Research on the Cost of Illness for Specific Occupational Diseases Caused by Isocyanates

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I. Aumann
K. Kreis
J. Zeidler
J.-M. Graf von der Schulenburg

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The responsibility for the contents of this publication lies with the authors.

Authors:
Ines Aumann, M. Sc.
Kristine Kreis, M. Sc.
Dr. Jan Zeidler
Prof. Dr. J.-Matthias Graf von der Schulenburg
Kompetenzzentrum Versicherungs-
wissenschaften GmbH
Otto-Brenner-Str. 1, 30159 Hannover, Germany

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Federal Institute for Occupational Safety and Health

Publisher: Federal Institute for Occupational Safety and Health
Friedrich-Henkel-Weg 1-25, 44149 Dortmund, Germany
Postal address: Postbox 17 02 02, 44061 Dortmund, Germany
Telephone +49 231 9071-2071
Fax +49 231 9071-2070
Email: *info-zentrum@baua.bund.de*
Web: *www.baua.de*

Berlin:
Nöldnerstr. 40-42, 10317 Berlin, Germany
Telephone +49 30 51548-0
Fax +49 30 51548-4170

Dresden:
Fabricestr. 8, 01099 Dresden, Germany
Telephone +49 351 5639-50
Fax +49 351 5639-5210

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Table of contents

Research on the Cost of Illness for Specific Occupational Diseases Caused by Isocyanates

Abstract

The aim of this study was to estimate costs of illness resulting from specific occupational lung and skin diseases caused by isocyanates in Europe.
First, we conducted a comprehensive systematic literature search in selected databases from the German Institute for Medical Documentation and Information (DIMDI) and the OSH Reference database to identify articles dealing with costs of illness as well as indicators of severity/duration of occupational lung and skin diseases and evaluated the quality of included studies. A detailed quality evaluation was carried out for all included studies with the support of quality assessment instruments. Second, we analysed aggregated claim data provided by the German Social Accident Insurance (DGUV) covering costs for medical rehabilitation, services for professional rehabilitation and pensions for the years 2004-2013. Third, we transferred both, costs of illness values identified through the systematic literature search as well as calculated costs of illness based on claims data analysis, to the EU-28 countries using different methodological approaches.
According to data from the DGUV, approximately 500 insured persons per year with recognised occupational lung disease and approximately 20 insured persons with recognised occupational skin disease used at least one service per year for medical rehabilitation, service for professional participation or pension. Per case of disease of an insured person average total costs of almost €9000 per year for lung diseases (BK1315), and approximately €7000 per year for skin diseases (BK-5101) caused by isocyanates over 2004-2013 were calculated. A share of about 20% of these average total costs can be attributed to the cost category “medical rehabilitation”.
The cost of illness data derived by claim data analysis and literature search was extrapolated to EU-28, and average costs per case of disease and year were calculated. In this extrapolation only medical rehabilitation costs and productivity losses were included. The extrapolation lead to a range of costs depending on the data sources used and methodological approaches applied: 2.100€ to 3.500€ per case of occupational asthma, and 1.800€ to 2.400€ per case of occupational contact dermatitis.

Key words:

Isocyanate, costs of illness, occupational diseases, skin, lung

Ermittlung von Krankheitskosten für spezifische arbeitsbedingte Erkrankungen durch Isocyanate

Kurzreferat

Die Studie analysierte die Krankheitskosten isocyanatbedingter Lungen- und Hauterkrankungen.
Zunächst wurde eine umfassende systematische Literaturrecherche in ausgewählten Datenbanken des Deutschen Institutes für medizinische Dokumentation und Information (DIMDI) sowie in der OSH Reference Datenbank durchgeführt, um Artikel zu identifizieren, die sowohl Krankheitskosten, als auch Indikatoren zur Schwere oder Dauer der berufsbedingten Lungen- und Hauterkrankungen beinhalten. Für alle einbezogenen Krankheitskostenstudien wurde anschließend eine Qualitätsbewertung durchgeführt. In einem zweiten Schritt wurden isocyanatebedingte Krankheitskosten auf Basis von Daten der deutschen gesetzlichen Unfallversicherung (DGUV) berechnet. Dafür wurden aggregierte Daten aus den Jahren 2004-2013 zur Inanspruchnahme von Leistungen für medizinische Heilbehandlungen, zur Teilhabe am Arbeitsleben sowie Rentenzahlungen verursacht durch isocyanatebedingte Berufskrankheiten ausgewertet. In einem dritten Schritt wurden die Daten der DGUV sowie die Ergebnisse der systematischen Literaturrecherche mit verschiedenen nicht-Modellierungs- und Modellierungsansätzen auf die EU-28 Staaten übertragen.
Gemäß der Daten der DGUV nehmen pro Jahr circa 500 Versicherte mit berufsbedingter Lungenerkrankung (BK-1315) und circa 20 Versicherte mit berufsbedingter Hauterkrankung (BK-5101) mindestens eine Leistung der medizinischen, der beruflichen Rehabilitation oder eine Rentenleistung in Anspruch. Pro erkranktem Versicherten und Jahr ergeben sich daraus jährliche Gesamtkosten von 9.000€ für die BK-1315 und 7000€ für die BK-5101. Die Kosten für die Kostenkategorie „medizinische Behandlungskosten“ haben bei beiden Berufskrankheiten einen Anteil von rd. 20% an den durchschnittlichen jährlichen Gesamtkosten pro Jahr und pro erkranktem Versicherten.
Die durch Auswertung der BK-Daten sowie durch die systematische Literaturrecherche ermittelten Krankheitskosten wurden mit verschiedenen Ansätzen auf die EU-28 Staaten übertragen und ein EU-Mittelwert ermittelt, wobei nur medizinische Behandlungskosten und Produktivitätsausfall berücksichtigt wurden. Je nach gewähltem Ansatz und verwendeten Daten ergeben sich die folgenden Bandbreiten von durchschnittlichen jährlichen Krankheitskosten durch Isocynanate pro Erkrankungsfall für EU-28: 2.100€ bis 3.500€ für berufsbedingtes Asthma und 1.800€ bis 2.400€ für berufsbedingte Kontaktdermatitis.

Schlagwörter:

Isocyanate; Krankheitskosten, berufsbedingte Erkrankungen, Lunge, Haut

1 Introduction

The aim of this project is to analyse the costs of illness attributed by isocyanates as a sensitizer for the respiratory system and for the skin. These kinds of occupational diseases unit cost values will be derived by a systematic literature review of cost of illness studies. A claims data analysis will be conducted in order to calculate costs of isocyanate-induced diseases.
Isocyanate can cause respiratory diseases like asthma, chronic obstructive pulmonary disease (COPD) and extrinsic allergic alveolitis but they can also be responsible for skin diseases like allergic and irritant contact dermatitis (Beck, Leung 2000; Baur, Latza, Butz 2003), (Wisnewski et al. 2000). Costs of illness will be analysed for the German population and afterwards the results will be transferred to the selected EU-28 states.
This project is classified into three main work packages. First, in order to identify the relevant cost of illness studies as well as studies addressing the indicators of duration and the severity of isocyanate-induced occupational diseases a systematic literature search will be performed. In addition, a quality assessment will be conducted (1). Second, the costs of illness will be calculated for Germany based on claims data (2). In the third work package, the costs of illness for the selected EU states will be estimated by transferring the results of the first two work packages (3).
For a detailed overview of the different aims and sub targets of this project see appendix 1.

In this preliminary final report, one special focus is on the following tasks:

1. Quality assessment of cost of illness studies identified through the systematic literature search
2. Transfer of costs of illness of occupational lung and skin diseases from the perspective of the DGUV to the EU-28 countries as well as integration of results from the systematic literature search
3. Extrapolation of healthcare costs per case inclusive calculation of ranges of the healthcare costs using different methodological approaches.

Each of these results will be described in the following sections.

2 Systematic literature review

2.1 Theoretical background

The aim of the systematic literature review is to identify all publications which include relevant information regarding the defined research question. A well-focused research question and a structured approach are of particular importance. Therefore, it is necessary to use systematic methods to identify, select and critically evaluate relevant research (Moher et al. 2009).
A sophisticated search strategy is rather sensitive than specific to identify all studies including the negative results. The positive results are often published in high quality journals and these journals are mostly quoted in the main databases. Hence, a sensitive systematic research will commonly identify more studies than necessary. Nevertheless, this approach is considered better than the potential lack of some relevant papers (Nightingale 2009). In order to structure the literature research and specify the research questions, the PICO framework has proven as a methodological standard and is often utilised in medicine and health economics (Richardson E et al. 1995).
PICO is defined as follows:

- P=Patient or population (e.g. children, adolescent, age, sex, ethnic groups…)
- I=Intervention (e.g. standard therapy, operation…)
- C=Comparison (interventions)
- O=Outcome (e.g. treatment effect, adverse effect, risk factors, diagnostic test…)

Based on this framework the research question can be classified into different categories or search terms. Moreover, relevant inclusion and exclusion criteria can be defined. For each category all possible search terms, sometimes in different languages, have to be compiled. In the next step, each category has to be linked into a logical way by a Boolean operator (AND, OR, NOT, AND NOT) (Sayers 2008).
Subsequently, after the deduction of the research question with the PICO scheme, a suitable database must be selected. In general, a huge number of potentially appropriate databases exist. Table 2.1 provides a brief overview of selected databases and their access information. Each database has a different research focus. Some databases provide general medical content. In contrast, the Oshline database, for example, only refers to occupational health as a specific data source. DIMDI, for example, is a platform that searches different databases (e.g. Medline, EMBASE) simultaneously**.** Each database has its own characteristics, thus the search strategy needs to be adapted to the individual requirements. In some databases, e.g. PubMed/Medline, it is possible to limit the search to specific search areas like author, title and abstract. However, researchers need to take into account that the quality of the search results depends on the coding quality of the databases (White et al. 2005). The MEDLINE database is directly searchable from the National Library of Medicine (NLM) as a subset of the PubMed database and through other search services. In comparison with the rest of PubMed, MEDLINE offers the advantage of using NLM controlled vocabulary (Medical Subject Headings) to index citations.

Table 2.1 Overview of selected databases and access

Medline/PubMed	• Largest bibliographic database for all fields of medicine • Free access via search interface PubMed: http://ncbi.nlm.nih.gov/sites/entrez?db-pubmed
Embase	• Bibliographic database with focus on pharmacology, pharmaceuticals, human medicine and its peripheral fields • Fee-based; Providers: Elsevier, Ovid, DIMDI
CENTRAL (Cochrane Controlled Trials Register)	• Circa 40k entries to controlled studies which have been identified by research in large databases (e. g. Medline, Embase etc.) and handsearching • Fee-based; Providers: Ovid, Wiley, DIMDI
CDSR (Cochrane Database of Systematic Reviews)	• Contains systematic reviews of the Cochrane Collaboration respectively meta-analyses which examine the effectiveness of interventions with regard to prevention, therapy and rehabilitation • Fee based; Providers: Ovid, Wiley, DIMDI • Abstracts and summaries searchable via: http://www.cochrane.org/reviews/
DARE (Database of Abstracts of Reviews of Effectiveness)	• Contains bibliographic information and abstracts of systematic reviews, suitable for therapeutic and diagnostic problems. • Free access via http://www.cre.york.ac.uk/crdweb/
NHS EED (National Health Service Economic Evaluation Database)	• Contains structured abstracts of studies in which a comparison of two or more interventions or care alternatives is undertaken and in which both the costs and outcomes of the alternatives are examined. • Free access via http://www.crd.york.ac.uk/crdweb/
HTA Database (Health Technology Assessment Database)	• Brings together details of completed and ongoing health technology assessments (HTA) from around the world. Contains information about HTA reports of HTA institutions; Does not claim to be exhaustive. • Free access: http://www.cre.york.ac.uk/crdweb/
Oshline	• OSHLINE(TM) continues the coverage of NIOSHTIC®, which is no longer being updated. • Provides an update service covering Occupational Safety and Heath related literature published in the world. Many new journals have been added to ensure that up-to-date, relevant and comprehensive information is included. Seamless searching of both NIOSHTIC® and OSHLINE(TM) is available.
NIOSHTIC (The National Institute for Occupational Safety and Health)	• Provides comprehensive international coverage of documents on occupational health and safety, as well as related fields. • It contains detailed summaries of over 200,000 articles, reports and publications, spanning over 100 years.

NIOSHTIC-2	• A bibliographic database of occupational safety and health publications, documents, grant reports, and other communication products supported in whole or in part by NIOSH.
HSELINE (Health and Safety Executive)	• HSELINE contains around 250,000 references to worldwide information covering all aspects of occupational safety and health, and approximately 3,000 additions are made each year.
CISILO	• CISILO is a bilingual, bibliographic database which provides references to international occupational health and safety literature. The database is created by the International Occupational Safety and Health Information Centre/Centre international d'informations de sécurité et d'hygiène du travail (CIS) in Geneva.

After the determination of relevant databases and transformation of the research question into appropriate search terms, a systematic approach to identify the relevant publications should be applied (Figure 2.1). Researchers should connect all records from the database search and further studies identified by an open desktop research or public institutional information. Afterwards, duplicates should be removed. Titles and abstracts of the remaining records must be screened independently by two researchers using the defined inclusion and exclusion criteria. Subsequently, full-text articles have to be assessed for eligibility. The final number of studies will be included in the qualitative analysis. Disagreements between the two researchers should be settled through discussion.

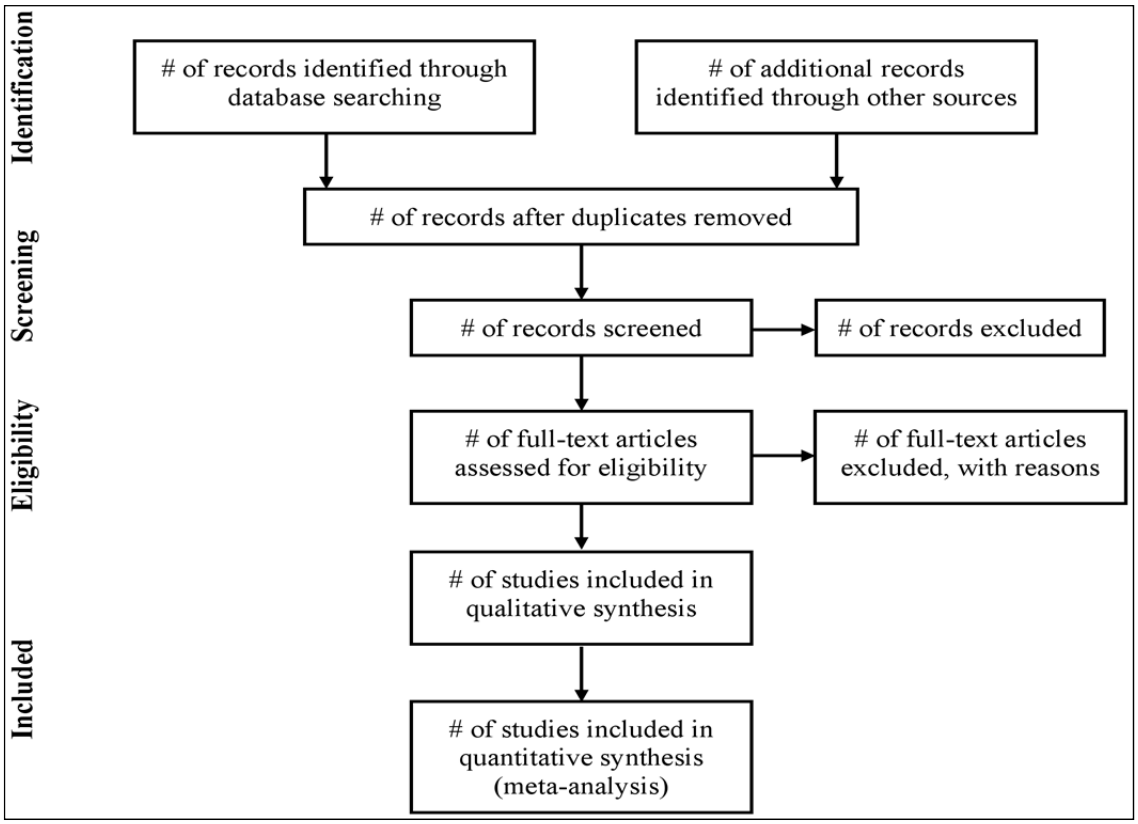


Figure 2.1 Flow of information through the different phases of a systematic review (Moher et al. 2009)

2.2 Methods

2.2.1 Formulation and selection of the search strategy for this project

We adapted the theoretical approach described above to this project in order to conduct a comprehensive systematic literature review to identify all relevant cost of illness studies and indicators for the disease severity and duration. Therefore, in the first step we structured the research question according to the PICO framework (Table 2.2).

Table 2.2 Research question according to PICO framework

Patient/ Population	Isocyanate-induced diseases: Airway diseases Asthma (especially allergic) chronic obstructive pulmonary disease (COPD) exogen allergic alveolitis skin diseases allergic contact dermatitis irritant contact dermatitis adults over 18 years
Intervention	Not relevant according to the research question
Comparison	Not relevant according to the research question
Outcome	Study type: cost of illness cohort studies RCT Cost effectiveness studies (to identify relevant cost categories) other aspects of outcomes: duration of the disease severity of the disease costs of specific areas: inpatient or outpatient care, pharmacotherapy, rehabilitation number of sickness days number of early retirement

In a second step, relevant databases were chosen. To identify relevant cost of illness studies and studies dealing with the indicators of disease (duration and severity), we defined a list with various search terms and different linkages in different databases. We decided to perform one joint systematic literature search regarding the costs and disease characteristics because it is possible that some publications provide information about costs as well as duration and severity of disease.
The first search strategy focused on the selected databases from DIMDI and OSH References and included the search term “Isocyanate” by simultaneously ignoring Isocyanate-related diseases like Asthma or COPD. The DIMDI database was used because it covers several databases like Medline, EMBASE and SciSearch. In addition, OSH Reference Databases were used because they also consist of a lot of specific databases that are related to occupational health and safety (for example OSHLINE, HSELINE, NIOSHTIC, CISILO). For a detailed description of the search terms

and the linkages see Table 2.3. An overview on the search history in DIMDI is shown in the appendix 2. Applying this search strategy resulted in 807 records.

Table 2.3 Search strategy 1 for studies on Isocyanate

Category	German search terms	English search terms
Selected databases (DIMDI): Medline, BIOSIS Previews, EMBASE alert, EMBASE, Gms, Gms Meetings, SciSearch		
Isocyanate	FT=Isocyanat?	FT=Isocyanat?
	CTG D "ISOCYNATE"	FT=Isothiocyanat?
		CT D ”Isocyanate”
	Results= 50,955 (Nr. 5)	
Linkage with AND		
Cost	FT=Kosten	FT=Cost
	FT=Kost?	FT=Cost?
		FT=Los* productivity
		CT D "PRODUCTIVITY LOSS"
		CT D "LOSS OF PRODUCTIVITY"
	CTG D ("KOSTEN UND KOSTENANA-LYSE"; "KOSTEN, KRANKHEITS-")	CT D "ABSENTEEISM"
		CT D ("HEALTH CARE COSTS"; "HEALTH CARE COSTS/"*)
		CT D ("COST OF ILLNESS"; "COST OF ILL-NESS ANALYSIS"; "COST, COST ANALYSIS")
		CT D ("ECONOMIC"; "ECONOMIC ANAL-YSES"; "ECONOMIC ANALYSIS"; "ECONOMIC ASPECTS OF ILLNESS"; "ECONOMIC BUR-DEN OF DISEASE")
	Results= 1,317,348 (Nr. 54)	
Linkage with OR		
Severity and duration of illness	FT=Dauer der Erkrankung	FT=Sickness duration
	FT=Krankheitslast	FT=Illness duration
	FT=Krankheitsschwere	CT D ("SEVERITY"; "SEVERITY OF ILLNESS")
	FT=Schwere der Erkrankung	CT D ("DURATION OF ILLNESS"; "DURA-TION,DISEASE")
	FT=Schweregrad	
	Results= 82,187 (Nr. 59) Linkage with Cost= 1,396,967 (Nr.60)	
Results		
ResultsDIMDI	N=747 (Nr. 5 and Nr 60)	
Search terms OSH References Databases	(isocyanate OR isocyanat*) AND ("Cost of illness" OR cost* OR economic* OR "burden of disease" OR (productivity loss*) OR (Los* productivity) OR absenteeism OR "sickness duration" OR "illness duration" OR "duration of illness" OR "severity of the disease" OR "Severity of illness")	
Results OSH References Databases	N=60	
Results DIMDI and OSH		
Results DIM-DI+OSH	N=807	
Explanation: ? replaces any number of characters; FT=free text, all fields; CT= Controlled Terms; N= number of records		

This might indicate that relevant publications are missing and that it might be necessary to expand the search to additional Isocyanate-induced diseases. Due to the low number of records in the first search strategy, we performed a second search strategy and expanded to Isocyanate-induced airway and skin diseases (Table 2.4). All other factors (databases, search terms and limitations) remained the same. This search resulted in 15,413 records. This number of hits is not feasible for the systematic literature search over a time period of less than one year. Moreover, the restriction of the results in the last ten years did not change the number of records significantly.

Table 2.4 Search strategy 2 - Integration of Isocyanate-induced diseases

Category	German search terms	English search terms
Selected databases (DIMDI): Medline, BIOSIS Previews, EMBASE alert, EMBASE, Gms, Gms Meetings, SciSearch		
Isocyanate	FT=Isocyanat?	FT=Isocyanat?
	CTG D "ISOCYANATE"	FT=Isothiocyanat?
		CT D ”Isocyanate”
	Results= 50,955 (Nr. 5)	
Linkage with OR (Nr. 5)		
Isocyanate-induced diseases	Asthma	
	CTG D ("ASTHMA"; "ASTHMA BRONCHIALE")	CT D ("ASTHMA"; "ASTHMA BRONCHIALE")
		CT D "BRONCHIAL ASTHMA"
	Pulmonary Disease, Chronic Obstructive	
	CTG D ("CHRONISCH OBSTRUKTIVE LUNGENKRANKHEIT"; "CHRONISCH OBSTRUKTIVE PULMONALE ERKRANKUNG"; "CHRONISCH OBSTRUKTIVE PULMONALE KRANKHEIT")	CT D COPD
		CT D ("CHRONIC OBSTRUCTIVE PULMONARY DISEASE"; "CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)")
		CT D COAD
		CT D ("CHRONIC OBSTRUCTIVE AIRWAY DISEASE"; "CHRONIC OBSTRUCTIVE AIRWAYS DISEASE"; "CHRONIC OBSTRUCTIVE LUNG DISEASE")
		CT D ("AIRFLOW OBSTRUCTION, CHRONIC"; "AIRFLOW OBSTRUCTIONS, CHRONIC")
		CT D ("CHRONIC AIRFLOW OBSTRUCTION"; "CHRONIC AIRFLOW OBSTRUCTIONS")
	Alveolitis, Extrinsic Allergic	
	FT=Exogen allergische alveolitis	FT=extrinsic allergic alveoliti?
	CTG D "EXOGEN-ALLERGISCHE ALVEOLITIS"	CT D ("HYPERSENSITIVITY PNEUMONITIS"; "HYPERSENSITIVITY PNEUMONITIDES”)
	CTG D "ALLERGISCHE ALVEOLITIS, EXOGENE"	CT D ("PNEUMONITIDES, HYPERSENSITIVITY"; "PNEUMONITIS, HYPERSENSITIVITY")

		CT D ("ALLERGIC ALVEOLITIS, EXTRINSIC"; "ALLERGIC ALVEOLITIS,EXTRINSIC")
		CT D "ALVEOLITIDES, EXTRINSIC ALLERGIC"
		CT D ("EXTRINSIC ALLERGIC ALVEOLITIDES"; "EXTRINSIC ALLERGIC ALVEOLITIS")
	Dermatitis, Allergic Contact	
	CTG D ("DERMATITIS, KONTAKT-"; "DERMATITIS, KONTAKT-, ALLERGISCHE")	CT D ("DERMATITIS, ALLERGIC CONTACT"; "DERMATITIS, ALLERGIC ECZEMATOUS"; "DERMATITIS, CONTACT, ALLERGIC")
	CTG D "ALLERGISCHE KONTAKTDERMATITIS"	CT D "DERMATITIDES, ALLERGIC ECZEMATOUS"
		CT D ("ALLERGIC ECZEMATOUS DERMATITIDES"; "ALLERGIC ECZEMATOUS DERMATITIS")
		CT D ("ECZEMATOUS DERMATITIDES, ALLERGIC"; "ECZEMATOUS DERMATITIS, ALLERGIC")
		CT D "ALLERGIC CONTACT DERMATITIS"
		CT D "ALLERGIC CONTACT DERMATITIDES"
		CT D ("CONTACT DERMATITIDES, ALLERGIC"; "CONTACT DERMATITIS, ALLERGIC")
	Dermatitis, Irritant	
	FT=Toxisches Kontaktekzem	FT=Irritant contact dermati?
		FT=Primary Irritant Dermatiti?
	FT=Toxische Kontaktdermatitis	CT D "IRRITANT CONTACT DERMATITIS"
	CTG D ("DERMATITIS, IRRITATIONS-"; "DERMATITIS, KONTAKT-"; "DERMATITIS, KONTAKT-, ALLERGISCHE")	CT D "DERMATITIS, PRIMARY IRRITANT"
		CT D ("DERMATITIDES, IRRITANT"; "DERMATITIDES, PRIMARY IRRITANT")
		CT D ("IRRITANT DERMATITIDES"; "IRRITANT DERMATITIDES, PRIMARY"; "IRRITANT DERMATITIS"; "IRRITANT DERMATITIS, PRIMARY")
		CT D "PRIMARY IRRITANT DERMATITIS"
	Dermatitis, Occupational	
	CTG D "BERUFSBEDINGTE DERMATOSE"	CT D ("OCCUPATIONAL DERMATITIDES"; "OCCUPATIONAL DERMATITIS")
	CTG D "DERMATITIS, BERUFSBEDINGTE"	CT D ("INDUSTRIAL DERMATOSES"; "INDUSTRIAL DERMATOSIS")

		CT D "DERMATITIDES, OCCUPATIONAL"
		CT D ("DERMATOSES, INDUSTRIAL"; "DERMATOSIS, INDUSTRIAL")
	Results: 266,220 (Nr. 44) With Isocyanate 316,351 (Nr. 45)	
Linkage with AND		
Cost	FT=Kosten	FT=Cost
	FT=Kost?	FT=Cost?
	CTG D ("KOSTEN UND KOSTENANALYSE"; "KOSTEN, KRANKHEITS-")	FT=Los* productivity
		CT D "PRODUCTIVITY LOSS"
		CT D "LOSS OF PRODUCTIVITY"
		CT D "ABSENTEEISM"
		CT D ("HEALTH CARE COSTS"; "HEALTH CARE COSTS/"*)
		CT D ("COST OF ILLNESS"; "COST OF ILLNESS ANALYSIS"; "COST, COST ANALYSIS")
		CT D ("ECONOMIC"; "ECONOMIC ANALYSES"; "ECONOMIC ANALYSIS"; "ECONOMIC ASPECTS OF ILLNESS"; "ECONOMIC BURDEN OF DISEASE")
	Results= 1,317,348 (Nr. 54)	
Linkage with OR		
Severity and duration of illness	FT=Dauer der Erkrankung	FT=Sickness duration
	FT=Krankheitslast	FT=Illness duration
	FT=Krankheitsschwere	CT D ("SEVERITY"; "SEVERITY OF ILLNESS")
	FT=Schwere der Erkrankung	CT D ("DURATION OF ILLNESS"; "DURATION,DISEASE")
	FT=Schweregrad	
	Results= 82,187 (Nr. 59); Linkage with Cost= 1,396,967 (Nr.60)	
Limitations	language: German and English	
Results		
Results DIMDI	N=14,604 (14,464– for the last 10 years) (Nr. 62,63)	
Search terms OSH References Databases	(Isocyanate OR Asthma OR "Chronic obstructive pulmonary disease" OR COPD OR (Airflow obstruction Chronic) OR “Chronic airflow obstruction” OR “Chronic Obstructive Airway Disease” OR “Pulmonary Emphysema” OR (Lung diseases obstructive) OR COAD OR "extrinsic allergic alveolitis" OR "Allergic contact dermatitis" OR "Irritant contact dermatitis") AND ("Cost of illness" OR cost* OR economic* OR "burden of disease" OR “Burden of Illness” OR (productivity loss*) OR (Los* productivity) OR absenteeism OR "sickness duration" OR "illness duration" OR "duration of illness" OR "severity of the disease" OR "Severity of illness")	
Results OSH References	N= 809	
Results DIMDI and OSH		
Results DIMDI and OSH	N= 15,413	
Explanation: ? replaces any number of characters; FT=free text, all fields; CT= Controlled Terms; N= number of records		

Due to the high number of records a third search strategy was performed (Table 2.5). For this purpose the second search was restricted to studies with an occupational or working focus. In order to narrow down the search to occupational studies, we tested a sensitive and specific string developed by Mattioli et al. (Mattioli et al. 2010). The sensitive search resulted in 3,992 records. The specific search strategy was extended to the search terms “occupation?” and “worker?” and it resulted in 1,105 records. This might both be a feasible and an appropriate search strategy. Due to the fact that the sensitive string finds more studies and that the number of records seems to be feasible in the project time, we prefer the search strategy one with the sensitive string for occupation.

Table 2.5 Search strategy 3 – Studies for Isocyanate and Isocyanate-induced airway and skin diseases in combination with a focus on occupation or work

Category	German search terms	English search terms
Selected databases (DIMDI): Medline, BIOSIS Previews, EMBASE alert, EMBASE, Gms, Gms Meetings, SciSearch		
(Isocyanate OR Isocyanate-induced diseases Nr.45) AND (Cost OR Severity and duration of illness Nr.60) *(for detail overview about the search terms see table 2.4)*		
Linkage with „AND“		
Alternative 1: Sensitive String occupation	FT=Beruf?	FT=work
	FT=Arbeit?	FT=Works?
	FT=Betrieb?	FT=work'?
		FT=worka?
		FT=worke?
		FT=workg?
		FT=worki?
		FT=workl?
		FT=workp?
		FT=occupation?
		FT=prevention?
		FT=protect?
	Results: 5,635,163 (Nr. 68)	
Alternative 2: Specific string for occupational	FT=Beruf?	FT=occupational diseases
	FT=Arbeit?	FT=occupational exposure
	FT=Betrieb?	FT=occupational medicine
		FT=occupational risk
		FT=occupational hazard
		FT=occupational group?
		FT=work-related
		FT=occupational air pollutants
		FT=working environment
		FT=Occupation?
		FT=Worker?
	Results: 575,986 (Nr. 72)	
Results		
Results DIMDI	N=3,732 (Alternative 1: sensitive string for occupation) N=845 (Alternative 2: specific string for occupation incl. occupation?, worker	
Search terms OSH References Databases	(Isocyanate OR Asthma OR "Chronic obstructive pulmonary disease" OR COPD OR (Airflow obstruction Chronic) OR	

	“Chronic airflow obstruction” OR “Chronic Obstructive Airway Disease” OR “Pulmonary Emphysema” OR (Lung diseases obstructive) OR COAD OR "extrinsic allergic alveolitis" OR "Allergic contact dermatitis" OR "Irritant contact dermatitis") AND ("Cost of illness" OR cost* OR economic* OR "burden of disease" OR “Burden of Illness” OR (productivity loss*) OR (Los* productivity) OR absenteeism OR "sickness duration" OR "illness duration" OR "duration of illness" OR "severity of the disease" OR "Severity of illness") AND (Work-related OR (Working environment) OR (Work environment) OR Workload OR Occupation? OR Prevention)
Search terms OSH References Databases	N= 260
Results DIMDI and OSH	
Results DIMDI and OSH	N=3,982 (Alternative 1: sensitive string for occupation) N=1,105 (Alternative 2: specific string for occupation incl. occupation?, worker?)
Explanation: ? replaces any number of characters; FT=free text, all fields; CT= Controlled Terms; N= number of records	

2.2.2 Data extraction and definition of quality criteria for the evaluation of economic studies

As written in the project proposal, the performance of a meta-analysis on the basis of cost-of-illness studies represents a challenge. Reasons for this are that the results are only partially comparable due to the various input parameters and cost areas considered (Egger et al. 2008). Therefore, a quality assessment of the cost of illness studies was carried out.
In the first step, we extracted certain features of all identified studies, for example the sample size, variable definition and operationalisation, data collection method, the survey period and type of study (Cooper 2010). We supplemented these data by the following areas: author, year, study aim, country, study population/medical indication, study perspective, data sources, results (direct costs, indirect costs and other). All these aspects were extracted of the studies and are listed in a table.
For a better comparison of cost of illness studies, we converted the costs and details of financial compensations in Euro (€) to the exchange rate on the publication year and then inflated them to the base-year 2014. For the inflation, we used the harmonized consumer price index (Statistisches Bundesamt 2015a) according to the recommendations of the G-BA.
In addition, studies that made both statements on indicators of the severity of the disease or the duration as well as applicable costs are listed and evaluated in both tables (cost and disease severity).

2.2.3 Quality assessment

To ensure that only high-quality studies are integrated, quality criteria were defined in the second step. A critical examination and questioning of the extracted features is essential in order to scrutinize the results of studies.
A detailed quality evaluation was carried out with the support of quality assessment instruments. Several detailed checklists exist for evaluating economic studies but most checklists focus on full economic evaluations like cost effectiveness, cost utility, cost minimisation or cost benefit analyses. For example, Dummond et al. developed

guidelines for authors and peer rereviewers of economic submission to the British Medical Journal (Drummond et al. 1996). In 2005, Drummond et al. duplicated a similar 10-point checklist for assessing economic evaluations (Drummond et al. 2005).

Table 2.6 Criteria and questionnaires for the evaluation of different disease-related studies

	Molnier et al. 2008 (Prostate Cancer)	**Costa et al. 2012 (Alzheimer)**	**Stuhldreher et al 2012[1] (Eating disorder)**	**Kleine-Budde et al. 2014[2] (Bipolar disorder)**
1	Was a clear definition of the illness given?	Was a clear definition of the illness given?	Scope	Aims and methods of the study
2	Were epidemiological sources carefully described?	Were epidemiological sources carefully described?	General economic	
3	Were direct/indirect costs sufficiently disaggregated?	Were costs sufficiently disaggregated?	Calculation of costs	Calculation of costs
4	Were activity data sources carefully described	Were activity data sources carefully described	Study design and analysis	
5	Were activity data appropriately assessed?	Were activity data appropriately assessed?	Presentation of results	Presentation of results
6	Were the sources of all cost values analytically described?	Were the sources of all cost values analytically described?	Discussion	Discussion
7	Were unit costs appropriately valued?	Were unit costs appropriately valued?		
8	Were the methods adopted carefully explained	Were the methods adopted carefully explained		
9	Were the major assumptions testes in a sensitivity analysis?	Were costs discounted?		
10	Was the presentation of study results consistent with the methodology of the study?	Were the major assumptions tested in a sensitivity analysis?		
11		Was the presentation of study results consistent with methodology of study?		

[1] Each category has different sub criteria
[2] Each category has different sub criteria

Apart from the large number of different checklists for cost effectiveness analyses, different checklists exist for cost of illness studies. Most of these checklists are developed for selected diseases. Table 2.6 gives an overview on questions and criteria for evaluating disease-related cost of illness studies. All questions and criteria are based on the checklist for full economic evaluation by Drummond et al. (Drummond et al. 2005). All questions can be answered by voting 'yes', 'no' or sometimes 'not applicable'.
Larg and Moss developed a checklist to assist readers and users, particularly those without a strong background in economics, to critically evaluate COI studies (Larg et al. 2011). The authors did not mention how they developed this checklist. Therefore, it is unclear if the checklist is based on a literature search, expert opinion or other methods. Another problem is that not all questions can be answered with "yes" or "no". As a result of these limitations, we would not choose this approach for the evaluation of our studies.
The method used by Kleine-Budde seemed to be suitable for evaluation of cost of illness studies due to occupational skin and airway diseases because this checklist has detailed questions that fit to our studies (see Table 2.7). In this setting possible answer options are: ✓=yes; x= no; n.a. = not applicable.

Table 2.7 Quality assessment by Kleine-Budde et al. 2014

Aims and methods of the study	**Options**
Study objective	
Inclusion and exclusion criteria	
Non-diseases comparison group or disease-specific costs	
Matching or regression analysis	
Sensitivity analysis	
Calculation of costs	
Data sources	
Perspective	
Cost calculation	
Cost categories	
Reference year (price)	
Currency	
Inflation rate and/or discount rate	
Monetary valuing of resource utilization	
Presentation of results	
Sample size	
Demographics	
Arithmetic mean costs	
Standard deviations	
Separate information number of services used and costs	
Discussion	
Discussion with respect to other studies	
Limitations	

With the help of the checklists, it is possible to discuss the quality of the studies. These results will be integrated into the transferability section and will be part in the discussion about the limitation of the transferability methods.

2.3 Results of the systematic literature review

2.3.1 Implementation of the systematic literature review

The search strategy with the sensitive string (Table 2.5) was performed on 8 June 2015 in the selected databases of the DIMDI. On 20 August 2015 we carried out a further database search in ”OSH Reference”. Overall, a total of 4,107 results were identified and exported to Citavi. Subsequently, 814 results were identified as duplicates and were then removed (see Figure 2.2). Main inclusion criteria were:

- Studies with a focus on occupational asthma, occupational COPD or occupational contact dermatitis
- Cost of illness studies
- Studies who calculated economic consequences due to the diseases
- Studies about the severity or duration of the diseases:

The results from the databases were then reduced based on the PRISMA Flow Chart (see Figure 2.2). Titles and abstracts were screened independently by two researchers using the defined inclusion and exclusion criteria. A total of 3,046 matches were excluded after the first investigation. The reasons for the exclusion of these results were different.

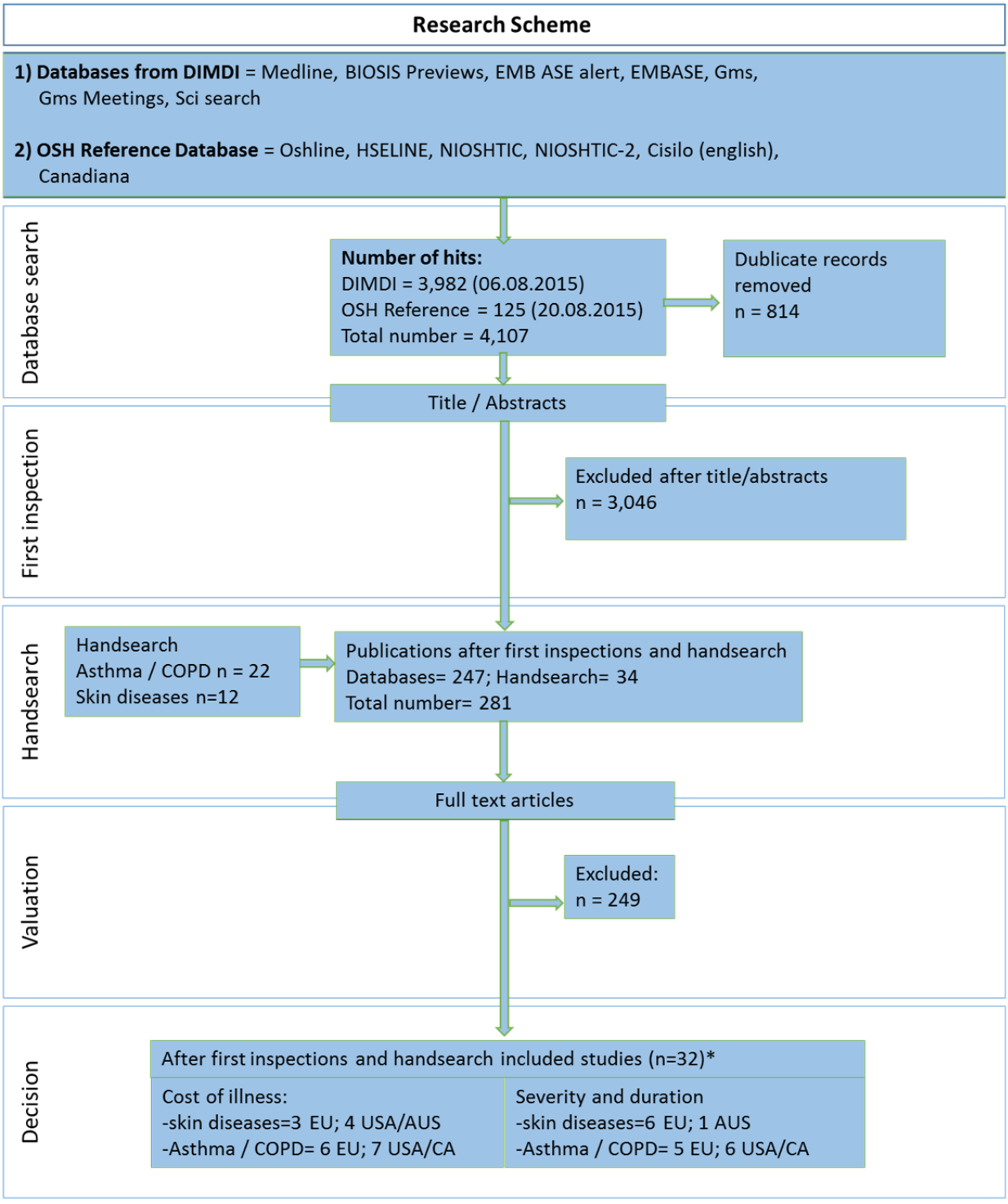
Studies of the following categories were excluded:

- Guidelines
- Children or schools
- No direct connection to one of the selected diseases
- Cell structures, genes or biomarkers
- About therapies, medication
- About the management of the disease (Treatment patterns, burden of disease studies)
- Other languages than English or German
- Infections and vaccinations
- Compliance and adherence
- Depression, anxiety, stress
- Cost-effectiveness analysis
- Prevention, Obesity, Dietary and Nutrition
- Telemedicine, E-Health
- Rehabilitation, education or training
- Risk factors
- Not transferable to the European states
- Smoking cessation
- Air pollution/Exposure
- Screening
- Quality of life
- Other reasons

Other studies were excluded because they dealt with other diseases like tuberculosis, cancer, allergic rhinitis or cardiovascular diseases. 34 additional publications were found by manual search. The manual search was carried out through google schoolar and through the reference lists of the integrated publications.

