

Hofbauer-Milan, Valeska

ESSAYS IN HEALTH ECONOMICS

Dissertation
for obtaining the degree of Doctor of Business and Economics
(Doctor rerum politicarum - Dr. rer. pol.)

at WHU – Otto Beisheim School of Management

04 / 2023

First Advisor: *Prof. Dr. Christian Hagist*

Second Advisor: *Prof. Dr. Ralf Fendel*

External Third Advisor: *Prof. Dr. Stefan Fetzer, Hochschule Aalen*

Preface

This thesis is the result of an external PhD program at the WHU – Otto Beisheim School of Management at the Chair of Economic and Social Policy, during which I was simultaneously employed professionally at the AOK Baden-Württemberg. For me, it was a challenging but, at the same time, incredibly enriching time, and I want to express my sincere gratitude to everyone who supported me during my PhD.

First and foremost, I would like to thank my supervisors, Prof. Dr. Christian Hagist and Prof. Dr. Stefan Fetzler. I could not have imagined better guidance and support. They were always available for me, got the best possible performance out of me, and I am most grateful to them for sharing their professional expertise with me and also for supporting me personally with words and deeds. In this way, they have had a decisive influence on my personal development and my path in life. Without the constant encouragement and motivation from Prof. Dr. Stefan Fetzler since my bachelor studies, I would never have made it to the dissertation, and I will never forget how warmly Prof. Dr. Christian Hagist welcomed me to his chair as a doctoral student.

I would also like to sincerely thank Prof. Dr. Ralf Fendel for taking on the role of the second supervisor. And I am very grateful to my employer, the AOK Baden-Württemberg, for supporting me during the PhD program and especially for providing the research data, without which this work would not have been possible. My special thanks also go to all the proofreaders of the individual contributions.

Finally, my very heartfelt thanks go to my family for their incredible support. My mother, my parents-in-law, my godmother and her family and all the other lovely people who always stood by me. And I am sure that I also received support from all the dear people who are sadly no longer in this world, especially my father. But most of all, I want to thank my husband. With his all-time positive nature, he was able to get me out of any low point, and there is no one who has ever believed in me more. I am so happy and grateful to have him and our wonderful son by my side.

Table of contents

Table of contents	3
List of figures	5
List of tables	5
List of abbreviations	6
List of formulas	6
Introduction.....	7
1 General introduction.....	7
2 Research questions	8
3 Contribution 1	9
4 Contribution 2	9
5 Contribution 3	10
Contribution 1: Healing, Surviving, or Dying? – Projecting the German future disease burden using a Markov Illness-Death Model.....	12
1 Background	12
2 Methods	14
2.1 Markov Illness-Death Model with Recovery	14
2.2 Scenarios	18
2.3 Dataset	19
3 Results.....	25
4 Discussion.....	30
5 Conclusion	32
Contribution 2: How to predict drug expenditure – A Markov model approach with risk classes	33
1 Introduction	33
2 Methods	34
3 Data	36
4 Scenarios	38
5 Results.....	40
6 Discussion.....	43
7 Conclusion	45
Contribution 3: Cost-risk groups in the SHI and the costs in the year of death	46
1 Introduction	46
2 Methods	47
3 Results.....	49
4 Discussion.....	54

5 Conclusion 57

Summary..... 58

References..... 60

Appendices 71

List of figures

Fig. 1 Relative change in <i>apr</i> until 2060 in the different scenarios.....	28
Fig. 2 Transition Matrix (illustrated by the example of female cohorts for the transition from 2018 to 2019)	36
Fig. 3 Initial affiliation probability in the different risk groups by age 2018.....	37
Fig. 4 Projection proportional change of annual per-capita pharmaceutical expenditure in Germany up to 2060 (without consideration of cost growth rates).....	41
Fig. 5 HCE distribution of survivors 2018 after risk group classification.....	49
Fig. 6 Daily per-capita HCE 2018 of survivors 2019, decedents 2019, and decedents 2018 ...	50
Fig. 7 Average affiliation probabilities and mortality rates in the different risk groups by age	53
Fig. 8 Search filter PubMed	71
Fig. 9 Flow chart of the literature selection process.....	72

List of tables

Tab. 1 Scenarios, assumptions and their effect on the future prevalence rate	18
Tab. 2 Diseases and selection criteria	21
Tab. 3 Determined disease-specific variables.....	23
Tab. 4 Projected average prevalence rates <i>apr</i> 2060 and percentage change compared to 2018.....	25
Tab. 5 Projected number of patients 2060 in the different scenarios	29
Tab. 6 Study population characteristics and modeling assumptions	38
Tab. 7 Projection scenarios and their model calculation.....	40
Tab. 8 Projected percentage change of annual per-capita pharmaceutical expenditure of the German population from 2019 to 2040 and 2060	42
Tab. 9 Risk group classification of the study population 2018	48
Tab. 10 HCE distribution between survivors and decedents 2018	52
Tab. 11 Bibliography and study characteristics	73

List of abbreviations

CA	-	Pulmonary, bronchial and tracheal cancer
CHD	-	Coronary heart disease
COPD	-	Chronic obstructive pulmonary disease
CVD	-	Cerebrovascular diseases
Fig.	-	Figure
HCE	-	Healthcare expenditure
HF	-	Heart failure
RG	-	Risk group
SHI	-	Statutory health insurance
SQ	-	Status quo
Tab.	-	Table

List of formulas

Formula (1)	15
Formula (2)	16
Formula (3)	16
Formula (4)	16
Formula (5)	16
Formula (6)	16
Formula (7)	17
Formula (8)	18

Introduction

1 General introduction

The German healthcare system, with its statutory health insurance (SHI) introduced already in 1883, can be regarded as a forerunner of modern healthcare systems and is considered well-equipped and generous in coverage by international standards [1]. However, the past few years of the Covid-19 pandemic have shown that even the German health care system has capacity limits. But while the pandemic was hardly predictable, the German SHI scheme faces a more calculable challenge in the medium and longer-term [2]. Germany is one of the fastest ageing countries in the world due to constantly low fertility rates since the 1970s and a continuously increasing life expectancy [3]. This demographic transition could also drive the German healthcare system to the limits of its capacity and fiscal sustainability, with fewer and fewer young working people facing a growing number of retirees with age-related diseases and healthcare expenditures (HCE) [3, 4].

But the question of whether the demographic change will lead to an increase in HCE is one of the most debated issues in the field of health economics. Various authors have reviewed this topic in detailed literature surveys (see for example Meijer et al. (2013), Sorensen et al. (2013), or Breyer & Lorenz (2021) [5–7]). Two basic theories can be distinguished in the literature: On the one hand, higher life expectancy could be accompanied by an increase in years spent in illness [8, 9]. This would lead to an expansion of morbidity in older age groups and thus to rising HCE [8, 9]. On the other hand, rising longevity could lead to a compression of morbidity in older age groups [10]. The years of life gained are thus spent in good health, which would result in no increase or even a decrease in HCE [10]. Similarly, proximity to death could be an important determinant of HCE, and high spending in the last year(s) of life could merely be postponed to a later age [11–15]. However, there is still no clear evidence on how increasing life expectancy will affect future disease burden and the related HCE. And since steadily rising HCE are a phenomenon observed for decades [4], also other factors influencing today's and future HCE like medical innovations, real income growth, or regulations like pricing policies for medical goods are up for debate [16].

Moreover, in many developed countries, we can observe not only an increase in HCE, but also a growing concentration on a few high-cost cases [17–20]. Tanke et al. (2019) provide an

overview of the cost distribution in different OECD member states and show that the top five percent of the most expensive patients account for 40 to 60 percent of total HCE [20]. In Germany, around 20 percent of expenditure is attributable solely to the most expensive one percent [19–21]. Despite this huge share in HCE, high-risk cases are so far not considered in HCE projections. In pharmaceutical spending, this concentration of expenditure on a small number of patients is even more significant [19], while these patients are additionally characterized by particular sustainability in high expenditure [22, 23]. So those who incur very high costs once are likely to do so in subsequent years. This trend is mainly attributable to the increasing approval of high-priced special therapies for rare diseases, so-called "orphan drugs", particularly in oncology [24–26].

2 Research questions

In view of the outlined trends and challenges for the German healthcare system, detailed analyses of expenditure distributions and projections of future disease burden and HCE can provide important guidance for policymakers. A contribution to these topics will be made by this dissertation. The dissertation consists of three papers, all based on data from a major sickness fund covering around four million insureds. In the first paper, we illustrate the impact of demographic change by looking at the morbidity in the German population and present projections for ten common non-infectious diseases. By modeling different scenarios regarding a possible compression or expansion of morbidity, we show the future range of disease burden in Germany. Since pharmaceutical expenditures are a key factor regarding the future development of HCE, the second paper focuses on modeling medium- and long-term drug expenditure projections with particular attention to the spending concentration on the small group of high-risk patients. Finally, the last paper addresses the overall distribution of HCE, both between different risk groups and with a special focus on the differential expenditures of survivors and decedents. This allows us to gain important insights into spending patterns in the German SHI and provide a new starting point for future projections of total HCE.

3 Contribution 1

In view of the upcoming demographic transition, there is still no clear evidence on how increasing life expectancy will affect future disease burden, especially regarding specific diseases. In our study, we project the future development of Germany's ten most common non-infectious diseases (arthrosis, coronary heart disease, pulmonary, bronchial and tracheal cancer, chronic obstructive pulmonary disease, cerebrovascular diseases, dementia, depression, diabetes, dorsal pain and heart failure) in a Markov illness-death model with recovery until 2060.

The disease-specific input data stem from a consistent data set of a major sickness fund covering about four million people, the demographic components from official population statistics. Using six different scenarios concerning an expansion and a compression of morbidity as well as increasing recovery and effective prevention, we can show the possible future range of disease burden and, by disentangling the effects, reveal the significant differences between the various diseases in interaction with the demographic components.

Our results indicate that, although strongly age-related diseases like dementia or heart failure show the highest relative increase rates, diseases of the musculoskeletal system, such as dorsal pain and arthrosis, still will be responsible for the majority of the German population's future disease burden in 2060, with about 25-27 and 13-15 million patients, respectively. Most importantly, for almost all considered diseases a significant increase in burden of disease can be expected even in case of a compression of morbidity.

A massive caseload is emerging on the German health care system, which can only be alleviated by more effective prevention. Immediate action by policy makers and health care managers is needed, as otherwise the prevalence of widespread diseases will become unsustainable from a capacity point-of-view.

4 Contribution 2

Although pharmaceutical expenditures have been rising for decades, the question of their drivers remains unclear, and long-term projections of pharmaceutical spending are still scarce. We use a Markov approach considering different cost-risk groups to show the possible range

of future drug spending in Germany and highlight the leverage effects of various determinants.

We compute different medium and long-term projections of pharmaceutical expenditure in Germany up to 2060 and compare extrapolations with constant shares, time-to-death scenarios, and Markov modeling based on transition probabilities. Our modeling is based on data from a large statutory sickness fund covering around four million insureds. We divide the population into six risk groups according to their share of total pharmaceutical expenditures, determine their cost growth rates, survival and transition probabilities, and compute different scenarios related to changes in life expectancy or spending trends in different cost-risk groups.

If the spending trends in the high-cost groups continue, per-capita expenditure will increase by over 40 percent until 2040. By 2060, pharmaceutical expenditures could more than double, even if these groups would not benefit from rising life expectancy. By contrast, the isolated effect of demographic change would "only" lead to a long-term increase of around 15 percent.

The long-term development of pharmaceutical spending in Germany will depend mainly on future expenditure and life expectancy trends of particularly high-cost patients. Thus, appropriate pricing of new expensive pharmaceuticals is essential for the sustainability of the German healthcare system.

5 Contribution 3

In view of steadily rising HCE, studies on spending distributions can provide important guidance for policy decisions. Since the majority of HCE is concentrated in a few high-cost cases, this study focuses on the spending distribution between different cost-risk groups. We show detailed allocation structures, distinguishing several categories of HCE and the survival status of insureds to gain insights regarding the share of mortality costs.

Our analyses rely on data from a large sickness fund covering around four million insureds. We classify the population into ten equal risk groups by costs and then determine expenditure shares of total HCE and daily per-capita expenditures depending on survival status and risk group affiliation.

Our results offer that mortality costs are only evident in lower-risk groups and almost exclusively attributable to hospitalization. Moreover, HCE in the calendar year of death is

equal for most risk groups. Only for the high-risk cases, HCE in the year of death is significantly higher, but the difference between survivors and decedents is proportionally small. It is primarily pharmaceutical spending accounting for the difference in per capita HCE between decedents in high-risk and other risk groups.

Short-term high HCE in the calendar year of death occur equally in all risk groups and are hardly avoidable. By contrast, the extremely high costs of high-risk cases already show up sometime before death. Regardless of the mortality cost share, this group remains the main target for influencing rising HCE, and their characteristics should be considered regarding future HCE projections.

Contribution 1: Healing, Surviving, or Dying? – Projecting the German future disease burden using a Markov Illness-Death Model¹

1 Background

The development of future patient numbers is an important concern for many stakeholders in the health systems. Rational decisions about the planning of hospital capacities, pharmaceutical investments, career choices of (future) healthcare professionals as well as the development of future HCE itself depend on the precise knowledge of the future development of specific diseases.

Germany is one of the fastest ageing countries in the world due to constantly low fertility rates since the 1970s and a continuously increasing life expectancy [3]. In the literature there are different rival theories and hypotheses how an increasing life expectancy will particularly affect the disease burden and the related HCE. Gruenberg (1977) [8] and Verbrugge (1984) [9] hypothesize that a rising longevity goes hand in hand with an increase in years spent in illness and therefore with an *expansion of morbidity* in older age groups. In contrast, Fries (1980) [10] assumes that an increasing life expectancy leads to a *compression of morbidity*. Given these somehow contradictory hypotheses, the influence of proximity to death and treatment spending as a function of remaining life expectancy are controversially discussed among health economists [7, 11, 15, 28].

However, even less evidence exists today concerning the (more epidemiological) question of specific diseases' future development in the light of the different hypotheses. A systematic literature review on PubMed searching for projections (or synonyms) in context of demography and using the keywords *prevalence*, *incidence* or *burden of disease* for specific or chronic non-infectious diseases in general shows 160 relevant publications. There are three categories of studies by their projection methodology: trend extrapolations (99/160), multistate models (57/160) and studies using both methodologies (4/160). In 54 of the studies

¹ Milan V, Fetzer S, Hagist C. Healing, surviving, or dying? - Projecting the German future disease burden using a Markov illness-death model. BMC Public Health. 2021;21:123. doi:10.1186/s12889-020-09941-6. [27].

using trend extrapolation (103/160) indeed current prevalence or incidence rates are transferred to population projections, which excludes a specific modelling of the various theses. This so-called status quo analysis is also commonly used in projections of health expenditures.² Out of the 61 studies using multistate modelling (61/160), 17 (17/61) are based on the classical structure of an illness-death model (even if only 7 explicitly define it that way). However, only nine of the studies (9/61) focus on an explicit modelling of a compression of morbidity, of them eight (8/9) related to dementia. Furthermore, just seven studies (7/61) compare the development of more than two different diseases, only one of them modelling compression scenarios [30] (see Fig. 8, Fig. 9 and Tab. 11 in the appendix for more detailed information and results on the systematic database search).

In our paper, we present projections for ten common non-infectious diseases (arthrosis, coronary heart disease, pulmonary, bronchial and tracheal cancer, chronic obstructive pulmonary disease, cerebrovascular diseases, dementia, depression, diabetes, dorsal pain and heart failure). The selected diseases represent the intersection between the most common and most expensive disease patterns in Germany [31]. For the projections we use a time-discrete Markov illness-death model with recovery. Our model allows us to regard the different hypotheses in context of demographic transition and to quantify the influence of potentially changing variables (disease-specific survival, incidence and recovery rate) on the future frequency of diseases. In addition, we show the influence of successful prevention on long-term prevalence of the different diseases.

The population-related components used for modelling stem from Destatis, the German Federal Statistical Office, whereas the disease-specific components are computed on the data of a major sickness fund covering approximately four million insureds during the period from 2009 to 2017. Our data set is unique as we calculated the input data ourselves using disease-specific validation criteria selected for this purpose (shown in Tab. 2). Hence, our study is one of the few that use insurance data (7/160), although the resulting treatment prevalence is of particular importance for decision makers and payers in the health care system. Data sources from other studies of the systematic literature review are surveys or other epidemiological

² See for example the Ageing Report published by the European Commission [29].

studies (61/160), a literature review for the different input factors (34/160), registries (28/160) or mixed data sources (30/160).

The paper is organized as follows: we start with the presentation of our time-discrete Markov illness-death model with recovery as well as our data set. Then, we show our results for the future development of the ten diseases (average prevalence rates and number of patients) in different populations and scenarios, also considering the results of other publications. This is followed by a discussion of the results in view of the current state of research and the limitations, finishing with a concluding summary.

2 Methods

2.1 Markov Illness-Death Model with Recovery

We will calculate the future number of patients and the future average prevalence rates for the total population from 2018 to 2060³ using a time-discrete Markov illness-death model with recovery. The model is based on the cohort-component-method [32], which is widely used for (official) population projections. Regarding epidemiologic modelling, it can be attributed to the work of Fix & Neyman (1951) [33] and is closely related to those of Manton et al. (1984), Brookmeyer et al. (1998), Brinks et al. (2012), and Andersson et al. (2015) [34–37], but differs in the detail level of the rich routine data set used. The specific cohort data by age and gender with corresponding detail diagnosis allows us to vary different variables over time (future development of the disease-specific survival rate, incidence rate and recovery rate). In contrast to most other studies using an illness-death approach (16/17) including the work of Milan & Fetzer (2019) [38], on which our modelling is based, the model also includes the possibility of recovery.

The starting point of our model is the number of patients $P_{a,g}$ (differentiated by age a between 0 and 100 and gender g which is men or women) in our starting year T . It results from the prevalence rate $p_{a,g,T}$ multiplied by the cohort size $K_{a,g,T}$.

$$P_{a,g,T} = K_{a,g,T} p_{a,g,T} \quad (1)$$

³ We chose the year 2060 as the end point of the projection as the official population projection of the German Federal Statistical Office also ends in 2060.

In models extrapolating current prevalence rates (status quo analysis) $p_{a,g,T}$ is assumed to be constant over time and only the future cohort sizes determine the future development of patients. In contrast to this, for all following years, age- and gender-specific incidence and recovery rates as well as the mortality rates of patients are used in our model to calculate the (future) number of patients $P_{a,g,T+t}$. At this point we distinguish between the group of patients which are comprised of the surviving patients of the previous year $D_{a,g,T+t}^{T+t-1}$ and the group of newly diseased patients $I_{a,g,T+t}$.

$$P_{a,g,T+t} = D_{a,g,T+t}^{T+t-1} + I_{a,g,T+t} \quad (2)$$

In order to calculate the surviving patients of the previous year $D_{a,g,T+t}^{T+t-1}$ we use the disease-specific mortality difference $md_{a-1,g,T+t-1}$ which is subtracted from the survival rate of each cohort $sr_{a-1,g,T+t-1}$.⁴ Also we consider disease-specific recovery rates $r_{a-1,g,T+t-1}$ as follows⁵:

$$D_{a,g,T+t}^{T+t-1} = P_{a-1,g,T+t-1}(sr_{a-1,g,T+t-1} - md_{a-1,g,T+t-1})(1 - r_{a-1,g,T+t-1}) \quad (3)$$

To determine the number of new patients $I_{a,g,T+t}$, the number of surviving non-diseased from the previous year is calculated as follows in a first step:

$$ND_{a,g,T+t}^{T+t-1} = K_{a-1,g,T+t-1}sr_{a-1,g,T+t-1} - D_{a,g,T+t}^{T+t-1} \quad (4)$$

In a second step the number of new patients $I_{a,g,T+t}$, which results from the age- and gender-specific incidence rate $i_{a,g,T+t}$, is multiplied with the surviving non-diseased from the previous year:

$$I_{a,g,T+t} = ND_{a,g,T+t}^{T+t-1}i_{a,g,T+t} \quad (5)$$

The total number of patients P_{T+t} in all years $T + t$ is finally calculated as:

$$P_{T+t} = \sum_{a=0}^{100}(D_{a,women,T+t}^{T+t-1} + I_{a,women,T+t}) + \sum_{a=0}^{100}(D_{a,men,T+t}^{T+t-1} + I_{a,men,T+t}) \quad (6)$$

⁴ This mortality difference can be interpreted as the difference between the mortality rates of the diseased persons $mr_{a,g}^D$ and the population $mr_{a,g}$ or as the (reverse) difference between the corresponding survival rates $sr_{a,g}$ and $sr_{a,g}^D$.

⁵ In the respective year under consideration, we still assume the survival rate of the diseased for the recovered persons before they are transferred to the healthy population in the following year.

In our model for all years $T + t$ the future cohort sizes, $K_{a,g,T+t}$ as well as the future survival rates $sr_{a,g,T+t}$ of the total population are derived from a population projection, which we calculate via the cohort component method. Within this framework we consider the disease-specific components. The calculation of the survival rate of the patients as the difference $sr_{a-1,g,T+t-1} - md_{a-1,g,T+t-1}$ and the surviving non-diseased $ND_{a,g,T+t}^{T+t-1}$ as the difference between all survivors of the cohort and the surviving patients from the previous period finally merge the population projection with the epidemiological developments. Thus, the design of our model also allows the use of input data from any other population projection or/and disease-specific statistic. This time-discrete approach is also more intuitive to understand for a broader audience, such as policy setters and health care decision makers.

Dividing the total number of patients by the total number of the population results in the average prevalence rate of the total population, apr , which we will present in addition to the total number of patients in the result section. Obviously, the apr highly depends on the share of the elderly and diseased within the total population. As the German demographic transition leads to an increasing proportion of elderly cohorts, we call this effect *cohort effect*, which can also be observed in models extrapolating current prevalence rates using the status quo analysis.

As for the further effects of our model, we will take a closer look at the future age- and gender-related prevalence rate p_{T+1} , which can be obtained by dividing the number of patients (equations 2 to 5) by the total corresponding cohort $K_{a,g,T+t} = K_{a-1,g,T+t-1} sr_{a-1,g,T+t-1}$ and therefore is independent of future cohort sizes:

$$p_{T+1} = \frac{p_T(1-i)(1-r)(sr-md)+isr}{sr} \quad (7)$$

For reasons of simplicity we use time-independent incidence, recovery and mortality rates and abstract from the indices of age and gender in equation (7). The total derivate can be used to determine the impact of changing incidence, recovery and mortality rates on the prevalence in year $T + 1$.

$$\begin{aligned}
dp_{T+1} = & \left((1-i)(1-r) \frac{(sr-md)}{sr} \right) dp_T \\
& + \left(\frac{P_T(1-i)(1-r) + i - p_{T+1}}{sr} \right) dsr \\
& - \left(\frac{P_T(1-i)(1-r)}{sr} \right) dmd \\
& - \left(P_T(1-i) \frac{(sr-md)}{sr} \right) dr \\
& + \left(1 - P_T \frac{(sr-md)}{sr} + P_T hr \frac{(sr-md)}{sr} \right) di
\end{aligned} \tag{8}$$

In our model specification, the variables p_T , sr , md , r and i can take on values between 0 and 1 and the disease-specific mortality difference md is less (or in theory equal) than the survival rate of the entire population sr . As equation (8) shows, a higher prevalence rate p in year T leads to a higher prevalence rate in year $T + 1$. The theoretical one-to-one impact of this effect is lowered by the degree of the incidence and recovery rate as well as the disease-specific mortality difference.

An increase of the survival rate sr initially leads to an increase in both, the diseased and the non-diseased population. In conjunction with the incidence rate i , a positive impact on the prevalence rate in year $T + 1$ can be observed as the rising survival rate leads to a higher "at risk" population. In contrast to this, a higher mortality difference md leads to a decline in the prevalence rate in year $T + 1$. Both effects combined can be interpreted as follows: The smaller the difference in mortality between the diseased and non-diseased, the higher the positive impact of an increasing survival rate.

The influence of the recovery rate is negative and linked to the life expectancy of the patients. The more patients survive until the following year, the more can recover again. However, the higher the incidence rate and thus the proportion of new patients, the lower the proportion of persons who could potentially recover, which mitigates the negative effect of the recovery rate.

Considering the impact of increasing incidence rates also offers a connection between the incidence and the recovery rate. A higher proportion of recovered people leads to a higher

"at-risk" population. The opposite effect results from a higher prevalence rate in year T which comes along with a lower "at-risk" population.

2.2 Scenarios

Regarding the effects outlined above, a change of one variable will always affect the future prevalence in interaction with the other components. To illustrate these effects and the sensitivity of the model, we model six scenarios of changing disease-specific variables $md_{a,g}$, $i_{a,g}$ and $r_{a,g}$ for each of the ten diseases up to 2060, especially regarding the different hypotheses of expansion and compression of morbidity (see Tab. 1). In all scenarios we assume increasing survival rates $sr_{a,g}$ according to the moderately increasing life expectancy scenario $L2$ [39].

