert Koch Institute, 2015). The prevalence rate was around 0.17–0.19%, which is below the estimation of 0.3–0.5% by Robert Koch Institute (2015). In absolute numbers, we found about 125,000 prevalent patients in 2011. This is lower than that reported in Bruggmann et al. (2014), who reported that in 2011, 12,700 patients were treated. Assuming that 4.7% of all CHC patients receive treatment (Hardtke and Wedemeyer, 2015), our number is half of what one would expect. One reason for this relatively low prevalence rate could be that because of unspecific symptoms of an HCV infection, about 75% of the infected patients remain undiagnosed for a long time (Maier et al., 2010; Robert Koch Institute, 2013; Robert Koch Institute, 2014; Younossi et al., 2014) and the fact that we could not exclude that diagnoses may have been made before the year 2004. In addition, cirrhosis develops in 10–20% of patients quite slowly during a 20- to 30-year timeframe, which may be the reason for the “silent” disease (European Association for the Study of the Liver, 2014). Overall, this lets us assume that both the incidence as well as the prevalence rate calculation until 2013 are influenced by two facts: first, that the diagnosis is sometimes years after the infection, and second, that a treatment with an IFN-containing therapy might be started with delay because of the severe side effects of IFN and its complex application (Maasoumy et al., 2013). This may have changed with the introduction of IFN-free therapies available since 2014 (Wilder and Muir, 2015).

Another reason for our findings on the prevalence may be that insurants in the SHI system are not equally distributed among German health insurance funds because of historical reasons. Before 1996, most Germans could not choose their preferred sickness fund, but were assigned to one according to their profession or place of residence. For the BKK system, it is known that the share of insurants with chronic diseases is lower than in other systems (e.g., than in the Allgemeine Ortskrankenkassen

(AOK) system). In addition, the share of low educated individuals that is presumably positively correlated with drug abuse is smaller in the BKK system (Gesundheitsmonitor, 2008). Therefore, another reason for the low prevalence rate could be that certain groups of high-risk individuals are generally under-represented in our sample from German company health insurance funds (BKKs). Instead, these groups are either more often insured by AOK or not insured at all. In contrast to the general German population, our sample may include less high-risk groups for CHC infection, especially fewer drug addicts, but also fewer immigrants from countries with higher infection rates (Hardtke and Wedemeyer, 2015), fewer individuals with certain CHC-related diseases such as HIV or hemophilia, as well as fewer individuals with transplanted organs or dialysis patients (Stahmeyer et al., 2014). It has to be stated, though, that this bias is becoming smaller. Since 1996, Germans are mostly free to choose their preferred sickness fund. Differences still exist because of limited willingness of insurants to switch to other sickness funds. If CHC risk factors or common comorbidities, such as HIV, exist, it will be regularly checked for CHC infection, which can then lead to an earlier diagnosis of CHC in these patients (Chen et al., 2014). Nevertheless, HIV is also usually diagnosed late (Wagenlehner et al., 2016).

Another reason for underestimation could be that we did not consider the ICD-10-GM codes B17.9 (acute virus hepatitis, not otherwise specified) and B18.9 (chronic virus hepatitis, not otherwise specified). Patients with these codes could have also had a chronic HCV infection.

In contrast, there are also reasons for an overestimation of the number of prevalent patients in our sample: because of the relatively infrequent contact of patients with the health insurance system, we were not able to follow the recommended „M2Q“ (German: „Mindestens zwei (2) Quartale“ / English: „at least two quarters“) criterion (Wagner, 2014). This criterion demands that the respective diagnosis appears in at least two quarters within 1 year to define an individual as a patient. In contrast, in our case, we used a single diagnosis to categorize a patient as prevalent. Finally, we could have overestimated CHC because we also used the ICD-10-GM code B17.1 (acute hepatitis C).

Because of the reasons mentioned above, the results may primarily apply to the BKK system rather than to the general SHI population. A recently published BKK analysis in CHC also reported a 1-year prevalence rate of 0.17% and a 3-year prevalence rate of 0.19%, which is consistent with our results (Tomeczkowski and Cornberg, 2015).

In terms of incidence, the incidence in this BKK data collection ($n \approx 10,000$) is higher than the number of new cases ($n=5,169$) estimated by the RKI for the year 2013 (Robert Koch Institute, 2015). This deviation can, to a small extent, be explained by the exclusion of healthy insurants because of incomplete insurance times if 12-quarter-insurance coverage is required before the quarter of identification. Also, young and well-educated insurants are generally more willing to change their sickness fund (Hoffmann and Icks, 2011). Therefore, they have a higher probability of being excluded from the analysis, which can lead to selection bias (Wagner, 2014). This led to the problem that the denominator of the incidence rate was often too small if the restrictions for inclusion/exclusion were considered. Although the absolute numbers were upwardly biased, the trend of the incidence rate over time was not. Our decrease in incidence for 2010–2011 was also observed by RKI ($n=5,303$ in 2010 to $n=5,057$ in 2011) (Robert Koch Institute, 2015).

Another reason for a possible overestimation of incidence rates could be that the preobservation period may be too short, which has been considered to be crucial for the estimation of incidence rates (Abbas et al., 2012; Prosser et al., 2015). Choosing a length of 3 years, we aimed to find a solution for the trade-off between having a preobservation period as long as possible and at the same time losing as few insurants with incomplete insurance time as possible. Finally, the relatively high incidence rates could again be a consequence of not applying the M2Q criterion. Nevertheless, this bias should apply to all quarters or years in the same way. Therefore, even if absolute numbers were overestimated, the evolution of the incidence rates is not.

Further research is needed to extend the database and to estimate the real effect of the second-generation DAA on the diagnosis rate after the year 2013.

3.5 Appendix

Table A 4: Age and gender of patients in 2013

Age groups	Male patients		Female patients	
	N	Share (in %)	N	Share (in %)
Under 15 years	9	0.2	7	0.1
15 to 19 years	5	0.1	5	0.1
20 to 24 years	19	0.4	20	0.4
25 to 29 years	74	1.6	77	1.6
30 to 34 years	216	4.5	94	2.0
35 to 39 years	302	6.4	118	2.5
40 to 44 years	315	6.6	154	3.2
45 to 49 years	406	8.5	196	4.1
50 to 54 years	415	8.7	256	5.4
55 to 59 years	295	6.2	259	5.4
60 to 64 years	211	4.4	176	3.7
65 to 69 years	122	2.6	120	2.5
70 to 74 years	131	2.8	187	3.9
75 to 79 years	98	2.1	154	3.2
80 to 84 years	69	1.5	103	2.2
85 to 89 years	35	0.7	77	1.6
90 and more years	8	0.2	22	0.5
Total	2,730	57.4	2,025	42.6
		N = 4,755		

Table A 5: Quarterly period prevalence

Quarter	Prevalence rate (in %)	N prevalent patients (predicted for SHI)
1/2007	0.157	110,609
2/2007	0.182	128,140
3/2007	0.164	115,361
4/2007	0.167	117,284
1/2008	0.167	117,477
2/2008	0.170	119,486
3/2008	0.175	122,751
4/2008	0.176	123,799
1/2009	0.177	123,631
2/2009	0.177	124,108
3/2009	0.179	125,513
4/2009	0.180	125,916
1/2010	0.180	125,349
2/2010	0.178	124,131
3/2010	0.178	124,096
4/2010	0.176	122,806
1/2011	0.174	121,321
2/2011	0.173	120,410
3/2011	0.173	120,220
4/2011	0.172	120,043
1/2012	0.172	120,003
2/2012	0.170	118,352
3/2012	0.168	116,879
4/2012	0.165	115,046
1/2013	0.162	112,856
2/2013	0.155	108,275
3/2013	0.147	102,345
4/2013	0.130	90,726

Table A 6: Annual period prevalence

Year	Prevalence rate (in %)	N prevalent patients (predicted for SHI)
2007	0.174	122,486
2008	0.185	129,882
2009	0.192	134,517
2010	0.193	134,661
2011	0.185	129,114
2012	0.183	127,623
2013	0.173	120,794

Table A 7: Prevalence at cutoff date July 1st

Year	Prevalence rate (in %)	N prevalent patients (predicted for SHI)
2007	0.164	115,425
2008	0.173	121,603
2009	0.179	125,566
2010	0.178	124,228
2011	0.173	120,360
2012	0.168	116,847
2013	0.147	102,382

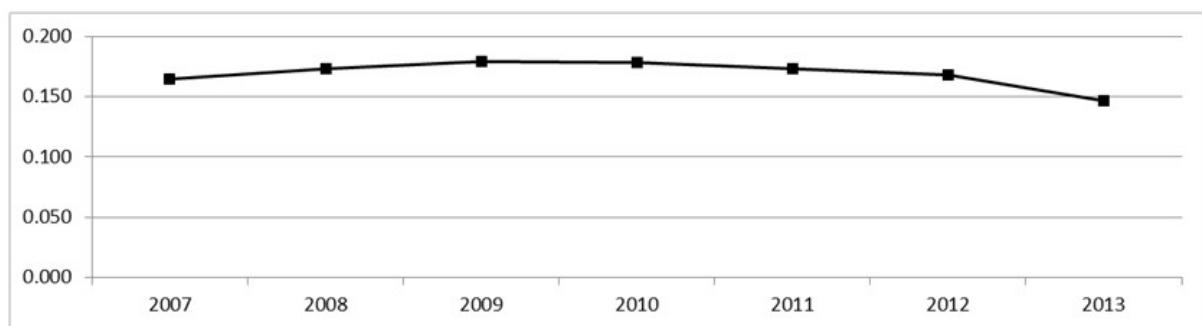
Table A 8: Quarterly incidence

Quarter	Incidence rate (in %)	N incident patients (predicted for SHI)
1/2007	0.007	4,900
2/2007	0.005	3,307
3/2007	0.007	4,689
4/2007	0.006	3,898
1/2008	0.005	3,436
2/2008	0.005	3,429
3/2008	0.006	4,527
4/2008	0.005	3,687
1/2009	0.006	4,071
2/2009	0.005	3,579
3/2009	0.005	3,547
4/2009	0.005	3,185
1/2010	0.005	3,613
2/2010	0.005	3,476
3/2010	0.005	3,763
4/2010	0.004	2,534
1/2011	0.004	3,095
2/2011	0.004	2,515
3/2011	0.003	2,277
4/2011	0.004	2,635
1/2012	0.005	3,306
2/2012	0.003	2,147
3/2012	0.004	2,465
4/2012	0.003	2,347
1/2013	0.005	3,357
2/2013	0.003	2,260
3/2013	0.003	1,889
4/2013	0.004	2,788

Table A 9: Annual incidence

Year	Incidence rate (in %)	N incident patients (predicted for SHI)
2007	0.024	16,721
2008	0.021	15,038
2009	0.020	14,343
2010	0.019	13,420
2011	0.015	10,490
2012	0.015	10,260
2013	0.015	10,391

Figure A 2: Prevalence rate at cut-off date July 1st (in %)



4. Clinical and Economic Burden of Hepatic and Extrahepatic Complications from Chronic Hepatitis C: A Retrospective Analysis of German Sickness Fund Data³⁸

4.1 Introduction

Hepatitis C virus (HCV) infection is a systemic disease presenting with hepatic and extrahepatic complications (EHCs) (Younossi et al., 2016). HCV represents a major global health burden with over 80 million people infected worldwide (Gower et al., 2014), including an estimated 14 million people chronically infected in the WHO European region (World Health Organization, 2017a). The incidence risk of HCV in the European Union (EU) is approximately 8.7 per 100,000 people (World Health Organization, 2017b), with a reported 2.6 million individuals infected with viremic HCV in Western Europe (Gower et al., 2014). While there are limited data estimating the prevalence of HCV infection in Germany specifically, one 2013 study reported a prevalence estimate of antibodies against HCV in the German population to be 0.3%, similar to the prevalence estimated 10 years prior (0.4%) (Poethko-Müller et al., 2013).

The estimated diagnosis rate of HCV is 57% (Razavi et al. 2014), which suggests a relatively large proportion of patients who are living with HCV yet who remain undiagnosed with this disease. Acute HCV infection is typically asymptomatic and often remains undiagnosed, with up to 85% of acutely infected individuals developing chronic hepatitis C (CHC) virus infection (World Health Organization, 2016). Complications resulting from HCV infection include cirrhosis, hepatocellular carcinoma, and liver failure (Younossi et al., 2017), all of which are associated with substantial healthcare costs (Nevens et al., 2012).

In the WHO European region, nearly 112,500 people die each year due to HCV-related liver diseases (World Health Organization, 2017a). In addition to the detrimental effects on the liver, HCV is associated with a number of EHCs, which affect other organ systems, causing progressive illness and possible death (Carrozzo and Scally, 2014). These EHCs include mixed cryoglobulinemia, cryoglobulinemic vasculitis, B cell non-Hodgkin lymphoma, arthralgia, immune thrombocytopenia, type 2 diabetes mellitus

³⁸ This study is joint work with Michael R. Kraus, Henning Kleine, Marc Pignot, and Yuri Sanchez Gonzalez. See Kraus et al. (2018a) for a published version of this chapter.

(T2DM), renal impairment, fatigue, cognitive impairment, depression, cancer, and cardiovascular disorders, among others (Cacoub et al., 2016).

A recent global meta-analysis showed the most common EHCs among patients diagnosed with CHC were mixed cryoglobulinemia (30.1%), depression (24.5%), T2DM (15.0%), Sjögren's syndrome (11.9%), and chronic renal disease (10.1%) (Younossi et al., 2016). The study also found that the most commonly-studied EHCs were mixed cryoglobulinemia, porphyria cutanea tarda, T2DM, and depression (Younossi et al., 2016). Other diseases also impact the overall burden associated with CHC. These include Parkinson's disease, behavioral and mental disorders due to psychoactive substance use, cardiovascular disorders, and non-hepatic malignancies, among others. A recent systematic review has shown that HCV-infected patients have approximately 35% higher risk of Parkinson's disease as compared with patients without HCV (Wijarnpreecha et al., 2018). Substance abuse also contributes to viral exposure due to use of contaminated needles (Khalsa et al., 2008). A direct link does not exist between cardiovascular disorders and HCV infection; however, HCV infection has been reported to increase cardiovascular risk (Petta, 2017). Furthermore, CHC patients are at an increased risk of cancer, not only because of the infection itself but also due to exposure to other substances such as tobacco and alcohol (Balakrishnan et al., 2017).

HCV-related clinical events pose a significant economic burden in terms of both direct medical costs (such as pharmacy- and treatment-related) and indirect costs (work productivity loss due to absenteeism and/or presenteeism) (Younossi et al., 2016). The economic burden of HCV has been documented in Europe (DiBonaventura et al., 2014; Vietri et al., 2013), including data from Germany (Stahmeyer et al., 2014). However, data that specifically estimate the economic impact attributable to CHC-related EHCs for Germany alone are unavailable. In addition, the clinical and economic burden of CHC-related EHCs is not yet fully understood, given that most studies report on a limited number of EHCs (Solinis et al., 2016). There is particularly a lack of available data pertaining to the prevalence and burden of CHC-related EHCs in Germany. The aim of this study was to utilize a comprehensive national database from the German *Betriebskrankenkasse* (BKK) sickness fund, to assess the clinical and economic burden of a broad range of CHC-related EHCs.

4.2 Methods

4.2.1 Data sources

Reimbursement data from the BKK sickness fund cover 5.2 million persons (as of 2012), which includes patients' medical (i.e., inpatient and outpatient claims), prescription drugs, and insurance eligibility information. Data from 2007 through 2014 were utilized for HCV-diagnosed patients and matched non-HCV controls. The BKK were informed about the project and all the required approvals were obtained. Patient data were fully anonymized according to accepted standard procedures.

4.2.2 Study definitions

Prevalent patients with CHC were identified using the International Classification of Diseases, 10th Edition German Modification (ICD-10-GM) code B18.2 in outpatient and/or inpatient care data in any of the quarters in the identification period (Q1/2008 through Q1/2014). Only patients with a diagnosis of CHC preceded and followed by at least 4 quarters of full insurance were considered for inclusion. For inpatient data, primary CHC discharge diagnoses as well as secondary diagnoses were checked. For outpatient data, only assured diagnoses (marked by "G" or "Z") were considered and required evidence of a second diagnosis code within 3 quarters pre- or post-identification.³⁹

4.2.3 Extrahepatic complications (EHCs)

EHCs included extrahepatic manifestations (EHMs), which have a documented clinical pathway with CHC, as well as other conditions and behavioral factors which, although no clinical pathway has been established, are prevalent among the patient population. EHMs investigated in this study included the broader disease categories of T2DM, cardiovascular disease (CVD), fatigue, renal impairment, and malignancies. Other prevalent diseases observed in the patient population were mental and behavioral disorders (due to opioids, multiple drug use, and other psychoactive substances); Parkinson's disease; and some cardiovascular, renal, and other diseases not documented as EHMs. EHMs, behavioral factors, and other prevalent conditions in the

³⁹ G (abbreviation for "gesicherte Diagnose") = assured diagnosis; Z ("Zustand nach") = condition after.

population are jointly called EHCs for this study. The complete list of diseases within each grouping and its disease category, as well as their associated ICD-10-GM codes, is presented in Table 10.

Table 10: ICD-10-GM codes for extrahepatic complications

Condition category	ICD-10-GM	Label
<i>Extrahepatic manifestations</i>		
Type 2 diabetes	E11.*	Diabetes mellitus, type 2
	E14.*	Diabetes mellitus, not further specified
Cardiovascular disease	I20.*-I25.*	Ischemic heart diseases
	I60.*-I69.*	Cerebrovascular diseases
	I70.*	Atherosclerosis
Fatigue	F32.*	Episode of depression
	G93.3	Chronic fatigue syndrome
	R53	Indisposition and fatigue
	F43.0	Fatigue in the context of an acute stress reaction, e.g., combat fatigue
	F48.0	Neurasthenia
	Z73	Problems related to life management difficulty, including burnout (state of total exhaustion)
Renal impairment	N18.*	Chronic kidney disease
	N19.*	Renal failure, not further specified
	D89.1	Cryoglobulinemia
Malignancies	C85.*	Other and not further specified types of Non-Hodgkin-lymphoma
<i>Behavioral factors</i>		
Mental and behavioral disorders (due to opioids, or multiple and other psychoactive substances)	F11.*	Mental and behavioral disorders due to use of opioids
	F19.*	Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances
<i>Conditions that are prevalent in the population</i>		
Cardiovascular disease	I10.*-I15.*	Hypertension
	E78.*	Disorders of lipoprotein metabolism and other lipoproteins
Parkinson's disease	F02.3	Dementia with primary Parkinson's syndrome
	G20.*	Primary Parkinson's syndrome
	G21.*	Secondary Parkinson's syndrome
	G22	Parkinson's syndrome with elsewhere classified diseases
	G23.2	Multiple system atrophy of Parkinson type
Renal impairment	N17.*	Acute renal failure
Malignancies	C20	Malign neoplasm of rectum
	C22.*	Malign neoplasm of liver and intra-hepatic bile ducts
	C25.*	Malign neoplasm of pancreas
	C34.*	Malign neoplasm of bronchia and lung
	C64	Malign neoplasm of kidney, except from renal pelvis
	C65	Malign neoplasm of renal pelvis
Other	H52.*	Disorders of refraction and accommodation
	K29.*	Gastritis and duodenitis
	M54.*	Dorsalgia

The following sources were used for the preparation of Table 10: Cacoub et al., 2016; Cacoub et al., 2017; Cheng et al., 2014; Mohammed et al., 2010; Reau et al., 2017; Tengen et al., 2017. ICD-10-GM: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification.

Clinical burden analyses: Cumulative prevalence and incidence of EHCs

The cumulative prevalence and incidence of the EHCs were compared between patients with prevalent CHC matched to controls with no evidence of CHC to assess the clinical burden of these diseases. Patients were required to be insured at least 4 quarters of look-back and at least 20 quarters of follow-up, as the prevalence and incidence were calculated for 5 years of follow-up. For patients with CHC, the index quarter was defined as the quarter of the first CHC diagnosis, using data from Q1/2008 to Q1/2014. Controls were identified as having no evidence of CHC in the entire study period. Matching was carried out 1:1 on index quarter, age (in 5-year-categories), sex, and the previous year's healthcare costs (in categories; 0 euro, and 23 quantiles of costs > 0 euro). The annual prevalence was calculated separately for both cohorts, and the number of patients suffering from each/any of the EHCs was measured in each of the 5 years of follow-up (F/U) to assess annual prevalence. Incidence was defined as the proportion of newly diagnosed patients in the period of interest among patients at risk at the start of the period of interest. Four-year cumulative incidence rates of the EHCs were calculated separately for both cohorts, based on F/U2 through F/U5. The prevalence, incidence, and risks of the EHCs were compared between the matched study cohorts using unadjusted logistic models, odds ratios (OR), and P values.

4.2.4 Economic burden analyses

Medical cost definitions

Annualized total costs were assessed from the index quarter until the end of patient follow-up, which corresponded to the end of continuous insurance time, based on whether the patient died or switched to another health insurance, or the end of data availability on December 31, 2014. Therefore, while follow-up time may have differed in length across patients, annualizing the costs served to make patients' follow-up time comparable. To quantify the economic burden of CHC, annual costs were compared between matched patients with and without CHC.