Overall, 281 publications have been obtained in full texts. Of these publications, 82 titles have been moved to a separate folder, since these publications were general cost studies, studies on productivity loss and general guidelines to the selected res-

piratory and skin diseases without references to occupational or work related diseases. Other studies were excluded because they focused on prevention, quality assurance or epidemiological analysis. Some studies also reported a case study (e.g. they analysed which substance are responsible for the diseases) or demonstrated different treatment options or guidelines. A total of 32 records were identified as eligible.



* Three studies have been included in both, cost of illness studies and indicators of severity/duration.

Figure 2.2 Results of the PRISMA Flow chart for the systematic literature search

In the following sections, the identified studies will be described. In this context we demonstrated the results separately for the diseases occupational Asthma and COPD; as well as those for skin diseases.

2.3.2 Description of the included cost of illness studies for occupational asthma and COPD

Overall, we identified six studies with a focus on the cost of illness and financial loss due to occupational asthma and COPD for the European countries. Two of them are cost of illness studies (Ayres et al. 2010; Gomez et al. 2012), two of them analysed the loss of income (Ameille et al. 1997; Moscato et al. 1999) and two assessed both the loss of income and potential compensation by the health insurance systems (Gannon et al. 1993; Leira et al. 2005). Table 2.8 gives an overview on the studies above.

In addition to the European studies, we identified seven studies with the same topic from the United States of America (USA) and Canada. Three studies evaluated the costs and loss of income in Quebec (Miedinger et al. 2011; Marlo et al. 2008; Marlo et al. 2008). Another study assessed the total compensable and medical cost for isocyanate-induced asthma in the USA (Rheeb-Whitaker et al. 2013). Two studies from the USA assessed the direct and indirect costs of occupational COPD and asthma (Leigh et al. 2003; Leigh et al. 2002). The last study focused on differences in healthcare use between workers with work-exacerbated asthma (WEA) and occupational asthma (OA) (Lemiére et al. 2007). These seven studies will be excluded from the further analysis because a cost transfer from the other countries to the European countries is challenging.

Ayres et al. estimated social costs of OA based on different exposures in the UK (Ayres et al. 2010). They calculated the costs for six hypothetical patients (male and female) with OA who are exposed to isocyanates. Direct and indirect costs were calculated for the three different perspectives like for example taxpayer, employers and individual patients. The calculation of direct costs included resource consumption for general practice, medications, hospital admission, outpatient services and payments by the department of Work and Pensions (taxpayer). Additionally, the costs for an individual person like for example prescription charges, commuting or additional transport costs were calculated. Total indirect costs for the society consisted of the payments from the statutory health insurance (taxpayer), the reduction in net income and the human costs of ill health (individual) as well as the costs for foregone productivity (employer). The calculation of indirect costs was based on four different assumptions from the literature. The authors made the assumptions, that in 25% of the cases the individual performs the same job, 25% switch jobs at the same employer and had a reduction in take home salary of 20%, 15% of the individuals changed their employer and had a reduction in take home salary of 50% and the last 15% will retire from the labor force and had a full salary reduction. The total direct costs and indirect costs for the society were calculated per person per year. Moreover, lifetime total costs for the different people were calculated. The lifetime costs for man with isocyanate induced asthma are much higher than the lifetime costs for a new male case. The authors argued that these costs reflecting the number of men exposed to relevant agents in the UK and their greater loss of income.

Table 2.8 Cost of illness studies and studies about financial consequences for occupational Asthma and COPD

Author/ Year	Study aim	Study population/ medical indication/Country	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Data sources/ study perspective	Results (direct costs, indirect costs and others)	results - subanalysis
Ayres et al./ 2010	Estimated the social costs of occupational asthma	6 hypothetical patients (m/f) with OA who are exposed to isocyanates, latex, biocides (e.g. glutaraldehyde) or flour/ UK	1) literature research to identify cost of illness studies for Asthma and OA 2) cost of illness study: calculate costs on the basis of different scenarios direct costs: resource consumption to diagnose, treat (the same like asthma), rehabilitation, non-medical costs indirect costs: 3 Scenarios: returned to work with the same employer, performing the same job or switching jobs, changing employer or retiring from the labor force	Survey of work-related and occupational respiratory disease costs are based on literature / Employers, Taxpayers, individual patient (sum of it= social cost)	Direct cost of occupational asthma (Society) due to Isocyanates per year/per patient= 915.88€-1,227.45€ (male) and 919.30€-1,225.74€ (female) **indirect cost** (Society) of occupational asthma due to isocyanate per year per patient=8,503.12€-8,770.18€€ (Male) and 6,296.45€-6,534.41€ (female) total present value costs to society over a lifetime (Isocyanate) per patient= 22768.56€-24,485.56€ (male), 664.23€-720.28€ (female)	Different perspective (Taxpayer, individual), resource areas (hospital, general practice…) and exposures (Isocyanate, Latex, Flour)
Gomez et al./ 2010	Estimated the number of asthma cases attributed to the work setting as well as the related **health care costs** for the same year.	OA (>20 years; CIE-9-MC diagnosis: CIE-9 493.0)/ Spain	1) Estimation of costs to patients who had received some type of specialized care (SC): Calculation of costs for hospital admission and specialized outpatient care; costs for primary care and pharmaceuticals were taken from other studies 2) Global health expenses: Based on the total expenses per patients with asthma	Statistical data: NHS Information through interactive consult/not mentioned	(1) Direct costs of specialized care (in-hospital and SOC for all patients per years: 9,809714.80€ (2) Primary Care cost= 4,934286.54€; Pharmaceutical Care cost= 4,660,381.36€; Total Health cost by disease (1+2)= 19,413425.59€ Further results: number of work-related asthma cases Total direct costs per patient per year: 1,764.52€	Subanalysis for (1) and (2): Gender
Leira et al./ 2005	Study the exposure and the consequences for work, health, and income for workers notified for OA	N=723 workers with physician's diagnosis of asthma, asthmatic complaints, asthma attacks, reactive airways dysfunction syndrome, bronchial hyperreactivity, or a combination of asthma and COPD/Norway	Cross sectional study: questionnaire, Information on working situation, symptoms, the relationship of symptoms to work, smoking, and socioeconomic consequences of the disease (study period 1995-1999); data for exposure coded by the doctor varied so that job was used as proxy for exposure.	Data about the patients who have the disease were given by Labor inspection Authority/not mentioned	Loss of income: 55% had a reduction in annual income; 5% temporarily reduction financial compensation from Occupational Injury Insurance Act: other industry: 10% <13,812.30€ 11% 13,812.30€-69,061.50€ ; 4% = >69,061.50€ aluminum industry group: 26% <13,812.30€, 8% 13,812.30€ - 69,061.50€; 0,4% = >69,061.50€	Subanalysis for different income reductions for other industries and aluminium industry

Author/ Year	Study aim	Study population/ medical indication/Country	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Data sources/ study perspective	Results (direct costs, indirect costs and others)	results - subanalysis
Moscato et al./ 1990	Evaluate the clinical outcome and socioeconomic consequences of OA	N=25 patients with OA to high and low-molecular-weight agents At 12 months: 13 patients (group A) had ceased exposure; 12 patients (group B) continued to be exposed/ Italy	Longitudinal study: Diagnosis: each patient received a diary on which to report peak expiratory flow rate (PEFR), symptoms, drug consumption, expenses directly or indirectly related to the disease, as well as information regarding personal socioeconomic status. Follow-up visit (1, 3, 6, 12 months) the patients underwent clinical examination, spirometry, methacholine (Mch) challenge, and assessment of diary-derived parameters and socioeconomic status. Asthma severity (AS): four levels, based on symptoms, drug consumption, and PEFR variability.	Self-collected data/not relevant	A significant loss of income was registered in patients of group A (10,917.89€ to 16,667.56€ on the year preceding diagnosis and 6,880.21€ to 13,622.82€ on the year after diagnosis; $p<0.01$), whereas no significant change was seen for patients in group B.	no
Gannon et al./ 1993	To study the health, employment, and financial outcome of OA	N=112 workers with OA based on a history of respiratory symptoms that improved on days away from work + at least one other confirmatory investigation PEF measurement, bronchial provocation tests, RAST/ UK	Cross sectional study: Self-administrated questionnaire one year after diagnosis with information about respiratory symptoms, employment state, and current financial situation (including compensation). Diagnostic data, respiratory function, and causative agent were obtained from the workers' case records.	Self-collected data/not mentioned	Of all patients who had changed the job, 74% reported a reduced income; Of all patients who remained exposed, 44% reported a reduction of income Median perceived annual loss= 6907.27€ (removed from exposure), 4500.03€ (remained exposed) Median perceived loss as a percentage of annual income was 54% (unexposed), 35% (remained exposed) 47% had attempted to claim statutory compensation for OA; 27 (52%) had settled the claim, 17 (33%) had claims outstanding, and 8 (15%) had had the claim rejected; Median amount of compensation= 2,687.53€ per year	Pulmonary function in workers with OA removed from exposure and remaining exposed

Author/ Year	Study aim	Study population/ medical indication/Country	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Data sources/ study perspective	Results (direct costs, indirect costs and others)	results - subanalysis
Ameille et al./ 1997	Changes in employment and income following a diagnosis of OA; determine what factors might affect these changes	N=257; diagnosis is based on a history of respiratory symptoms that improved on days away from work, and generally on at least one other confirmatory investigation/Paris	Follow Up Study: Baseline: lung function test, socio-demographic information, medical information (Duration of symptoms), severity of asthma (based on hospital admission, frequency of asthma symptoms, past and current use of steroids and/or other asthma medications), additional information: e.g. type of employment, number of employees 1 year later: interviewed via telephone or self-administered questionnaire by post. Information about working status, financial situation and whether a compensation claim had been submitted were collected	Self-collected data at the occupational medicine departments for OA/not relevant	Financial consequences of OA: 46% of patients had suffered from a reduction of income Mean loss of annual income were significantly higher in subjects who left their employer than in those who remained in the same company Of the 103 workers whose claim for compensation was accepted, 58 (56%) suffered from a reduction of income.	no

Abbreviations: OA= occupational Asthma; NHS=National Health Service; SC= specialized care; SOC= specialized outpatient care; COPD= chronic obstructive pulmonary disease, FEV1= Forced Expiratory Pressure in 1 Second; PEF= peak expiratory flow; RAST=Radio-Allergo-Sorbent-Test

Another cost of illness study was conducted by Gomez et al. (2011) in Spain. The authors estimated the number of asthma cases attributable to the work. The estimation of the costs for specialized care, like inpatient care and specialized outpatient care was based on statistical data of the National Health Service (NHS) in Spain. The cost for primary care and pharmaceuticals were taken from secondary data sources. The perspective for calculating the costs is not mentioned but it seems to be a third party payer perspective because the data from the NHS in Spain was used. The costs for the specialised care are calculated for all men and women with asthma attributed to occupational exposures. Costs per patient were not specified and had to be calculated.
The cost of illness study reported by Ares et al. analysed direct annual costs between 915.88€-1,227.45€ for a male patient with Isocynate and 919.30€-1,225.74€ for a female patient. In comparison, Gomez et al. analysed costs in dependency of the source of cost calculation between 1,665,90€-1,863.15€.
Ameille et al. (1997) analysed the financial consequences especially changes in income and employment. This analysis is based on a follow up study with 257 patients with a diagnosis of OA in Paris. One year after a medical based diagnosis, patients were interviewed via telephone or questionnaire by post. The authors calculated the mean loss of income in the different groups (same employer, unemployment or other employer).
Moscato et al. (1990) evaluated the socioeconomic consequences of patients with OA in Italy. It is a longitudinal study with 25 patients who underwent follow up visits (1, 3, 6 and 12 months) after their diagnosis. They calculated the monthly and annual income at the time of the diagnosis and after the 12 month for Group A (patients who ceased exposure) and Group B (patients who continued the exposure).
Gannon et al. (1993) and Leira et al. (2005) studied the employment and financial situation of workers with OA in UK and Norway with a cross sectional study design. 723 patients with different forms of physician diagnosed OA were asked questions about working status and socioeconomic consequences. Besides the loss of income, information on the financial compensation from occupational injury insurance act was collected. This compensation included costs of chronic medical impairment, disability, and for incurring medical expenses, compensation for an anticipated reduction of future income. These regulations are supposed to compensate 100% up to a yearly income of the present Norwegian kroner (NOK) 570,000. The authors differentiated in their study between workers from the aluminium industry and workers from other industry areas.

2.3.3 Description of studies for indicators of disease severity and duration for occupational asthma and COPD

During the systematic literature review we identified five studies that analysed the disease severity and the duration of occupational asthma or COPD for the European countries. Three of the five studies were also mentioned in the section before (Moscato et al. 1999; Gannon et al. 1993; Leira et al. 2005) (see Table 2.9).
All studies performed a comparison of medical outcomes between the time of diagnosis and a follow up date (usually one year after diagnosis). Four studies also compared people who have changed their job after diagnosis and the people who were still exposed on job (Moscato et al. 1999; Gannon et al. 1993; Pisati et al. 1993, Piirilä et al. 2005).

At the time of diagnosis Moscato et al. found out that patients who have changed their job had a higher asthma severity and less lung functions than the patients who are still exposed after diagnosis. Pisati et al. identified other results. They analysed that both groups were similar according to the symptoms score, medication score and lung function test.
The Health status at follow up diagnosis was reported by five different studies (Moscato et al. 1999; Gannon et al. 1993; Pisati et al. 1993; Piirilä et al. 2005). Pisati et al. (1993) pointed out that in both groups asthma severity and lung function tests improved at the time of follow up compared to the time of the diagnosis. Nevertheless, disease severity (especially the FEV1 and symptoms) improved more in the group which is no longer exposed. Also Gannon et al. confirmed that the lung function (FEV1) improved by 5% in the group who was no longer exposed but contrary results were found for the group that was still exposed. FEV1 fell by 2% as predicted in this group. Moscato et al. (1999) confirmed the results that the asthma severity was improved in the group which has changed their job.
The analyses by Pisati et al. went much further. They also analysed factors that influenced the disease prognosis of the persons who had TDI-induced asthma and who have changed their job after diagnosis. Therefore, the patients were divided into three different groups according to their health status at the follow up (recovered, improved and not improved). The characteristics and health status at the time of the diagnosis were compared between these groups. Patients who have changed their job could have a new job in which irritant factors for the airways (dusts, fumes or gases) are present. These irritant factors could be found in one of the 12 (8.3%) subjects who have recovered, in four of the 10 (40%) patients who have improved, and in five of the 21 (23.8%) who have not improved. One main factor is the duration of exposure to the TDI or the symptomatic work. Patients who have recovered at the time of the follow up, the duration for exposure was significantly shorter than in those who had not improved at all. People who have recovered at the time of the diagnosis have a maximum exposure to TDI for ten years. Another result from the study by Gannon et al. was that there was no significant difference in the number of exposed in either groups to any one of the five most common agents. This result supports our decision to take the whole study about occupational asthma regardless of whether they were exposed to isocyanates or other agents.
Besides the studies from the European setting we identified six studies from Canada and the USA (see Table 2.10). Three studies compared the work-relating asthma (WRA) with non-WRA (Knoeller et al. 2013; Breton et al. 2006, Lemiére et al. 2012). All studies found a higher burden of the disease if asthma is work-related compared to non-WRA. Patients with WRA have more asthma attacks, emergency room or doctor visits and more symptoms than patients with non-WRA (Knoeller et al. 2013; Breton et al. 2006).
Lemiere et al. (2012) also studied the differences between individuals with work-exacerbated asthma (WEA) and OA. WEA is characterised by pre-existing or coincidental asthma that is exacerbated by a workplace-related stimulus and OA is induced by sensitization to a specific substance exposure or an inhaled irritant at work (Lemiére et al. 2012). They found that the disease severity and the status of asthma control are not different between both groups. Nevertheless, patients with WEA are often smokers and tend to have a lower FEV1.

Table 2.9 Studies analysing indicators of disease severity and duration in occupational Asthma and COPD (Europe)

Author/ Year	Study aim/ Country	Study population/ medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Leira et al./ 2005	Study the exposure and the consequences for work, health, and income for workers notified for OA/ Norway	n=723 workers with physician's diagnosis of asthma, asthmatic complaints, asthma attacks, reactive airways dysfunction syndrome, bronchial hyperreactivity, or a combination of asthma and COPD	Cross sectional study: questionnaire, Information on working situation, symptoms, the relationship of symptoms to work, smoking, and socioeconomic consequences of the disease (study period 1995-1999); data for exposure coded by the doctor varied so that job was used as proxy for exposure.	- smoking have an influence on the prevalence of daily cough; - need for medication was lower in smokers than in non-smokers - Prevalence of self-reported respiratory symptoms during the last 12 month between aluminium and other industries were also reported
Piirilä et al./ 2005	Conduct a follow-up study of working status and life satisfaction of patients with diisocyanate-induced asthma/Finnland	213 patients with diisocyanate-induced asthma	All diagnosed patients at Finnish Institute of occupational Health (FIOH) between 1976-1992 were studied in 1995. - Follow-up questionnaire on average 10 years (3-19 years) after diagnosis - Questionnaire included information about: employment status, diisocyanate exposure, smoking habits, symptoms of asthma, use of asthma medication and satisfaction with life	- persons still working had fewer asthma symptoms, less asthma medication, less PEF variability than unemployed persons - persons who had continued in their original exposed work had more nocturnal asthma symptoms than those who changed job - unemployment was not associated with duration of exposure to diisocyanates - control examination (subsample n=91): short-acting beta-sympathomimetic medication (62%), inhaled steroids (60%), long acting beta-sympathomimetic (27%) theophyllamines (3%)
Moscato et al./ 1999	To evaluate the clinical outcome and socioeconomic consequences of OA/Italy	N=25 patients with OA to high and low-molecular-weight agents At 12 months: 13 patients (group A) had ceased exposure; 12 patients (group B) continued to be exposed	Longitudinal study: Diagnosis: each patient received a diary on which to report peak expiratory flow rate (PEFR), symptoms, drug consumption, expenses directly or indirectly related to the disease, as well as information regarding personal socioeconomic status. Follow-up visit (1, 3, 6, 12 months) the patients underwent clinical examination, spirometry, methacholine (Mch) challenge, and assessment of diary-derived parameters and socioeconomic status. Asthma severity (AS): four levels, based on symptoms, drug consumption, and PEFR variability	At diagnosis: Group A higher asthma severity; FEV1 percent and provocative dose causing a 20% fall in FEV1 (PD20) of Mch were lower in group A than in group B; patients group A were also characterized by significantly higher basal AS levels. At 12 months: no significant variation in FEV1 percent or PD20 was found; AS levels improved in both groups, the change being more marked for group A than group B. - Pharmaceutical expense at 12 months significantly ($p<0.05$) decreased, as compared with the first month, in group A, whereas it tended to increase in group B. - Further analysis for the distribution of AS level in the whole group at diagnosis, 1, 6 and 12 month; Duration of exposure before symptoms

Author/ Year	Study aim/ Country	Study population/ medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Gannon et al./ 1993	To study the health, employment, and financial outcome of OA/UK	N=112 workers with OA based on a history of respiratory symptoms that improved on days away from work + at least one other confirmatory investigation PEF measurement, bronchial provocation tests, RAST	Cross sectional study: Self-administrated questionnaire one year after diagnosis with information about respiratory symptoms, employment state, and current financial situation (including compensation). Diagnostic data, respiratory function, and causative agent were obtained from the workers' case records.	- Of those who had changed job,78% said this was because of OA - The median lag time between diagnosis and changing job was 12 months (range -36 to 36 months; one worker presented for the first time three years after he had changed his job because of symptoms). - 66% (who no longer exposed) thought that their symptoms had improved - FEV1 in the group who remained exposed fell by 2% of predicted (95% CI -7,23 - 3,23) whereas in the group removed from exposure it improved by 5% (95% CI 0,77-8,43) (p = 0 06). - There was no significant difference in the number exposed in either group to any one of the five most common agents
Pisati et al./ 1993	Examine the characteristic features of 60 patients with OA due to TDI five years after the initial diagnosis according to the persistence or not of exposure to the offending agent/Italy	65 patients with TDI induced asthma; - Group B= away from exposure within six months after the diagnosis) - Group A= persistent occupational exposure to TDI)	65 patients with TDI induced asthma diagnosed between 1980 and 1985 were recalled five years (±7 months) later; At diagnosis all subjects filled in a questionnaire (characteristics of the risk of exposure to TDI at the workplace , severity of the asthmatic symptoms, need for medication and stays in hospital for asthma over the past 12 months) Tests: (1) skin test (2) lung function tests (3) methacholine inhalation test (4) Inhalation challenge to TDI Follow-up: questions were asked again and the same treatment steps were carried out	At diagnosis: symptoms score, medication score, lung function tests, and PD15 methacholine of group A and B were similar Re-evaluation: Group B had significantly less severe symptoms and a threefold increase in PD15 methacholine than at diagnosis (paired t test) (n=12 completely recovered, n=10 improved but still required treatment for asthmatic symptoms, n=16 stable, n=5 worse). The rate of decline of FEV1 was 120 (SD 128 ml/y) in patients of group A and 12 (SD 88) ml/y in group B; Factors affected the prognosis of the TDI induced OA: Group B was divided into three subsets according to the clinical outcome (group I, recovered; group II, improved; group III, not improved-that is, stable plus deteriorated) and their initial data were compared. - Irritant factors for the airways (dusts, fumes or gases) were present in the new workplace in one of the 12 (8.3%) subjects who had recovered, in four of the 10 (40%) patients who had improved, and in five of the 21 (23.8%) who had not improved; the ratios were not statistically different on X 2 analysis. - The duration of exposure to TDI and of symptomatic work was significantly shorter in patients who had recovered than in those who had not improved at all; intermediate values characterized the subjects who had improved but had not completely recovered. None of the workers who recovered had had occupational exposure to TDI longer than 10 years and a duration of exposure after the onset of asthmatic symptoms longer than three years.
Abbreviations: OA= occupational Asthma; TDI=Toluene diisocyanate; AS= asthma severity; FEV1=forced expiratory volume in one second				

Table 2.10 Studies analysing indicators of disease severity and duration in occupational Asthma and COPD (Canada, USA)

Author/ Year	Study aim/Country	Study population/medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Knoeller et al./ 2013	Exam the number of days with asthma symptoms among individuals with WRA and non-WRA/USA	N=38,306 people who ever have been diagnosed to asthma -current asthma status based on self-reported physician diagnosis -WRA based on a positive response to 4 different questions (9% physician diagnosed WAR, 37.4% possible WRA)	telephone survey: Behavioural Risk Factor Surveillance System (2006-2009) -survey data for employed adults, Subset of people were called back within 3 weeks -Questions about frequency and duration of asthma symptoms -Resource consumption: urgent care visits, emergency room visits, overnight hospital visits, frequency of routine check ups	-health professional WRA had significantly higher mean number of days with Asthma symptoms, trouble sleeping, activity limitations, asthma attacks routine check-ups for asthma, urgent treatment visits, hospitalization than non-WRA -association of activity limitation due to asthma with asthma symptoms were weaker among current employed adults with current asthma and stronger not currently employed with current asthma than the observed associations for all ever-employed adults
Lemière et al./ 2012	1) Compare the clinical, functional, and inflammatory characteristics of workers with WEA and OA and 2) Compare health care use and related costs between workers with WEA and OA and with WRA and NWRA/ Canada (Quebec)	N=154 patients with WRA and NWRA Diagnosis of OA and WEA was based on the positivity and negativity of results on specific inhalation challenges	Prospective cohort (2003-2008) study of workers with and without WRA with a 2-year follow-up. First visit: medical and occupational questions were asked, Skin prick tests, respiratory function tests, severe asthma exacerbations: emergency department visit or a hospitalization during the study period Calculation of costs: Lining the medical and administrative database (physical services, emergency department, hospitalization)	-WEA was associated with more frequent prescription of inhaled corticosteroids, a noneosinophilic phenotype, a trend toward a lower FEV1, and a higher proportion of smokers than the diagnosis of OA. Asthma control or asthma severitie were not associated with the type of diagnosis (WEA vs OA). -WRA had asthma for a shorter period of time, were older, more severe asthma, and tended to be less atopic than subjects with NWRA Cost: WEA and OA had more physician's office and emergency department visits for asthma than NWRA in the year preceding the first assessment. -Predictor of severe asthma exacerbations= persistent work exposure in subjects with WRA -WRA was associated with a much higher cost than NWRA in the year before and after diagnosis.
Miedinger et al./ 2010	Identify socioeconomic factors that can influence the delay in submitting a claim to a medicolegal agency, with removal from exposure after the onset of asthmatic symptoms/Canada (Montreal)	N=60 subjects who claimed compensation for OA at the Workers' Compensation Board of Quebec in 2004–2006	-Cross-sectional study -Questionnaire: medication, tobacco consumption, the type of agent causing the OA, information about the workplace, sociodemographic and socioeconomic outcomes, information about the Workers' Compensation Board's Social Rehabilitation Program. -Data were collected at re-evaluation, 2.5 years after diagnosis.	-Being older, having a revenue of 30,000 Canadian dollars and having OA due to high molecular weight agents were all positively associated with the number of years of exposure with symptoms before removal from exposure. Subjects with persistent airway hyperresponsiveness at follow-up had a higher number of years with symptoms. Experiencing symptoms in the workplace for,1 yr generated lower direct costs.

Author/ Year	Study aim/Country	Study population/medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Breton et al./ 2006	Investigation of differences in asthma control measures such as frequency of asthma symptoms, number of asthma attacks in the past year, medication usage, sleeping difficulty, and inhibition of usual activity/ USA (Massachusetts)	N=2007 individuals with ever physician reported asthma; 133=WRA; 1874=non WRA	Data from the Massachusetts Behavioral Risk Factor Surveillance System for 2001 - 2002 were used for this analysis. Healthcare measures evaluated were emergency room visits and physician visits for worsening asthma and for routine care. Characteristics of asthma control evaluated were frequency of asthma symptoms, asthma attacks, difficulty sleeping, and asthma medication usage in the last 30 days and limited activity in the past 12 months.	In the past 12 months, individuals with work related current asthma were 4.8 times (95% CI 2.0 to 11.6) as likely to report having an asthma attack, 4.8 times (95% CI 1.8 to 13.1) as likely to visit the emergency room at least once, and 2.5 times (95% CI 1.1 to 6.0) as likely to visit the doctor at least once for worsening asthma compared to individuals with non-work related asthma.
Tarlo et al./ 1997	Comparison the outcome of OA induced by isocyanates, with the outcome of OA induced by other work agents/ Canada (Ontario)	patients were classified in: a) occupational asthma b) aggravation of asthma c) unrelated asthma d) other decision	-Files were reviewed of all claims for occupational asthma submitted to the Ontario Workers' Compensation Board between 1984 -1988 -Information included: demographic details, type and duration of work exposure, details of symptoms attributed to work, history of any previous asthma, medication, and results of investigations. -Follow up results obtained one to two years later, including work status, symptoms, medication, and pulmonary function results.	-136/235 compensated claims were attributed to isocyanates. -attributed to isocyanates had a shorter latent period before onset (5.9 v 7.9 years, P<0.05), shorter duration of symptoms before diagnosis (2.0 v 3.0 years, P<0.05), and less associated atopy (43% v 58%, P<0.05). -Outcome at a mean of 1.9 years after initial assessment was significantly better in those with OA induced by isocyanates; 73% cleared or improved (56% with other causes) -n=10 OA induced by isocyanates stayed at the same work; n=0 cleared, n=4 had worsened at follow up. -A better outcome in OA induced by isocyanates was associated with early diagnosis (P<0.05), and early removal from isocyanates after the onset of asthma.
WRA= Work-related Asthma; WEA= work-exacerbated asthma; NWRA= non–work-related asthma; OA= occupational Asthma				

Tarlo et al. (1997) made a comparison for different OA claims (Isocyanates compared with other causes of OA) in Ontario. The results are based on mean follow up period of 1.9 years after initial assessment. 73% of the patients with Isocyanate-induced OA are cleared or improved compared to 56% of patients with other causes.
Miedinger et al. (2010) analysed in a cross sectional study based on questionnaire the socioeconomic factors that are correlated with the number of years of exposure with symptoms before removal from exposure. This study was carried out in Montreal (Canada). The authors showed that having an income of 30.000 Canadian dollars, being older and having OA due to high molecular weight agents is correlated with a longer interval for which a subject is symptomatic in the workplace. This also increases the probability for an increase severity at diagnosis.

2.3.4 Description of the included cost of illness studies for occupational skin diseases

Through the systematic literature search we identified three studies executing cost of illness analyses for occupational skin diseases, whereby two studies were performed in Germany (Diepgen et al. 2013a, Diepgen et al. 2013b) and one study in Denmark (Satterstrom et al. 2014). Moreover, the systematic search revealed four publications analysing compensations claims data from outside Europe (Horwitz et al. 2006, Lyons et al. 2013, Keegel et al. 2013, McCall et al. 2005).
All three European studies performed their cost of illness analysis from the societal perspective calculating direct (healthcare), indirect (loss of productivity) and total societal costs. As shown in Table 2.11, studies differ strongly in the estimated amount of annual costs per patient. However, in all studies the main cost driver were indirect costs, that is costs attributable to loss of productivity. Discrepancies in calculated costs might be due to cross-country differences in the healthcare system, different populations under study as well as varying methods/data sources used.
All studies focused on occupational skin diseases (contact dermatitis (CD) and hand eczema (HE)), but different severity groups were taken into account. While Satterstrom et al. 2014 included all patients with CD (covering also those with no current or minor symptoms), Diepgen et al. 2013b distinguished between two severity groups of occupational HE and the analysis of Diepgen et al. 2013a involved only refractory chronic HE patients.
Moreover, identified studies differed also significantly in the methods and data sources used for cost of illness analysis. To investigate the effects of CD on labour market affiliation and societal costs Satterstrom et al. (2014) linked data from a clinical database to patient, healthcare service and drug registries. In order to avoid an overestimation of costs of illness, only those costs should be taken into account which are associated with the target disease. Therefore, by means of propensity score matching, a control group was selected from a 30% random sample of the population and five controls were assigned to each case of CD. In order to receive costs attributable to the disease, costs of controls were subtracted from costs of cases (i.e. 21,441 patients with CD). These attributable costs were calculated annually from four years prior to recognition (i.e. patch testing) until 1 year after recognition (patch testing). Results revealed that direct costs attributable to occupational CD remained stable for the first three years, but one year before recognition and in particular one year after recognition they increased strongly.

Table 2.11 Cost of illness studies and studies about financial consequences for occupational skin diseases

Author/ Year	Study aim	Study population/ medical indication/Country	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Data sources/study perspective	Results (direct costs, indirect costs and others)	Results – subanalysis
Satterstrom et al. (2014)	Investigation of the effects of CD on labour market affiliation and societal costs (healthcare costs and productivity loss)	N=21,441 incident individuals with CD (patch tested/ MOAHLFA index) in the period 2004-2009: (a) children (0-15 years), (b) OCD (16-65 years), (c) non-OCD (>15 years) / Denmark	Register-based cost of illness study with case-control design (propensity score matching): 'Attributable' healthcare costs=Difference between costs for cases and controls; Yearly 'attributable' costs were estimated from 4 years prior to patch testing (date of recognition) until 1 year after patch testing; Healthcare costs: include drugs, primary care, outpatient care, inpatient care Productivity loss (for individuals in the labour market force aged 18-65 years): long-term sick leave (>24 days) for both adult cohorts, cost of vocational rehabilitation for adults with OCD	Clinical database (National Allergy Research Centre), Danish National Health Service Register, Danish National Patient Register, Danish National Prescription Registry, National Labour Market Authority's database DREAM/societal perspective	'Attributable' total healthcare costs per year/case: (b) OCD: before recognition: €48.62 (year 1)- €163.84 (year 4) after recognition: €412.23 (year 5) (c) non-OCD: before recognition: €227.26 (year 1)- €514.76 (year 4) after recognition: €592.98 (year 5) 'Attributable' productivity loss per case (year 1-5): (b) OCD: Sickness: €8,982.39 Vocational rehabilitation: €2,350.77 (c) non-OCD: Sickness: €3,249.22	Analyses were stratified by healthcare sector (drugs, primary care, outpatient care, inpatient care)
Diepgen et al. (2013) (a)	Comparison of the cost-of-illness for patients with refractory CHE, in relation to whether the disease was occupational or unrelated to work factors.	N=310 patients with CHE insured by SHI and/or OHI and recruited from / Germany	Surveys were conducted in 2008. First survey: Was conducted at 24 dermatology practices and clinics across Germany and included patients insured by SHI: SHI-1: non-working patients SHI-2: work-unaffected patients SHI-3: work-impaired patients Second survey: Was conducted in two specialized centers linked with OHI system and included only patients insured by OHI: work-diseased patients	Two virtually identical cross-sectional surveys/ societal perspective	Direct annual costs (healthcare costs) per patient: SHI-1: €1,362.52 SHI-2: €1,545.84 SHI-3: €3,391.83 OHI: €3,547.27 Indirect annual costs (productivity loss) per patient: SHI-3: €2,006.80 OHI: €3,668.41	no

Author/ Year	Study aim	Study population/ medical indication/ Country	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Data sources/study perspective	Results (direct costs, indirect costs and others)	Results - subanalysis
Diepgen et al. (2013) (b)	Estimation of the societal costs of patients with OHE in Germany	N=151 patients recruited in one specialized hand eczema clinic in Germany which needed to have OHE that had been diagnosed, treated and reported by a dermatologist using a special report (Hautarztbericht)/ Germany	Medical-record- and interview-based cost of illness analysis of OHE patients (recruited 2006/2007) 12 months prior to inclusion in inpatient rehabilitation program. As not all data was available, some data were estimated by using assumptions. Two severity groups were distinguished: Severity group A: no signs/mild and severity group B (moderate to severe)	Medical records (covering medical history, diagnostic and therapeutic procedures) and 1-hr structured interview/ societal perspective	Direct annual costs per patient (medical care costs): All patients: €2,836.53 Severity A: €2,899.78 Severity B: €2,797.94 Indirect annual costs per patient (productivity loss): All patients: €6,594.99 Severity A: €5,488.68 Severity B: €7,285.37 Total annual societal costs per patient: All patients: €9,432.60 Severity A: €8,388.46 Severity B: €10,083.31	Different cost components

Abbreviations: CD=contact dermatitis; OCD=occupational contact dermatitis; CHE=chronic hand eczema; OHE=occupational hand eczema; SHI=statutory health insurance; OHI=occupational health insurance

Regarding indirect costs (productivity loss) the overall trend was similar. The comparison of occupational and non-occupational CD showed higher attributable total costs for non-occupational compared to occupational CD patients.
To compare costs of illness for patients with refractory chronic HE (either occupational or unrelated to work), Diepgen et al. (2013a) used data from a cross-sectional-data-survey performed in 2008 among SHI-insured patients (Augustin et al. 2011). They additionally carried out a second virtually identical survey among patients with chronic HE in two German specialized centres linked with the occupational health insurance (OHI) system. This means that in order to facilitate comparison, patients were recruited from OHI centres using the same inclusion/exclusion criteria as defined in the study of Augustin et al. (2011) and the same survey methods and instruments. Afterwards, four groups depending on the impact of chronic HE on work were defined by differentiating between non-working (SHI-1), work-unaffected (SHI-2), work-impaired (SHI-3)[3] and work-diseased patients (OHI)[4]. Analyses of 310 patients showed that annual direct costs of work-impaired (SHI-3) and work-diseased (OHI) patients were approximately twice as high as costs of non-working (SHI) and work-unaffected (SHI) patients. Moreover, costs attributable to loss of productivity were also higher for work-diseased compared work-impaired chronic HE patients.
Using information from medical records covering medical history, diagnostic/therapeutic procedures as well as 1-hour structured interviews Diepgen et al. (2013b) estimated annual societal costs of 151 patients with occupational HE in Germany 12 month prior to entering a special rehabilitation program. Due to unavailability of some data, some calculations were based on assumptions. Moreover, analyses were stratified by two severity groups, that is group A (no signs/mild) and group B (moderate to severe). While there was no significant difference in annual direct costs per patient between group A and B, the analyses revealed a trend towards higher indirect costs in patients suffering from moderate to severe severity occupational HE (group B). In sum, total annual societal costs were higher in severity group B compared to A.

2.3.5 Description of studies for indicators of disease severity and duration in occupational skin diseases

By means of the systematic search we identified six studies dealing with indicators of disease severity and duration in occupational skin diseases of which one was detected by manual search (Meding et al. 2005). The six studies were conducted in Germany (Brans et al. 2014), Finland (Malkönen et al. 2010), Sweden (Meding et al. 2005) and Denmark (Cvetkovski et al. 2005, Skoet et al. 2004). In addition to that, we identified one systematic literature search including studies from inside and outside Europe. For an overview of included studies see Table 2.12. Apart from six European studies, we also identified one study which has been carried out in Australia dealing with severity of worker impairment (Keegel et al. 2007).

[3] Work-impaired patients (SHI-3) are defined as “SHI patients in work for whom work is affected by CHE (i.e. disease causes days off work or with job loss/change due to CHE). In such patients, CHE might be caused by work, although (at the time of the study) the relationship was not confirmed by OHI” (Diepgen et al. 2013a, p. 539).
[4] Work-diseased patients (OHI) are defined as “OHI patients, i.e. subjects with known work-related CHE and in whom the correlation between CHE and work has been confirmed by the occupational health insurance” (Diepgen et al. 2013a, p. 539).