Tab. 1 Scenarios, assumptions and their effect on the future prevalence rate

		Variables				Effect on dp_{T+1}	Implementation
		md	sr	i	r		
Expansion 1 (Exp1)	Scenario		+			+	Increasing $sr_{a,g}$ according to $L2$ scenario
	Effect		+				
Expansion 2 (Exp2)	Scenario		+	+		++	Increasing $sr_{a,g}$ according to $L2$ scenario Linearly increasing i of 30 percent until 2060
	Effect		+	+			
Compression 1 (Comp1)	Scenario	+	+			?	Increasing $sr_{a,g}$ according to $L2$ scenario Increasing $md_{a,g}$ corresponding to increasing sr
	Effect	-	+				
Compression 2 (Comp2)	Scenario		+	-		?	Increasing $sr_{a,g}$ according to $L2$ scenario Shift of $i_{a,g}$ corresponding to increasing $sr_{a,g}$ resulting in a continuous decrease of i
	Effect		+	-			
Prevention (Prev)	Scenario		+	- -		?	Increasing $sr_{a,g}$ according to $L2$ scenario Linearly decreasing $i_{a,g}$ of 30 percent until 2035
	Effect		+	- -			
Extended Recovery (Rec)	Scenario		+		+	?	Increasing $sr_{a,g}$ according to $L2$ scenario Linearly increasing $r_{a,g}$ of 50 percent until 2060
	Effect		+		-		

Source: Own depiction.

In the first scenario, we hold all disease-specific variables constant over the time horizon. However, the assumption of a constant mortality difference and rising survival rates ($sr_{a,g,T+t} > sr_{a,g,T+t-1}$) leads to an increase in life expectancy of both the non-diseased and the diseased. In conjunction with constant incidence rates ($i_{ag} = \text{const}$), this results in an increasing duration of disease. Thus, the scenario *Expansion 1* can be interpreted as a type of *expansion of morbidity hypothesis*. This scenario serves as our baseline scenario in the following. The scenario *Expansion 2* is a more extreme scenario of the *expansion of morbidity*

hypothesis, assuming an additional 30 percent increase in incidence rates until 2060 ($i_{a,g,T+t} > i_{a,g,T+t-1}$).

The *compression of morbidity hypothesis* is considered in two different scenarios: In the scenario *Compression 1* only the healthy population benefits from the increasing life expectancy ($sr_{a,g}^D = \mathbf{const}$) which leads to a continuous increase in the mortality difference between the diseased and the healthy population. In the scenario *Compression 2* a shift of diseased cases in relation to increasing life expectancy is modelled which is in line with the "traditional" *compression of morbidity hypothesis* and leads to continuously decreasing incidence rates ($i_{a,g,T+t} < i_{a,g,T+t-1}$).

To highlight the long-term impact of effective prevention programmes, a scenario *Prevention* is modelled with temporarily decreasing incidence rates ($i_{a,g,T+t} < i_{a,g,T+t-1}$) up to 30 percent until 2035. In order to simulate possible effects of better medical care, e.g. due to disease management programmes, the scenario *Extended Recovery* assumes increasing recovery rates up to 50 percent until the year 2060 ($r_{a,g,T+t} > r_{a,g,T+t-1}$).

Interestingly (and as discussed in the section on the total differential of the prevalence rate), the total effect of the scenarios *Compression 1* and *2* as well as of the scenarios *Extended Recovery* and *Prevention* on the future (age- and gender-related) prevalence rate is not defined a priori and depends on the numerical ratio of disease-related input data and the increase of survival rates.

2.3 Dataset

The average disease-specific input data for each cohort and gender⁶ derives from a routine dataset of around four million insureds of the AOK Baden-Württemberg from 2009 to 2017.⁷ Due to this large number of people insured by the AOK in Baden-Württemberg, this population is approximately representative of the German population regarding the disease-rates within the age cohorts. Tab. 2 shows the specific selection criteria for each of the ten diseases. Since there are no coding guidelines for outpatient diagnoses in Germany, we use the criteria of the

⁶ An exception are age cohorts between 95 and 100 years, whose disease rates were determined in groups because of relatively few data points.

⁷ The disease-specific input data is determined in the pseudonymised database environment of the AOK Baden-Württemberg via SQL scripts, resulting in only anonymised rates being used for the model calculations. Further calculations are executed using Microsoft Excel.

AOK Research Institute published in various reports [40–43]. The M2Q⁸/M3Q criterion, for instance, only defines patients as diseased if they have a confirmed diagnosis in at least two and three out of four quarters of the year, respectively. Inpatient primary and secondary diagnosis are included without additional validation criteria. We complete missing data by the following procedure: If the selection criteria are satisfied the year before and the year after, insureds are classified as patients also in the incompletely coded year. Patients are classified as "new patients" when they fail to fulfil the prevalence criteria in any of the four previous years. The days of insurance of the patients identified by diagnosis are then set in relation to those of all insureds to calculate period prevalence $p_{a,g}$ and cumulative incidence $i_{a,g}$ for the years 2015 to 2017 [45]. For pulmonary cancer we use a five-year pre-observation period for the derivation of the incidence. To take into account the periodic character of depression, we use additional selection criteria for new cases and divergent diagnoses to determine prevalence and incidence.⁹

⁸ In Germany, this methodology is also used for allocating insureds to risk groups as part of the morbidity-based risk-adjustment scheme in the SHI [44].

⁹ Insureds with single diagnoses F34.1 or F38.1 (short depressive episodes) or isolated outpatient diagnosis in the previous year are not excluded from incidence calculation in order to identify new cases with a documented beginning depressive episode in the pre-observation year.

Tab. 2 Diseases and selection criteria

Disease	ICD-10	Validation criteria for outpatient diagnosis
Arthrosis	M15-M19	M2Q
Pulmonary, bronchial and tracheal cancer (CA)	C33, C34	M2Q
Coronary heart disease (CHD)	I20-I25	M3Q and prescription of at least 50 DDD of specific medication ^a
Chronic obstructive pulmonary disease (COPD)	J44	M2Q
cerebrovascular diseases (CVD)	I60-I69	M2Q
Dementia	F00-F03, F05.1, G23.1, G30, G31.0, G31.82	M2Q
Depression	Prevalence: F32, F33, F34.1 Incidence: only F32, not F33 (recurrent depressive disorders)	M2Q
Diabetes	E10-E14	M2Q or at least two prescriptions of antidiabetics/blood glucose test strips ^b
Dorsal pain	M40-M54	M2Q
Heart failure (HF)	I50, I11.0, I13.0, I13.2	M3Q and prescription of at least 50 DDD of specific medication ^c

Source: Own depiction using the ICD-10 classification system and according to the criteria published by AOK Research Institute [40-43].

^a ATC groups B01AC, C07, C01D, C08, C09A, C09BB, C09C, C09DB-

^b ATC groups A10A, A10B, A10X, V04CA03

^c ATC groups C09A, C09B, C07, C01A, C03, C08, C09C, C09D

For the calculation of recovery rates $r_{a,g}$ all surviving patients without a coded diagnosis in the following years are set in relation to the total of all surviving patients. For the definition of recovery we use a four-year follow-up period for diseases with realistic cure probabilities (dorsal pain, depression and CVD) and a five-year follow-up period for pulmonary cancer. The maximum follow-up period of eight years is used for all other diseases since there are still no cure possibilities available for their most common manifestations. Since dementia is (as of yet) characterized by an irreversible disease progression, no recovery rates are considered in these calculations.¹⁰ For chronic diseases, the recovery rates are to be interpreted as being symptom-free. A recurrence of the disease after years of asymptomatic illness is taken into account by the incidence rate. For each cohort, we calculate mortality differences $md_{a,g}$ as the difference between the 1-year survival rates of the diseased and all insureds in a given year and subtract them from the German population's survival probability $sr_{a,g}$ as described

¹⁰ However, for dementia we will assume emerging recovery rates in the scenario *Extended Recovery* for reason of comparability to the other diseases.

above.¹¹ Tab. 3 shows the population weighted determined input data as the average value for different age groups and overall average in the base year 2018 for each disease, in parentheses differentiated by gender (female vs male). In addition, Tab. 3 illustrates the demographic characteristics of the study population as average values of all years analyzed in millions and as percentage compared to those of the entire German population in 2018.¹²

¹¹ According to other studies, no mortality difference was found for arthrosis and dorsal pain [46, 47].

¹² The group of 0-17-year-olds is left out because the considered diseases are very rare in these cohorts.

Tab. 3 Determined disease-specific variables

	Total	Age cohort				
		18-29	30-44	45-64	65-84	>85
German population						
Million	83.0 (5.5, 6.0)	11.5 (7.6, 7.9)	15.5 (12.3, 12.3)	24.6 (8.5, 7.1)	15.6 (8.5, 7.1)	2.3 (1.5, 0.7)
%		13.8 (6.6, 7.2)	18.7 (9.2, 9.5)	29.7 (14.8, 14.8)	18.9 (10.3, 8.5)	2.8 (1.8, 0.9)
Study population						
Million	4.0 (2.1, 1.9)	0.6 (0.3, 0.3)	0.7 (0.4, 0.3)	1.1 (0.6, 0.5)	0.8 (0.4, 0.3)	0.13 (0.09, 0.03)
%		15.3 (7.6, 7.7)	17.9 (9.1, 8.8)	27.8 (14.4, 13.4)	19.4 (11.1, 8.3)	3.1 (2.3, 0.8)
Life expectancy total population						
	98.89	99.97	99.92	99.51	97.11	85.51
	(98.90, 98.88)	(99.98, 99.96)	(99.94, 99.90)	(99.65, 99.37)	(97.67, 96.43)	(86.08, 84.31)
Arthrosis						
<i>p</i> (%)	13.4 (15.8, 10.8)	0.4 (0.3, 0.4)	2.1 (2.1, 2.1)	15.6 (17.6, 13.5)	37.3 (41.6, 32.1)	46.9 (49.5, 41.5)
<i>i</i> (%)	1.5 (1.6, 1.3)	0.2 (0.2, 0.2)	0.7 (0.7, 0.7)	2.6 (2.8, 2.3)	2.7 (2.8, 2.5)	2.1 (2.0, 2.2)
<i>r</i> (% of patients)	1.6 (1.4, 1.8)	11.5 (12.4, 10.8)	6.3 (6.0, 6.6)	2.2 (2.0, 2.5)	1.0 (1.0, 1.1)	0.2 (0.2, 0.2)
<i>md</i> (%-points)	-	-	-	-	-	-
CA						
<i>p</i> (%)	0.20 (0.14, 0.26)	0.00 (0.00, 0.00)	0.01 (0.01, 0.01)	0.22 (0.17, 0.27)	0.63 (0.39, 0.92)	0.35 (0.21, 0.63)
<i>i</i> (%)	0.07 (0.05, 0.09)	0.00 (0.00, 0.00)	0.01 (0.01, 0.01)	0.08 (0.06, 0.11)	0.21 (0.13, 0.32)	0.12 (0.07, 0.22)
<i>r</i> (% of patients)	1.9 (2.5, 1.6)	-	0.5 (0.7, 0.2)	2.2 (2.7, 1.9)	1.8 (2.4, 1.4)	1.8 (2.2, 1.5)
<i>md</i> (%-points)	24.4 (22.0, 25.7)	-	14.9 (14.2, 15.8)	23.4 (20.9, 25.0)	24.8 (22.7, 25.8)	29.1 (25.1, 31.9)
CHD						
<i>p</i> (%)	5.9 (4.5, 7.3)	0.0 (0.0, 0.0)	0.3 (0.1, 0.5)	4.8 (2.5, 7.2)	19.2 (14.1, 25.4)	29.2 (25.8, 36.4)
<i>i</i> (%)	0.7 (0.6, 0.8)	0.0 (0.0, 0.0)	0.1 (0.1, 0.2)	0.8 (0.5, 1.0)	1.9 (1.6, 2.1)	2.0 (1.9, 2.1)
<i>r</i> (% of patients)	1.4 (2.0, 1.0)	-	8.3 (13.2, 6.9)	2.7 (5.2, 1.8)	1.0 (1.7, 0.6)	0.2 (0.3, 0.1)
<i>md</i> (%-points)	1.3 (1.3, 1.2)	-	1.1 (1.6, 0.9)	1.0 (1.0, 1.0)	1.4 (1.5, 1.4)	0.9 (0.9, 0.9)
COPD						
<i>p</i> (%)	4.1 (3.6, 4.6)	0.3 (0.3, 0.3)	0.9 (0.9, 1.0)	4.9 (4.2, 5.6)	10.8 (8.7, 13.3)	11.3 (9.1, 15.7)
<i>i</i> (%)	0.5 (0.4, 0.5)	0.1 (0.1, 0.1)	0.2 (0.2, 0.2)	0.7 (0.6, 0.8)	1.0 (0.8, 1.2)	0.9 (0.8, 1.1)
<i>r</i> (% of patients)	2.5 (2.9, 2.2)	7.8 (8.3, 7.3)	6.3 (6.5, 6.1)	2.8 (3.2, 2.5)	1.6 (2.2, 1.2)	0.4 (0.6, 0.2)
<i>md</i> (%-points)	1.4 (1.2, 1.7)	0.0 (0.0, 0.0)	0.3 (0.1, 0.4)	0.9 (0.7, 1.1)	2.0 (1.6, 2.3)	1.7 (1.2, 2.2)
CVD						
<i>p</i> (%)	4.6 (4.4, 4.8)	0.1 (0.1, 0.1)	0.4 (0.4, 0.4)	3.2 (2.7, 3.8)	15.1 (13.3, 17.4)	25.5 (24.2, 28.3)
<i>i</i> (%)	0.7 (0.7, 0.7)	0.0 (0.0, 0.0)	0.1 (0.1, 0.1)	0.7 (0.6, 0.8)	2.2 (2.0, 2.4)	3.0 (3.0, 3.0)
<i>r</i> (% of patients)	2.9 (3.2, 2.5)	8.9 (9.0, 8.9)	6.7 (7.3, 6.0)	4.1 (3.1, 3.7)	2.6 (3.1, 2.2)	1.7 (1.9, 1.3)
<i>md</i> (%-points)	1.4 (1.4, 1.4)	1.2 (1.1, 1.3)	1.4 (1.2, 1.6)	1.1 (1.0, 1.3)	1.5 (1.5, 1.5)	1.6 (1.7, 1.3)
Dementia						
<i>p</i> (%)	2.0 (2.4, 1.6)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.4 (0.3, 0.5)	6.3 (6.3, 6.2)	26.4 (28.1, 22.9)
<i>i</i> (%)	0.4 (0.5, 0.4)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.1 (0.1, 0.1)	1.4 (1.4, 1.5)	4.8 (4.9, 4.7)
<i>r</i> (% of patients)	-	-	-	-	-	-
<i>md</i> (%-points)	6.0 (5.2, 7.2)	-	1.5 (1.5, 1.5)	3.3 (2.5, 3.9)	6.3 (5.4, 7.3)	5.9 (5.1, 8.1)
Depression						
<i>p</i> (%)	12.5 (16.1, 8.7)	5.0 (6.6, 3.6)	9.9 (12.7, 7.2)	17.7 (22.3, 13.1)	20.8 (25.9, 14.7)	24.8 (28.5, 17.1)
<i>i</i> (%)	0.9 (1.0, 0.8)	0.8 (1.1, 0.7)	0.9 (1.1, 0.7)	1.0 (1.1, 1.0)	1.1 (1.2, 1.0)	1.4 (1.5, 1.4)
<i>r</i> (% of patients)	3.2 (2.9, 3.6)	5.8 (5.8, 5.8)	4.1 (4.0, 4.4)	3.1 (2.8, 3.6)	2.6 (2.4, 3.0)	1.3 (1.4, 1.1)
<i>md</i> (%-points)	0.1 (0.0, 0.1)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.1 (0.0, 0.1)	0.1 (0.0, 0.2)	-
Diabetes						
<i>p</i> (%)	11.1 (10.9, 11.2)	0.8 (0.9, 0.6)	2.5 (2.7, 2.3)	12.1 (10.4, 13.8)	31.6 (29.6, 34.1)	34.3 (34.2, 34.5)
<i>i</i> (%)	0.7 (0.7, 0.7)	0.2 (0.3, 0.1)	0.5 (0.6, 0.4)	1.0 (0.9, 1.2)	1.4 (1.3, 1.5)	1.1 (1.0, 1.2)
<i>r</i> (% of patients)	0.6 (0.7, 0.5)	3.4 (4.8, 1.4)	2.1 (3.1, 1.0)	0.7 (0.7, 0.6)	0.4 (0.5, 0.4)	0.2 (0.2, 0.1)
<i>md</i> (%-points)	0.4 (0.4, 0.4)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)	0.2 (0.1, 0.3)	0.4 (0.4, 0.4)	0.3 (0.3, 0.3)

Dorsal pain							
p (%)	28.3 (31.7, 24.8)	12.0 (13.8, 10.3)	22.7 (25.3, 20.1)	39.4 (43.3, 35.5)	48.7 (52.1, 44.5)	45.2 (46.5, 42.4)	
i (%)	2.5 (2.5, 2.4)	3.0 (3.3, 2.8)	3.3 (3.5, 3.2)	2.8 (2.8, 2.9)	2.1 (2.1, 2.1)	1.6 (1.6, 1.8)	
r (% of patients)	1.7 (1.6, 1.9)	3.1 (3.0, 3.1)	2.0 (1.9, 2.2)	1.5 (1.3, 1.7)	1.5 (1.4, 1.6)	1.5 (1.5, 1.3)	
md (%-points)	-	-	-	-	-	-	
HF							
p (%)	4.5 (4.6, 4.4)	0.0 (0.0, 0.1)	0.2 (0.2, 0.3)	2.5 (1.8, 3.2)	14.4 (13.4, 15.7)	35.3 (35.7, 34.5)	
i (%)	0.9 (0.9, 0.9)	0.0 (0.0, 0.0)	0.1 (0.1, 0.1)	0.7 (0.5, 0.9)	2.8 (2.6, 3.1)	4.9 (4.6, 5.4)	
r (% of patients)	2.6 (2.3, 2.9)	14.1 (15.3, 13.5)	11.4 (13.3, 10.4)	6.9 (7.1, 6.8)	2.1 (2.2, 2.0)	0.2 (0.2, 0.1)	
md (%-points)	4.3 (3.7, 4.9)	4.1 (5.0, 3.7)	3.3 (3.6, 3.1)	3.1 (2.9, 3.3)	4.5 (3.8, 5.2)	4.7 (4.0, 6.2)	

Source: Own Data and depiction in combination with data of Destatis and mortality.org, in parentheses differentiated by gender (female/male) Abbreviations: p = prevalence rate, i = incidence rate, r = recovery rate, md = mortality difference, CA = pulmonary, bronchial and tracheal cancer, CHD = coronary heart disease, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular diseases, HF = heart failure.

In order to derive the (future) cohort sizes $K_{a,g}$ and survival rates $sr_{a,g}$, we build different population projections based on input data from Destatis and statistics of mortality.org. As our starting point serves a *Stationary Population* with constant absolute births and constant life expectancy to separate the effects resulting from disease-specific (epidemiological) components from the effects of the composition of future cohort sizes on the *apr*. In our second population projection *Population (LE constant)* we abstract from a further increase in life expectancy. This projection is based on the German population in 2018 under the assumption of a fertility rate of 1.55 children per woman of fertile age. For our third population projection, *Standard Population (LE increasing)*, we further assume an increase of life expectancy from 83.3 to 88.1 years at birth for women and 78.5 to 84.4 at birth for men according to the moderate increase scenario *L2* of the 14th population projection [39]. Migration movement is not taken into account, as too little is known about whether disease rates of the German population are transferrable to migrants [48, 49]. Hence, the *Standard Population (LE increasing)* represents an absolute decline in population from 83.0 to 66.2 million by 2060, accompanied by an increasing old-age dependency ratio from 35.9 to 69.7 percent.¹³ However, for reason of comparability to other studies, we build a fourth population projection, *Population (Migration)*, where future migration is integrated according to the

¹³ Age a is limited between 0 and 100 years and with regard to gender, a distinction is made between male and female cohorts. We model our own population projection as Destatis does not publish a scenario without a future shift in migration. For this purpose, we use the data of mortality.org to model the survival rate for persons older than 100 years and calibrate the data on the life tables publishes by Destatis for the *L2* scenario. In a last step we aggregate the numbers for all persons older than 100 years as our disease specific input data has only few data points for cohorts of age 100 and older.

scenario *W2* of the 14th population projection [39].¹⁴ In this case the total population is 79.1 million people in 2060 and the old-age dependency is 58.8 percent.

3 Results

The presentation of our results starts in Tab. 4 with a comparison of the average prevalence rates *apr* (i.e. the total number of patients divided by the total number of the population) in the years 2018 and 2060 under the assumption of constant disease-specific variables over the time horizon. We use the three different population projections Stationary Population, Population (LE constant) and Standard Population (LE increasing) to separate the effects resulting from disease-specific (epidemiological) components and those occurring from the demographic components (initial population structure and increasing life expectancy). The values resulting from Standard Population (LE increasing) correspond to the baseline scenario Expansion 1.

Tab. 4 Projected average prevalence rates *apr* 2060 and percentage change compared to 2018

	<i>apr</i>		% change for different populations		
	2018	2060	Stationary population (only epidemiology)	Population (LE constant)	Expansion 1 Standard Population (LE increasing)
Arthrosis	13.4%	22.7%	30.8%	56.0%	69.8%
CA	0.2%	0.3%	16.2%	42.2%	53.9%
CHD	5.9%	9.5%	5.0%	38.5%	60.4%
COPD	4.1%	7.1%	31.0%	56.2%	71.9%
CVD	4.6%	8.7%	22.7%	63.2%	89.9%
Dementia	2.0%	4.4%	8.1%	67.7%	117.9%
Depression	12.5%	14.4%	3.3%	10.1%	15.7%
Diabetes	11.1%	14.4%	0.3%	18.8%	29.7%
Dorsal pain	28.3%	41.4%	39.9%	43.4%	46.1%
HF	4.5%	8.5%	15.4%	60.3%	90.4%

Source: Own depiction.

Abbreviations: CA = pulmonary, bronchial and tracheal cancer, CHD = coronary heart disease, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular diseases, HF = heart failure.

The results show a high increase in the *apr* for strongly age-related diseases like dementia, heart failure or CVD, with the ageing of the German population due to its current structure (Population (LE constant)) and rising life expectancy being the key factors driving the large growth rates. The ratio of people with dementia could more than double by 2060 within the

¹⁴ In line with the *W2* scenario published by Destatis, we assume an average positive net migration of 220,000 persons and consider their composition of age groups published by Destatis.

Standard Population (LE increasing). In contrast, the increase of the apr of dorsal pain is mainly driven by the epidemiological effect. Regarding arthrosis and COPD, the increase of apr can be attributed to both, the epidemiological as well as the demographic effects. The smallest increase of apr emerges for diabetes and depression. For both, the epidemiological effect is comparatively low. However, an increase in the average prevalence rate is to be expected for all diseases given the baseline scenario Expansion 1. Even when abstracting from an increasing life expectancy, the ageing of the German population in conjunction with the epidemiological effects will lead to a substantial increase of all diseases.

Fig. 1 presents the results for the apr in the year 2060 that occur under the different model scenarios (see Tab. 1) as well as under a simple extrapolation of age- and gender-related prevalence rates for the population of 2060 (status quo (SQ) principle). For this purpose, we use the Standard Population (LE increasing). The y-axis of Fig. 1 shows the relative change of the apr between 2018 and 2060 whereas the x-axis displays the value of the apr for the different scenarios in 2060. Additionally, the x-axis depicts the numbers of apr in 2018.