The sum of all-cause medical and pharmacy costs is referred to as total cost. All-cause medical costs were further broken down into medical costs related to hepatic and extrahepatic complications. Pharmacy costs were split into CHC-related and non-CHC-related costs. CHC-related costs were defined as those associated with esophageal varices, spontaneous bacterial peritonitis, cirrhosis of the liver, hepatic

encephalopathy (liver failure), portal hypertension, ascites, splenomegaly, hepatorenal syndrome, hepatocellular carcinoma, porphyria cutanea tarda, and liver transplantation. Costs attributable to CHC-related EHCs were identified using relevant German Uniform Assessment Standard (EBM) codes, Diagnosis Related Groups (DRG) codes, and Operation and Procedure (OPS) codes. EBM codes are relevant in the setting of medical practitioners, while DRG and OPS codes are relevant in the setting of hospitals (in- and outpatient care). In addition, claims from sickness benefits (medical leave benefits received by employees after 6 weeks of inability to work), which were based on relevant ICD-10-GM codes, were included in the EHC costs. Likewise, medical costs related to hepatic complications were identified by searching for relevant EBM, DRG, OPS, and ICD-10-GM codes that are associated with hepatic complications. Claims associated with both CHC-associated EHCs and hepatic complications were attributed to both categories. Total all-cause medical costs contain costs for practitioner, hospital in- and outpatient care, as well as sickness benefits. In addition to EHC-related or hepatic complications-related medical costs, all other costs that occur due to any disease were included in total all-cause medical costs. CHC-related pharmacy costs were identified for 12 CHC drugs, while all other pharmacy costs were summarized as non-CHC-related pharmacy costs (Table 11). Costs were calculated as average, annualized charged amounts and adjusted to reflect average 2016 Euro exchange rates.

Mean costs differences estimated from unadjusted and adjusted ordinary least squares regression models were used to compare the medical costs between study cohorts. Models were adjusted for age (in years), gender, and the previous year's total healthcare costs.

Table 11: German ATC codes and OPS codes for substances defined as CHC-related drugs

ATC code	OPS code	Substance
J05AE12	---	Boceprevir
J05AX14	6-008.d	Daclatasvir
L03AB**	8-812.1*/8-812.2*/8-547.2	Interferon
J05AX65	6-007.g (combined with Sofosbuvir)	Ledipasvir
J05AB04	---	Ribavirin
J05AE14	6-008.2	Simeprevir
J05AX15	6-007.g (combined with Ledipasvir)/6-008.3	Sofosbuvir
J05AE11	6-009.6	Telaprevir

ATC code: anatomical therapeutic chemical code; CHC: chronic hepatitis C;
OPS code: operation and procedure code.

Economic burden of CHC

A retrospective cohort study was performed to estimate the medical costs between patients with and without CHC. Patients with a CHC diagnosis were matched to controls with no evidence of CHC ever in the study period. Controls were selected from the same index quarter and met the same insurance criteria, requiring four quarters of insurance coverage pre- and post-index. One random quarter between Q1/2008 and Q1/2014 in which CHC patients showed a relevant diagnosis was used as their identification/index quarter, and this anchored their look-back and follow-up. The CHC cohort was matched 1:5 to controls on age (in categories of 5 years each), gender, and the previous year's total healthcare costs (in 38 categories, i.e., 0 euro, and 37 quantiles for costs > 0 euro).

All analyses were conducted using SAS version 9.4. Alpha of 0.05 was used as the cut-off for determining statistical significance.

4.2.5 Compliance with ethics guidelines

This article is based on previously available data, and does not involve any new studies of human or animal subjects performed by any of the authors. However, appropriate approvals from the BKK were obtained in order to use their data for this study.

Similar data were used in a study assessing the role of treatment in reducing the economic burden of hepatic and EHCs associated with CHC in Germany. That study found that treatment may reduce the burden of CHC and result in substantial cost

savings, even when initiated at earlier stages of the disease, subject to similar limitations as the present study (Kraus et al., 2018b).

4.3 Results

4.3.1 Clinical burden: Cumulative prevalence and incidence and risk of CHC-related EHCs

In general, the prevalence and incidence of the EHCs was greater in the CHC cohort ($n = 3,994$) versus the cohort without CHC ($n = 3,994$) (Table 12). The exceptions were cardiovascular and Parkinson's disease, though the prevalence gap was significantly different only for CVD. The prevalence in the CHC cohort for any of the EHCs was significantly higher than the controls with no-CHC for each year of follow-up (F/U), with a 3-fold greater risk (OR = 3.0; $P < 0.05$; Table 12) in the fifth year of F/U (data for F/U2 through F/U4 not shown). Patients with CHC had significantly greater annual risks in the majority of follow-up years for mental and behavioral disorders (due to opioids, multiple drug use, and other psychoactive substances; F/U5 OR = 22.0), fatigue (F/U5 OR = 1.9), renal impairment (F/U5 OR = 1.4), and malignancies (F/U5 OR = 1.9), all $P < 0.05$. The 4-year cumulative incidence rate for any of the EHCs was also significantly higher in the CHC cohort than in the no-CHC cohort (OR = 1.1; $P < 0.05$). The EHCs with significantly greater 4-year cumulative incidence risk (F/U2 through F/U5) in CHC patients were mental and behavioral disorders (due to opioids, multiple drug use, and other psychoactive substances; OR = 4.0), malignancies (OR = 2.9), fatigue (OR = 1.6), and renal impairment (OR = 1.4), all $P < 0.05$.

Table 12: Clinical burden of CHC-related extrahepatic complications risk in the matched CHC versus no-CHC cohorts

Extrahepatic complications	Prevalence in F/U1			Prevalence in F/U5			4-year cumulative incidence in F/U5 ^a		
	CHC cohort (n=3,994)	No-CHC cohort (n=3,994)	OR	CHC cohort (n=3,994)	No-CHC cohort (n=3,994)	OR	CHC cohort (n=3,994)	No-CHC cohort (n=3,994)	OR
Any extrahepatic complication	3,593 (90.0%)	3,200 (80.1%)	2.2*	3,913 (98.0%)	3,757 (94.1%)	3.0*	320 (79.8%) ^b	557 (70.2%) ^b	1.1*
Type 2 diabetes	609 (15.2%)	555 (13.9%)	1.1	830 (20.8%)	788 (19.7%)	1.1	221 (6.5%)	233 (6.8%)	1.0
Cardiovascular disease	1,863 (46.6%)	2,079 (52.1%)	0.8*	2,439 (61.1%)	2,629 (65.8%)	0.8*	576 (27.0%)	550 (28.7%)	0.9
Parkinson's disease	14 (0.4%)	25 (0.6%)	0.6	38 (1.0%)	52 (1.3%)	0.7	24 (0.6%)	27 (0.7%)	0.9
Mental and behavioral disorders	912 (22.8%)	27 (0.7%)	43.5*	1,016 (25.4%)	61 (1.5%)	22.0*	104 (3.4%)	34 (0.9%)	4.0*
Fatigue	1,413 (35.4%)	918 (23.0%)	1.8*	2,147 (58.2%)	1,552 (42.3%)	1.9*	911 (35.3%)	770 (25.0%)	1.6*
Renal impairment	227 (5.7%)	173 (4.3%)	1.3*	468 (11.7%)	352 (8.8%)	1.4*	241 (6.4%)	179 (4.7%)	1.4*
Malignancies	81 (2.0%)	60 (1.5%)	1.4	170 (4.3%)	91 (2.3%)	1.9*	89 (2.3%)	31 (0.8%)	2.9*
Other	2,540 (63.6%)	2,468 (61.8%)	1.1	3,495 (87.5%)	3,421 (85.7%)	1.2*	955 (65.7%)	953 (62.5%)	1.2

CHC and no-CHC patients were matched on age (in 5-year-categories), gender, and the previous year's healthcare costs (in categories; 0 euro, and 23 categories for costs > 0 euro).

F/U: follow-up year; CHC: chronic hepatitis C virus infection; F/U: follow-up; OR: odds ratio.

*P<0.05

^a I.e., F/U2-F/U5. In F/U1, all individuals that suffer from some extrahepatic complication were prevalent. Therefore, incidence can only be analyzed from F/U2 onwards.

^b The denominator is the population under risk, i.e., the number of patients or controls that is not prevalent in F/U1.

4.3.2 Economic burden of HCV

A total of 8,425 patients with CHC were identified and matched to 42,125 patients without HCV to compare the economic burden associated with HCV. Patients with HCV were 55.7% male with a mean age of 52.0 years (standard deviation (SD) = 28.7), while those without HCV were also 55.7% male with a mean age of 52.4 years (SD = 13.8) (Table 13). The total costs (€10,108 vs. €5,430, adjusted difference €3,628), hepatic complications-related medical costs (€1,425 vs. €556, adjusted difference €865), EHC-related costs (€3,547 vs. €1,921, adjusted difference €1,606), CHC-related pharmacy costs (€577 vs. €116, adjusted difference €454), and non-CHC-related pharmacy costs (€3,719 vs. €1,479, adjusted difference €1,272) were all significantly higher for the CHC cohort than the no-CHC cohort ($P < 0.01$ for all; Table 14). EHC-related medical costs were a major contributor to the higher all-cause medical (84.4%) and total (44.3%) adjusted cost differences observed.

Table 13: Comparison of patient characteristics among patients in the matched CHC vs. no-CHC cohorts

Characteristics	Patients with prevalent CHC and matched CHC-free controls		
	CHC cohort (n = 8,425)	No-CHC cohort (n = 42,125)	
Age (years)			
	mean \pm SD	52.0 \pm 28.7	52.4 \pm 13.8
	[median]	[50]	[51]
Males	N (%)	4,694 (55.7%)	23,470 (55.7%)
Previous year's healthcare cost (euro)	mean \pm SD	8,666 \pm 52,293	7,798 \pm 11,523
	[median]	[2,893]	[3,037]
Previous year's healthcare cost (euro), per category	0	0	0
	1st quartile	875	901
	2nd quartile	2,893	3,037
	3rd quartile	8,989	9,126
	4th quartile	1,312,098	476,544
Index year	N (%)		
	2008	1,229 (14.6%)	6,145 (14.6%)
	2009	1,151 (13.7%)	5,755 (13.7%)
	2010	1,121 (13.3%)	5,605 (13.3%)
	2011	1,184 (14.1%)	5,920 (14.1%)
	2012	1,355 (16.1%)	6,775 (16.1%)
	2013	1,795 (21.3%)	8,975 (21.3%)
	2014	590 (7.0%)	2,950 (7.0%)

CHC: Chronic hepatitis C virus infection; SD: standard deviation.

Table 14: All-cause, hepatic complication-related, and extrahepatic complication-related annual costs among patients in the matched CHC versus no-CHC cohorts

Cost category	Weighted mean costs (2016 euro) per patient per year of follow-up after the randomly selected index quarter			Adjusted cost difference (95% CI) ^a
	CHC cohort [A] (n = 8,425) (mean ± SD)	No-CHC cohort [B] (n = 42,125) (mean ± SD)	Mean cost difference [A]–[B] (95% CI)	
Total cost (all-cause medical + pharmacy)	10,107.5 ± 86,851.3	5,429.7 ± 9,069.5	4,677.8* (3,635.2; 5,720.5)	3,628.4* (3,213.8; 4,042.9)
Total all-cause medical costs	5,811.6 ± 21,441.4	3,834.2 ± 6,598.6	1,977.4* (1,710.4; 2,244.5)	1,902.1* (1,679.5; 2,124.7)
Hepatic complications-related medical costs	1,425.2 ± 11,116.1	555.9 ± 2,229.4	869.3* (734.1; 1,004.6)	865.4* (751.4; 979.4)
Extrahepatic complication-related medical costs (any of the conditions listed below)	3,547.3 ± 16,107.6	1,921.2 ± 4,357.0	1,626.2* (1,427.4; 1,824.9)	1,605.8* (1,433.7; 1,777.9)
Type 2 diabetes	1,100.5 ± 8,845.9	659.8 ± 2,285.5	440.7* (331.8; 549.6)	440.5* (348.0; 533.0)
Cardiovascular disease	1,220.8 ± 10,628.1	688.0 ± 2,524.7	532.8* (402.6; 663.0)	536.2* (433.2; 639.2)
Parkinson's disease	595.2 ± 5,535.7	414.6 ± 1,617.7	180.6* (112.0; 249.3)	181.6* (123.3; 239.9)
Mental and behavioral disorders	1,204.8 ± 6,889.5	478.6 ± 1,743.9	726.2* (641.5; 810.9)	712.1* (637.1; 787.2)
Fatigue	714.8 ± 4,816.0	322.1 ± 1,273.0	392.7* (333.4; 452.1)	381.9* (327.9; 435.9)
Renal impairment	1,147.0 ± 10,429.2	522.1 ± 2,642.3	624.9* (496.7; 753.0)	615.4* (503.3; 727.4)
Malignancies	1,278.6 ± 8,634.0	781.8 ± 2,642.9	496.8* (389.3; 604.3)	494.1* (407.4; 580.9)
Other	889.8 ± 7,511.1	473.2 ± 1,606.4	416.6* (325.0; 508.1)	418.3* (344.8; 491.7)
All pharmacy costs				
CHC-related pharmacy costs	576.9 ± 4,058.4	116.1 ± 1,139.0	460.9* (410.7; 511.1)	453.9* (402.1; 505.8)
Non-CHC-related pharmacy costs	3,719.0 ± 81,637.5	1,479.4 ± 5,132.8	2239.6* (1,262.6; 3,216.5)	1,272.3* (911.6; 1,633.1)

Patients with and without CHC were matched on age (in 5-year-categories), gender, and the previous year's healthcare costs (in categories; 0 euro, and 37 quantiles for costs > 0 euro).

CHC: chronic hepatitis C virus infection; CI: confidence interval; OLS: ordinary least squares; SD standard deviation.

*P<0.01.

^a Weighted OLS regression models to estimate adjusted mean cost difference between the CHC and no-CHC cohorts.

4.4 Discussion and limitations

In the current German BKK sickness fund data analysis, for the first time, the all-cause medical, pharmacy, hepatic complication- and EHC-related medical costs were compared between matched patients with and without CHC. The results showed that CHC was significantly associated with clinical and economic burden attributable to hepatic and EHCs. Results concerning the economic burden associated with CHC were consistent with recent evidence from the US (Reau et al., 2017). However, in contrast to previous results (Solinis et al., 2016; Tengan et al., 2017), the prevalence of cardiovascular disease was significantly higher in the cohort without CHC than in the CHC cohort. This also contrasts the difference in economic burden attributed to cardiovascular EHCs observed in the present study, where the CHC cohort incurs a greater cost (Table 14). As the clinical burden analysis was limited to people with at least 5 years of data, it is possible that the sample was skewed to a healthier population resulting from the exclusion of patients with CVD passing away or lost to follow-up within this 5-year period.

CHC patients in this study had 3-fold higher risks in the last follow-up year of this study for any EHC, and higher total cost, all-cause medical, and EHC-related medical costs (adjusted annual cost differences €3,628, €1,902, and €1,606, respectively) compared to patients without CHC. Similarly, a meta-analysis by Younossi et al. (2016) found HCV to be a risk factor for developing new EHMs including kidney disease, lymphoma, depression, and T2DM. Using a US claims database, Reau et al. (2017) demonstrated that EHMs contributed to the overall clinical and economic burden of HCV and its treatment. Of the EHMs assessed, kidney disease and CVD were the costliest EHMs across HCV versus no-HCV. The results observed in our study are comparable to Reau et al.'s US study, with the share of the all-cause medical costs attributable to EHCs being 84.4% for HCV versus no-HCV cohorts. Regarding clinical burden, the HCV cohort in the current study showed greater risk of contracting any EHC compared to the US study (OR 3.0 vs. 2.2).

A European study evaluating all-cause medical costs from 5 countries, including Germany, showed that costs were greater for patients with HCV compared with patients without HCV (Vietri et al., 2013). However, the all-cause medical costs were lower in the European study compared with the current study (€1,147 vs. €5,812). A major driver of this difference may be that the European study used medical costs calculated using an average price reported in literature and adjusting for 2010 inflation

values. The current study used a single data source to calculate German costs through 2014 and, hence, these price and time-period differences could have influenced the costs in addition to inflation.

Cacoub et al. (2017) recently used an economic model to estimate the burden of EHMs in European HCV patients. These authors analyzed EHMs not included in the present study, such as lichen planus, Sjögren's syndrome, and rheumatoid-like arthritis. The EHC-related medical costs in the current study were almost 3-fold higher (€3,547 vs. €1,247) than in the European study (Cacoub et al., 2017). The higher cost observed in the current study could be due to the data collection methods used; for example, Cacoub et al. obtained data from various sources including literature, national databases, and expert opinion, whereas the current study used data from a single database.

The strength of our study is the inclusion of a broad range of EHCs, including some that have not been studied extensively (e.g., mental disorders, gastric disorders), which enabled us to understand the clinical and economic burden of CHC in Germany. EHC is a broader term than EHM because the former only encompasses conditions that have a documented clinical pathway to CHC, while the latter also includes conditions that are prevalent among the patient population but are not yet shown to be related to CHC.

The limitations of the current study must be kept in mind while interpreting the results. The BKK data only represent ~8% of all people within the statutory health insurance system. Residual confounding may persist despite sample matching and covariate adjustment in the analyses. Patients could be misclassified due to misinterpretation of EBM, DRG, OPS, and ICD-10-GM codes. CHC is a chronic disease; hence, a possibility of lag between infection and diagnosis cannot be excluded. It is possible that some of the patients in the no-CHC cohort were infected but undiagnosed, potentially underestimating the risk of EHCs; however, with a HCV prevalence of 0.3% in Germany (Poethko-Müller et al., 2013), the bias introduced by undiagnosed HCV patients in the no-HCV cohort must be very small. Some EHC categories such as cardiovascular disorders and renal impairment are comprised of both EHMs documented in the literature and other conditions that are prevalent in this population. The medical costs were measured as charged amounts, and not paid amounts, which may result in overestimation of the actual cost. However, this is likely to affect all the cohorts equally. In addition, a single medical claim could be associated with multiple procedure codes, resulting in the same medical cost being counted under multiple

EHM categories. However, these costs were only included once while performing summation. Also, not all EHCs were included in the analysis and those included were grouped together which could affect the respective cost analyses. Moreover, data are used from a large span of time (2007–2014), which introduces a high level of heterogeneity regarding patient characteristics, making interpretation of the data and results more difficult.

4.5 Conclusion

The current study findings reveal that CHC is associated with a high risk of EHCs and imposes a substantial economic burden. Not treating CHC or delaying treatment to advanced stages of liver disease may result in additional expenditures, mainly due to EHC-related complications. The results observed in this study may help guide clinical decision making for the improvement of care for patients with CHC, which in turn could lead to significant cost savings for payers and society alike.

5. Improvement of Hepatic and Extrahepatic Complications from Chronic Hepatitis C after Antiviral Treatment: A Retrospective Analysis of German Sickness Fund Data⁴⁰

5.1 Introduction

Hepatitis C virus (HCV) infection is a major health burden in Europe, reportedly affecting 14 million people in the WHO European region (World Health Organization, 2017a) and 2.6 million individuals in Western Europe (Gower et al., 2014). While there is a paucity of data estimating the prevalence of HCV infection in Germany specifically, a 2013 study reported the overall prevalence of antibodies against HCV in the German population to be 0.3%, similar to the prevalence estimated 10 years prior (0.4%) (Poethko-Müller et al., 2013). Furthermore, the estimated diagnosis rate among those living with HCV is 57% (Razavi et al., 2014).

Acute HCV infection is typically asymptomatic and often remains undiagnosed, with up to 85% of acutely infected individuals developing chronic hepatitis C (CHC) virus infection (World Health Organization, 2016). HCV infection presents with hepatic complications such as cirrhosis, hepatocellular carcinoma, and liver failure (Younossi et al., 2017), apart from extrahepatic complications (EHCs) (Younossi et al., 2016), which affect other organ systems, causing progressive illness and possible death (Carrozzo and Scally, 2014). These include common and well-studied EHCs, such as mixed cryoglobulinemia, depression, and type 2 diabetes mellitus (T2DM) (Younossi et al., 2016), apart from others such as cryoglobulinemic vasculitis, B cell non-Hodgkin lymphoma, arthralgia, immune thrombocytopenia, renal impairment, fatigue, cognitive impairment, cancer, and cardiovascular disorders (Cacoub et al., 2016).

Beyond the direct burden of HCV, other diseases, such as Parkinson's disease (Wijarnpreecha et al., 2018), behavioral and mental disorders due to psychoactive substance use (Khalsa et al., 2008), cardiovascular disorders (Petta, 2017), and non-hepatic malignancies (Balakrishnan et al., 2017), also impact the overall burden associated with CHC. A recent systematic review has shown that HCV-infected patients have approximately 35% higher risk of Parkinson's disease compared with patients

⁴⁰ This study is joint work with Michael R. Kraus, Henning Kleine, Marc Pignot, and Yuri Sanchez Gonzalez. See Kraus et al. (2018b) for a published version of this chapter.

without HCV (Wijarnpreecha et al., 2018), while substance abuse contributes to viral exposure due to usage of contaminated needles (Khalsa et al., 2008).