Table 2.12 Studies analysing indicators of disease severity and duration in occupational skin diseases

Author/ Year	Study aim/Country	Study population/ medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Brans et al. 2014	Evaluation of relations between smoking status, severity and prognosis of OHE patients/ Germany	N=1,788 patients with OHE taking part in a tertiary individual prevention programme	- Prospective, multicentre cohort study - Patients were recruited and followed up for 3 years - Clinical and self-reported outcome data of smokers and non-smokers were compared	Worse prognosis of smoking: - The severity of OHE is increased in smokers (at all-time points in the study) - Smoking is associated with higher absenteeism and giving up occupation (due to OHE)
Malkönen et al. 2010	Identification of prognostic risk factors for persistent OHE/ Finland	N=605 patients diagnosed with OHE at the Finnish Institute of Occupational Health	- Survey: Patients examined at the Finnish Institute of Occupational Health in 1994-2001 completed a follow-up questionnaire 7-14 years after diagnosis	Risk factors for the continuation of OHE: - long duration of hand eczema before diagnosis - respiratory atopy - skin atopy - continuation of the same occupation No risk factors: age, sex, diagnosis (irritant/allergic), contact allergies (except chromate allergy)
Meding et al. 2005	Study of the long-term prognosis of occupational skin diseases/ Sweden	N=517 patients who in 1987 reported occupational skin disease to the Social Insurance Office in Sweden	- Microfilm records were reviewed by an dermatologist regarding diagnoses, patch test results, location of skin symptoms, skin atopy and perceived cause of skin disease - Additional survey: In 1999, patients were sent a questionnaire; non-responders were interviewed by telephone	- Occupational skin disease has poor long-term prognosis - >80% had performed occupational changes (most common job changes) Unfavourable factors for the prognosis: - skin atopy - contact allergy - Female sex
Cvetkovski et al. 2005	Evaluation and comparison of the severity and consequences of recognised OHE in different diagnostic and subdiagnostic groups/ Denmark	N=758 new cases of recognised OHE identified from the Danish National Board of Industrial Injuries Registry	- Basis: Identification of new cases of recognised OHE (October 2001-November 2002) through registry; severity grading depending on the intensity of skin response and the frequency of relapse - Additional information by means of postal questionnaires - Stratification by five subdiagnoses of OHE	Risk factors for higher severity of OHE: - Greater severity among those with occupational irritant CD and AD than for other diagnoses - Age >50 was associated with increased severity of OHE - Prolonged sick leave due to OHE was associated with AD and severe OHE - Higher proportion of prolonged sick leave among those in food-related occupations compared with wet/other occupations

Author/ Year	Study aim/Country	Study population/ medical indication (data sources)	Methods (Modell, cross sectional vs longitudinal Surveys, data analysis); analysis period	Severity and duration of disease
Skoet et al. 2004	Characterisation of OHE in Denmark/ Denmark	N=758 new cases of OHE, who were 18 years or above at the time of registration of the case (Danish National Board of Industrial Injuries Registry)	- Prospective information from the National Board of Industrial Injuries Registry - Additional information through self-administered questionnaires	Causes of OHE: - Most frequently recognised diagnosis was irritant CD, mainly caused by wet occupations - Disease duration was not associated with occupation - Cooks/kitchen workers were found to have a mean disease duration of 4.7 years, and 27.1% had severe hand eczema, compared to healthcare workers with a mean duration of 4.9 years and 14.3% with severe hand eczema - Construction workers were found to have long disease duration of 8.2 years and 14.3% had severe eczema
Cahill et al. 2004	Identification of common variables influencing the prognosis of OCD/ In and outside Europe	N=15 studies reviewed	- Systematic literature search (databases Medline and Web of Science were searched between 1966 and 2004) using the terms OCD, occupational skin disease, prognosis, allergic and irritant CD - Review of 15 studies published between 1958 and 2002	- Factors influencing prognosis: age, sex, atopy, patient knowledge, disease aetiology, duration of symptoms, job change, as well as clinical, financial and social issues - Improved patient knowledge and early diagnosis may be associated with improved prognosis - Job change does not make a significant difference
Study outside Europe				
Keegel et al. 2007	Comparison of treatment between general practitioners and dermatologists; Evaluation of predictors for OCD disease severity measured in terms of worker impairment/ Australia	N=123 workers with suspected OCD recruited by the report of clinicians (as part of their routine practice) or who attended a tertiary referral occupational dermatology clinic in the study area	- Data collection through reporting forms - Apart from recording demographic and clinical information from the reported workers, the reporting form asked clinicians to list the suspected diagnosis, the current or recommended treatment, and their normal management/referral practice for a patient with this type of illness - Patient assessment: diagnosis, atopy (personal history of asthma), occupational causation, level of severity	- General practitioners were more likely to treat a patient independently, referring if the patient did not improve, whereas dermatologists were more likely to refer for patch testing on initial presentation - When adjusted for all variables including age, sex, duration and diagnostic subgroup, workers with atopy as a cofactor had the most severe impairment

Abbreviations: OHE=occupational hand eczema; CD=contact dermatitis; OCD=occupational contact dermatitis; AD=atopic dermatitis

Again, a comparison of the results is difficult because publications differ in the population under study/severity of indication and data sources used vary from registries and medical records to questionnaires and interviews per telephone. All studies (except the systematic literature search) additionally used patient questionnaires to enrich information obtained from medical record or registry data.
With the aim of examining the relations between smoking status, severity and prognosis of occupational hand eczema (OHE), Brans et al. (2014) compared clinical and self-reported outcome data of smokers and non-smokers followed up for three years after taking part in an tertiary individual prevention program in Germany. The authors found higher severity of OHE and a higher amount of work absenteeism/more patients being forced to give up their work due to OHE in smokers compared to non-smokers, thus resulting in a worse prognosis for smokers.
In order to investigate factors associated with the long-term continuation of OHE in Finland/Sweden, Malkönen et al. (2010) and Meding et al. (2005) sent follow-up questionnaires to patients 7-14 years (Malkönen et al. 2010) or 12 years (Meding et al. 2005) after diagnosis of OHE/occupational skin disease. Malkönen et al. (2010) identified a long duration of hand eczema before diagnosis, respiratory atopy, skin atopy and not changing the job as unfavourable factors for prognosis. Moreover, age, sex, diagnosis (allergic/irritant) and contact allergies (except chromate allergy) were not correlated with the continuation of OHE. By comparison, Meding et al. (2005) also identified skin atopy as an unfavourable factor for prognosis, but in contrast to Malkönen et al. (2010) the authors also found contact allergy and female sex to be associated with the long-term continuation of occupational skin diseases.
Focusing on indicators of severity of OHE in Denmark, Cvetkovski et al. (2005) and Skoet et al. (2004) collected information from questionnaires sent to incident cases of OHE which have been identified from the Danish National Board of Industrial Injuries Registry. The authors found out that there is a greater severity among workers with irritant contact or atopic dermatitis than for other diagnoses and increased severity is also correlated with age above 50 years. Moreover, there was a higher proportion of long-term sick leave among those workers in food-related compared to other occupations. Likewise, Keegel et al. (2007) focusing on OCD outside of Europe (Australia), observed that workers with atopy as a cofactor had the most severe impairment. In sum, most studies reported risk factors, among other things for the continuation of chronic HE (e.g. Malkönen et al. 2010) or higher severity of occupational HE. Several factors were reported more frequently to be associated with a negative prognosis, for example smoking (Brans et al. 2014), respiratory/skin atopy (Malkönen et al. 2010, Meding et al. 2005) or special occupations (Cvetkovski et al. 2005).
With the aim to identify common variables influencing the prognosis of occupational CD, Cahill et al. 2004 performed a systematic literature search in the databases Medline and Web of Science covering the years 1966-2004. They identified 15 studies from inside and outside of Europe. Variables which could exert (positive or negative) influence on prognosis included inter alia age, sex, atopy, patient knowledge, disease aetiology, duration of symptoms, job change, as well as clinical, financial and social issues. However, included studies presented opposite findings.

2.3.6 Quality assessment of cost of illness studies

As already described in the methods section, we assessed the quality of all cost of illness studies identified through the systematic search. Table 2.13 gives an overview

on the evaluation of cost of illness studies concerning occupational lung and skin diseases.

2.3.6.1 Occupational lung diseases

Quality assessment was carried out for four different cost of illness studies according to respiratory diseases. One of these studies is not a typical cost of illness study because it analysed the loss of income due to occupational asthma (Gannon et al. 1993). All studies described the study objective and the inclusion and exclusion criteria. Gomez et al. (2012) and Ayres et al. (2010) both analysed the costs for a hypothetical sample and adapted relevant healthcare costs to this hypothetical sample. Gomez et al. only analysed direct costs whereby Ayres et al. included the analysis of indirect costs.
The study by Ayres et al. focused on one hypothetical man and one hypothetical woman that are in each case exposed to isocyanate, latex and biocides or flour. For each patient the direct and indirect costs identified by a systematic literature search were adopted to each patient. Therefore, the authors did not calculate costs, but adopted costs from other studies.
It is unusual to use two hypothetical patients and adopt other study results to this patients, but the implementation of the study by Ayres et al. (2010) is of good quality. Nevertheless, it is important to take into account that the results are aggregated by other cost of illness studies, mostly for patients with asthma in general and not for patients with occupational asthma. Furthermore, this study does not include a primary data analysis. It is also necessary to see that the identified studies possibly used other methods, other study populations and especially other cost perspectives and that some results are based on assumptions.
The calculation of indirect costs by Ayres et al. (2010) is very detailed. They used for example results for employment and income rate following diagnosis of occupational asthma by another study (Ameillle et al. 1997). Overall, this study reported the costs for patients with occupational asthma very detailed, the quality is sufficient but the named limitations should be taken into account.
Gomez et al. (2012) and Moscato et al. (1990) did not report the perspective of the study. Moscato et al. (1990) calculated the pharmaceutical expenses via a diary by the patients, but it remains unclear whether the pharmaceutical costs are the costs payed only by the insurance company or also the co-payments of the patients. Therefore, the perspective of cost calculation remains unclear. It is likely that Gomez et al. (2012) calculated the costs from the perspective of the insurance because they only reported specialised care, primary care and pharmaceutical care costs.
In comparison with Gomez et al. (2012) and Ayres et al. (2010), the study by Moscato et al. (1990) was based on self-reported questionnaires and did not use secondary sources to calculate costs.Furthermore this study had great deficits regarding the criteria for cost calculation. Therefore, a comparison with other studies is difficult and associated with an unusually high degree of uncertainty.
Despite the uncertainty resulting from the adaption of costs for asthma in general, no study performed a good univariate or probabilistic sensitivity analysis. None of the included studies discussed their study sample in terms of representativeness but most of the studies described the limitations.

Table 2.13 Overview on quality assessment of included cost of illness studies concerning occupational lung and skin diseases

Aims and methods of the study		Occupational asthma and COPD				Occupational skin diseases		
		Ayres et al. (2010)	**Gomez et al. (2012)**	**Mos-cato et al. (1990)**	**Gannon et al. (1993)**	**Satter-strom et al. (2014)**	**Diepgen et al. (2013a)**	**Diepgen et al. (2013b)**
Study objective	The objective(s) and research question(s) of the study was (were) described clearly	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Inclusion and exclusion criteria	At least the objective diagnostic criteria (e.g. ICD code and DSM-IV) used to identify eligible patients were reported. The study population was specified	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Non-diseases comparison group or disease-specific costs	The study included a non-diseased control group in order to calculate excess costs or, if no control group was involved, the costs were due to the disease of interest (e.g. diagnostic codes)	No[5]	No	Yes	No	Yes	Yes	Yes
Matching or regression analysis	If comparison groups were used: a) they were matched, at least in terms of age and/or gender, to allow a direct comparison between equally dispersed groups with regard to their characteristics or b) regression analysis was carried out in order to control differences	N.a.	N.a.	N.a.	N.a.	Yes	N.a.	N.a.
Sensitivity analysis	Relevant parameters were varied in univariate and/or in probabilistic sensitive analyses in order to address parameter uncertainties (e.g. different unit costs)	No	No	No	No	No	No	No
Calculation of costs								
Data sources	The source of information on healthcare utilization or costs was reports and mentioned specifically	Yes	Yes	No	Yes	Yes	Yes	Yes
Perspective	The perspective of the cost calculation was reported (e.g. from payer, employer, or societal perspective)	Yes	No	No	n.a.	Yes	Yes	Yes
Cost calculation	The method of cost calculation was clearly documented	Yes	Yes	No	No	Yes	No	Yes
Cost categories	The study estimated costs from the utilization of different kinds of healthcare services or areas, which meant that more than one category was given, in order to consider, at best, all costs that accrued from the disease under study	Yes	Yes	No	No	Yes	Yes	Yes
Reference year (price)	All costs were valued at the price level of a stated base year	Yes	Yes	No	No	Yes	Yes	No

Aims and methods of the study		Occupational lung diseases				Occupational skin diseases		
		Ayres et al. (2010)	Gomez et al. (2012)	Mos-cato et al. (1990)	Gannon et al. (1993)	Satter-strom et al. (2014)	Diepgen et al. (2013a)	Diepgen et al. (2013b)
Currency	The currency in which the costs were calculated was reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Inflation rate and/or dis-count rate	If data were collected from or estimated for a period longer than one year, costs were adjusted for differential timing and the inflation rate/discount rate was mentioned	Yes	N.a.	N.a.	N.a.	Yes	N.a.	N.a.
Monetary valu-ing of resource utilization	If data on resource utilization were collected that were valued with unit costs, the latter were reported; if cost data were used, these reflected actual charges	Yes	Yes	No	No	No	No	Yes
Presentation of results								
Sample size	The sample size was reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Demographics	The characteristics of the sample were described; at least (mean) age and gender were reported	Yes	No	Yes	Yes	Yes	Yes	Yes
Arithmetic mean costs	The cost estimates were (partly) presented as arithmetic means	No	Yes	Yes	Yes	Yes	Yes	Yes
Standard de-viations	Standard deviations of cost estimates were (partly) re-ported as a measure of variability	Yes	No[6]	No[6]	Yes	No[6]	No[6]	No[6]
Separate in-formation number of services used and costs	Separate information about the number of (health) ser-vices and cost were given for all cost categories that were described	No[4]	Yes	No	No	No[1]	No[2]	No[2]
Discussion								
Discussion with respect to other studies	The results were discussed in relation to other studies on the same topic	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Limitations	The limitations regarding the calculation of costs and the representativeness of the study population, in particular, were discussed in detail	No	No[3]	No	No	No[3]	No	Yes

[1] Separate information about the costs were given for all cost categories that were described, but there was no separate information about the number of health services
[2] Separate information about the number of health services were given, but there was no separate information about all cost categories that were described
[3] The limitations regarding the calculation of costs were discussed in detail, but the representativeness of the study population was not (fully) addressed
[4] Separate information about the number of health services were not given, but there was separate information about all cost categories that were described
[5] The limitations regarding the calculation of costs were discussed in detail, but the representativeness of the study population was not (fully) addressed
[6] The authors reported 95%CI

In summary, the quality assessment of the studies with a focus on occupational respiratory diseases shows that two studies are of good quality (Ayres et al. 2010; Gomez et al. 2012) and have a comparable study perspective. They both calculated costs from the perspective of taxpayer or the social insurance so that these results are more comparable with data from the DGUV than costs based on the patient perspective. They also calculated direct costs for occupational asthma and took at least the costs for inpatient and outpatient treatment as well as medication costs into account. Ayres et al. (2010) also reported further cost categories like administration costs or indirect costs. This should be taken into account if the results of the study will be transferred to the different EU-28 countries.
The result of quality assessment for the study by Moscato et al. (1990) is very insufficient. The study has a lot of methodological missings e.g. an unclear documentation of the methods for cost calculation and they only reported costs for monthly pharmaceutical expenses. This cost category is not enough to cover the costs due to occupational asthma from one perspective. Therefore, we would suggest neglecting these results for cost transfer in chapter 4.5. The same applies to the study by Gannon et al. (1993). The quality of the study may be better but they reported only the loss of income due to occupational asthma. Therefore, we would also suggest neglecting these study results for cost transfer.

2.3.6.2 Occupational skin diseases

Through the systematic literature search, we identified three European cost of illness studies concerning occupational skin diseases (Table 2.13). The quality assessment of these three studies shows that while study objective and inclusion/exclusion criteria have been described adequately and all studies included a comparison group or disease-specific costs were otherwise calculated, none of the studies reported the performance of sensitivity analyses in order to address parameter uncertainties. However, Diepgen et al. (2013b) reported using a conservative approach to handle missing data, thus rather underestimating costs.
Regarding the calculation of costs, we identified deficits in the documentation of cost calculation (Diepgen et al. 2013a) and the valuation of costs at the price level of a stated base year (Diepgen et al. 2013b). Furthermore, Satterstrom et al. (2014) and Diepgen et al. (2013a) did not report the unit costs that were used with the valuation of resource utilisation, thus showing a lack of methodological transparency and making replicability impossible.
Concerning the presentation of results, none of the studies on costs of occupational skin diseases reported standard deviations of costs, but 95% confidence intervals were given. Moreover, studies either presented separate information about the number of health services used (Diepgen et al. 2013a, Diepgen et al. 2013b) or costs for all cost categories that were described (Satterstrom et al. 2014). All studies discussed their results in relation to other studies on the same topic, but we identified deficits in the reporting of limitations regarding the calculation of costs and/or the representativeness of the study population in two studies. Diepgen et al. (2013b) provided a broad discussion about limitations, whereas Satterstrom et al. (2014) did not address the representativeness of the study population and Diepgen et al. (2013a) did not report any limitations. Conclusion of the systematic literature review
The aim of this systematic literature search was to identify all studies conducted in Europe which include information on costs of illness of work-related lung and skin diseases and indicators of duration and severity of these diseases. A total of 29 stud-

ies have been included in this review showing low evidence for cost of illness studies as well as publications on indicators of severity and duration of the diseases.
Concerning cost of illness studies for work-related lung diseases, only two usable cost of illness studies for occupational lung diseases were identified. Ayres et al. used a holistic approach which is based on assumptions and hypothetical patients. Therefore the inclusion criteria are good explained and best source for adapting the costs were chosen. For the cost transfer it is necessary to reduce the calculated direct costs by pensions payments. Another limitation is the adoption of results from other cost of illness studies to the hypothetical population. Therefore it is possible that different study settings, perspectives and populations are combined. While Ayres et al. calculated indirect costs Gomez et al. only reported direct costs. In this study also a primary research have been implemented.
With regard to work-related skin diseases, three studies from Germany and Denmark on costs of illness have been identified showing a wide range of average annual costs, but all studies have in common that they identified indirect costs as the main cost driver. The wide range of costs might be due to the different methods/data sources used and the inclusion of different study populations, thus making the comparability of these studies almost impossible. While Satterstrom et al. (2014) focused on individuals with work-related CD reported to the Board of Occupational Health including also cases in which all symptoms had already cleared, Diepgen et al. (2013a) and Diepgen et al. (2013b) included patients with work-related chronic HE refractory to treatment (Diepgen et al. 2013a) or at risk of losing their ability to work due to the disease (Diepgen et al. 2013b), i.e. individuals with higher disease severity.
The quality assessment of these cost of illness studies reveals some deficits, especially a lack of sensitivity analyses, transparency of the methodological approach, level of detail in shown results as well as discussed limitations of the study. Nevertheless, from a methodological point of view, out of the three cost of illness analyses the study by Satterstrom et al. (2014) might be of best quality, because the analysis was based on a linkage between a clinical database and registries whereby healthcare costs were calculated using appropriate tariffs. Moreover, in order to estimate only those costs attributable to the disease, a control-group design was implemented. By comparison, in the cost of illness studies performed by Diepgen et al. (2013a) and Diepgen et al. (2013b) information on healthcare utilisation was obtained from patients and physicians and medical costs were also calculated by applying insurance-specific tariffs. However, as information on the exact quantification of resource use was not available, for the purpose of the cost analysis, a number of assumptions needed to be made. In general, these assumptions have been conservative, thus rather underestimating costs.
Concerning indicators of severity and duration of work-related lung diseases, the evidence is very low, i.e. results are to a high extent very general and details are missing. Likewise, studies focusing on indicators of severity and duration of work-related skin diseases are rare and results are very diverse depending on the study population and research question. Most often (skin/lung) atopy as a co factor was reported to be associated with a negative prognosis of work-related skin diseases.
In sum, the results of the systematic literature review show a high need for research. This is especially true for cost of illness studies, where primary research should be performed. Only then it is possible to evaluate cost differences between patients with occupational asthma and patients with asthma unrelated to work.

3 Cost of illness analysis using claims data

3.1 Theoretical approach

In this working package the cost of illness analysis for the German setting based on claims data will be performed. Therefore, in the following section we will give an overview on the main components of a cost of illness analysis and different study perspectives.

“Cost-of-illness studies are descriptive analyses assessing the economic burden of health problems on the population” (Rice et al. 1990). This research type provides evidence regarding the maximum amount that could potentially be saved or gained if a disease can be prevented (Segel 2006). There are different categories of costs and the definition of relevant cost categories depends to a large extend on the study perspective. Three main perspectives may be distinguished: perspective of the society, the payer (e.g. third-party payers) and the participants or their families (Prenzler et al. 2010). For each project the study perspective has to be defined clearly. For instance, the National Health Service in GB adopts the payer perspective while the IQWIG in Germany prefers the perspective of the society which additionally includes the costs which have to be beard by the patients themselves.

Depending on the study perspective, different cost components should be included. In general, three different forms of costs can be distinguished. Direct costs comprise all costs that are directly linked with the provision of therapy (Schöffski 2012), e.g. costs for inpatient care, outpatient care, rehabilitation, pharmacy prescriptions, remedies and medical aids (Segel 2006; Rice et al. 1990; Gold et al. 1996). Apart from direct costs, indirect costs can be calculated by measuring the economic loss of productivity due to sick leave, invalidity or premature mortality. Indirect costs can be calculated by using three different approaches: ‘Human Capital Method’, ‘Friction Cost Method’ and the ‘Willingness to Pay Method’ (Koopmanschap et al. 2001). However, pension payments or sick leave payments are not a part of the indirect costs as these costs belong to transfer payments (Gold et al. 1996). Transfer costs can cause a significant load on social insurance agencies and might even be more relevant from a quantitative point of view than direct costs, especially in the course of chronic diseases. Nevertheless, from a macroeconomic point of view, these payments are not real costs as they are means of redistribution and do not indicate resource consumption. Thus, in the cost analyses, transfer costs should be shown separately. Intangible costs are those costs that cannot be directly measured in monetary terms including physical, psychological and social factors, e.g. anxiety, stress, and quality of life. Due to their challenging measurement, intangible costs are often excluded in cost of illness studies.

After identifying the choice of study perspective and cost components, costs can be calculated using two different approaches, either the bottom-up or the top-down approach. Moreover, costs can be calculated per patient or for the whole economy. The top-down approach is based on a highly aggregated database which can be broken down into research question (e.g. total costs divided through the number of patients). In comparison, the bottom-up approach estimates costs by calculating the average disease-related costs on the patients’ (individual) level and multiplies these results by the prevalence of the illness (Segel 2006; Bloom et al. 2001). Both approaches have advantages and disadvantages and the choice depends on data availability and quality for each research question.

Bottom-up analyses in cost of illness studies can be performed using claims data derived from different social insurance agencies. Claims data are a form of secondary data and belong to the category of administrative data. In Germany, researchers can request access to different claims data sources, for example data of the statutory health insurance (GKV), the statutory accident insurance (DGUV) or the statutory pension insurance (GRV). Because this data is primarily recorded for billing and reimbursement, it could offer insight into real-life healthcare provision (on the basis of a huge data set with largely complete cases of insured persons). However, this data is not predominantly collected for scientific purposes, which means that it has specific limitations which need to be taken into account (Zeidler et al. 2012; Swart et al. 2005; Swart et al. 2014).

3.2 Methods

3.2.1 DGUV claims data

3.2.1.1 Aim

The aim of this claims data analysis is to estimate the costs of illness for specific occupational diseases caused by isocyanates affecting the respiratory tract, the lungs and the skin. In particular, this analysis focuses on individuals insured by the DGUV which suffer from the following occupational diseases listed in Annex 1 of the Occupational Disease Ordinance (Federal Institute for Occupational Safety and Health 15.06.2015): Asthma, COPD, and alveolitis (mainly number 1315), as well as dermatitis (number 5101).
Data from the DGUV will serve as a basis for this analysis for several reasons: When an employee becomes sick as a result of his work or work circumstances, this impairment can be confirmed and recognised as an occupational disease. In this case, according to articles 26 and 27 of the Social Security Code VII, the DGUV is exclusively responsible for paying the medical services. These expenditures are an important component of the total social costs of these occupational diseases. Moreover, as described by Lohsträter (Lohträter 2005), DGUV claims data are a suitable data source for scientific purposes as they largely comprise complete cases. In sum, this analysis focuses on recognised cases as a subset of confirmed cases, because confirmed cases do not lead to a performance obligation.
By comparison, as other social insurance agencies, e.g. the statutory health insurance (GKV), are not obliged to pay medical services in the case of recognised occupational diseases they do not provide information about costs of occupational diseases. In general, GKV claims data can be used to estimate costs of illness of specific diseases based on ICD-Codes or medications without a direct focus on the cause of illness.

3.2.1.2 Analysis strategy

First, a separate cost analysis for each of the before mentioned indications will be conducted. It is intended to analyse the costs of every occupational disease per case over the course of the disease, thus enabling to report case-related costs of illness. Moreover, since the disease duration of the insured differ, a uniform time base (e.g., costs per year) has to be defined. Second, it will be clarified, whether a stratification of the cost analysis, for example into age at the onset of disease; gender and if pos-

sible disease severity, is realisable and necessary. Third, if possible, we will examine the evolution of costs from the time of the onset of disease.
Moreover, the data analysis will be conducted from the perspective of the DGUV (Payer perspective). Besides those (so called) direct costs of illness, which arise in the use of health care services and can be extracted directly from the data set (bottom-up approach), the indirect costs of illness will also be calculated. These indirect costs emerge by an increased number of sick leave days. Further information regarding the duration of sick leave in the above mentioned respiratory and skin diseases can be gathered, for instance, at the Federal Health Monitoring (e.g. sick leave among German Public Health Insurance compulsory members). However, this data has its limitation that the cause of sick leave is missing. This difference might be fairly important for the severity and the progression of the asthmatic disease, which in turn has to be considered when using this indicator. Under these circumstances, we will proof whether the occupational disease data of the DGUV will allow drawing inferences about duration and time of sick leave.
Nonetheless, it needs to be weighed, whether the evaluation of indirect costs will be performed by applying the human capital or the friction cost approach. The advantage of applying the friction cost approach is that it wipes out some unrealistic assumptions of the human capital approach. Namely, that it assumes perfect competition in the labor market and full employment respectively (Greiner et al. 2012).
Finally, in order to calculate costs of isocyanate-induced diseases, the time period is considered to be of great importance. That is, the precision and reliability of the cost evaluation increases with the length of time period observed.

3.2.1.3 Statistical analysis

As defined by “Good Practice Secondary Data Analysis” (GPS) (Swart et al. 2015) and according to the classical approach in claims data analysis from statutory health insurances (Horenkamp-Sonntag et al. 2014), completeness, plausibility and validity of data obtained have to be verified, because this data is primarily recorded for accounting purposes and not for research purposes. In the case of conspicuity, a repeated reconciliation with the data owner will take place.
After verifying the data, the first step is to perform a descriptive analysis, i.e. absolute and relative frequency distributions. In the course of analysing metric data which applies particularly to costs, measures central tendencies (mean value, median) and dispersion measures (variance, standard deviation) will be used. In order to investigate how precise the estimated means correspond to the truth, but unknown mean of the population, we will calculate 95% confidence intervals.
Moreover, we will conduct comparative analysis between the patient groups by means of statistical tests, whereby the choice of tests depends on data characteristics. Apart from the descriptive presentation of indication-specific costs, we will perform subgroup analysis, e.g. among gender, age group and medical indication.
The second step consists of applying multivariate methods of data analysis (especially regression analysis) to identify indicators of duration and of severity of occupational diseases (e.g. exacerbation of lung diseases). Nevertheless, at the present time it cannot be determined if disease severity can be measured adequately. We will execute data preparation and analysis by means of SPSS Statistics, SAS and/or STATA.

3.2.1.4 Process of data extraction

As displayed in Table 3.1 the study population consists of individuals insured by the German statutory accident insurance (DGUV), who suffer from specific occupational diseases caused by isocyanates, i.e. isocyanate-induced respiratory and lung diseases (bronchial asthma, chronic obstructive bronchitis, alveolitis) as well as skin diseases (dermatitis); in accordance to the Ordinance on Occupational Diseases (Federal Institute for Occupational Safety and Health 15.06.2015). Depending on the analysis period and the number of cases provided by the German statutory accident insurance, we will discuss which cases (i.e. diseases according to ICD, German Modification) will be included in the analysis.

Table 3.1 Overview inclusion criteria DGUV

Group of disease	Medical indication	ICD (GM)	Occupational disease Nr.
Respiratory and lung diseases	Allergic bronchial asthma	J45.0	1315/4301
	Non-allergic bronchial asthma[5]	J45.1	1315
	Chronic obstructive bronchitis	J44.8	1315/4302
	Extrinsic allergic alveolitis	J68.4/ J67.8	1315
Skin diseases	Irritant contact dermatitis	L24-	5101
	Allergic contact dermatitis	L23-	5101

In the case of identifying relevant diagnoses/occupational disease numbers in the given analysis period, we will extract all relevant information from the following resource and cost domains: Patient characteristics, basic documentation, follow-up documentation as well as costs of occupational diseases caused by isocyanates.
The most important variables are those providing information about (framework conditions of) service provision, resulting (monetary) resource use as well as the reason for using health care services (documented by ICD). Table 3.2 gives an overview of these variables by resource and cost domains. However, this overview should be interpreted as an ideal concept. Thus, exact availability, preparation and quality of chosen variables should be brought into agreement by the DGUV and the BAuA/Leibniz University of Hannover (LUH).

Table 3.2 Variables by resource and cost domains[2]

Resource and cost domains	Specification
Patient characteristics	Identification number (primary key) Insurance status and type of pension Begin of status End of status Reason for leaving
Basic documentation: demographical pa-	Identification number (primary key) Reporting year Number of occupational disease ordinance

[5] Very rare disease; perhaps there is no separate cost evaluation needed

tient characteristics and reporting of suspicion of occupational disease	Year of birth Gender Nationality Primary disease Secondary diseases Job role code
Follow-up documentation	Identification number (primary key) Day of fist compensation Amount of reduction in earning capacity Maximum admissible concentration in the workplace Duration of exposure Assessment of exposure as well as potential multi-factorial event
Inpatient care	Identification number (primary key) Case number Admission day Dismissal day Main diagnosis at dismissal All secondary diagnoses All procedures DRG Costs Co-payments of the insured Regional code of the hospital
Outpatient care	Identification number (primary key) Doctor identifier number Specialist's group Diagnoses Diagnostic reliability German Uniform Assessment Standard (EBM) Number of provided services (separate lines) GONR Date of service provision EBM-Points All procedures Costs Co-payments of the insured Regional code of doctor
Pharmacy data	Identification number (primary key) Doctor identifier number German anatomical therapeutic chemical classification (ATC) Pharmaceutical registration number (PZN) Date of prescription Date of delivery Number of prescribed units (Daily defined doses) Costs

Remedies and medical aids	Identification number (primary key) Doctor identifier number Date of prescription Date of (service) delivery Position number (type of remedies and medical aids) Number of prescribed units Costs
Rehabilitation	Identification number (primary key) Begin of rehabilitation End of rehabilitation Main diagnosis Type of rehabilitation Costs
Sick leave and sick leave payments	Identification number (primary key) Begin of sick leave End of sick leave Number of days in sick leave Diagnoses Type of sick leave Begin of sick leave payments End of sick leave payments Number of days with sick leave payments Sum of sick leave payments (costs)
Other	Sum of transitional payments Begin of transitional payments End of transitional payments Sum of pension payments Begin of pension payments End of pension payments

[2] Own table following Lohsträter (Lohträter 2005) and Prenzler (Prenzler et al. 2010))

3.2.1.5 Data protection

Within this project, we will comply with the statutory provisions relating to data protection: Claims data of the DGUV (in a temporary pseudonymous form) will be transmitted through the Competence Center for Insurance Science (KVW) in a factual anonymous form. In the course of the pseudonym, personally identified characteristics will be removed from the extracted data and replaced by a unique identifier, e.g. an ongoing identification number. Hereby, identification of the affected person will be impossible. Factual anonymization means that the process of replacing personally identifying data cannot be reversed. The data owner guarantees that this factual anonymization by destroying pseudonym key before transmitting the data. Thus, for both cooperation partners, data is given in a factual anonymous form and this anonymised data is not covered by provisions in data protection with regards to the processing of personal data.
Moreover, in signing this obligation, data users commit themselves to comply with the data protection rules during the whole duration of the project. All transmitted data will be kept under tight wraps in order to ensure confidential handling with the data. For the realisation of the project, generally accepted operating systems (MS Windows XP and MS Windows 7) and software applications will be used, ensuring safeguarding of

the system and user authentication, i.e. only personal responsible for data preparation and analysis will gain access. Non-required network interfaces will be deactivated or removed. If possible, processing computer will be disconnected from the internet in order to prevent external access. Only authorised staff have administrative credentials. The establishment and maintenance of the used hardware and protection systems will be conducted with the support of qualified internal IT student assistants. Data preparation and analysis will be performed exclusively at the KVW (Competence Center for Insurance Science, Managing Director: Prof. Dr. J.-Matthias Graf von der Schulenburg).

3.2.1.6 Originally planned procedure

Unfortunately, it was not possible to get access to individual DGUV claims data as originally planned in the way described above. However, the DGUV offered the opportunity to analyse claims data on request and to provide aggregated results tables. Therefore, we placed two requests with regard to the annual costs from 2004-2013 of insured persons suffering from the confirmed occupational diseases 1315 and 5101, broken down by cost domains as well as age groups and gender. The second request related to an additional analysis of the costs further subdivided by ICD-codes.
After the delivery of aggregated tables, we put all costs on a comparable basis by adjusting them for inflation to the year 2013 using the consumer price index. Afterwards, we calculated average costs per insurant and per case. To quote average costs per insurant, we divided the sum of costs (of a resource domain) by the total number of insured persons (irrespective of whether they have used that special service). In comparison, average costs per case were calculated by dividing the sum of costs (of a resource domain) by number of insured persons that used that special service.

3.2.2 DIMDI database

Since we did not get full access to DGUV claims data, in coordination with the BAuA we decided to apply for the use of the information system for healthcare data derived from the German Institute for Medical Documentation and Information (DIMDI). The DIMDI claims database provides comprehensive aggregated claims data based on morbidity-oriented risk structure compensation (Risikostrukturausgleich - RSA) from all statutory health insurance (SHI) funds, thus including information from 86% of the German population. Although the DIMDI database has some methodological disadvantages compared to data from an individual SHI fund (e.g. a smaller extent of variables), it provides representative data for approximately 70 million individuals (all publicly insured). Access to the DIMDI database is regulated by the German Social Security Code (§§ 303a to 303e SGB V) and depends on the type of institution and intended use. Entitled users can apply for provision of claims data by a formal request which also includes the development of SQL/SAS analyses programmes and a project description. All documents have to be submitted to the DIMDI data processing centre. The centre will check these programmes and in case of positive evaluation, data will be analysed according to the SQL/SAS analyses programmes and the project description, and finally results tables will be transmitted to the applicant. In November, we submitted our application to the DIMDI data processing centre. Please note that is uncertain how long the checking of documents with regard to content and

form will take and how much time passes between the confirmation and data transfer of aggregated results.
The following section contains the project description for submission to the DIMDI data processing centre. As in the case of confirmed occupational diseases the DGUV is exclusively responsible for paying the medical services in connection with the disease, the DIMDI database does not include costs attributable to confirmed occupational diseases, but information on publicly insured persons with certain diseases (independent of whether they are work-related or not). Thus, this cost of illness analysis using the DIMDI database enables an approximate estimation of costs attributable to selected lung and skin diseases.

3.2.2.1 Aim

The aim of this project is to determine the health care costs for publicly insured patients with specific respiratory and skin disease. Of interest are the average total costs, sector-specific costs as well as costs for asthma patients comparing intermittent and persistent cases. In order to calculate average costs, we will take the sum of the total annual costs of all the insured individuals with the relevant target disease (according to the ICD code) and divide them by the respective number of the insured. For the following medical indications (Table 3.3) which were defined respectively through the three-digit ICD-10-GM code, we will conduct separate cost analyses:

Table 3.3 Overview on inclusion criteria (DIMDI database)

Group of disease	**Medical indication**	**ICD (GM)***
Respiratory diseases	Asthma	J45.-
	Other chronic obstructive pulmonary disease (COPD)	J44.-
	Respiratory conditions due to inhalation of chemicals, gases, fumes and vapours	J68.-
Skin diseases	Atopic dematitis	L20.-
	Allergic contact dermatitis	L23-
	Irritant contact dermatitis	L24.-
	Other dermatitis	L30.-

*International classification of diseases and related health problems

3.2.2.2 Selection process

As a basis we analysed data from the reporting years 2009-2011, because only these three years comprise a largely complete picture on the relevant sectors of master data, inpatient diagnoses, outpatient diagnoses and expenditures from the corresponding compensation years (for an overview of all processed data elements see appendix 3). Unfortunately, in the DIMDI database, data for expenditures for the compensation years 2009 and 2010 are only available as a sample (DIMDI 2015). Therefore, we limited the study population to insured persons for which costs in the relevant resource domains are available. In order to get a complete picture of disease-related costs, it is essential to distinguish between individuals who did not incur any healthcare costs because they have not used healthcare services and those individuals for which costs are not documented as they are not part of the DIMDI sam-

ple. The inclusion of both groups would result in an underestimation of disease-related costs.
In the second step, we identified the study population using inpatient and outpatient diagnosis codes. In the area of lung disease, the study population included the insured with the following diagnoses: asthma (ICD: J45.-), other chronic obstructive pulmonary disease (ICD: J44.-) or respiratory conditions due to inhalation of chemicals, gases, fumes and vapours (ICD: J68.-). In the area of skin diseases, the study population included the insured with the following diagnoses: atopic dermatitis (ICD: L20.-), allergic contact dermatitis (ICD: L23.-), irritant contact dermatitis (ICD: L24.-) or other dermatitis (ICD: L30.-). Every target indication had to be documented in 2010 (index year) as either a stationary primary or secondary diagnosis, and/or a secured outpatient diagnosis. In the case of outpatient diagnosis, a second secured outpatient diagnosis in one of the following three quarters was compulsory. We excluded insured persons with the diagnosis addition “state after diagnosis”, as well as suspicion and exclusion diagnoses. The diagnosis addition “state after diagnosis” is coded in ambulatory care if the diagnosis no longer exists and disease specific diagnostics and therapies are completed. However, the underlying disease has caused medical treatment which has to be coded (e.g. administration of ASS after completed stroke treatment). As this project focuses on chronic skin and lung diseases in contrast to healed up diseases, the inclusion of patients with this diagnosis additional would presumably lead to an underestimation of disease-related costs. As part of the determination of the study population, patients can be repeatedly included, because of the different indicators.
In the third step, we concretised the study population using the following inclusion and exclusion criteria: In addition to the presence of the relevant diagnoses, we only allowed insured adults (minimum age of 18). We calculated the age for the baseline year of 2009. To ensure that individuals have complete cost data and not any gaps in the documentation of services, we considered only those individuals which were insured for the whole year (>364 days) over the entire analysis period (2009-2011). In addition, we also excluded insured persons who became deceased during the analysis period. The insured with a (temporary) residence or living abroad were also excluded from the analysis, since the diagnosis and cost documentation could not be acquired.
Moreover, the insured with a reimbursement agreement according to the articles 13 (para. 2) and 53 (para. 4) of the Social Security Code V were also excluded. Reimbursement agreement means that statutory insureds become self-payer, that is, first, they balance accounts directly with healthcare provider and then, costs will be reimbursed wholly or partly less an administration fee by their statutory health insurance fund. According to article 30 (para. 1 (9)) of the regulation of risk adjustment among the statutory health insurance funds (RSAV), health insurance funds document the number of days of reimbursement agreement for each person individually. We excluded individuals with at least one day of reimbursement agreement from the analysis, due to the fact that the payment of performed services takes a different path (e.g. there might be delays in administration and billing and medical services might not be fully reimbursed) thus resulting in incomplete documentation of disease-related costs.
In the course of the selection process, we also distinguished between incident and prevalent cases using the reporting year 2009. This distinction served for later sub group analyses. Patients were referred as prevalent if they had the same diagnosis (ICD three plates) in both the index year 2010 and the year before (2009). Similar to the general identifications of the study population, it had to be a stationary primary or

secondary diagnosis or a secured outpatient diagnosis. In contrast, patients were referred as incident if a diagnosis was documented in 2010, but not in 2009.

3.2.2.3 Analysis methods

Control group design:
In order to avoid overestimation of the medical costs for the target diseases, only resource consumption associated with the diseases should be taken into account. To determine indication-specific costs, we applicated a control group design (Zeidler et al. 2013), that is the matched pairs method. The potential insured who were going to be included in the control group, must not have any of the relevant target diagnoses in the reporting years 2009-2011. Moreover, the same inclusion and exclusion criteria as described above were applied to the potential control group.
As matching criteria we used age, gender, the Elixhauser comorbidity score (Van Walraven et al. 2009) as well as pharmaceutical and inpatient costs from the last year (2009). The Elixhauser classification system including 30 comorbidity groups is an instrument for measuring patient comorbidities based on ICD-10 codes, originally used to predict hospital resource use and mortality. For use in administrative data, it has been modified into a single numeric comorbidity score ranging from -19 to +89. (van Walraven et al. 2009).
We performed an exact 1:5 matching. This means that five comparison partners (“twins”) were assigned to each intervention participant, either by the exact expression of the intervention participant (e.g. by gender) or within a defined radius (caliper). Initially, we set the caliper to 10% above or below pharmaceutical and inpatient costs of the intervention participant. If there will be no adequate match with the caliper, it needs to be extended. With regard to the year of birth and the Elixhauser score we determined an absolute value of +/- 3 years (year of birth) and +/- 5 points (Elixhauser Score). The setting of percentage deviations would not be effective here, because there are neither ages during the year nor decimals for the Elixhausercomorbidity score. The comparison partner was determined by "sampling with replacement". This means that a comparison partner may also be associated with two or more intervention participants. However, it was ruled out that the same comparison partner was assigned several times to one intervention participant. The method "sampling with replacement" was selected in comparison to the „sampling without replacement" to minimize the risk of failure of the comparison partner assignment.

Determining the incremental average costs:
The objective of the analysis is to determine the average total costs for the years 2009 and 2011 in the intervention and control groups in order to ultimately estimate incremental average costs per indication (Zeidler et al. 2013). To isolate disease-specific costs of the intervention group, we will perform a cost comparison for the years 2009 (before disease index) and 2011 (after index disease) between prevalent and incident patients. By means of the differences-in-differences estimator we will additionally subtract the cost difference between the years 2011 and 2009 of the control group from the cost difference between the years 2011 and 2009 of the intervention group. It is assumed that any increase in costs between 2009 and 2011, which does not occur in the control group, is attributable to the target indications and associated costs of the intervention group.