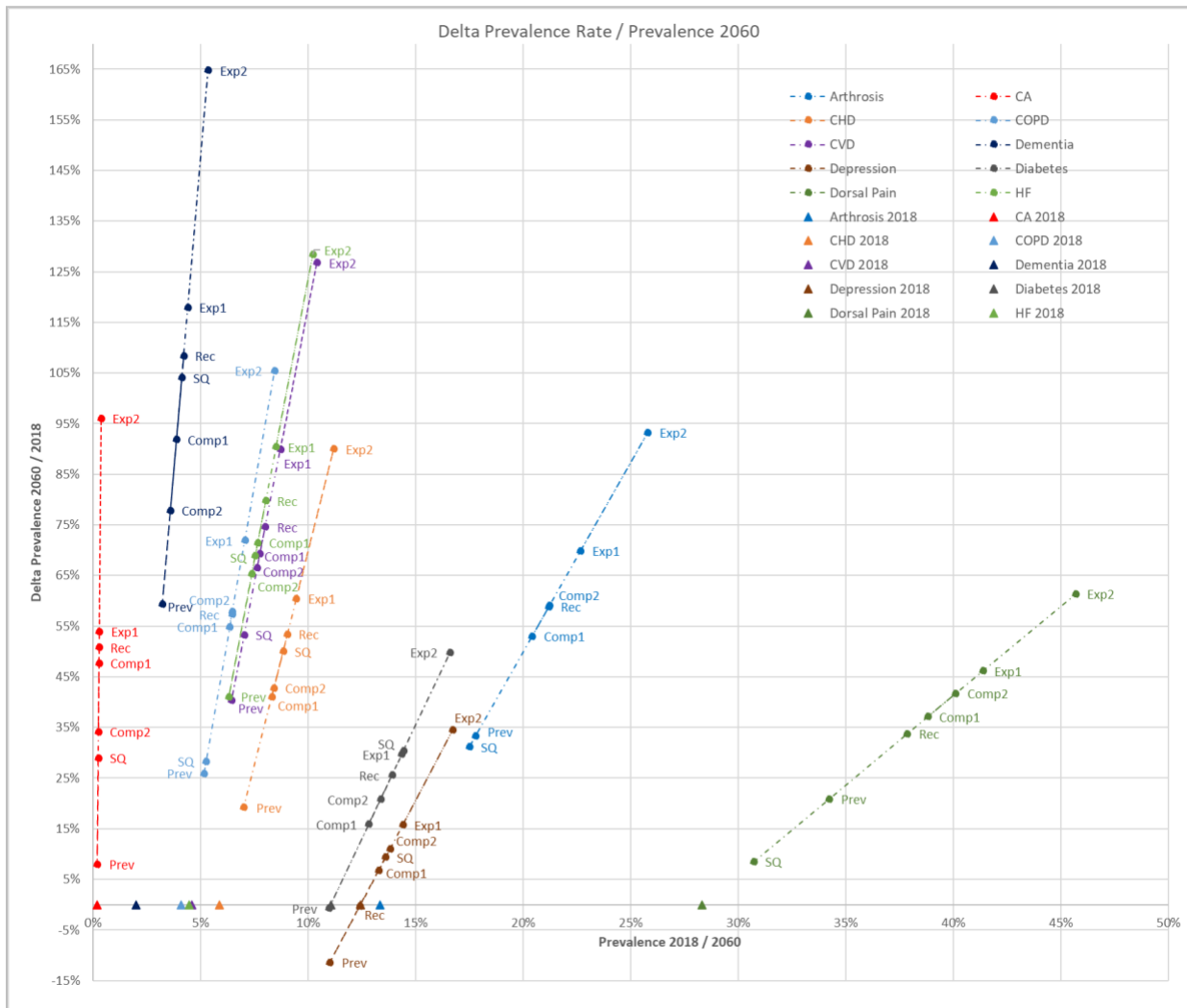
As a first result, Fig. 1 illustrates that the ranking of the ten diseases with respect to the value of the apr in 2060 is the same as in 2018, even though the relative change of the apr differs significantly between the ten diseases. That means that dorsal pain and arthrosis are expected to be the two major diagnoses in 2060, although e.g. dementia offers a significantly higher change in the apr in all scenarios.

Second, the results show a different impact of the rival hypotheses regarding the consequences of increasing life expectancy on future disease burden: The expansion of morbidity scenarios Expansion 1 and 2 lead to a soaring increase of all diseases compared to the other scenarios. Especially the scenario of Expansion 2 (with an assumed increase of the incidence rate by 30 percent until 2060) offers a strong increase of the apr. For strongly age-related diseases such as dementia, CVD or HF, the Compression 2 scenario (shifting the incidence to higher age groups) has a stronger impact on the apr than the Compression 1 scenario, in which the life expectancy for patients is constant over time and only the healthy population benefits from the increasing life expectancy. Yet even in the compression of morbidity scenarios, an increase in all the common diseases can be expected. In other words: The increase in burden of disease due to increasing life expectancy and high incidence rates in older age groups can be mitigated but not fully compensated by a compression.

The assumption of continuously rising recovery rates (scenario Extended Recovery) has an even smaller impact on future apr, although this is also attributable to the low chances of recovery for the considered diseases in general. Only for depression an increasing recovery rate would lead to a constant prevalence rate in the long term. A diminishing effect on future long-term prevalence for all diseases can only be seen in the scenario Prevention. For diabetes and depression, the Prevention scenario even leads to a small decline in the apr. This highlights the importance of effective prevention regarding the upcoming demographic transition.

At a first glance a (simple) extrapolation of current prevalence rates should range between the expansion and compression scenarios, our results offer that this is not true for all diseases. In particular, for dorsal pain, arthrosis, COPD, and cancer the status quo principle leads to an apr in 2060 which is smaller than the scenarios of Prevention. Hence, our results show a wide range future developments of the different diseases depending on the chosen parameters for modelling.

Fig. 1 Relative change in *apr* until 2060 in the different scenarios



Source: Own depiction.

Abbreviations: Exp1 = scenario Expansion 1, Exp2 = scenario Expansion 2, Comp1 = scenario Compression 1, Comp2 = scenario Compression 2, Rec = scenario Extended Recovery, Prev = scenario Prevention, CA = pulmonary, bronchial and tracheal cancer, CHD = coronary heart disease, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular diseases, HF = heart failure.

Tab. 5 shows the absolute results of the projection for 2040 and 2060. As the Standard Population (LE increasing) neglects future migration, the total number of people in Germany will decline between 2040 and 2060. Thus, for the most scenarios and diseases the total numbers of patients are higher in 2040 than 2060. However, the results given the projection Population (Migration) in parentheses offer the opposite effect. Hereby we assume identical disease-related input data for migrants.

All in all, our calculations show that all of the ten diseases are expected to increase up until 2060: Diseases of the musculoskeletal system like dorsal pain and arthritis will be responsible for the majority of the future disease burden within the German population, possibly affecting about 25-27 and 13-15 million people, respectively, by 2060. Diabetes, which is closely related

to other diseases like CHD, is expected to impact at least 9.5 million patients in case of expanding morbidity. With up to 7.4 million people affected in 2060, CHD will continue to be the most common cardiovascular disease. The high growth rates of primarily age-related diseases such as CVD or HF are also steep in absolute terms. Only if prevention strategies are successful, the significant increase in number of patients could be alleviated in the long run.

Tab. 5 Projected number of patients 2060 in the different scenarios

	Number of patients <i>P</i> (million) in 2060												
	2018	Expansion 1		Expansion 2		Compression 1		Compression 2		Extended Recovery		Prevention	
		2040	2060	2040	2060	2040	2060	2040	2060	2040	2060	2040	2060
Arthrosis	11.1	15.7 (16.1)	15.0 (16.5)	16.7 (17.0)	17.1 (18.8)	15.1 (15.5)	13.5 (14.9)	15.3 (15.6)	14.1 (15.3)	15.3 (15.7)	14.0 (15.4)	13.5 (13.7)	11.8 (12.9)
CA	0.16	0.22 (0.22)	0.20 (0.22)	0.25 (0.25)	0.26 (0.28)	0.22 (0.22)	0.19 (0.21)	0.21 (0.21)	0.17 (0.19)	0.22 (0.22)	0.20 (0.21)	0.16 (0.16)	0.14 (0.15)
CHD	4.9	6.4 (6.4)	6.3 (6.7)	6.9 (6.9)	7.4 (7.9)	6.0 (6.1)	5.5 (5.9)	6.1 (6.1)	5.6 (5.9)	6.2 (6.3)	6.0 (6.4)	5.2 (5.2)	4.7 (5.0)
COPD	3.4	4.9 (5.0)	4.7 (5.1)	5.3 (5.4)	5.6 (6.1)	4.7 (4.8)	4.2 (4.6)	4.7 (4.8)	4.3 (4.7)	4.7 (4.8)	4.3 (4.7)	4.0 (4.1)	3.4 (3.7)
CVD	3.8	5.8 (5.9)	5.8 (6.2)	6.3 (6.4)	6.9 (7.4)	5.5 (5.6)	5.2 (5.5)	5.5 (5.5)	5.1 (5.4)	5.6 (5.7)	5.3 (5.7)	4.6 (4.7)	4.3 (4.5)
Dementia	1.7	2.6 (2.6)	2.9 (3.0)	2.9 (2.9)	3.5 (3.7)	2.5 (2.5)	2.6 (2.7)	2.4 (2.4)	2.4 (2.5)	2.5 (2.6)	2.8 (3.0)	2.0 (2.0)	2.1 (2.2)
Depression	10.3	10.6 (11.0)	9.5 (10.7)	11.3 (11.7)	11.1 (12.4)	10.3 (10.7)	8.8 (9.9)	10.5 (10.8)	9.1 (10.2)	10.1 (10.4)	8.2 (9.2)	9.1 (9.4)	7.3 (8.1)
Diabetes	9.2	10.1 (10.3)	9.5 (10.4)	10.7 (11.0)	11.0 (12.0)	9.7 (9.9)	8.5 (9.4)	9.9 (10.1)	8.9 (9.6)	10.0 (10.2)	9.2 (10.1)	8.7 (8.9)	7.3 (7.9)
Dorsal pain	23.5	29.4 (30.7)	27.4 (31.1)	30.7 (32.1)	30.3 (34.5)	28.6 (29.9)	25.7 (29.3)	29.0 (30.3)	26.6 (30.0)	28.5 (29.7)	25.1 (28.5)	26.1 (27.1)	22.7 (25.5)
HF	3.7	5.6 (5.6)	5.6 (6.0)	6.1 (6.2)	6.8 (7.2)	5.3 (5.4)	5.1 (5.4)	5.2 (5.3)	4.9 (5.2)	5.4 (5.5)	5.3 (5.6)	4.3 (4.4)	4.2 (4.4)

Source: Own depiction.

Abbreviations: CA = pulmonary, bronchial and tracheal cancer, CHD = coronary heart disease, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular diseases, HF = heart failure.

Our results can be compared with other recent studies for Germany. From the 16 (16/160) studies for Germany in our literature review (concerning our ten most common non-infectious diseases) only six (6/16) were published in the last five years and most of them focussing on cancer (3/6), dementia (2/6) or diabetes (1/6). For diabetes, Tönnies et al. (2019) [50] calculate with the help of an illness-death model and under the assumption of constant incidence rates a higher number of 11.0 million patients for 2040. The discrepancy to our projection (10.3 million) for 2040 is probably due to their older input data, which stem from 2010. The most recent study on dementia by Alzheimer Europe (2020) [51] project 2.7 million patients for 2050 with a status quo projection which lies in the interval of our forecast with 2.5 to 3.0

million people affected. Milan & Fetzer (2019) [38] project 2.6 to 3.3 dementia patients for 2060 by using the same model. The slight differences to their results are attributable to more recent population statistics and disease-specific input data. A comparison of our results with the three studies focusing on cancer is difficult as two of them consider the disease pattern of lung cancer and take a short-term perspective (up to the year 2020), whereas the third focuses on a trend projection of incidence rates.

4 Discussion

A projection of ten common non-infectious diseases in concurrent scenarios based on a rich and consistent data set is expanding the literature on the development of future disease burden in light of the demographic transition. In this context, ours is one of the few studies using an illness-death approach with recovery and modelling compression of morbidity and prevention scenarios. Furthermore, due to its time-discrete specification, our model could be directly linked to any (official) population projection, and therefore adapted by institutions in the field of policy consulting.

In contrast to a naïve extrapolation (status quo principle), our analysis highlights the importance of focusing on the interdependence between demographic and disease-specific components in projecting future disease burden. Based on six different scenarios we show the possible future range of disease burden and reveal the large differences between the various diseases in interaction with the demographic components. Considering these differences, it becomes clear that the extrapolation of prevalence rates can only reflect the cohort effect caused by population structure and not epidemiologically induced changes in the burden of disease, as observed e.g. for dorsal pain. In contrast, for CHD the status quo projection ranges, as expected, between the compression and expansion scenarios due to minor epidemiological influences.

With regard to the probability of the different hypotheses on future disease burden, the study situation remains inconclusive. Chatterji et al. (2015) [52] show with their detailed review of studies across the world how much the results vary for observed compression or expansion in recent years. However, just looking on the prevalence of chronic diseases (not e.g. in the quality of life) resulted more frequently in an expansion. Considering very similar diseases as our study in connection with proximity to death, Beltrán-Sánchez et al. (2016) [53] show for

the United States that those who died in recent times had a higher prevalence of chronic diseases in periods far from death, especially of those chronic diseases with low mortality and high frequency.

Interestingly, even in international studies there are only a few projections for the two major common diseases dorsal pain and arthrosis (1/160 dorsal pain, 10/160 arthrosis or joint replacement procedures), although these diseases are expected to increase the most in total numbers of patients according to our calculations. Our results can be compared with those of Kingston et al. (2018) [54], who use a population sample to model multimorbidity and prevalence of similar diseases for over 65-year-olds in England until 2035. In line with our findings, they predict a significant increase for all diseases considered except depression, but with the largest increases for cancer, diabetes and respiratory diseases. In line with our findings, the only study that also compares different compression scenarios, but with regard to disability due to similar diseases in the UK, by Jagger et al. (2006) [30], concludes that improvements in population health cannot fully compensate the effect of population ageing and that there will still be an increase in number of older people with disabilities.

Of course, our results are also subject to limitations. The Markov assumption of the illness-death model implies that the transition probabilities depend only on the current state and are not influenced by past events. But complex long-term studies, e.g. on the probability of re-disease after a successful recovery, would be necessary to heal this caveat, which are not available for such a large number of insureds. However, regarding the fit with observed incidence or prevalence rates, multistate models used in a retrospective analysis of epidemiological study data (in contrast to regression models) score well [55, 56].

Even if our discrete model has certain advantages, modelling in discrete time might be overestimating epidemiological effects. By comparing the results of a discrete-time model with those of a continuous model, Brinks & Landwehr (2014) [57] show that a projection in discrete time can overestimate future prevalence. However, the authors also state that smaller projection intervals lead to smaller deviations. Our chosen one-year interval leads to about a ten percent overestimation in their model.

Nonetheless, this overestimation effect might be somehow offset by the conservative estimates generated by using insurance data, which constitutes another limitation of our measure. Insurance or routine data is primarily collected for invoicing medical services when

patients visit a physician. Thus, the resulting prevalence and incidence rates can only be interpreted as treatment rates and are usually slightly lower than those obtained by surveys. In conjunction with the required validation procedures, the actual population incidence could be underestimated. Due to the incomplete coding observed for some diseases, it is also questionable whether the documented onset of illness corresponds to the real date of incidence.

A third limitation could be our data set: The rates determined from the AOK Baden-Württemberg might differ from the rates of the total German population. However, regarding gender-specific differences or frequencies in older cohorts that are particularly relevant for this analysis, various studies indicate that large AOK data sets are representative [58–60].

Further insights could be obtained by including multi-morbidity in our model. Comorbidity analyses could also provide more detailed insights into causes of mortality differences, which would help limiting the range of possible future scenarios. Despite the limitations mentioned, our results can offer an important guide to rational decisions in health care, especially due to the actuality and detail level of the data used. Although the strongly age-related diseases such as dementia or heart failure show the highest relative increase rates, the enormous prevalence of musculoskeletal diseases and depression should not be ignored. Most importantly, for almost all considered diseases a significant increase in burden of disease can be expected even in case of a compression of morbidity.

5 Conclusion

We think that our approach is useful for consulting health care professionals and politicians in preparing for the upcoming pressure on health care capacities. As the current COVID-19 crisis is showing, health care capacities are quite scarce. Even in our most optimistic scenario we would have the same pressure – at least in numbers – from chronic diseases as currently experienced during the pandemic. The lesson from our analysis is clear: A massive caseload is emerging on the German health care system, which can only be alleviated by more effective prevention. Immediate action by policy makers and health care managers is needed, as otherwise the prevalence of widespread diseases will become unsustainable from a capacity point-of-view.

Contribution 2: How to predict drug expenditure – A Markov model approach with risk classes¹⁵

1 Introduction

Expenditures for pharmaceuticals are one of healthcare systems' most dynamic cost drivers. However, the widespread use of expensive biologics and the ongoing increase in launch prices makes it difficult to predict the future development of expenditures for pharmaceuticals [62, 63]. Furthermore, in light of the ageing of OECD societies, the sustainable financing of drug spending becomes a challenge [62–64]. The OECD provides an overview of forecasting activities for pharmaceutical expenditures of its member states [62]. In contrast to short-term forecasts (1-5 years), the OECD identifies only a few studies with a medium- and long-term perspective. Moreover, none of these studies consider the influence of different patient groups with specific profiles of drug consumption and thus different cost risks for the healthcare system in detail.

The pharmaceutical market can be divided into the market segment of off-patent drugs, characterized by high price competition and/or a high degree of price regulation, and the market segment of patent-protected drugs with, for the most part, stand-alone products [65]. For Germany, most top-selling drugs are patent-protected blockbusters like oncologics, immunotherapeutics, or pharmaceuticals for cardiovascular diseases [26]. However, in the last few years, most of the increase in pharmaceutical spending in Germany and many other countries is attributable to pharmaceuticals for rare diseases (so-called orphan drugs) [24, 25]. The presumable reason for this is a less stringent legal framework for drug evaluation and reimbursement for new launches of orphan drugs compared to new launches of blockbusters [66, 67]. Overall, in 2019 half of all newly launched pharmaceuticals in Germany were orphan drugs, most of them for cancers [26]. Consequently, this trend is leading to an increasing concentration of spending on high-risk patients [68].

In this paper, we compute different medium and long-term projections of pharmaceutical expenditure in Germany from 2019 to 2060. For this purpose, we use a Markov approach with different risk groups by costs and transition probabilities between the risk groups. Even

¹⁵ Hofbauer-Milan V, Fetzter S, Hagist C. How to Predict Drug Expenditure: A Markov Model Approach with Risk Classes. *Pharmacoeconomics*. 2023;41:561–572. <https://doi.org/10.1007/s40273-023-01240-3> [61].

though discrete-time Markov models are widely used in Pharmacoeconomics, their application tends to focus on cost-benefit, cost-effectiveness, or cost-utility analyses [69, 70] rather than on population-based expenditure projections. Our model is based on a large statutory sickness funds dataset covering approximately four million insureds. All our modeling is done within a population projection in which we simulate the distribution and development of risk groups for the German population. This allows us to distinguish projections with constant shares (status quo), projections with the time-to-death assumption, and projections via the Markov modeling mentioned above. With this comprehensive approach, we can extend the literature both in terms of medium- and long-term drug expenditure projections and on the impact of the increasing high-cost cases on future pharmaceutical spending. By making different assumptions about gains in life expectancy and risk group-specific future growth trends of pharmaceutical costs, we can show the possible future range of pharmaceutical spending for the healthcare system. As many scholars support the assumption that healthcare spending is determined less by age itself than by proximity to death [11, 12, 14], we also account for the costs of dying in one projection model.

The paper is organized as follows: First, we describe the projection model, the underlying data set, and the different projection scenarios for the future development of pharmaceutical spending in Germany. We then present our projection results, followed by a discussion of the results considering current literature and limitations. At the end, we draw the respective conclusions and provide policy implications.

2 Methods

We project future pharmaceutical expenditures for Germany until 2060. As usual for this long time horizon, we focus on the demand side [62] and, particularly, on the impact of high-cost patients. We follow the work of Thiébaud et al. (2013) [71] and use a Markov model approach based on transition probabilities to simulate future pharmaceutical expenditure in various scenarios. Our model operates with different risk groups by costs, which can transition among themselves and also transition to death with group-specific mortality (see Pritchard (2006) [72], Sherris & Wei (2021) [73] or Rickayzen & Walsh (2002) [74]). Since we focus on the influence of patients with very high drug spending, the risk in our model is determined by prior year pharmaceutical expenditure, as this has proven to be a good predictor of high spending in the future [22, 23]. In line with Kildemoes et al. (2006) [75] and Morgan & Cunningham

(2011) [76], we distinguish the costs of survivors and deceased to account for the costs of dying. Following the Intergenerational Report of the Commonwealth of Australia (2021) [77], we also include risk-group-specific cost growth rates in our projection.

The data in our model is calibrated to the pharmaceutical expenditures in 2019 of the German SHI, covering about 90 percent of the German population. The population in our model is split into six (different-in-size) risk groups based on their share of total pharmaceutical spending. Risk group one represents the most expensive one percent, risk group two the second most expensive four percent, and the other risk groups the following five, ten, 30, and 50 percent. For each risk group, we calculate age- and sex-related affiliation probabilities.

We use a deterministic Markov approach to determine how the different risk groups transition over time. For each cohort by age a and sex s , we calculate transition probabilities and mortality rates as shown in Fig. 2. The initial risk groups rg_t (R1-R6) are shown in row one. Every cohort of a risk group has a certain transition probability $tp_{rg_t,rg_{t+1}}^{a,s}$ to move to another risk group rg_{t+1} or to die with a certain mortality rate $mr_{rg_t,rg_{t+1}}^{a,s}$ in year $t + 1$. The rates $tp_{rg_t,rg_{t+1}}^{a,s}$ and $mr_{rg_t,rg_{t+1}}^{a,s}$ are calibrated to the life tables associated with the projection of the German population up to 2060. For each risk group, we calculate average daily per-capita pharmaceutical costs differentiated by deceased and survivors. In the Markov model, the origin risk group in year t determines the amount of expenditure in year $t + 1$. Thus, in year $t = 2018$, we use age and sex-related (affiliation) probabilities to distribute the population among the six risk groups to begin modeling from year $t + 1 = 2019$ using the transition probabilities and mortality rates. In allocating expenditure to survivors and decedents, we calibrate the model assuming a daily spending of 360 days for survivors and 180 days for decedents.

Fig. 2 Transition Matrix (illustrated by the example of female cohorts for the transition from 2018 to 2019)

Cohort 1918, women		$t + 1$											
Risk groups	R1	R2	R3	R4	R6	R6	m_1	m_2	m_3	m_4	m_5	m_6	
Cohort 2016, women		$t + 1$											
Risk groups	R1	R2	R3	R4	R6	R6	m_1	m_2	m_3	m_4	m_5	m_6	
Cohort 2017, women		$t + 1$											
Risk groups	R1	R2	R3	R4	R6	R6	m_1	m_2	m_3	m_4	m_5	m_6	
Cohort 2018, women		$t + 1$											
Risk groups	R1	R2	R3	R4	R6	R6	m_1	m_2	m_3	m_4	m_5	m_6	
t	R1	$tp_{1,1}$	$tp_{1,2}$	$tp_{1,3}$	$tp_{1,4}$	$tp_{1,5}$	$tp_{1,6}$	$mr_{1,1}$	0	0	0	0	0
	R2	$tp_{2,1}$	$tp_{2,2}$	$tp_{2,3}$	$tp_{2,4}$	$tp_{2,5}$	$tp_{2,6}$	0	$mr_{2,2}$	0	0	0	0
	R3	$tp_{3,1}$	$tp_{3,2}$	$tp_{3,3}$	$tp_{3,4}$	$tp_{3,5}$	$tp_{3,6}$	0	0	$mr_{3,3}$	0	0	0
	R4	$tp_{4,1}$	$tp_{4,2}$	$tp_{4,3}$	$tp_{4,4}$	$tp_{4,5}$	$tp_{4,6}$	0	0	0	$mr_{4,4}$	0	0
	R5	$tp_{5,1}$	$tp_{5,2}$	$tp_{5,3}$	$tp_{5,4}$	$tp_{5,5}$	$tp_{5,6}$	0	0	0	0	$mr_{5,5}$	0
	R6	$tp_{6,1}$	$tp_{6,2}$	$tp_{6,3}$	$tp_{6,4}$	$tp_{6,5}$	$tp_{6,6}$	0	0	0	0	0	$mr_{6,6}$

Source: Own depiction.

3 Data

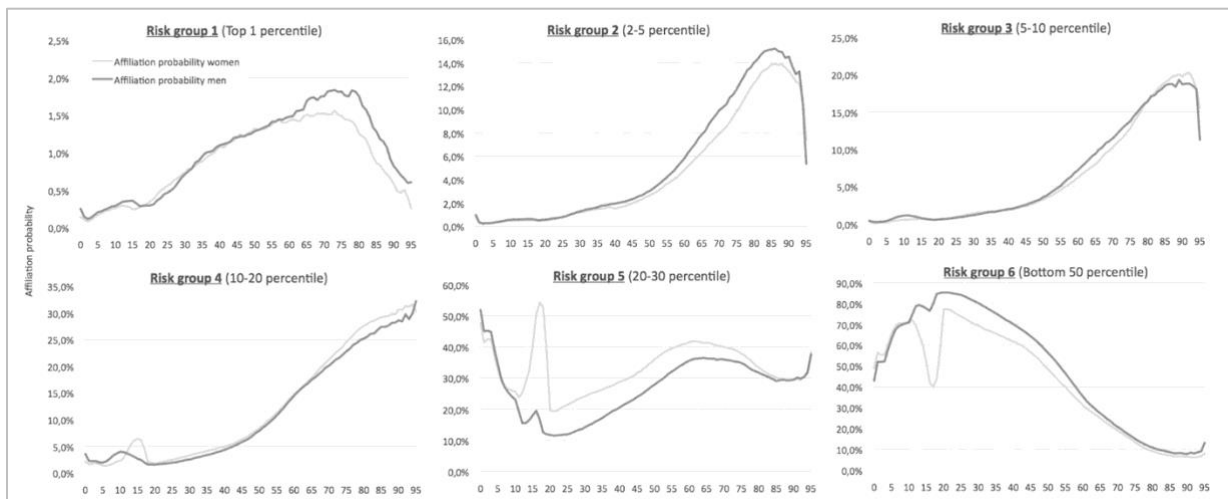
As input data for the population projection, we use official population statistics and life tables from Destatis [78] and mortality.org [79] to derive (future) cohort sizes and survival rates. In line with the fertility assumption G2 and mortality assumption L2 of the official forecast [39], we assume a constant total fertility rate of 1.55 children per woman of childbearing age and an increase in the life expectancy at birth from 83.4 (78.6) in the year 2019 to 88.1 (84.4) in the year 2060 for women (men). Further, we abstract from future migration movements.