Complications resulting from HCV infection are associated with substantial healthcare costs (Nevens et al., 2012). Economic modeling showed that the cost of extrahepatic manifestations (EHM) in Germany was €1,247 per patient per year (PPPY), amounting to a total annual cost of €301.9 million (Cacoub et al., 2017). Moreover, treatment costs increase incrementally according to disease stage, with patients requiring liver transplants spending more than patients with mild disease (Nevens et al., 2012). To quickly reduce HCV progression, global treatment guidelines encourage the use of newer, all-oral, direct-acting antiviral (DAA) regimens for HCV treatment rather than interferon-based regimens because of the former's higher sustained virologic response (SVR) at >90%, shorter treatment duration, and better tolerability (World Health Organization, 2016). Based on model estimates, DAA regimens could provide substantial short- and long-term benefits to patients and reduce the overall economic burden of HCV on the healthcare system. However, there is limited evidence from actual clinical practice on the extent to which these benefits compare with the up-front costs of treatment (Van Nuys et al., 2015; Linthicum et al., 2016). A recent Japanese study reported that utilizing DAAs avoided approximately €8,968 in per-patient complication costs (Younossi et al., 2018). In India, too, DAA usage was tied to cost-savings for both non-cirrhotic (€446) and cirrhotic (€1,205) patients (Aggarwal et al., 2017). Moreover, after taking the SVR rate and treatment duration into consideration, the cost per SVR for DAAs was found to be cheaper than that of interferon-based regimens (Rosenthal and Graham, 2016).

HCV treatment has been shown to reduce both clinical (Mehta et al., 2017) and economic (Reau et al., 2017) EHM-related burden. A post-hoc analysis of phase 3 clinical trials revealed that DAA treatment improved multiple EHM biomarkers such as triglycerides (cardiovascular EHM biomarker), serum glucose (metabolic EHM biomarker), and the estimated glomerular filtration rate (renal EHM biomarker). Moreover, these effects lasted for at least a year post-treatment completion (Mehta et al., 2017). Economic analysis of a large US claims database showed that HCV treatment reduced EHM-related costs by \$12,773 (or approximately €10,295). Additionally, starting treatment at an early disease stage reduced EHM-related costs by \$10,409 (or approximately €8,389) (Reau et al., 2017).

The economic burden of CHC-related EHCs is not yet fully understood, given that most studies report on a limited number of EHCs (Solinis et al., 2016). Moreover, the economic impact of CHC-related EHCs in Germany has not been estimated in the literature. Therefore, the aim of this study was to utilize a comprehensive national database from the German *Betriebskrankenkasse* (BKK) sickness fund to assess the role of treatment in mitigating the economic burden of CHC, both hepatic and extrahepatic, especially at early (i.e., non-cirrhotic) stages of liver disease.

5.2 Methods

5.2.1 Data sources

The BKK sickness fund was originally meant for employees of a certain organization; however, since the 1990s, mergers between multiple funds and open enrollment for individuals have broadened the original conception of the BKK (Schut et al., 2003). As of 2012, reimbursement data from the BKK sickness fund cover 5.2 million persons and include patients' medical (i.e., in- and outpatient claims), prescription drug, and insurance eligibility information. Data from 2007 through 2014 were utilized for HCV-diagnosed patients. The BKK was informed about the project, and all the required approvals were obtained. Patient data were fully anonymized according to the accepted standard procedures.

5.2.2 Study definitions

Prevalent patients with CHC were identified using the International Classification of Diseases, 10th Edition German Modification (ICD-10-GM) code B18.2 in outpatient and/or inpatient care data in any of the quarters in the identification period (Q1/2008 through Q1/2014). Only patients with a diagnosis of CHC preceded and followed by at least four quarters of full insurance were considered for inclusion. For inpatient data, primary CHC discharge diagnoses as well as secondary diagnoses were checked. For outpatient data, only assured diagnoses (marked by "G" or "Z") were considered and also required evidence of a second diagnosis code within three quarters pre- or post-identification.⁴¹

⁴¹ G (abbreviation for "gesicherte Diagnose") = assured diagnosis; Z ("Zustand nach") = condition after.

5.2.3 Extrahepatic complications (EHCs)

EHCs included EHMs, which have a documented clinical pathway in CHC, as well as other conditions and behavioral factors that, although no clinical pathway has been established, are prevalent among the patient population. EHMs investigated in this study included the broader disease categories of T2DM, cardiovascular disease (CVD), fatigue, renal impairment, and malignancies. Other prevalent diseases observed in the patient population were mental and behavioral disorders (due to opioids, multiple drug use, and other psychoactive substances), Parkinson's disease, and some cardiovascular, renal, and other diseases not documented as EHMs. EHMs, behavioral factors, and other prevalent conditions in the population are jointly called EHCs in this study. The complete list of diseases within each grouping and their disease category, as well as their associated ICD-10-GM codes, is presented in Table 15.

Table 15: ICD-10-GM codes for extrahepatic complications

Condition category	ICD-10-GM	Label
<i>Extrahepatic manifestations</i>		
Type 2 diabetes	E11.*	Diabetes mellitus, type 2
	E14.*	Diabetes mellitus, not further specified
Cardiovascular disease	I20.*-I25.*	Ischemic heart diseases
	I60.*-I69.*	Cerebrovascular diseases
	I70.*	Atherosclerosis
Fatigue	F32.*	Episode of depression
	G93.3	Chronic fatigue syndrome
	R53	Indisposition and fatigue
	F43.0	Fatigue in the context of an acute stress reaction, e.g., combat fatigue
	F48.0	Neurasthenia
	Z73	Problems related to life management difficulty, including burnout (state of total exhaustion)
Renal impairment	N18.*	Chronic kidney disease
	N19.*	Renal failure, not further specified
	D89.1	Cryoglobulinemia
Malignancies	C85.*	Other and not further specified types of Non-Hodgkin-lymphoma
<i>Behavioral factors</i>		
Mental and behavioral disorders (due to opioids, or multiple and other psychoactive substances)	F11.*	Mental and behavioral disorders due to use of opioids
	F19.*	Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances
<i>Conditions that are prevalent in the population</i>		
Cardiovascular disease	I10.*-I15.*	Hypertension
	E78.*	Disorders of lipoprotein metabolism and other lipoproteins
Parkinson's disease	F02.3	Dementia with primary Parkinson's syndrome
	G20.*	Primary Parkinson's syndrome
	G21.*	Secondary Parkinson's syndrome
	G22	Parkinson's syndrome with elsewhere classified diseases
	G23.2	Multiple system atrophy of Parkinson type
Renal impairment	N17.*	Acute renal failure
Malignancies	C20	Malign neoplasm of rectum
	C22.*	Malign neoplasm of liver and intra-hepatic bile ducts
	C25.*	Malign neoplasm of pancreas
	C34.*	Malign neoplasm of bronchia and lung
	C64	Malign neoplasm of kidney, except from renal pelvis
	C65	Malign neoplasm of renal pelvis
Other	H52.*	Disorders of refraction and accommodation
	K29.*	Gastritis and duodenitis
	M54.*	Dorsalgia

The following sources were used for the preparation of Table 15: Cacoub et al., 2016; Cacoub et al., 2017; Cheng et al., 2014; Mohammed et al., 2010; Reau et al., 2017; Tengen et al., 2017. ICD-10-GM: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification.

5.2.4 Economic burden analyses

Medical cost definitions

Annualized total costs were assessed from the index quarter until the end of patient follow-up, which corresponded to the end of continuous insurance time, based on whether the patient died or switched to another health insurance, or the end of data availability on 31 December 2014. Therefore, while follow-up time may have differed in length across patients, annualizing the costs served to make patients' follow-up time comparable. To quantify (1) the benefits of treatment in reducing economic burden and (2) the benefits of early treatment, annual costs were compared between (1) time post CHC treatment and time without CHC treatment for patients with CHC and (2) CHC patients that initiated treatment 'early' (i.e., without cirrhosis) vs. 'late' (i.e., with cirrhosis).

The sum of all-cause medical and pharmacy costs is referred to as total cost. All-cause medical costs were further broken down into medical costs related to hepatic and extrahepatic complications. Pharmacy costs were split into CHC-related and non-CHC-related costs. CHC-related costs were defined as those associated with esophageal varices, spontaneous bacterial peritonitis, cirrhosis of the liver, hepatic encephalopathy (liver failure), portal hypertension, ascites, splenomegaly, hepatorenal syndrome, hepatocellular carcinoma, porphyria cutanea tarda, and liver transplantation. Costs attributable to CHC-related EHCs were identified using relevant German Uniform Assessment Standard (EBM) codes, Diagnosis Related Groups (DRG) codes, and Operation and Procedure (OPS) codes. EBM codes are relevant in the setting of medical practitioners, while DRG and OPS codes are relevant in the setting of hospitals (in- and outpatient care). In addition, claims from sickness benefits (medical leave benefits received by employees after 6 weeks of inability to work), which were based on relevant ICD-10-GM codes, were included in the EHC costs. Likewise, medical costs related to hepatic complications were identified by searching for relevant EBM, DRG, OPS, and ICD-10-GM codes associated with hepatic complications. Claims associated with both CHC-associated EHCs and hepatic complications were attributed to both categories. Total all-cause medical costs contain costs for practitioner, hospital in- and outpatient care, as well as sickness benefits. In addition to EHC-related or hepatic complication-related medical costs, all other costs that occur because of any disease were included in total all-cause medical costs. CHC-related pharmacy costs were identified for 12 CHC drugs, while all other pharmacy costs were summarized as

non-CHC-related pharmacy costs (Table 16). Costs were calculated as average annualized charged amounts and adjusted to reflect average 2016 euro exchange rates.

Table 16: German ATC codes and OPS codes for substances defined as CHC-related drugs

ATC code	OPS code	Substance
J05AE12	---	Boceprevir
J05AX14	6-008.d	Daclatasvir
L03AB**	8-812.1*/8-812.2*/8-547.2	Interferon
J05AX65	6-007.g (combined with Sofosbuvir)	Ledipasvir
J05AB04	---	Ribavirin
J05AE14	6-008.2	Simeprevir
J05AX15	6-007.g (combined with Ledipasvir)/6-008.3	Sofosbuvir
J05AE11	6-009.6	Telaprevir

ATC code: anatomical therapeutic chemical code; CHC: chronic hepatitis C;

OPS code: operation and procedure code.

Economic impact of CHC treatment

Treatment was identified by using relevant German Anatomical Therapeutic Chemical (ATC) classification and OPS codes (Table 16). Medical costs between treated and untreated time of patients newly diagnosed with CHC were compared using data from Q1/2008 to Q4/2014. The random quarter of CHC diagnosis between Q1/2008 to Q4/2014 served as the patients' identification/index quarter and anchored their 4-month lookback and follow-up. Medical costs for treated time were summarized from the quarter of treatment initiation until end of follow-up. Medical costs for untreated time were summarized from the quarter of diagnosis to the end of follow-up or initiation of treatment, whichever came first. Patients that initiated treatment after the quarter of diagnosis contributed data from diagnosis until treatment initiation to untreated time and data to treated time from treatment initiation until end of follow-up. Patients that initiated treatment in the same quarter of diagnosis contributed no data to untreated time while patients that never initiated treatment contributed no data to treated time.

Economic impact of early treatment

Medical costs for patients diagnosed with CHC who had received treatment were compared for whether treatment was initiated early or late. Comparison groups were created based on a four-quarter lookback from treatment initiation for evidence of cirrhosis. Patients without evidence of cirrhosis prior to treatment initiation were considered to have had early treatment, whereas those with evidence of cirrhosis prior to treatment initiation were considered to have had late treatment. Cirrhosis was identified using ICD-10-GM codes (K74.3–K74.6).

5.2.5 Statistical analysis

Mean cost differences estimated from unadjusted and adjusted ordinary least squares (OLS) regression models were used to compare the medical costs between all study cohorts. Models were adjusted for age (in years), gender, and the previous year's total healthcare costs. Additionally, cost models for treated vs. untreated and early vs. late treatment cohorts were adjusted for their index quarter year. The former comparison was also adjusted for presence of cirrhosis. Mean \pm standard deviation (SD), medians, and proportions were used to depict patient characteristics. Age, gender, and EHM type were independent variables, while the previous year's healthcare costs and current medical costs were dependent variables. All analyses were conducted using SAS version 9.4. Alpha of 0.05 was used as the cutoff for determining statistical significance.

5.2.6 Compliance with ethics guidelines

This article is based on previously available data and does not involve any new studies of human or animal subjects performed by any of the authors. However, appropriate approvals from the BKK were obtained to use their data for this study.

Similar data were used in a study assessing the clinical and economic burden of hepatic and EHCs associated with CHC in Germany (Kraus et al., 2018a). In that study, CHC was associated with a substantial burden (e.g., medical costs) largely due to hepatic complications and EHCs, subject to limitations similar to those of the present study (Kraus et al., 2018a).

5.3 Results

5.3.1 Patient characteristics

Of patients with CHC, 1,714 were identified as ever receiving treatment (61.4% male, average age 45.6 years (SD = 12.2)) and 7,124 were identified as ever being untreated (54.9% male, average age 52.6 years (SD = 16.8)). Among the treated patients, 1,552 received treatment early (61.5% male, average age 44.5 years (SD = 12.0)) and 162 received treatment late (60.5% male, average age 55.5 years (SD = 8.9), Table 17).

Table 17: Comparison of patient characteristics between study cohorts

Characteristics	Patients with newly diagnosed CHC		Treated patients with newly diagnosed CHC	
	Treated time (n = 1,714)	Untreated time (n = 7,124)	Early treatment cohort (n = 1,552)	Late treatment cohort (n = 162)
Age (years)				
	mean ± SD	45.6 ± 12.2	52.6 ± 16.8	44.5 ± 12.0
	[median]	[46]	[51]	[45]
Males	N (%)	1,052 (61.4%)	3,910 (54.9%)	954 (61.5%)
Previous year*s healthcare cost (euro)	mean ± SD	10,114 ± 40,915	6,719 ± 24,004	9,652 ± 41,122
	[median]	[3,309]	[2,038]	[3,246]
Previous year's healthcare cost (euro), per category	0	0	0	0
	1st quartile	922	600	897
	2nd quartile	3,309	2,038	3,246
	3rd quartile	12,455	6,373	12,378
	4th quartile	1,508,911	1,239,866	1,508,911
Index year	N (%)			
	2008	396 (23.1%)	3,191 (44.8%)	363 (23.4%)
	2009	278 (16.2%)	891 (12.5%)	261 (16.8%)
	2010	238 (13.9%)	758 (10.6%)	215 (13.9%)
	2011	295 (17.2%)	790 (11.1%)	274 (17.7%)
	2012	267 (15.6%)	722 (10.1%)	228 (14.7%)
	2013	175 (10.2%)	617 (8.7%)	160 (10.3%)
	2014	65 (3.8%)	155 (2.2%)	51 (3.3%)
				14 (8.6%)

CHC: Chronic hepatitis C virus infection; SD: standard deviation.

5.3.2 Association between treatment and economic burden

The economic burden from CHC-related hepatic complications and EHCs was reduced after initiating treatment. Annual medical costs related to hepatic complications (€1,384 vs. €1,022, adjusted difference €398) and EHCs (€3,573 vs. €2,287, adjusted difference €1,363) were significantly higher during the untreated time than the treated time ($P<0.01$ for all; Table 18). However, the average annual total costs (€15,843 vs. €8,206, adjusted difference -€2,125; $P = 0.01$) and non-HCV-related pharmacy costs (€7,174 vs. €2,243, adjusted difference €342; $P = 0.70$) were higher during the treated time. The €1,363 saved in EHC-related medical costs (adjusted cost difference between untreated and treated time) by patients in treatment was a major contributor to the all-cause medical cost savings observed (72.3%). However, both hepatic complication- (€3,761 vs. €779, adjusted difference €2,822) and EHC-related costs (€4,561 and €2,085, adjusted difference €2,255) were significantly higher for the late than the early treatment cohort ($P<0.01$ for both; Table 19). Savings due to EHC-related medical costs were again a major contributor to the savings from early treatment observed in all-cause medical (66.5%) and total (58.9%) adjusted cost differences.

Table 18: All-cause, hepatic complication-related, and extrahepatic complication-related annual costs for treated vs. untreated time

Cost category	Weighted mean costs (2016 euro) per patient per year of treated and untreated time			Adjusted cost difference [B] – [A] (95% CI) ^a
	Treated time [A] (n = 1,714) (mean ± SD)	Untreated time [B] (n = 7,124) (mean ± SD)	Mean cost difference between untreated and treated time [B] – [A] (95% CI)	
Total cost (all-cause medical + pharmacy)	15,842.5 ± 173,555.5	8,206.1 ± 47,770.1	-7,636.5* (-11,715.9; -3,557.0)	-2124.9# (-3,759.6; -490.2)
Total all-cause medical costs	4,243.9 ± 16,553.2	5,962.9 ± 22,398.3	1,719.0* (1,259.8; 2,178.2)	1,885.5* (1,339.1; 2,431.8)
Hepatic complication-related medical costs	1,022.2 ± 10,263.3	1,384.3 ± 10,870.8	362.1* (94.1; 630.1)	397.9* (199.1; 596.7)
Extrahepatic complication-related medical costs (any of the conditions listed below)	2,287.1 ± 12,015.6	3,572.9 ± 15,999.0	1,285.8* (954.1; 1,617.6)	1,363.2* (1,044.0; 1,682.5)
Type 2 diabetes	577.8 ± 6,357.2	1,134.8 ± 8,734.1	557.0* (379.8; 734.1)	409.1* (259.8; 558.4)
Cardiovascular disease	630.0 ± 7,592.2	1,191.7 ± 9,305.9	561.6* (356.7; 766.6)	442.5* (272.3; 612.6)
Parkinson's disease	380.0 ± 4,914.3	587.2 ± 5,216.9	207.2# (78.8; 335.6)	167.5* (55.2; 279.7)
Mental and behavioral disorders	777.1 ± 4,071.6	1,202.9 ± 7,030.6	425.8* (302.9; 548.8)	748.4* (620.9; 875.9)
Fatigue	524.3 ± 3,474.5	693.7 ± 4,869.8	169.5* (72.1; 266.9)	429.2* (326.9; 531.6)
Renal impairment	731.2 ± 8,428.8	1,178.3 ± 10,953.3	447.1* (215.9; 678.2)	322.6* (113.0; 532.1)
Malignancies	854.0 ± 7,735.8	1,236.2 ± 8,438.3	382.1* (178.9; 585.4)	299.1* (127.8; 470.5)
Other	554.5 ± 6,420.1	894.5 ± 7,398.2	340.0* (169.2; 510.7)	261.0* (129.1; 392.8)
All pharmacy costs				
CHC-related pharmacy costs	4,424.3 ± 10,319.9	---	---	---
Non-CHC-related pharmacy costs	7,174.3 ± 171,880.4	2,243.2 ± 36,162.2	-4931.1# (-8,957.0; -905.3)	341.9 (-1,390.7; 2,074.5)

CHC: chronic hepatitis C virus infection; CI: confidence interval; OLS: ordinary least squares; SD: standard deviation.

*P < 0.01, #P = 0.02.

^a Weighted OLS regression models to estimate adjusted mean cost difference between the treated and untreated follow-up time.