Sub group analysis:
The costs per indication were displayed across sectors and sector-specific (outpatient care, inpatient care, drug supply, sickness benefits). Concerning the indication asthma costs were presented separately according to approximated severity. Analogous to Jacob et al. (2015) we distinguished between intermittent (rather mild cases) and persistent asthma (rather moderate to severe cases). Patients with a documented hospitalisation with a primary diagnosis of asthma (secondary diagnoses were excluded) or at least one prescription of as specific long-acting therapeutic (Table 3.4) were classified as having persistent asthma whereas all other insured were classified as intermittent asthma cases. The latter only received reliever medication or no asthma-specific drugs were documented. In order to identify asthma-specific medication based on ATC-codes, we require the WidO drug master file. In case of positive preliminary review of this application, we will seek the consent of the WidO for the use of the WidO drug master file.

Table 3.4 Definition of intermittent and persistent asthma cases

Service Sector	**Intermittent asthma („light“)**	**Persistent asthma („medium/strong“)**
Drugs	• Reliever medication (i.e. at least one prescription of a short-acting b2-mimetics; ATC: R03AC04, R03AK03, 03AK05, R03AC02, R03CC02, R03AC03, R03CC03) • No asthma-specific medication	• Long-acting b2-agonist (LABA; ATC: R03AC13, R03AK07, R03AK72, R03AC12, R03AK61, R03AK06, R03CC12, R03CC13, R03CC14, R03CC63, R03AK71) • Leukotriene modifiers (LTRA, ATC: R03DC03) • Inhaled corticosteroids (ICS; ATC: R01AD01, R03BA01, R03BA02, R03BA08, R03BA05, R03BA07) • Oral corticosteroids (OCS; ATC: H02AB03, H02AB04, H02AB07, H02AB06, H02AB56, H02AB08) • Anti-IgE; ATC: R03DX05 • Theophylline (ATC: R03DA04, R03DA54) • Ipratropium bromide (ATC: R03BB01)
Inpatient care	-	• Stationary primary diagnosis of asthma (ICD: J45.-); no secondary diagnosis

Aggregation method:
We aggregated average costs on an annual basis (reporting years 2009-2011). In the course of subgroup analyses costs were also issued at the sector and annual basis. Our analyses do not permit statistical inference to single patients.

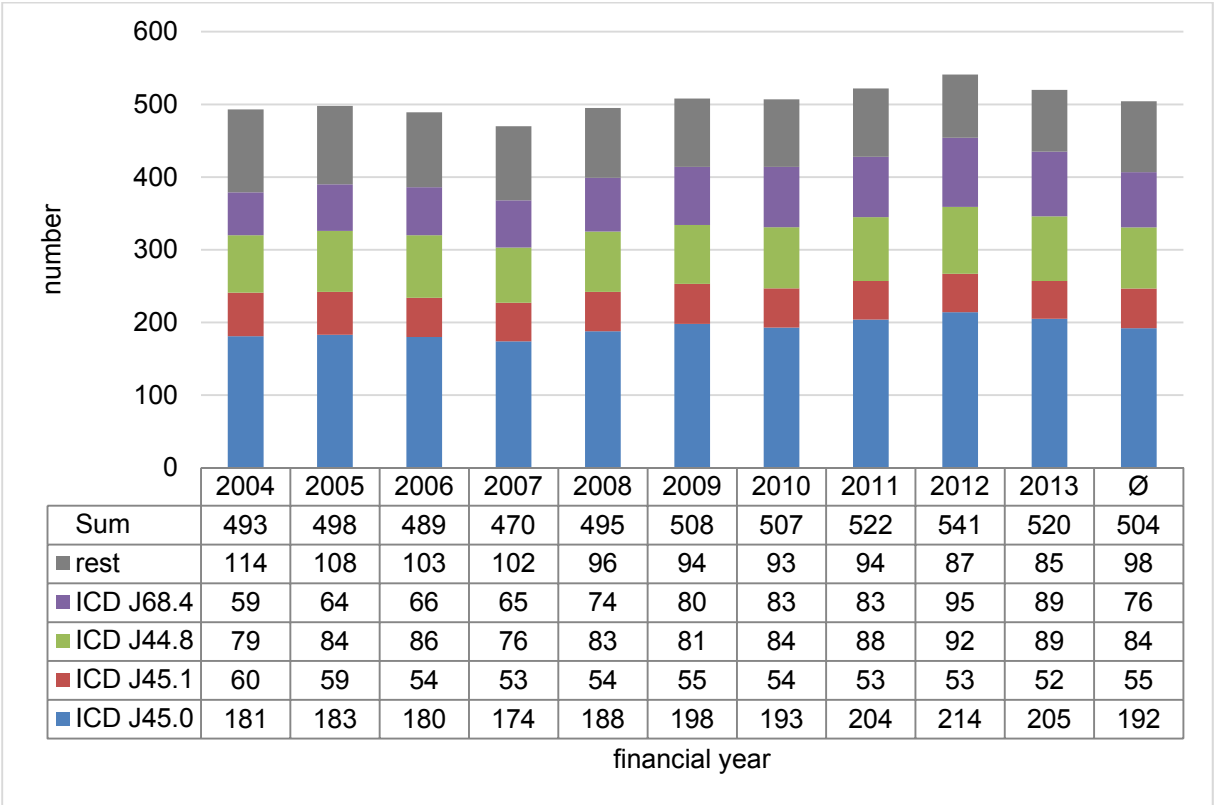
3.3 Results

3.3.1 Costs of illness of occupational lung and skin diseases from the perspective of the DGUV

The following section gives an overview of prepared results concerning costs of recognised occupational diseases nr. 1315 and 5101 (cause: isocyanates) from the perspective of the DGUV based on aggregated results tables (from the DGUV). The original results tables derived from the DGUV can be found in appendix 4. Selected figures will be presented in the following two sections.

3.3.1.1 Development and costs of occupational lung diseases due to isocyanates

As shown in Figure 3.1, the total annual number and composition regarding diagnosed disease of insured persons suffering from occupational lung diseases remained relatively stable over time. Every year approximately 500 insured persons used at least one healthcare service/received at least one benefit. Please note that this figure does not provide information about the date of recognition of the occupational disease, but only the number of benefit recipients.

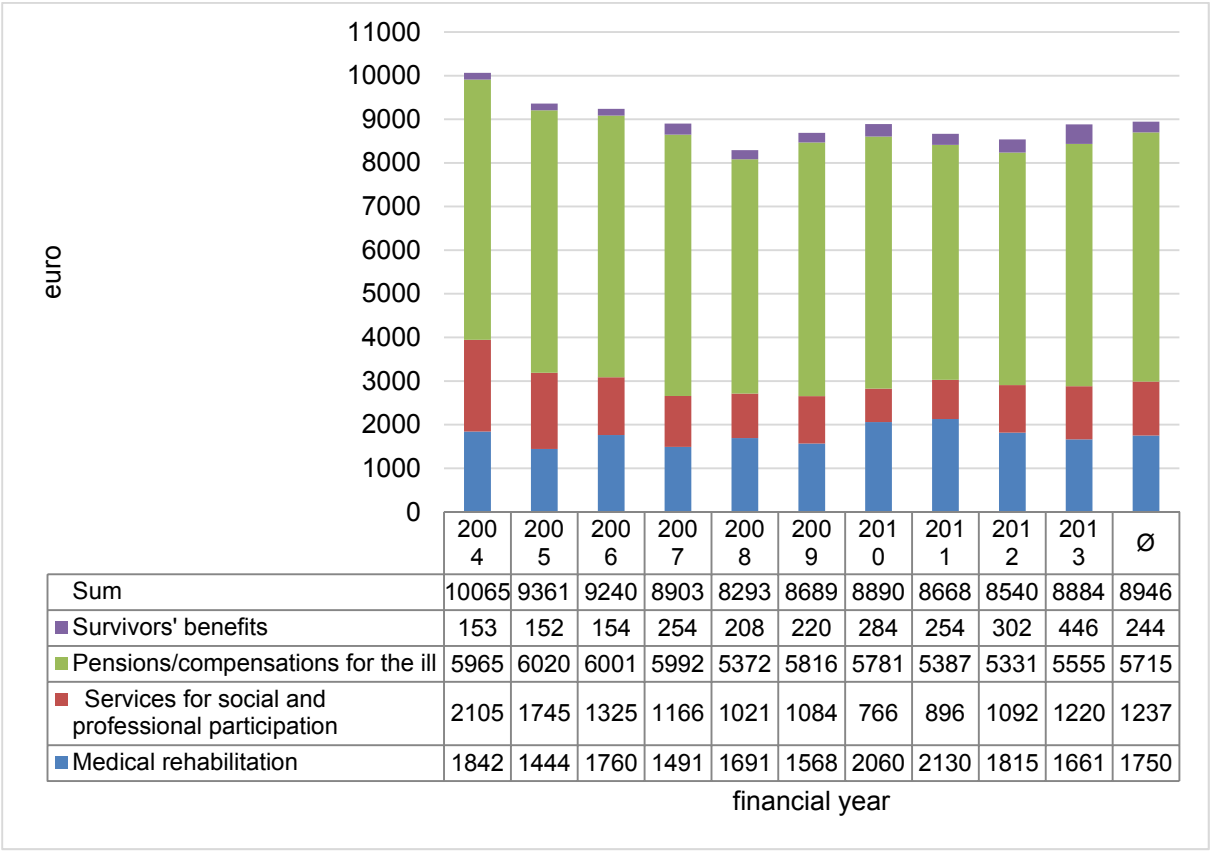


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	493	498	489	470	495	508	507	522	541	520	504
rest	114	108	103	102	96	94	93	94	87	85	98
ICD J68.4	59	64	66	65	74	80	83	83	95	89	76
ICD J44.8	79	84	86	76	83	81	84	88	92	89	84
ICD J45.1	60	59	54	53	54	55	54	53	53	52	55
ICD J45.0	181	183	180	174	188	198	193	204	214	205	192

Figure 3.1 Number and composition of insured persons suffering from occupational lung diseases (OD 1315)

Most of the insured were attributable to ICD J45.0, which is allergic asthma. The remaining occupational disease patients were distributed almost equally between the other three ICD-codes. However, there remains a rest of approximately 100 insured persons which could not be assigned due to a structural break concerning diagnosis coding in 2002. The DGUV tried to assign diagnosis codes before the structural

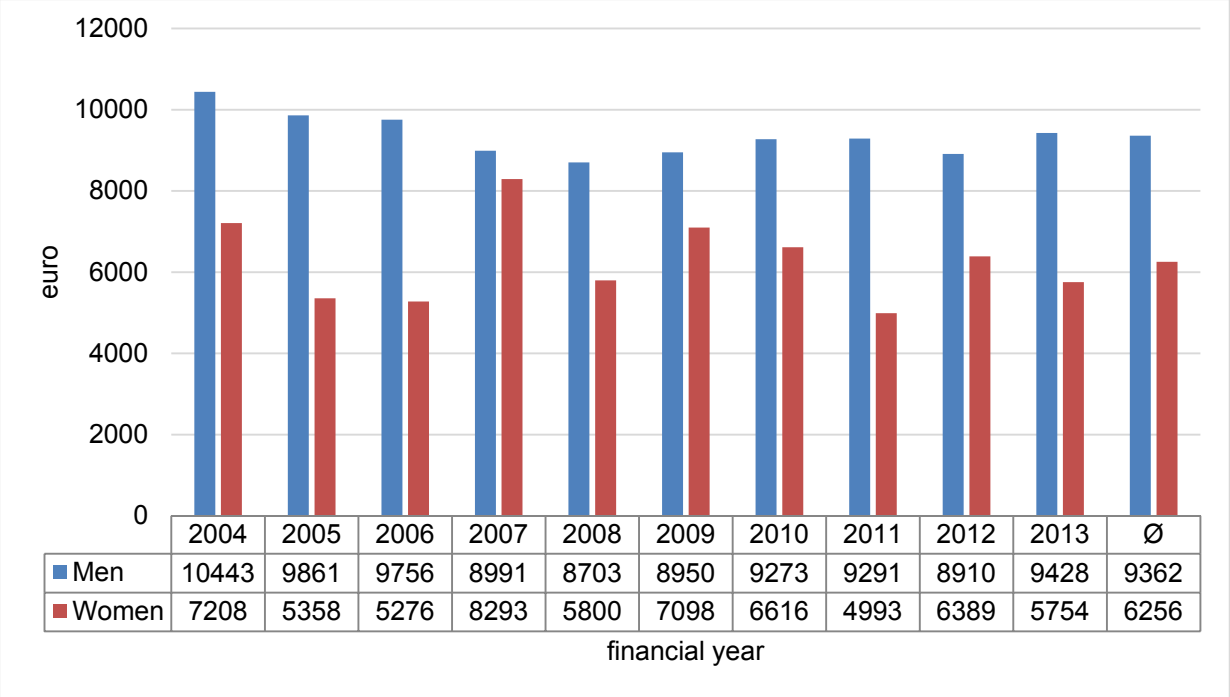
break to the corresponding IVD-10-codes. Thus, the residual category includes non-allocable patients, not specified patients as well as insured persons suffering from diagnosis H18.9 (only few cases).
With regard to the average annual costs of occupational lung diseases per patient, Figure 3.2 shows that these costs are estimated at approximately €8,000-10,000 across all ICD-groups, with an average over ten years with almost €9,000. The main cost driver, covering approximately two thirds of the costs, were pensions and compensations for the ill. Services for social and professional participation and medical rehabilitation accounted for nearly about one third of the costs, whereby survivors' benefits were of minor importance. Detailed information on DGUV sectors and services provided is given in appendix 5.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	10065	9361	9240	8903	8293	8689	8890	8668	8540	8884	8946
Survivors' benefits	153	152	154	254	208	220	284	254	302	446	244
Pensions/compensations for the ill	5965	6020	6001	5992	5372	5816	5781	5387	5331	5555	5715
Services for social and professional participation	2105	1745	1325	1166	1021	1084	766	896	1092	1220	1237
Medical rehabilitation	1842	1444	1760	1491	1691	1568	2060	2130	1815	1661	1750

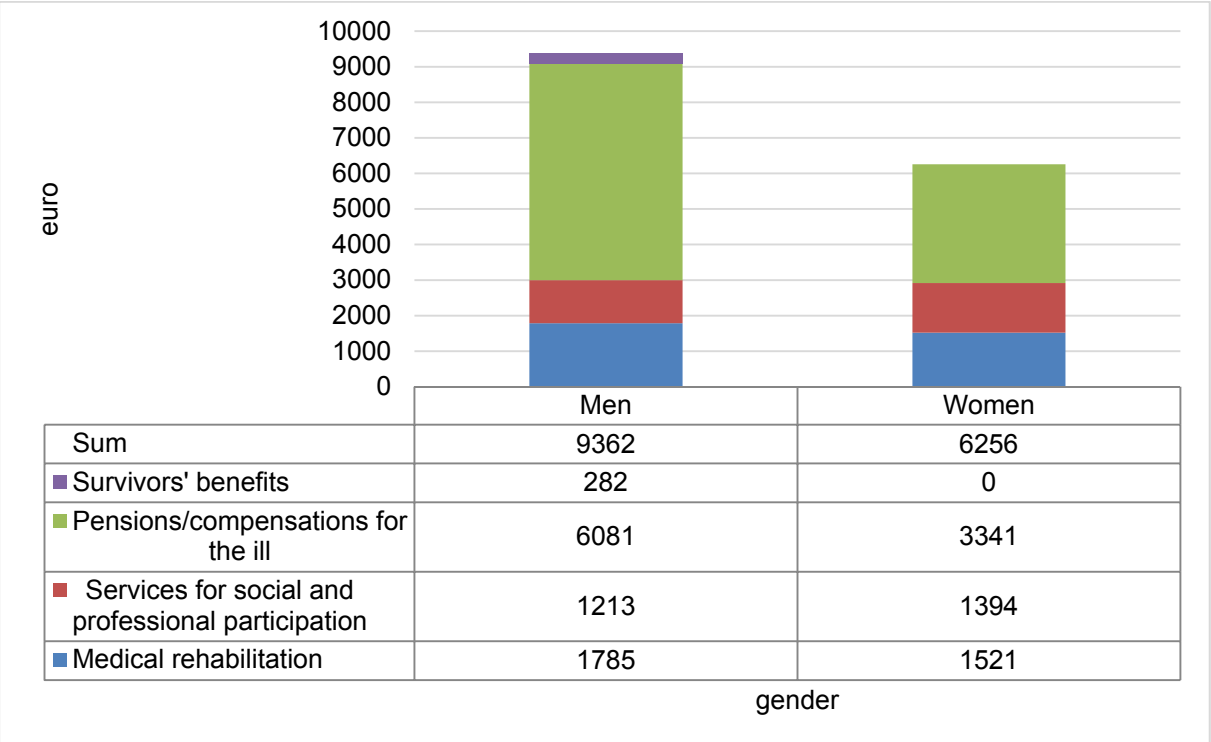
Figure 3.2 Average annual costs of occupational lung diseases per insured person with target disease (OD 1315, n=5,043)

Moreover, we performed a gender comparison which showed that on average over ten years, 13.4% of all beneficiaries were female. The cost analysis revealed that male patients caused considerably higher average annual costs than female insured persons. For example, in 2005 costs of male patients were nearly twice as high as costs of female patients (Figure 3.3). These gender-specific cost differences can be explained by the composition of total average costs over the years 2004-2013 (Figure 3.4). Whereas costs for social services and professional participation as well as medical rehabilitation accounted for about €3,000 per year for both genders, pensions and compensations for the ill were on average nearly twice as high for male patients compared to female patients. Here again, survivors' benefits are of minor importance.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Men	10443	9861	9756	8991	8703	8950	9273	9291	8910	9428	9362
Women	7208	5358	5276	8293	5800	7098	6616	4993	6389	5754	6256

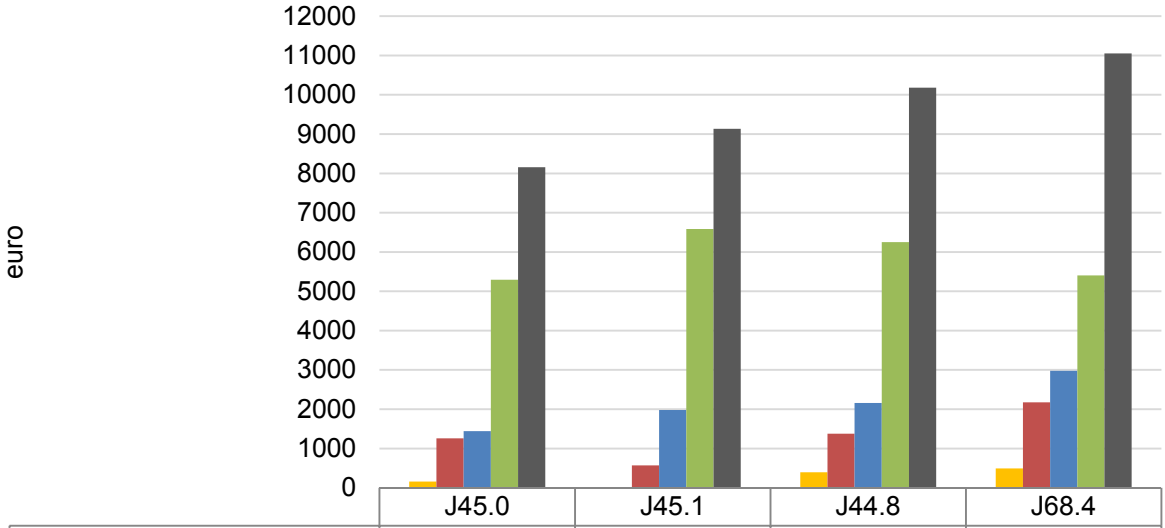
Figure 3.3 Average annual costs (2004-2013) of occupational lung diseases per insured person with target disease stratified by gender (OD 1315, n=5,043)



	Men	Women
Sum	9362	6256
Survivors' benefits	282	0
Pensions/compensations for the ill	6081	3341
Services for social and professional participation	1213	1394
Medical rehabilitation	1785	1521

Figure 3.4 Composition of average total costs of occupational lung diseases per insured person with target disease by gender (OD 1315, n=5,043)

As already mentioned, with regard to occupational lung diseases in general, by far the main cost factor were pensions/compensations for the ill. As shown in Figure 3.5, this also applies to every single ICD-subgroup. However, total average costs were highest among patients suffering from occupational alveolitis, followed by COPD, non-allergic asthma and allergic asthma. Again, survivors' benefits accounted only for a small proportion.

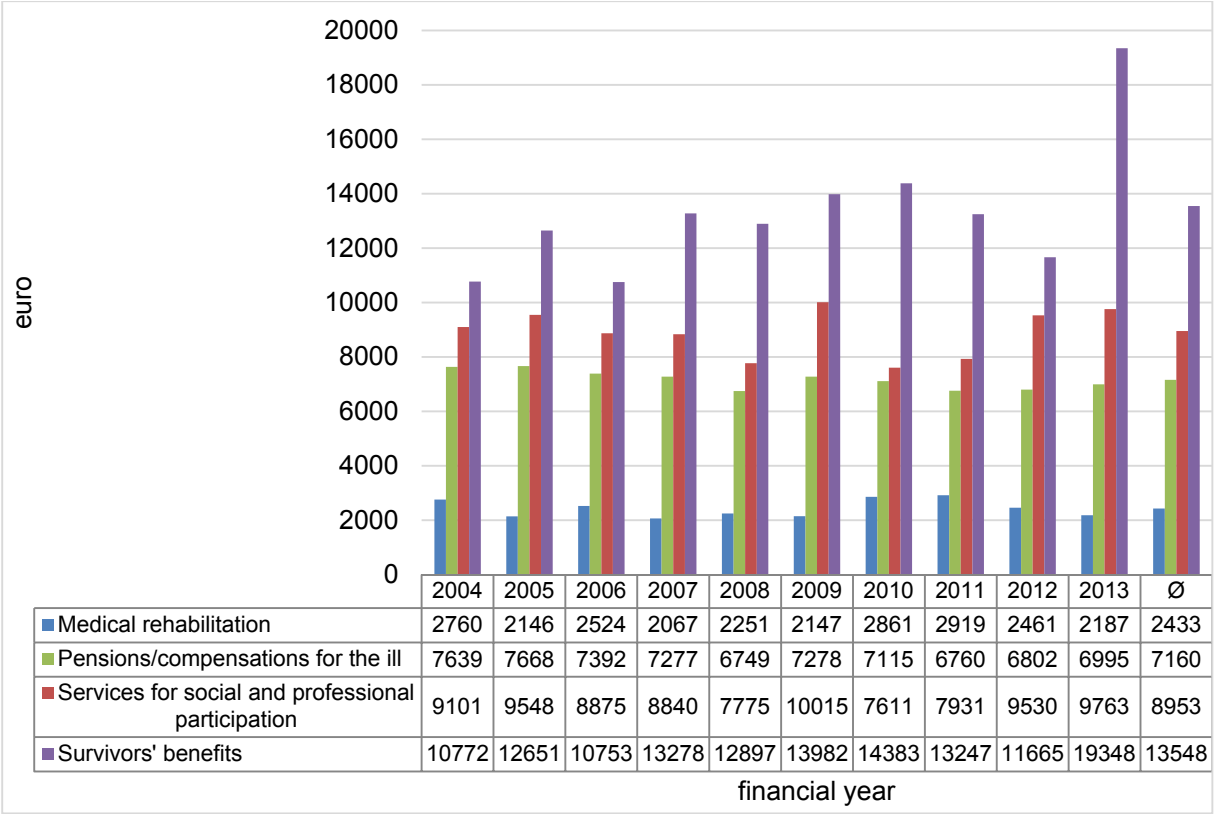


	J45.0	J45.1	J44.8	J68.4
Survivors' benefits	160	0	397	495
Services for social and professional participation	1259	569	1375	2174
Medical rehabilitation	1442	1979	2159	2979
Pensions/compensations for the ill	5296	6586	6249	5403
Sum	8157	9134	10180	11051

ICD

Figure 3.5 Average annual costs (2004-2013) of occupational lung diseases per insured person with target disease stratified by ICD-subgroup (OD 1315, n=4,067)

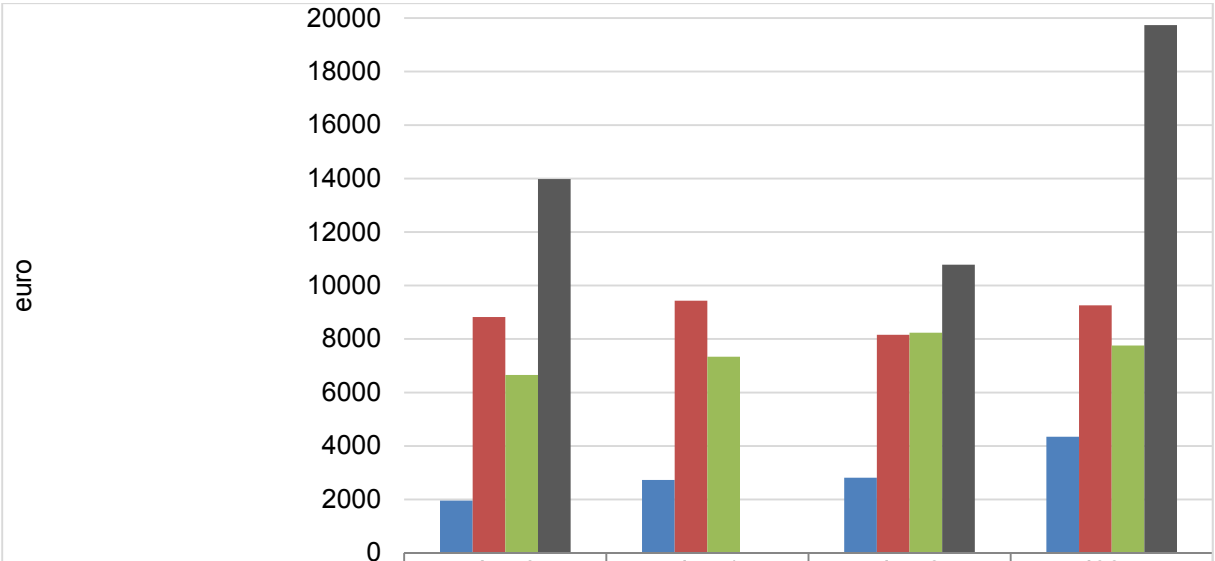
All the results described above were reported as average costs per insured person (with a least one healthcare service used/benefit received). In comparison, the following two tables give an overview on average costs per case, that is the total costs of a resource domain (e.g. medical rehabilitation) were divided by the number of patients that actually used these medical services (e.g. outpatient care) and/ or received benefits.Figure 3.6 illustrates that if survivors' benefits are paid, these are by far the largest cost factor (up to almost €20,000 in 2013), followed by services for social and professional participation and pensions/compensation for the ill. Costs of medical rehabilitation remained relatively constant over time accounting for slightly more than €2,000 per year.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	2760	2146	2524	2067	2251	2147	2861	2919	2461	2187	2433
Pensions/compensations for the ill	7639	7668	7392	7277	6749	7278	7115	6760	6802	6995	7160
Services for social and professional participation	9101	9548	8875	8840	7775	10015	7611	7931	9530	9763	8953
Survivors' benefits	10772	12651	10753	13278	12897	13982	14383	13247	11665	19348	13548

Figure 3.6 Average annual costs of occupational lung diseases per case (OD 1315, n=5,043)

Further information regarding average costs per case over ten years stratified by ICD-subgroups can be gathered from Figure 3.7. In all ICD-subgroups except non-allergic asthma (ICD 45.1), if paid, survivors' benefits were by far the highest average costs, followed by services for social and professional rehabilitation (in most sub-groups).
Further information regarding average costs per insured and per case stratified by ICD-subgroups are provided in appendices 6 (allergic asthma), 7 (non-allergic asthma), 8 (COPD) and 9 (alveolitis).

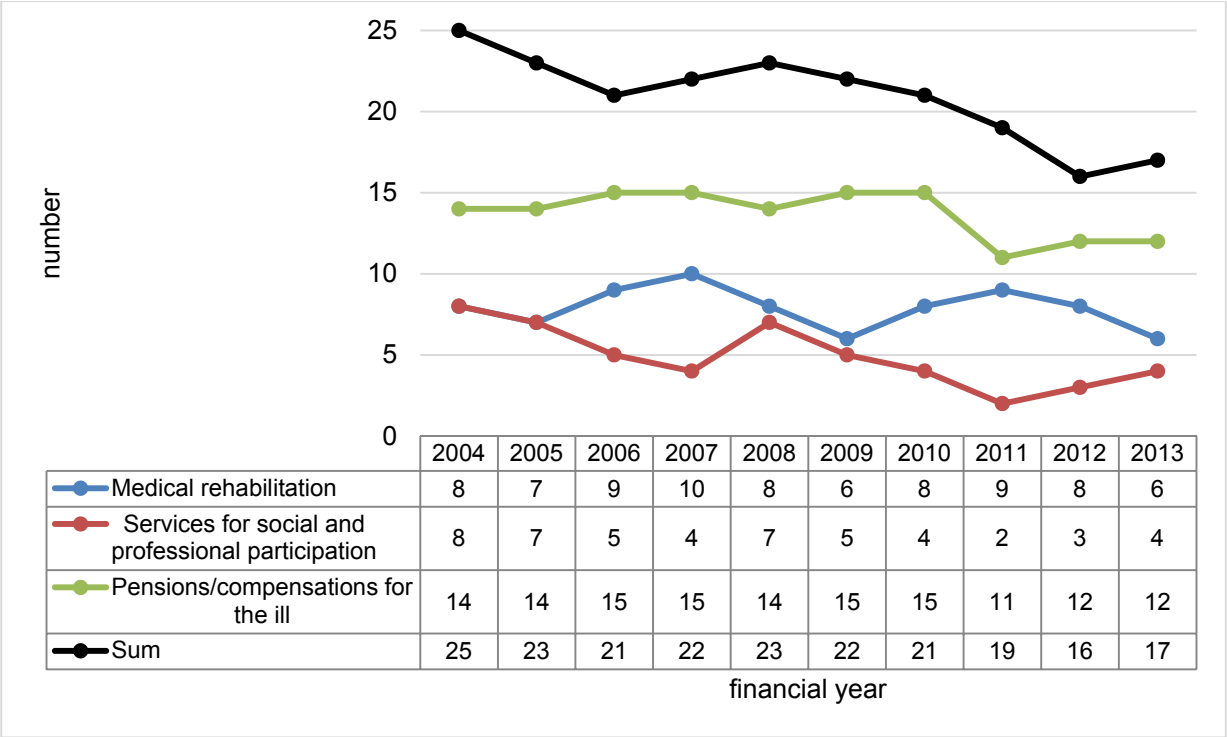


	J45.0	J45.1	J44.8	J68.4
Medical rehabilitation	1960	2727	2814	4343
Services for social and professional participation	8824	9433	8155	9257
Pensions/compensations for the ill	6654	7337	8235	7757
Survivors' benefits	13979	0	10776	19737

Figure 3.7 Average annual costs of occupational lung diseases per case stratified by ICD-subgroup (OD 1315, n=5,043)

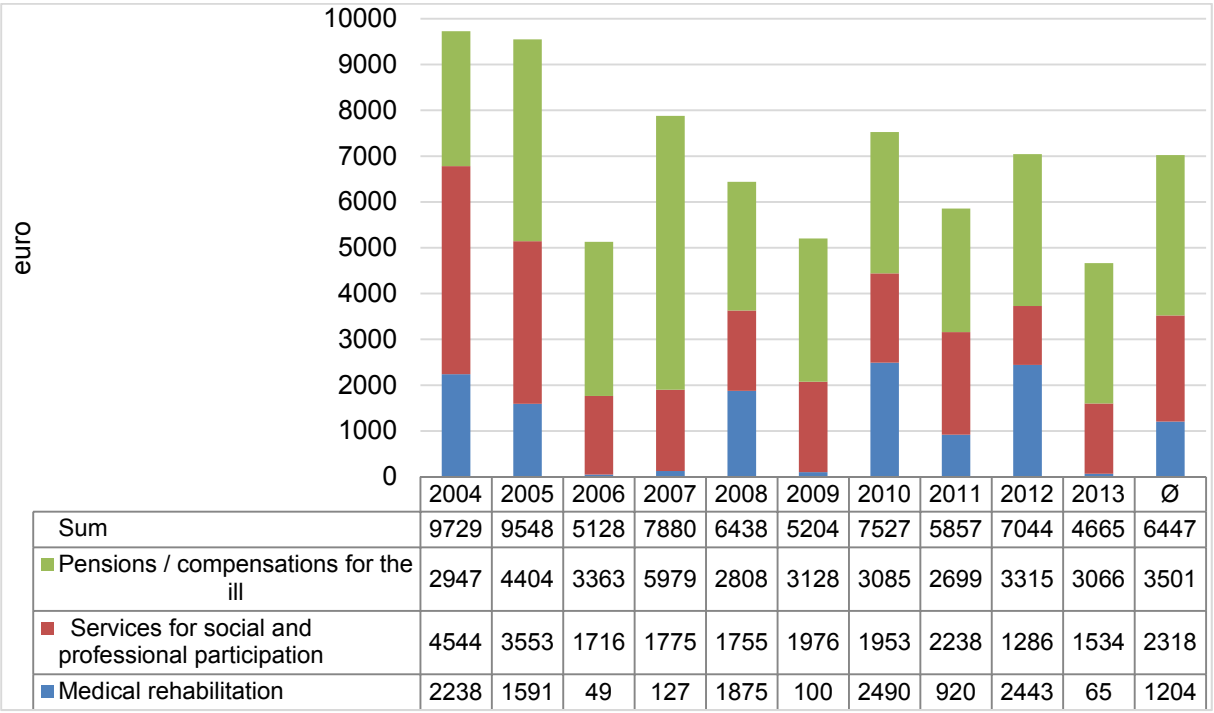
3.3.1.2 Development and costs of occupational skin diseases due to isocyanates

As illustrated in Figure 3.8, over time the total number of patients with newly confirmed occupational skin disease (nr. 5101) by definition making use of at least one healthcare service or receiving at least one benefit, decreased over the years from 25 insured persons in 2004 to 17 insured persons in 2013. Accordingly, the number of patients using healthcare services also decreased over the years, with most of occupational skin disease patients receiving pensions/compensations for the ill. Please note that one insured person may have used several services and that no survivors' benefits have been provided. However, for reasons of data protection, a further evaluation stratified by ICD-codes L23.- and L24.- as well as age and gender was impossible.
In most years, the main cost driver of average annual costs per insured person were pensions and compensations for the ill, followed by services for social and professional participation (Figure 3.9). In comparison, average annual costs of medical rehabilitation varied strongly over the years.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Medical rehabilitation	8	7	9	10	8	6	8	9	8	6
Services for social and professional participation	8	7	5	4	7	5	4	2	3	4
Pensions/compensations for the ill	14	14	15	15	14	15	15	11	12	12
Sum	25	23	21	22	23	22	21	19	16	17

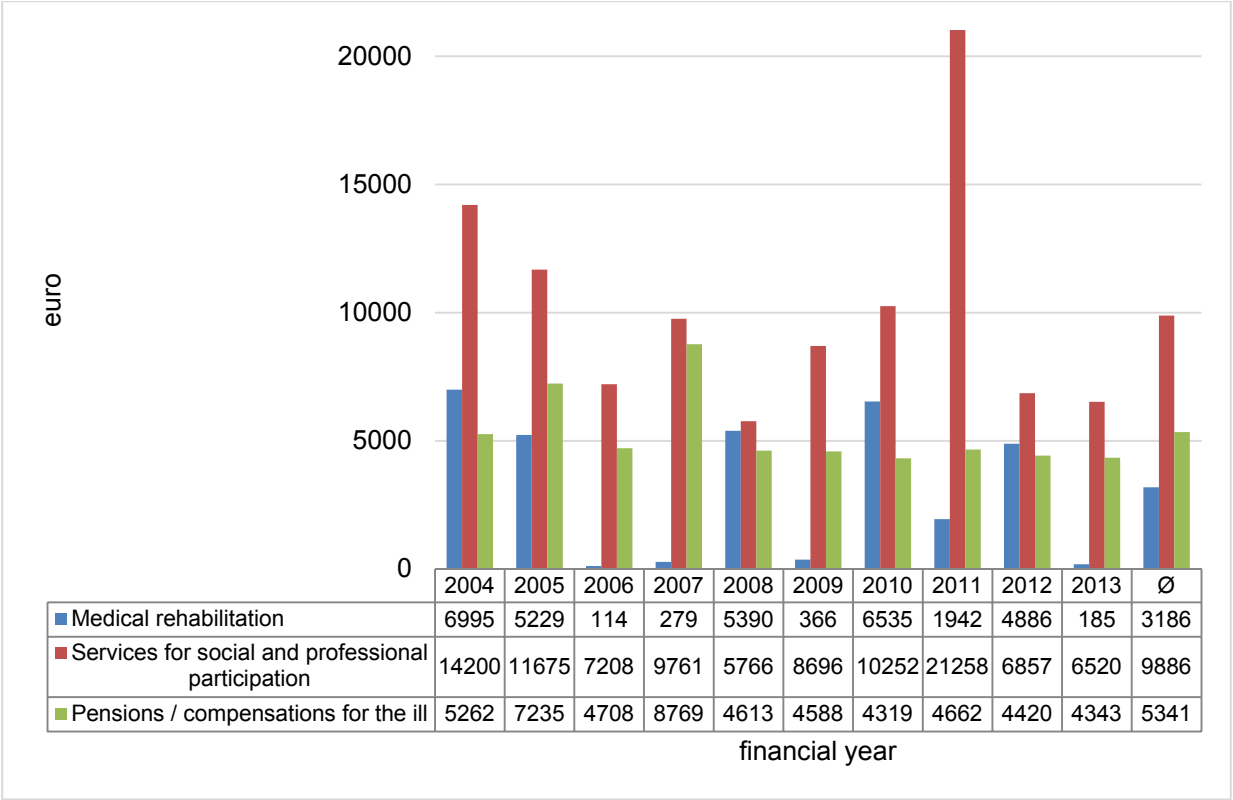
Figure 3.8 Number of insured persons suffering from occupational skin diseases making use of at least one healthcare service/receiving benefits (OD 5101, n=209)



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	9729	9548	5128	7880	6438	5204	7527	5857	7044	4665	6447
Pensions / compensations for the ill	2947	4404	3363	5979	2808	3128	3085	2699	3315	3066	3501
Services for social and professional participation	4544	3553	1716	1775	1755	1976	1953	2238	1286	1534	2318
Medical rehabilitation	2238	1591	49	127	1875	100	2490	920	2443	65	1204

Figure 3.9 Average annual costs of occupational skin diseases per insured person with target disease (OD 5101, n=209)

Figure 3.10 gives an overview on average annual costs per case that is the total costs of a resource domain divided by the number of patients that actually used these medical services and/or received benefits. The highest average annual costs per case were by far attributable to services for social and professional participation.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	6995	5229	114	279	5390	366	6535	1942	4886	185	3186
Services for social and professional participation	14200	11675	7208	9761	5766	8696	10252	21258	6857	6520	9886
Pensions / compensations for the ill	5262	7235	4708	8769	4613	4588	4319	4662	4420	4343	5341

Figure 3.10 Average annual costs of occupational skin diseases per case (OD 5101, n=209)

3.3.2 Costs of illness of lung and skin diseases from DIMDI

The results for the DIMDI analysis are not available in to the date of final report. Therefore the results could not be demonstrated in this chapter.

4 Transferability of the results from the routine analysis and the systematic literature search to the EU-28

4.1 Theoretical approaches for transferability in the literature

This work package aims to transfer the results from the working packages one and two to the EU-28-countries. Therefore, all relevant external factors which could have an influence on the transferability of the results have to be identified. Furthermore the influence of the factors should be quantified to ensure transferability.
The transfer of results from the cost of illness study to other countries has certain challenges. Health care systems often differ from each other with regards to the attributes of financing, insurance coverage, care structures, and degree of co-payments by the patients, as well as quality of care (Schöffski 2012). These different characteristics can cause limitations concerning transferability. Therefore, literature was searched for these factors that have an influence on transferability and existing approaches for the transfer.
Ten studies have been identified which address this topic (Greiner, Schöffski, Graf v. d. Schulenburg, J.-Matthias 2000; Koopmanschap, Touw, Rutten 2001; Sculpher et al. 2004; Goeree et al. 2007; Welte et al. 2004; Wordsworth, Ludbrook 2005; Tchouaket, Brousselle 2013; Ready, R et al. 2004; Drummond et al. 2005; Drummond et al. 2009). The publications by Koopmanschap et al. 2001, Drummond et al. 2005 and Wordsworth et al. 2005 focus more on the generalisability of economic evaluations conducted in different countries rather than on the transfer of the results to other countries and due to this fact these studies were disregarded from further analysis. In contrast to that, the other publications developed different approaches to transfer economic study results to other countries.
The latest publication by Goeree et al. integrates the results of the previous studies, this is relevant for our purpose and will be described on the following pages (Goeree et al. 2007). First, the authors performed a systematic literature review (a) examining factors that affect the transferability of economic study results to different countries. Second, they summarized approaches (b) used in the identified studies and developed a modelling approach based on the main factors.
a) Systematic literature review: During the systematic review several factors that have had an impact on the transferability were identified by Goeree et al (Goeree et al. 2007). They classified these factors in the following five categories: patient characteristics, disease characteristics, provider characteristics, health care system characteristics and methodological characteristics (Table 4.1). The following table comprises all the previous published factors and adds further factors identified by the systematic literature search. This table clearly shows that the transferability of results is complex and that it is almost impossible to have country specific data for all the relevant factors.
b) Different approaches: Based on the approaches identified in the studies, Goeree et al. developed a classification system that differentiated between non-modelling and modelling approaches.