The risk group-specific data is based on a dataset from the AOK Baden-Württemberg, a large German sickness fund with around four million insureds, spanning the years 2010 to 2019. We divide the insured population into the six (different-sized) risk groups, considering only individuals with at least 360 insurance days. Since we need both a pre-observation year with a full insurance period and a post-observation year to distinguish between deceased and survivors, the data used stems from the period 2011 to 2018. Tab. 6.a provides an overview of the study population. For every cost group, it offers for the year 2018 the number of insureds, the share of total pharmaceutical costs, the distribution of women and men, and the average age. Given the overall size of the dataset, the sex distribution, and the total population's mortality rate compared to official population statistics, it can be assumed that the data is representative [80, 81].

Tabl. 6.b shows the average daily per-capita costs per risk group differentiated by survivors and deceased, which we calibrate to the total pharmaceutical expenditures of the SHI for Germany in 2019.¹⁶ To account for spending trends, we calculate the expenditure growth rates per risk group from 2010 to 2018, additionally differentiated by survivors and deceased.

The age and sex-related (affiliation) probabilities for every risk group obtained from the AOK Baden-Württemberg dataset are illustrated in Fig. 3. We can see that the probability of incurring high costs is clearly dependent on age, especially evident in risk groups 2 to 4. In risk group 1, the curve is less steep, with exceptionally high costs compared to the other groups. The observed swings in the cohorts of 14- to 21-year-old women in groups 4 and 5 are attributable to contraceptives that are reimbursed by SHI in Germany for these age groups.

Fig. 3 Initial affiliation probability in the different risk groups by age 2018



Source: Own data and depiction. Please note the varying axis scaling.

The data set allows us to follow each insured over the complete years 2010 to 2018. Thus, we can also track how frequently risk classes are changed (or individuals die). The transition probabilities for the survivors (as a weighted average over sex and age) as well as the share of decedents per initial risk group and their average age are illustrated in Table 6.c. As the probability of changing the risk class is constant across years, we use the average of the age-, sex- and risk-group-specific one-year transition probabilities $tp_{rg_t,rg_{t+1}}^{a,s}$ and mortality rates $mr_{rg_t,rg_{t+1}}^{a,s}$ from 2011 to 2018 in the simulation. The transition probabilities of zero-year-olds

¹⁶ For the cohort of zero-year-olds, we use only total costs without dividing them into cost groups.

are estimated based on the risk group affiliations of one-year-olds. In the next step, all values are calibrated to the corresponding years' life tables associated with the German population.¹⁷

Tab. 6 Study population characteristics and modeling assumptions

a. Study population characteristics 2018							
Risk group	Population percentile	Cost-share	Sex distribution		Average age		
			Women	Men	Women	Men	Total
1	Top 1%	46%	52.9%	47.1%	54.0	52.6	53.4
2	2-5%	23%	51.3%	48.7%	68.0	64.0	66.1
3	5-10%	12%	54.0%	46.0%	69.1	64.6	67.0
4	10-20%	10%	57.2%	42.8%	63.2	60.1	61.9
5	20-50%	8%	58.9%	41.1%	46.6	44.9	45.9
6	Bottom 50%	1%	47.1%	52.9%	35.3	33.7	34.5
Total	100%	100%	52.2%	47.8%	45.7	42.1	44.0
b. Average cost structure							
Risk group	Calibrated average daily costs 2019		Cost growth rates per year 2010-2018				
	Survivors	Deceased	Survivors	Deceased			
1	56.5 €	68.6 €	6.3%	8.0%			
2	8.6 €	12.7 €	2.3%	3.0%			
3	3.8 €	6.3 €	1.6%	2.2%			
4	1.9 €	4.5 €	1.1%	1.8%			
5	0.6 €	4.7 €	-0.2%	4.2%			
6	0.1 €	3.4 €	1.0%	1.6%			
Total	1.4 €	11.7 €	3.2%	3.5%			
c. Average transition probabilities							
Risk group Year t	Risk group Year $t + 1$						Mortality rate
	1	2	3	4	5	6	
1	65.3%	15.2%	1.7%	1.8%	2.6%	1.9%	11.5%
2	5.4%	63.1%	15.7%	4.2%	2.9%	1.9%	6.8%
3	1.0%	14.6%	45.9%	23.8%	6.7%	3.4%	4.8%
4	0.4%	2.3%	11.4%	50.2%	25.7%	6.4%	3.6%
5	0.2%	0.5%	1.5%	9.5%	60.2%	25.7%	2.5%
6	0.1%	0.2%	0.5%	1.7%	19.3%	76.0%	2.1%

Source: Own data and depiction.

4 Scenarios

We use different scenarios, all presented in Tab. 7, to simulate the range of future drug spending in the German SHI. The benchmark is a *Status quo* simulation, as often done in the literature. In this scenario, the cost distribution per age and sex of the projection's base year ("status quo") is linked to the future demographic development of the population. In the

¹⁷ The aggregate claim data is determined in the pseudonymized database environment of the AOK Baden-Württemberg via SQL scripts, resulting in only anonymized data being used for the model calculations. Further calculations are executed using Microsoft Excel and Matlab.

second scenario (scenario *Cost of dying*), we additionally distinguish between the sex- and age-specific costs of survivors and decedents. As our population projection comes along with an increase in life expectancy, this approach mimics the cost-of-dying theory (for the costs occurring in the last half-year before dying).

In scenarios 3 to 5, we use the Markov model described above to simulate future pharmaceutical expenditure. Scenario 3 serves as our *Baseline* scenario, where we use the transition probabilities $tp_{rg_t,rg_{t+1}}^{a,s}$ and the risk group-specific mortality rates $mr_{rg_t,rg_{t+1}}^{a,s}$ to model future pharmaceutical spending. Since the mortality rates are calibrated to the moderately increasing life expectancy assumed for the underlying population, this results in a continuous gain in life expectancy for all cost groups. In scenarios 4 and 5, we also show the impact of an uneven gain in life expectancy for different risk groups. In scenario 4, *Expensive Ageing*, the high-cost groups 1-4 benefit from the increasing survival rate. In contrast to this, in scenario 5, *Inexpensive Ageing*, the very low-cost groups 5 and 6 drive the increase in life expectancy.

In all scenarios, we initially apply constant pharmaceutical costs over time (no pharma growth surplus). In a further step, we consider uniform and finally risk group-specific growth rates of per-capita pharmaceutical costs (pharma growth surplus). For this purpose, we use the observed average cost growth rates of our dataset from 2010 to 2018 (see Tab. 6.b) less an alternative economic nominal growth rate of three percent per year. The latter amount follows the annual real GDP growth projected by the European Commission [82] (one percent per year) plus the European Central Bank's inflation target [83] of two percent per year.

Tab. 7 Projection scenarios and their model calculation

No	Scenario	Description	Model calculation		
			Pharmaceutical costs	Transition probability	Mortality rate
1	Status quo	<ul style="list-style-type: none"> Extrapolation of age and sex distribution 	Daily pharmaceutical average costs per sex and age	-	<ul style="list-style-type: none"> Age and sex-specific mortality rate Decreasing according to the L2 scenario
2	Costs of dying	<ul style="list-style-type: none"> Extrapolation of age and sex distribution Additional distinction of costs between deceased and survivors 	Daily pharmaceutical average costs per sex and age differentiated by survivors (360 days) and decedents (180 days)	-	<ul style="list-style-type: none"> Age and sex-specific mortality rate Decreasing according to the L2 scenario
3	Baseline	<ul style="list-style-type: none"> Markov model simulation Consideration of risk group-specific transition probabilities and mortality rates All cost groups benefit from increasing life expectancy 	Costs $t + 1$ according to risk group membership in t , differentiated by survivors and deceased in year $t + 1$	$tp_{rg_t,rg_{t+1}}^{a,s}$	<ul style="list-style-type: none"> $mr_{rg_t,rg_{t+1}}^{a,s}$ Calibrated to L2 scenario Uniform decrease across all risk groups
4	Expensive Ageing	<ul style="list-style-type: none"> Markov model simulation Consideration of risk group-specific transition probabilities and mortality rates High-cost groups 1-4 benefit from increasing life expectancy 	Cost $t + 1$ according to risk group membership in t , differentiated by survivors and deceased in year $t + 1$	$tp_{rg_t,rg_{t+1}}^{a,s}$	<ul style="list-style-type: none"> $mr_{rg_t,rg_{t+1}}^{a,s}$ Calibrated to L2 scenario Decreasing only for RG1-4
5	Inexpensive Ageing	<ul style="list-style-type: none"> Markov model simulation Consideration of risk group-specific transition probabilities and mortality rates Low-cost groups 5-6 benefit from increasing life expectancy 	Cost $t + 1$ according to risk group membership in t , differentiated by survivors and deceased in year $t + 1$	$tp_{rg_t,rg_{t+1}}^{a,s}$	<ul style="list-style-type: none"> $mr_{rg_t,rg_{t+1}}^{a,s}$ Calibrated to L2 scenario Decreasing only for RG5-6

Source: Own depiction.

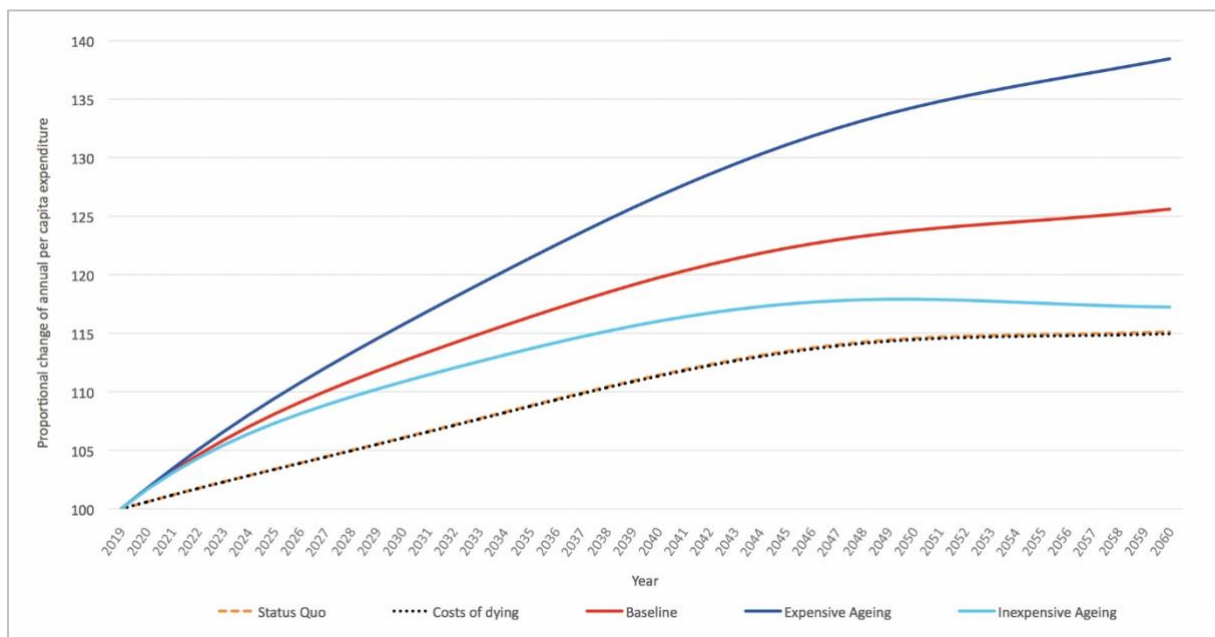
5 Results

We first consider the results of a simplified projection of the change of annual per-capita drug spending for the five scenarios in which we neglect the case of future cost growth due to pharma growth surplus (Fig. 4). The two dashed lines in Fig. 4 show the extrapolations of the scenarios *Status quo* and *Costs of dying*. Both scenarios lead to more or less the same increase in pharmaceutical per-capita spending (562€ Euro in 2019 [84]) of around 15 percent until 2060. The reason for this increase is the upcoming ageing of the German population.

Interestingly, in contrast to other kinds of HCE (e.g., expenditures for hospital services), proximity to death seems to have a minor influence on future pharmaceutical spending (see for this point also Kildemoes et al. (2006) [75] or Moore et al. (2014) [85]).

The *Baseline* scenario of the Markov simulation, where we take the risk group-specific mortality rates and transition probabilities into account, shows a moderately higher increase in drug spending of around 25 percent. In all scenarios so far, every risk group benefits equally from the assumed increase in life expectancy. By contrast, in scenario 4, *Expensive Ageing*, only the high-risk groups 1-4 benefit from a gain in life expectancy, which leads to a significantly stronger increase in per-capita spending of almost 40 percent. The opposite result can be seen in scenario 5, *Inexpensive Ageing*, where only the less cost-intensive groups 5-6 benefit from the gain in life expectancy, resulting in a spending increase of only about 17 percent.

Fig. 4 Projection proportional change of annual per-capita pharmaceutical expenditure in Germany up to 2060 (without consideration of cost growth rates)



Source: Own calculation and depiction.

In general, one can notice that the Markov modeling predicts higher expenditure increases than the status quo projection, even without any increase in life expectancy of the high-risk groups. This illustrates the crucial difference between the two forecasting methods. In our Markov modeling, we first define the six risk groups, followed by calculating age-related transition probabilities. Resultantly, the high-cost groups 1-4 have a significantly higher age with a mean of 63.6 years, compared to the risk groups 5 and 6 with 38.8 years. Thus, the

further increase in high expenditures in the high-cost groups due to their increasing age has a decisive impact on total spending, especially in the medium term. Only in the long run (after 2080) is this effect compensated by higher mortality in these groups. A status quo projection with a mere extrapolation of average values cannot account for such determining socioeconomic characteristics and may underestimate future spending especially in the medium term.

So far, the results are based on the assumption of no pharma growth surplus (compared to GDP-per-capita) in the future. However, the cost growth rates presented in the data section (Tab. 6.b) for the years 2010 to 2018 differ significantly from zero. The consequence of a continuing trend of cost increase is shown in Tab. 8 for all scenarios. It depicts the projection results as a percentage change from 2019 to 2040 and 2060. The results using a uniform growth rate for all cost-risk groups of 3.2 percent for survivors and 3.5 percent for decedents are compared to the results using risk group-specific growth rates. All scenarios are additionally based on an assumed alternative nominal economic growth of three percent per year.

Tab. 8 Projected percentage change of annual per-capita pharmaceutical expenditure of the German population from 2019 to 2040 and 2060

Scenario	2040			2060		
	No cost growth	Uniform growth rate across all risk groups*	Risk group-specific growth rates**	No cost growth	Uniform growth rate across all risk groups*	Risk group-specific growth rates**
1. Status quo	11.9%	17.5%	17.5%	15.2%	27.4%	27.4%
2. Costs of dying	11.8%	17.4%	17.4%	15.0%	27.3%	27.3%
3. Baseline	20.3%	26.8%	44.0%	25.8%	39.9%	121.2%
4. Expensive Ageing	27.7%	34.3%	54.8%	38.9%	54.4%	151.7%
5. Inexpensive Ageing	16.4%	22.7%	39.0%	17.2%	30.4%	104.8%

Source: Own calculation and depiction.

*3.2% per year for survivors, 3.5% per year for decedents adjusted by an alternative economic growth rate of three percent per year

** Based on the calculated growth rates shown in Tab. 6.b and adjusted by an alternative economic growth rate of three percent per year

We can see that even at a uniform growth rate, annual per-capita spending on pharmaceuticals in Germany would increase by 40 percent up to 2060 in our *Baseline* scenario. However, the gap between the extrapolations of per-capita spending by age and sex (1-2) and the Markov scenarios (3-5) is even more prominent when applying risk-group-specific growth rates in our model. The *Baseline* scenario of the Markov model projects an increase of more than 40 percent already by 2040. By 2060, pharmaceutical per-capita spending would more

than double, compared with an increase of only about 27 percent in scenarios 1 and 2. The combination of increasing life expectancy to the benefit of high-cost risk groups 1-4 and a continued trend in risk-group specific growth leads to a pharmaceutical per-capita expenditure increase by more than 150 percent in scenario 4, *Expensive Ageing*.

6 Discussion

To our knowledge, this study is the first to project pharmaceutical expenditures for Germany, considering different cost risk groups and their development in the medium- and long-term horizon. We can show that although the probability of incurring high drug spending depends significantly on age, the key determinant of future expenditure growth is the cost trend within the different risk groups, together with an increasing life expectancy for high-risk groups. In contrast, other demographic trends, including mortality costs, play a minor role in influencing pharmaceutical expenditure growth. If the observed spending trend in the high-risk groups continues, the German SHI must prepare for a significant increase in pharmaceutical expenditure already in the medium term.

There are only a few studies that can be compared with our results. Boecking et al. (2012) [86] project the pharmaceutical spending for Germany and France up to 2050, solely considering the demographic development in an extrapolation of per-capita expenditures. For Germany, they calculate a demographically driven increase in pharmaceutical spending of 26 percent from 2004 to 2050 [86], which is comparable with our results for the *Status quo* scenario. Our slightly lower projected rate of increase is probably attributable to the underlying population projection assuming a smaller proportion of older people. Thiébaud et al. (2013) [71] use a similar Markov simulation model to predict future drug spending in France until 2029. Using an aggregate indicator of morbidity–mortality, they model different scenarios of chronic morbidity and forecast growth in pharmaceutical spending for France between 33 percent (scenario healthy ageing) and 55 percent (scenario medical progress) by 2029 [71]. Kildemoes et al. (2006) [75] project the Danish pharmaceutical expenditures from 2003 to 2030, also focusing on the effect of population ageing. In line with our findings, they arrive at nearly the same results with and without accounting for the costs of dying, projecting an increase of 17.9 and 16.9 percent, respectively [75]. They also conclude that the predicted demographically driven increase is small compared to recently observed increases in pharmaceutical expenditures [75]. Morgan & Cunningham (2011) [76] reach the same conclusion in their

analysis and forecast of prescription drug spending for British Columbia. Many studies show that, instead, most of the past increases in drug spending stemmed from changes in therapies and amount, as well as new pharmaceuticals [87]. Thus, not only the future demographic development needs to be considered for medium- and long-term forecasts.

At the same time, there are certain limitations to our results. Firstly, Markov models have a key limitation: their lack of memory. That means that with each cycle, individuals' possible transitions depend only on their current state, not on how they got to it [70, 88]. In our case, we assume that the identified transition probabilities are age-dependent and remain constant in the future. With regard to the cost of dying, these model specifications imply a risk group-specific probability of dying. It is possible, however, that there is reverse causality, namely that high costs of dying lead to higher risk classification.

Furthermore, the assumption of an ongoing pharma growth surplus must be explored more in detail. Indeed, Newhouse (1992) [89] identified medical-technological progress as the main cause of past increases in healthcare spending, and many studies confirm that health spending in OECD countries is higher than GDP growth [90, 91]. An overview of possible reasons for this phenomenon can be found in Chernew & Newhouse (2011) [92]. Meijer et al. (2013) [93] found the same phenomenon for pharmaceutical spending in the Netherlands. And in line with our findings, they showed that the high-cost cases are the main drivers [93]. Nevertheless, more recent studies show that the amount of cost-increasing innovations strongly varies between different diseases [94, 95]. In turn, these are expected to develop very differently within demographic change [27, 96]. Thus, future pharmaceutical spending will be influenced by several factors whose interaction should be explored in more detail.

Despite the abovementioned limitations, we can derive the following implications from our results. First, our analysis shows that the choice of projection model significantly impacts the forecast results. Even if the widely discussed mortality costs are considered, status quo projections may not adequately reflect the decisive socioeconomic differences of certain population groups. This leads to the second key point: Future drug expenditures depend significantly on the life expectancy and expenditure development of a specific population group, namely the high-cost cases. Therefore, additional research is needed on which population groups are really driving the current increase in life expectancy to better forecast

future drug spending. Especially since a benefit in longevity in the high-risk groups is associated with enormous financial input.

Whether this high investment leads to the intended goals should be monitored more closely, also considering the quality of life gained. Especially because the high-cost groups drive the identified excessive growth in drug spending¹⁸, which, if continued, would have an even greater impact on future spending than rising life expectancy. This pharma growth surplus is not only influenced by the upcoming amount of innovations and new therapies but also by the pricing policies of the German SHI. Thus, policymakers should question the current less restrictive requirements for the evaluation and reimbursement of orphan drugs in Germany to ensure the sustainability of the German health care system.¹⁹

7 Conclusion

When forecasting pharmaceutical spending in the medium and long term, particular focus should be placed on the small group of high-cost patients responsible for a large share of drug expenditures. If the current spending growth on high-cost therapies continues, the German SHI must prepare itself for a significant increase in pharmaceutical spending. Policymakers should address this with adequate pricing policies in the orphan drug segment and increased monitoring regarding the impact of these therapies on life expectancy and quality.

¹⁸ The annual growth rates determined are consistent with other studies on the development of the pharmaceutical market in Germany, see for example, Wasem et al. (2021) [97].

¹⁹ The current draft law of the "GKV-Finanzstabilisierungsgesetz" includes an item concerning this point [98].

Contribution 3: Cost-risk groups in the SHI and the costs in the year of death²⁰

1 Introduction

Steadily rising HCE are a phenomenon observed for decades in many OECD countries [4]. Possible causes for the increase of HCE are medical innovations, real income growth, regulations like pricing policies for medical goods, as well as the ageing of the population [16]. The latter is one of the most controversial topics in health economics. Indeed, there are fears that the changing demographic structure, with fewer and fewer working people facing a growing number of retirees incurring higher HCE at older ages, will jeopardize the fiscal sustainability of the health care system in countries like Germany [3, 4]. However, in 1999, Zweifel et al. (1999) identified the latter effect of higher HCE in older age groups as a possible "red herring" and pinpointed mortality costs as the decisive determinant of high HCE [11]. Accordingly, a longer life expectancy would merely shift high spending in the last year(s) of life to a later age [11–15].

Taking an actuarial perspective, insureds are usually divided into risk groups based on different socio-demographic factors to quantify their risk of incurring high expenses [100]. In many developed countries, a growing concentration of HCE in a small risk group of high-cost patients has been observed [17–20]. In the German SHI, which covers around 90 percent of the population, the most expensive ten percent of insureds account for 60 percent of total HCE [19]. But 20 percent of HCE are accountable solely to the group of the most expensive one percent, with an increasing trend [19, 20].

However, if proximity to death is a key factor in high spending, it also should play an important role in an insured's individual cost risk. Thus, the question arises of how far mortality costs are related to high-cost cases (and vice versa). Several studies examined Germany's high-cost cases' characteristics and spending profiles in detail [17, 19–21]. They are also repeatedly discussed regarding possible risk selection in the German SHI and legal structures to avoid it [101–103]. However, we are not aware of any study to date that has examined the cost of dying as a function of different risk groups for Germany.

²⁰ Hofbauer-Milan V, Fetzter S, Hagist C. Cost risk groups in the SHI and the costs in the year of death. Unpublished working paper. 2022 [99].

Our paper aims to fill this research gap by looking at mortality costs of different risk groups. The analysis is based on data of a large German sickness fund covering around four million insureds from 2011 to 2019. We first divide the entire study population into ten risk groups by costs of equal size, followed by a detailed examination of their expenditures in various categories of HCE, particularly depending on survival or death. This allows us to show which type of expenditures dominate in the several risk groups and to what extent they are attributable to mortality costs.

The paper is organized as follows: We first describe our methods of analysis and then present the results on HCE distribution and structure in the different risk groups differentiated by survivors and deceased. This is followed by a detailed discussion of the results in the context of other studies, also considering our approach's limitations. Finally, we conclude the paper with policy implications and our conclusion.

2 Methods

Our analyses rely on a comprehensive data set of a large statutory sickness fund, the AOK Baden-Württemberg, spanning the periods from January 2010 to December 2019. The data set includes socio-economic characteristics such as age, gender, insurance duration, and date of death. In addition, it contains all related expenditures eligible for the risk structure compensation scheme according to §4 of the "Risikostuktur-Ausgleichsverordnung" (RSAV) [104], representing around 95 percent of total SHI-covered HCE. The expenditures are already cumulated by the respective seven main categories: expenses for physicians, dental care, hospitalization, sick pay, pharmaceuticals, dialysis, and other expenses.²¹

The study population used for the analysis contains only individuals with a full insurance period of at least 360 days in all years 2011 to 2019 unless they were born or died in one of the analysis years. The insurance period after birth or before death must also be complete in the latter two cases. For each calendar year, we first divide the study population into survivors and decedents. All survivors with at least 360 days of insurance are then classified into ten risk groups by costs, based on their share of total health care spending in the categories listed

²¹ "Other expenses" include, for example, expenses for remedies, aids, patient transport, or rehabilitation. For details on the eligible services and allocations to the main categories, see the Federal Office of Social Security databases [105].

above.²² The risk groups consist of deciles, starting with risk group one as the most expensive ten percent of insureds in descending order to the least expensive ten percent. For some analyses, the top ten percent are again subdivided into risk group *1a* as the most expensive one percent, risk group *1b* as the second most expensive four percent, and risk group *1c* as the third most expensive five percent. Tab. 9 shows the risk group classification, applied to all analysis years, exemplified by the study population of 2018.

Tab. 9 Risk group classification of the study population 2018

Risk group	Number of insured	Population share
1	1a	28,478
	1b	113,909
	1c	142,386
2	284,773	10%
3	284,769	10%
4	284,776	10%
5	284,769	10%
6	284,776	10%
7	284,768	10%
8	284,775	10%
9	284,768	10%
10	284,779	10%
Total Survivors	2,847,726	100%
Survivors	2,847,726	98%
Deceased	49,012	2%
Total population	2,896,738	100%

Source: Own depiction.