Table 19: All-cause, hepatic complication-related, and extrahepatic complication-related annual costs among patients in the early vs. late treatment cohorts

Cost category	Weighted mean costs (2016 euro) per patient per year of follow-up after treatment initiation				Adjusted cost difference [B]–[A] (95% CI) ^a	
	Early CHC treatment cohort [A] (n = 1,552) (mean ± SD)	Late CHC treatment cohort [B] (n = 162) (mean ± SD)	Mean cost difference between late and early treatment cohorts [B]–[A] (95% CI)			
Total cost (all-cause medical + pharmacy)	15,092.3 ± 181,540.5	24,295.7 ± 52,098.6	9,203.4** (3,066.0; 15,340.7)	3,831.1 (-3,036.0; 10,698.2)		
Total all-cause medical costs	3,931.4 ± 13,916.7	7,765.5 ± 31,641.6	3,834.1** (1,212.1; 6,456.2)	3,393.5** (1,318.6; 5,468.5)		
Hepatic complication-related medical costs	779.1 ± 6,678.7	3,760.8 ± 25,724.6	2,981.7** (861.4; 5,102.0)	2,821.8** (1,323.7; 4,319.9)		
Extrahepatic complication-related medical costs (any of the conditions listed below)	2,085.3 ± 11,023.2	4,560.8 ± 18,583.4	2,475.5** (925.3; 4,025.8)	2,255.4** (880.0; 3,630.8)		
Type 2 diabetes	508.1 ± 6,363.3	1,363.3 ± 6,124.9	855.3** (329.0; 1,381.5)	716.3* (169.3; 1,263.3)		
Cardiovascular disease	517.3 ± 6,498.4	1,900.6 ± 14,147.7	1,383.4# (210.1; 2,556.6)	1,233.7* (294.9; 2,172.5)		
Parkinson's disease	336.6 ± 4,305.9	869.8 ± 8,797.8	533.2 (-197.2; 1,263.7)	536.3 (-152.3; 1,224.9)		
Mental and behavioral disorders	775.8 ± 4,083.5	791.3 ± 3,968.3	15.5 (-325.2; 356.2)	331.8 (-67.1; 730.8)		
Fatigue	523.7 ± 3,478.7	530.0 ± 3,444.1	6.2 (-289.0; 301.5)	226.1 (-128.9; 581.1)		
Renal impairment	603.5 ± 7,508.1	2,170.6 ± 14,309.1	1,567.1* (377.3; 2,757.0)	1,297.8** (334.5; 2,261.0)		
Malignancies	705.9 ± 6,250.8	2,522.6 ± 15,793.4	1,816.7** (510.0; 3,123.4)	1,548.5** (480.7; 2,616.3)		
Other	417.5 ± 4,738.1	2,099.1 ± 14,593.0	1,681.6** (476.8; 2,886.4)	1,515.6** (566.2; 2,465.1)		
All pharmacy costs						
CHC-related pharmacy costs	4,276.9 ± 10,141.3	6,085.1 ± 11,471.7	1,808.2** (834.1; 2,782.2)	1,020.4* (246.8; 1,794.0)		
Non-CHC-related pharmacy costs	6,884.0 ± 180,187.6	10,445.1 ± 38,850.0	3,561.1 (-1,850.6; 8,972.8)	-582.8 (-7,719.0; 6,553.3)		

CHC: chronic hepatitis C virus infection; CI: confidence interval; OLS: ordinary least squares; SD: standard deviation.

P = 0.02, *P = 0.01, **P < 0.01.

^a Weighted OLS regression models to estimate adjusted mean cost difference between the early (i.e., without cirrhosis) and late (i.e., with cirrhosis) relative to the time of treatment initiation.

5.4 Discussion and limitations

Using German BKK sickness fund data, for the first time, the all-cause medical, pharmacy, hepatic complication- and EHC-related medical costs were compared between CHC patients' time of treatment and non-treatment as well as between CHC patients treated early and late. The results showed that CHC treatment may significantly mitigate the economic burden of hepatic and EHCs, especially if initiated early. The results concerning the economic burden associated with CHC's late treatment were consistent with recent evidence from the US (Reau et al., 2017).

CHC treatment saved €1,885 in all-cause medical costs per patient per year, mainly because of the reduced EHC-related medical costs (adjusted annual cost differences, €1,363), but average annual total costs and non-HCV related pharmacy costs were higher during the treated time. Moreover, early treatment of CHC could save €3,831 in total costs, which includes €3,394 of all-cause medical costs and €2,255 in EHC-related costs, compared with late treatment.

Benefits of CHC treatment can be experienced both clinically and economically. CHC treatment reduces the number of hepatocellular carcinoma and decompensated cirrhosis cases (Younossi et al., 2018), which results in economic savings. Furthermore, DAA treatment costs can be offset by the benefits incurred within a few years (Aggarwal et al., 2017; Reau et al., 2017). On the clinical side, some benefits of CHC treatment include seroconversion of anti-HCV, normalization of biologic enzymes, reduction of the risk of cirrhosis or even cirrhosis reversion, reduction of liver cancer progression, disappearance of sexual or perinatal transmission risk, improved quality of life, improvement of any EHM, and reduced risk of death (Marinho et al., 2014). Therefore, it makes sense to tackle CHC as early as possible. Sbarigia et al. (2017) studied the economic value of expanding the HCV treatment capacity in Germany and reported that increasing treatment capacity would reduce disease transmission and prevalence in addition to increasing quality-adjusted life years and net treatment savings.

Using a US claims database, Reau et al. (2017) demonstrated that EHMs contributed to the overall economic burden of HCV and its treatment. Of the EHMs assessed, kidney disease and CVD were the costliest EHMs across all comparisons (treated HCV vs. untreated HCV and early HCV treatment vs. late HCV treatment). The results observed in our study are comparable to Reau et al.'s US study, with the share of the all-cause medical costs attributable to EHCs being 72.3% for treated vs. untreated time

and 66.5% for early vs. late HCV treatment. It should also be noted that economic modeling may not always reflect real-life conditions, such as the evidence observed in the current study. In this study, early treatment was associated with savings of €3,831 for total costs, with €2,255 saved in EHC-related medical costs alone. Economic modeling in the Spanish (Buti et al., 2016) and Italian (Marcellusi et al., 2016) settings have echoed similar conclusions.

The strength of our study is the inclusion of a broad range of EHCs, including some that have not been studied extensively (e.g., mental disorders, gastric disorders), which enabled us to understand the clinical and economic burden of CHC in Germany. EHC is a broader term than EHM because the former only encompasses conditions that have a documented clinical pathway to CHC, while the latter also includes conditions that are prevalent among the patient population but are not yet shown to be related to CHC. Analyzing pharmacy cost data separately from the medical expenditure is another advantage of this study. In fact, the observed higher total cost for CHC treatment compared with non-treatment is attributable to CHC-related pharmacy costs, which by definition the latter cohort did not have.

The limitations of the current study must be kept in mind while interpreting the results. The BKK data only represent ~8% of all people within the statutory health insurance system. Residual confounding may persist despite covariate adjustment in the analyses. Patients could be misclassified because of misinterpretation of the EBM, DRG, OPS, and ICD-10-GM codes. CHC is a chronic disease; hence, a possibility of lag between infection and diagnosis cannot be excluded. Some EHC categories such as cardiovascular disorders and renal impairment are comprised of both EHMs documented in the literature and other conditions that are prevalent in this population. The medical costs were measured as charged amounts, not paid amounts, which may result in overestimation of the actual cost. However, this is likely to affect all the cohorts equally. In addition, a single medical claim could be associated with multiple procedure codes, resulting in the same medical cost being counted under multiple EHM categories. However, these costs were only included once while performing summation. Also, not all EHCs were included in the analysis, and those included were grouped together – this could affect the respective cost analyses. Moreover, data are used from a large span of time (2007–2014), which introduces a high level of heterogeneity regarding patient characteristics and treatment options, making interpretation of the data and results more difficult. However, the results are robust to

show that costs incurred during CHC treatment are less than when CHC is not being treated for all costs considered in this study. In addition, the analyses included CHC treatments available between 2007 and 2014, but there has been a rapid evolution in the treatment landscape since. Finally, the comparisons between patients receiving early vs. late treatment should be interpreted with caution as those receiving late treatment could include patients with end-stage liver disease, a life-threatening complication of CHC resulting in significant medical costs.

5.5 Conclusion

The current study findings reveal that not treating CHC or delaying treatment to advanced stages of liver disease may result in additional expenditures, mainly due to EHC-related complications. This burden suggests that an unmet economic need exists for timely initiation of treatment. The results observed in this study may help guide clinical decision making for the improvement of care for patients with CHC, which in turn could lead to significant cost savings for payers and the healthcare system.

6. Sickness Absence and Unemployment Revisited⁴²

6.1 Introduction

Sickness absence is costly. Even in the case of no sick pay, sickness absence leads to considerable output losses (see, e.g., Koopmanschap et al., 1995). These costs are aggravated by the fact that sickness absence tends to be procyclical (see for instance Leigh, 1985; Johansson and Palme, 1996, for early studies on this topic). Thus, in times when there is a higher labor demand due to a booming economy (Audas and Goddard, 2001), sickness absence is usually higher than during recessions.

So far the literature has evolved around two main explanations for this procyclical pattern. The first explanation is based on a selection of healthier workers into the labor force during recessions, while in boom times employment increases and workers with worse health find employment as well. Another (complementary) explanation is due to changing incentives over the business cycle.⁴³ For instance Leigh (1985) suggests the fear of job loss during recessions might lead to going to work sick – commonly referred as presenteeism – and lower sickness absence.⁴⁴ On the other hand, presenteeism in combination with a contagious disease can also lead to increased sickness absence due to associated infections, as shown for instance by Pichler and Ziebarth (2017).

In this paper, we analyze these incentives in more detail. In particular, the incentives faced by workers differ, depending on their job stability and likelihood of unemployment. For instance, within the SOEP dataset, a representative panel data set on German households, between 1999 and 2009 more than 50% of respondents thought that their probability of job loss is 10% or lower (SOEPGroup, 2013). Therefore, we will analyze two subgroups of individuals based on their job mobility in order to evaluate how changing incentives over the business cycle affect their sickness absence behavior. We focus on job mobility because economic research has shown that job mobility is determined mostly by worker heterogeneity and firm specific human capital (Farber, 1999; Topel, 1991). In particular, we hypothesize the following

⁴² This study is joint work with Stefan Pichler. See Pichler and Thönnes (2019) for a published version of this chapter.

⁴³ Many health variables are found to change over the business cycle. Ruhm (2000) and Miller et al. (2009) find changing mortality rates over the business cycle and Davies et al. (2009) analyzes occupational injuries. Finally, Schaller (2016) looks at fertility.

⁴⁴ This explanation is related to unemployment being a disciplining device as suggested by Shapiro and Stiglitz (1984).

relationship between job mobility and fear of unemployment: Workers who fear unemployment will prefer a stable work situation and thus move less. Moreover, workers who acquire firm specific capital will tend to move less and thus exhibit a larger fear of unemployment.

Moreover, how incentives are reflected in sickness absence strongly depends on the disease group. For contagious diseases Pichler (2015) suggests that the procyclical relationship is largely driven by infections and not by the fear of job loss. Another reason why the disease matters is that for small health shocks sickness absence is a choice while for larger health shocks sickness absence is (almost) unavoidable. In order to take this heterogeneity into account we will look at business cycle effects of different causes for sickness absence.

Throughout the paper we will largely disregard the selection issue mentioned above for two reasons. Firstly, incentives are easier to change in order to counteract procyclical sickness absence, while selection reflects the general level of health of the workforce. Thus, selection is less interesting from a policy perspective. Moreover, different articles suggest that incentives play a more important role in explaining procyclical sickness absence as compared to selection (Arai and Thoursie, 2005; Askildsen et al., 2005; Nordberg and Røed, 2009).

With respect to incentives, there is some degree of heterogeneity throughout the workforce. For instance, marginal workers and workers with mainly firm specific human capital rightly fear that sickness absence will lead to job loss (as for instance confirmed by Scoppa and Vuri, 2014). This will result in more sickness absence and shirking during booms, when the risk of job loss is lower, and more presenteeism during recessions. However, as argued by Pichler (2015), income opportunities change as well over the business cycle. For instance, labor demand tends to be higher during booms (Audas and Goddard, 2001). Therefore, more career-oriented workers have incentives to engage in presenteeism during booms in order to be present when needed most and thereby increase their probability of promotion. Moreover, workers who advanced in their career and have many responsibilities might find it hard to be on sick leave when they are needed. In this paper we will look at individual level data, in order to analyze the heterogeneous incentives faced by individuals and examine how these incentives aggregate to the overall procyclical variation of sickness absence.

Other papers that analyze how sickness absence changes due to (external) changes of opportunity costs are Goerke and Pannenberg (2015), Johansson and Palme (2005), Puhani and Sonderhof (2010), and Ziebarth and Karlsson (2010). Ziebarth and Karlsson (2010) and Puhani and Sonderhof (2010) find that German employees reduced sickness absence significantly after a cut in sick pay. Goerke and Pannenberg (2015) look at the same law change but find smaller effects for union members. Moreover, Johansson and Palme (2005) find evidence for lower sickness absence after a sick pay cut in Sweden. Furthermore, Ichino and Riphahn (2005) and Olsson (2009) find that as employment protection decreases sickness absence decreases as well. In particular, Ichino and Riphahn (2005) find that sickness absence is lower during probation than during regular employment. Olsson (2009) looks at a law change in Sweden that exempts workers from the seniority rule which also led to lower sickness absence. Finally, Røed and Fevang (2007) find that after downsizing sickness absence increases significantly. In this paper we do not look at incentives that change due to a particular regulation, but rather at changing incentives over the business cycle.

Finally, this is the first paper to look at detailed health diagnoses in combination with individual level data in order to analyze how the heterogeneous incentives are reflected in differing sickness absence. Looking at the diagnoses is important for several reasons. Firstly, Pichler and Ziebarth (2017) in a recent paper show that the sickness absence effects due to lower sick pay strongly differ by the cause for sickness absence. In their paper Pichler and Ziebarth (2017) suggest that the differences arise due to increased presenteeism and infections after the sick pay cut. For contagious diseases workers create negative externalities for coworkers. Secondly, for large negative health shocks the incentives might not translate into lower sickness absence, because the opportunity costs of sick leave are too large. Thus, different causes for sickness absence can help to understand the mechanisms at work. Furthermore, Adda (2016) shows that economic activity has a direct influence on the spread of diseases. Thus, it is important to separate these dynamics from sickness absence behavior due to non-contagious diseases.

In the theoretical model discussed in this paper we distinguish two kinds of workers: workers with procyclical income opportunities who have incentives to reduce their sickness absence during booms due to career incentives and increased labor demand. The second group of workers have countercyclical income opportunities and have incentives to reduce their sickness absence in recessions due to fear of unemployment.

Moreover, depending on the distribution of the disease in terms of severity more severe diseases are less elastic. Finally, infections vary over the business cycle as well, providing additional dynamics.

In the empirical part of the paper we estimate these patterns by forming subgroups both in terms of diseases and workers. In particular, we cannot reject the hypothesis that diseases associated with a longer sickness absence, and thus related to larger health shocks, have no cyclical variation. For short diseases we distinguish between contagious and non-contagious diseases. Our results show that contagious diseases seem to drive procyclical sickness absence. Finally, analyzing worker heterogeneity we find that among workers who do not change jobs sickness absence due to non-contagious diseases is procyclical, most likely due to fear of job loss. For workers that are found to change jobs sickness absence due to non-contagious diseases is countercyclical. In line with our model this last finding suggests that these workers have additional income opportunities during booms and therefore the opportunity cost of sickness absence during booms is higher.

Our paper is structured as follows. In the next section, we provide a short theoretical model. In Section 6.3, we briefly introduce the German health care system and describe the data and the empirical specification. The results are presented and discussed in Section 6.4. Section 6.5 concludes.

6.2 A model of sickness absence with moral hazard and infections

Our model builds upon standard leisure work models (cf. Barmby et al., 1994; Brown, 1994) used in the sickness absence literature. The individual utility u at time t is a function of consumption c and leisure l and reads as

$$U_t = (1 - \sigma_t)c_t + \sigma_t l_t, \text{ with } \sigma_t \in [0,1]. \quad (4)$$

The relative weights attributed to consumption and leisure depend on the current health status σ_t . Higher values of σ represent a higher degree of sickness. Thus, when the person is very sick, leisure used for recuperation has a higher utility, while when in good health consumption becomes more important.

Assuming that workers spend all their wage income w the utility when working becomes

$$U_t^{work} = (1 - \sigma_t)w_t + \sigma_t(T - h), \quad (5)$$

with T denoting total time available and h representing the contracted working time. Similarly, for individuals on sick leave the utility function reads

$$U_t^{absent} = (1 - \sigma_t)s + \sigma_t T, \quad (6)$$

where s stands for sick pay, which we assume to be fixed over time. The worker will then compare these utilities and decide when to go to work and when to stay at home. At $\sigma^*(w_t)$ the worker is indifferent between these two options:

$$\sigma^*(w_t) = \frac{(w_t - s)}{(w_t - s) + h}. \quad (7)$$

Thus, if $\sigma_t < \sigma^*$ workers will work, while they will be on sick leave otherwise. Moreover, we assume that $w_t - s \geq 0$, otherwise there would be no incentives to work even for perfectly healthy workers with no leisure preferences ($\sigma_t = 0$).

Finally, we assume that there is an exogenous level $\tilde{\sigma}$, which determines the degree of sickness where sickness absence becomes “acceptable”.⁴⁵ More in particular, $\tilde{\sigma}$ determines shirking and presenteeism: Absent workers with $\sigma_t < \tilde{\sigma}$ are shirking, while present workers with $\sigma_t > \tilde{\sigma}$ engage in presenteeism. All other workers are either “rightly” absent or present.

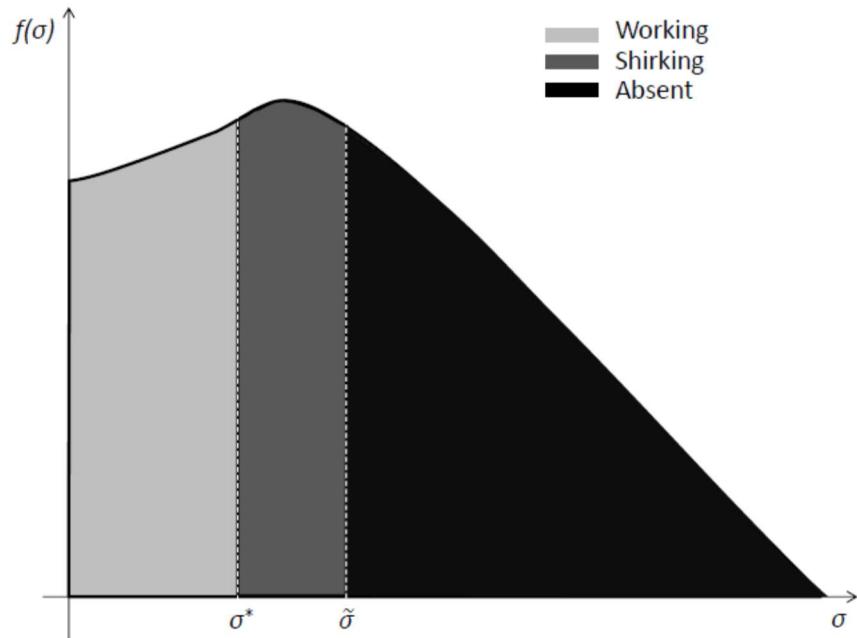
This relationship is illustrated in Figure 7. On the extremes we have either healthy individuals who are working or sick individuals who are absent. However, the relationship between σ^* and $\tilde{\sigma}$ determines whether we are in a shirking or presenteeism regime. In particular, if the indifference point σ^* is to the left of the acceptable sickness level $\tilde{\sigma}$ as depicted in Panel A, there will be a share of workers who are absent given their incentives and sickness level, but should work from a society point of view. We

⁴⁵ This acceptable level for sickness absence might for instance result from the maximization problem of the firm or the social welfare, which are not explicitly modeled in our context.

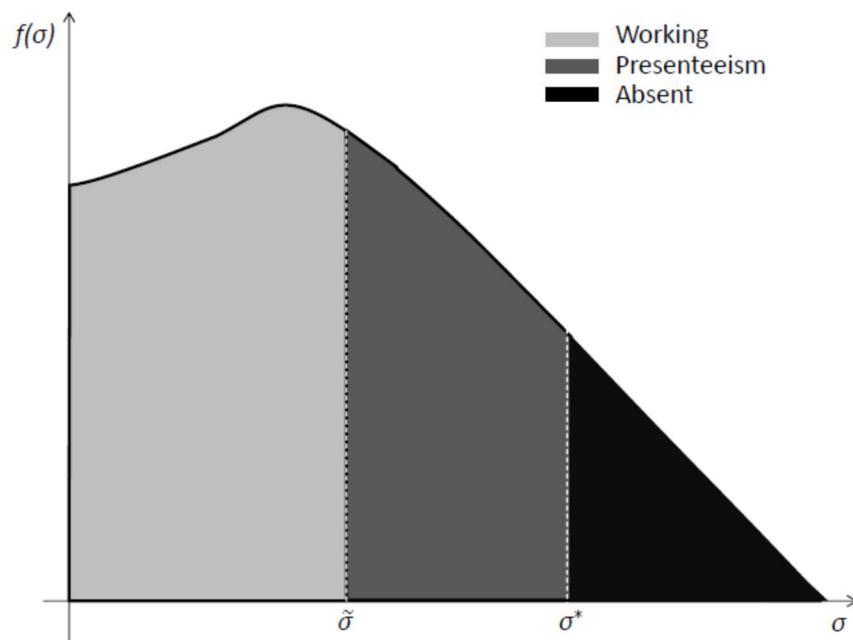
refer to this behavior as shirking. To the contrary, if σ^* is to the right of the acceptable sickness level $\tilde{\sigma}$ (Panel B), we have workers who are present, even though they should be at home. This latter situation is commonly described as presenteeism.

Figure 7: Presence, absence, shirking, and presenteeism

Panel A: Presence, absence, and shirking



Panel B: Presence, absence, and presenteeism



The two graphs show the density of sickness σ for two situations that differ by individual and time specific indifference point σ^* . In the first graph, the acceptable disease level $\tilde{\sigma}$ is above the indifference point, which leads to shirking. For the second graph, the contrary is true and thus some workers engage in presenteeism.