Table 4.1 Factors cited in conceptual and empirical papers as potentially affecting transferability (Goeree et al. 2007)

Patient characteristics:	**Disease characteristics:**	**Provider characteristics:**	**Health care system characteristics:**	**Methodological characteristics:**
Demographics (age, gender, race), education, socio economic status	Epidemiology (incidence/prevalence, disease progression, spread)	Clinical practice, conventions, guidelines, norms	Absolute or relative prices	Costing methodology, estimation procedures (e.g. productivity cost)
Risk factors, medical history, genetic factors	Disease severity, case mix	Experience, education, training skills, learning curves position	Available resources (staff, facilities, equipment), programs, services	Study perspective
Lifestyle, environmental factors	Disease interaction, comorbidity, concurrent medications	Quality of care provided	Organization of delivery system, structure, level of competition	Study factors (artificial trial conditions, industry-related bias)
Mortality rates, life expectancy	Mortality due to disease	Method of remuneration (supplier-induces demand)	Level of technological advancement, innovation and availability	Timing of the economic evaluation
Attitudes towards treatment, culture, religion, hygiene, nutrition		Patient identification	Market form of suppliers, payment of suppliers, supplier incentives	Clinical endpoints/outcome measures
Compliance and adherence rates, ethical standards		Cultural attitudes	Capacity utilization, economies of scale, technical efficiency	Discount rates
Population values (utilities)		Incentives for provides, liability	Waiting list, referral patterns	Exchange rates, purchasing power parties
Population density, immigration, emigration, traveling patterns			Access to programs and services, gatekeepers, historical differences	
Income, employment rates, productivity, work loss time, friction time			Input mix (personnel, equip), specialization of labor, joint production	
Type of insurance coverage, user fees, co-payments, deductibles			Regulatory and organizational infrastructure, licensing of products	
Incentives for patients			Availability of generics or substitutes	
			Available treatment options (comparators)	

The *non-modelling approach* is a simple transfer of the study results to another country based on the exchange rates or Purchasing Power Parities (PPP). A major issue is the use of gross domestic product (GDP) PPP in comparison to the use of a more specific health or medical care PPP. The health or medical specific PPPs are calculated using the prices of a basket of health related goods and services. In comparison, the global GDP, PPPs are based on the prices of a basket of all goods in the economy and not only on medical specific goods (Gosden 2002). The studies have tested different methods (Health PPP, GDP PPP) for converting international cost utility analysis into UK prices. The results showed different cost utility ratios, so that both methods do not lead to the same result (Wordsworth, Ludbrook 2005; Gosden 2002). The GDP PPP has the disadvantage that it does not reflect the differences in medical cost. The medical PPP also has the disadvantage that it does not address the differences in medical care cost structures between countries.
Due to the methodological disadvantages of the calculation of the health PPP at that time, the OECD developed a new methodology for calculating the health PPP in 2012 (OECD 2012). This new approach moves “away from the input perspective towards an output perspective and should allow productivity differences between countries to be captured and paves the way for more meaningful comparisons of the volume of health services provided to consumers in the different countries” (Koechlin 2014). The input perspective is normally used for comparison of costs for non-market products like health products. In this approach especially wage rates are used to compare the costs for one treatment. This does not include differences in the qualifications, so the productivity between the countries is not possible to compare with an input approach. The output approach has the advantage that the costs per treatment are calculated. Therefore the OECD uses the reimbursement per treatments. The method of cost calculation for health PPP is presented in Table 4.2.

Besides the non-modelling approach, Goeree et al. summarized all approaches that integrate country-specific data into the category of *modelling approaches*.
Developing a framework that fits to all factors (Table 4.3) is not realistic, leading Goeree et al. to develop a framework based on the three most frequently named and therefore important factors mentioned in the studies which have the biggest influence on transferability. These include relative clinical efficacy, resource utilisation data and the data about unit costs. This framework compares five different approaches that integrated between one (1) to all (5) relevant country-specific parameters for relative clinical efficacy, resource utilization and unit cost data (Table 4.3). The results of the systematic literature review reveal that one third of the identified studies used the modelling approach 1 or 2. In most cases they integrate country specific unit costs. Only 5% of the identified studies use the modelling approach, where the targeted country’s specific data was adopted for the relative clinical efficacy, resource utilization and unit costs (5).

Table 4.2 Health expenditure by basic heading (OECD 2012)

BH Code	Basic heading	PPPs used
Individual consumption expenditure by households		
11.06.11.1	Pharmaceutical products	PPPs calculated with prices from six survey of the three-year cycle of price surveys for consumer goods and services: Furniture and health
11.06.12.1	Other medical products	
11.06.13.1	Therapeutic appliances and equipment	
11.06.21.1	Out-patient medical services	
11.06.22.1	Out-patient dental services	
11.06.23.1	Out-patient paramedical services	
11.06.31.1	Hospital services	PPPs for production of health services by government (without receipts from sales)
Individual consumption expenditure by NPISHS		
12.02.11.1	Health services	PPPs for production of health services by government (without receipts from sales)
Individual consumption expenditure by government		
Health benefits and reimbursements		
13.02.11.1.	Pharmaceutical products	PPPs calculated with prices from six survey of the three-year cycle of price surveys for consumer goods and services: Furniture and health
13.02.11.2	Other medical products	
13.02.11.3.	Therapeutic appliances and equipment	
13.02.12.1	Out-patient medical services	
13.02.12.2	Out-patient dental services	
13.02.12.3	Out-patient paramedical services	
13.02.12.4	Hospital services	PPPs for production of health services by government
Production of health services		
13.02.21.1	Compensation of employees: Physicians	PPPs calculates with prices from annual survey of compensation of government employees
13.02.21.2	Compensation of employees: Nurses and other medical staff	
13.02.21.3	Compensation of employees: Non-medical staff	
13.02.22.1	Intermediate consumption: Pharmaceutical products	PPPs for pharmaceutical products
13.02.22.2	Intermediate consumption: Other medical products	PPPs for other medical products
13.02.22.3	Intermediate consumption: therapeutic appliances and equipment	PPPs for therapeutic appliances and equipment
13.02.22.4	Intermediate consumption n.e.c	PPPs for individual market consumption (see BOX 12.3B for coverage)
13.02.23.1	Gross operating surplus	PPPs for gross fixed capital formation
13.02.24.1	Net taxes on production	PPPs for production of health services by government (without net taxes on production and receipts from sales)
13.02.25.1	Receipts from sales	PPPs for production of health services by government (without receipts from sales)

Explanation: NPISH = non-profit institutions serving households

Table 4.3 Modelling approaches based on the three most commonly advocated transferability factors (Goeree et al. 2007)

Modelling approach		Source of data by transferability factor		
		Relative clinical efficacy data	Resource utilization data	Unit cost data
Least to most country specific analysis	1	Studied country only	Studied country only	Mixture of studies and target country
	2	Studied country only	Studied country only	Target country only
	3	Studied country only	Mixture of studies and target country	Target country only
	4	Studied country only	Target country only	Target country only
	5	Target country only	Target country only	Target country only

4.2 Methods and approaches for cost transfer

In this study the results from the systematic literature search and the costs of illness derived from the DGUV and DIMDI will be transferred to the EU-28 States. Due to different health systems and challenges in the transfer, we will use a mixed method approach which consists of the following priority list (Figure 4.1). For reason of comparability, we will use the same approach for the transfer of DGUV and DIMDI data. As the results of the DIMDI cost of illness analysis are not yet available, the following methodological description focuses only on the results of the DGUV analysis.

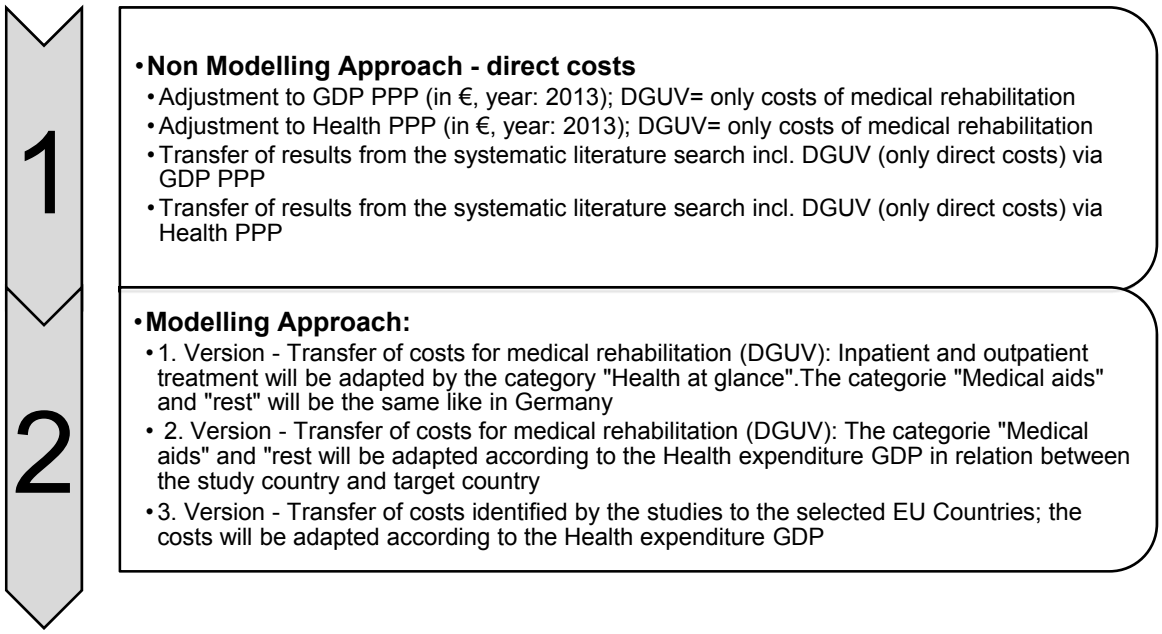


Figure 4.1 Overview of the modelling and non-modelling approach

4.2.1 Non-modelling approach

As shown in Figure 4.2, in the course of the non-modelling approach, direct costs obtained from the DGUV and DIMDI will be transferred to the other EU-28 countries using two approaches by adjusting them to a) GDP PPP and b) Medical PPP of each

country in relation to Germany. Direct costs cover average costs (in €) of medical rehabilitation in 2013 in Germany per insured person with recognised target disease, that is occupational lung diseases nr. 1315 (as a whole and subdivided by the ICD-codes J45.0, J45.1, J44.8 and J68.4) as well as the occupational skin disease nr. 5101. Due to the fact that the mean costs of occupational skin diseases according to data from the DGUV vary strongly over the years (due to the low number of insured persons with recognised occupational skin disease), we will use mean costs over the years 2004-2013 as basis for the transfer to other countries.
As already mentioned, data from the DIMDI database are not yet available, but with regard to lung diseases it will also cover costs for the ICD groups J45.-, J44.- and J68.-. Moreover, concerning skin diseases, costs will be separately shown for the ICD codes L20.- (atopic dermatitis), L23.- (allergic contact dermatitis), L24.- (irritant contact dermatitis) as well as L30.- (other dermatitis), thus providing a higher level of detail compared to DGUV data, but without work-relatedness of the target diseases.

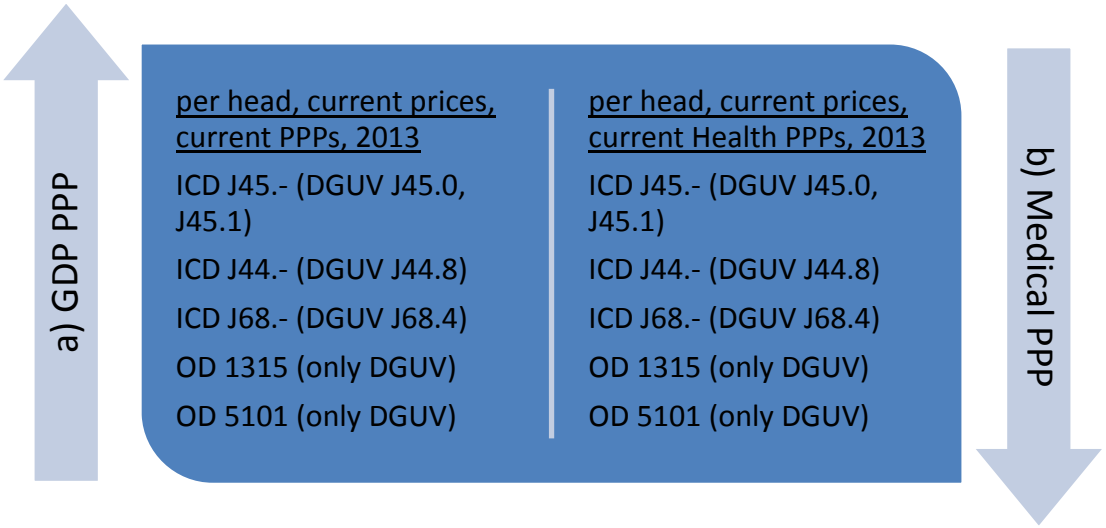


Figure 4.2 Non-modelling approach: Adjustment to GDP PPP and Medical PPP

a) Data including the **GDP PPP** of each EU-28 country have been obtained from the world bank (World Bank 2016a), where GDP PPP has been calculated per capita for the year 2013 using current prices and current PPPs. Please note that data on GDP PPP has been calculated in current international $ (but we are interested in euros), but as we only use the GDP PPP to calculate the adjustment factor, the currency is not of importance. We computed the adjustment factor as the quotient of GDP PPP of each country with GDP PPP of Germany.
b) Data covering the **Medical PPP** have been received by the OECD (OECD Statistics 2016), but please note that for some countries, data on health PPP was not available. Medical PPP covers current expenditure on healthcare and includes all healthcare providers. Again, it has been calculated per capita for the year 2013 using current prices and current PPPs. We used the same methodology for the computation of the adjustment factor as for GDP PPP.

Aside from the transfer of the DGUV data to other EU countries, we also integrated the results from the systematic literature search on cost of illness studies. In order to

allow better comparison of all cost of illness studies, we only used total direct costs of included cost of illness studies. We first inflated them to the year 2013 and second, we used them as base countries and transferred them to the other countries according to the methodology as described above (via GDP PPP and medical PPP). Each Table includes the mean across all 28 countries which has been weighted according to the population of each country.
Apart from direct costs, indirect costs due to loss of productivity will also be calculated and transferred to the EU-28 countries using two different approaches. In the **first approach**, we calculated the indirect costs for Germany based on the following formula:

Average compensation per day per employee (Germany)
(Eurostat 2015)
x
Average days of absence from work per disease case
(Federal Ministry of Health 2013)
=
Loss of productivity per patient per case

The first approach is more conservative then the second approach. In the **second approach**, we used the same calculation methods but instead of using the variable "average compensation per day per employee" we used the variable "gross value added as factor cost" (World Bank 2016b), because the use of the average compensation per day per employee might result in an underestimation of actual costs from the perspective of the company, and from an social welfare perspective. The results of both approaches for the German setting will be transferred via GDP PPP to the other EU-28 states. Results of all approaches will be compared and discussed. Please note that the average days of absence from work are only available on case level, i.e. we only know the average duration of inability to work per case of illness, but we don't know how often cases of illness occur per year per patient.

4.2.2 Modelling approach

According to Goree et al. all approaches that integrate country-specific data will be summarised into a modelling approach. Goree et al. described the three most frequently named and therefore important factors which have the biggest influence on transferability. These include relative clinical efficacy, resource utilisation data and data on unit costs. The factor of "relative clinical efficacy" is not relevant for our model, because we only focus on cost of illness and not on cost effectiveness ratios. Therefore, this factor will be excluded for further analysis. In contrast to that, the factor of "**resource utilisation**" is relevant for transferability, because countries differ with respect to the types and magnitude of resources, programs, or services that are available. A quantification of the services in the selected countries is challenging because of the various structures of the health care systems. For example, patients in the European countries have different access rules to health services. In Great Britain and Italy, they operate with the gatekeeper system which means that patients go first to a general practitioner before consulting a specialist. In contrast, in Germany or France, patients have free access to all health services. These differences can lead to different resource utilisations. Given the fact that there are various influencing factors on resource utilisation in different countries and the project time is restricted to

one year, we will make the assumption that resource utilisation, identified in the routine analyses for the German population, is equal in the other countries. Therefore, we will only include country data from Germany for the factor resource utilisation. The third important factor for transferability addresses **unit costs**. If possible, target country specific unit costs will be calculated for different categories.
In the course of the modelling approach we will use three different versions with different assumptions for the transfer of direct costs (seeTable 4.4)

Table 4.4 Description of different versions of cost transfer

	1st version	**2nd version**	**3rd version**
Aim	Transfer of costs for medical rehabilitation (DGUV)	Transfer of costs for medical rehabilitation (DGUV)	Transfer of costs identified by the studies to the selected EU Countries
Assumptions	• Inpatient and outpatient treatment will be adapted by the category "Health at glance" (OECD) • The categories "medical aids" will be the same like in Germany	• Inpatient and outpatient treatment will be adapted by the category "Health at glance" (OECD) • all other categories will be adapted according to the Health expenditure GDP in relation between the study country and target country	The costs will be adapted according to the Health expenditure GDP in relation to the study and target country
Selected diseases/ sudies	• ICD J45.0 • ICD J45.1 • ICD J44.8 • ICD J68.4	• ICD J45.0 • ICD J45.1 • ICD J44.8 • ICD J68.4 • OD 1315 • OD 5101	Lung diseases: • Medical rehabilitation OD1315 (DGUV) • Gomez et al. • Ayres et al. Skin diseases: • Medical rehabilitation OD5101 (DGUV) • Satterstrom et al. 2014 • Diepgen et al. 2013a • Diepgen et al. 2013b

The **first version** uses the cost categories “inpatient and outpatient treatment” of the cost calculation based on the DGUV data for Germany and adapts them to 17 different European countries. We have chosen these 17 countries because the OECD has calculated the current health expenditure by function (inpatient, outpatient, long-term care, medical good and collective services) of health care for these countries (OECD 2015). The category medical rehabilitation of the DGUV data can be differentiated for the lung diseases into inpatient treatment, outpatient treatment (rest), medical aids

and the rest. Costs for pharmaceuticals are part of the category outpatient treatment (rest). Therefore, we had to combine the percentage of the expenditure for medical goods and outpatient care from the OECD statistics (see Table 4.5). Please note that only the costs for the different lung diseases can be transferred to the other countries because costs for occupational skin diseases are not further differentiated by DGUV.

Table 4.5 Classification by function of health care used by the OECD Health Statistics and the DGUV

Medical rehabilitation DGUV	**Classification of health care functions (OECD)**
Inpatient Treatment: ⟶ Inpatient Treatment (460) Home care (465)	Inpatient care (HC1.1.+HC1.2)
Outpatient Treatment (rest) ⟶ Outpatient medical and dental treatment Drugs, medicine and medical aids	Medical goods and outpatient care

In the **second approach**, we use the same countries compared with the first approach. However, we transferred the costs of the categoriy “medical aids” from the DGUV according to the health expenditure GDP in relation between the study country and target country (OECD Health Statistics 2015).
In the **third version**, we will use the direct costs identified by the systematic literature review and inflate them to the year 2013. The study country represents the basis country. The costs will then be adapted according to the health expenditure GDP in relation between the study country and target country. Due to the fact that one study is based on UK, we need to integrate the UK to the countries mentioned in Version 2 and 3. For all different versions we calculated mean costs and provided the costs ranges for each approach. The mean costs are weighted according to the population in each country.
Each approach for calculation of direct costs has advantages and disadvantages. It is expected that the results of the first and second approach will not differ too much. The only different aspect is that the cost category “medical aids” will be adapted according to the GDP in the second approach. Nevertheless the Range of costs will be higher for the second approach. The mean results for the first approach will be near the costs for Germany. The third approach differs from approaches one and two. The results based on this approach are not good comparable to the other results, because the study used heterogonous disease severity, different study perspective and integrated different cost components. Therefore, it is expected that the range for the results will be higher than for the other two approaches. Another limitation is that the costs for the occupational skin diseases will be overestimated because we could not differentiated these data according to the categories of medical rehabilitation. Therefore the category “Rest” is included in the results and this category refers to the second largest cost category.
Apart from direct costs, we will also calculate indirect costs due to loss of productivity in the course of the modelling approach. In contrast to the non-modelling approach we will use country specific data for the average compensation per day per employee (Eurostat 2015) and for the variable “gross value added at factor cost” (World Bank 2016b). For both approaches we assume that the average days of absence from

work per disease case are the same in the EU-28 states than in Germany, but the average compensation per day per employer is different for each country.
As costs of illness might vary strongly between European countries due to different health care systems, the discussion of results should take significant characteristics of health care system into account. Therefore, we first build three clusters of the European countries (see Table 4.6, Table 4.7, Table 4.8).

- Group 1: Belgium, France, Italy, Greece, Spain, Czech Republic, Lithuania, Estonia, Latvia, Cyprus, Portugal, Slovenia
- Group 2: Bulgaria, Hungary, Croatia, Poland, Romania, Slovakia, Malta
- Group 3: Denmark, Germany, Austria, United Kingdom, Netherlands, Sweden, Ireland, Finland, Luxembourg

The composition of the three groups is based on two different cluster analyses (hierarchical and non-hierarchical) and resulted in similar results. Firstly, the cluster analysis was built on three structural economic indicators: GDP per capita, total employment rate and comparative price levels. The hierarchical cluster analysis and non-hierarchical cluster analysis were applied and both gave similar results (Kurnoga Zivadinovic, Dumicic, Ceh Casni 2009). For the three groups of EU-28 states, we created a table (see Table 4.6, Table 4.7, Table 4.8) which will be used to discuss the results of the cost transfer.

Table 4.6 Country characteristics of group 1

Country	Health care system		Public Hospital	Outpatient System	Calculation indirect costs		Calculation pharmaceutical costs	Occupational diseases	
	Access to	Social security system	Type of DRG	Payment system outpatient care	average salary	sick leave days	Price Information about Pharmaceuticals	Institution for occupational diseases	Services/compensation forms from the institute for occupational diseases
Belgium	Free access	Bismarck	Prospective global budget	25% co-payment	46.340 US$ (2013)	6.94 days (2008)	Co- payments: 25-80% Institut national d'assurance maladie-invalidité Link: http://www.inami.fgov.be/	Fonds des accidents du travail - FAT (Accidents at work Fund)	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions - case of death
France	Free access	Bismarck	DRG: GHM	Common Classification of Medical Procedures (CCAM): all medical procedures reimbursable and excluded. Grouping criteria: anatomic classification, medical specialties (17 chapters); Co-payments higher if patient is treated without being referred by a treating doctor; flat-rate charge for extensive procedures, a 1€ charge for visiting a doctor and for examinations and tests and a flat charge for medicines, paramedical procedures and travel for medical purposes.	43.550 US$ (2013)	8.3 days (2013)	http://medicprix.sante.gouv.fr/medicprix/welcome.do but: patients co-payment (35$-100%)	Local Health Insurance Fund (in the case of Metropolitan France) or the General Social Security Fund (in the case of the Overseas Departments).	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions
Italy	Gatekeeper	Bismarck	Prospective global budget	"National contract for Primary care, Decree on specialist outpatient services": Contract for primary care describes obligations of GP. Individual services are not further itemized. Decree on specialist outpatient services lists services in three sections: available, availability restricted to specific indications, excluded. Some services can only be provided in special settings (i.e. out-patient services in hospitals). 16 categories based on anatomical site, each subdivided into different chapters containing several items (single services)	35.430 US$ (2013)	1.54 days (2008)	L'Agenzia Italiana del farmaco (AIFA) Link: http://farmaco.agenziafarmaco.it/index.php	Inail: National Institute for Insurance against Accidents at Work;	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions

Greece	Free access	Bis-marck	DRG	Co-payments in public hospital: outpatient departments: €3 for a physician visit. Afternoon outpatient visits:. €25 for doctors in rural hospitals, €90 for medical professors in university-affiliated hospitals. These services are direct payments (non-reimbursable by insurance)	22.610 US$ (2013)	4.87 days (2000)	List: not found; 25 % out of pocket payments	The Fund for occupational diseases Ika-Etam;	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions
Spain	Gatekeeper	Bis-marck	Line-item remu-ne-ration	„Royal Decree 63/1995, Law 16/2003“; Services are listed explicitly in decree under “Primary Care”-category, with 9 subdivisions (ranging from prevention and health promotion to palliative care for the terminally ill) In some cases, services are restricted to specific patient groups; Health Care Centres receive an administrative budget based on historical patterns that take into account the number of patients that belong to the health area or primary care administration (no fixed prices)	29.940 US$ (2013)	9.4 days (2014)	Agencia Espana de Medicamentos y Productos Sanitarios (AEMPS) Link: http://www.vademecum.es/	Spanish National Institute of Social Security (INSS)	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions
Czech Republic	Free access	Bis-marck	DRG: IR-DRG	Care provided by ambulatory specialists and hospital outpatient services up to a predefined threshold is reimbursed on a fee-for service basis according to the List of Health Services provided. Beyond this threshold is also reimbursed on a fee-for-service basis, but using lower service prices	18.970 US$ (2013)	13.2 days (2013)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	Reimbursement from the insurance of the employer.	Compensation for: - temporary inability to work, - permanent unemployment - health care costs - survivors' pensions
Lithuania	Gatekeeper	Bis-marck/B everidge	DRG: AR-DRG oder Nord-DRG?	Without a referral from a primary health-care physician the patient must pay a fee for the consultation as set by the NHIF. Outpatient care is financed mainly through case payment, and through fee for service for diagnostic tests.	15.100 US$ (2013)	7.19 days (2008)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/ (WHO)	The Fund for occupational diseases (FBZ-FMP) Valstybinio Socialinio Draudimo Fondo Valdyba - SoDra (State Social Insurance Fund Board)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions

Estonia	Gatekeeper	Bis-marck	DRG: Nord-DRG	Health services provided by general practitioners are free. Patients can be charged for a maximum amount of 5 euros for GPs' home visits and for ambulatory service.	17.970 US$ (2013)	15.3 days (2008)	Not found	No specific insurance against employment injuries and occupational diseases. These risks are covered by the health insurance (short-term benefits) and pension insurance (long-term benefits).	In cases of occupational diseases, sickness benefit is covered by the Estonian Health Insurance Fund. In work-related sickness, the compensation amounts to 100% of the employee's average wages and is paid from the first sickness day.
Latvia	Gatekeeper	Beve-ridge	Intro-duc-tion of a NordDRGs	If a patient is treated without being referred by a treating doctor the patient has to pay the service by themselves	15.280 US$ (2013)	No data	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/ (WHO)	Valsts Sociâlâs Ap-drosinâsanas Agentûra - VSAA (State Social Insurance Agency)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions
Cyprus	Gatekeeper	Beve-ridge	DRG	User charges are depending on the beneficiary group (A,B or C), Outpatient coverage, where available, is reimbursed in cash at typically 90% of the cost borne by the insured	27.520 US$ (2013)	No data	Not found	The Department of Social Insurance Services of the Ministry of Labour and Social Insurance	The insurance covers "employment accidents" and "occupational diseases" and provides injury benefits (temporary incapacities), disablement benefits and death benefits.
Portugal	Gatekeeper	Beve-ridge	Pro-spec-tive global budget	The health subsystems and private insurance schemes reimburse on a fee-for-service basis for ambulatory services provided to their beneficiaries. In some cases, patients are expected to pay and then be reimbursed retroactively for the cost of services	21.310 US$ (2013)	6.8 days (2007)	National Authority of Medicines and Health products) INFARMED Link: http://www.infarmed.pt/infomed/inicio.php	Centro Nacional de Protecção contra os Riscos Profissionais - CNPRD (National Centre of Protection against occupational risks)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions

Slovenia	Gatekeeper	Bis-marck	DRG	Primary health care services provided by chosen personal physicians (GPs and pri-mary-level paediatricians and gynaecol-ogists) in health centres are paid through a combined system of capitation and fee-for-service payments, implemented in 2001	23.220 US$ (2013)	11.6 days (2013)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	Health Insurance Institute of Slovenia (Zavod za zdravstveno zava-rovanje Slovenije) and the Institute of Pension and Invalidi-ty Insurance of Slo-venia (Zavod za pokojninsko in inva-lidsko zavarovanje Slovenije)	Compulsory health insur-ance: -health services, medicines and medical devices -salary compensation during temporary work absence, funeral, death + reimburse-ment of travel expenses The Institute of Pension and Invalidity Insurance of Slo-venia: -provider of compulsory pension and invalidity insur-ance.

Abbreviations: AP-DRG= All Patient Diagnosis Related Group; APR-DRG= All Patient Refined Diagnosis Related Group; CMS-DRG= Medicare Severity-Diagnosis Related Groups; DRG= Diagnosis Related Groups; GHM= Groupes Homogènes de Malade; GP= general practitioner; IR-DRG= International Refined Diagnosis Related Groups; NHIF= National Health Insurance Fund; Nord-DRG= Nordic Diagnosis Related Groups; WHO= World Health Organisation

Table 4.7 Country characteristics of group 2

Country	health care system: Access to	health care system: Social security system	Public Hospital: Type of DRG	Outpatient System: Payment system outpatient care	Calculation indirect costs: average salary	Calculation indirect costs: sick leave days	Calculation pharmaceutical costs: Price Information about Pharmaceuticals	Occupational diseases: Institution for occupational diseases	Occupational diseases: Services/compensation forms from the institute for occupational diseases
Bulgaria	Gatekeeper	Bismarck	Introduction of a DRG-based payment system based on Nord DRGs	Choose between a reimbursement (they first pay the provider out of pocket after which the health insurance company reimburses the insured person fully or partially for health costs) and a benefits in-kind model (VHIC pays contracted healthcare providers directly for providing predetermined health services and goods).	7.280 US$ (2013)	7.4 days (2007)	No information	National Revenue Agency (Национална агенция за приходите)[	-Disability due to sickness, in case the insured hasn't got the needed period of insurable service to be granted disability pension for sickness; -death of an insured person
Hungary	Gatekeeper	Bismarck	Self-developed, based on HCFA-DRGs	"Governmental decrees and reimbursement catalogues": Similar services are listed in groups. Governmental decrees relate to different areas of care (e. g. dental care, specialist services): Items in reimbursement catalogues are listed with the respective ICPM code and a point value. Most outpatient specialist services are financed by fee-for-service points, based on the German point system; Since 2007 excess points above the providers' own output limit are not reimbursed at all	13.260 US$ (2013)	6.8 days (2013)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	No specific institution	Compensation for: - temporary inability to work - permanent unemployment -health care costs
Croatia	Gatekeeper	Bismarck	AR-DRG	No information	13.470 US$ (2013)	No data	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	The Croatian Institute for Health Insurance (Hrvatski zavod za zdravstveno osiguranje)	No information

Poland	Free access	Bis-marck	DRG-like PCS: JGP (like British HRGs)	"Governmental decrees and Catalogue of Benefits"; Overall benefit catalogue of all services covered by NHF Services listed include consultation, diagnostic tests and also separate group of imaging techniques	13.440 US$ (2013)	7 days	The Common European Drug Database (CEDD) Quelle: http://cedd.oep.hu/	Social Insurance Institution (Zakład Ubezpieczeń Społecznych, ZUS)	Unique compensation for: sickness benefits, reduction in earning capacity, in case of death of the family procider
Romania	Gatekeeper	Bis-marck	AR-DRG	payment for services provided by the outpatient departments of the hospitals, consisting of fee for service (paid from the budget dedicated to ambulatory care)	9.050 US$ (2013)	5.98 days (2009)	No information	Casa Nationala de Pensii si Alte Drepturi de Asigurari Sociale (National House of Pensions and Other Social Insurance Rights)	-Medical rehabilitation of workers and recovery of their working capacity -Workers' rehabilitation and reintegration -Indemnities for temporary loss of working capacity, decease, etc
Slovakia	Gatekeeper	Bis-marck	Procedure service payment	outpatient specialists are paid using capped fee-for-service payments; Specialists in outpatient care are paid on a fee-for-service basis. Each medical procedure has an assigned number of points, and health insurance companies negotiate the fee for one point	17.810 US$ (2013)	11.9 days per case (2014)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	Workplace accident insurance (different)	-additional accidental benefit, accidental rent, lump-sum settlement, survivor's rent, lump–sum compensation, professional rehabilitation and rehabilitation benefit, retraining and retraining benefit, pain compensation and compensation for difficulties with social reintegration, compensation for medical expenses, funeral expenses reimbursement.
Malta	Gatekeeper	Beve-ridge	No infor-mation	Aside from GP services, all public primary and ambulatory services require physician referral; all services are free of charge.	21.000 US$ (2013)	2.10 (2008)	No information	Maltese Social Security Division: entitled Injury Benefit/Industrial Disease; All organization requires Industrial accident insurance, which is in the hands of private insurers.	No information

Abbreviations: AR-DRG= All Patient Diagnosis Related Group; DRG= Diagnosis Related Groups; GP= general practitioner; HCFA-DRG= Health Care Financing Administration Diagnosis Related Groups; HRG= Healthcare Resource Group; ICPM= International Classification of Procedures in Medicine; JGP= Homogeneous groups of patients (Polish patient classificationsystem); NHF= National Health Fund; PCS= Patient Classification System; VHIC= Voluntary health insurance companies

Table 4.8 Country characteristics of Group 3 (without Germany)

Country	health care system		Public Hospital	Outpatient System	Calculation indirect costs		Calculation pharmaceutical costs	Occupational diseases	
	Access to	Social security system	Type of DRG	Payment system outpatient care	average salary	sick leave days	Price Information about Pharmaceuticals	Institution for occupational diseases	Services/compensation forms from the institute for occupational diseases
Denmark	Gatekeeper	Beveridge	Prospective global budget	Services are grouped according to medical specialty and for GPs additionally in basic, supplementary, laboratory and miscellaneous services. Each service has an item number. It is referred to the respective legislation decree specifying the benefit, certain goods, and procedures or in rare cases indications.	61.740 US$ (2013)	7.7 days (2014)	Medicin priser Link: http://www.medicinpriser.dk/	Arbejdsskadestyrelsen (National Board of Industrial Injuries)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions
Austria	Free access	Bismarck	DRG-like PCS: LKF	Performance-oriented hospital financing system	50.390 US$ (2013)	10.2 days (2013)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/ (WHO)	Allgemeine Unfallversicherungsanstalt - AUVA (Austrian Workers' Compensation Board)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions
UK	Gatekeeper	Beveridge	DRG-like PCS: HRG	"National Service Framework General Medical Services Contract Clinical Guidelines"; General medical services contract, Taxonomy based on specific conditions, Some individual items listed (e.g. vaccinations)	41.590 US$ (2013)	7.4 days (2009)	Drug Tariff for Scotland Link: http://www.isdscotland.org/isd/2245.html	Employers are required to insure against liability for injury or disease	invalidity allowance according to the severity of the invalidity
Netherlands	Gatekeeper	Beveridge	DRG-like PCS: DBC	"Health Insurance (Treatment and Services) Decree" (Diagnose Behandeling Combinaties [DBC] (DRG-like system)): GP services are regulated in generic terms only by decree. DBC-catalogue also relevant for hospital out-patient services Grouping criteria: medical specialty, product group	51.060 US$ (2013)	10 days (2013)	College voor Zorgverzekeringen (CVZ) Link: http://www.medicijnkosten.nl/	Public organisation Uitvoeringsinstituut Werknemersverzekeringen (UWV)	An employer must pay at least 70% (and no less than the minimum wage) of the wage for two years, weeks. Aid of the UWV after the two years

Sweden	Gatekeeper	Beveridge	Prospective global budget	From a patient's perspective, the reform introduced fixed co-payments for outpatient services (SEK 7/€0.8)	61.750 US$ (2013)	9.4 days (2013)	The Dental and Pharmaceutical Benefits Agency (TLV) Quelle: http://www.tlv.se/in-english/	Försakringskassan (Swedish Social Insurance Agency)	Compensation for: - temporary inability to work, - permanent unemployment -health care costs -survivors' pensions
Ireland	Gatekeeper	Beveridge	Prospective global budget	Those providing public sector services enter into a contractual agreement with the National Primary Care Reimbursement Board. Fees are based primarily on weighted capitation, plus additional payments for special services	43.080 US$ (2013)	No data	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	Department of Social Protection	-Injury Benefit, death benefit -Disablement Benefit -Incapacity Supplement -Constant Attendance Allowance -Medical Care Scheme
Finland	Gatekeeper	Beveridge	DRG: Nord-DRG	Health centers can impose fees for physician appointments. They differentiate between single and annual payments. The former is 11 € and can be charged for max 3x a year. The latter equates to 22 EUR once a year. At the weekends and bank holidays patients maybe have to pay a higher fee of 15 EUR. Additionally, there can be "penalty charges" of 27 EUR for visits without appointment	48.910 US$ (2013)	8.9 days (2014)	The Common European Drug Database (CEDD) Link: http://cedd.oep.hu/	Tapaturmavakuutuslaitosten Liitto - TVL (Federation of accident insurance institutions - FAII)	Compensation for: -temporary inability to work, -permanent unemployment -health care costs -survivors' pensions
Luxembourg	Free access	Bismarck	Prospective global budget	Fee for a home visit by a general practitioner are reimbursed by 80% (20% co-payment) in any 28-day period. Subsequently the co-payment decreases; visits are reimbursed at a rate of 95%. Pre- and post-natal care is reimbursed at a rate of 100%. When doctors are summoned by the emergency services the cost is 100% reimbursed. There are limitations on the number of GP visits, or visits to more than one doctor of the same specialism, within certain time periods	69.880 US$ (2013)	12 days (2013)	No information found	Association d'Assurance Accident - AAA (Accident insurance association)	Compensation for: -temporary inability to work, -permanent unemployment -health care costs -survivors' pensions

Abbreviations: AR-DRG= All Patient Diagnosis Related Group; DBC= Diagnose Behandeling Combinaties; DkDRG= Denmark DRG; DRG= Diagnosis Related Groups; HRG= Healthcare Resource Group; LKF= Leistungsorientierte Krankenanstalten-Finanzierung; Nord-DRG= Nordic Diagnosis Related Groups, PCS= Patient Classification System

4.3 Results for cost transfer to the EU-28

4.3.1 Non-Modelling approach

4.3.1.1 Direct costs

Table 4.9 shows the average direct costs of medical rehabilitation per insured person of the DGUV with the target disease after adjustment to a) GDP PPP that is transfer to the other EU-28 countries. Total direct costs are separately shown for both, recognised occupational lung and skin diseases in the last two columns. Moreover, costs of occupational lung diseases are further subdivided by the respective ICD codes.
From the perspective of the DGUV, direct costs are costs of medical rehabilitation covering outpatient treatment (medical and dental care as well as drugs, medicine and medical aids), inpatient treatment (including home care) as well as other services ("residual category"), including for example injury benefit, special assistance, granting of care, nursing allowance, other medical expenses and services for participation in the community. As the residual category also contains transfer payments, we wanted to exclude them from the transfer of direct costs by subtracting them from total costs of medical rehabilitation. Thus, results for the ICD subgroups J45.0, J45.1, J44.8 and J68.4 are based on costs of medical rehabilitation minus the residual category. However, in the OD groups 1315 and 5101, due to the high level of aggregation of DGUV data, there is no information available about the composition of medical rehabilitation, i.e. the costs displayed are based on medical rehabilitation including the residual category.
Moreover, please note that total direct costs of occupational lung diseases (second-last column) do not represent the average over the ICD subgroups J45.0, J45.1, J44.8 and J68.4, because approximately 20% of insured persons with recognised occupational lung disease could not be assigned to one of the ICD subgroups due to a structural break in diagnosis coding in 2002.
As shown in Table 4.9, direct costs of occupational lung diseases per insured person in 2013 varied considerably between the countries ranging from €605.48 in Bulgaria to €3526.94 in Luxembourg with a weighted mean of €1334.68 across countries (and Germany being much higher than the mean). Among the occupational lung diseases, average direct costs across the countries are highest in insured persons suffering from COPD (€922.46), followed by extrinsic allergic alveolitis (€822.82), non-allergic bronchial asthma (€808.36) and finally, allergic bronchial asthma (€784.25). Compared with lung diseases, occupational skin diseases caused lower average costs (mean: €967.46) over the years 2004-2013, ranging from €438.89 in Bulgaria to €2556.58 in Luxembourg. However, across all medical indications highest costs are displayed in group 3, followed by group 1 and 2.
As part of the sensitivity analyses, we additionally transferred the direct costs obtained from cost of illness analyses (identified by the systematic literature search) on occupational or work-related lung and skin diseases to the EU-28 countries using the same methodological approach (via GDP PPP). As shown in Table 4.10, where costs of base countries are marked in grey, average direct costs of occupational lung diseases across the EU-28 countries vary between €365.32 (obtained from Ayres et al. 2010) and €1920.76 (taken from Gomez et al. 2012), with costs obtained from the DGUV (€1334.68) being positioned between them.