We can then determine the expenditure shares of total HCE depending on survival status and risk group affiliation and the related distribution between the several categories. In addition, we calculate daily per-capita expenditures in the various risk groups by category and survival status. For this purpose, daily HCE by category of the study population are calibrated to the category's expenditures of the total German SHI according to official annual statistics [106]. Thus, our results are comparable with other studies on spending by the German SHI.

Our data spanning the years 2010 to 2019 allows us to follow individuals after risk classification. Thus, we can differentiate the cost in the year after risk classification between survivors and deceased. This enables us to compute risk-group-related mortality rates as well as the risk-group-related costs of the deceased in the year of death. As we require both a pre-observation year with a full insurance period and a post-observation year to distinguish

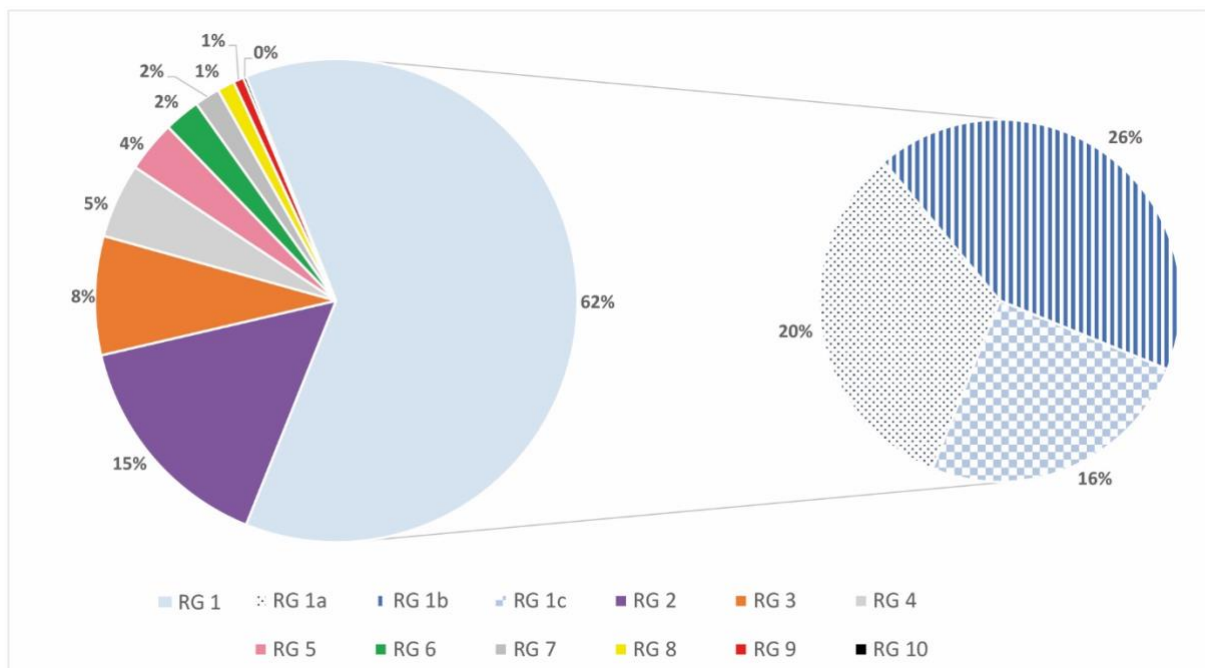
²² To eliminate risk group classification bias due to incomplete insurance years and costs after birth, we exclude the cohort of zero-year-olds for each calendar year.

between deceased and survivors, we can present analysis results on HCE for the years 2011 through 2018.²³

3 Results

We start the presentation of our results with the distribution of total HCE between all survivors of the year 2018 after the risk group classification. Fig. 5 shows in the left circle the spending distribution between the main risk groups; in the right circle, the distribution of risk group 1 is broken down again into subgroups 1a, 1b, and 1c. We can see that 62 percent of survivors' HCE are incurred by the most expensive ten percent (risk group 1), with 26 percent generated solely by the most expensive one percent (risk group 1a), which is in line with the results of other studies on HCE distribution for Germany [19, 20].

Fig. 5 HCE distribution of survivors 2018 after risk group classification



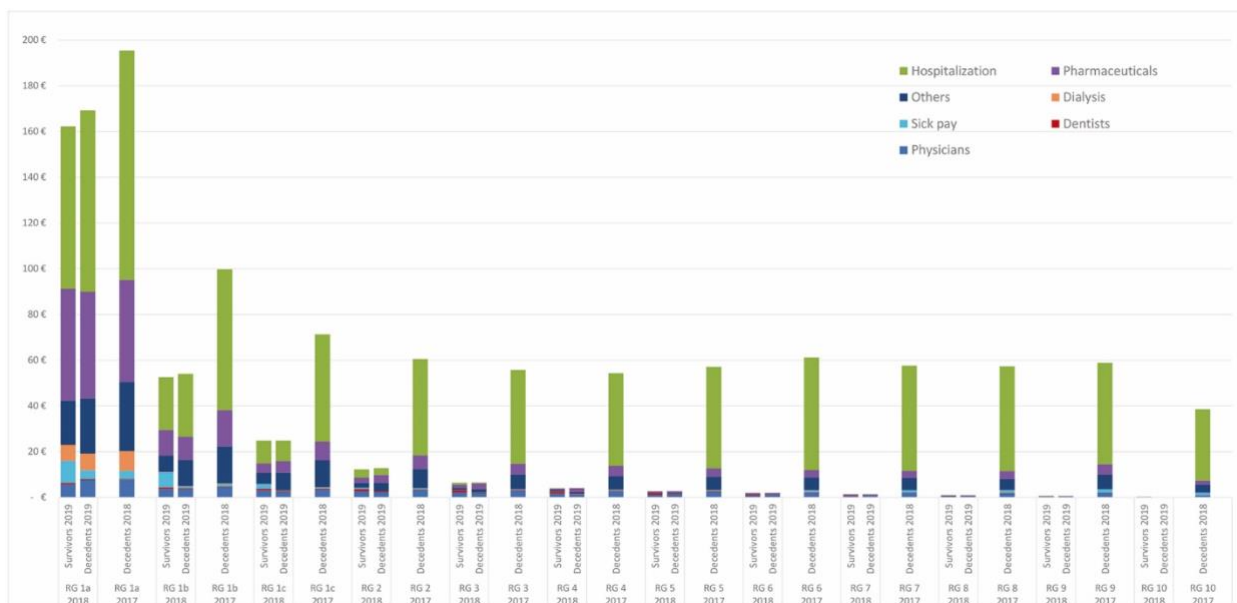
Source: Own depiction. RG = Risk group

In a next step, we want to show to what extent spending is additionally distributed between survivors and decedents. We use per-capita daily spending in 2018 for this purpose to make HCE of decedents and survivors comparable. First, we can distinguish per-capita spending of survivors in 2018 depending on whether they died in 2019 (*Decedents 2019*) or survived 2019

²³ The aggregate claim data is determined in the pseudonymized database environment of the AOK Baden-Württemberg via SQL scripts, resulting in only anonymized data being used for further calculations in Microsoft Excel.

(*Survivors 2019*). The risk group membership of these two groups is based on the risk group classification of 2018. In addition, we would like to contrast the daily per-capita HCE of those who died in 2018 (*Decedents 2018*). Their risk group affiliation, in turn, stems from the 2017 risk group classification. Fig. 6 shows the daily per-capita HCE of the three groups just described according to their risk group affiliation. Furthermore, the spending distribution among the categories of HCE (*physicians, dental care, hospitalization, sick pay, pharmaceuticals, dialysis, and others*) is also apparent.

Fig. 6 Daily per-capita HCE 2018 of survivors 2019, decedents 2019, and decedents 2018



Source: Own depiction. RG = Risk group

Fig. 6 shows that the *Decedents 2018* have the highest daily per-capita HCE in all risk groups. Thus, as might be expected, HCE are highest in the calendar year of death. But, remarkably, the *Decedents 2018* daily spending is nearly the same across all risk groups, with around 60 € per capita and day. Only the most and least expensive ten percent differ significantly. Daily per-capita spending of the most expensive one percent (risk group 1a) reaches nearly 200 €. In contrast, the cheapest ten percent of *Decedents 2018* generate only 39 € in daily expenses.

But comparing now the *Decedents 2018* expenditures with those of the *Survivors 2019* and the *Decedents 2019*, we can see that the difference is proportionally small for the most expensive one percent. Thus, the costs in the year of death do not appear to drive these insureds to become high-cost cases at first glance. Comparing the daily per-capita costs 2018 of the *Decedents 2019* and *Survivors 2019*, we observe almost no difference between annual

per-capita HCE, which applies to all risk groups. Thus, mortality costs do not appear to reach a relevant level in the calendar year prior to death but only in the year of death.

Observing the daily per-capita costs of the different categories shows that hospital expenditures are almost exclusively responsible for the cost difference between survivors and decedents in the calendar year of death. Pharmaceutical expenses and expenditure subsumed under "*Other*" also play a subordinate role. But to be among the most expensive insureds, however, these two groups, together with dialysis expenses, seem to play the decisive role. Furthermore, it is remarkable that all dialysis spending is only found in risk group *1a*.

Tab. 10 shows the proportional distribution of total HCE between *Survivors 2018* and *Decedents 2018*, along with the related breakdown between categories. Taking this approach, we see that the deceased account for only eight percent of total HCE, with five percent attributable to risk group *1*. Thus, the mortality costs of the great majority of insureds play hardly any role in total HCE.

Considering the deceased distribution between the categories by risk group, it is again clear that dying in a hospital causes the costs in the year of death. Hospital expenditures account for 70 to 80 percent of decedents' expenditures, except in risk group *1*. Their hospital expenditures already account for around 40 percent among survivors but then increase only slightly in the case of death. With an expenditure share of 30 percent, pharmaceutical spending plays a significant role in the most expensive one percent (risk group *1a*). In the lower-risk groups of survivors, spending on physicians accounts for the majority of HCE, as well as on dental care and, to a smaller extent, pharmaceuticals.

Tab. 10 HCE distribution between survivors and decedents 2018

a. Survivors 2018									
Risk group affiliation 2018	Share of total expenditure 2018		Distribution among categories						
			Physicians	Dental care	Hospitalization	Pharmaceuticals	Sick pay	Dialysis	Others
1	57%		7%	1%	43%	23%	9%	2%	15%
1a	19%		4%	0%	44%	30%	5%	4%	12%
1b	24%		7%	1%	44%	21%	12%	0%	14%
1c	14%		12%	3%	40%	17%	8%	0%	20%
2	14%		23%	8%	29%	19%	4%	0%	17%
3	7%		34%	15%	12%	23%	2%	0%	14%
4	5%		40%	23%	4%	22%	1%	0%	11%
5	3%		44%	27%	2%	18%	1%	0%	9%
6	2%		48%	27%	1%	16%	1%	0%	7%
7	2%		53%	25%	0%	15%	1%	0%	5%
8	1%		57%	26%	0%	13%	1%	0%	4%
9	1%		59%	28%	0%	10%	0%	0%	2%
10	0%		63%	29%	0%	7%	0%	0%	1%
Total	92%		17%	7%	33%	22%	6%	1%	14%
b. Decedents 2018									
Risk group affiliation 2017	Share of total expenditure 2018		Distribution among categories						
			Physicians	Dental care	Hospitalization	Pharmaceuticals	Sick pay	Dialysis	Others
1	5%		4%	0%	59%	17%	1%	2%	16%
1a	2%		4%	0%	51%	23%	2%	4%	15%
1b	2%		5%	0%	62%	16%	1%	0%	16%
1c	2%		5%	0%	66%	11%	1%	0%	17%
2	1%		5%	1%	70%	10%	1%	0%	14%
3	1%		5%	1%	74%	8%	1%	0%	11%
4	0%		5%	0%	75%	8%	1%	0%	11%
5	0%		4%	1%	78%	6%	0%	0%	10%
6	0%		4%	0%	80%	5%	1%	0%	9%
7	0%		4%	0%	80%	5%	1%	0%	9%
8	0%		3%	0%	80%	6%	2%	0%	9%
9	0%		3%	0%	75%	8%	2%	0%	11%
10	0%		2%	0%	81%	5%	3%	0%	9%
Total	8%		5%	0%	65%	14%	1%	1%	14%

Source: Own depiction.

All in all, our analysis so far indicates that proximity to death is probably not the main factor explaining HCE when controlling for different cost risks. Thus, it might be interesting if the different risk groups vary in socio-economic characteristics. Fig. 7 shows the risk groups' age- and gender-specific affiliation probabilities (primary axis) and mortality rates (secondary axis). They are computed as averages of all available analysis years 2012 to 2018, as only small numbers of cases are available in some age groups.

Fig. 7 Average affiliation probabilities and mortality rates in the different risk groups by age



Source: Own depiction.

One can see that the probability of belonging to the most expensive ten percent clearly depends on age, reaching its maximum for men and women at about 87 years. But at the same time, these high-risk cases also die with a high probability of 30 and 35 percent, respectively. The older age groups are also significantly more frequently represented in risk groups 2 and 3. From risk group 4, the curves flatten, then the trend reverses. Also noticeable is that middle-aged women are more likely to belong to a more expensive risk group.

Considering all the results presented, one can say that there seems to be a kind of chicken-and-egg situation regarding the causality of high-cost cases since we don't know whether they are particularly expensive because they are about to die in the following year(s). Or on the other hand, high HCE, in general, could be associated with high mortality.

4 Discussion

Our results extend the literature as we show the relationship between cost-risk groups and the costs in the year of dying (and the year before). By looking at both daily spending and the proportional distribution of spending in relation to the total population, we can provide a comprehensive overview of the expenditure structure, broken down by categories of spending. Our results offer that mortality costs are only evident in lower-risk groups and almost exclusively attributable to hospitalization. Moreover, HCE in the calendar year of death is equal for the majority of risk groups. The spending difference between survivors and decedents is only evident in the calendar year of death, not in the year before death. For the high-risk groups, HCE in the year of death is significantly higher than in all other risk groups, but the difference between survivors and decedents is proportionally small. Pharmaceutical spending, with an increasing concentration in a few high-cost cases, is primarily responsible for the crucial difference in spending between the decedents in high-risk and other risk groups.

The results can be placed in the previous literature. With 51.2 percent hospital and 23.3 percent drug expenditures, Lange et al. (2020) can also identify these two categories as the main cost pools of high-risk patients [21]. In line with national and international studies, we show that the probability of belonging to the most expensive cases is strongly related to age, with a substantially increased mortality rate compared with the overall population [20, 21,

107].²⁴ The higher proportion of women in the high-risk groups is also consistent with the findings of other studies [20, 21, 108]. For a comprehensive literature review on other socio-demographic characteristics or frequently diagnosed diseases of high-risk insureds, see Wammes et al. (2018) [109].

The work of Stahmeyer et al. (2021) presents a detailed analysis of decedents' and survivors' spending characteristics for Germany based on a similar dataset from 2017 [110]. They also find a massive increase in pre-death hospitalization spending and a nine percent share of total HCE attributable to decedents [110]. The slight difference from our result of eight percent is probably due to their consideration of the last year before the date of death rather than the calendar year of death as we do. By looking at spending each quarter before death, they determine that half of all health care spending in the last year of life is attributable to the previous quarter before death [110]. This is consistent with our findings of a significant difference in spending between survivors and decedents only in the calendar year of death. Karlsson et al. (2016) also confirm this result based on data from a private German sickness fund [17]. In their analysis, the spending difference between survivors and decedents drops by half when looking back more than a year before death, which suggests pure mortality costs and less an age effect [17].

Bynum et al. (2017) find in their analysis for the USA that high-cost Medicare and Medicaid insureds can be divided into two distinct groups: older beneficiaries facing the end of life and younger beneficiaries with ongoing functional support needs [111]. Aldridge & Kelley (2015) also take a closer look at the deceased within the high-cost cases for the United States [112]. Although they find that most decedents are in the high-cost group, the majority of high-cost cases are still not in their last year of life [112]. Wammes et al. (2017) also show for the Netherlands that dying increases the risk of incurring high costs, but less than ten percent of beneficiaries with high costs are in their last year of life [107]. Davis et al. (2016) try to find cost drivers at the end of life of older Medicare beneficiaries [113]. Their findings suggest that HCE at the end of life is often an indicator of the general spending profile, beginning long before death [113], which is in line with our results for the group of the most expensive one percent.

²⁴ According to Lange et al. (2020), German high-risk insureds are particularly old in an international comparison, although the generally higher average age of the German population must also be considered [21].

Our results also may have implications on the optimal design of risk adjustment schemes between sickness funds. In 2020, Germany introduced a new regulation for high-risk patients in the SHI's morbidity-based risk adjustment scheme. An additional risk pool covers 80 percent of the expenditures for high-cost insureds with more than 100,000 euros annual spending [114, 115]. In the light of our results, this is indeed an important advancement. But despite the 2014 adjustment to account for deceased expenses in the risk adjustment scheme²⁵, the decedents are still heavily underfunded. On average, only about 35 percent of decedents' expenses are covered by risk adjustment [118], depending on the age cohort ranging from 7.3 percent for under-5-year-olds to 57.8 percent for 94-year-olds [117].²⁶ Accordingly, death is a risk difficult to capture, which insurers have to bear. Proposals to include lump-sum payments for each case of death in a risk adjustment have existed for some time [119–121].

Our results also have some limitations, firstly regarding the study population. As we examined a closed study population, which can be entered only by birth or exit by death, we could not include individuals who changed their insurance during this period. In addition, it is important to note the small cohort sizes in the high-risk groups for those younger than ten years and older than 92 years (*n* between ten and 20) and in the very low-risk groups for those older than 93 years (*n* between six and 20).

Secondly, the expenditures considered are also subject to some limitations. The classification of risk groups only allowed an analysis of expenditures from full calendar years, which means that the period until the deceased's death is not always the same for every person. However, Karlsson et al. (2016) show in their analysis that there is no difference in the expenditure differential between decedents and survivors depending on whether taking an exact view of the year before death or the calendar year of death [17].

Despite the limitations above, we can finally derive three cases regarding policy recommendations from the relationship between individual cost risk and mortality costs: Firstly, death can occur suddenly and accidentally, without any mortality costs being incurred

²⁵ Consideration of deceased expenditures has been adjusted to the international standard of annualization, i.e., deceased expenditures are divided by the insured's days of coverage and multiplied by the number of days in the year [116]. The German government thus followed a recommendation of the scientific advisory board mandated to regularly evaluate the risk adjustment scheme [117].

²⁶ The evaluation of the risk adjustment scheme back in 2009 found that the introduction of the risk pool would have the same slightly positive effect on deceased coverage rates as the implementation of decedent expenditure annualization [117].

at all. In the second case, there is a short-term illness treated mainly in the hospital until death, clearly showing up as a cost difference to survivors in the lower risk groups in the year of death. These cases are hardly predictable and barely preventable. Considering their small share in total HCE and the small timeframe until death, we also do not see any potential for significantly influencing HCE.

This is quite different in the last case, in which a severe chronic illness turns the insureds into high-cost cases already sometime before death. We cannot conclusively answer the question of the extent that mortality costs contribute toward turning these insureds into high-cost cases. More research is needed to determine which ones of the high-cost cases pass to other high-risk groups and which ones die. Despite their high mortality rate, we see this risk group's huge proportion of total spending as the main target for policy reforms. On the one hand, some hospitalizations in this group are certainly avoidable through better outpatient care, as Lange and colleagues (2020) also deduce from their study [21]. In addition, policymakers should also focus on the high pharmaceutical expenditures that distinguish the dying high-risk cases from those in other risk groups. In line with Wende & Schmitt (2021) as well as Hofbauer-Milan et al. (2022), we see a significant increase in drug spending concentration, which could be counteracted by pricing policies for new therapies, especially regarding orphan drugs [19, 61].

5 Conclusion

Our analysis shows that clear mortality costs are only evident in the lower-risk groups. The extremely high HCE of the high-risk groups show up already some time before and increase only slightly toward death compared with the other risk groups. Since the high-risk groups also have the highest mortality rate, we could not finally answer to what extent mortality costs contribute to turning these insureds into high-cost cases. The causality question remains open: Are high-cost risk patients expensive because they are about to die in the following year(s), or is a high cost risk, in general, associated with high mortality? However, the answer to this question may not be essential. Especially for projections of future HCE, considering the high-cost cases' characteristics, like expenditure shares and specific life expectancy, seems to be much more relevant than mortality costs of both high-cost cases and the rest of the population.

Summary

In summary, all three contributions of this dissertation could show that the German SHI is facing major challenges. These result not only from the demographic transition in the German population but also from new medical developments and changing spending trends, particularly in the field of pharmaceuticals.

In the first paper, we focused on the disease burden in the German population and presented projections of ten widespread non-infectious diseases. Using a Markov illness-death model with recovery, our analysis highlighted the importance of focusing on the interdependence between demographic and disease-specific components in projecting future disease burden. We could show that the increase in disease burden due to increasing life expectancy and high incidence rates in older age groups can be mitigated but not fully compensated in case of a compression of morbidity. As a result, we must expect a significant increase for almost all considered diseases, even in optimistic scenarios. Especially the strong increase of primary age-related and care-intensive diseases like dementia or heart failure could bring the German SHI to its capacity limits. Only more effective prevention could alleviate the massive caseload, but this requires immediate action by policymakers and healthcare managers.

But there is also a clear need for action in the field of drug pricing policy, as we showed in the second paper. Here, the increasing approval of high-priced special therapies for rare diseases has led to a growing spending concentration on a small group of high-cost cases that have not previously been considered in projections of future drug spending. In our approach, we projected pharmaceutical expenditures for Germany, taking into account the demographic characteristics and spending trends of different cost-risk groups. We showed that the key determinants of future spending growth are less general demographic trends including mortality costs, but rather the development of costs and life expectancy in the small group of high-cost cases. Although these developments result from emerging innovations and their impact on life expectancy, they can be decisively influenced by the pricing policies of the German SHI. For example, the current less restrictive requirements for orphan drug evaluation and reimbursement might be reconsidered.

Similarly, the third contribution of this dissertation reveals the strong impact of the small group of high-cost cases, also in terms of total HCE. In the German SHI, more than 60 percent of total HCE is caused by the most expensive ten percent of the insureds. However, there are

hardly any findings regarding the role of mortality costs in these high-risk groups. Thus, we analyzed the spending distribution of HCE between different cost-risk groups and distinguished between several categories of HCE and the survival status. We found that short-term high HCE in the year of death occur equally in all risk groups and are probably hardly avoidable. Costs in the year of death were significantly higher only in the high-risk groups, but the difference between decedents and survivors was proportionally small. Thus, the extremely high costs of high-risk cases already show up sometime before death. Moreover, the key difference in spending between decedents in high-risk and other risk groups was attributable to pharmaceutical spending. Since the high-risk group also had the highest mortality rate, we could not finally answer the question to what extent potentially longer-term mortality costs contribute to becoming a high-cost case. Nevertheless, the enormous share of this risk group in total HCE becomes clear and independently offers the main target to influence rising HCE.

Taken together, the three contributions to this dissertation could provide important guidance for policymakers to address the challenges facing the German SHI. In particular, all contributions made clear that we cannot rely solely on the mitigating effect of optimistic scenarios, like compression of morbidity and a mere shift in HCE with rising life expectancy. In terms of projections for future HCE, the focus needs to be shifted away from the ongoing debate about expansion, compression, and mortality costs, towards the small group of high-cost cases that have a critical impact on healthcare spending. It is the high-cost therapies, especially in the area of pharmaceuticals, and the simultaneous expected massive caseload of age-related diseases that we must counter in the future. Better prevention regarding widespread diseases is urgently needed, as is the evaluation of high-priced drug therapies in terms of life expectancy increase and quality. Because only an efficient healthcare system can withstand the current developments and future challenges.

References

1. Blümel M, Spranger A, Achstetter K, Maresso A, Busse R. Germany: Health system review. *Health Systems in Transition*. 2020;22(06):i–273.
2. Hofbauer-Milan V, Fetzer S, Hagist C. Gesunden, Überleben oder Sterben: Prognosen für zehn nicht-infektiöse Volkskrankheiten. In: Hagist C, Kohlstruck T, editors. *Fiskalische Nachhaltigkeit: Von der ökonomischen Theorie zum politischen Leitbild*; 2022. p. 145–156.
3. DeStatis. Bevölkerung im Wandel: Ergebnisse der 14. koordinierten Bevölkerungsvorausberechnung. 2019. https://www.destatis.de/DE/Themen/Querschnitt/Demografischer-Wandel/_inhalt.html;jsessionid=28B0C78CF8E6EE9C38EE1CF5FC95BABE.live711#sprg233552. Accessed 19 Aug 2022.
4. OECD. *Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives*. Paris: OECD Publishing; 2015.
5. Meijer C de, Wouterse B, Polder J, Koopmanschap M. The effect of population aging on health expenditure growth: a critical review. *Eur J Ageing*. 2013;10:353–61. doi:10.1007/s10433-013-0280-x.
6. Sorenson C, Drummond M, Bhuiyan Khan B. Medical technology as a key driver of rising health expenditure: disentangling the relationship. *Clinicoecon Outcomes Res*. 2013;5:223–34. doi:10.2147/CEOR.S39634.
7. Breyer F, Lorenz N. The "red herring" after 20 years: ageing and health care expenditures. *Eur J Health Econ*. 2021;22:661–7. doi:10.1007/s10198-020-01203-x.
8. Gruenberg EM. The Failures of Success. *The Milbank Memorial Fund Quarterly. Health and Society*. 1977;55:3. doi:10.2307/3349592.
9. Verbrugge LM. Longer Life but Worsening Health? Trends in Health and Mortality of Middle-Aged and Older Persons. *The Milbank Memorial Fund Quarterly. Health and Society*. 1984;62:475. doi:10.2307/3349861.
10. Fries JF. Aging, natural death, and the compression of morbidity. *N Engl J Med*. 1980;303:130–5. doi:10.1056/NEJM198007173030304.
11. Zweifel P, Felder S, Meiers M. Ageing of population and health care expenditure: a red herring? *Health Econ*. 1999;8:485–96. doi:10.1002/(sici)1099-1050(199909)8:6<485::aid-hec461>3.0.co;2-4.