6.2.1 Income opportunities in booms and recessions

To this basic model we add different incentives over the business cycle. In particular, let the variable $u_t \in \{\underline{u}, \bar{u}\}$ represent the unemployment rate in the economy, with $u_t = \bar{u}$ representing a high unemployment rate and therefore a recession, and $u_t = \underline{u}$ representing a boom. We assume that the current state of the economy will affect income opportunities of individuals and thereby affect the opportunity costs of working and sick leave.

The effect of the current state of the economy on workers is worker specific. In particular, we distinguish two types of workers. Firstly, during booms income opportunities might increase. There are several reasons such as (i) more overtime possibilities due to increased production (Hamermesh, 1996), (ii) incentive contracts and better sales opportunities leading to higher bonuses, (iii) more meetings and deadlines during booms, (iv) specialized tasks and an overall higher workload during booms, and (v) an overall higher labor demand leading to more pressure by the employer (Audas and Goddard, 2001). We refer to workers with these income dynamics as individuals with procyclical income opportunities $\frac{\partial w}{\partial u} < 0$.

Since workers are heterogeneous we also have a share of workers with countercyclical income opportunities $\frac{\partial w}{\partial u} > 0$. The reason usually brought forward in the literature is fear of job loss. For this group of workers, income opportunities in recessions are higher, because they can reduce the likelihood of job loss by avoiding sickness absence. Thus, wages w do not only include wages today, but are also related to future income which is directly affected by job loss. In terms of the business cycle, the risk of job loss becomes more eminent during a recession and since sick leave is associated with higher dismissal probabilities (see, for instance, Scoppa and Vuri, 2014), workers with countercyclical income opportunities will try to avoid sick leave in order to avoid job loss and increase their future income opportunities.

Due to $\frac{\partial \sigma^*}{\partial w} > 0$ and a fixed acceptable level of sickness $\tilde{\sigma}$, the following hypothesis directly follows:

Hypothesis 1: *Individuals with procyclical income opportunities ($\frac{\partial w}{\partial u} < 0$) will increase their indifference point σ^* during booms, which, depending on the acceptable level of sickness $\tilde{\sigma}$, will lead to more presenteeism and/or less shirking.*

Moreover, workers with countercyclical income opportunities $\frac{\partial w}{\partial u} > 0$ will increase shirking and/or reduce presenteeism during booms.

6.2.2 Different diseases

Finally, we follow Pichler and Ziebarth (2017) and consider different diseases. Firstly, a fraction $1 - q - p_t$ of workers will be healthy $\sigma_t = 0$ at any point in time. Moreover, a share of q workers will be sick due to a non-contagious disease $\sigma_t = \sigma_n$. Finally, p_t workers will be sick due to a contagious disease $\sigma_t = \sigma_c$. This last share p_t is time varying, and depends upon infections in the previous period. The severity of the disease follows from the densities $f_n(\sigma_n)$ and $f_c(\sigma_c)$. Finally, we allow the “acceptable” sickness level $\tilde{\sigma}$ to vary by disease group. In particular, contagious diseases lead to externalities through infections and, thus, we assume that the societal costs are higher and the resulting level of acceptable sickness for sickness absence is smaller for contagious diseases ($\tilde{\sigma}_n > \tilde{\sigma}_c$). This implies more presenteeism (less shirking) for contagious diseases.

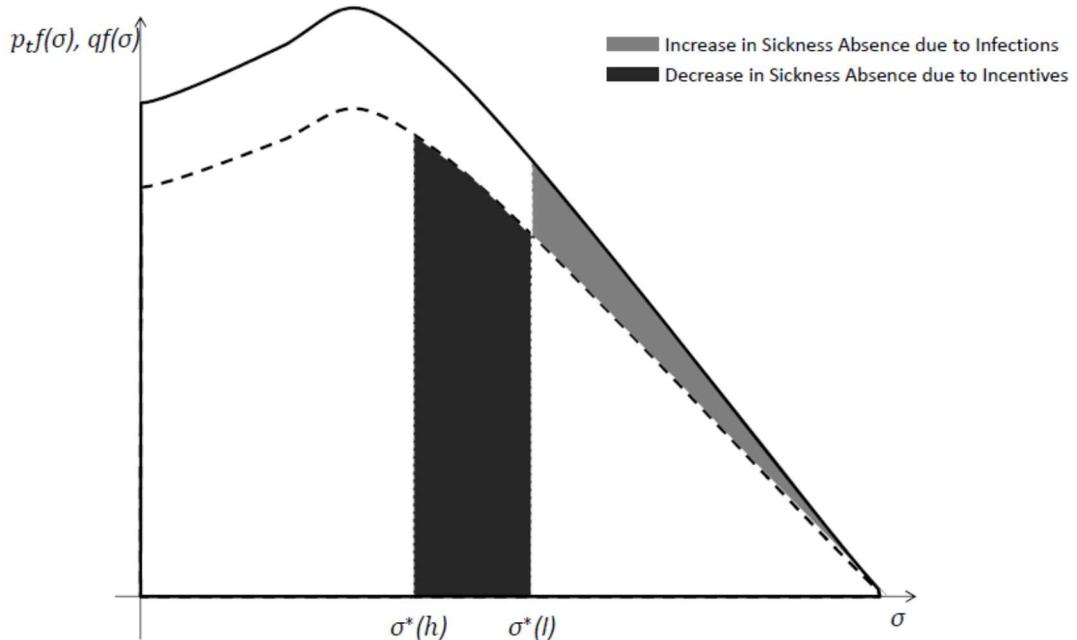
While we do not model infections explicitly, following a standard SIS (susceptible-infected-susceptible) endemic model – based on Ross (1916) and Kermack and McKendrick (1927) – the share of individuals with a contagious disease can be approximated by a multiplicative combination of the share of susceptibles (healthy individuals present at work), the infected (contagious individuals present at work), and the infection rate. As discussed above, individuals with procyclical income opportunities increase their presence during booms, leading to an increase in the share of susceptibles and the share of infected. Contrarily, individuals with countercyclical income opportunities decrease their presence. Depending on the size of the two groups infections might spread countercyclically or procyclically. What prevails might differ from workplace to workplace and from sample to sample and is thus an empirical question.

6.2.3 Combining disease characteristics with individual incentives

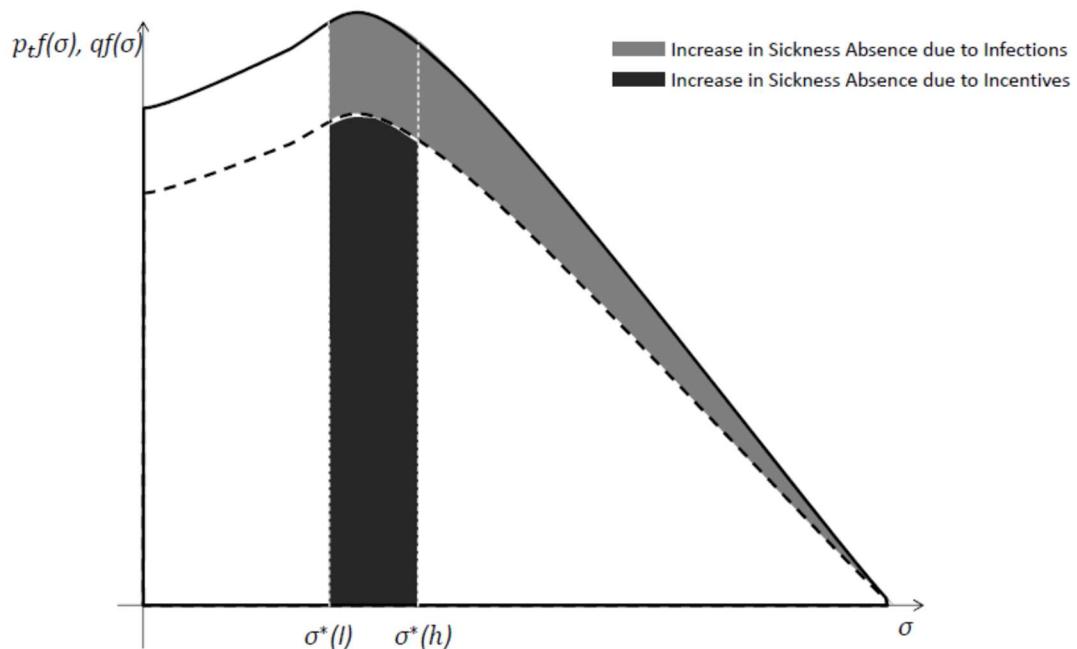
The consequences for the overall labor market are highlighted in Figure 8 below.

Figure 8: Sick leave effects

Panel A: Sick leave effects for individuals with procyclical income opportunities



Panel B: Sick leave effects for individuals with countercyclical income opportunities



The two graphs show the density of sickness σ for booms (solid lines) and recessions (dashed lines) for infectious diseases. During booms, the probability of drawing an infectious disease p_t increases, which is represented by an increase in the overall density. The density for non-infectious diseases is represented by the dashed lines and does not change over the business cycle. σ^* represents the individual indifference point. For $\sigma > \sigma^*$, individuals are absent, while they are present otherwise. The shaded areas represent the difference in absence between booms ($u_t = l$) and recessions ($u_t = h$).

Over the course of a business cycle, sickness absence due contagious diseases is affected in two distinct ways. Firstly, income opportunities change, which leads to a shift of the individual indifference point σ^* , while the acceptable disease level $\tilde{\sigma}$ is unchanged. Given Hypothesis 1, going from a recession to a boom will lead to an increase (decrease) in σ^* for individuals with procyclical (countercyclical) income opportunities, leading to more (less) presenteeism and/or less (more) shirking – depending on the acceptable disease level $\tilde{\sigma}$.

Furthermore, the share of individuals with contagious diseases changes over the business cycle. Thus, when looking at the changes in sickness absence for contagious diseases, we see a combination of changing incentives and changing infections over the business cycle. For non-contagious diseases, on the other hand, the share of individuals with a disease q is not time varying. Thus, what we observe in the data only reflects changing incentives over the business cycle.

This results in four combinations: Individuals with procyclical and countercyclical sickness absence, and sickness absence due to contagious and non-contagious diseases. The sickness absence behavior of these four groups is summarized in the following hypothesis:

Hypothesis 2: *The behavior of sickness absence over the business cycle depends both on worker characteristics and sickness characteristics. In particular, denoting with A_c and A_n the sickness absence due to contagious and non-contagious diseases, the following list summarizes all possible combinations:*

- (a) *Individuals with procyclical income opportunities will increase their sickness absence for non-contagious diseases during recessions due to higher work incentives, i.e., if $\frac{\partial w}{\partial u} < 0$ then $\frac{\partial A_n}{\partial u} > 0$.*
- (b) *The change in sickness absence due to contagious diseases for individuals with procyclical income opportunities is unclear. If incentive effects are large enough there will be a positive relationship as well. However, if infections are procyclical, the additional infections might outweigh incentive effects during booms, i.e., if $\frac{\partial w}{\partial u} < 0$ then $\frac{\partial A_c}{\partial u} \leq 0$.*
- (c) *Individuals with countercyclical income opportunities will decrease their sickness absence for non-contagious diseases during recessions due to lower work incentives, i.e., if $\frac{\partial w}{\partial u} > 0$ then $\frac{\partial A_n}{\partial u} < 0$.*

(d) *The change in sickness absence due to contagious diseases for individuals with countercyclical income opportunities is unclear. If incentive effects are large enough there will be a negative relationship as well. However, if infections are countercyclical, the additional infections might outweigh incentive effects during booms, i.e., if $\frac{\partial w}{\partial u} > 0$ then $\frac{\partial A_c}{\partial u} \leq 0$.*

In the empirical model that follows, we will distinguish between workers with procyclical and countercyclical income opportunities by looking at their job mobility. This is inspired by economic research of Farber (1999) and Topel (1991).

Farber (1999) suggests that job mobility is mainly a function of worker heterogeneity and firm specific human capital. In terms of worker heterogeneity, it is easy to imagine that individuals with a higher fear of unemployment prefer job stability and thus will change jobs less frequently. Individuals with large firm specific capital usually get a wage premium as shown already in early research by Topel (1991). Therefore, also these workers are less mobile and have a larger fear of unemployment, if for instance their firm faces difficulties due to a recession.

6.3 Institutional settings and data

6.3.1 The German sick pay scheme and monitoring system

The health insurance system in Germany is organized in public and private funds. In the total population about 90% are with state funded insurance providers, while the remaining 10% are with private providers, which are reserved for public servants, self-employed, and employees with an income above 46,350 € in 2004 (the exact income needed is adjusted by average yearly salary growth). At the beginning of 2015, there were 124 sickness funds in Germany (German Federal Ministry of Health, 2015). The public system is financed by a premium that is paid as a share of the salary. Moreover, employees are free in their choice of funds. Sickness funds offer a very similar package which is regulated by law at the federal level (Buchner and Wasem, 2003). Nevertheless, the funds compete by offering different prices, even though switching rates are rather low (Schmitz and Ziebarth, 2017).

Sick pay in Germany is very generous. In the case of sickness, sick pay equals 100% of previous wage for six weeks. Payments are made directly by the employer during this

interval. After these six weeks, the replacement rate is reduced to 70% and insurance funds step in.

Employees who are sick have to notify their employer and have to provide a doctor's certificate starting from day 4, or earlier if asked by the employer. Thus, doctors act as gatekeepers and monitor workers. However, most sickness absence is certified by the family doctor and therefore a personal relationship might change the incentives to act as gatekeepers. For instance, Markussen et al. (2013) show for Norway that changing the family doctor has a significant influence on individual sickness absence.

The medical service of the sickness health insurance provides additional monitoring. This institution employs doctors who examine absence spells. Employers and/or sickness funds may ask for assistance from the medical service if doubts on sickness absences arise. Such doubts may occur due to excessive sickness absence from particular employees or an increased frequency of certified sickness spells from the same doctor. In 2012, about 2,000 full-time equivalent and independent doctors worked for the medical service and examined 1.5 million cases of absenteeism (Medical Review Board of the Statutory Health Insurance Funds, 2014).

6.3.2 Data from sickness fund

Our data is based on administrative data on certified sickness absence spells. These spells are recorded by the sickness insurance providers.

Our data comes from one company insurance fund (BKK) and contains individual data on a total of 178,967 sick fund enrollees. The data ranges from 2005 to mid-2011. Before we look at the data in more detail, we compare our sample of individuals to data from other insurance funds in order to identify a potential selection in Table 20.

Table 20: Sickness absence in percent by sickness fund

	2005	2006	2007	2008	2009	2010	2011
All public sickness funds	3.32	3.31	3.22	3.37	3.40	3.69	3.86
Regional sickness funds (AOK)	3.30	3.55	3.61	3.73	3.66	3.96	4.06
Company-based sickness funds (BKK)	3.23	2.93	2.88	3.02	3.01	3.28	3.54
Our sample	2.25	2.29	2.21	2.38	2.45	2.57	2.24

This table shows the annual average of the percentage of employees who are sick on the first day of each month. In the first row we present the overall statistics for Germany. The second and third row show the average for regional sickness fund members and company-based sickness fund members, respectively. Finally, in the last row follows the same statistics from our sample.

Data Source: Federal Health Monitoring, 2019 – Quota of inability to work of obligatory members of the statutory health insurance and own calculations.

Table 20 shows that our sample is on average healthier as compared to overall sickness absence. Also comparing the data to overall regional sickness funds and company sickness funds, we observe a lower frequency of sickness absence in our sample. In order to partly take care of this selection, we use the profession specific unemployment rate (instead of the overall unemployment rate) in order to capture the movement of the business cycle.

Since we focus on working age individuals, we exclude enrollees aged below 16 and above 65. Moreover, we restrict our sample to working individuals, i.e., we drop unemployed individuals from our sample as their sickness absence behavior might differ from working individuals.

Our main outcome variable is sickness absence, which is available on a daily basis, for all diseases lasting 4 days or more (for shorter diseases our dataset is incomplete as the doctor's certificate is not mandatory). We aggregate this daily sickness absence to quarterly data, in order to merge the data with quarterly unemployment data provided by Institute for Employment Research (IAB) (2012). Overall we have 25 quarters in our sample, which runs from the second quarter of 2005 to mid-2011. Moreover, all sickness absences exhibit the medical cause for sickness absence based on the International Statistical Classification of Diseases, 10th Revision, German Modification (ICD-10-GM). This data is merged with administrative information that individuals are required to provide to their insurance fund. This data includes information on gender, age, profession, and the establishment identification number where individuals are working. Since one major focus of our analysis is infections at the workplace, we focus on firms where we have more than one worker per establishment in our data.

Table 21: Summary statistics

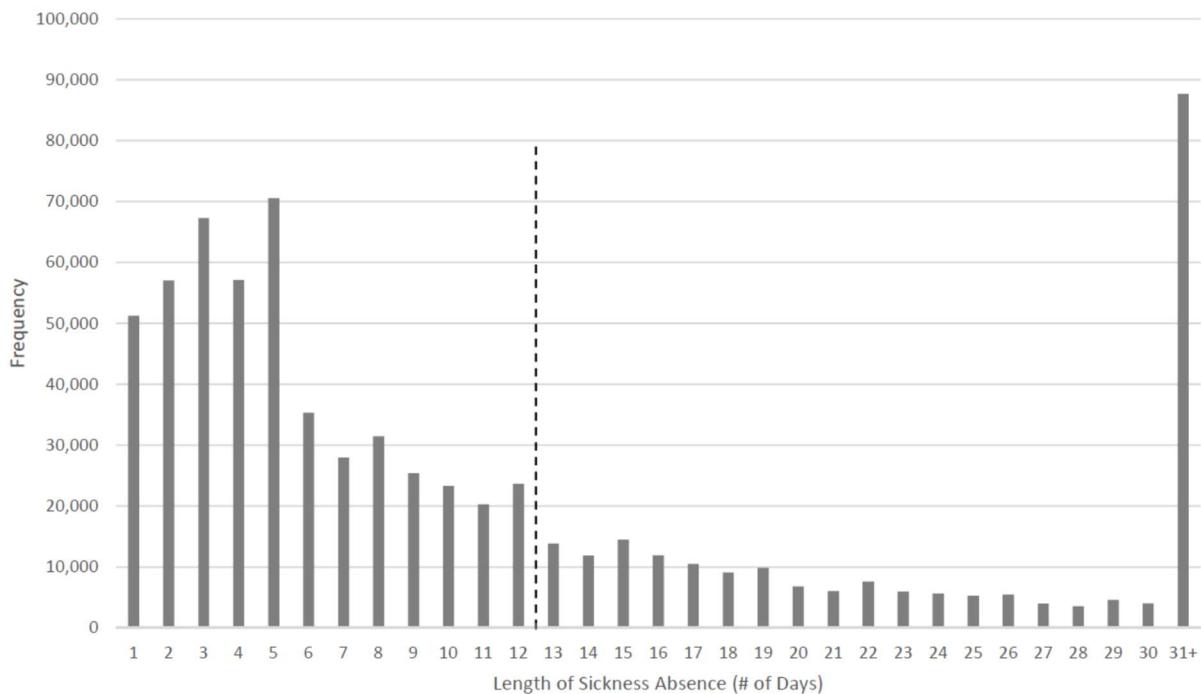
Variable	Mean	SD	N
Sickness absence days	3.788	11.836	2,768,303
Sickness absence days long (> 12 days)	2.857	11.816	2,768,303
Sickness absence days short (≤ 12 days)	0.931	2.409	2,768,303
Sickness absence short (contagious)	0.408	1.605	2,768,303
Sickness absence short (non-contagious)	0.534	1.896	2,768,303
Unemployment rate (UE)	0.099	0.083	2,768,303
Male	0.599	0.490	2,768,303
Male*Age16-29	0.132	0.339	2,768,303
Male*Age30-49	0.355	0.478	2,768,303
Male*Age50-65	0.112	0.316	2,768,303
Female*Age16-29	0.106	0.308	2,768,303
Female*Age30-49	0.228	0.420	2,768,303
Female*Age50-65	0.067	0.250	2,768,303
Changers	0.186	0.389	2,768,303

This table shows the summary statistics for the variables used in our regression. The first five form our dependent variables: overall sickness absence days, followed by sickness absence days separated in long sickness absences > 12 days and short sickness absences ≤ 12 days. Finally, we split short sickness absences into absences due to contagious and non-contagious diseases. Our main explanatory variable is the profession specific unemployment rate (UE). Finally, we have a set of dummy variables on socioeconomic controls, such as gender, age and whether or not the person changed jobs over the observation period.

Table 21 shows the summary statistics. In total, we have 2.75 million observations which come from roughly 179,000 individuals that are observed over 25 quarters. Individuals who change sickness fund or who are unemployed drop out of our sample, which is the main reason for having an unbalanced panel.

On average, individuals are on sick leave around four days per quarter. In Figure 9 we present the frequency of various lengths of sickness absences. We observe positive sick days for about one quarter of the 2.75 million observations. This equates to one sickness absence per person per year. However, the length of these absences can be quite different, as seen in the figure.

Figure 9: Distribution of sickness absences



This graph shows the distribution of sickness absences. Roughly one fourth of the data points of our dependent variable shows some sickness absence. The graph shows how these sickness absences are distributed in terms of number of days. The graph also shows the cutoff at 12 days, which we use for dividing short and long sickness absences.