Table 4.9 Average direct costs (medical rehabilitation) of recognised occupational lung and skin diseases per insured person (DGUV) after adjustment to GDP PPP (in €, year 2013)

		Occupational lung diseases[3]				**Lung diseases (OD 1315)[2]**	**Skin diseases (OD 5101)[1,2]**
		Allergic bronchial asthma (ICD J45.0)	Non-allergic bronchial asthma (ICD J45.1)	Chronic obstructive bronchitis (ICD J44.8)	Extrinsic allergic alveolitis (ICD J68.4)		
Group 1	Belgium	914.88	943.00	1076.11	959.88	1556.99	1128.61
	France	832.63	858.23	979.37	873.58	1417.01	1027.14
	Italy	775.65	799.49	912.34	813.80	1320.03	956.85
	Greece	562.12	579.39	661.18	589.76	956.63	693.43
	Spain	720.46	742.61	847.43	755.90	1226.12	888.77
	Czech Republic	641.29	661.00	754.30	672.83	1091.37	791.10
	Lithuania	569.67	587.18	670.07	597.69	969.49	702.75
	Estonia	580.40	598.24	682.68	608.94	987.75	715.98
	Latvia	488.33	503.34	574.39	512.35	831.07	602.41
	Cyprus	691.02	712.26	812.80	725.00	1176.01	852.44
	Portugal	612.46	631.28	720.39	642.58	1042.31	755.53
	Slovenia	635.02	654.54	746.93	666.25	1080.70	783.36
Group 2	Bulgaria	355.78	366.72	418.48	373.28	605.48	438.89
	Hungary	520.67	536.68	612.43	546.28	886.10	642.30
	Croatia	472.09	486.61	555.29	495.31	803.43	582.38
	Poland	529.43	545.71	622.73	555.47	901.01	653.11
	Romania	424.54	437.59	499.35	445.42	722.50	523.71
	Slovakia	588.81	606.91	692.58	617.77	1002.07	726.36
	Malta	645.14	664.97	758.83	676.87	1097.93	795.85
Group 3	Denmark	969.75	999.56	1140.65	1017.44	1650.36	1196.29
	Austria	999.40	1030.12	1175.53	1048.56	1700.83	1232.87
	UK	858.12	884.50	1009.35	900.33	1460.39	1058.59
	Netherlands	1035.19	1067.01	1217.63	1086.11	1761.74	1277.02
	Sweden	987.55	1017.91	1161.59	1036.12	1680.66	1218.25
	Ireland	1038.67	1070.60	1221.72	1089.75	1767.66	1281.31
	Finland	886.35	913.59	1042.55	929.94	1508.43	1093.41
	Luxembourg	2072.44	2136.14	2437.67	2174.37	3526.97	2556.58
	Germany	976	1006	1148	1024	1661.00	1204.00
Mean (weighted)[4]		784.25	808.36	922.46	822.82	1334.68	967.46
Median		668.08	688.61	785.81	700.94	1136.97	824.15
Min		355.78	366.72	418.48	373.28	605.48	438.89
Max		2072.44	2136.14	2437.67	2174.37	3526.97	2556.58
Standard deviation		179.83	185.36	211.52	188.67	306.04	221.84

Note: Base countries are marked in grey

[1] Mean costs over the years 2004-2013 were used as basis for calculation

[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category

[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category

[4] mean weighted according to population structure

Source: Own calculation on the basis of data from the DGUV for Germany

Table 4.10 Average annual direct cost per insured person of occupational/work-related lung and skin diseases after adjustment to GDP PPP (in €, year 2013)

		Occupational/work-related lung diseases			Occupational/work-related skin diseases			
		DGUV[2] (nr.1315)	Ayres et al. 2010	Gomez et al. 2012	DGUV[1,2] (nr.5101)	Satter-strom et al. 2014	Diepgen et al. 2013 (a)	Di-epgen et al. 2013 (b)
Group 1	Belgium	1556.99	426.17	2240.69	1128.61	388.91	3325.14	2658.91
	France	1417.01	387.86	2039.25	1027.14	353.94	3026.20	2419.86
	Italy	1320.03	361.31	1899.69	956.85	329.72	2819.10	2254.25
	Greece	956.63	261.84	1376.71	693.43	238.95	2043.01	1633.67
	Spain	1226.12	335.61	1764.53	888.77	306.26	2618.52	2093.87
	Czech Republic	1091.37	298.72	1570.61	791.10	272.60	2330.76	1863.76
	Lithuania	969.49	265.36	1395.22	702.75	242.16	2070.48	1655.63
	Estonia	987.75	270.36	1421.49	715.98	246.72	2109.45	1686.80
	Latvia	831.07	227.47	1196.01	602.41	207.59	1774.85	1419.23
	Cyprus	1176.01	321.89	1692.41	852.44	293.74	2511.50	2008.29
	Portugal	1042.31	285.29	1500.01	755.53	260.35	2225.98	1779.97
	Slovenia	1080.70	295.80	1555.26	783.36	269.94	2307.97	1845.54
Group 2	Bulgaria	605.48	165.73	871.36	438.89	151.24	1293.08	1034.00
	Hungary	886.10	242.54	1275.21	642.30	221.33	1892.38	1513.22
	Croatia	803.43	21991	1156.23	582.38	200.68	1715.83	1372.04
	Poland	901.01	246.62	1296.67	653.11	225.06	1924.22	1538.68
	Romania	722.50	197.76	1039.76	523.71	180.47	1542.98	1233.83
	Slovakia	1002.07	274.28	1442.10	726.36	250.30	2140.04	1711.25
	Malta	1097.93	300.52	1580.05	795.85	274.24	2344.76	1874.96
Group 3	Denmark	1650.36	451.73	2375.07	1196.29	412.23	3524.54	2818.36
	Austria	1700.83	465.54	2447.70	1232.87	388.91	3632.33	2904.55
	UK	1460.39	399.73	2101.68	1058.59	353.94	3118.85	2493.95
	Netherlands	1761.74	482.21	2535.36	1277.02	329.72	3762.41	3008.57
	Sweden	1680.66	460.02	2418.67	1218.25	238.95	3589.25	2870.10
	Ireland	1767.66	483.83	2543.87	1281.31	306.26	3775.05	3018.67
	Finland	1508.43	412.88	2170.81	1093.41	272.60	3221.44	2575.98
	Luxembourg	3526.97	965.38	5075.74	2556.58	242.16	7532.28	6023.10
	Germany	1661.00	454.64	2390.38	1204.00	246.72	3547.27	2836.53
Mean (weighted)[3]		1334.68	365.32	1920.76	967.46	294.49	2850.37	2279.26
Median		1136.97	311.20	1636.23	824.15	265.14	2428.13	1941.63
Min		605.48	165.73	871.36	438.89	151.24	1293.08	1034.00
Max		3526.97	965.38	5075.74	2556.58	412.23	7532.28	6023.10
Standard deviation		306.04	83.77	440.43	221.84	59.74	653.58	522.63

Note: Base countries are marked in grey

[1] Mean costs over the years 2004-2013 were used as basis for calculation

[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category

[3] mean weighted according to population structure

Source: Own calculation on the basis of data from the DGUV for Germany and results of the systematic literature search

In comparison, average direct costs of occupational skin diseases across all EU countries show a much higher variation between the different data sources ranging from €294.49 according to Satterstrom et al. (2014) to €2850.37 obtained from Diepgen et al. (2013a). As already mentioned in chapter 2.3.4, these differences might be due to the fact that the identified cost of illness studies focused on different study populations: While Satterstrom et al. (2014) included individuals with occupational contact dermatitis independent of the severity of symptoms (cases in which all symptoms have cleared have also been included), Diepgen et al. (2013a) focused on patients with occupational chronic refractory hand eczema and Diepgen et al. (2013b) recruited patients with occupational hand eczema which were at risk of loosing their ability to continue to work.
In the second step, we transferred all costs described above using b) medical PPP as adjustment factor. Results of the transfer of DGUV data are displayed in

Please note that for one quarter of the countries (Cyprus, Bulgaria, Croatia, Romania, Malta, Ireland, Luxembourg) data on medical PPP was not available so that these countries have been excluded from cost transfer. Again, average costs of occupational lung diseases vary considerably between the countries ranging from €419.31 in Latvia to €1768.54 in the Netherlands with a mean of €1196.57 across all countries. By comparison, the adjustment by GDP PPP (Table 4.10) showed average direct costs of €1334.68 across the EU-28 countries. Concerning occupational skin diseases, Table 4.11 shows average direct costs of €867.35 per years across all countries compared with €967.46 using GDP PPP.
Table 4.12 additionally shows the transfer of direct costs obtained from cost of illness analyses on occupational or work-related lung and skin diseases to the EU-28 countries using the same methodological approach, i.e. via Medical PPP.

Table 4.11 Average direct costs (medical rehabilitation) of recognised occupational lung and skin diseases per insured person (DGUV) after adjustment to Medical PPP (in €, year 2013)

		Occupational lung diseases[3]				**Lung diseases (OD 1315)[2]**	**Skin diseases (OD 5101)[1,2]**
		Allergic bronchial asthma (ICD J45.0)	Non-allergic bronchial asthma (ICD J45.1)	Chronic obstructive bronchitis (ICD J44.8)	Extrinsic allergic alveolitis (ICD J68.4)		
Group 1	Belgium	861.97	888.47	1013.88	904.36	1466.94	1063.33
	France	835.22	860.89	982.41	876.29	1421.41	1030.33
	Italy	623.12	642.28	732.93	653.77	1060.46	768.69
	Greece	479.28	494.01	563.74	502.85	815.66	591.24
	Spain	587.03	605.07	690.48	615.90	999.03	724.16
	Czech Republic	413.09	425.79	485.89	433.41	703.02	509.59
	Lithuania	318.51	328.30	374.64	334.17	542.05	392.91
	Estonia	312.33	321.93	367.37	327.69	531.54	385.29
	Latvia	246.38	253.96	289.81	258.50	419.31	303.94
	Portugal	509.26	524.91	599.00	534.30	866.67	628.22
	Slovenia	508.61	524.24	598.24	533.62	865.57	627.42
Group2	Hungary	348.26	358.97	409.63	365.39	592.68	429.62
	Poland	309.92	319.45	364.54	325.16	527.44	382.32
	Slovakia	407.14	419.65	478.89	427.16	692.88	502.25
Group 3	Denmark	922.23	950.57	1084.75	967.58	1569.49	1137.66
	Austria	922.17	950.51	1084.68	967.52	1569.38	1137.59
	UK	655.16	675.30	770.62	687.38	1114.99	808.21
	Netherlands	1039.19	1071.13	1222.33	1090.30	1768.54	1281.95
	Sweden	993.26	1023.79	1168.30	1042.10	1690.37	1225.29
	Finland	697.11	718.54	819.96	731.39	1186.37	859.96
	Germany	976	1006	1148	1024	1661.00	1204.00
Mean (weighted)[4]		703.10	724.71	827.01	737.68	1196.57	867.35
Median		587.03	605.07	690.48	615.90	999.03	724.16
Min		246.38	253.96	289.81	258.50	419.31	303.94
Max		1039.19	1071.13	1222.33	1090.30	1768.54	1281.95
Standard deviation		219.62	226.37	258.32	230.42	373.76	270.92

Note: Base countries are marked in grey
[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category
[4] Mean weighted according to population structure
Source: Own calculation on the basis of data from the DGUV for Germany

Table 4.12 Average annual direct cost per insured person of occupational/work-related lung and skin diseases after adjustment to Medical PPP (in €, year 2013)

		Occupational/work-related lung diseases			Occupational/work-related skin diseases			
		DGUV[2] (nr.1315)	Ayres et al. 2010	Gomez et al. 2012	DGUV[1,2] (nr.5101)	Satter-strom et al. 2014	Diepgen et al. 2013 (a)	Di-epgen et al. 2013 (b)
Group 1	Belgium	1466.94	525.91	2590.97	1063.33	385.30	3132.84	2505.13
	France	1421.41	509.59	2510.55	1030.33	373.34	3035.60	2427.38
	Italy	1060.46	380.18	1873.02	768.69	278.53	2264.73	1810.97
	Greece	815.66	292.42	1440.65	591.24	214.24	1741.95	1392.92
	Spain	999.03	358.16	1764.53	724.16	262.40	2133.56	1706.07
	Czech Republic	703.02	252.04	1241.70	509.59	184.65	1501.38	1200.56
	Lithuania	542.05	194.33	957.39	392.91	142.37	1157.62	925.67
	Estonia	531.54	190.56	938.82	385.29	139.61	1135.16	907.72
	Latvia	419.31	150.33	740.60	303.94	110.13	895.49	716.06
	Portugal	866.67	310.71	1530.75	628.22	227.63	1850.89	1480.04
	Slovenia	865.57	310.31	1528.80	627.42	227.34	1848.53	1478.16
Group2	Hungary	592.68	212.48	1046.82	429.62	155.67	1265.75	1012.14
	Poland	527.44	189.09	931.58	382.32	138.53	1126.40	900.72
	Slovakia	692.88	248.40	1223.80	502.25	181.99	1479.74	1183.26
Group 3	Denmark	1569.49	562.67	2772.08	1137.66	412.23	3351.83	2680.25
	Austria	1569.38	562.63	2771.90	1137.59	412.20	3351.61	2680.07
	UK	1114.99	399.73	1969.33	808.21	292.85	2381.19	1904.09
	Netherlands	1768.54	634.03	3123.66	1281.95	464.51	3776.94	3020.18
	Sweden	1690.37	606.01	2985.59	1225.29	443.98	3609.99	2886.68
	Finland	1186.37	425.32	2095.41	859.96	311.60	2533.64	2025.99
	Germany	1661.00	595.48	2933.72	1204.00	436.27	3547.27	2836.53
Mean (weighted)[3]		1106.60	396.73	1954.53	802.14	290.65	2363.29	1889.78
Median		999.03	358.16	1764.53	724.16	262.40	2133.56	1706.07
Min		419.31	150.33	740.60	303.94	110.13	895.49	716.06
Max		1768.54	634.03	3123.66	1281.95	464.51	3776.94	3020.18
Standard deviation		478.28	171.47	844.75	346.69	125.62	1021.42	816.76

Note: Base countries are marked in grey
[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
[3] Mean weighted according to population structure
Source: Own calculation on the basis of data from the DGUV for Germany and results of the systematic literature search

In order to summarise and compare both adjustment factors used in the non-modelling approach, Table 4.13 gives an overview on the average annual direct costs across all countries (weighted mean) obtained from the DGUV after adjustment to a) GDP PPP and b) Health PPP. Using GDP PPP as adjustment factor, average direct costs of the target diseases are approximately 10% higher compared to the adjustment via Health PPP.

Table 4.13 Overview of the average annual direct costs obtained from DGUV after adjustment to a) GDP PPP and b) Health PPP

		Occupational lung diseases[3]				**Lung diseases (OD 1315)[2]**	**Skin diseases (OD 5101)[1,2]**
		Allergic bronchial asthma (ICD J45.0)	Non-allergic bronchial asthma (ICD J45.1)	Chronic obstructive bronchitis (ICD J44.8)	Extrinsic allergic alveolitis (ICD J68.4)		
a) GDP PPP	**Mean**	**784.25**	**808.36**	**922.46**	**822.82**	**1334.68**	**967.46**
	Median	668.08	688.61	785.81	700.94	1136.97	824.15
	Min	355.78	366.72	418.48	373.28	605.48	438.89
	Max	2072.44	2136.14	2437.67	2174.37	3526.97	2556.58
	SD	179.83	185.36	211.52	188.67	306.04	221.84
b) Health PPP	**Mean**	**703.10**	**724.71**	**827.01**	**737.68**	**1196.57**	**867.35**
	Median	587.03	605.07	690.48	615.90	999.03	724.16
	Min	246.38	253.96	289.81	258.50	419.31	303.94
	Max	1039.19	1071.13	1222.33	1090.30	1768.54	1281.95
	SD	219.62	226.37	258.32	230.42	373.76	270.92

[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category
Source: Own calculation on the basis of data from the DGUV for Germany

Moreover, Table 4.14 additionally gives an overview of the average direct costs obtained from the systematic literature search. With regard to studies focusing on occupational/work-related lung diseases, average direct costs are a little lower after adjustment to a) GDP PPP compared to the adjustment to b) Health PPP, whereas the transfer of costs obtained from studies focusing on occupational/work-related skin diseases shows the opposite picture.

Table 4.14 Overview of the average annual direct costs obtained from the DGUV/systematic literature search after adjustment to a) GDP PPP and b) Health PPP

		Occupatinal/work-related lung diseases			Occupational/work-related skin diseases			
		DGUV[1] (nr.1315)	Ayres et al. 2010	Gomez et al. 2012	DGUV[1,2] (nr.5101)	Satter-strom et al. 2014	Diepgen et al. 2013 (a)	Diepgen et al. 2013 (b)
a) GDP PPP	**Mean**	**1334.68**	**365.32**	**1920.76**	**967.46**	**294.49**	**2850.37**	**2279.26**
	Median	1136.97	311.20	1636.23	824.15	265.14	2428.13	1941.63
	Min	605.48	165.73	871.36	438.89	151.24	1293.08	1034.00
	Max	3526.97	965.38	5075.74	2556.58	412.23	7532.28	6023.10
	SD	306.04	83.77	440.43	221.84	59.74	653.58	522.63
b) Health PPP	**Mean**	**1196.57**	**396.73**	**1954.53**	**867.35**	**290.65**	**2363.29**	**1889.78**
	Median	999.03	358.16	1764.53	724.16	262.40	2133.56	1706.07
	Min	419.31	150.33	740.60	303.94	110.13	895.49	716.06
	Max	1768.54	634.03	3123.66	1281.95	464.51	3776.94	3020.18
	SD	373.76	171.47	844.75	270.92	125.62	1021.42	816.76

[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
Source: Own calculation on the basis of data from the DGUV for Germany

All costs transferred to the EU-28 in this chapter were calculated per insured person, i.e. the sum of all costs has been divided by the number of insured person (irrespective of whether they have used that special service). In comparison, average costs per case which were calculated by dividing the sum of costs of a resource domain by number of insured persons that used that special service, are shown in appendix 11. Please note that due to the high level of aggregation of costs obtained from the DGUV, costs of medical rehabilitation on case level include the residual category (category “other” in appendix 5), and thus might be overestimated.

4.3.1.2 Indirect costs

Apart from direct costs, indirect costs in terms of loss of productivity due to lung and skin diseases are of great importance. Table 4.15 gives an overview on the loss of productivity due to selected lung and skin diseases. Please note that first, days of absence displayed in the table do not indicate anything about the cause of illness, i.e. if the disease has been caused by work. As data on the average number of days of absenteeism due to occupational skin and lung diseases were not available, we used this general number. Second, indirect costs are not shown per insured person or patient per year, but per case of illness. We only know the average duration of inability to work per case of illness, but we don’t know how often cases of illness occur per year per patient. Thus, our calculation represents a conservative approach assuming one case of illness per patient per year which might result in an underestimation of indirect costs.
As shown in Table 4.15, concerning lung diseases individuals suffering from ICD J44 cause average indirect costs of €1482.21 per disease case across all countries, followed by €984.08 for ICD J68 and €898.71 for ICD J45. In comparison, indirect costs of skin diseases are a little bit lower, resulting in €1121.67 per disease case across all countries.

Table 4.15 Average indirect costs of lung and skin diseases per case using the average compensation of employees and after adjustment to GDP PPP (in €, year: 2013)

Country		Compensation per day	Days of absence from work due to lung and skin diseases per case				Loss of productivity (in euro) per case			
			ICD J45	ICD J44	ICD J68	ØL20. 23. 24. 30	ICD J45	ICD J44	ICD J68	Ø L20. 23. 24. 30
Group 1	Belgium	129.76	9.58	15.80	10.49	10.08	883.87	1457.74	967.83	929.54
	France	109.75	9.58	15.80	10.49	10.08	804.41	1326.69	880.82	845.97
	Italy	95.82	9.58	15.80	10.49	10.08	749.36	1235.89	820.54	788.08
	Greece	73.65	9.58	15.80	10.49	10.08	543.06	895.65	594.65	571.12
	Spain	96.20	9.58	15.80	10.49	10.08	696.04	1147.96	762.16	732.01
	Czech Republic	60.41	9.58	15.80	10.49	10.08	619.55	1021.80	678.40	651.56
	Lithuania	54.27	9.58	15.80	10.49	10.08	550.36	907.70	602.64	578.80
	Estonia	59.52	9.58	15.80	10.49	10.08	560.72	924.78	613.99	589.70
	Latvia	47.39	9.58	15.80	10.49	10.08	471.78	778.09	516.59	496.16
	Cyprus	84.82	9.58	15.80	10.49	10.08	667.59	1101.04	731.01	702.09
	Portugal	72.61	9.58	15.80	10.49	10.08	591.70	975.87	647.90	622.27
	Slovenia	82.95	9.58	15.80	10.49	10.08	613.49	1011.81	671.77	645.19
Group 2	Bulgaria	38.15	9.58	15.80	10.49	10.08	343.72	566.89	376.37	361.48
	Hungary	55.48	9.58	15.80	10.49	10.08	503.02	829.62	550.80	529.01
	Croatia	71.25	9.58	15.80	10.49	10.08	456.09	752.22	499.42	479.66
	Poland	58.09	9.58	15.80	10.49	10.08	511.49	843.58	560.07	537.92
	Romania	42.18	9.58	15.80	10.49	10.08	410.15	676.44	449.11	431.34
	Slovakia	59.61	9.58	15.80	10.49	10.08	568.85	938.19	622.89	598.25
	Malta	75.37	9.58	15.80	10.49	10.08	623.27	1027.94	682.48	655.48
Group 3	Denmark	104.30	9.58	15.80	10.49	10.08	936.88	1545.16	1025.87	985.28
	Austria	103.20	9.58	15.80	10.49	10.08	965.53	1592.41	1057.24	1015.42
	UK	99.62	9.58	15.80	10.49	10.08	829.04	1367.30	907.78	871.87
	Netherlands	111.34	9.58	15.80	10.49	10.08	1000.10	1649.44	1095.10	1051.78
	Sweden	95.99	9.58	15.80	10.49	10.08	954.08	1573.53	1044.70	1003.37
	Ireland	109.19	9.58	15.80	10.49	10.08	1003.46	1654.98	1098.78	1055.31
	Finland	102.13	9.58	15.80	10.49	10.08	856.30	1412.28	937.64	900.55
	Luxembourg	141.83	9.58	15.80	10.49	10.08	2002.19	3302.15	2192.38	2105.64
	Germany	98.43	9.58	15.80	10.49	10.08	942.92	1555.12	1032.48	991.64

Mean EU-28[1]						898.71	1482.21	984.08	1121.67
Mean[2]						757.67	1249.60	829.64	945.64
Median						645.43	1064.49	706.74	805.56
Min						343.72	566.89	376.37	428.99
Max						2002.19	3302.15	2192.38	2498.91
Standard deviation[3]						173.73	286.53	190.23	216.83

Note: Base countries are marked in grey
[1] Weighted mean calculated on the basis of the EU-28 average compensation of employees per day (€93.81)
[2] Mean weighted according to the population structure
[3] SD calculated on the basis of the weighted mean according to the population structure
Source: Own calculation

In order to avoid underestimation of actual costs from the perspective of companies, in the second step indirect costs have been calculated using the average gross value added at factor costs. Results are displayed in Table 4.16.

Table 4.16 Average indirect costs of lung and skin diseases per case using the average gross value added at factor cost and after adjustment to GDP PPP (in €, year: 2013)

Country		**Gross value added at factor cost per day**	**Days of absence from work due to lung and skin diseases PER CASE**				**Loss of productivity (in euro) per case**			
			ICD J45	**ICD J44**	**ICD J68**	**ØL20. 23. 24. 30**	**ICD J45**	**ICD J44**	**ICD J68**	**Ø L20. 23. 24. 30**
Group 1	Belgium	212.45	9.58	15.80	10.49	10.08	1579.59	2605.18	1729.64	1661.21
	France	202.09	9.58	15.80	10.49	10.08	1437.58	2370.96	1574.14	1511.86
	Italy	178.58	9.58	15.80	10.49	10.08	1339.20	2208.70	1466.41	1408.40
	Greece	124.76	9.58	15.80	10.49	10.08	970.52	1600.65	1062.71	1020.67
	Spain	150.47	9.58	15.80	10.49	10.08	1243.92	2051.56	1362.08	1308.19
	Czech Republic	78.07	9.58	15.80	10.49	10.08	1107.22	1826.10	1212.39	1164.43
	Lithuania	67.07	9.58	15.80	10.49	10.08	983.57	1622.17	1077.00	1034.39
	Estonia	73.20	9.58	15.80	10.49	10.08	1002.09	1652.71	1097.27	1053.87
	Latvia	62.05	9.58	15.80	10.49	10.08	843.13	1390.55	923.22	886.70
	Cyprus	125.21	9.58	15.80	10.49	10.08	1193.08	1967.71	1306.41	1254.73
	Portugal	92.64	9.58	15.80	10.49	10.08	1057.44	1744.00	1157.89	1112.08
	Slovenia	93.64	9.58	15.80	10.49	10.08	1096.39	1808.25	1200.54	1153.04
Group 2	Bulgaria	33.67	9.58	15.80	10.49	10.08	614.27	1013.10	672.62	646.01
	Hungary	60.04	9.58	15.80	10.49	10.08	898.97	1482.64	984.36	945.42
	Croatia	65.93	9.58	15.80	10.49	10.08	815.10	1344.31	892.52	857.21

	Poland	61.95	9.58	15.80	10.49	10.08	914.09	1507.59	1000.92	961.33
	Roma-nia	40.79	9.58	15.80	10.49	10.08	732.99	1208.89	802.61	770.86
	Slova-kia	79.26	9.58	15.80	10.49	10.08	1016.62	1676.67	1113.18	1069.14
	Malta	n.a.	9.58	15.80	10.49	10.08	1113.87	1837.07	1219.68	1171.42
Group 3	Den-mark	222.22	9.58	15.80	10.49	10.08	1674.32	2761.40	1833.36	1760.83
	Austria	191.92	9.58	15.80	10.49	10.08	1725.52	2845.85	1889.43	1814.68
	UK	167.10	9.58	15.80	10.49	10.08	1481.59	2443.55	1622.33	1558.15
	Nether-lands	192.17	9.58	15.80	10.49	10.08	1787.32	2947.77	1957.09	1879.67
	Swe-den	224.44	9.58	15.80	10.49	10.08	1705.06	2812.10	1867.02	1793.16
	Ireland	240.24	9.58	15.80	10.49	10.08	1793.32	2957.67	1963.67	1885.98
	Finland	194.40	9.58	15.80	10.49	10.08	1530.33	2523.93	1675.69	1609.40
	Luxem-xem-bourg	479.00	9.58	15.80	10.49	10.08	3578.18	5901.38	3918.07	3763.06
	Ger-many	175.90	9.58	15.80	10.49	10.08	1685.12	2779.21	1845.18	1772.19
Mean[1] (weighted)							1354.05	2233.20	1482.68	1424.23
Median							1153.47	1902.39	1263.04	1439.64
Min							614.27	1013.10	672.62	646.01
Max							3578.18	5901.38	3918.07	3763.06
Standard deviation							310.48	512.07	340.03	326.58

Note: Base countries are marked in grey
[1] Mean weighted according to the population structure
Source: Own calculation

To give an overview of both approaches, Table 4.17 displays average indirect costs per case over all countries using the average compensation per employee (approach 1) or the gross value added as factor cost (approach 2). As expected, in comparison with the average compensation of employees, the second approaches in which costs per case have been calculated by multiplying the average days of absence from work with the gross value added as factor cost, indirect costs are considerably higher, approximately 70%.

Table 4.17 Overview of the average indirect costs per case using 1) the average compensation or 2) the gross value added as factor cost

		Loss of productivity (in euro) per case			
		ICD J45	**ICD J44**	**ICD J68**	**Ø L20, 23, 24, 30**
Approach 1: Average compensation	**Mean EU-28[1]**	**898.71**	**1482.21**	**984.08**	**1121.67**
	Mean[2]	**757.67**	**1249.60**	**829.64**	**945.64**
	Median	645.43	1064.49	706.74	805.56
	Min	343.72	566.89	376.37	428.99
	Max	2002.19	3302.15	2192.38	2498.91
	SD[3]	173.73	286.53	190.23	216.83
Approach 2: Gross value added as factor cost	**Mean[2]**	**1354.05**	**2233.20**	**1482.68**	**1689.98**
	Median	1153.47	1902.39	1263.04	1439.64
	Min	614.27	1013.10	672.62	646.01
	Max	3578.18	5901.38	3918.07	3763.06
	SD[3]	310.48	512.07	340.03	326.58

[1] Weighted mean calculated on the basis of the EU-28 average compensation of employees per day (€93.81)
[2] Mean weighted according to the population structure
[3] SD calculated on the basis of the weighted mean according to the population structure
Source: Own calculation

4.3.2 Modelling approach

4.3.2.1 Direct costs

We calculated direct costs for the different occupational lung and skin diseases using three different approaches. The results of the first approach can be seen in Table 4.18. In this approach no costs for skin diseases could be calculated because the costs for skin diseases (OD5101) are no further differentiated into categories of medical rehabilitation. Thus it was assumed that the category “medical aids” is the same as in Germany for all other integrated EU-28 states. The categories “inpatient treatment” and “outpatient treatment” differ between the countries. Only 18 of the 28 European countries were included the first and second version of the modelling approach, because only for these countries information on health expenditure by functions are available.
The mean (population-weighted) costs for the diseases are between €770.54 (J45.0) and up to €929.24 (J45.1). The highest costs for occupational lung diseases refers to Luxemburg (€1553.62 J45.0; €1589.95 J45.1; €1708.55J44.8; €1710.62 J68.4). Estonia has the lowest costs for the different occupational lung diseases. The highest costs are caused by patients with occupational non-allergic asthma (€923.26) followed by allergic alveolitis (€804.93), COPD (€929.24) and allergic asthma (€770.54).
In the second approach, we also transferred the cost categoriy “Medical aids” to the other countries. The results for this approach are shown in Table 4.19. The mean (weighted) costs of the diseases are lower than in the first approach and range between €751.88 (J45.0) and €885.95. Nevertheless, the spread of the results is larger than in version 1, but the difference is marginal.

Table 4.18 Version 1: Average direct costs (medical rehabilitation) of recognised occupational lung diseases per insured person (DGUV) (in €, year 2013)

		ICD J45.0 allergic asthma				ICD J45.1 non-allergic Asthma				ICD J44.8 COPD				ICD J68.4 allergic alveolitis			
		IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**
Group 1	**Belgium**	571	213	75	**859.11**	424	237	241	**902.24**	656	193	174	**1023.16**	530	275	94	**898,79**
	France	673	229	75	**977.16**	500	255	241	**995.70**	774	207	174	**1155.00**	625	295	94	**1014,04**
	Greece	458	105	75	**637.91**	340	117	241	**697.93**	526	95	174	**795.24**	425	135	94	**654,51**
	Spain	336	99	75	**510.26**	250	110	241	**600.86**	386	90	174	**650.08**	312	127	94	**533,75**
	Czech Rep.	297	78	75	**449.61**	220	86	241	**547.98**	341	70	174	**585.54**	276	100	94	**469,82**
	Estonia	205	48	75	**328.08**	152	54	241	**446.89**	235	44	174	**453.00**	190	62	94	**346,45**
	Portugal	308	77	75	**459.63**	229	86	241	**555.12**	353	70	174	**597.24**	286	99	94	**478,84**
	Slovenia	355	92	75	**522.05**	264	102	241	**607.07**	408	83	174	**665.30**	330	119	94	**542,23**
Group 2	**Hungary**	232	49	75	**355.77**	172	55	241	**467.73**	266	45	174	**484.64**	215	63	94	**372,43**
	Poland	255	55	75	**384.64**	189	61	241	**491.32**	293	50	174	**516.39**	236	71	94	**401,32**
	Slovak Rep.	225	54	75	**353.54**	167	60	241	**467.84**	258	49	174	**480.93**	209	70	94	**372,07**
Group 3	**Denmark**	592	235	75	**902.07**	440	261	241	**942.05**	681	213	174	**1067.35**	550	302	94	**946,35**
	Austria	740	302	75	**1117.49**	550	336	241	**1127.03**	851	274	174	**1298.48**	688	389	94	**1170,67**
	Nether-lands	773	326	75	**1173.98**	574	363	241	**1178.00**	887	296	174	**1357.47**	717	420	94	**1231,89**
	Sweden	537	217	75	**828.76**	399	241	241	**880.94**	617	196	174	**987.48**	499	279	94	**871,81**
	Finland	487	176	75	**738.35**	362	196	241	**798.88**	560	160	174	**893.39**	452	227	94	**773,37**
	Luxem-bourg	801	678	75	**1553.62**	595	754	241	**1589.95**	920	614	174	**1708.55**	744	873	94	**1710,62**
	Germany	645	257	75	**977.00**	479	286	241	**1006.00**	741	233	174	**1148.00**	599	331	94	**1024,00**
Mean[4]		515	181	75	**770.54**	591	201	131	**923.26**	591	164	174	**929.24**	478	233	94	**804.93**
Median		473	141	75	**688.13**	351	157	241	**748.41**	543	128	174	**844.32**	439	181	94	**713.94**
Min		205	49	75	**328.08**	152	54	131	**446.89**	235	44	174	**453.00**	190	62	94	**346.45**
Max		801	678	75	**1553.62**	595	754	241	**1589.95**	920	614	174	**1708.55**	744	873	94	**1710.62**
SD4		181	90	0	**269.81**	135	101	0	**233.42**	208	82	0	**288.42**	169	116	0	**282.63**

Abbreviation: IP= inpatient treatment. OP= Outpatient treatment. MA= Medical aids. COPD= Chronic Obstructive Pulmonary Disease;
[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category
[4] mean and SD weighted according to population structure; Source: Own calculation
[5] rounded

Table 4.19 Version 2: Average direct costs (medical rehabilitation) of recognised occupational lung diseases per insured person (DGUV) (in €. year 2013)

		ICD J45.0 allergic asthma 2013				ICD J45.1 non-allergic Asthma 2013				ICD J44.8 COPD 2013				ICD J68.4 allergic alveolitis 2013			
	Countries	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**	IP[5]	OP (rest)[5]	MA[5]	**Sum[3]**
Group 1	**Belgium**	571	213	66	**849.90**	424	237	211	**872.64**	656	193	153	**1001.79**	530	275	82	**887,24**
	France	673	229	64	**966.14**	500	255	206	**960.30**	774	207	148	**1129.44**	625	295	80	**1000,23**
	Greece	458	105	36	**599.36**	340	117	117	**574.08**	526	95	85	**705.82**	425	135	46	**606,20**
	Spain	336	99	45	**479.95**	250	110	144	**503.49**	386	90	104	**579.77**	312	127	56	**495,77**
	Czech Rep.	297	78	32	**406.71**	220	86	103	**410.12**	341	70	74	**486.01**	276	100	40	**416,05**
	Estonia	205	48	25	**277.63**	152	54	79	**284.78**	235	44	57	**335.96**	190	62	31	**283,22**
	Portugal	308	77	39	**423.92**	229	86	126	**440.38**	353	70	91	**514.40**	286	99	49	**434,08**
	Slovenia	355	92	39	**486.00**	264	102	125	**491.22**	408	83	90	**581.66**	330	119	49	**497,05**
Group 2	**Hungary**	232	49	27	**307.93**	172	55	87	**314.02**	266	45	63	**373.66**	215	63	34	**312,47**
	Poland	255	55	24	**333.52**	189	61	77	**327.08**	293	50	55	**397.81**	236	71	30	**337,26**
	Slovak Rep.	225	54	32	**310.09**	167	60	101	**328.22**	258	49	73	**380.12**	209	70	40	**317,61**
Group 3	**Denmark**	592	235	71	**898.17**	440	261	228	**929.52**	681	213	165	**1058.30**	550	302	89	**941,47**
	Austria	740	302	71	**1113.65**	550	336	229	**1114.69**	851	274	165	**1289.58**	688	389	89	**1165,86**
	Nether-lands	773	326	81	**1179.98**	574	363	260	**1197.31**	887	296	188	**1371.40**	717	420	102	**1239,42**
	Sweden	537	217	77	**830.34**	399	241	246	**886.03**	617	196	178	**991.16**	499	279	96	**873,79**
	Finland	487	176	54	**717.09**	362	196	173	**730.56**	560	160	125	**844.07**	452	227	67	**746,72**
	Luxem-bourg	801	678	96	**1575.05**	595	754	310	**1658.81**	920	614	224	**1758.26**	744	873	121	**1737,48**
	Germany	645	257	75	**977.00**	479	286	241	**1006.00**	741	233	174	**1148.00**	599	331	94	**1024,00**
Mean[4]		515	181	56	**751.88**	382	201	181	**764.54**	591	164	131	**885.95**	478	233	71	**781.54**
Median		472	141	49	**658.23**	351	157	158	**652.32**	543	128	114	**774.94**	439	181	62	**676.46**
Min		205	49	24	**277.63**	152	54	77	**284.78**	235	44	55	**335.96**	190	62	30	**283.22**
Max		801	678	96	**1575.05**	595	754	310	**1658.81**	920	614	224	**1758.26**	744	873	121	**1737.48**
SD[4]		181	90	19	**288.03**	135	101	62	**292.61**	208	82	44	**330.76**	169	116	24	**305.55**

Abbreviation: IP= inpatient treatment. OP= Outpatient treatment. MA= Medical aids

[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category

[4] mean and SD weighted according to population structure

[5] rounded

Source: Own calculation

In the second approach, we also transferred the costs of occupational skin diseases. The mean costs for skin diseases were €904.42in the year 2013 (see Table 4.20).
In the third approach, we additionally integrated costs of illness obtained from the studies by the systematic literature search and transferred them to the EU. The studies focused on four base countries (marked in grey, see Table 4.21). Mean (weighted) costs for occupational lung diseases based on studies ranged between €431.89 €2193.32. Mean costs calculated by the approaches 1 and 2 are in between. For the skin diseases the spread of the results is bigger compared to the lung diseases. These calculated costs ranged between €322.12 and €627.76 per year.

Table 4.20 Version 2: Average direct costs (medical rehabilitation) of recognised occupational lung and skin diseases per insured person (DGUV) (in €. year 2013) continuation

		OD1315 2013[2]	OD5101 2013[1,2]
		sum	sum
Group 1	Belgium	1457.00	1056,13
	France	1417.01	1027,14
	Greece	807.43	585,28
	Spain	989.89	717,54
	Czech Rep.	710.89	515,30
	Estonia	543.71	394,12
	Portugal	870.18	630,76
	Slovenia	862.58	625,25
Group 2	Hungary	601.57	436,06
	Poland	529.03	383,48
	Slovak Rep.	698.69	506,45
Group 3	Denmark	1574.65	1141,41
	Austria	1576.00	1142,39
	Netherlands	1794.07	1300,45
	Sweden	1696.08	1229,43
	Finland	1190.14	862,69
	Luxembourg	2135.60	1548,02
	Germany	1661.00	1204,00
Mean[4]		**1247,71**	**904.42**
Median		**1090,01**	**790.11**
Min		**529,03**	**383.48**
Max		**2135,60**	**1548.02**
SD[4]		**424,65**	**307.81**

[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category
[4] Mean weighted according to population structure
Source: Own calculation
Abbreviation: IP= inpatient treatment. OP= Outpatient treatment. MA= Medical aids

Table 4.21 Transfer of results of the identified studies

		DGUV[2]	Gomez et al. 2012	Ayres et al. 2010	DGUV[2,1]	Satter-strom et al. 2014	Diepgen et al. 2013a	Diepgen et al. 2013b
		Germany	Spain	UK	Germa-ny	Denmark	Germany	Germany
		OD 1315 2013	Occupati-onal Asthma	Isocynate induced Asthma	OD 5101 2013			
Group 1	Belgium	1457.00	2597.17	511.41	1056.13	381.43	3111.60	2488.15
	France	1417.01	2525.89	497.37	1027.14	370.96	3026.20	2419.86
	Greece	807.43	1439.29	283.41	585.28	211.38	1724.37	1378.87
	Spain	989.89	1764.53	347.45	717.54	259.14	2114.04	1690.46
	Czech Rep.	710.89	1267.20	249.52	515.30	186.11	1518.20	1214.01
	Estonia	543.71	969.20	190.84	394.12	142.34	1161.17	928.51
	Portugal	870.18	1551.14	305.44	630.76	227.81	1858.38	1486.03
	Slovenia	862.58	1537.59	302.77	625.25	225.82	1842.14	1473.05
Group 2	Hungary	601.57	1072.33	211.15	436.06	157.49	1284.73	1027.32
	Poland	529.03	943.03	185.69	383.48	138.50	1129.82	903.45
	Slovak Rep.	698.69	1245.45	245.24	506.45	182.91	1492.14	1193.17
Group 3	Denmark	1574.65	2806.90	552.71	1141.41	412.23	3362.87	2689.08
	Austria	1576.00	2809.29	553.18	1142.39	412.58	3365.74	2691.37
	Netherlands	1794.07	3198.01	629.72	1300.45	469.67	3831.45	3063.77
	Sweden	1696.08	3023.34	595.33	1229.43	444.02	3622.18	2896.43
	Finland	1190.14	2121.48	417.74	862.69	311.57	2541.68	2032.43
	Luxembourg	2135.60	3806.80	749.60	1548.02	559.08	4560.83	3647.01
	Germany	1661.00	2960.81	583.01	1204.00	434.83	3547.27	2836.53
	UK	1138.84	2030.03	399.73	825.50	298.14	2432.13	1944.82
Mean[4]		**1230.44**	**2193.32**	**431.89**	**891.90**	**322.12**	**2627.76**	**2101.26**
Median		**1457.00**	**2597.17**	**511.41**	**844.10**	**304.85**	**2486.91**	**1988.62**
Min		529.03	943.03	185.69	383.48	138.50	1129.82	903.45
Max		2135.60	3806.80	749.60	1548.02	559.08	4560.83	3647.01
SD[4]		391.55	697.96	137.44	283.82	102.51	836.21	668.67

Abbreviation: SD= standard deviation;
[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including residual category
[3] Basis for the calculation of direct costs: costs of medical rehabilitation minus the residual category
[4] Mean weighted according to population structure
Source: Own calculation

4.3.2.2 Indirect costs

Besides the direct costs we calculated indirect costs based on two different approaches. In the first approach, we used the average number of sick leave days per case and multiplied them with the average compensation per day (see Table 4.22). The mean costs were for J45 = €798.33, J44 = €1316.66, J68 = €874.16 and for the skin diseases = €839.58. The lowest indirect costs were calculated for Bulgaria (€365.52 J45) and the highest for Luxembourg. The highest indirect costs are caused by COPD (€1316.66) with an average of 15.80 days per case. Group number 2 has

the lowest average costs (J45 = €772.11€) followed by group number 1 (€772.11) and group number 3 (€1028.29).
The second approach used instead of average compensation the gross value added at factor cost per day per employee (see Table 4.23). Mean costs are 72% higher than the average costs in the first approach but the distribution in the countries is the same. Again, Luxembourg has the highest costs. The standard deviation of both approaches shows that the indirect costs on the basis of the gross value added at factor costs (SD J44= 1476) spread much more than the costs based on the average co-compensation (SD J44=421.90).