12. Zweifel P, Felder S, Werblow A. Population Ageing and Health Care Expenditure: New Evidence on the “Red Herring”. *Geneva Pap Risk Insur Issues Pract.* 2004;29:652–66. doi:10.1111/j.1468-0440.2004.00308.x.
13. Howdon D, Rice N. Health care expenditures, age, proximity to death and morbidity: Implications for an ageing population. *J Health Econ.* 2018;57:60–74. doi:10.1016/j.jhealeco.2017.11.001.
14. Felder S, Werblow A, Zweifel P. Do red herrings swim in circles? Controlling for the endogeneity of time to death. *J Health Econ.* 2010;29:205–12. doi:10.1016/j.jhealeco.2009.11.014.
15. Fuchs VR. "Though much is taken": reflections on aging, health, and medical care. *The Milbank Memorial Fund Quarterly. Health and Society.* 1984:143–66.
16. Bodenheimer T. High and rising health care costs. Part 1: seeking an explanation. *Ann Intern Med.* 2005;142:847–54. doi:10.7326/0003-4819-142-10-200505170-00010.
17. Karlsson M, Klein TJ, Ziebarth NR. Skewed, Persistent and High before Death: Medical Spending in Germany. *Fiscal Studies.* 2016;37:527–59. doi:10.1111/J.1475-5890.2016.12108.
18. French E, Kelly E. Medical Spending around the Developed World. *Fiscal Studies.* 2016;37:327–44. doi:10.1111/j.1475-5890.2016.12127.
19. Wende D, Schmitt N. Hochkostenpatienten und Auswirkung des Risikopools in der GKV. In: Repschläger et al. (Hg.) 2021 - Gesundheitswesen aktuell 2021. p. 126–147. doi:10.30433/GWA2021-126.
20. Tanke MAC, Feyman Y, Bernal-Delgado E, Deeny SR, Imanaka Y, Jeurissen P, et al. A challenge to all. A primer on inter-country differences of high-need, high-cost patients. *PLoS ONE.* 2019;14:e0217353. doi:10.1371/journal.pone.0217353.
21. Lange L, Pimperl A, Schulte T, Groene O, Tanke M. Hochkostenversicherte in Deutschland: Leistungs- und Kostenprofile. *Z Evid Fortbild Qual Gesundhwes.* 2020;153-154:76–83. doi:10.1016/j.zefq.2020.05.007.
22. Xu Y, Joyce G. Persistence And Concentration Of Prescription Drug Expenditure Among Medicare Beneficiaries 2006-2013. *Value in Health.* 2017;20:A664. doi:10.1016/j.jval.2017.08.1604.
23. Hanley GE, Morgan S. Chronic catastrophes: exploring the concentration and sustained nature of ambulatory prescription drug expenditures in the population of British Columbia, Canada. *Soc Sci Med.* 2009;68:919–24. doi:10.1016/j.socscimed.2008.12.008.

24. Morgan SG, Bathula HS, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. *BMJ*. 2020;368:l4627. doi:10.1136/bmj.l4627.
25. Danzon PM. Affordability Challenges to Value-Based Pricing: Mass Diseases, Orphan Diseases, and Cures. *Value Health*. 2018;21:252–7. doi:10.1016/j.jval.2017.12.018.
26. Lohmüller J, Bauckmann J, Schröder M, Niepraschk-von Dollen K, Telschow C, Sollmann S, et al. Der GKV-Arzneimittelmarkt. doi:10.4126/FRL01-006423607.
27. Milan V, Fetzer S, Hagist C. Healing, surviving, or dying? - projecting the German future disease burden using a Markov illness-death model. *BMC Public Health*. 2021;21:123. doi:10.1186/s12889-020-09941-6.
28. Seshamani M, Gray AM. A longitudinal study of the effects of age and time to death on hospital costs. *J Health Econ*. 2004;23:217–35. doi:10.1016/j.jhealeco.2003.08.004.
29. European Commission. The 2018 ageing report: Economic & budgetary projections for the 28 EU Member States (2016-2070). 2018.
30. Jagger C, Matthews R, Spiers N, Brayne C, Comas-Herrera A, Robinson T. Compression or expansion of disability?: Forecasting future disability levels under changing patterns of diseases. 2006.
31. Federal Statistical Office. Federal Health Reporting. 2019. bund.de/gbe10/pkg_isgbe5.prc_isgbe?p_uid=gastg&p_aid=97182139&p_sprache=E. Accessed 25 May 2022.
32. Whelpton PK. An empirical Model of Calculating Future Population // An Empirical Method of Calculating Future Population. *Journal of the American Statistical Association*. 1936;31:457–73. doi:10.1080/01621459.1936.10503346.
33. Fix, E., Neyman, J. A simple stochastic model of recovery, relapse, death and loss of patients. *Human Biology*. 1951:205–41.
34. Manton KG, Liu K. Projecting chronic disease prevalence. *Med Care*. 1984;22:511–26. doi:10.1097/00005650-198406000-00002.
35. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. *Am J Public Health*. 1998;88:1337–42. doi:10.2105/ajph.88.9.1337.
36. Brinks R, Tamayo T, Kowall B, Rathmann W. Prevalence of type 2 diabetes in Germany in 2040: estimates from an epidemiological model. *Eur J Epidemiol*. 2012;27:791–7. doi:10.1007/s10654-012-9726-2.

37. Andersson T, Ahlbom A, Carlsson S. Diabetes Prevalence in Sweden at Present and Projections for Year 2050. *PLoS ONE*. 2015;10:e0143084. doi:10.1371/journal.pone.0143084.
38. Milan V, Fetzer S. Die zukünftige Entwicklung von Demenzerkrankungen in Deutschland – ein Vergleich unterschiedlicher Prognosemodelle. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2019;62:993–1003. doi:10.1007/s00103-019-02981-3.
39. DeStatis. Bevölkerung Deutschlands bis 2060: Ergebnisse der 14. koordinierten Bevölkerungsvorausberechnung. 2019. https://www.destatis.de/DE/Themen/Querschnitt/Demografischer-Wandel/_inhalt.html;jsessionid=28B0C78CF8E6EE9C38EE1CF5FC95BABE.live711#spring233552. Accessed 19 Aug 2022.
40. Günster C, Altenhofen L, editors. *Versorgungs-Report 2011: Schwerpunkt: Chronische Erkrankungen*. Stuttgart: Schattauer GmbH; 2011.
41. Günster C, Klose J, Schmacke N, editors. *Versorgungs-Report 2012*. Stuttgart: Schattauer GmbH; 2012.
42. Klauber J, Günster C, Gerste B, Robra B-P, Schmacke N, editors. *Versorgungs-Report 2013/2014: Schwerpunkt: Depression*. Stuttgart: Schattauer GmbH; 2014.
43. Günster C, Klauber J, Robra B-P, Schmacke N, Schmuker C, editors. *Versorgungs-Report Früherkennung*. Berlin: Medizinisch Wissenschaftliche Verlagsgesellschaft; 2019.
44. Drösler S, Garbe E, Hasford J, Schubert I, Ulrich V, van de Ven W, et al. *Sondergutachten zu den Wirkungen des morbiditätsorientierten Risikostrukturausgleichs*. 2011.
45. Swart E. Health Care Utilization Research using Secondary Data. In: Swart E, Lengerke T von, Janssen C, editors. *Health Care Utilization in Germany: Theory, Methodology, and Results*. New York, NY: Springer; 2014. p. 63–86.
46. Veronese N, Cereda E, Maggi S, Luchini C, Solmi M, Smith T, et al. Osteoarthritis and mortality: A prospective cohort study and systematic review with meta-analysis. *Semin Arthritis Rheum*. 2016;46:160–7. doi:10.1016/j.semarthrit.2016.04.002.
47. Kuperman EF, Schweizer M, Joy P, Gu X, Fang MM. The effects of advanced age on primary total knee arthroplasty: a meta-analysis and systematic review. *BMC Geriatr*. 2016;16:41. doi:10.1186/s12877-016-0215-4.
48. Schouler-Ocak M, Aichberger MC. Versorgung von Migranten. [Providing Care for Migrants]. *Psychother Psychosom Med Psychol*. 2015;65:476-85; quiz 485. doi:10.1055/s-0034-1399972#.

49. Robert Koch-Institut. Migration und Gesundheit: Schwerpunktbericht der Gesundheitsberichterstattung des Bundes. 2008. https://www.rki.de/DE/Content/Gesundheitsmonitoring/Gesundheitsberichterstattung/GBEDownloadsT/migration.pdf?__blob=publicationFile. Accessed 25 May 2022.
50. Tönnies T, Röckl S, Hoyer A, Heidemann C, Baumert J, Du Y, et al. Projected number of people with diagnosed Type 2 diabetes in Germany in 2040. *Diabet Med*. 2019;36:1217–25. doi:10.1111/dme.13902.
51. Alzheimer Europe. Dementia in Europe Yearbook 2019: Estimating the prevalence of dementia in Europe. 2020.
52. Chatterji S, Byles J, Cutler D, Seeman T, Verdes E. Health, functioning, and disability in older adults—present status and future implications. *The Lancet*. 2015;385:563–75. doi:10.1016/S0140-6736(14)61462-8.
53. Beltrán-Sánchez H, Jiménez MP, Subramanian SV. Assessing morbidity compression in two cohorts from the Health and Retirement Study. *J Epidemiol Community Health*. 2016;70:1011–6. doi:10.1136/jech-2015-206722.
54. Kingston A, Robinson L, Booth H, Knapp M, Jagger C. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. *Age Ageing*. 2018;47:374–80. doi:10.1093/ageing/afx201.
55. Barendregt JJ, Ott A. Consistency of epidemiologic estimates. *Eur J Epidemiol*. 2005;20:827–32. doi:10.1007/s10654-005-2227-9.
56. Binder N, Balmford J, Schumacher M. A multi-state model based reanalysis of the Framingham Heart Study: Is dementia incidence really declining? *Eur J Epidemiol*. 2019;34:1075–83. doi:10.1007/s10654-019-00567-6.
57. Brinks R, Landwehr S. Age- and time-dependent model of the prevalence of non-communicable diseases and application to dementia in Germany. *Theor Popul Biol*. 2014;92:62–8. doi:10.1016/j.tpb.2013.11.006.
58. Geyer S, Kowalski C. GKV-Routinedaten in der onkologischen Versorgungsforschung.
59. Jaunzeme J, Eberhard S, Geyer S. Wie "repräsentativ" sind GKV-Daten? Demografische und soziale Unterschiede und Ähnlichkeiten zwischen einer GKV-Versichertenpopulation, der Bevölkerung Niedersachsens sowie der Bundesrepublik am Beispiel der AOK Niedersachsen. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56:447–54. doi:10.1007/s00103-012-1626-9.

60. Hartmann J, Weidmann C, Biehle R. Validierung von GKV-Routinedaten am Beispiel von geschlechtsspezifischen Diagnosen. *Gesundheitswesen*. 2016;78:e53-e58. doi:10.1055/s-0035-1565072.
61. Hofbauer-Milan V, Fetzer S, Hagist C. How to predict drug expenditure: A Markov model approach with risk classes. *Pharmacoeconomics*. 2023;41:561–572. <https://doi.org/10.1007/s40273-023-01240-3>.
62. OECD. Improving Forecasting of Pharmaceutical Spending - Insights from 23 OECD and EU Countries. 2019.
63. WHO. Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research. 2015. <https://apps.who.int/iris/bitstream/handle/10665/159405/WHO-EURO-2015-3211-42969-60044-eng.pdf?sequence=3&isAllowed=y>. Accessed 25 Aug 2022.
64. Mills M, Kanavos P. Do pharmaceutical budgets deliver financial sustainability in healthcare? Evidence from Europe. *Health Policy*. 2020;124:239–51. doi:10.1016/j.healthpol.2019.12.002.
65. Danzon PM, Chao L-W. Does Regulation Drive Out Competition in Pharmaceutical Markets? *The Journal of Law and Economics*. 2000;43:311–58. doi:10.1086/467458.
66. Czech M, Baran-Kooiker A, Atikeler K, Demirtshyan M, Gaitova K, Holownia-Voloskova M, et al. A Review of Rare Disease Policies and Orphan Drug Reimbursement Systems in 12 Eurasian Countries. *Front Public Health*. 2019;7:416. doi:10.3389/fpubh.2019.00416.
67. Worm F, Dintsios C-M. Determinants of Orphan Drug Prices in Germany. *Pharmacoeconomics*. 2020;38:397–411. doi:10.1007/s40273-019-00872-8.
68. Mestre-Ferrandiz J, Palaska C, Kelly T, Hutchings A, Parnaby A. An analysis of orphan medicine expenditure in Europe: is it sustainable? *Orphanet J Rare Dis*. 2019;14:287. doi:10.1186/s13023-019-1246-7.
69. Carta A, Conversano C. On the Use of Markov Models in Pharmacoeconomics: Pros and Cons and Implications for Policy Makers. *Front Public Health*. 2020;8:569500. doi:10.3389/fpubh.2020.569500.
70. Stahl JE. Modelling methods for pharmacoeconomics and health technology assessment: an overview and guide. *Pharmacoeconomics*. 2008;26:131–48. doi:10.2165/00019053-200826020-00004.

71. Thiébaud SP, Barnay T, Ventelou B. Ageing, chronic conditions and the evolution of future drugs expenditure: a five-year micro-simulation from 2004 to 2029. *Applied Economics*. 2013;45:1663–72. doi:10.1080/00036846.2011.633895.
72. Pritchard DJ. Modeling Disability in Long-Term Care Insurance. *North American Actuarial Journal*. 2006;10:48–75. doi:10.1080/10920277.2006.10597413.
73. Sherris M, Wei P. A Multi-state Model of Functional Disability and Health Status in the Presence of Systematic Trend and Uncertainty. *North American Actuarial Journal*. 2021;25:17–39. doi:10.1080/10920277.2019.1708755.
74. Rickayzen BD, Walsh DEP. A Multi-State Model of Disability for the United Kingdom: Implications for Future Need for Long-Term Care for the Elderly. *Br. Actuar. J*. 2002;8:341–93. doi:10.1017/S1357321700003755.
75. Kildemoes HW, Christiansen T, Gyrd-Hansen D, Kristiansen IS, Andersen M. The impact of population ageing on future Danish drug expenditure. *Health Policy*. 2006;75:298–311. doi:10.1016/j.healthpol.2005.03.013.
76. Morgan S, Cunningham C. Population aging and the determinants of healthcare expenditures: the case of hospital, medical and pharmaceutical care in british columbia, 1996 to 2006. *Health Policy*. 2011;7:68–79.
77. Commonwealth of Australia. 2021 Intergenerational Report. 2021. https://treasury.gov.au/sites/default/files/2021-06/p2021_182464.pdf. Accessed 17 Jan 2022.
78. DeStatis. Population. 2022. https://www.destatis.de/EN/Themes/Society-Environment/Population/_node.html;jsessionid=5EDEE3AF26A891247D7E9DB1DD47E158.live712. Accessed 29 Jun 2022.
79. The Human Mortality Database. Germany, Total population. <https://mortality.org/cgi-bin/hmd/country.php?cntr=DEU&level=2>. Accessed 8 May 2022.
80. Statistisches Bundesamt. Sterbefälle: Fallzahlen nach Tagen, Wochen, Monaten, Altersgruppen, Geschlecht und Bundesländern für Deutschland 2016 - 2022. 2022. <https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Bevoelkerung/Sterbefaelle-Lebenserwartung/Tabellen/sonderauswertung-sterbefaelle.html>. Accessed 1 Jun 2022.
81. Statistisches Bundesamt. Bevölkerung nach Nationalität und Geschlecht. 2021. <https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Bevoelkerung/Bevoelkerungsstand/Tabellen/deutsche-nichtdeutsche-bevoelkerung-nach-geschlecht-deutschland.html>. Accessed 2 Jun 2022.

82. European Commission. The 2021 ageing report. Luxembourg: Publication Office of the European Union; 2020.
83. European Central Bank. An overview of the ECB's monetary policy strategy. 2022. https://www.ecb.europa.eu/home/search/review/html/ecb.strategyreview_monpol_strategy_overview.en.html#toc3. Accessed 27 May 2022.
84. Bundesgesundheitsministerium. Gesetzliche Krankenversicherung Vorläufige Rechnungsergebnisse 1. bis 4. Quartal 2019. 2019. https://www.bundesgesundheitsministerium.de/fileadmin/Dateien/3_Downloads/Statistiken/GKV/Finanzergebnisse/KV45_1-4_Quartal_2019_Internet.pdf. Accessed 15 Jul 2022.
85. Moore PV, Bennett K, Normand C. The importance of proximity to death in modelling community medication expenditures for older people: evidence from New Zealand. *Appl Health Econ Health Policy*. 2014;12:623–33. doi:10.1007/s40258-014-0121-x.
86. Boecking W, Klamar A, Kitzmann F, Kirch W. Pharmaco-economic impact of demographic change on pharmaceutical expenses in Germany and France. *BMC Public Health*. 2012;12:894. doi:10.1186/1471-2458-12-894.
87. Mousnad MA, Shafie AA, Ibrahim MI. Systematic review of factors affecting pharmaceutical expenditures. *Health Policy*. 2014;116:137–46. doi:10.1016/j.healthpol.2014.03.010.
88. Ademi Z, Kim H, Zomer E, Reid CM, Hollingsworth B, Liew D. Overview of pharmacoeconomic modelling methods. *Br J Clin Pharmacol*. 2013;75:944–50. doi:10.1111/j.1365-2125.2012.04421.x.
89. Newhouse JP. Medical care costs: how much welfare loss? *J Econ Perspect*. 1992;6:3–21. doi:10.1257/jep.6.3.3.
90. OECD. Health at a Glance 2019. Paris: OECD Publishing; 2019.
91. Hagist C, Kotlikoff L. Who's Going Broke? Comparing Growth in Healthcare Costs in Ten OECD Countries. 2005.
92. Chernew ME, Newhouse JP. Health Care Spending Growth. In: Pauly MV, McGuire TG, Barros PP, editors. *Handbook of Health Economics*: Elsevier; 2011. p. 1–43. doi:10.1016/B978-0-444-53592-4.00001-3.
93. Meijer C de, O'Donnell O, Koopmanschap M, van Doorslaer E. Health expenditure growth: looking beyond the average through decomposition of the full distribution. *J Health Econ*. 2013;32:88–105. doi:10.1016/j.jhealeco.2012.10.009.

-
94. Breyer F, Lorenz N, Pruckner GJ, Schober T. Looking into the black box of “medical progress”: Rising health expenditures by illness type and age. 2021. <https://www.econstor.eu/handle/10419/231468>. Accessed 11 Dec 2021.
95. Starr M, Dominiak L, Aizcorbe A. Decomposing growth in spending finds annual cost of treatment contributed most to spending growth, 1980-2006. *Health Aff (Millwood)*. 2014;33:823–31. doi:10.1377/hlthaff.2013.0656.
96. Fetzer S, Moog S. Indicators for Measuring Intergenerational Fairness of Social Security Systems—The Case of the German Social Health Insurance. *Sustainability*. 2021;13:5743. doi:10.3390/su13105743.
97. Wasem J, Hüer T, Abels C. Gesellschaftliche und volkswirtschaftliche Sicht auf die (zukünftige) Finanzierbarkeit von Arzneimitteln. In: Schröder H, Thürmann P, Telschow C, Schröder M, Busse R, editors. *Arzneimittel-Kompass 2021*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2021. p. 19–34. doi:10.1007/978-3-662-63929-0_2.
98. German Bundestag. Entwurf eines Gesetzes zur finanziellen Stabilisierung der gesetzlichen Krankenversicherung (GKV-Finanzstabilisierungsgesetz); July 2022.
99. Hofbauer-Milan V, Fetzer S, Hagist C. Cost risk groups in the SHI and the costs in the year of death. Unpublished Working Paper. 2022.
100. Crocker KJ, Snow A. The Theory of Risk Classification. In: Dionne G, editor. *Handbook of Insurance*. New York, NY: Springer New York; 2013. p. 281–313. doi:10.1007/978-1-4614-0155-1_11.
101. McGuire TG, Schillo S, van Kleef RC. Very high and low residual spenders in private health insurance markets: Germany, The Netherlands and the U.S. Marketplaces. *Eur J Health Econ*. 2021;22:35–50. doi:10.1007/s10198-020-01227-3.
102. Schillo S, Lux G, Wasem J, Buchner F. High cost pool or high cost groups-How to handle high(est) cost cases in a risk adjustment mechanism? *Health Policy*. 2016;120:141–7. doi:10.1016/j.healthpol.2016.01.003.
103. Wasem J, Buchner F, Lux G, Schillo S. Health Plan Payment in Germany. In: *Risk Adjustment, Risk Sharing and Premium Regulation in Health Insurance Markets*: Elsevier; 2018. p. 295–329. doi:10.1016/B978-0-12-811325-7.00011-7.
104. Bundesgesundheitsministerium. Verordnung über das Verfahren zum Risikostrukturausgleich in der gesetzlichen Krankenversicherung (Risikostruktur-Ausgleichsverordnung): RSAV.
105. Federal Office for Social Security. Bestimmungen des GKV-Spitzenverbandes: Anlage 1.1 - Archiv.

- <https://www.bundesamtsozialesicherung.de/de/themen/risikostrukturausgleich/datengrundlagen/archiv-bestimmungen-des-gkv-spitzenverbandes/-/anlage-11/>. Accessed 9 Aug 2022.
106. Bundesgesundheitsministerium. Finanzergebnisse der GKV. 01.08.2022. <https://www.bundesgesundheitsministerium.de/themen/krankenversicherung/zahlen-und-fakten-zur-krankenversicherung/finanzergebnisse.html>. Accessed 17.08.222.
107. Wammes JG, Tanke M, Jonkers W, Westert GP, van der Wees P, Jeurissen PP. Characteristics and healthcare utilisation patterns of high-cost beneficiaries in the Netherlands: a cross-sectional claims database study. *BMJ Open*. 2017;7:e017775. doi:10.1136/bmjopen-2017-017775.
108. Joynt KE, Figueroa JF, Beaulieu N, Wild RC, Orav EJ, Jha AK. Segmenting high-cost Medicare patients into potentially actionable cohorts. *Healthc (Amst)*. 2017;5:62–7. doi:10.1016/j.hjdsi.2016.11.002.
109. Wammes JG, van der Wees PJ, Tanke MAC, Westert GP, Jeurissen PPT. Systematic review of high-cost patients' characteristics and healthcare utilisation. *BMJ Open*. 2018;8:e023113. doi:10.1136/bmjopen-2018-023113.
110. Stahmeyer JT, Hamp S, Zeidler J, Eberhard S. Gesundheitsausgaben und die Rolle des Alters: Eine detaillierte Analyse der Kosten von Überlebenden und Verstorbenen. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2021. doi:10.1007/s00103-021-03385-y.
111. Bynum JPW, Austin A, Carmichael D, Meara E. High-Cost Dual Eligibles' Service Use Demonstrates The Need For Supportive And Palliative Models Of Care. *Health Aff (Millwood)*. 2017;36:1309–17. doi:10.1377/hlthaff.2017.0157.
112. Aldridge MD, Kelley AS. The Myth Regarding the High Cost of End-of-Life Care. *Am J Public Health*. 2015;105:2411–5. doi:10.2105/AJPH.2015.302889.
113. Davis MA, Nallamotheu BK, Banerjee M, Bynum JPW. Identification Of Four Unique Spending Patterns Among Older Adults In The Last Year Of Life Challenges Standard Assumptions. *Health Aff (Millwood)*. 2016;35:1316–23. doi:10.1377/hlthaff.2015.1419.
114. Federal Office for Social Security. Weiterentwicklung des Risikostrukturausgleichs. <https://www.bundesamtsozialesicherung.de/de/themen/risikostrukturausgleich/weiterentwicklung/>. Accessed 9 Aug 2022.