Most sickness absences last for 5 days and after 12 days we experience a sharp drop by more than 40%. This is where we set the cutoff in terms of short and long sickness days. For short sickness absences, lasting 12 days or less, there is much more variation and thus the individual has potentially more influence whether to go on sick leave or not. For longer sickness absences, on the other hand, sick leave is almost unavoidable and, thus, incentives should play only a minor role. We also provide robustness checks with respect to this cutoff below. Finally, Figure 9 shows an extremely long tail as often observed for many health variables.

Long sickness absences are much less frequent. However, due to their length they account for more of overall sickness absence as compared to short ones. Around 75% of sick days are due to long term sicknesses. Finally, about half of short term sickness absences are due to non-contagious diseases. Table A 10 (in the appendix) lists all diseases which we categorize as contagious based on their ICD-10-GM code.

Our main explanatory variable is the lagged profession specific unemployment rate, which is close to 10% on average. We use the lag for mainly two reasons. Firstly, it is hard to imagine that the average unemployment rate over a full quarter influences

sickness absence, especially during the first weeks of the quarter, when it is not yet clear how the remaining quarter will evolve. Secondly, using the lagged unemployment rate avoids endogeneity due to reverse causality.

We also control for a set of binary socioeconomic variables. Firstly, we observe the gender of the enrollee. In terms of age, we have about 23% below 30, and 18% above 50. Furthermore, the Table 21 indicates that around 60% of our sample are men, and also within each age group around 60% are male. Finally, we group individuals by whether they were changing jobs over the observation period. This is the case for roughly one fifth of the sample. This is in line with official statistics. Following a study by Nisic and Trübswetter (2012) from the German Institute of Employment Research (IAB), about 3.4% of the workforce change their employer every year. Given that our data spans over 7 years, the observed 20% seems roughly in line with this statistic. Finally, looking at the reason for such job changes, individuals in the SOEP answered that the most common cause for job changes and terminations is own resignation (SOEPGroup, 2013).

Table 22: Descriptive statistics: Most frequent ICD-10-GM codes

Panel A: Sickness absence				
	ICD-10-GM code	Number of cases	Average duration	Sickness absence days
J06	Acute upper respiratory infections	73,478	6.44	0.17
M54	Dorsalgia (back pain)	68,694	14.95	0.37
K52	Other non-infective gastroenteritis and colitis	31,737	5.08	0.06
K08	Disorders of teeth and supporting structures	31,363	2.41	0.03
J20	Acute bronchitis	30,658	7.87	0.09
			Total	0.71
Panel B: Long sickness absences (> 12 days)				
	ICD-10-GM code	Number of cases	Average duration	Sickness absence days
M54	Dorsalgia (back pain)	20,549	37.06	0.28
J06	Acute upper respiratory infections	5,399	23.84	0.05
F32	Depressive episode	4,893	71.29	0.13
M23	Internal derangement of knee	3,883	43.14	0.06
T14	Injury of unspecified body region	3,804	37.28	0.05
			Total	0.56
Panel C: Short sickness absences (≤ 12 days)				
	ICD-10-GM code	Number of cases	Average duration	Sickness absence days
J06	Acute upper respiratory infections	68,079	5.06	0.12
M54	Dorsalgia (back pain)	48,145	5.52	0.10
K08	Disorders of teeth and supporting structures	31,093	2.23	0.03
K52	Other non-infective gastroenteritis and colitis	30,324	3.87	0.04
J20	Acute bronchitis	26,887	5.67	0.06
			Total	0.34
Panel D: Short contagious diseases				
	ICD-10-GM code	Number of cases	Average duration	Sickness absence days
J06	Acute upper respiratory infections	68,079	5.06	0.12
J20	Acute bronchitis	26,887	5.67	0.06
A09	Other gastroenteritis and colitis	26,230	3.86	0.04
J40	Bronchitis, not specified as acute or chronic	21,787	5.62	0.04
B34	Viral infection of unspecified site	15,265	4.89	0.03
			Total	0.29
Panel E: Short non-contagious diseases				
	ICD-10-GM code	Number of cases	Average duration	Sickness absence days
M54	Dorsalgia (back pain)	48,145	5.52	0.10
K08	Disorders of teeth and supporting structures	31,093	2.23	0.03
K52	Other non-infective gastroenteritis and colitis	30,324	3.87	0.04
K29	Gastritis and duodenitis	11,513	3.94	0.02
T14	Injury of unspecified body region	9,626	5.51	0.02
			Total	0.20

This table shows the most frequent causes for overall sickness absence and for subgroups based on causes of sickness absence used in the regressions below. For each cause, we present the number of sickness absence spells, the average duration per spell in days, and the number of sickness absence days per quarter.

Table 22 presents the most common medical causes for sickness absence in our sample. Over the 25 quarters we observe 73,478 sickness spells starting due to upper respiratory infections (J06). These last for 6.44 days on average. In terms of our quarterly measure of absence days, upper respiratory infections account for 0.17 days per quarter out of a total absence days of 3.788 (first variable in Table 21). Back pain (M54) is the cause for slightly fewer sickness spells started (68,694), but they last longer on average (almost 15 days) and thus account for 0.37 sickness absence days per quarter. Overall, the five most common causes account for one fifth of total sickness absence.

For our analysis we split these sickness absences into long sickness absences lasting for more than 12 days and short sickness absences. In terms of differing incentives, we expect individuals to have more control over short term sickness absences, while for long sickness absences the opportunity costs of no sick leave are too high and, thus, individuals are on sick leave, independently of the incentives provided by the business cycle.⁴⁶ The cause for sickness absence seems to be in line with this reasoning as well. Long sickness absences are caused mostly by severe back pain leading to sickness absences of more than a month on average, depressions lasting more than two months, and knee problems and injuries both leading to sickness absences of over one month on average. For short sickness absences, on the other hand, we have respiratory infections and back pain, both lasting for five days on average, as the most common medical causes for sickness absence.

Finally, we split short term sickness absences into sickness absences due to contagious and non-contagious diseases. We do this because the business cycle directly affects the spread of diseases, as shown by Adda (2016).

6.3.3 Empirical model

We estimate the following model for the 25 quarters starting from April 2005 to June 2011:

$$y_{ipt} = \alpha_i + \beta UR_{p,t-1} + \delta_t + u_{ipt} \quad (8)$$

where y_{ipt} represents the number of days worker i , working in industry p , is on sick leave during quarter t . Since the dependent variable only takes on integer values, we

⁴⁶ We present robustness checks with respect to the exact split into long and short sickness absences below.

will estimate both a linear model and a count data model. The variables a_i and δ_t are individual and time fixed effects. In terms of time, we only include year and quarter dummies and no interactions for a more parsimonious model. However, in the appendix we also provide the results when we include a full set of quarter dummies. Finally, the variable $UR_{p,t-1}$ represents the lagged profession specific unemployment rate. Standard errors will be clustered at the level of the unemployment rate which corresponds to the “treatment” variable within our setting.

Finally, with regards to endogeneity, reverse causality should be limited as we employ the unemployment rate of the previous quarter.

6.4 Results

6.4.1 Overall results

Table 23 looks at overall absence days in the first two columns. In the first column we present the results of a standard fixed effects model, while in the second column we estimate a count data model with fixed effects. The constant for the fixed effects regression in the first column shows the average fixed effect. This average fixed effect suggests that each individual had slightly more than 3 absence days on average. Moreover, sickness absence seems to be increasing over time and the first quarter usually has the highest level of sickness absence.

In the next two columns we only look at absence days that last longer than 12 days. In terms of average absences and absence length this captures two thirds of all absence days. In columns (5) and (6) we look at short absences representing the remaining third. Finally, in the last four columns we split up short absences into short absences due to contagious diseases ((7) and (8)) and short absences due to non-contagious diseases ((9) and (10)) both representing roughly half of all short absences.

Table 23: Regression results

	All diseases		Absence > 12 days		Absence ≤ 12 days		Short contagious		Short non-contagious											
	(1)		(2)		(3)		(4)		(5)		(6)		(7)		(8)		(9)		(10)	
	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count						
Unemployment	-0.594 (0.515)	0.087 (0.119)	-0.469 (0.528)	0.143 (0.156)	-0.124** (0.059)	-0.057 (0.051)	-0.103** (0.040)	-0.198** (0.078)	-0.050 (0.042)	-0.064 (0.062)										
Year 2006	0.281*** (0.034)	0.090*** (0.009)	0.317*** (0.035)	0.132*** (0.012)	-0.036*** (0.004)	-0.036*** (0.005)	-0.041*** (0.003)	-0.094*** (0.008)	0.004 (0.004)	0.007 (0.008)										
Year 2007	0.663*** (0.063)	0.202*** (0.014)	0.650*** (0.062)	0.263*** (0.018)	0.013* (0.007)	0.020*** (0.008)	0.003 (0.004)	0.023** (0.010)	0.012** (0.005)	0.023** (0.010)										
Year 2008	0.930*** (0.068)	0.275*** (0.017)	0.896*** (0.068)	0.353*** (0.022)	0.034*** (0.007)	0.042*** (0.008)	0.020*** (0.004)	0.065*** (0.010)	0.015*** (0.006)	0.029*** (0.011)										
Year 2009	1.362*** (0.079)	0.378*** (0.021)	1.344*** (0.079)	0.495*** (0.027)	0.017 (0.013)	0.024* (0.015)	0.041*** (0.006)	0.109*** (0.015)	-0.014 (0.009)	-0.026 (0.017)										
Year 2010	1.514*** (0.085)	0.418*** (0.020)	1.494*** (0.089)	0.547*** (0.028)	0.020** (0.009)	0.027*** (0.010)	0.001 (0.005)	0.019 (0.013)	0.028*** (0.006)	0.053*** (0.012)										
Year 2011	1.800*** (0.106)	0.486*** (0.026)	1.747*** (0.106)	0.628*** (0.035)	0.052*** (0.008)	0.057*** (0.010)	0.038*** (0.005)	0.093*** (0.013)	0.029*** (0.007)	0.053*** (0.014)										
Q2	-0.680*** (0.029)	-0.175*** (0.010)	-0.317*** (0.024)	-0.111*** (0.008)	-0.363*** (0.011)	-0.374*** (0.013)	-0.374*** (0.008)	-0.868*** (0.010)	-0.008 (0.005)	-0.014 (0.010)										
Q3	-0.635*** (0.037)	-0.162*** (0.013)	-0.283*** (0.028)	-0.096*** (0.011)	-0.353*** (0.011)	-0.363*** (0.013)	-0.379*** (0.009)	-0.896*** (0.012)	0.008 (0.006)	0.015 (0.011)										
Q4	-0.154*** (0.032)	-0.033*** (0.008)	-0.007 (0.026)	0.001 (0.009)	-0.147*** (0.008)	-0.132*** (0.007)	-0.146*** (0.005)	-0.249*** (0.008)	-0.008** (0.004)	-0.015** (0.007)										
Constant	3.387*** (0.089)		2.231*** (0.090)		1.156*** (0.010)		0.645*** (0.008)		0.532*** (0.006)											
Observations	2,768,303	2,377,726	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,667,414	2,768,303	2,183,843										
Persons	178,967	132,809	178,967	77,220	178,967	123,864	178,967	87,970	178,967	118,014										

This table presents the regression results with five different dependent variables: The first two columns show the results for overall sickness absence days per quarter as the dependent variable. The second two columns exhibit the results with sickness absence days lasting for more

than 12 days, while columns (5) and (6) are short term absences. Finally, in the last four columns we split short term diseases into contagious and non-contagious diseases. For each dependent variable we estimate a standard fixed effects model and a count data fixed effects model. The number of observations is smaller for the count data model as only individuals exhibiting variation over time are taken into consideration by the estimator. The second row presents standard errors clustered at the profession level. The stars represent significance at the following p-values: * $p \leq 0.10$, ** $p \leq 0.05$, *** $p \leq 0.01$.

In terms of number of observations, the fixed effects regression uses all observations, while the count data model uses only observations that have variation over the dependent variable. Thus, in terms of variation we observe a higher variation in the short term absences as there are more observations included in the count data model in column (6) as compared to column (4).

Our explanatory variable of interest is the lagged unemployment rate. Looking at all sickness absences independent of the cause we find no significant relationship between sickness absence and the unemployment rate after controlling for year and quarter fixed effects in the first two columns. Moreover, the two point estimates show opposite signs.

Long absences are driven by bad health and, thus, the unemployment rate should have little or no influence. The results are in line with this prediction. Finally, for short absences both columns show the sign commonly observed in the literature: a higher unemployment rate leads to lower sickness absence. In column (5) this result is highly significant, while using the count data model in column (6) we get the same sign, but no significant result. Since this classification of long and short term absences is somewhat arbitrary we present results for alternative classifications in Table A 11 (in the appendix). In all models in the appendix we find differing signs and no significant results for the relationship between the unemployment rate and long term sickness absences. For short term sickness absences, on the other hand, the sign is always negative. Finally, only the short sickness absences due to contagious diseases show a significant relationship with the unemployment rate.

Columns (7) and (8) suggest that the negative overall relationship for short term absences is driven by contagious diseases: the point estimates are negative and significant. This result implies that sickness absence due to contagious diseases is higher (lower) when the unemployment rate is low (high). This relationship is similar to the finding in Pichler (2015), who also finds that the negative relationship between sickness absence and unemployment is mainly due to contagious diseases. A potential explanation was given in the theoretical section of this paper: Employees come to work because of a high work load in times of low unemployment and infect other individuals, leading to an overall higher sickness absence due to contagious diseases.

In terms of effect size, the estimated coefficient in column (7) suggests that an increase in the profession specific unemployment rate by one standard deviation will decrease short term sickness absence due to contagious diseases by 0.01 days. Column (8), on the other hand, estimates a count data model and, thus, the interpretation is slightly different. In particular, the point estimate implies that an increase in the profession specific unemployment rate by one standard deviation will decrease sickness absence by 1.6%. Finally, the results for non-contagious diseases are inconclusive, as they are negative but insignificant.

A more robust version of the main results table may be found in Table A 12 (in the appendix). In this table we include all 24 quarter dummies. The results are hardly affected by this change.

6.4.2 Results depending on job mobility

So far, we only calculated results for the overall sample and did not include any individual characteristics except for the profession specific unemployment rate and individual fixed effects. In what follows we will look at two subsamples in order to analyze whether the incentives faced differ among them.

The first group is represented by individuals who change jobs at least once over the observation period (about 20% of our sample), while individuals who never change jobs fall into the second category. As stated earlier, the main cause for job change is own resignation. Moreover, economic research has shown that worker heterogeneity and firm specific human capital are the main determinants for job mobility (Farber, 1999; Topel, 1991). Thus, it is likely that the incentives between these two groups differ.

Table 24: Regression results for job changers and stayers

		Absence ≤ 12 days		Short contagious		Short non-contagious	
		(1) FE model	(2) FE count	(3) FE model	(4) FE count	(5) FE model	(6) FE count
Changers	Unemployment	-0.047 (0.105)	0.003 (0.076)	-0.226*** (0.062)	-0.506*** (0.120)	0.165** (0.073)	0.322*** (0.098)
	Constant	1.112*** (0.025)		0.659*** (0.014)		0.470*** (0.016)	
	Observations	516,021	401,951	516,021	294,834	516,021	346,806
	Persons	38,997	25,041	38,997	17,475	38,997	20,700
	Stayers	-0.156** (0.069)	-0.082 (0.063)	-0.063 (0.046)	-0.097 (0.085)	-0.127*** (0.048)	-0.185** (0.074)
	Constant	1.168*** (0.010)		0.642*** (0.008)		0.549*** (0.008)	
		Observations	2,252,282	1,858,511	2,252,282	1,372,580	2,252,282
		Persons	139,970	98,823	139,970	70,495	139,970
							84,550

This table presents the regression results with three different dependent variables: The first two columns show the results short term absences, while the last four columns split short term diseases into contagious and noncontagious diseases. For each dependent variable we estimate a standard fixed effects model and a count data fixed effects model. The number of observations is smaller for the count data model as only individuals exhibiting variation over time are taken into consideration by the estimator. Each group of 6 rows represents estimation results from a different subsample of the overall population including the same time dummies as in the previous table. Time dummies are omitted for a more convenient representation. The second row presents standard errors clustered at the profession level. The stars represent significance at the following p values: * $p \leq 0.10$, ** $p \leq 0.05$, *** $p \leq 0.01$.

Table 24 shows the results for these two subgroups. The constant reveals that sickness absence in general is very similar across these two groups and also the split between contagious and noncontagious diseases is quite similar. In terms of the relationship with the business cycle, however, the two groups behave very differently. For individuals who switch jobs we find a significant and positive relationship for non-contagious diseases. Following the implications of our model this suggests that in this group we have many individuals with procyclical income opportunities or career concerns. Moreover, when it comes to contagious diseases we observe a significant and negative relationship for this group that in line with our model can be explained by infections leading to more sickness absence during booms.

For individuals who do not change jobs, on the other hand, we observe a significant and negative relationship for non-contagious diseases. This pattern is in line with fear of job loss. Finally, for contagious diseases we find no significant relationship.

6.5 Conclusion

Sickness absence is related to the business cycle. This paper has identified two important channels of this relationship: different incentives of workers and different dynamics of contagious diseases over the business cycle.

Our theoretical model analyzes how incentives of individuals vary over the business cycle and how infections are affected by behavior of individuals. Our empirical results reveal that, in line with our predictions, workers who change jobs exhibit countercyclical sickness absence due to non-contagious diseases, i.e., sick leave due to non-contagious diseases is higher during recessions. On the other hand, workers who stay with the same employer exhibit procyclical sickness absence due to non-contagious diseases.

Our theoretical model explains this behavior by better income opportunities during booms for the first group. Because of higher labor demand during booms this is good news. However, this group is also responsible for an increased spread of contagious diseases during booms. Our results show that for individuals who change jobs sickness absence due to contagious diseases is procyclical. Overall short term sickness absence, which is the combination of contagious and non-contagious sickness absence, is unaffected by the business cycle for this group.

The procyclical sickness absence due to non-contagious diseases for individuals who stay with the same employer can be explained by fear of job loss in recessions leading to less sickness absence due to non-contagious diseases.

Finally, the analysis of all workers in our sample shows that overall procyclical sickness absence is driven by sickness absence due to contagious diseases.

Thus, firms who want to reduce procyclical sickness absence should incentivize workers to be absent when they are subject to a contagious disease. In particular, our results suggest that contagious diseases spread mainly during booms and, thus, workers need to be aware that even in times of high work pressure due to booms going to work sick is not desirable, especially when faced with a contagious disease.

6.6 Appendix

Table A 10: List of contagious diseases based on ICD-10-GM codes

Chapter	Disease categories
Chapter I - Certain infectious and parasitic diseases (A00-B99)	all
Chapter X - Diseases of the respiratory system (J00-J99)	Acute upper respiratory infections (J00-J06)
Chapter X - Diseases of the respiratory system (J00-J99)	Influenza and pneumonia (J09-J18)
Chapter X - Diseases of the respiratory system (J00-J99)	Other acute lower respiratory infections (J20-J22)
Chapter X - Diseases of the respiratory system (J00-J99)	Chronic rhinitis, nasopharyngitis and pharyngitis (J31)
Chapter X - Diseases of the respiratory system (J00-J99)	Other diseases of upper respiratory tract (J39)
Chapter X - Diseases of the respiratory system (J00-J99)	Bronchitis, not specified as acute or chronic (J40)
Chapter X - Diseases of the respiratory system (J00-J99)	Simple and mucopurulent chronic bronchitis (J41)
Chapter X - Diseases of the respiratory system (J00-J99)	Unspecified chronic bronchitis (J42)
Chapter X - Diseases of the respiratory system (J00-J99)	Other chronic obstructive pulmonary disease (J44)
Chapter X - Diseases of the respiratory system (J00-J99)	Pneumoconiosis associated with tuberculosis (J65)
Chapter X - Diseases of the respiratory system (J00-J99)	Pyothorax (J86)

This table shows all the diseases that were categorized as contagious. All others were categorized as non-contagious.