Table 4.22 Indirect costs based on average compensation per year

	Country	**Average compensation per day**	**Days of absence from work due to lung and skin diseases PER CASE**				**Loss of productivity (in euro) per case**			
			ICD J45	**ICD J44**	**ICD J68**	**ØL20. 23. 24. 30**	**ICD J45**	**ICD J44**	**ICD J68**	**Ø L20. 23. 24. 30**
Group 1	Belgium	129.76	9.58	15.80	10.49	10.08	1243.12	2050.24	1361.20	1307.35
	France	109.75	9.58	15.80	10.49	10.08	1051.40	1734.04	1151.27	1105.72
	Italy	95.82	9.58	15.80	10.49	10.08	917.98	1514.00	1005.18	965.41
	Greece	73.65	9.58	15.80	10.49	10.08	705.61	1163.73	772.63	742.06
	Spain	96.20	9.58	15.80	10.49	10.08	921.59	1519.96	1009.14	969.21
	Czech Republic	60.41	9.58	15.80	10.49	10.08	578.69	954.42	633.66	608.59
	Lithuania	54.27	9.58	15.80	10.49	10.08	519.94	857.53	569.33	546.81
	Estonia	59.52	9.58	15.80	10.49	10.08	570.24	940.48	624.41	599.70
	Latvia	47.39	9.58	15.80	10.49	10.08	453.97	748.72	497.09	477.43
	Cyprus	84.82	9.58	15.80	10.49	10.08	812.53	1340.08	889.71	854.51
	Portugal	72.61	9.58	15.80	10.49	10.08	695.58	1147.20	761.65	731.52
	Slovenia	82.95	9.58	15.80	10.49	10.08	794.70	1310.67	870.18	835.76
Group 2	Bulgaria	38.15	9.58	15.80	10.49	10.08	365.52	602.85	400.24	384.41
	Hungary	55.48	9.58	15.80	10.49	10.08	531.49	876.57	581.98	558.95
	Croatia	71.25	9.58	15.80	10.49	10.08	682.54	1125.69	747.37	717.80
	Poland	58.09	9.58	15.80	10.49	10.08	556.47	917.76	609.33	585.22
	Romania	42.18	9.58	15.80	10.49	10.08	404.08	666.44	442.46	424.96
	Slovakia	59.61	9.58	15.80	10.49	10.08	571.09	941.89	625.34	600.60
	Malta	75.37	9.58	15.80	10.49	10.08	722.01	1190.79	790.59	759.32
Group 3	Denmark	104.30	9.58	15.80	10.49	10.08	999.23	1648.00	1094.15	1050.86
	Austria	103.20	9.58	15.80	10.49	10.08	988.67	1630.58	1082.58	1039.75

	UK	99.62	9.58	15.80	10.49	10.08	954.40	1574.07	1045.06	1003.72
	Nether lands	111.34	9.58	15.80	10.49	10.08	1066.62	1759.15	1167.94	1121.73
	Swe-den	95.99	9.58	15.80	10.49	10.08	919.60	1516.67	1006.95	967.11
	Ireland	109.19	9.58	15.80	10.49	10.08	1046.02	1725.16	1145.38	1100.06
	Fin-land	102.13	9.58	15.80	10.49	10.08	978.39	1613.63	1071.33	1028.94
	Luxem xem-bourg	141.83	9.58	15.80	10.49	10.08	1358.76	2240.96	1487.83	1428.97
	Ger-many	98.43	9.58	15.80	10.49	10.08	942.92	1555.12	1032.48	991.64
Mean EU -28[1]		93.81	9.58	15.80	10.49	10.08	898.71	1482.21	984.08	945.15
Mean[2]							869.62	1434.24	952.23	914.56
SD[3]							199.73	329.41	218.70	210.05
Min							365.52	602.85	400.24	384.41
Max							1358.76	2240.96	1487.83	1428.97
Median							803.61	1325.37	879.95	845.14

Abbreviation: SD= standard deviation;
[1] Weighted mean calculated on the basis of the EU-28 average compensation of employees per day (€93.81)
[2] Mean weighted according to the population structure
[3] SD calculated on the basis of the weighted mean according to the population structure
Source: Own calculation

Table 4.23 Indirect costs based on gross value added at factor cost per year (2013)

	Country	**Gross value added at factor cost per day per em-ployee**	**Days of absence from work due to lung and skin dis-eases PER CASE**				**Loss of productivity (in euro) per case**			
			ICD J45[2]	**ICD J44[2]**	**ICD J68[2]**	**Ø L20. 23. 24. 30[2]**	**ICD J45**	**ICD J44**	**ICD J68**	**Ø L20. 23.24. 30**
Group 1	Belgium	212.45	10	16	11	10	2035.27	3356.72	2228.60	2140.44
	France	202.09	10	16	11	10	1935.99	3192.97	2119.89	2036.03
	Italy	178.58	10	16	11	10	1710.80	2821.57	1873.31	1799.20
	Greece	124.76	10	16	11	10	1195.21	1971.23	1308.75	1256.97
	Spain	150.47	10	16	11	10	1441.49	2377.41	1578.42	1515.97
	Czech Republic	78.07	10	16	11	10	747.92	1233.53	818.97	786.57
	Lithuania	67.07	10	16	11	10	642.53	1059.70	703.56	675.73
	Estonia	73.20	10	16	11	10	701.23	1156.51	767.84	737.46
	Latvia	62.05	10	16	11	10	594.48	980.45	650.95	625.19
	Cyprus	125.21	10	16	11	10	1199.54	1978.37	1313.49	1261.52
	Portugal	92.64	10	16	11	10	887.46	1463.66	971.76	933.31
	Slovenia	93.64	10	16	11	10	897.09	1479.54	982.30	943.44
Group 2	Bulgaria	33.67	10	16	11	10	322.58	532.02	353.22	339.25
	Hungary	60.04	10	16	11	10	575.19	948.65	629.83	604.91
	Croatia	65.93	10	16	11	10	631.65	1041.75	691.64	664.28

	Poland	61.95	10	16	11	10	593.44	978.75	649.82	624.11
	Romania	40.79	10	16	11	10	390.77	644.49	427.89	410.96
	Slovakia	79.26	10	16	11	10	759.31	1252.31	831.44	798.54
	Malta	n.a.	10	16	11	10	n.a.	n.a.	n.a.	n.a.
Group 3	Denmark	222.22	10	16	11	10	2128.88	3511.10	2331.10	2238.88
	Austria	191.92	10	16	11	10	1838.57	3032.30	2013.22	1933.57
	UK	167.10	10	16	11	10	1600.86	2640.24	1752.92	1683.57
	Nether-lands	192.17	10	16	11	10	1841.02	3036.34	2015.90	1936.15
	Sweden	224.44	10	16	11	10	2150.18	3546.22	2354.42	2261.28
	Ireland	240.24	10	16	11	10	2301.54	3795.87	2520.17	2420.47
	Finland	194.40	10	16	11	10	1862.32	3071.47	2039.22	1958.55
	Luxem-bourg	479.00	10	16	11	10	4588.87	7568.28	5024.76	4825.97
	Germany	175.90	10	16	11	10	1685.12	2779.21	1845.18	1772.19
Mean[1]							1469.52	2423.63	1609.11	1545.45
Median							1199,54	1978,37	1313,49	1261,52
Min							322.58	532.02	353.22	339.25
Max							4588.87	7568.28	5024.76	4825.97
SD[1])							519,98	857,58	569,37	546,84

Abbreviation: SD= standard deviation;
[1] Mean weighted and SD according to the population structure
[2] rounded
Source: Own calculation

4.3.3 Comparison of Non-modelling and modelling approach

The total costs for the occupational skin and lung diseases are shown in Table 4.24 and Table 4.25. We calculated each possible alternative which can be combined of the direct and indirect costs. For the modelling approach only direct costs of the second version were integrated because the first version only transfers the costs for the lung diseases and not for the skin diseases. Moreover, the third approach was also excluded because some studies did not integrate all cost categories or transparency of methods was lacking. Therefore, a comparison with the other approaches is not useful and may lead to misinterpretations.

Total costs for occupational lung diseases due to isocyanates ranged between €2142.21 and €3491.05. The lowest total costs for occupational lung diseases refer to the approach 2a using Health PPP and the indirect costs based on average compensation (mean weighted). The highest costs are calculated by approach 3a which used the GDP PPP for adjusting direct costs and the gross value added at factor cost. The highest mean direct costs were calculated by using GDP PPP (€1334.68), the highest mean indirect costs in the modelling approach by using the gross value added as factor cost (€1834.09). Therefore the most conservative approach with the lowest costs is the approach 2a (Health PPP, average compensation). The highest standard deviation for the lung diseases is calculated in the modelling approach3b (SD 648.97) which calculated the indirect costs using the gross value added at factor cost.

Table 4.24 Total costs for occupational lung diseases (in €, year 2013)

		OD 1315	Ø J45, J44, J68	
Non-modelling approach	**1a.**	**DC: GDP PPP**	**IC: average compensation**	**Total costs**
	Mean	1334.68	1121.67 (EU-28) 945.64 (mean weighted)	2456.35 (EU-28) 2280.32 (mean weighted)
	SD	306.04	216.83	
	1b.	**DC: GDP PPP**	**IC: gross value added**	**Total costs**
	Mean*	1334.68	1690.23	3024.91
	SD	306.04	387.57	
	2a.	**DC: Health PPP**	**IC: average compensation**	**Total costs**
	Mean*	1196.57	1121.67 (EU-28) 945.64 (mean weighted)	2318.24 (EU-28) 2142.21 (mean weighted)
	SD	373.76	216.83	
	2b.	**DC: Health PPP**	**IC: gross value added**	**Total costs**
	Mean*	1196.57	1690.23	2886.80
	SD	373.76	387.57	

		OD 1315	Ø J45, J44, J68	
Modelling Approach	**3a.**	**DC: Version 2**	**IC: average compensation**	**Total costs**
	Mean	1247.71	1121.67 (EU-28) 1085.36 (mean weighted)	3491.05 (EU-28) 2333.07 (mean weighted)
	SD	424.65	249.28	
	3b.	**DC: Version 2**	**IC: gross value added**	**Total costs**
	Mean*	1247.71	1834.09	3081.80
	SD	424.65	648.97	

Non-Modelling:
Total costs:
2142.21€-3024.91€
Modelling Approach:
Total costs:
2333.07€-3491.05€

Abbreviations: IC= indirect costs, DC= direct costs; mean= weighted according to population structure

Table 4.25 Total costs for occupational skin diseases (€, year 2013)

		OD 5101	Ø L20, 23, 24, 30	
Non-modelling approach	**1a.**	**DC: GDP PPP**	**IC: average compensation**	**Total costs**
	Mean*	967.46	1121.67 (EU-28) 945.64 (mean weighted)	2089.13 (EU-28) 1913.10 (mean weighted)
	SD	221.84	216.83	
	1b.	**DC: GDP PPP**	**IC: gross value added**	**Total costs**
	Mean*	967.46	1424.23	2391.69
	SD	221.84	326.58	
	2a.	**DC: Health PPP**	**IC: average compensation**	**Total costs**
	Mean*	867.35	1121.67 (EU-28) 945.64 (mean weighted)	1989.02 (EU-28) 1812.99 (mean weighted)
	SD	270.92	216.83	
	2b.	**DC: Health PPP**	**IC: gross value added**	**Total costs**
	Mean*	867.35	1424.23	2291.58
	SD	270.92	326.58	

Modelling Approach				
		OD 5101	**Ø L20, 23, 24, 30**	
	3b.	**DC: Version 2**	**IC: average compensation**	**Total costs**
	Mean	904.42	945.15 (EU-28) 914.56 (mean weighted)	1849,57 (EU-28) 1818.98 (mean weighted)
	SD	307.81	210.05	
	3b.	**DC: Version 2**	**IC: gross value added**	**Total costs**
	Mean*	904.42	1545.45	2449.87
	SD	307.81	546.84	

Non-Modelling:
Total costs:
1812.99€-2391.69€
Modelling Approach:
Total costs:
1818.98€-2449.87€

Abbreviations: IC= indirect costs, DC= direct costs; mean= weighted according to population structure

The same applies to occupational skin diseases whereby the mean costs are lower for skin diseases with a range of €1812.99 to €2449.87. The costs of the modelling approach are also between the conservative non-modelling approach (3a) and the optimistic non-modelling approach (1b). Again, the standard deviation for the skin diseases is highest for the modelling approach 3b (SD direct costs=424.65; indirect costs=648.97).

4.4 Discussion of results

This is the first study that analysed the costs for occupational skin and lung diseases due to isocyanates in Germany based on DGUV data. All analysed costs were transferred via different approaches to the EU-28 states. The different approaches were compared. Due to the different limitations of the methods and the high level of aggregation, the results will be discussed in the following.

The first limitation of the transfer is that the costs were not sufficiently differentiated into cost categories. A differentiated analysis according to the different categories of medical rehabilitation was only possible for occupational lung diseases. By comparison, for occupational skin diseases costs for medical rehabilitation are not further differentiated. Moreover, information on the type of pharmaceuticals that were prescribed, the length of hospital stay, the numbers of sick leave days and so on out of the DGUV data are lacking. This makes it difficult to transfer the results of the DGUV analysis in a well and differentiated modelling approach. Therefore, we focused on a mixed method approach using a non-modelling and a modelling approach.

In addition to that, the DGUV data are also very special, because the services paid by the DGUV are much higher compared to the statutory health insurance system in Germany. In other European countries, such a payment system does not exist. Moreover, due to structures of the health care systems, the transfer of costs represents a challenge. It is seen that besides the normal differences in the payment system (Beveridge vs. Bismarck), type of DRG or payment system of the outpatient care, also differences in the services and compensation forms from the institute of occupational diseases in the countries exists. Thus, we may have overestimated costs transferred to other countries.

In both approaches we calculated direct and indirect costs. The calculation of direct costs was associated with the limitation that not all cost categories that are integrated in the part “medical rehabilitation” can be assigned to the category of direct costs. It may be possible that some transfer payments are part of the medical rehabilitation, especially those costs that are part of the residual category. Therefore, we wanted to exclude them from the transfer of direct costs by subtracting them from total costs of medical rehabilitation. Unfortunately, due to the high level of aggregation of DGUV data, this was not possible in all models (e.g. costs on case level). The calculation of indirect costs also represented a major challenge, because the DGUV data do not include information on sick leave days. Therefore, we had to use the number of sick leave days from published statistics in Germany. However, these statistics only report the number of sick leave per case of illness for the different lung and skin diseases which could have led to an underestimation of costs.

Another specific challenge is the transfer of the results of cost of illness studies identified by the systematic literature search. During the systematic literature review some studies were identified but they are very heterogeneous, so that the results are significantly different. Especially the range of direct costs for occupational skin diseases was extremely large (modelling approach=€322.12-€2627.76; non-modelling

approach using GDP PPP: €294.49-€2850.37; non-modelling approach using Medical PPP: €290.65-€2363.29). One reason could be different study times and populations under study. Costs can be very differently if the person with the skin disease has a current eczema or is under exposure. Other differences are the perspectives of the analysis as well as integrated cost categories. Some studies do not include all relevant cost categories (at least inpatient/outpatient treatment and pharmaceuticals). All these reasons should be taken into account when comparing results. Another difference is that not all studies focused on the same diseases. One study reported the costs for occupational asthma, but another study focused on patients with asthma due to isocyanate. It is not clear if the costs between occupational asthma in general and occupational asthma due to isocyanate are different.

One aim of the study was to calculate average costs per insured person with isocyanate induced diseases for the whole EU-28. Therefore, we calculated mean costs per country. We decided to calculate the mean of the results by attaching specific weights to countries. It should be discussed if this is the right way to calculate the mean for the EU-28 but it is unclear how many people have an occupational asthma or an occupational skin disease due to isocyanate in each European country. Weighing the results with the population size in each country might lead to a miscalculation, because it is not clear if there is a correlation between the population size and the number of diseases due to isocyanates. Another option could be to weight the countries with a higher proportion of chemical industry but again, it is also not clear whether the size of chemical industry is associated with the number of cases of illness.

Besides the limitations of the different transfer approaches, there are several strengths. During the non-modelling approach we used two different adjustment factors, GDP PPP and Health PPP. The results show that the mean direct costs for J45.0 using Health PPP are lower compared to GDP PPP (Health PPP=€703.10; GDP PPP=€784.25). Moreover, the standard deviation is higher for Health PPP (SD=219.62) than for GDP PPP (SD=179.83).

In the course of the modelling approach, we integrated country specific data in the cost transfer that is e.g. the distribution of health expenditure according to the different cost categories was taken from the different countries. The results show that the cost ranges are higher between the countries compared to the non-modelling approach.

In general, the choice of the method of cost transfer depends on whether a more or less conservative model should be estimated. For the transfer of costs to the EU-28 we would prefer to use a mixed model approach with a combination of modelling and non-modeling approach. The calculations of direct costs based on health PPP are more conservative than the calculations with the GDP PPP. We also prefer this approach because the Health PPPs are calculated using the prices of a basket of health related goods and services and are therefore closer to the real health care costs in the countries.

For the calculation of indirect costs we prefer the modelling approach using average compensation rates. There are three reasons for this choice. First, it is also the most conservative approach compared to the calculation based on gross value added as factor costs and second, the values for the average compensations are based on country specific data. The third reason is that we have a mean for the EU-28 countries so that limitations that refer to the calculation of weighted mean are reduced. Therefore, this approach fits more to the realistic situation in the countries.

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List of figures

List of tables

Appendices

Appendix 1 Aims and sub targets of the research project

AIM: Calculate the cost of illness and indicators for the severity of the disease due to Isocyanate
Sub targets:
1. Implementation of a systematic literature review to identify studies about the costs of illness and the sickness duration or sickness severity and establishing a meta-analysis. 1. Choosing the search strategy for selected diseases to identify relevant studies 2. Performing the literature search 3. Defining quality criteria and data sources for meta-analysis 4. Implementation of meta-analysis
2. Calculation of cost of illness due to Isocyanate on the basis of claims data for Germany 1. Selection of suitable databases in coordination with data owner 2. Providing a concept for analysis 3. Analysis of routine data
3. Calculation the cost of illness for selected European countries 1. Ascertaining the external factors influencing the amount of sickness costs 2. Defining methods for cost transfer 3. Extrapolation of healthcare costs per case; inclusive calculation of the range of the healthcare costs
4. Publication

Appendix 2 Search history in DIMDI for search strategies 1-3

Suchhistorie

Nr.	Suchformulierung	Trefferzahl	Aktionen
63	62 AND PY=2005 to 2015	14464	
62	61 AND LA=(ENGLISH; GERMAN)	14604	
61	45 AND 60	15358	
60	54 OR 59	1396967	
59	55 OR 56 OR 57 OR 58	82187	
58	CT D ("DURATION OF ILLNESS"; "DURATION,DISEASE")	79129	
57	CT D ("SEVERITY"; "SEVERITY OF ILLNESS")	13	
56	FT=Sickness duration OR FT=illness duration	2807	
55	(((FT=Dauer der Erkrankung OR FT=Krankheitslast) OR FT=Krankheitsschwere) OR FT=Schwere der Erkrankung) OR FT=Schweregrad	629	
54	46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53	1317348	
53	CT D ("ECONOMIC"; "ECONOMIC ANALYSIS"; "ECONOMIC ASPECTS OF ILLNESS"; "ECONOMIC BURDEN OF DISEASE")	23706	
52	CT D ("COST OF ILLNESS"; "COST OF ILLNESS ANALYSIS"; "COST, COST ANALYSIS")	83446	
51	CT D ("HEALTH CARE COSTS"; "HEALTH CARE COSTS/"*)	150972	
50	CT D "ABSENTEEISM"	9213	
49	CT D "LOSS OF PRODUCTIVITY"	1	
48	CT D "PRODUCTIVITY LOSS"	8	
47	CTG D ("KOSTEN UND KOSTENANALYSE"; "KOSTEN, KRANKHEITS-")	72557	
46	(((FT=Kosten OR FT=cost) OR FT=cost?) OR FT=Kost?) OR FT=los* productivity	1304849	
45	5 OR 44	316351	
44	6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43	266220	
43	CT D ("DERMATOSES, INDUSTRIAL"; "DERMATOSIS, INDUSTRIAL")	1154	
42	CT D "DERMATITIDES, OCCUPATIONAL"	1154	
41	CT D ("INDUSTRIAL DERMATOSES"; "INDUSTRIAL DERMATOSIS")	1154	
40	CT D ("OCCUPATIONAL DERMATITIDES"; "OCCUPATIONAL DERMATITIS")	2187	
39	CTG D "DERMATITIS, BERUFSBEDINGTE"	1156	
38	CTG D "BERUFSBEDINGTE DERMATOSE"	1154	
37	CT D "PRIMARY IRRITANT DERMATITIS"	926	
36	CT D ("IRRITANT DERMATITIDES"; "IRRITANT DERMATITIDES, PRIMARY"; "IRRITANT DERMATITIS"; "IRRITANT DERMATITIS, PRIMARY")	2042	
35	CT D ("DERMATITIS, IRRITANT"; "DERMATITIS, PRIMARY IRRITANT")	2042	
34	CT D "IRRITANT CONTACT DERMATITIS"	1248	

☐	33	CTG D ("DERMATITIS, IRRITATIONS-"; "DERMATITIS, KONTAKT-"; "DERMATITIS, KONTAKT-, ALLERGISCHE")	6809
☐	32	((FT=Toxisches Kontaktekzem OR FT=Toxische Kontaktdermatitis) OR FT=irritant contact dermati?) OR FT=primary Irritant Dermatiti?	1871
☐	31	CTG D "ALLERGISCHE KONTAKTDERMATITIS"	4135
☐	30	CTG D ("DERMATITIS, KONTAKT-"; "DERMATITIS, KONTAKT-, ALLERGISCHE")	6809
☐	29	CT D ("CONTACT DERMATITIDES, ALLERGIC"; "CONTACT DERMATITIS, ALLERGIC")	4135
☐	28	CT D ("ALLERGIC CONTACT DERMATITIDES"; "ALLERGIC CONTACT DERMATITIS")	13116
☐	27	CT D ("ECZEMATOUS DERMATITIDES, ALLERGIC"; "ECZEMATOUS DERMATITIS, ALLERGIC")	4135
☐	26	CT D ("ALLERGIC ECZEMATOUS DERMATITIDES"; "ALLERGIC ECZEMATOUS DERMATITIS")	4140
☐	25	CT D "DERMATITIDES, ALLERGIC ECZEMATOUS"	4135
☐	24	CT D ("DERMATITIS, ALLERGIC CONTACT"; "DERMATITIS, ALLERGIC ECZEMATOUS"; "DERMATITIS, CONTACT, ALLERGIC")	13563
☐	23	CT D ("EXTRINSIC ALLERGIC ALVEOLITIDES"; "EXTRINSIC ALLERGIC ALVEOLITIS")	4219
☐	22	CT D "ALVEOLITIDES, EXTRINSIC ALLERGIC"	667
☐	21	CT D ("ALLERGIC ALVEOLITIDES, EXTRINSIC"; "ALLERGIC ALVEOLITIS, EXTRINSIC")	667
☐	20	CT D ("PNEUMONITIDES, HYPERSENSITIVITY"; "PNEUMONITIS, HYPERSENSITIVITY")	667
☐	19	CT D ("HYPERSENSITIVITY PNEUMONITIDES"; "HYPERSENSITIVITY PNEUMONITIS")	4485
☐	18	CTG D "ALLERGISCHE ALVEOLITIS, EXOGENE"	667
☐	17	CTG D "EXOGEN-ALLERGISCHE ALVEOLITIS"	667
☐	16	FT=Exogen allergische alveolitis OR FT=extrinsic allergic alveoliti?	631
☐	15	CTG D ("CHRONISCH OBSTRUKTIVE LUNGENERKRANKUNG"; "CHRONISCH OBSTRUKTIVE PULMONALE ERKRANKUNG"; "CHRONISCH OBSTRUKTIVE PULMONALE KRANKHEIT")	22410
☐	14	CT D ("CHRONIC AIRFLOW OBSTRUCTION"; "CHRONIC AIRFLOW OBSTRUCTIONS")	75255
☐	13	CT D ("AIRFLOW OBSTRUCTION, CHRONIC"; "AIRFLOW OBSTRUCTIONS, CHRONIC")	22410
☐	12	CT D ("CHRONIC OBSTRUCTIVE AIRWAY DISEASE"; "CHRONIC OBSTRUCTIVE AIRWAYS DISEASE"; "CHRONIC OBSTRUCTIVE LUNG DISEASE")	75590
☐	11	CT D "COAD"	22413
☐	10	CT D ("CHRONIC OBSTRUCTIVE PULMONARY DISEASE"; "CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)")	87649
☐	9	CT D "COPD"	80787
☐	8	CT D "BRONCHIAL ASTHMA"	138603
☐	7	CT D ("ASTHMA"; "ASTHMA BRONCHIALE")	170820
☐	6	CTG D ("ASTHMA"; "ASTHMA BRONCHIALE")	34819
☐	5	2 OR 3 OR 4	50955
☐	4	CT D "ISOCYANATE"	1025
☐	3	CTG D "ISOCYANATE"	5776
☐	2	FT=Isocyanat? OR FT=Isothiocyanat?	50436
	1	Datenbankauswahl: ME05 BA05 EA08 EM05 GA03 GM03 IS05	44228012

Appendix 3 Overview of processed data elements (variables/characteristics) using the DIMDI database

Record type	Reporting year			Comment
	2009	2010	2011	
Master Data I				
ID	V2009SA151_PSID	V2010SA151_PSID	V2011SA151_PSID	About Perennial insured ID (Pseudonym)
Reporting year	V2009SA151_BERICHTSJAHR	V2010SA151_BERICHTSJAHR	V2011SA151_BERICHTSJAHR	YYYY year in which the data was collected
Year of birth	V2009SA151_GEBURTSJAHR	V2010SA151_GEBURTSJAHR	V2011SA151_GEBURTSJAHR	Year of birth of the Insured YYY
Gender	V2009SA151_GESCHLECHT	V2010SA151_GESCHLECHT	V2011SA151_GESCHLECHT	1=Female. 2=Male
Insured days	V2009SA151_VERSICHERTENTAGE	V2010SA151_VERSICHERTENTAGE	V2011SA151_VERSICHERTENTAGE	Insured days of the insured during the reporting year in accordance with § 30 para. 1 no. 1 RSAV
Master Data II				
ID	V2010SA152_PSID	V2011SA152_PSID	V2012SA152_PSID	About Perennial Insured ID (Pseudonym)
Reporting year	V2010SA152_BERICHTSJAHR	V2011SA152_BERICHTSJAHR	V2012SA152_BERICHTSJAHR	YYYY year in which the data was collects
Disability pension	V2010SA152_ERWERBSMINDERUNGS_VT	V2011SA152_ERWERBSMINDERUNGS_VT	V2012SA152_ERWERBSMINDERUNGS_VT	Disability pension: insured days during the reporting year
Insured days overseas	V2010SA152_VERSICHERTENTAGEAUSLAND	V2011SA152_VERSICHERTENTAGEAUSLAND	V2012SA152_VERSICHERTENTAGEAUSLAND	Insured days with domicile or habitual residence overseas in accordance with § 30 para. 1 No. 8 RSAV
Insured daily reimbursement	V2010SA152_VERSICHERTENTAGE13II	V2011SA152_VERSICHERTENTAGE13II	V2012SA152_VERSICHERTENTAGE13II	Insured days with reimbursement according to § 13 para. 2 SGB V corresponding to the field of contractual medical care § 30 Para. 1 Nr. 9 RSAV
Insured daily reimbursement	V2010SA152_VERSICHERTENTAGE53IV	V2011SA152_VERSICHERTENTAGE53IV	V2012SA152_VERSICHERTENTAGE53IV	Insured days with reimbursement according to § 53 para. 4 SGB V

	2009	2010	2011	
Inpatient diagnosis				
ID	V2010SA551_PSID	V2011SA551_PSID	V2012SA551_PSID	About Perennial Insured ID (Pseudonym)
Reporting year	V2010SA551_BERICHTSJAHR	V2011SA551_BERICHTSJAHR	V2012SA551_BERICHTSJAHR	YYYY year in which the data was collects
Diagnosis	V2010SA551_ICD_CODE	V2011SA551_ICD_CODE	V2012SA551_ICD_CODE	ICD 10 GM Code without a dotted notation and also without special characters
Prima-ry/secondary diagnosis	V2010SA551_ARTDIAGNOSE	V2011SA551_ARTDIAGNOSE	V2012SA551_ARTDIAGNOSE	1=Primary diagnosis. 2=Secondary diagnosis
Outpatient diagnosis				
ID	V2010SA651_PSID	V2011SA651_PSID	V2012SA651_PSID	About Perennial Insured ID (Pseudonym)
Reporting year	V2010SA651_BERICHTSJAHR	V2011SA651_BERICHTSJAHR	V2012SA651_BERICHTSJAHR	YYYY year in which the data was collects
Quarter	V2010SA651_LEISTUNGSQUARTA	V2011SA651_LEISTUNGSQUARTA	V2012SA651_LEISTUNGSQUARTA	Quarter 1-4
Diagnosis	V2010SA651_ICD_CODE	V2011SA651_ICD_CODE	V20122A651_ICD_CODE	ICD 10 GM Code without a dotted notation and also without special characters
Qualification of diagnosis	V2010SA651_QUALIFIZIERUNG	V2011SA651_QUALIFIZIERUNG	V2012SA651_QUALIFIZIERUNG	V = suspected diagnosis. Z = State after the respec-tive diagnosis. A = ex-cluded diagnostics. G = definite Diagnosis
Service expenses				
ID	V2009SA751_PSID	V2010SA751_PSID	V2011SA751_PSID	About Perennial Insured ID (Pseudonym)
Reporting year	V2009SA751_BERICHTSJAHR	V2010SA751_BERICHTSJAHR	V2011SA751_BERICHTSJAHR	YYYY year in which the data was collects
Doctors	V2009SA751_AERZTE	V2010SA751_AERZTE	V2011SA751_AERZTE	Expenditure in Euro cents
Pharmacies	V2009SA751_APOTHEKEN	V2010SA751_APOTHEKEN	V2011SA751_APOTHEKEN	Expenditure in Euro cents
Hospitals	V2009SA751_KRANKENHAEUSER	V2010SA751_KRANKENHAEUSER	V2011SA751_ KRANKENHAEUS-ER	Expenditure in Euro cents
Other Services	V2009SA751_SONSTIGELA	V2010SA751_SONSTIGELA	V2011SA751_SONSTIGELA	Expenditure in Euro cents
Material costs dialysis	V2009SA751_SACHKOSTENDIALYSE	V2009SA751_SACHKOSTENDIALYSE	V2009SA751_SACHKOSTENDIALYSE	Expenditure in Euro cents
Sick pay	V2009SA751_KRANKENGELD	V2010SA751_KRANKENGELD	V2011SA751_KRANKENGELD	Expenditure in Euro cents
Legend:	compensatory year 2009	compensatory year 2010	compensatory year 2011	compensatory year 2012

Appendix 4 Original data from the DGUV

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

1315 Isocyanate

		Medizinische Rehabilitation		Leistungen zur Teilhabe		Renten/Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt	
		Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl
Geschäftsjahr	2004	781702	329	893273	114	2531920	385	64915	7	4271810	493
	2005	629222	335	760323	91	2623606	391	66427	6	4079578	498
	2006	764634	341	575530	73	2607032	397	66867	7	4014063	489
	2007	637009	339	498297	62	2560294	387	108645	9	3804245	470
	2008	780990	372	471415	65	2480562	394	96248	8	3829215	495
	2009	745296	371	515389	55	2764671	406	104660	8	4130016	508
	2010	987927	365	367226	51	2773121	412	136075	10	4264349	507
	2011	1074085	381	452004	59	2716305	416	127962	10	4370356	522
	2012	967198	399	581919	62	2840332	424	160839	14	4550288	541
	2013	863934	395	634574	65	2888818	413	232175	12	4619501	520
Gesamt		**8231997**	**3627**	**5749950**	**697**	**26786661**	**4025**	**1164813**	**91**	**41933421**	**5043**

* Erfassung der UVTöH in der BK-KOST ab 2009/2010.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

5101 Hautkrankheiten

		Medizinische Rehabilitation		Leistungen zur Teilhabe		Renten/Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt	
		Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl
Geschäftsjahr	2004	48178	8	97801	8	63420	14		0	209399	25
	2005	32030	7	71519	7	88638	14		0	192187	23
	2006	913	9	32018	5	62742	15		0	95673	21
	2007	2541	10	35499	4	119583	15		0	157623	22
	2008	40225	8	37653	7	60250	14		0	138128	23
	2009	2055	6	40681	5	64391	15		0	107127	22
	2010	49463	8	38796	4	61291	15		0	149550	21
	2011	16883	9	41067	2	49535	11		0	107485	19
	2012	38499	8	20259	3	52236	12		0	110994	16
	2013	1111	6	26079	4	52120	12		0	79310	17
Gesamt		**231898**	**79**	**441372**	**49**	**674206**	**137**		**0**	**1347476**	**209**

* Erfassung der UVTöH in der BK-KOST ab 2009/2010.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle BK-Nr. 1315 und ihre Kosten

Geschlecht: männlich

		Medizinische Rehabilitation		Leistungen zur Teilhabe		Renten/Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt	
		Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl
Geschäftsjahr	2004	667729	288	818885	96	2366689	344	64915	7	3918218	436
	2005	596071	298	713039	76	2446205	350	66427	6	3821742	443
	2006	720439	299	523397	63	2440942	353	66867	7	3751645	433
	2007	543381	299	377683	53	2329704	341	108645	9	3359413	411
	2008	672442	313	385878	57	2295942	348	96248	8	3450510	425
	2009	631839	313	400752	45	2521304	356	104660	8	3658555	437
	2010	849645	308	260421	41	2561302	361	136075	10	3807443	434
	2011	991943	320	374190	45	2509655	364	127962	10	4003750	446
	2012	848572	338	470286	47	2567053	368	160839	14	4046750	461
	2013	750836	333	547563	51	2645898	359	232175	12	4176472	443
Gesamt		**7272897**	**3109**	**4872094**	**574**	**24684694**	**3544**	**1164813**	**91**	**37994498**	**4369**

* Erfassung der UVTöH in der BK-KOST ab 2009/2010.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle BK-Nr. 1315 und ihre Kosten

Geschlecht: weiblich

		Medizinische Rehabilitation		Leistungen zur Teilhabe		Renten/Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt	
		Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl
Geschäftsjahr	2004	113973	41	74388	18	165231	41		0	353592	57
	2005	33151	37	47284	15	177401	41		0	257836	55
	2006	44195	42	52133	10	166090	44		0	262418	56
	2007	93628	40	120614	9	230590	46		0	444832	59
	2008	108548	59	85537	8	184620	46		0	378705	70
	2009	113457	58	114637	10	243367	50		0	471461	71
	2010	138282	57	106805	10	211819	51		0	456906	73
	2011	82142	61	77814	14	206650	52		0	366606	76
	2012	118626	61	111633	15	273279	56		0	503538	80
	2013	113098	62	87011	14	242920	54		0	443029	77
Gesamt		**959100**	**518**	**877856**	**123**	**2101967**	**481**		**0**	**3938923**	**674**

* Erfassung der UVTöH in der BK-KOST ab 2009/2010.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

Primärkrankheit: J44.8 Sonstige näher bezeichnete chronische obstruktive Lungenkrankheit bzw. Bronchitis. Emphysembronchitis

	Medizinische Rehabilitation								Leistungen zur Teilhabe		Renten/ Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt		Alter im Jahr der Anzeige		
	darunter: Ambulante Heilbehandlung		darunter: Stationäre Heilbehandlung		darunter: Hilfsmittel		Insgesamt												
Geschäftsjahr	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Mittelwert	Standardabweichung	Frauenanteil
2004	14032	46	32045	12	2500	3	170699	54	155163	21	410477	59	28877	3	765216	79	47.1	11.4	11.4%
2005	16990	55	54874	14	4100	4	198991	59	220396	22	471864	62	29332	3	920583	84	46.5	11.8	11.9%
2006	22037	57	73693	19	2378	5	221052	61	170634	22	443543	60	30031	3	865260	86	46.4	11.7	14.0%
2007	17620	55	37144	10	2321	6	113660	56	38989	12	475268	57	41861	4	669778	76	47.2	11.1	11.8%
2008	20047	59	60030	15	4683	4	155502	65	101034	13	394662	60	31438	3	682636	83	47.4	11.6	13.3%
2009	34580	60	48139	12	17326	6	103033	63	29424	6	614200	66	31780	3	778437	81	48.1	11.8	12.3%
2010	41237	66	28745	8	20562	6	188380	69	40438	7	493091	67	32159	3	754068	84	48.4	11.4	13.1%
2011	41629	63	32058	12	21362	7	150301	67	71773	12	472754	67	32316	3	727144	88	48.5	11.2	17.0%
2012	55651	73	74745	15	22827	7	219759	79	129558	13	519522	69	29472	4	898311	92	48.7	11.3	18.5%
2013	36226	69	65987	11	15499	6	163682	73	102420	14	605928	72	22076	2	894106	89	48.2	11.2	20.2%
Gesamt	300049	603	507460	128	113558	54	1685059	646	1059829	142	4901309	639	309342	31	7955539	842	47.7	11.4	14.5%

* Erfassung der UV-Träger der öffentlichen Hand in der BK-KOST erst seit 2009.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

Primärkrankheit: J45.0 Vorwiegend allergisches Asthma bronchiale bzw. Obstruktive Atemwegserkrankung. allergisch (Asthma)

Geschäftsjahr	Medizinische Rehabilitation								Leistungen zur Teilhabe		Renten/ Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt		Alter im Jahr der Anzeige		
	darunter: Ambulante Heilbehandlung		darunter: Stationäre Heilbehandlung		darunter: Hilfsmittel		Insgesamt												
	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Mittelwert	Standardabweichung	Frauenanteil
2004	40534	110	79283	26	2221	4	169204	117	323966	38	891507	145	15448	2	1400125	181	45.3	11.3	9.9%
2005	36726	118	81916	23	8613	5	179950	126	217588	29	935947	147	11308	1	1344793	183	45.8	11.5	9.3%
2006	39711	126	93781	23	3803	3	236772	135	130078	18	876542	147	11308	1	1254700	180	46.0	11.2	9.4%
2007	42286	116	120087	32	8307	10	229976	124	171190	25	936897	144	11338	1	1349401	174	45.1	11.8	10.3%
2008	42048	136	81613	22	8447	4	191914	144	231661	28	911456	148	24116	2	1359147	188	44.7	11.7	12.2%
2009	65772	143	125522	33	23259	11	303434	150	229434	28	915615	153	31412	2	1479895	198	44.9	11.7	12.1%
2010	58496	141	93181	25	17877	11	403751	146	185197	23	929934	157	46215	3	1565097	193	44.8	11.7	13.5%
2011	63710	145	114270	28	20976	10	268015	154	154319	25	1003163	162	29364	2	1454861	204	45.0	11.8	14.2%
2012	70638	144	109137	35	24451	9	336572	158	263011	29	1015234	165	62546	4	1677363	214	45.1	11.7	14.0%
2013	67945	151	132199	32	15318	8	270050	158	341805	31	1036802	160	49296	4	1697953	205	45.4	11.5	13.7%
Gesamt	527866	1330	1030989	279	133272	75	2589638	1412	2248249	274	9453097	1528	292351	22	14583335	1920	45.2	11.6	12.0%

* Erfassung der UV-Träger der öffentlichen Hand in der BK-KOST erst seit 2009.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

Primärkrankheit:

J45.1 Nichtallergisches Asthma bronchiale bzw. Obstruktive Atemwegserkrankung. chemisch-irritativ (Asthma) und Obstruktive Atemwegserkrankung. toxisch

	Medizinische Rehabilitation								Leistungen zur Teilhabe		Renten/ Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt		Alter im Jahr der Anzeige		
	darunter: Ambulante Heilbehandlung		darunter: Stationäre Heilbehandlung		darunter: Hilfsmittel		Insgesamt												
Geschäftsjahr	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Mittelwert	Standardabweichung	Frauenanteil
2004	12728	38	26469	8	213	1	82315	44	37330	7	322823	52		0	442468	60	45.4	12.3	15.0%
2005	9568	39	20714	7	984	2	63779	40	30492	6	311140	52		0	405411	59	45.6	12.2	13.6%
2006	7256	34	37975	11	621	2	52549	38	49931	5	393798	51		0	496278	54	45.8	12.1	14.8%
2007	17877	35	31051	6	2992	2	51010	35	76116	4	291798	48		0	418924	53	46.4	11.9	17.0%
2008	21088	37	40716	11	5510	3	159047	37	28043	3	308849	49		0	495939	54	46.6	12.0	16.7%
2009	25440	38	20559	7	6728	2	128330	40	6364	1	322778	50		0	457472	55	46.6	12.0	16.4%
2010	28472	38	45182	9	14156	4	135090	40	759	1	334646	48		0	470495	54	46.4	12.4	13.0%
2011	26455	42	23884	8	11134	5	67838	43	9390	2	375805	47		0	453033	53	46.0	12.6	11.3%
2012	27996	40	39842	9	11875	4	155830	40	11214	1	348832	48		0	515876	53	46.4	12.5	11.3%
2013	27426	39	24893	6	12557	4	119984	40	34325	3	334350	46		0	488659	52	46.3	12.1	13.5%
Gesamt	204306	380	311285	82	66770	29	1015772	397	283964	33	3344819	491		0	4644555	547	46.1	12.1	14.3%

* Erfassung der UV-Träger der öffentlichen Hand in der BK-KOST erst seit 2009.