115. German Bundestag. Gesetz für einen fairen Kassenwettbewerb in der gesetzlichen Krankenversicherung: Fairer-Kassenwettbewerb-Gesetz - GKV-FKG); 22.03.2020.
116. van de ven WPMM, Ellis RP. Risk adjustment in competitive health plan markets. In: Culyer AJ, Newhouse JP, editors. *Handbook of Health Economics*. Amsterdam: Elsevier; 2000. p. 755–845. doi:10.1016/S1574-0064(00)80173-0.
117. Drösler S, Hasford J, Kurth B-M, Schaefer M, Wasem J, Wille E. Evaluationsbericht zum Jahresausgleich 2009 im Risikostrukturausgleich. 22.06.2011. https://www.bundesamtsozialesicherung.de/fileadmin/redaktion/Risikostrukturausgleich/Wissenschaftlicher_Beirat/20210204Evaluationsbericht_zum_Jahresausgleich_2009.pdf. Accessed 10 Aug 2022.
118. Federal Office for Social Security. Risikostrukturausgleich: Ergebnisse des Jahresausgleichs 2020. 10.01.2022. https://www.bundesamtsozialesicherung.de/fileadmin/redaktion/Risikostrukturausgleich/Info-Dateien%20und%20Auswertungen/20220111_JA2020_Anlage_3.pdf. Accessed 10 Aug 2022.
119. Beck K, Zweifel P. Cream-skimming in deregulated social health insurance: evidence from Switzerland. *Dev Health Econ Public Policy*. 1998;6:211–27. doi:10.1007/978-1-4615-5681-7_11.
120. Breyer F, Heineck M, Lorenz N. Determinants of health care utilization by German sickness fund members--with application to risk adjustment. *Health Econ*. 2003;12:367–76. doi:10.1002/hec.757.
121. Breyer F, Bundorf MK, Pauly MV. Health Care Spending Risk, Health Insurance, and Payment to Health Plans. In: Pauly MV, McGuire TG, Barros PP, editors. *Handbook of Health Economics*: Elsevier; 2011. p. 691–762. doi:10.1016/B978-0-444-53592-4.00011-6.

Appendices

Fig. 8 Search filter PubMed

```

(("forecasting"[MeSH Terms] OR "forecasting"[All Fields] OR "forecast"[All Fields]) OR ("projection"[MeSH Terms] OR "projection"[All Fields]
OR "projecting"[All Fields]))

AND

(("prevalence"[All Fields] OR "prevalence"[MeSH Terms]) OR ("incidence"[All Fields] OR "incidence"[MeSH Terms]) OR "burden of disease"
[All Fields]))

AND

(("chronic disease"[All Fields] OR "non communicable disease"[All Fields]) OR (("joint diseases"[MeSH Terms] OR "joint diseases"[All Fields]
OR "arthrosis"[All Fields]) OR ("osteoarthritis"[MeSH Terms] OR "osteoarthritis"[All Fields])) OR ("coronary heart disease"[All Fields] OR
"coronary artery disease"[All Fields]
OR "ischemic heart disease"[All Fields])
OR ("chronic obstructive pulmonary disease"[All Fields] OR "chronic obstructive lung disease"[All Fields])
OR (("dementia"[MeSH Terms] OR "dementia"[All Fields]) OR "Alzheimer's"[All Fields]) OR ("depressive disorder"[MeSH Terms]
OR "depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive disorder"[All Fields] OR "depression"[All Fields] OR
"depression"[MeSH Terms])
OR ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields] OR
"diabetes"[All Fields])
OR ("heart failure"[All Fields] OR "cardiac insufficiency"[All Fields] OR "congestive heart failure"[All Fields] OR "cardiac failure"[All Fields]
OR "heart insufficiency"[All Fields] OR "cardial insufficiency"[All Fields] OR "cardiac insufficiency"[All Fields])
OR ("pulmonary cancer"[All Fields] OR "bronchial cancer"[All Fields] OR "tracheal cancer"[All Fields] OR "lung cancer"[All Fields])
OR (("back pain"[MeSH Terms] OR "back pain"[All Fields] OR "backache"[All Fields]) OR "back pain"[All Fields])
OR ("cerebrovascular disorder"[All Fields] OR "cerebrovascular disease"[All Fields]))

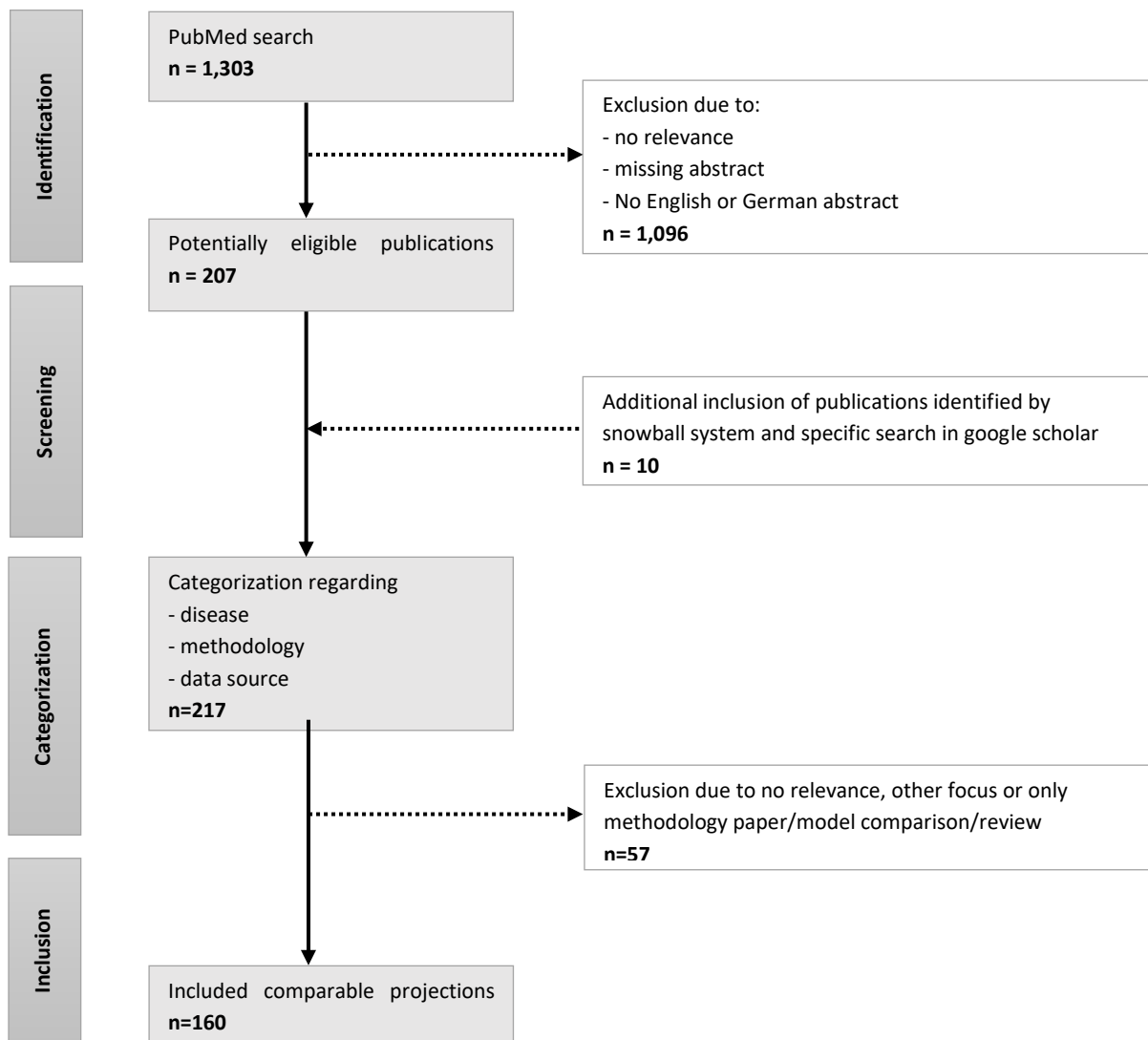
AND

(("demography"[MeSH Terms] OR "demography"[All Fields]) OR "demographic change"[All Fields] OR "demographic transition"[All Fields]
OR ("population"[MeSH Terms] OR "population"[All Fields]))
OR ("illness death model"[All Fields] OR "markov model"[All Fields] OR "cohort model"[All Fields]))

```

Source: Own depiction.

Fig. 9 Flow chart of the literature selection process



Source: Own depiction.

Tab. 11 Bibliography and study characteristics

#	Study	Country	Disease	Data source	Methodology	Projected year	DOI/PMID	Source
1	Cho et al. (2018): "IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045"	Global	Diabetes	Literature review	Trend extrapolation (Status quo)	2045	DOI: 10.1016/j.diabres.2018.02.023	Diabetes Research and Clinical Practice
2	Hebert et al. (2013): "Alzheimer disease in the United States (2010-2050) estimated using the 2010 census"	USA	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model	2050	DOI: 10.1212/WNL.0b013e31828726f5	Neurology
3	Shaw et al. (2010): "Global estimates of the prevalence of diabetes for 2010 and 2030"	Global	Diabetes	Literature review	Trend extrapolation (Status quo)	2030	DOI: 10.1016/j.diabres.2009.10.007	Diabetes Research and Clinical Practice
4	Guariguata et al. (2014): "Global estimates of diabetes prevalence for 2013 and projections for 2035"	Global	Diabetes	Literature review	Trend extrapolation (Status quo)	2035	DOI: 10.1016/j.diabres.2013.11.002. Epub 2013 Dec 1.	Diabetes Research and Clinical Practice
5	Ferri et al. (2005): "Global prevalence of dementia: a Delphi consensus study"	Global	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2040	DOI: 10.1016/S0140-6736(05)67889-0	The Lancet
6	Rowley et al. (2017): "Diabetes 2030: Insights from Yesterday, Today, and Future Trends"	USA	Diabetes	Literature review	Multistate model	2030	DOI: 10.1089/pop.2015.0181	Population Health Management

7	Meza et al. (2015): "Burden of type 2 diabetes in Mexico: past, current and future prevalence and incidence rates"	Mexico	Diabetes	Survey	Multistate model and trend extrapolation	2050	DOI: 10.1016/j.jpmed.2015.10.015	Preventive Medicine
8	Brookmeyer et al. (2018): "Forecasting the prevalence of preclinical and clinical Alzheimer's disease in the United States"	USA	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model	2060	DOI: 10.1016/j.jalz.2017.10.009	Alzheimers and Dementia
9	Etkind et al. (2017): "How many people will need palliative care in 2040? Past trends, future projections and implications for services"	GB	Sundries	Mixed data sources	Trend extrapolation (Status quo)	2040	DOI: 10.1186/s12916-017-0860-2	BMC Medicine
10	Bommer et al. (2018): "Global Economic Burden of Diabetes in Adults: Projections From 2015 to 2030"	Global	Diabetes	Literature review	Trend extrapolation (Status quo)	2030	DOI: 10.2337/dc17-1962	Diabetes Care
11	Wong et al. (2017): "Projection of prediabetes and diabetes population size in Singapore using a dynamic Markov model"	Singapore	Diabetes	Registries	Multistate model	2035	DOI: 10.1111/1753-0407.12384	Journal of Diabetes
12	Morrell et al. (2016): "Diabetes incidence and projections from prevalence surveys in Fiji"	Fiji	Diabetes	Survey	Trend extrapolation	2020	DOI: 10.1186/s12963-016-0114-0	Population Health Metrics
13	Kingston et al. (2016): "Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model"	GB	Various	Survey	Multistate model	2040	DOI: 10.1093/ageing/afx201	Age and Ageing
14	Brookmeyer et al. (1998): "Projections of Alzheimer's disease in the United States and the public	USA	Dementia/ Alzheimer's	Literature review	Multistate model (Illness-death model)	2050	DOI: 10.2105/ajph.88.9.1337	American Journal of Public Health

	health impact of delaying disease onset"												
15	Gonzales-Gonzales et al. (2017): "Projecting diabetes prevalence among Mexicans aged 50 years and older: the Future Elderly Model-Mexico (FEM-Mexico)"	Mexico	Diabetes	Survey	Trend extrapolation	2050	DOI: 10.1136/bmjopen-2017-017330	BMI Open					
16	Ziegler-Graham et al. (2008): "Estimating the prevalence of limb loss in the United States: 2005 to 2050"	USA	Others	Routine data	Multistate model (Illness-death model)	2050	DOI: 10.1016/j.apmr.2007.11.005	Archives of Physical Medicine and Rehabilitation					
17	Lin et al. (2018): "Projection of the future diabetes burden in the United States through 2060"	USA	Diabetes	Survey	Multistate model (Illness-death model)	2060	DOI: 10.1186/s12963-018-0166-4	Population Health Metrics					
18	Matthews et al. (2019): "Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015-2060) in adults aged ≥65 years"	USA	Dementia/ Alzheimer's	Routine data	Trend extrapolation (Status quo)	2060	DOI: 10.1016/j.jalz.2018.06.3063	Alzheimers & Dementia					
19	Awad et al. (2018): "Forecasting the burden of type 2 diabetes mellitus in Qatar to 2050: A novel modeling approach"	Qatar	Diabetes	Survey	Multistate model	2050	DOI: 10.1016/j.diabres.2017.11.015	Diabetes Research and Clinical Practice					
20	Meo (2016): "Prevalence and future prediction of type 2 diabetes mellitus in the Kingdom of Saudi Arabia: A systematic review of published studies"	Saudi Arabia	Diabetes	Literature review	Trend extrapolation (Status quo)	2030	PMID: 27339576	Journal of the Pakistan Medical Association					

21	Hebert et al. (2003): "Alzheimer disease in the US population: prevalence estimates using the 2000 census"	USA	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model	2050	DOI: 10.1001/archneur.60.8.1119	Archives of Neurology
22	Savica et al. (2018): "Parkinson disease with and without Dementia: A prevalence study and future projections"	USA	Others	Other epidemiological studies	Trend extrapolation (Status quo)	2060	DOI: 10.1002/mds.27277	Movement Disorders
23	Ackerman et al. (2018): "Projected Burden of Osteoarthritis and Rheumatoid Arthritis in Australia: A Population-Level Analysis"	Australia	Various	Survey	Trend extrapolation (Status quo)	2030	DOI: 10.1002/acr.23414	Arthritis Care & Research
24	Ahmadi-Abhari et al (2017): "Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040: modelling study"	GB	Dementia/ Alzheimer's	Survey	Multistate model	2040	DOI: 10.1136/bmj.j2856.	British Medical Journal
25	Sugiyama et al. (2017): "Construction of a simulation model and evaluation of the effect of potential interventions on the incidence of diabetes and initiation of dialysis due to diabetic nephropathy in Japan"	Japan	Diabetes	Survey	Trend extrapolation	2035	DOI: 10.1186/s12913-017-2784-0	BMC Health Services Research
26	Sarink et al. (2016): "Projected age- and sex-specific prevalence of cardiovascular diseases in Western Australian adults from 2005-2045"	Australia	Various	Mixed data sources	Multistate model	2045	DOI: 10.1177/2047487314554865	European Journal of Preventive Cardiology
27	Imperatore et al. (2012): "Projections of type 1 and type 2 diabetes burden in the U.S. population aged <20 years through 2050: dynamic modeling of	USA	Diabetes	Other epidemiological studies	Multistate model	2050	DOI: 10.2337/dc12-0669	Diabetes Care

	incidence, mortality, and population growth"											
28	Andersson et al. (2015): "Diabetes Prevalence in Sweden at Present and Projections for Year 2050"	Sweden	Diabetes	Mixed data sources	Multistate model (Illness-death model)	2050	DOI: 10.1371/journal.pone.0143084					PLoS One
29	Kainz et al. (2015): "Prediction of prevalence of chronic kidney disease in diabetic patients in countries of the European Union up to 2025"	Various	Various	Other epidemiological studies	Trend extrapolation	2025	DOI: 10.1093/ndt/gfv073.					Nephrology Dialysis Transplantation
30	Manuel et al. (2016): "Alzheimer's and other dementias in Canada, 2011 to 2031: a microsimulation Population Health Modeling (POHEM) study of projected prevalence, health burden, health services, and caregiving use"	Canada	Dementia/ Alzheimer's	Routine data	Trend extrapolation	2031	DOI: 10.1186/s12963-016-0107-z					Population Health Metrics
31	de Sousa-Uva et al. (2016): "Trends in diabetes incidence from 1992 to 2015 and projections for 2024: A Portuguese General Practitioner's Network study"	Portugal	Diabetes	Other epidemiological studies	Trend extrapolation	2024	DOI: 10.1016/j.pcd.2016.05.003					Primary Care Diabetes
32	Saidi et al. (2015): "Forecasting Tunisian type 2 diabetes prevalence to 2027: validation of a simple model"	Tunisia	Diabetes	Mixed data sources	Multistate model	2027	DOI: 10.1186/s12889-015-1416-z					BMC Public Health
33	Olajide et al. (2015): "Lung cancer trend in England for the period of 2002 to 2011 and projections of future burden until 2020"	GB	Pulmonary cancer	Registries	Trend extrapolation	2020	DOI: 10.3892/ijo.2015.3049					International Journal of Oncology

34	Javanbakht et al. (2015): "Projection of Diabetes Population Size and Associated Economic Burden through 2030 in Iran: Evidence from Micro-Simulation Markov Model and Bayesian Meta-Analysis"	Iran	Diabetes	Survey	Multistate model	2030	DOI: 10.1371/journal.pone.0132505. eCollection 2015.	PLoS One
35	Turkiewicz et al. (2014): "Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032"	Sweden	Arthritis	Routine data	Trend extrapolation (Status quo)	2032	DOI: 10.1016/j.joca.2014.07.015. Epub 2014 Jul 30.	Osteoarthritis and Cartilage
36	Bilandzic & Rosella (2017): "The cost of diabetes in Canada over 10 years: applying attributable health care costs to a diabetes incidence prediction model"	Canada	Diabetes	Survey	Trend extrapolation	2022	DOI: 10.24095/hpcdp.37.2.03	Health Promotion and Chronic Disease Prevention in Canada: Research, Policy and Practice
37	Al Ali et al. (2013): "Forecasting future prevalence of type 2 diabetes mellitus in Syria"	Syria	Diabetes	Survey	Multistate model	2022	DOI: 10.1186/1471-2458-13-507.	BMC Public Health
38	Park et al. (2013): "Burden of disease due to dementia in the elderly population of Korea: present and future"	Korea	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2050	DOI: 10.1186/1471-2458-13-293.	BMC Public Health
39	Waldeyer et al. (2013): "Projection of the burden of type 2 diabetes mellitus in Germany: a demographic modelling approach to estimate the direct medical excess costs from 2010 to 2040"	Germany	Diabetes	Survey	Multistate model (Illness-death model)	2040	DOI: 10.1111/dme.12177	Diabetic Medicine
40	Milan & Fetzer (2019): "The future development of dementia diseases in	Germany	Dementia/ Alzheimer's	Routine data	Multistate model (Illness-death model)	2060	DOI: 10.1007/s00103-019-02981-3	Bundesgesundheitsblatt Gesundheitsforschung

	Germany-a comparison of different forecast models"											Gesundheits- schutz
41	Loef & Walach (2013): "Midlife obesity and dementia: meta-analysis and adjusted forecast of dementia prevalence in the United States and China"	Various	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2030	DOI: 10.1002/oby.20037	Obesity				
42	Png et al. (2016): "Current and future economic burden of diabetes among working-age adults in Asia: conservative estimates for Singapore from 2010-2050"	Singapore	Diabetes	Mixed data sources	Trend extrapolation (Status quo)	2050	DOI: 10.1186/s12889-016-2827-1.	BMC Public Health				
43	Al-Quwaidhi et al. (2014): "Comparison of type 2 diabetes prevalence estimates in Saudi Arabia from a validated Markov model against the International Diabetes Federation and other modelling studies"	Saudi Arabia	Diabetes	Survey	Multistate model	2030	DOI: 10.1016/j.diabres.2013.12.036	Diabetes Research and Clinical Practice				
44	Backholer et al. (2013): "Diabetes Prevention and Treatment Strategies - Are we doing enough?"	Australia	Diabetes	Other epidemiological studies	Multistate model	2025	DOI: 10.2337/dc12-2501	Diabetes Care				
45	Huang et al. (2009): "Projecting the Future Diabetes Population Size and Related Costs for the U.S."	USA	Diabetes	Survey	Multistate model	2033	DOI: 10.2337/dc09-0459	Diabetes Care				
46	Tobias et al. (2008): "Burden of Alzheimer's disease: population-based estimates and projections for New Zealand, 2006-2031"	New Zealand	Dementia/ Alzheimer's	Literature review	Multistate model	2031	DOI: 10.1080/00048670802277297.	Australian and New Zealand Journal of Psychiatry				
47	Dall et al. (2013): "An aging population and growing disease burden will require a large and	USA	Various	Survey	Trend extrapolation	2025	DOI: 10.1377/hlthaff.2013.0714.	Health Affairs				

	specialized health care workforce by 2025"											
48	Boyle et al. (2001): "Projection of diabetes burden through 2050: impact of changing demography and disease prevalence in the U.S."	USA	Diabetes	Survey	Trend extrapolation	2050	DOI: 10.2337/diacare.24.11.1936	Diabetes Care				
49	Burgel et al. (2018): "An attempt at modeling COPD epidemiological trends in France"	France	COPD	Mixed data sources	Multistate model	2025	DOI: 10.1186/s12931-018-0827-7.	Respiratory Research				
50	Jorm et al. (2005): "Projections of future numbers of dementia cases in Australia with and without prevention"	Australia	Dementia/ Alzheimer's	Other epidemiological studies	Trend extrapolation (Status quo)	2050	DOI: 10.1080/j.1440-1614.2005.01713.x	Australian and New Zealand Journal of Psychiatry				
51	Sloane et al. (2002): "The public health impact of Alzheimer's disease, 2000-2050: potential implication of treatment advances"	USA	Dementia/ Alzheimer's	Literature review	Multistate model	2050	DOI: 10.1146/annurev.publhealth.23.100901.140525	Annual Review of Public Health				
52	Heo et al. (2008): "Population projection of US adults with lifetime experience of depressive disorder by age and sex from year 2005 to 2050"	USA	Depression	Survey	Trend extrapolation (Status quo)	2050	DOI: 10.1002/gps.2061	International Journal of Geriatric Psychiatry				
53	Brookmeyer & Gray (2000): "Methods for projecting the incidence and prevalence of chronic diseases in aging populations: application to Alzheimer's disease"	USA	Dementia/ Alzheimer's	Literature review	Multistate model (Illness-death model)	2050	DOI: 10.1002/(sici)1097-0258(20000615/30)19:11/12<1481::aid-sim440>3.0.co;2-u	Statistics in Medicine				

54	Centers for Disease Control and Prevention (CDC) (2003): "Public health and aging: projected prevalence of self-reported arthritis or chronic joint symptoms among persons aged >65 years--United States, 2005-2030"	USA	Arthritis	Survey	Trend extrapolation (Status quo)	2030	PMID: 12809109	MMWR Morbidity and Mortality Weekly Report
55	Odden et al. (2011): "The Impact of the Aging Population on Coronary Heart Disease in the U.S."	USA	CHD	Mixed data sources	Multistate model	2040	DOI: 10.1016/j.amjmed.2011.04.010	American Journal of Medicine
56	Brinks et al. (2012): "Prevalence of type 2 diabetes in Germany in 2040: estimates from an epidemiological model"	Germany	Diabetes	Survey	Multistate model (Illness-death model)	2040	DOI: 10.1007/s10654-012-9726-2.	European Journal of Epidemiology
57	Stewart et al. (2003): "Heart failure and the aging population: an increasing burden in the 21st century?"	GB	Heart failure	Mixed data sources	Trend extrapolation (Status quo)	2020	DOI: 10.1136/heart.89.1.49	Heart
58	Holt et al. (2011): "Forecasting the burden of advanced knee osteoarthritis over a 10-year period in a cohort of 60-64 year-old US adults"	USA	Arthritis	Mixed data sources	Multistate model	2020	DOI: 10.1016/j.joca.2010.10.009	Osteoarthritis and Cartilage
59	Saaddine et al. (2008): "Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus: United States, 2005-2050"	USA	Various	Survey	Multistate model (Illness-death model)	2050	DOI: 10.1001/archophth.126.12.1740.	Archives of Ophthalmology
60	Vickland et al. (2011): "Who pays and who benefits? How different models of shared responsibilities between formal and informal carers influence	Australia	Dementia/ Alzheimer's	Literature review	Trend extrapolation	2040	DOI: 10.1186/1471-2458-11-793	BMC Public Health

	projections of costs of dementia management"												
61	Moran et al. (2008): "The future impact of population growth and aging on coronary heart disease in China: projections from the Coronary Heart Disease Policy Model-China"	China	CHD	Mixed data sources	Multistate model	2030	DOI: 10.1186/1471-2458-8-394	BMC Public Health					
62	Jagger et al. (2009): "The effect of dementia trends and treatments on longevity and disability: a simulation model based on the MRC Cognitive Function and Ageing Study (MRC CFAS)"	GB	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model	2026	DOI: 10.1093/ageing/afp016	Age and Ageing					
63	Ackerman et al. (2019): "The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030"	Australia	Joint replacement	Registries	Trend extrapolation (Status quo)	2030	DOI: 10.1186/s12891-019-2411-9	BMC Musculoskeletal Disorders					
64	Schaubel et al. (1995): "End-stage renal disease projections for Canada to 2005 using Poisson and Markov models"	Canada	Kidney disease	Registries	Multistate model and trend extrapolation	2005	DOI: 10.1093/jje/27.2.274	International Journal of Epidemiology					
65	Mura et al. (2010): "How many dementia cases in France and Europe? Alternative projections and scenarios 2010-2050"	Various	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model	2050	DOI: 10.1111/j.1468-1331.2009.02783.x	European Journal of Neurology					
66	Parsons & Somerville (2000): "Estimation and projection of population lung cancer trends (United Kingdom)"	GB	Pulmonary cancer	Registries	Trend extrapolation	2015	DOI: 10.1023/a:1008966125578	Cancer Causes & Control					