Table A 11: Alternative grouping of long and short sickness absences

Panel A: Threshold at 10 days

	Absence > 10 days		Absence ≤ 10 days		Short contagious		Short non-contagious	
	(1) FE model		(3) FE model		(5) FE model		(7) FE model	
	(2) FE count	FE count	FE model	FE count	FE model	FE count	FE model	FE count
Unemployment	-0.522 (0.525)	0.129 (0.145)	-0.072 (0.056)	-0.044 (0.061)	-0.061* (0.035)	-0.163** (0.076)	-0.025 (0.040)	-0.046 (0.079)
Observations	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,621,110	2,768,303	1,931,807
Persons	178,967	77,220	178,967	123,864	178,967	85,369	178,967	101,426

Panel B: Threshold at 11 days

	Absence > 11 days		Absence ≤ 11 days		Short contagious		Short non-contagious	
	(1) FE model		(3) FE model		(5) FE model		(7) FE model	
	(2) FE count	FE count	FE model	FE count	FE model	FE count	FE model	FE count
Unemployment	-0.526 (0.526)	0.127 (0.150)	-0.067 (0.055)	-0.020 (0.055)	-0.080** (0.040)	-0.185** (0.081)	-0.022 (0.038)	-0.030 (0.070)
Observations	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,642,118	2,768,303	1,961,411
Persons	178,967	77,220	178,967	123,864	178,967	86,565	178,967	103,225

Panel C: Threshold at 13 days

	Absence > 13 days		Absence ≤ 13 days		Short contagious		Short non-contagious	
	(1) FE model		(3) FE model		(5) FE model		(7) FE model	
	(2) FE count	FE count	FE model	FE count	FE model	FE count	FE model	FE count
Unemployment	-0.420 (0.529)	0.160 (0.157)	-0.174*** (0.066)	-0.093* (0.056)	-0.120*** (0.044)	-0.222** (0.087)	-0.087* (0.047)	-0.115* (0.066)
Observations	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,678,395	27,68,303	2,010,525
Persons	178,967	77,220	178,967	123,864	178,967	88,566	178,967	106,258

Panel D: Threshold at 14 days

	Absence > 14 days		Absence ≤ 14 days		Short contagious		Short non-contagious	
	(1) FE model		(3) FE model		(5) FE model		(7) FE model	
	(2) FE count	FE count	FE model	FE count	FE model	FE count	FE model	FE count
Unemployment	-0.436 (0.532)	0.155 (0.162)	-0.158** (0.071)	-0.064 (0.055)	-0.136*** (0.047)	-0.252*** (0.088)	-0.056 (0.054)	-0.052 (0.067)
Observations	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,685,252	2,768,303	2,024,079
Persons	178,967	77,220	178,967	123,864	178,967	88,946	178,967	107,099

This table shows the results for alternative classifications into short and long term sickness absence spells. Results are directly comparable to columns (3)-(10) of Table 23.

Table A 12: Regression results including all quarterly dummies

	All diseases		Absence > 12 days		Absence \leq 12 days		Short contagious		Short non-contagious	
	(1)		(3)		(5)		(7)		(9)	
	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count	FE model	FE count
Unemployment	-0.817 (0.533)	0.033 (0.125)	-0.691 (0.546)	0.073 (0.164)	-0.126** (0.060)	-0.060 (0.054)	-0.097** (0.039)	-0.227*** (0.078)	-0.056 (0.043)	-0.074 (0.065)
Constant	4.507*** (0.084)		2.231*** (0.090)		1.156*** (0.010)		0.645*** (0.008)		0.532*** (0.006)	
Observations	2,768,303	2,377,726	2,768,303	1,506,807	2,768,303	2,260,462	2,768,303	1,667,414	2,768,303	2,183,843
Persons	178,967	132,809	178,967	77,220	178,967	123,864	178,967	87,970	178,967	118,014

This table presents the regression results with all 24 time dummies. In Table 23 we included only year and quarter dummies. Here, we only use the variation of the unemployment rate over different professions for identification. As in Table 23, the first two columns show the results for overall sickness absence days per quarter as the dependent variable. The second two columns exhibit the results with sickness absence days lasting for more than 12 days, while columns (5) and (6) are short term absences. Finally, in the last four columns we split short term diseases into contagious and non-contagious diseases. For each dependent variable we estimate a standard fixed effects model and a count data fixed effects model. The number of observations is smaller for the count data model as only individuals exhibiting variation over time are taken into consideration by the estimator. The second row presents standard errors clustered at the profession level. The stars represent significance at the following p values: * $p \leq 0.10$, ** $p \leq 0.05$, *** $p \leq 0.01$.

7. Conclusion

This thesis intended to find possibilities on how to mitigate the rise of contributions to the SHI. Contributions rise, amongst others, due to increasing health care expenditures. As pointed out in the introduction section, health care expenditures increase due to demographic change (which cannot be influenced in the short or medium term), technological progress (which is of utmost importance for society), as well as inefficiencies. In the studies of this thesis, several sources of inefficiency were examined. The studies search for channels to improve efficiency which includes that the same outcome can be achieved with less budget, or that a better outcome can be achieved using the same budget. The first point relates to reducing direct or indirect costs and is examined in Chapters 2, 4, 5, and 6. The latter point relates to preventing (avoidable) diseases or complications and is examined in Chapter 4 as well. Chapter 3 provides an analysis that serves as a basis for efficiency. To be concrete, it estimates the number of prevalent and incident patients which is important for decision makers to be able to allocate resources in an efficient way.

The results of the studies show that there are indeed inefficiencies in the health care sector that could be decreased. For example, in Chapter 2, participating in the premium refund tariff is associated with a lower probability of visiting a doctor, a lower probability of treating a minor ailment such as a common cold, as well as with reduced costs at the practitioner. Unfortunately, only a relatively small share of all insured individuals chooses such a tariff. Since the SHI is based on the principle of mutual solidarity (National Association of Statutory Health Insurance Funds, 2019), from a social perspective, individuals in worse health should not pay higher contributions, which would actually be the case: individuals under continuous treatment do not have a chance of receiving the premium refund. However, at the moment, the premium refund tariff is rarely advertised by the sickness funds. If more insureds were encouraged to participate in the tariff voluntarily, the efficiency gains found in the study could be realized in a bigger dimension.

In Chapters 4 and 5 it also shows that treating a systemic disease can decrease costs, the earlier the better. Given that we identified 1,552 HCV patients that received treatment early and only 162 HCV patients that received treatment late, doctors already seem to have noticed the advantages of an early treatment start. However, the number of patients under treated time is far lower than the number of patients under

no treatment (1,714 vs. 7,124). This finding is alarming because it indicates that only a small number of diagnosed patients receives treatment at all. To improve the study's credibility, it would be beneficial to find out why so many patients remain untreated. For example, it is imaginable that the disease was already cured and the patient was only diagnosed because of periodic follow-up care to exclude a re-infection (Robert Koch Institute, 2019). Unfortunately, we would need additional data to conduct further research on this topic (see below).

Finally, Chapter 6 finds that during economic booms especially employees with procyclical earnings opportunities are at risk of going to work although they are affected by some infectious disease. When doing so, they infect colleagues at work and as a consequence, all in all, more employees are on sickness absence as if the sick employees would have stayed at home to cure the disease. Through this channel, it comes to indirect costs for the employer, namely, to output losses. Although for sickness absences shorter than six weeks, the sickness fund does not have to pay sickness benefits, from an economic perspective it would be efficient to encourage employees suffering from an infectious disease to stay at home.

To sum up, in this thesis several channels on how the health care sector can be made more efficient were highlighted. Anyway, further research is needed because there are still many other sources of inefficiency and because the tools for researchers to study this field need to be further improved. To start with, although sickness fund data contain a variety of variables, they also lack important information on the insured individuals. For example, there is no information on health behavior like drinking, smoking, or doing sports. Neither is there information on attitudes or opinions nor on test results from the laboratory. It would be a major improvement if billing data of sickness funds were complemented with data that are asked from the doctor or hospital or from the insured individuals themselves. However, there are four difficulties: First, individuals that are insured with one sickness fund visit a high multitude of different doctors and hospital departments. For organizational reasons, it is not possible to collect data on the insured at so many different service providers. Instead, it would be a solution to select only some doctors and restrict analyses to those individuals that are insured with the sickness fund(s) in our data and that additionally visit the selected doctors. Second, answering questionnaires for research purposes is time-consuming for service providers and they will not be willing to spend much time on this without getting remunerated. As a consequence, this way of data collection is costly. Third, if

insured individuals are asked for personal information for research purposes by mail, the rate of return will be low. On the other hand, conducting personal interviews with the insureds will be very costly. Finally, understandably, sickness funds are concerned with data protection. Although it would be technically feasible to merge anonymized billing data with anonymized additional data collected from doctors, hospitals, or the insured, data protection specialists from sickness funds frequently do not allow this. Therefore, it would be beneficial for the whole research community if standard procedures were developed on how billing data can be extended by additional information needed for study purposes. One important step on this way can be to demonstrate sickness funds why research using sickness fund data is also beneficial for them, and why extending the available data is important in order to achieve unbiased results. For each single project, researchers should demonstrate which information is needed, and why. This can help gain understanding and acceptance from data protection specialists.

This additional information would be important in all studies in this thesis. In Chapter 2, it would be helpful to know about the insureds' health related behavior and their attitudes towards risk. Although being participant in a bonus program controls for some of the variation in risk aversion, it is only a dichotomous measure, and an ordinal or a continuous measure would improve credibility of the study. It would be a further improvement of the study if individual fixed effects were added to the regression to control for residual unobserved heterogeneity. This had been tested but could not be implemented due to low intra-individual variation in the treatment status. There were too few participants of the premium refund tariff in 2010 that did not take part in earlier years. Using data from other sickness funds may provide more variation and enable fixed effects regression. Another way could be to use instrumental variables, but it is hard to find instruments for participation in the premium refund tariff that are both relevant and exogenous.

Chapters 3 to 5 have in common that it is difficult to differentiate acute from chronic hepatitis C in the data. Although an acute HCV infection should be coded as chronic after six months, in practice it is frequently coded as acute for a longer time (Tomeczkowski and Cornberg, 2015). In addition, because HCV infection is often undiagnosed for a long time, it is difficult to decide whether an infection is actually new or only newly diagnosed. This makes it hard to differentiate incident from prevalent patients. However, also blood test results would not help much because only in the very

first two months of an acute infection it is possible to differentiate acute from chronic HCV infection by monitoring of viral RNA (ribonucleic acid) and antibodies (Robert Koch Institute, 2019). From the third month onwards, blood test results would not help differentiate acute from chronic hepatitis C. Yet, blood test results would help differentiate active virus infection from follow-up care.

Furthermore, it would be interesting to extend the analyses beyond 2014. At the time when the studies were conducted, data of later years were not available, but it has been shown that the introduction of the second-generation DAAs in 2014 was even more important than the introduction of the first-generation DAAs in 2011. Improved treatment options may not only have affected the number of prevalent and incident patients (Chapter 3) but also the effect that (early) treatment has on costs and risk of EHMs (Chapters 4 and 5).

Additional information on the insured individuals would also improve Chapter 6. In this study, we use the information whether individuals changed the employer to approximate whether they have pro- or countercyclical income opportunities. The disadvantage is that there is no information on why individuals changed their job. Asking for such important information in a questionnaire, e.g., would improve the study substantially.

Finally, for all of the studies, it would be an improvement to analyze data that are completely representative of the SHI. Although representativeness with respect to age and gender can be stated for the data used, one can think of a variety of other factors for which representativeness can be questioned. For example, for historical reasons, individuals insured with company health insurance funds on average have fewer chronic diseases compared to individuals insured in other parts of the SHI, and the share of low educated individuals is smaller (Gesundheitsmonitor, 2008). Moreover, certain groups of high-risk individuals with respect to HCV are underrepresented in company health insurance funds, and the data in this study may include fewer drug-addicts, fewer immigrants from countries with higher infection rates (Hardtke and Wedemeyer, 2015), fewer individuals with certain CHC-related diseases like HIV or hemophilia, and fewer individuals with transplanted organs or dialysis (Stahmeyer et al., 2014). Since 1996, individuals have been mostly free to choose their preferred sickness fund, and differences decrease by the time, but they still exist. For the research community, it would be beneficial to create a data set that is representative of the SHI in all important aspects.

Bibliography

Abbas, S., Ihle, P., Koster, I., and Schubert, I. (2012). Estimation of disease incidence in claims data dependent on the length of follow-up: A methodological approach. *Health Services Research Journal*, 47(2), 746–755.

Adda, J. (2016). Economic activity and the spread of viral diseases: Evidence from high frequency data. *Quarterly Journal of Economics*, 131(2), 891–941.

Aggarwal, R., Chen, Q., Goel, A., Seguy, N., Pendse, R., Ayer, T., and Chhatwal, J. (2017). Cost-effectiveness of hepatitis C treatment using generic direct-acting antivirals available in India. *PLoS One*, 12(5), e0176503.

Altonji, J. G., Elder, T. E., and Taber, C. R. (2005). Selection on observed and unobserved variables: Assessing the effectiveness of catholic schools. *Journal of Political Economy*, 113(1), 151–184.

Arai, M. and Thoursie, P. (2005). Incentives and selection in cyclical absenteeism. *Labour Economics*, 12(2), 269–280.

Aron-Dine, A., Einav, L., Finkelstein, A., and Cullen, M. (2015). Moral hazard in health insurance: Do dynamic incentives matter? *The Review of Economics and Statistics*, 97(4), 725–741.

Arrow, K. J. (1963). Uncertainty and the welfare economics of medical care. *American Economic Review*, 53(5), 941–973.

Askildsen, J., Bratberg, E., and Nilsen, Ø. (2005). Unemployment, labor force composition and sickness absence: A panel data study. *Health Economics*, 14(11), 1087–1101.

Association of Supplementary Health Insurance Funds (2019). Daten zum Gesundheitswesen: Versicherte. Available at: https://www.vdek.com/presse/daten/b_versicherte.html [Accessed July 24, 2019].

Audas, R. and Goddard, J. (2001). Absenteeism, seasonality, and the business cycle. *Journal of Economics and Business*, 53(4), 405–419.

Balakrishnan, M., Glover, M. T., and Kanwal, F. (2017). Hepatitis C and risk of nonhepatic malignancies. *Clinics in Liver Disease*, 21(3), 543–554.

Banerjee, D. and Reddy, K. R. (2016). Review article: Safety and tolerability of directacting anti-viral agents in the new era of hepatitis C therapy. *Alimentary Pharmacology and Therapeutics*, 43(6), 674–696.

Barmby, T., Sessions, J., and Treble, J. (1994). Absenteeism, efficiency wages and shirking. *The Scandinavian Journal of Economics*, 96(4), 561–566.

Boes, S. and Gerfin, M. (2016). Does full insurance increase the demand for health care? *Health Economics*, 25(11), 1483–1496.

Borghans, L., Golsteyn, B. H. H., Heckman, J. J., and Meijers, H. (2009). Gender differences in risk aversion and ambiguity aversion. *Journal of the European Economic Association*, 7(2-3), 649–658.

Breyer, F., Zweifel, P., and Kifmann, M. (2012) *Gesundheitsökonomik*. Springer-Verlag, Berlin, Heidelberg, 6th edition.

Brown, S. (1994). Dynamic implications of absence behaviour. *Applied Economics* 26(12), 1163–1175.

Bruggmann, P., Berg, T., Øvrehus, A. L., Moreno, C., Brandão Mello, C. E., Roudot-Thoraval, F., et al. (2014). Historical epidemiology of hepatitis C virus (HCV) in selected countries. *Journal of Viral Hepatitis*, 21(Suppl 1), 5–33.

Buchner, F. and Wasem, J. (2003). Needs for further improvement: Risk adjustment in the German health insurance system. *Health Policy*, 65(1), 21–35.

Buti, M., Dominguez-Hernandez, R., Oyagüez, I., and Casado, M. Á. (2016). Cost-effectiveness analysis of sofosbuvir, peginterferon and ribavirin in patients with chronic hepatitis C: early treatment in the initial stage of fibrosis vs. delayed treatment in advanced fibrosis. *Journal of Gastroenterology and Hepatology*, 39(7), 449–457.

Cacoub, P., Buggisch, P., Beckerman, R., and Younossi, Z. (2017). Direct medical costs associated with the extrahepatic manifestations of hepatitis C infection. *Journal of Hepatology*, 66(1 Suppl), S499.

Cacoub, P., Comarmond, C., Domont, F., Savey, L., Desbois, A. C., and Saadoun, D. (2016). Extrahepatic manifestations of chronic hepatitis C virus infection. *Therapeutic Advances in Infectious Disease*, 3(1), 3–14.

Caliendo, M. and Kopeinig, S. (2008). Some practical guidance for the implementation of propensity score matching. *Journal of Economic Surveys*, 22(1), 31–72.

Carrozzo, M. and Scally, K. (2014). Oral manifestations of hepatitis C virus infection. *World Journal of Gastroenterology*, 20(24), 7534–7543.

Chandra, A., Gruber, J., and McKnight, R. (2010). Patient cost-sharing and hospitalization offsets in the elderly. *American Economic Review*, 100 (1), 192–213.

Chen, J. Y., Feeney, E. R., and Chung, R. T. (2014). HCV and HIV co-infection: Mechanisms and management. *Nature Reviews Gastroenterology & Hepatology*, 11(6), 362–371.

Cheng, Z., Zhou, B., Shi, X., Zhang, Y., Zhang, L., Chen, L., et al. (2014). Extrahepatic manifestations of chronic hepatitis C virus infection: 297 cases from a tertiary medical center in Beijing, China. *Chinese Medical Journal*, 127(7), 1206–1210.

Cutler, D. M., Finkelstein, A., and McGarry, K. (2008). Preference heterogeneity and insurance markets: Explaining a puzzle of insurance. *American Economic Review: Papers & Proceedings*, 98(2), 157–162.

Davies, R., Jones, P., and Nuñez, I. (2009). The impact of the business cycle on occupational injuries in the UK. *Social Science & Medicine*, 69(2), 178–182.

DiBonaventura, M. d., Yuan, Y., Lescrauwaet, B., L'Italien, G., Lia, G. G., Kamae, I., et al. (2014). Multicountry burden of chronic hepatitis C viral infection among those aware of their diagnosis: A patient survey. *PLoS ONE*, 9(1), e86070.

Einav, L., Finkelstein, A., Ryan, S. P., Schrimpf, P., and Cullen, M. R. (2013). Selection on moral hazard in health insurance. *American Economic Review*, 103(1), 178–219.

European Association for the Study of the Liver (2014). EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. *Journal of Hepatology*, 60(2), 392–420.

European Medicines Agency (2019). Anhang 1: Zusammenfassung der Merkmale des Arzneimittels (Sovaldi 400 mg Filmtabletten). Available at: https://www.ema.europa.eu/en/documents/product-information/sovaldi-epar-product-information_de.pdf [Accessed August 09, 2019].

Farber, H. S. (1999). Mobility and stability: The dynamics of job change in labor markets. *Handbook of labor economics*, 3 (Part B), 2439–2483.

Farbmacher, H., Ihle, P., Schubert, I., Winter, J., and Wuppermann, A. (2017). Heterogeneous effects of a nonlinear price schedule for outpatient care. *Health Economics*, 26(10), 1234–1248.

Farbmacher, H. and Winter, J. (2013). Per-period co-payments and the demand for health care: Evidence from survey and claims data. *Health Economics*, 22(9), 1111–1123.

Federal Health Monitoring (2019). Available at: <https://www.gbe-bund.de> [Accessed August 05, 2019].

Federal Statistical Office (2019). Available at: <https://www.destatis.de> [Accessed August 8, 2019].

Felder, S. and Werblow, A. (2008). A physician fee that applies to acute but not to preventive care: Evidence from a German deductible program. *Schmollers Jahrbuch: Journal of Applied Social Science Studies/Zeitschrift für Wirtschafts- und Sozialwissenschaften*, 128(2), 191–212.

Finkelstein, A., Arrow, K. J., Gruber, J., Newhouse, J. P., and Stiglitz, J. E. (2015). Moral hazard in health insurance. Columbia University Press, New York, 1st edition.

García-Gómez, P. (2011). Institutions, health shocks and labour market outcomes across Europe. *Journal of Health Economics*, 30(1), 200–213.

García Gómez, P. and López Nicolás, A. (2006). Health shocks, employment and income in the Spanish labour market. *Health Economics*, 15(9), 997–1009.

Gerfin, M., Kaiser, B., and Schmid, C. (2015). Healthcare demand in the presence of discrete price changes. *Health Economics*, 24(9), 1164–1177.

German Federal Ministry of Health (2015). Mitglieder und Versicherte. Available at: <http://bmg.bund.de/themen/krankenversicherung/zahlen-und-fakten-zur-krankenversicherung/mitglieder-und-versicherte.html> [Accessed March 10, 2015].

Gesundheitsmonitor (2008). Sozioökonomische Strukturen und Morbidität in den gesetzlichen Krankenkassen. Available at: [http://gesundheitsmonitor.de/studien/detail/?tx_itaoarticles_pi1\[article\]=220&tx_itaoarticles_pi1\[action\]=show&tx_itaoarticles_pi1\[controller\]=Article](http://gesundheitsmonitor.de/studien/detail/?tx_itaoarticles_pi1[article]=220&tx_itaoarticles_pi1[action]=show&tx_itaoarticles_pi1[controller]=Article) [Accessed December 6, 2016].

Goerke, L. and Pannenberg, M. (2015). Trade union membership and sickness absence: Evidence from a sick pay reform. *Labour Economics*, 33 (Issue C), 13–25.

Gower, E., Estes, C., Blach, S., Razavi-Shearer, K., and Razavi, H. (2014). Global epidemiology and genotype distribution of the hepatitis C virus infection. *Journal of Hepatology*, 61(1 Suppl), S45–57.

Hagan, R., Jones, A. M., and Rice, N. (2009). Health and retirement in Europe. *International Journal of Environmental Research and Public Health*, 6(10), 2676–2695.

Hamermesh, D. S. (1996). Labor demand. Princeton University Press.