67	Soerjomataram et al. (2011): "Reducing inequalities in lung cancer incidence through smoking policies"	Netherlands	Pulmonary cancer	Survey	Trend extrapolation	2050	DOI: 10.1016/j.lungcan.2011.01.009	Lung Cancer
68	Robertsson et al. (2000): "Past incidence and future demand for knee arthroplasty in Sweden: a report from the Swedish Knee Arthroplasty Register regarding the effect of past and future population changes on the number of arthroplasties performed"	Sweden	Joint replacement	Registries	Trend extrapolation (Status quo)	2030	DOI: 10.1080/000164700317393376	Acta Orthopaedica Scandinavica
69	Murakami & Ohashi (2001): "Projected number of diabetic renal disease patients among insulin-dependent diabetes mellitus children in Japan using a Markov model with probabilistic sensitivity analysis"	Japan	Kidney disease	Literature review	Multistate model	2015	DOI: 10.1093/ije/30.5.1078	International Journal of Epidemiology
70	Pritzkeleit et al. (2010): "Disease numbers in pneumology - a projection to 2060"	Germany	Various	Literature review	Trend extrapolation (Status quo)	2060	DOI: 10.1055/s-0030-1255637	Pneumologie
71	Rowley & Bezold (2012): "Creating public awareness: state 2025 diabetes forecasts"	USA	Diabetes	Literature review	Multistate model	2025	DOI: 10.1089/pop.2011.0053	Population Health Management
72	Narayan et al. (2006): "Impact of recent increase in incidence on future diabetes burden: U.S., 2005-2050"	USA	Diabetes	Survey	Multistate model (Illness-death model)	2006	DOI: 10.2337/dc06-1136	Diabetes Care
73	Fontaine et al. (2007): "Projected prevalence of US adults with self-reported doctor-diagnosed arthritis, 2005 to 2050"	USA	Arthritis	Survey	Trend extrapolation (Status quo)	2050	DOI: 10.1007/s10067-007-0556-7	Clinical Rheumatology

74	Ruwaard et al. (1993): "Forecasting the number of diabetic patients in The Netherlands in 2005"	Netherlands	Diabetes	Mixed data sources	Multistate model (Illness-death model)	2005	DOI: 10.2105/ajph.83.7.989	American Journal of Public Health
75	Hebert et al. (2004): "State-specific projections through 2025 of Alzheimer disease prevalence"	USA	Dementia/ Alzheimer's	Other epidemiological studies	Trend extrapolation (Status quo)	2025	DOI: 10.1212/01.wnl.0000123018.01306.10	Neurology
76	Gao et al. (2017): "Nephrology Dialysis Transplantation"	Canada	Various	Mixed data sources	Trend extrapolation	2025	DOI: 10.1186/s12882-017-0699-y	BMC Nephrology
77	Feenstra et al. (2001): "The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands"	Netherlands	COPD	Other epidemiological studies	Multistate model	2015	DOI: 10.1164/ajrccm.164.4.2003167	American Journal of Respiratory and Critical Care Medicine
78	Danielsen et al. (2017): "Prevalence of heart failure in the elderly and future projections: the AGES-Reykjavik study"	Iceland	Heart failure	Other epidemiological studies	Trend extrapolation (Status quo)	2060	DOI: 10.1080/14017431.2017.1311023	Scandinavian Cardiovascular Journal
79	Sharif et al. (2015): "Projecting the direct cost burden of osteoarthritis in Canada using a microsimulation model"	Canada	Arthritis	Mixed data sources	Trend extrapolation	2031	DOI: 10.1016/j.joca.2015.05.029	Osteoarthritis and Cartilage
80	Gouveia et al. (2019): "The current and future burden of heart failure in Portugal"	Portugal	Heart failure	Mixed data sources	Trend extrapolation (Status quo)	2036	DOI: 10.1002/ehf2.12399	ESC Heart Failure
81	Standfield et al. (2018): "A simulation of dementia epidemiology and resource use in Australia"	Australia	Dementia/ Alzheimer's	Literature review	Trend extrapolation	2050	DOI: 10.1111/1753-6405.12700	Australian and New Zealand Journal of Public Health

82	Menvielle et al. (2010): "Scenarios of future lung cancer incidence by educational level: Modelling study in Denmark"	Denmark	Pulmonary cancer	Mixed data sources	Trend extrapolation	2050	DOI: 10.1016/j.ejca.2010.07.027	European Journal of Cancer
83	Peters et al. (2010): "Demographic change and disease rates: a projection until 2050"	Germany	Various	Literature review	Trend extrapolation (Status quo)	2050	DOI: 10.1007/s00103-010-1050-y	Bundesgesundheitsblatt Gesundheitsforschung Gesundheitschutz
84	Brinks et al. (2014): "Age-specific prevalence of diagnosed systemic lupus erythematosus in Germany 2002 and projection to 2030"	Germany	Others	Routine data	Trend extrapolation (Status quo)	2030	DOI: 10.1177/0961203314540352	Lupus
85	Oberaigner & Geiger-Gritsch (2014): "Prediction of cancer incidence in Tyrol/Austria for year of diagnosis 2020"	Austria	Cancer	Registries	Trend extrapolation	2020	DOI: 10.1007/s00508-014-0596-3	Wiener klinische Wochenschrift
86	Nowossadeck et al.: (2014): "The future incidence of colorectal and lung cancers: results of the calculation of different scenarios for the year 2020"	Germany	Cancer	Registries	Trend extrapolation (Status quo)	2020	DOI: 10.1007/s00103-013-1873-4	Bundesgesundheitsblatt Gesundheitsforschung Gesundheitschutz
87	Bonneux et al. (1994): "Estimating clinical morbidity due to ischemic heart disease and congestive heart failure: the future rise of heart failure"	Netherlands	Heart failure	Mixed data sources	Multistate model	2010	DOI: 10.2105/ajph.84.1.20	American Journal of Public Health

88	Nowatzki et al. (2011): "Projection of future cancer incidence and new cancer cases in Manitoba, 2006-2025"	Canada	Cancer	Registries	Trend extrapolation	2025	PMID: 21466757	Chronic Diseases in Canada
89	Salomaa et al. (2013): "Aging of the population may not lead to an increase in the numbers of acute coronary events: a community surveillance study and modelled forecast of the future"	Finland	CHD	Registries	Trend extrapolation	2050	DOI: 10.1136/heartjnl-2012-303216	Heart
90	Didkowska et al. (2011): "Future lung cancer incidence in Poland and Finland based on forecasts on hypothetical changes in smoking habits"	Various	Pulmonary cancer	Mixed data sources	Trend extrapolation	2030	DOI: 10.3109/0284186X.2010.488247	Acta Oncologica
91	Estes et al. (2018): "Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030"	Various	Others	Literature review	Multistate model	2030	DOI: 10.1016/j.jhep.2018.05.036	Journal of Hepatology
92	McLean et al. (2016): "Projecting the COPD population and costs in England and Scotland: 2011 to 2030"	GB	COPD	Mixed data sources	Multistate model	2030	DOI: 10.1038/srep31893	Scientific Reports
93	Firlei et al. (2007): "The prevalence of COPD in Austria--the expected change over the next decade"	Austria	COPD	Other epidemiological studies	Trend extrapolation (Status quo)	2020	DOI: 10.1007/s00508-007-0867-3	Wiener klinische Wochenschrift
94	Cobiac & Scarborough (2017): "Translating the WHO 25x25 goals into a UK context: the PROMISE modelling study"	GB	Various	Mixed data sources	Trend extrapolation	2030	DOI: 10.1136/bmjopen-2016-012805	BMJ Open

95	Marimuthu (2008): "Projection of cancer incidence in five cities and cancer mortality in India"	India	Cancer	Registries	Trend extrapolation (Status quo)	2008	PMID: 18453733	Indian Journal of Cancer
96	Soerjomataram et al. (2010): "Impact of a smoking and alcohol intervention programme on lung and breast cancer incidence in Denmark: An example of dynamic modelling with Prevent"	Denmark	Pulmonary cancer	Mixed data sources	Trend extrapolation	2050	DOI: 10.1016/j.ejca.2010.07.051	European Journal of Cancer
97	Edwards et al. (2014): "A novel approach for the accurate prediction of thoracic surgery workforce requirements in Canada"	Canada	Pulmonary cancer	Survey	Trend extrapolation	2030	DOI: 10.1016/j.jtcvs.2014.03.031	The Journal of Thoracic and Cardiovascular Surgery
98	Estes et al. (2018): "Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease"	USA	Others	Literature review	Multistate model	2030	DOI: 10.1002/hep.29466	Hepatology
99	Perruccio et al. (2006): "Revisiting arthritis prevalence projections--it's more than just the aging of the population"	Canada	Arthritis	Survey	Trend extrapolation	2021	PMID: 16960946	Journal of Rheumatology
100	Nepal et al. (2014): "Rising midlife obesity will worsen future prevalence of dementia"	Australia	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2050	DOI: 10.1371/journal.pone.0099305	PLoS One
101	Rahib et al. (2014): "Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States"	USA	Cancer	Mixed data sources	Trend extrapolation (Status quo)	2030	DOI: 10.1158/0008-5472.CAN-14-0155	Cancer Research
102	Orenstein & Shi (2016): "Microsimulation Modeling of Coronary Heart Disease: Maximizing	USA	CHD	Survey	Trend extrapolation	2030	DOI: 10.1177/0046958016666009	INQUIRY: The Journal of Health Care

	the Impact of Nonprofit Hospital-Based Interventions"										Organization, Provision, and Financing
103	Quante et al. (2016): "Projections of cancer incidence and cancer-related deaths in Germany by 2020 and 2030"	Germany	Cancer	Registries	Trend extrapolation	2030	DOI: 10.1002/cam4.767				Cancer Medicine
104	Gilbertson et al. (2005): "Projecting the number of patients with end-stage renal disease in the United States to the year 2015"	USA	Kidney disease	Survey	Multistate model	2005	DOI: 10.1681/ASN.2005010112				Journal of the American Society of Nephrology
105	Beele et al. (2008): "Lung cancer incidence and mortality: current trends and projections based on data from Schleswig-Holstein"	Germany	Pulmonary cancer	Registries	Trend extrapolation (Status quo)	2020	DOI: 10.1055/s-2008-1081095				Deutsche Medizinische Wochenschrift
106	Tsoi et al. (2017): "Cancer burden with ageing population in urban regions in China: projection on cancer registry data from World Health Organization"	China	Cancer	Registries	Trend extrapolation	2030	DOI: 10.1093/bmb/ldw050				British Medical Bulletin
107	Okura et al. (2008): "Impending epidemic: future projection of heart failure in Japan to the year 2055"	Japan	Heart failure	Other epidemiological studies	Trend extrapolation (Status quo)	2055	DOI: 10.1253/circj.72.489				Circulation Journal
108	Ansah et al. (2018): "Projection of Eye Disease Burden in Singapore"	Singapore	Others	Other epidemiological studies	Trend extrapolation (Status quo)	2040	PMID: 29493707				Annals Academy of Medicine Singapore
109	Heidenreich et al. (2011): "Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association"	USA	Various	Survey	Trend extrapolation (Status quo)	2030	DOI: 10.1161/CIR.0b013e31820a55f5				Circulation

110	Bahr et al. (2015): "Prognosis of population-related morbidity for common cancers in Germany--Effects on health care"	Germany	Cancer	Registries	Trend extrapolation (Status quo)	2020	DOI: 10.1055/s-0041-101356	Deutsche Medizinische Wochenschrift
111	Weinstein et al. (1987): "Forecasting coronary heart disease incidence, mortality, and cost: the Coronary Heart Disease Policy Model"	USA	CHD	Mixed data sources	Multistate model	2010	DOI: 10.2105/ajph.77.11.1417	American Journal of Public Health
112	Campbell et al. (2018): "The present and future burden of previously treated advanced non-small cell lung cancer (NSCLC) by histology and line of therapy in France, Germany, Italy, and Spain: model-based predictions"	Various	Pulmonary cancer	Registries	Trend extrapolation	2020	DOI: 10.1186/s12963-018-0174-4	Population Health Metrics
113	Moran et al. (2010): "Future cardiovascular disease in china: markov model and risk factor scenario projections from the coronary heart disease policy model-china"	China	CHD	Other epidemiological studies	Multistate model and trend extrapolation	2020	DOI: 10.1161/CIRCOUTCOMES.109.910711	Circulation: Cardiovascular Quality and Outcomes
114	Kingston et al. (2018): "Forecasting the care needs of the older population in England over the next 20 years: estimates from the Population Ageing and Care Simulation (PACSim) modelling study"	GB	Various	Other epidemiological studies	Multistate model	2035	DOI: 10.1016/S2468-2667(18)30118-X	The Lancet Public Health
115	Baik (2019): "Projection of Diabetes Prevalence in Korean Adults for the Year 2030 Using Risk Factors Identified from National Data"	Korea	Diabetes	Survey	Trend extrapolation	2030	DOI: 10.4093/dmj.2018.0043	Diabetes and Metabolism Journal
116	Lee et al. (2016): "Epidemiology of Heart Failure in Korea: Present and Future"	Korea	Heart failure	Routine data	Trend extrapolation (Status quo)	2040	DOI: 10.4070/kcj.2016.46.5.658	Korean Circulation Journal

117	Mukasheva et al. (2019): "Forecasting the Prevalence of Diabetes Mellitus Using Econometric Models"	Kazakhstan	Diabetes	Registries	Trend extrapolation	2018	DOI: 10.1007/s13300-019-00684-1	Diabetes Therapy
118	Pandya et al. (2013): "More americans living longer with cardiovascular disease will increase costs while lowering quality of life"	USA	CHD	Survey	Trend extrapolation	2030	DOI: 10.1377/hlthaff.2013.0449	Health Affairs
119	Pan et al. (2010): "Burden of diabetes in the adult Chinese population: A systematic literature review and future projections"	China	Diabetes	Literature review	Trend extrapolation (Status quo)	2016	DOI: 10.2147/jigm.s6343	International Journal of General Medicine
120	Chen et al. (2011): "Bayesian age-period-cohort prediction of lung cancer incidence in China"	China	Pulmonary cancer	Registries	Trend extrapolation	2020	DOI: 10.1111/j.1759-7714.2011.00062.x	Thoracic Cancer
121	Brookmeyer et al. (2007): "Forecasting the global burden of Alzheimer's disease"	Global	Dementia/ Alzheimer's	Literature review	Multistate model	2050	DOI: 10.1016/j.jalz.2007.04.381	Alzheimers and Dementia
122	Boyle et al. (2010): "Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence"	USA	Diabetes	Literature review	Multistate model and trend extrapolation	2050	DOI: 10.1186/1478-7954-8-29	Population Health Metrics
123	Wong et al. (2018): "Projecting the Burden of Chronic Kidney Disease in a Developed Country and Its Implications on Public Health"	Singapore	Kidney disease	Registries	Multistate model	2035	DOI: 10.1155/2018/5196285	International Journal of Nephrology

124	Bai et al. (2018): "The trends and projections in the incidence and mortality of liver cancer in urban Shanghai: a population-based study from 1973 to 2020"	Shanghai	Cancer	Registries	Trend extrapolation	2020	DOI: 10.2147/CLEP.S153951	Clinical Epidemiology
125	Islek et al. (2016): "Estimating the potential contribution of stroke treatments and preventative policies to reduce the stroke and ischemic heart disease mortality in Turkey up to 2032: a modelling study"	Turkey	CHD	Mixed data sources	Multistate model	2032	DOI: 10.1186/s12889-015-2655-8	BMC Public Health
126	Guzman-Castillo et al. (2017): "Forecasted trends in disability and life expectancy in England and Wales up to 2025: a modelling study"	GB	Various	Other epidemiological studies	Multistate model	2025	DOI: 10.1016/S2468-2667(17)30091-9	The Lancet Public Health
127	Phan et al. (2014): "Forecasting the burden of type 2 diabetes in Singapore using a demographic epidemiological model of Singapore"	Singapore	Diabetes	Mixed data sources	Multistate model	2050	DOI: 10.1136/bmjdr-2013-000012	BMJ Open Diabetes Research and Care
128	Suka et al. (2004): "The national burdens of rheumatoid arthritis and osteoarthritis in Japan: projections to the year 2010, with future changes in severity distribution"	Japan	Various	Survey	Trend extrapolation (Status quo)	2010	DOI: 10.3109/s10165-004-0310-9	Modern Rheumatology
129	Earnest et al. (2019): "Forecasting annual incidence and mortality rate for prostate cancer in Australia until 2022 using autoregressive integrated moving average (ARIMA) models"	Australia	Cancer	Registries	Trend extrapolation	2022	DOI: 10.1136/bmjopen-2019-031331	BMJ Open
130	Wancata et al. (2003): "Number of dementia sufferers in Europe between the years 2000 and 2050"	Various	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2050	DOI: 10.1016/j.eurpsy.2003.03.003	European Psychiatry

131	Li et al. (2019): "Prevalence, incidence and future projection of diabetic eye disease in Europe: a systematic review and meta-analysis"	Various	Others	Literature review	Trend extrapolation (Status quo)	2050	DOI: 10.1007/s10654-019-00560-z	European Journal of Epidemiology
132	Joly et al. (2013): "Prevalence Projections of Chronic Diseases and Impact of Public Health Intervention"	France	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model (Illness-death model)	2030	DOI: 10.1111/j.1541-0420.2012.01827.x	Biometrics
133	Mathers & Loncar (2008): "Projections of Global Mortality and Burden of Disease from 2002 to 2030"	Global	Various	Other epidemiological studies	Trend extrapolation	2030	DOI: 10.1371/journal.pmed.0030442	PLoS Medicine
134	Jagger et al. (2006): "Compression or expansion of disability?: forecasting future disability levels under changing patterns of diseases"	GB	Various	Mixed data sources	Multistate model	2025	http://eprints.lse.ac.uk/4459/1/Compression_or_expansion_of_disability_forecasting_future_disability_levels_under_changing_patterns_of_diseases.%28LSERO%29.pdf	Kings's Fund
135	Xie et al. (2015): "Cancer incidence in Canada: trends and projections (1983-2032)"	Canada	Cancer	Registries	Trend extrapolation	2032	PMID: 26011811	Health Promotion and Chronic Disease Prevention in Canada
136	Jacqmin-Gadda et al. (2013): "20-Year prevalence projections for dementia and impact of preventive policy about risk factors"	France	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model (Illness-death model)	2030	doi: 10.1007/s10654-013-9818-7	European Journal of Epidemiology
137	Culliford et al. (2015): "Future projections of total hip and knee arthroplasty in the UK: results from	GB	Joint replacement	Mixed data sources	Trend extrapolation (Status quo)	2035	DOI: 10.1016/j.joca.2014.12.022	Osteoarthritis and Cartilage

	the UK Clinical Practice Research Datalink"												
138	Van Meigaard et al. (2011): "Forecasting diabetes prevalence in California: a microsimulation"	USA	Diabetes	Mixed data sources	Trend extrapolation	2020	PMID: 21672404	Preventing Chronic Disease					
139	Honeycutt et al. (2003): "A dynamic Markov model for forecasting diabetes prevalence in the United States through 2050"	USA	Diabetes	Survey	Multistate model (Illness-death model)	2050	DOI: 10.1023/a:10244467522972	Health Care Management Science					
140	Terschüren et al. (2009): "Health status of 'Ruhr-City' in 2025--predicted disease burden for the metropolitan Ruhr area in North Rhine-Westphalia"	Germany	Various	Mixed data sources	Trend extrapolation (Status quo)	2025	DOI: 10.1093/eurpub/ckp060	European Journal of Public Health					
141	Bagust et al. (2002): "The projected health care burden of Type 2 diabetes in the UK from 2000 to 2060"	GB	Diabetes	Literature review	Trend extrapolation (Status quo)	2060	DOI: 10.1046/j.1464-5491.19.s4.2.x	Diabetic Medicine					
142	Bickel (2002): "Dementia in advanced age: estimating incidence and health care costs"	Germany	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2050	PMID: 11393002	Zeitschrift für Gerontologie und Geriatrie					
143	Morrison et al. (1995): "The impending Canadian prostate cancer epidemic"	Canada	Cancer	Registries	Trend extrapolation	2016	PMID: 7497416	Canadian Journal of Public Health					
144	Heidenreich et al. (2013): "Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association"	USA	Heart failure	Survey	Trend extrapolation (Status quo)	2030	DOI: 0.1161/HHF.0b013e318291329a	Circulation: Heart Failure					
145	Manton & Liu (1984): "Projecting chronic disease prevalence"	USA	Various	Registries	Multistate model (Illness-death mode with recovery)	2000	DOI: 10.1097/00005650-198406000-00002	Medical Care					

146	Van Meijgaard et al. (2009): "Assessing and forecasting population health: integrating knowledge and beliefs in a comprehensive framework"	USA	CHD	Mixed data sources	Trend extrapolation	2020	DOI: 10.1177/003335490912400604	Public Health Reports
147	Bray & Piñeros (2015): "Cancer patterns, trends and projections in Latin America and the Caribbean: a global context"	Various	Cancer	Registries	Trend extrapolation (Status quo)	2030	DOI: 10.21149/spm.v58i2.7779	Salud Pública de México
148	Evans (1990): "Estimated prevalence of Alzheimer's disease in the United States"	USA	Dementia/ Alzheimer's	Other epidemiological studies	Trend extrapolation (Status quo)	2050	PMID: 2233632	The Milbank Quarterly
149	Holman et al. (2011): "The Association of Public Health Observatories (APHO) Diabetes Prevalence Model: estimates of total diabetes prevalence for England, 2010-2030"	GB	Diabetes	Survey	Trend extrapolation	2030	DOI: 10.1111/j.1464-5491.2010.03216.x	Diabetic Medicine
150	Wille et al. (2010): "Modelling the costs of care of hypertension in patients with metabolic syndrome and its consequences, in Germany, Spain and Italy"	Various	Hypertension	Literature review	Trend extrapolation	2020	DOI: 10.1007/s10198-010-0223-9	The European Journal of Health Economics
151	Hitzl et al. (2019): "Projected numbers of primary total knee replacement in Austria from 2015-2075"	Austria	Joint replacement	Registries	Trend extrapolation (Status quo)	2075	DOI: 10.1007/s00132-018-3605-9	Der Orthopäde
152	Fox et al. (2011): "Estimating the costs of caring for people with Alzheimer disease in California: 2000-2040"	USA	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2040	PMID: 11382092	Journal of Public Health Policy
153	Zissimopoulos et al. (2018): "The Impact of Changes in Population Health and Mortality on Future	USA	Dementia/ Alzheimer's	Survey	Trend extrapolation	2040	DOI: 10.3233/JAD-150233	The journals of gerontology. Series B,

	Prevalence of Alzheimer's Disease and Other Dementias in the United States"									Psychological sciences and social sciences
154	Wanneveich et al. (2018): "Impact of intervention targeting risk factors on chronic disease burden"	France	Dementia/ Alzheimer's	Other epidemiological studies	Multistate model (Illness-death model)	2030	DOI: 10.1177/0962280216631360		Statistical Methods in Medical Research	
155	Vickland et al. (2010): "A computer model of dementia prevalence in Australia: foreseeing outcomes of delaying dementia onset, slowing disease progression, and eradicating dementia types"	Australia	Dementia/ Alzheimer's	Literature review	Trend extrapolation	2040	DOI: 10.1159/000272436		Dementia and Geriatric Cognitive Disorders	
156	Hooper et al. (2014): "Current trends and projections in the utilisation rates of hip and knee replacement in New Zealand from 2001 to 2026"	New Zealand	Joint replacement	Registries	Trend extrapolation (Status quo)	2026	PMID: 25225759		The New Zealand medical journal	
157	Amos et al. (1997): "The rising global burden of diabetes and its complications: estimates and projections to the year 2010"	Global	Diabetes	Literature review	Trend extrapolation (Status quo)	2010	PMID: 9450510		Diabetic Medicine	
158	Modig et al. (2012): "The aging population in Sweden: can declining incidence rates in MI, stroke and cancer counterbalance the future demographic challenges?"	Sweden	Various	Registries	Trend extrapolation (Status quo)	2050	DOI 10.1007/s10654-012-9653-2		European Journal of Epidemiology	
159	Tönnies et al. (2019): "Projected number of people with diagnosed Type 2 diabetes in Germany in 2040"	Germany	Diabetes	Mixed data sources	Multistate model (Illness-death model)	2040	DOI: 10.1111/dme.13902		Diabetic Medicine	
160	Alzheimer Europe (2020): "Dementia in Europe Yearbook 2019 - Estimating	Global	Dementia/ Alzheimer's	Literature review	Trend extrapolation (Status quo)	2050	https://www.alzheimer-europe.org/Publications/Dementia-in-Europe-Yearbooks		Alzheimer Europe	

	the prevalence of dementia in Europe"									
--	---------------------------------------	--	--	--	--	--	--	--	--	--

Source: Own depiction.