Hardtke, S. and Wedemeyer, H. (2015). Eradikation des Hepatitis-C-Virus und Verhinderung klinischer Endpunkte. *Der Gastroenterologe*, 10(4), 305–309.

Hayen, A., Klein, T. J., and Salm, M. (2018). Does the framing of patient cost-sharing incentives matter? The effects of deductibles vs. no-claim refunds. IZA Discussion Paper No. 11508.

Health Policy Brief (2015). The Oregon Health Insurance Experiment. *Health Affairs*. Available at <https://www.healthaffairs.org/do/10.1377/hpb20150716.236899/full/> [Accessed July 16, 2015].

Hemken, N., Schusterschitz, C., and Thöni, M. (2012). Optional deductibles in GKV (statutory German health insurance): Do they also exert an effect in the medium term? *Journal of Public Health*, 20(3), 219–226.

Hoffmann, F. and Icks, A. (2011). Do persons that changed health insurance differ from those who did not? The case of diabetes. *Experimental and Clinical Endocrinology & Diabetes*, 119 (9), 569–572.

Hofmann, W. P., Sarrazin, C., and Zeuzem, S. (2012). Current standards in the treatment of chronic hepatitis C. *Deutsches Ärzteblatt International*, 109(19), 352–358.

Hüppé, D., Zehnter, E., Mauss, S., Böker, K. H. W., Lutz, T., Racky, S., et al. (2008). Epidemiology of chronic hepatitis C in Germany – An analysis of 10,326 patients in hepatitis centres and outpatient units. *Zeitschrift für Gastroenterologie*, 46(1), 34–44.

Ichino, A. and Riphahn, R. (2005). The effect of employment protection on worker effort: Absenteeism during and after probation. *Journal of the European Economic Association*, 3(1), 120–143.

Imbens, G. W. (2015). Matching methods in practice: Three examples. *Journal of Human Resources*, 50(2), 373–419.

Imbens, G. W. and Wooldridge, J. M. (2009). Recent developments in the econometrics of program evaluation. *Journal of Economic Literature*, 47(1), 5–86.

Institute for Employment Research (IAB) (2012). Unemployment rates by profession (Arbeitslosenquoten nach Beruf aus der Beschäftigten- und Arbeitslosenstatistik der Bundesagentur für Arbeit; Berechnungen des IAB).

Johansson, P. and Palme, M. (1996). Do economic incentives affect work absence? Empirical evidence using Swedish micro data. *Journal of Public Economics*, 59(2), 195–218.

Johansson, P. and Palme, M. (2005). Moral hazard and sickness insurance. *Journal of Public Economics*, 89(9), 1879–1890.

Kahle, C. (2015). 480 Euro pro Tablette: Neuer Preis für Sofosbuvir. Available at: <https://www.meine-gesundheit.de/service/news/hepatitis-c-preis-fuer-sovaldi-gesenkt> [Accessed August 09, 2019].

Kermack, W. and McKendrick, A. (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London. Series A*, 115(772), 700–721.

Khalsa, J. H., Treisman, G., McCance-Katz, E., and Tedaldi, E. (2008). Medical consequences of drug abuse and co-occurring infections: Research at the National Institute on Drug Abuse. *Substance Abuse*, 29(3), 5–16.

Knieps, F. and Reiners, H. (2015). *Gesundheitsreformen in Deutschland: Geschichte – Intentionen – Konfliktlinien*. Verlag Hans Huber, Bern, 1st edition.

Koç, Ç. (2011). Disease-specific moral hazard and optimal health insurance design for physician services. *Journal of Risk and Insurance*, 78(2), 413–446.

Koopmanschap, M. A., Rutten, F. F., van Ineveld, B. M., and Van Roijen, L. (1995). The friction cost method for measuring indirect costs of disease. *Journal of Health Economics*, 14(2), 171–189.

Korzilius, H. (2014). Arzneimittel: Fragwürdige Preispolitik der Industrie. *Deutsches Ärzteblatt International*, 111(47), 2056–2058.

Kraus, M. R., Kleine, H., Thönnnes, S., Pignot, M., and Sanchez Gonzalez, Y. (2018a). Clinical and economic burden of hepatic and extrahepatic complications from chronic hepatitis C: A retrospective analysis of German sickness fund data. *Infectious Diseases and Therapy*, 7(3), 327–338.

Kraus, M. R., Kleine, H., Thönnnes, S., Pignot, M., and Sanchez Gonzalez, Y. (2018b). Improvement of hepatic and extrahepatic complications from chronic hepatitis C after antiviral treatment: A retrospective analysis of German sickness fund data. *Infectious Diseases and Therapy*, 7(3), 339–352.

Kunz, J. S. and Winkelmann, R. (2017). An econometric model of healthcare demand with non-linear pricing. *Health Economics*, 26(6), 691–702.

Leigh, J. (1985). The effects of unemployment and the business cycle on absenteeism. *Journal of Economics and Business*, 37(2), 159–170.

Linthicum, M. T., Gonzalez, Y. S., Mulligan, K., Moreno, G. A., Dreyfus, D., Juday, T., et al. (2016). Value of expanding HCV screening and treatment policies in the United States. *American Journal of Managed Care*, 22(6 Spec No.), SP227–235.

Maasoumy, B., Port, K., Markova, A. A., Serrano, B. C., Rogalska-Taranta, M., Sollik, L., et al. (2013). Eligibility and safety of triple therapy for hepatitis C: Lessons learned from the first experience in a real world setting. *Plos One*, 8(2), e55285.

Maier, K.-P. (2002) Akute und chronische Hepatitis C: Epidemiologie – Diagnostik – Therapie. Georg Thieme Verlag, Stuttgart, New York, 2nd edition.

Maieron, A., Metz-Gercek, S., Hackl, F., Luger, C., Ziachehabi, A., Strauss, R., et al. (2010). Chronic hepatitis C in Austria, 1992–2006: Genotype distribution and demographic factors. *Eurosurveillance*, 15(8), 19492.

Malin, E.-M. and Schmidt, E. M. (1995). Beitragsrückzahlung in der GKV: Ein Instrument zur Kostendämpfung? *Die Betriebskrankenkasse* 12/1995, 759–763.

Manning, W. G., Newhouse, J. P., Duan, N., Keeler, E. B., and Leibowitz, A. (1987). Health insurance and the demand for health care. Evidence from a randomized experiment. *American Economic Review*, 77(3), 251–277.

Marcellusi, A., Viti, R., Damele, F., Cammà, C., Taliani, G., and Mennini, F. S. (2016). Early treatment in HCV: Is it a cost-utility option from the Italian perspective? *Clinical Drug Investigation*, 36(8), 661–672.

Marcus, J. (2014). Does job loss make you smoke and gain weight? *Economica*, 81(324), 626–648.

Marinho, R. T., Vitor, S., and Velosa, J. (2014). Benefits of curing hepatitis C infection. *Journal of Gastrointestinal and Liver Diseases*, 23(1), 85–90.

Markussen, S., Røed, K., and Røgeberg, O. (2013). The changing of the guards: Can family doctors contain worker absenteeism? *Journal of Health Economics*, 32(6), 1230–1239.

Medical Review Board of the Statutory Health Insurance Funds (2014). Available at: www.mdk.de [Accessed April 27, 2014].

Mehta, D. A., Cohen, E., Charafeddine, M., Cohen, D. E., Bao, Y., Sanchez Gonzalez, Y., and Tran, T. T. (2017). Effect of hepatitis C treatment with Ombitasvir/Paritaprevir/R + Dasabuvir on renal, cardiovascular and metabolic extrahepatic manifestations: A post-hoc analysis of phase 3 clinical trials. *Infectious Diseases and Therapy*, 6(4), 515–529.

Miller, D., Page, M., Stevens, A., and Filipski, M. (2009). Why are recessions good for your health? *The American Economic Review*, 99(2), 122–127.

Mohammed, R. H., ElMakhzangy, H. I., Gamal, A., Mekky, F., El Kassas, M., Mohammed, N., et al. (2010). Prevalence of rheumatologic manifestations of chronic hepatitis C virus infection among Egyptians. *Clinical Rheumatology*, 29(12), 1373–1380.

National Association of Statutory Health Insurance Funds (2019). Available at: <https://www.gkv-spitzenverband.de> [Accessed August 31, 2019].

Nevens, F., Colle, I., Michielsen, P., Robaeys, G., Moreno, C., Caekelbergh, K., et al. (2012). Resource use and cost of hepatitis C-related care. *European Journal of Gastroenterology & Hepatology*, 24(10), 1191–1198.

Nisic, N. and Trübswetter, P. (2012). Berufswechsler in Deutschland und Großbritannien. *IAB Kurzbericht* 1/2012.

Nordberg, M. and Røed, K. (2009). Economic incentives, business cycles, and long-term sickness absence. *Industrial Relations: A Journal of Economy and Society*, 48(2), 203–230.

OECD (2015). Focus on Health Spending. *OECD Health Statistics 2015*. Available at: <https://www.oecd.org/health/health-systems/Focus-Health-Spending-2015.pdf> [Accessed March 20, 2016].

Olsson, M. (2009). Employment protection and sickness absence. *Labour Economics*, 16(2), 208 – 214.

Oster, E. (2016). Unobservable selection and coefficient stability: Theory and evidence. Unpublished working paper. Available at: https://www.brown.edu/research/projects/oster/sites/brown.edu.research.projects.oster/files/uploads/Unobservable_Selection_and_Coefficient_Stability_o.pdf [Accessed February 21, 2019].

Pauly, M. (1968). The economics of moral hazard: Comment. *American Economic Review*, 58(3), 531–537.

Petta, S. (2017). Hepatitis C virus and cardiovascular: A review. *Journal of Advanced Research*, 8(2), 161–168.

Pichler, S. (2015). Sickness absence, moral hazard, and the business cycle. *Health economics*, 24(6), 692–710.

Pichler, S. and Thöennes, S. (2019). Sickness absence and unemployment revisited. *Working Papers Dissertations No. 53*, Paderborn University, Faculty of Business Administration and Economics.

Pichler, S. and Ziebarth, N. R. (2017). The pros and cons of sick pay schemes: Testing for contagious presenteeism and noncontagious absenteeism behavior. *Journal of Public Economics*, 156(C), 14–33.

Poethko-Müller, C., Zimmermann, R., Hamouda, O., Faber, M., Stark, K., Ross, R. S., et al. (2013). Epidemiology of hepatitis A, B, and C among adults in Germany: Results of the German Health Interview and Examination Survey for Adults (DEGS1). *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz*, 56(5–6), 707–715.

Private Medical Insurance (2019). Beitragsentwicklung der PKV und GKV im Vergleich. Available at: <https://www.pkv.de/themen/krankenversicherung/pkv-beitrag-2019/> [Accessed August 09, 2019].

Prosser, C., Altevers, L., and Hickstein, J. (2015). Incidence and prevalence estimations based on claims data – New methodological considerations. ISPOR 18th Annual European Congress. Milan, Italy.

Puhani, P. and Sonderhof, K. (2010). The effects of a sick pay reform on absence and on health-related outcomes. *Journal of Health Economics*, 29(2), 285–302.

Pütz, C. and Hagist, C. (2006). Optional deductibles in social health insurance systems. Findings from Germany. *European Journal of Health Economics*, 7(4), 225–230.

Razavi, H., Waked, I., Sarrazin, C., Myers, R. P., Idilman, R., Calinas, F., et al. (2014). The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *Journal of Viral Hepatitis*, 21(Suppl 1), 34–59.

Reau, N., Vekeman, F., Wu, E., Bao, Y., and Sanchez Gonzalez, Y. (2017). Prevalence and economic burden of extrahepatic manifestations of hepatitis C virus are underestimated but can be improved with therapy. *Hepatology Communications*, 1(5), 439–452.

Robert Koch Institute (2011). Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Virushepatitis B, C and D im Jahr 2010. *Epidemiologisches Bulletin*, 29, 261–274.

Robert Koch Institute (2013). Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Virushepatitis C im Jahr 2012. *Epidemiologisches Bulletin*, 30, 273–280.

Robert Koch Institute (2014). Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Virushepatitis C im Jahr 2013. *Epidemiologisches Bulletin*, 31, 275–288.

Robert Koch Institute (2015). Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Hepatitis C im Jahr 2014. *Epidemiologisches Bulletin*, 30, 289–299.

Robert Koch Institute (2018). Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Hepatitis C im Jahr 2017. *Epidemiologisches Bulletin*, 29, 271–284.

Robert Koch Institute (2019). RKI-Ratgeber: Hepatitis C. Available at: https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_HepatitisC.html [Accessed August 10, 2019].

Røed, K. and Fevang, E. (2007). Organizational change, absenteeism, and welfare dependency. *Journal of Human Resources*, 42(1), 156–193.

Rosenthal, E. S. and Graham, C. S. (2016). Price and affordability of direct-acting antiviral regimens for hepatitis C virus in the United States. *Infectious Agents and Cancer*. DOI: 10.1186/s13027-016-0071-z.

Ross, R. (1916). An application of the theory of probabilities to the study of a priori pathometry. Part I. *Proceedings of the Royal Society of London. Series A*, 92(638), 204–230.

Ruhm, C. (2000). Are recessions good for your health? *The Quarterly Journal of Economics*, 115(2), 617–650.

Sarrazin, C., Berg, T., Buggisch, P., Dollinger, M., Hinrichsen, H., Hüppe, D., et al. (2014). Aktuelle Empfehlung zur Therapie der chronischen Hepatitis C. *Zeitschrift für Gastroenterologie*, 52(10), 1185–1197.

Sarrazin, C., Berg, T., Cornberg, M., Dollinger, M., Ferenci, P., Hinrichsen, H., et al. (2012). Expert opinion on boceprevir- and telaprevir-based triple therapies of chronic hepatitis C. *Zeitschrift für Gastroenterologie*, 50(1), 57–72.

Sbarigia, U., Wirth, D., Van Nuys, K., Huber, C., Brookmeyer, R., Stahmeyer, J., et al. (2017). Economic study of the value of expanding HCV treatment capacity in Germany. *BMJ Open Gastroenterology*, 4(1), e000130.

Schaller, J. (2016). Booms, busts, and fertility testing the becker model using gender-specific labor demand. *Journal of Human Resources*, 51(1), 1–29.

Schmitz, H. (2012). More health care utilization with more insurance coverage? Evidence from a latent class model with German data. *Applied Economics*, 44 (34), 4455–4468.

Schmitz, H. and Westphal, M. (2015). Short- and medium-term effects of informal care provision on female caregivers' health. *Journal of Health Economics*, 42, 174–185.

Schmitz, H. and Ziebarth, N. R. (2017). How framing prices affects the consumer price sensitivity of health plan choice. *Journal of Human Resources*, 52(1), 88–127.

Schut, F. T., Greß, S., and Wasem, J. (2003). Consumer price sensitivity and social health insurer choice in Germany and The Netherlands. *International Journal of Health Care Finance and Economics*, 3(2), 117-138.

Scoppa, V. and Vuri, D. (2014). Absenteeism, unemployment and employment protection legislation: Evidence from Italy. *IZA Journal of Labor Economics*, 3(1), 1–25.

Shapiro, C. and Stiglitz, J. (1984). Equilibrium unemployment as a worker discipline device. *The American Economic Review*, 74(3), 433–444.

SOEPGroup (2013). German Socio-economic Panel Study (SOEP), data of the years 1984 – 2012.

Solinis, R. N., Ugarte, P. A., Rojo, A., and Sanchez Gonzalez, Y. (2016). Value of treating all stages of chronic hepatitis C: A comprehensive review of clinical and economic evidence. *Infectious Diseases and Therapy*, 5(4), 491–508.

Stahmeyer, J. T., Rossol, S., Bert, F., Abdelfattah, M., and Krauth, C. (2014). Costs of a guideline-based treatment of patients with chronic hepatitis C in Germany. *Zeitschrift für Gastroenterologie*, 52(9), 1041–1049.

Stahmeyer, J. T., Rossol, S., Bert, F., Antoni, C., Demir, M., Hinrichsen, H., et al. (2014). Cost of treating hepatitis C in Germany: A retrospective multicenter analysis. *European Journal of Gastroenterology & Hepatology*, 26(11), 1278–1285.

Tagesschau (2019). Regelung zu Soli-Abschaffung: Hohes Risiko der Verfassungswidrigkeit. Available at: <https://www.tagesschau.de/inland/soli-verfassung-103.html> [Accessed August 30, 2019].

Tengan, F. M., Levy-Neto, M., Miziara, I. D., Dantas, B. P., and Maragno, L. (2017). Extrahepatic manifestations of chronic hepatitis C infection: A consecutive study in Brazilian patients. *The Brazilian Journal of Infectious Diseases*, 21(2), 203–204.

Thönnnes, S. (2019). Ex-Post Moral Hazard in the Health Insurance Market – Empirical Evidence from German Data. *European Journal of Health Economics*. DOI: 10.1007/s10198-019-01091-w.

Thönnnes, S., Friedel, H., and Fröhlich, H. (2017). The number of patients with chronic hepatitis C in times of new therapy options: A retrospective observational study on German health insurance funds data. *European Journal of Gastroenterology & Hepatology*, 29(5), 503-508.

Tomeczkowski, J. and Cornberg, M. (2015). Hepatitis C in Germany: An analysis of statutory sickness funds claims data. *Deutsche Medizinische Wochenschrift*, 140(8), e67–e73.

Topel, R. (1991). Specific capital, mobility, and wages: Wages rise with job seniority. *Journal of Political Economy*, 99(1), 145–176.

Van Nuys, K., Brookmeyer, R., Chou, J. W., Dreyfus, D., Dieterichs, D., and Goldman, D. P. (2015). Broad hepatitis C treatment scenarios return substantial health gains, but capacity is a concern. *Health Affairs (Millwood)*, 34(10), 1666-1674.

Vietri, J., Prajapati, G., and El Khoury, A. C. (2013). The burden of hepatitis C in Europe from the patients' perspective: A survey in 5 countries. *BMC Gastroenterology*. DOI: 10.1186/1471-230X-13-16.

Wagenlehner, F. M. E., Brockmeyer, N. H., Discher, T., Friese, K., and Wichelhaus, T. A. (2016). The presentation, diagnosis and treatment of sexually transmitted infections. *Deutsches Ärzteblatt International*, 113(1-02), 11–22.

Wagner, C. (2014). Die Population unter Risiko bei Prävalenz- und Inzidenzschätzungen – Nennerkonzepte. In: Swart, E., Ilhe, P., Gothe, H., and Matusiewicz, D. (editors) (2014). *Routinedaten im Gesundheitswesen: Handbuch Sekundärdatenanalyse: Grundlagen, Methoden und Perspektiven*. Bern: Hans Huber, pp. 376–388.

Wijarnpreecha, K., Chedsachai, S., Jaruvongvanich, V., and Ungprasert, P. (2018). Hepatitis C virus infection and risk of Parkinson's disease: A systematic review and metaanalysis. *European Journal of Gastroenterology & Hepatology*, 30(1), 9–13.

Wilder, J. M. and Muir, A. J. (2015). Strategies for treating chronic HCV infection in patients with cirrhosis: latest evidence and clinical outcomes. *Therapeutic Advances in Chronic Disease*, 6(6), 314–327.

Wooldridge, J. M. (2015). *Introductory econometrics: A modern approach*. South Western Educational Publishing, Mason, 6th edition.

World Health Organization (2016): Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection. Available at: https://apps.who.int/iris/bitstream/handle/10665/205035/9789241549615_eng.pdf;jsessionid=AD654ACF118CAB670469D47FoEC1DoAC?sequence=1 [Accessed September 13, 2017].

World Health Organization (2017a). Hepatitis C in the WHO European Region. Available at: http://www.euro.who.int/__data/assets/pdf_file/0010/283357/factsheeten-hep-c-edited.pdf [Accessed September 13, 2017].

World Health Organization (2017b). Data and statistics. Available at: <http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/data-and-statistics> [Accessed September 13, 2017].

Younossi, Z. M., Kanwal, F., Saab, S., Brown, K. A., El-Serag, H. B., Kim, W. R., et al. (2014). The impact of hepatitis C burden: An evidence-based approach. *Alimentary Pharmacology and Therapeutics*, 39(5), 518–531.

Younossi, Z., Park, H., Henry, L., Adeyemi, A., and Stepanova, M. (2016). Extrahepatic manifestations of hepatitis C: a meta-analysis of prevalence, quality of life, and economic burden. *Gastroenterology*, 150(7), 1599–1608.

Younossi, Z. M., Tanaka, A., Eguchi, Y., Henry, L., Beckerman, R., and Mizokami, M. (2018). Treatment of hepatitis C virus leads to economic gains related to reduction in cases of hepatocellular carcinoma and decompensated cirrhosis in Japan. *Journal of Viral Hepatitis*, 25(8), 945-951.

Younossi, Z. M., Tanaka, A., Eguchi, Y., Lim, Y. S., Yu, M. L., Kawada, N., et al. (2017). The impact of hepatitis C virus outside the liver: Evidence from Asia. *Liver International*, 37(2), 159-172.

Ziebarth, N. and Karlsson, M. (2010). A natural experiment on sick pay cuts, sickness absence, and labor costs. *Journal of Public Economics*, 94(11), 1108–1122.