Berufskrankheiten-Kostenerhebung (BK-KOST) - Gewerbliche Wirtschaft und Öffentlicher Dienst*
Leistungsfälle mit Isocyanat-Einwirkung und ihre Kosten

Primärkrankheit: J68.4 Chronische Krankheiten der Atmungsorgane durch chemische Substanzen. Gase. Rauch und Dämpfe

Geschäftsjahr	Medizinische Rehabilitation: darunter: Ambulante Heilbehandlung		Medizinische Rehabilitation: darunter: Stationäre Heilbehandlung		Medizinische Rehabilitation: darunter: Hilfsmittel		Medizinische Rehabilitation: Insgesamt		Leistungen zur Teilhabe		Renten/ Abfindungen an Erkrankte		Leistungen an Hinterbliebene		Leistungen insgesamt		Alter im Jahr der Anzeige		Frauenanteil
	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Betrag	Anzahl	Mittelwert	Standardabweichung	
2004	6497	30	43322	14	953	2	171686	39	194923	23	284238	35	17478	1	668325	59	43.5	12.0	15.3%
2005	9205	32	34954	12	2281	3	109779	38	132894	20	384649	44	17478	1	644800	64	44.9	11.7	14.1%
2006	16962	37	41066	13	6211	4	183939	41	128054	16	356740	48	17478	1	686211	66	44.8	11.8	12.1%
2007	15366	43	48807	9	2965	5	180845	49	122985	14	342792	52	22040	2	668662	65	46.0	10.9	18.5%
2008	15423	46	77505	13	2034	3	194760	55	98262	18	354507	54	17669	1	665198	74	45.1	11.5	24.3%
2009	21395	51	47608	10	3185	4	152665	56	246624	19	401892	55	17979	1	819160	80	45.2	11.8	25.0%
2010	31198	48	114502	13	12292	4	200330	53	131337	19	495585	58	33937	2	861189	83	44.7	11.3	25.3%
2011	35694	56	462126	15	15870	7	535595	59	202292	18	332766	58	42391	3	1113044	83	44.4	11.4	22.9%
2012	35594	60	73463	15	8857	7	194365	66	147236	16	460657	64	36118	3	838376	95	45.0	11.4	20.0%
2013	37849	56	53282	15	8406	6	191869	64	123307	15	401409	60	136230	4	852815	89	45.5	11.6	18.0%
Gesamt	225183	459	996635	129	63054	45	2115833	520	1527914	178	3815235	528	358798	19	7817780	758	44.9	11.5	19.9%

* Erfassung der UV-Träger der öffentlichen Hand in der BK-KOST erst seit 2009.

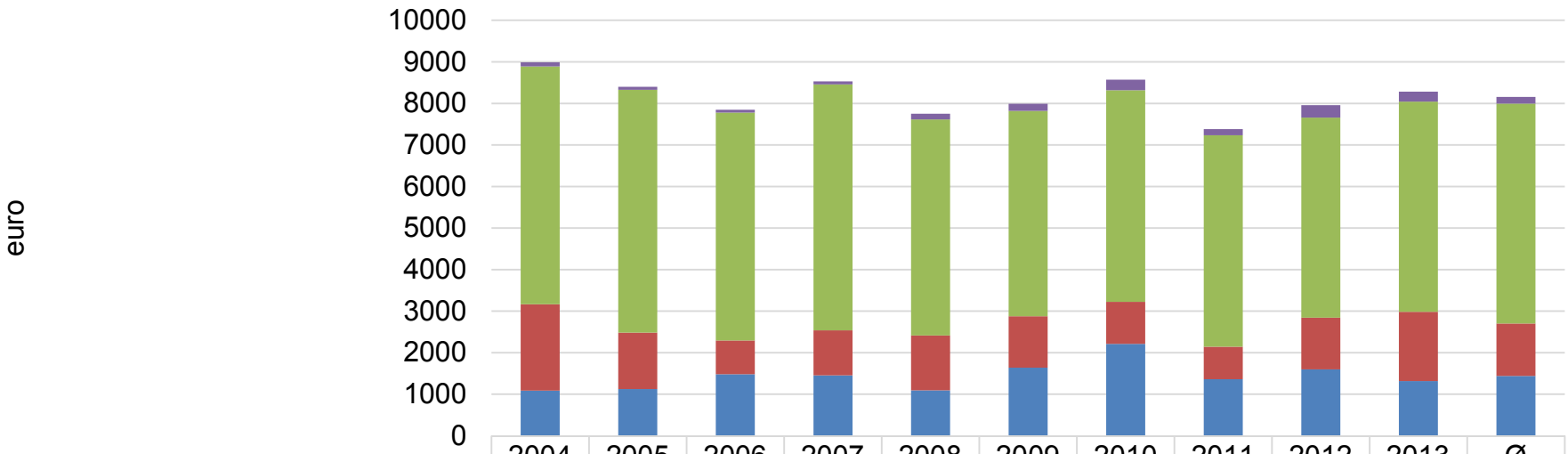
Appendix 5 Services of the GUV sector

Sector	Service (account type)	Summary from the accounting System
Medical Rehabilitation	**Outpatient Treatment** (400) • Outpatient medical and dental treatment • Drugs. medicine and medical aids	Costs of primary care and outpatient medical and dental care include the non-cash benefits. Furthermore, the cost of drugs, medicines and medical aids. Medical aids: These include in particular prostheses, orthopedic and other aids, including the necessary changes, repair and replacement and training in the use of these tools.
	Inpatient Treatment: • Inpatient Treatment (460) • Home care (465)	All expenses for benefits in-patient and day-care treatment according to § 33 para. 1 SGB VII. Does not include the cost of a (partially) inpatient stay for valuation purposes (see to 770). All expenses for nursing home care according to § 27 para. 1 no. 5 in conjunction with § 32 SGB VII.
	„Other":	
	• Dental prosthesis (450)	All costs for dentures regardless of whether the denture is granted for outpatient treatment or inpatient treatment, etc. Will the cost of dentures be billed with those for dental treatment in an amount (flat rate), the amount is to be posted here. Moreover, the costs of dental treatment (including orthodontic treatment) under account type 400 and 460 are to be recorded.
	• Injury benefit(470)	Injury benefit in accordance with § 45 para. 2 SGB VII, including the recipients of cash benefits to supporting post contributions to social insurance. From those accident insurance institutions to support social security contributions are booked in account type 484. But not yet the offsetting entry for the paid contributions in account type 119. 80 percent of the stabile payments, but not higher than the regular net pay. In addition to the deductions from the contributions paid to pension and unemployment insurance
	• Special assistance (475)	Special support in accordance with § 39 para 2 SGB VII by medical treatment. In addition to the calculation of compensation for the injured for loss of earnings during outpatient treatment.
	• Granting of Care (480)	All expenditures from home care and in residential care according to § 44 SGB VII.
	• Nursing Allowance(481)	Expenditure on care allowance according to § 44 SGB VII.
	• Compensation for laundry and clothes wear (482)	
	• Other Medical Expenses (483)	All other expenses in connection with the medical treatment that cannot be included among the types of accounts 400-482. for example flat-rate allowances to emergency rooms, to the German Red Cross, at first aid stations and similar facilities.
	• Social security contributions for injury benefits(484)	Contributions and contributions paid by the accident insurance institutions for social security in respect to injury benefits.

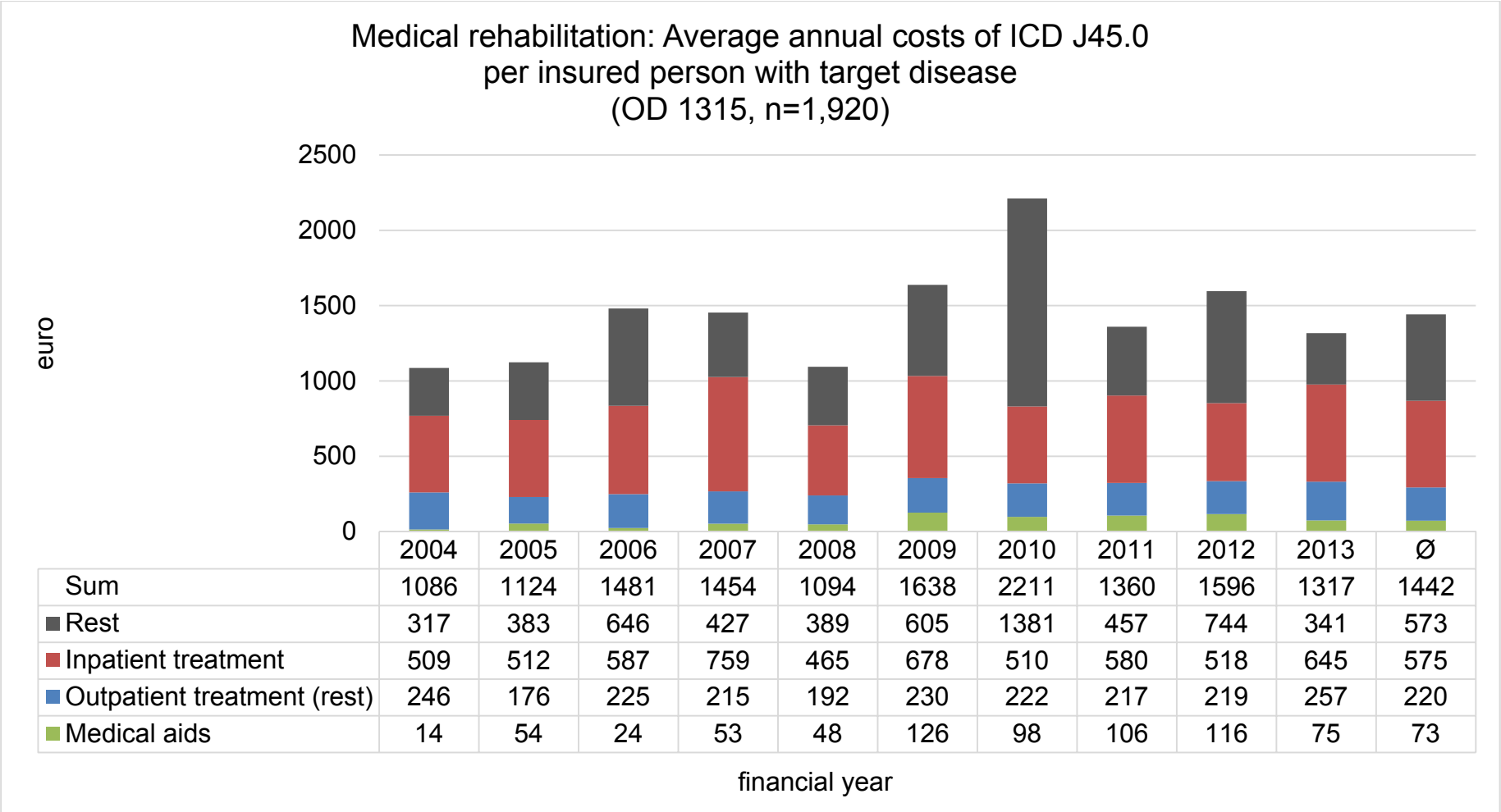
	• Transport - and travel expenses for medical treatment and care (485)	All transport and travel costs for outpatient and inpatient treatment and care. This also includes the (share) expenditures on own ambulances of the insurance carrier, including personal and material costs for the motorist. Not booked here are the costs associated with the benefits for participation in work force (see 49), with accommodation in nursing homes (see to 530) and Accident Investigation Bureau (see to 770).
	• Home- and child-care costs for medical treatment (486)	Benefits under § 42 SGB VII § 54 para 1 to 3 SGB IX. The agricultural trade associations detect here the benefits under § 54 para 2 SGB VII.
	• Services for participation in the community (488)	Benefits under § 39 of the SGB VII., unless they are attributable to the benefits of medical rehabilitation or the benefits for the participation in work force.
	• Injury benefit due to an accident of a child (489)	Allowance payments to child care according to § 45 para 4 SGB VII § 45 SGB V.
Services for social and professional participation	• Non-cash Benefit (490)	
	• Temporary Allowance (491)	Also transitional allowance according to § 50 SGB VII §§ 45 to 51 SGB IX.
	• Other cash benefits with benefits for participation in work field (492)	Special support in accordance with § 39 para 2 SGB VII at the participation in work force.
	• Social security contributions for a temporary allowance (494)	Contributions and contributions paid by the accident insurance institutions for social security in respect to transitional allowance; also subsidies from private health insurance.
	• Travel expenses on benefits for participation in the work force (495)	Benefits under § 43 SGB VII under the benefits for participation in work force.
	• Home care benefits for participation in the work force (496)	Benefits according to § 42 SGB VII § 54 para 1 to 3 SGB IXthe agricultural BGs detect here the benefits according to § 54 para 2 SGB VII.
	• Other supplementary services (498)	Additional benefits of participation in the work force. as far as they are not recognised in other types of accounts of account group 49 or account type 580.
	• Transitional Benefit (499)	Tansitional Benefits according to § 3 para 2 Occupational Disease Ordinance.
Pension/compensation for the ill	• Pension benefits for the insured (500)	Also pension increases by §§ 57 und 58 SGB VII and children allowances. Also payments to the pension insurance institution according to § 270 SGB VI.
	• Compensation payments to the insured (520)	
	• Compensation package according to § 75 SGB VII (521)	
Survivors' benefits	• Widows 'and widowers' pensions according to § 65 para 2 (2) SGB VII (501) and § 65 para 2 (3) SGB VII (502)	Also Corresponding benefits under the § 217 para 2 SGB VII. Also pensions to former spouses.
	• Pension after death according to § 65 Abs. 2 Nr. 1 SGB VII (503)	Also Corresponding benefits under the § 217 para 2 SGB VII. Also pensions to former spouses.

	• Orphans' pensions (504)	
	• Parent pension according to § 69 SGB VII (505)	
	• One time widow and widower aid (510)	Also Corresponding benefits under the § 217 para 2 SGB VII.
	• Ongoing widow and widower aid (511)	Also Corresponding benefits under the § 217 para 2 SGB VII.
	• Orphan aid (512)	
	• Severance payments to widows and widowers (525)	
	• Burial allowance (570)	§ 64 para 1 SGB VII
	• Transfer money (571)	§ 64 para 2 SGB VII

Appendix 6 Further DGUV results with regard to allergic asthma

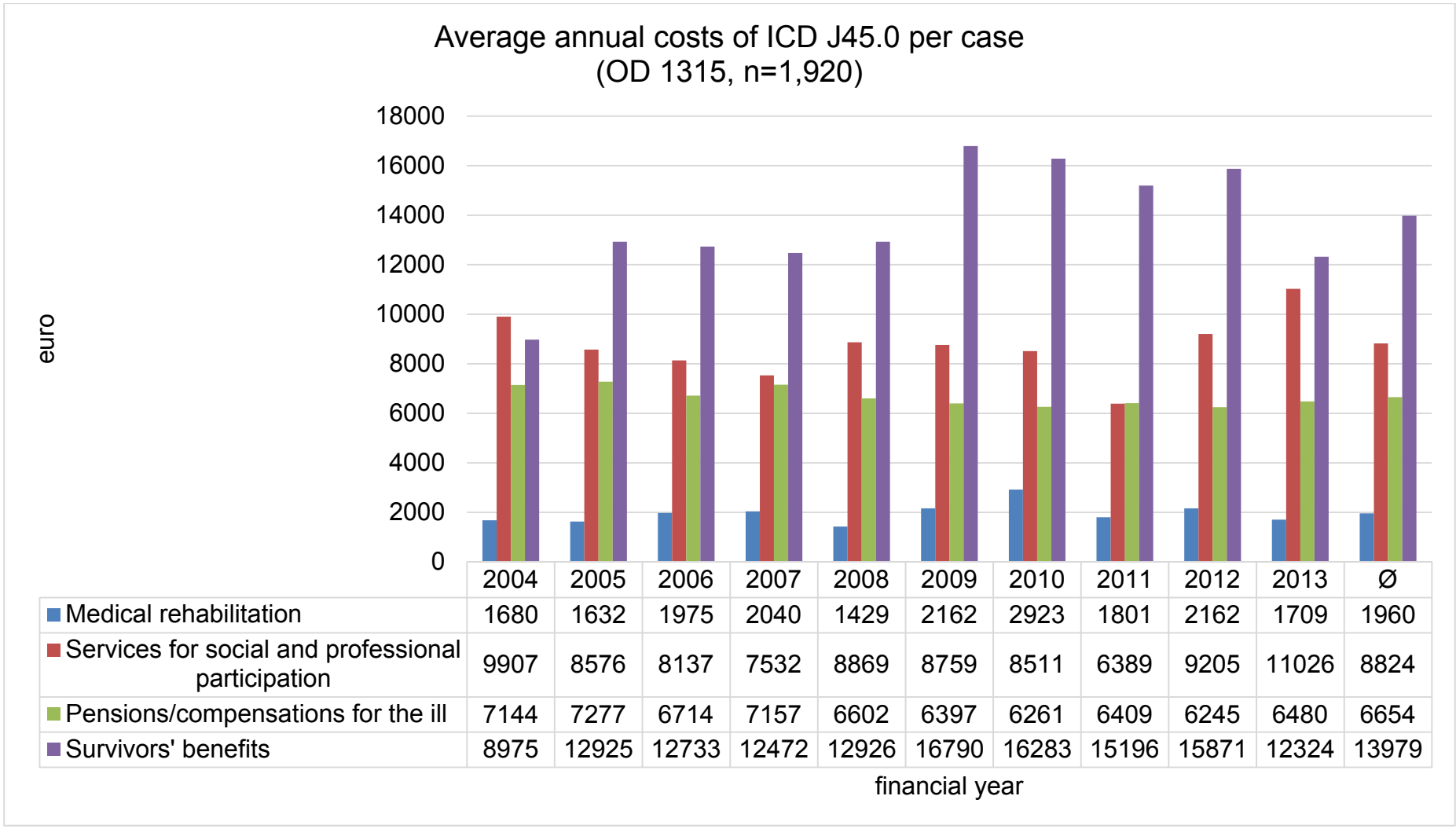


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Summe	8989	8399	7849	8531	7750	7990	8572	7381	7956	8283	8157
Survivors' benefits	99	71	71	72	138	170	253	149	297	240	160
Pensions/compensations for the ill	5723	5846	5483	5923	5197	4943	5093	5090	4815	5058	5296
Services for social and professional participation	2080	1359	814	1082	1321	1239	1014	783	1247	1667	1259
Medical rehabilitation	1086	1124	1481	1454	1094	1638	2211	1360	1596	1317	1442



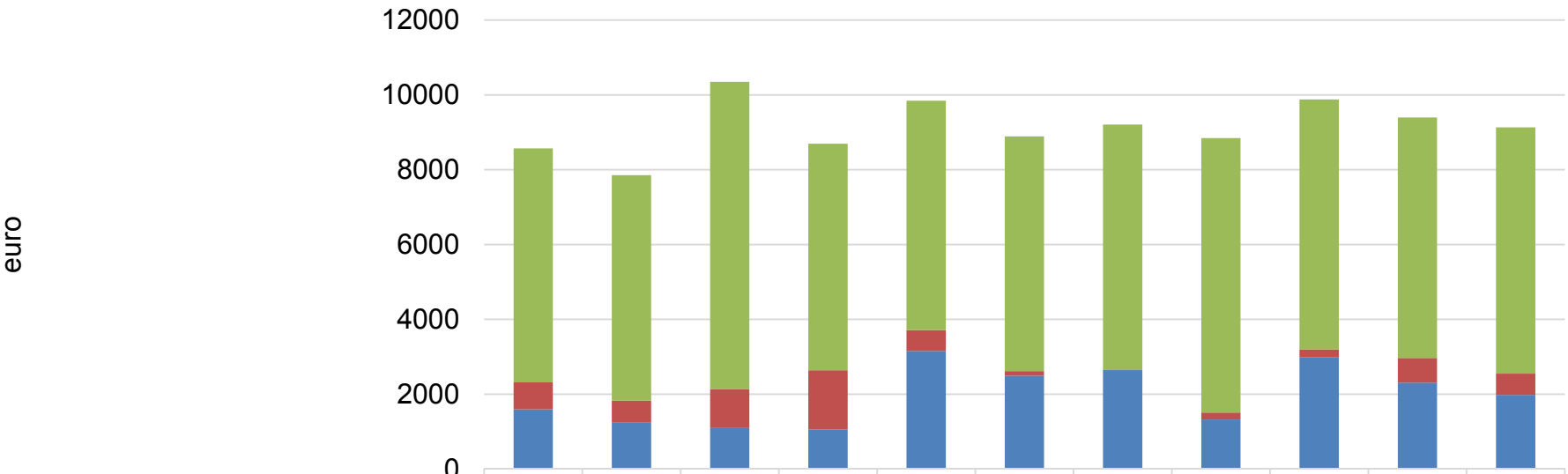
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	1086	1124	1481	1454	1094	1638	2211	1360	1596	1317	1442
Rest	317	383	646	427	389	605	1381	457	744	341	573
Inpatient treatment	509	512	587	759	465	678	510	580	518	645	575
Outpatient treatment (rest)	246	176	225	215	192	230	222	217	219	257	220
Medical aids	14	54	24	53	48	126	98	106	116	75	73

Please note that according to services of the DGUV sector (appendix 5) costs of medical aids are part of the outpatient treatment. In this figure medical aids are shown separately and subtracted from overall outpatient treatment costs.

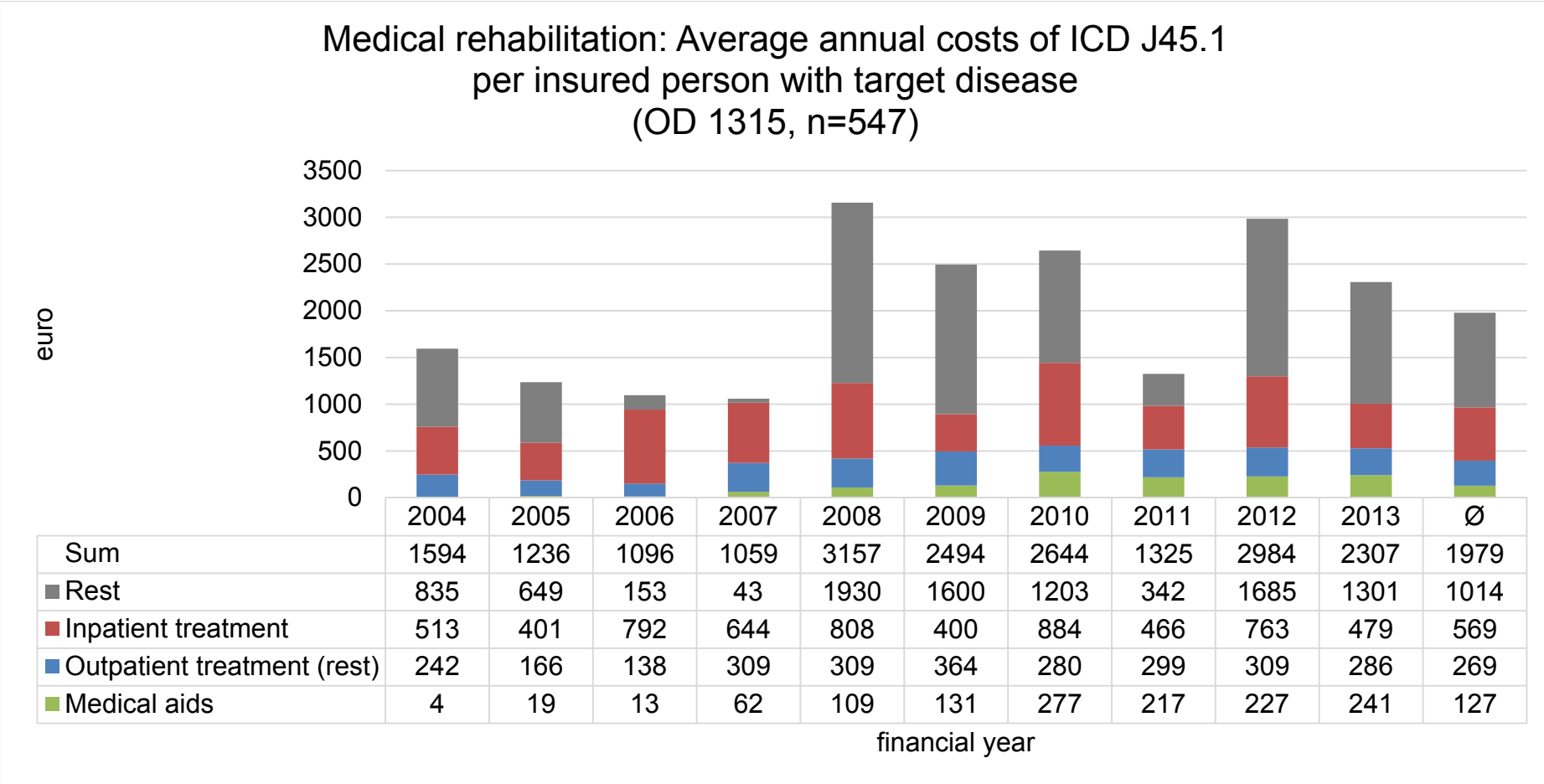


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	1680	1632	1975	2040	1429	2162	2923	1801	2162	1709	1960
Services for social and professional participation	9907	8576	8137	7532	8869	8759	8511	6389	9205	11026	8824
Pensions/compensations for the ill	7144	7277	6714	7157	6602	6397	6261	6409	6245	6480	6654
Survivors' benefits	8975	12925	12733	12472	12926	16790	16283	15196	15871	12324	13979

Appendix 7 Further DGUV results with regard to non-allergic asthma

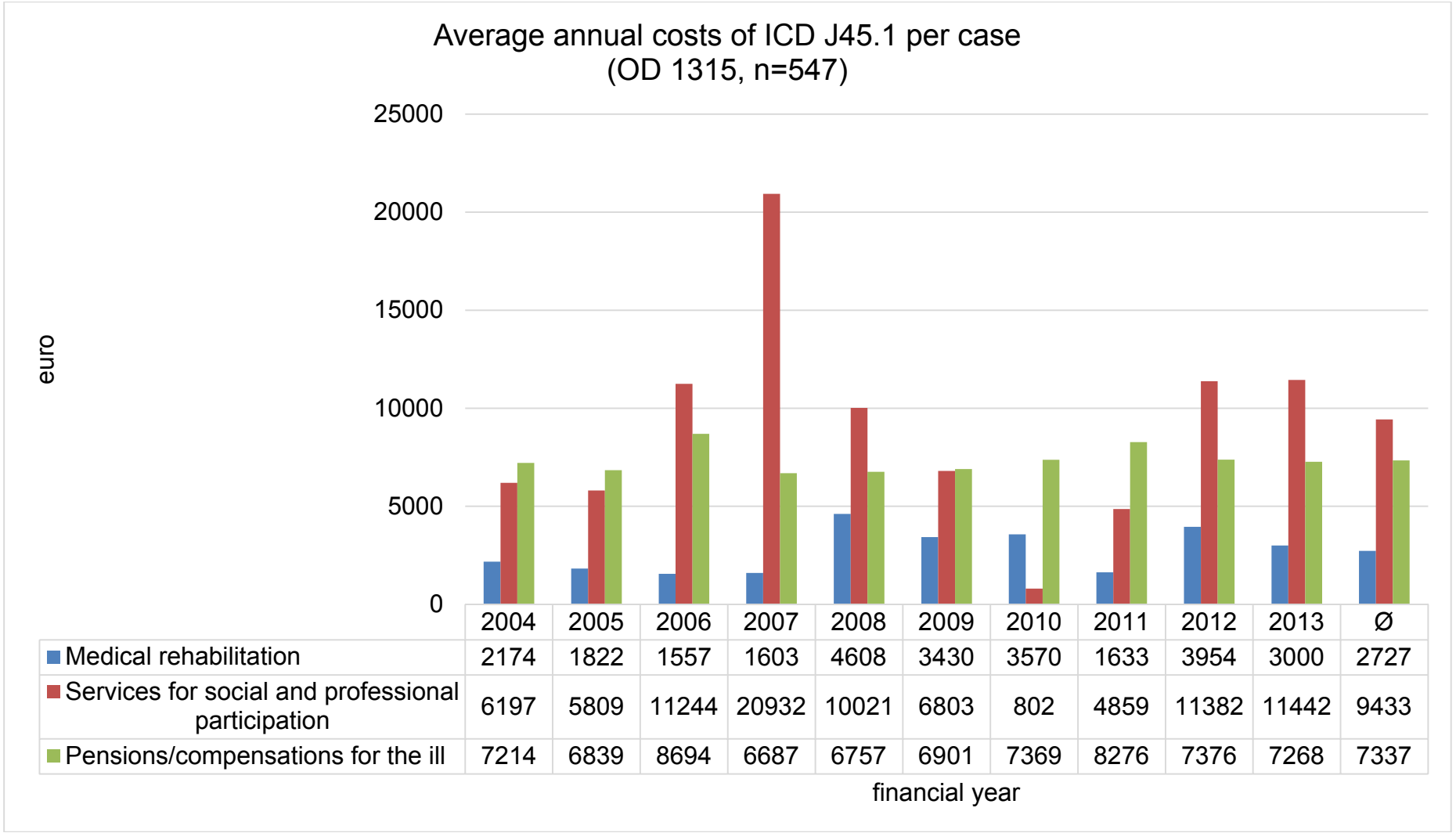


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Summe	8569	7854	10348	8695	9845	8892	9210	8847	9880	9397	9134
Pensions/compensations for the ill	6252	6028	8211	6056	6131	6274	6550	7339	6680	6430	6586
Services for social and professional participation	723	591	1041	1580	557	124	15	183	215	660	569
Medical rehabilitation	1594	1236	1096	1059	3157	2494	2644	1325	2984	2307	1979



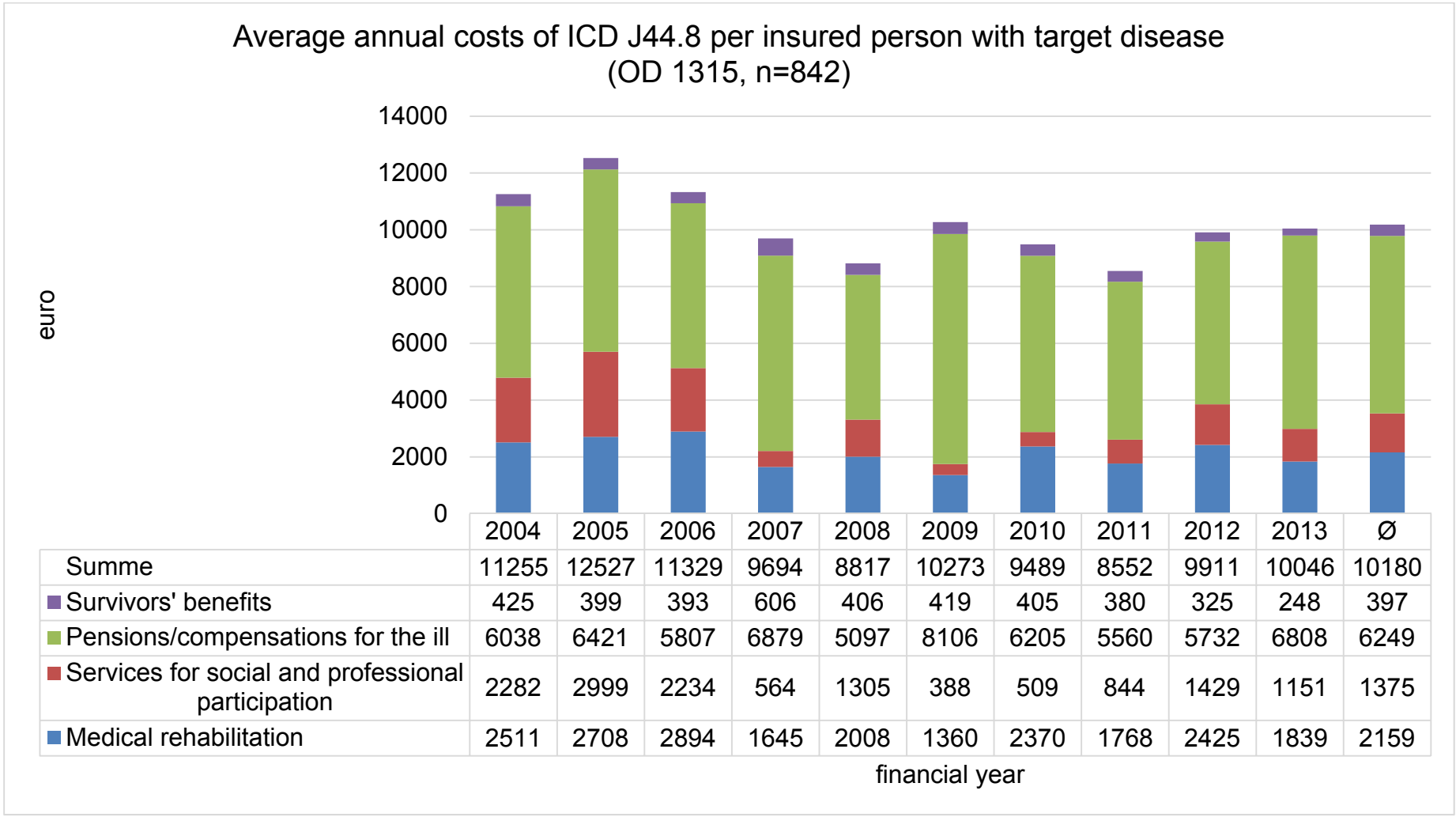
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	1594	1236	1096	1059	3157	2494	2644	1325	2984	2307	1979
Rest	835	649	153	43	1930	1600	1203	342	1685	1301	1014
Inpatient treatment	513	401	792	644	808	400	884	466	763	479	569
Outpatient treatment (rest)	242	166	138	309	309	364	280	299	309	286	269
Medical aids	4	19	13	62	109	131	277	217	227	241	127

Please note that according to services of the DGUV sector (appendix 5) costs of medical aids are part of the outpatient treatment. In this figure medical aids are shown separately and subtracted from overall outpatient treatment costs.

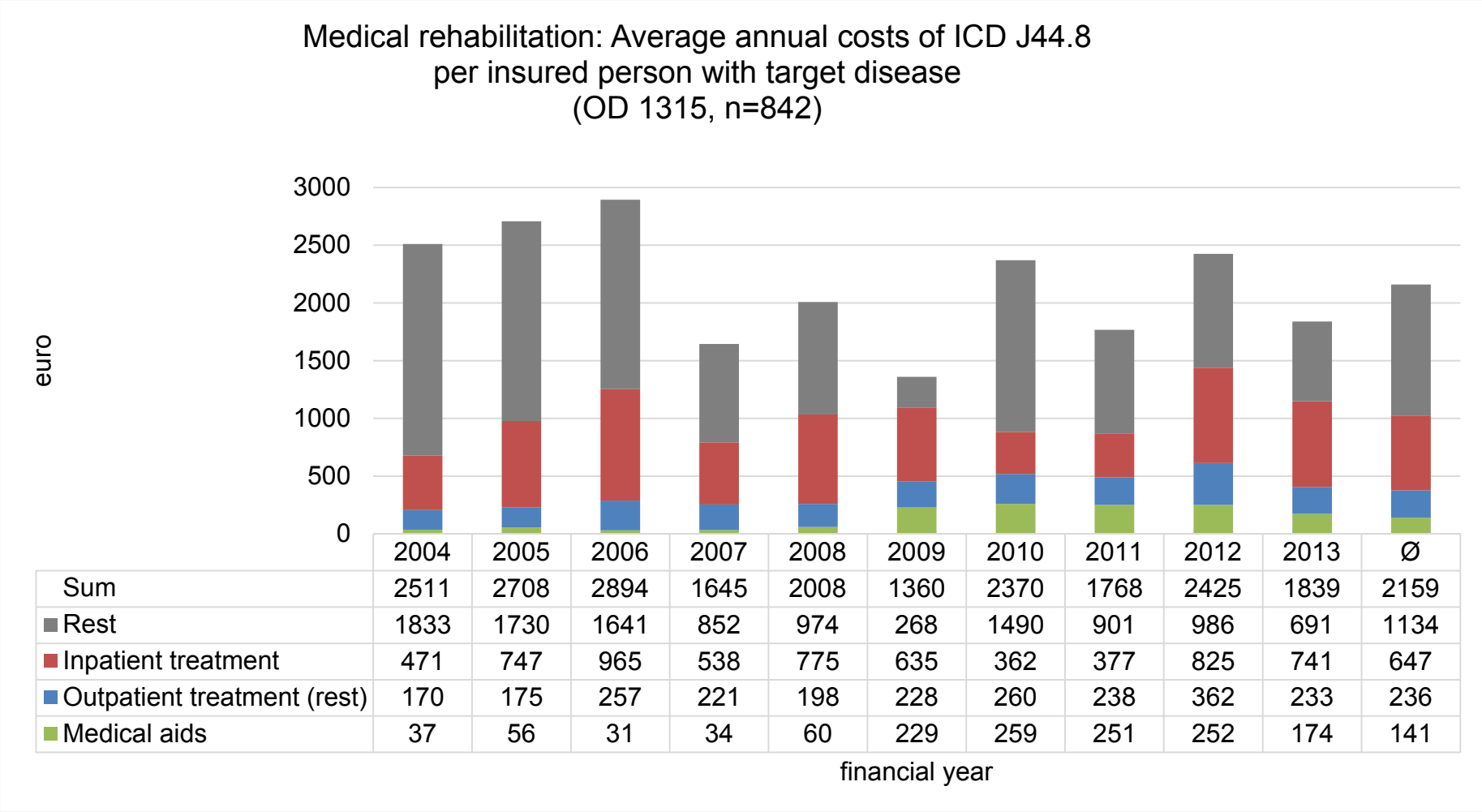


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	2174	1822	1557	1603	4608	3430	3570	1633	3954	3000	2727
Services for social and professional participation	6197	5809	11244	20932	10021	6803	802	4859	11382	11442	9433
Pensions/compensations for the ill	7214	6839	8694	6687	6757	6901	7369	8276	7376	7268	7337

Appendix 8 Further DGUC results with regard to COPD

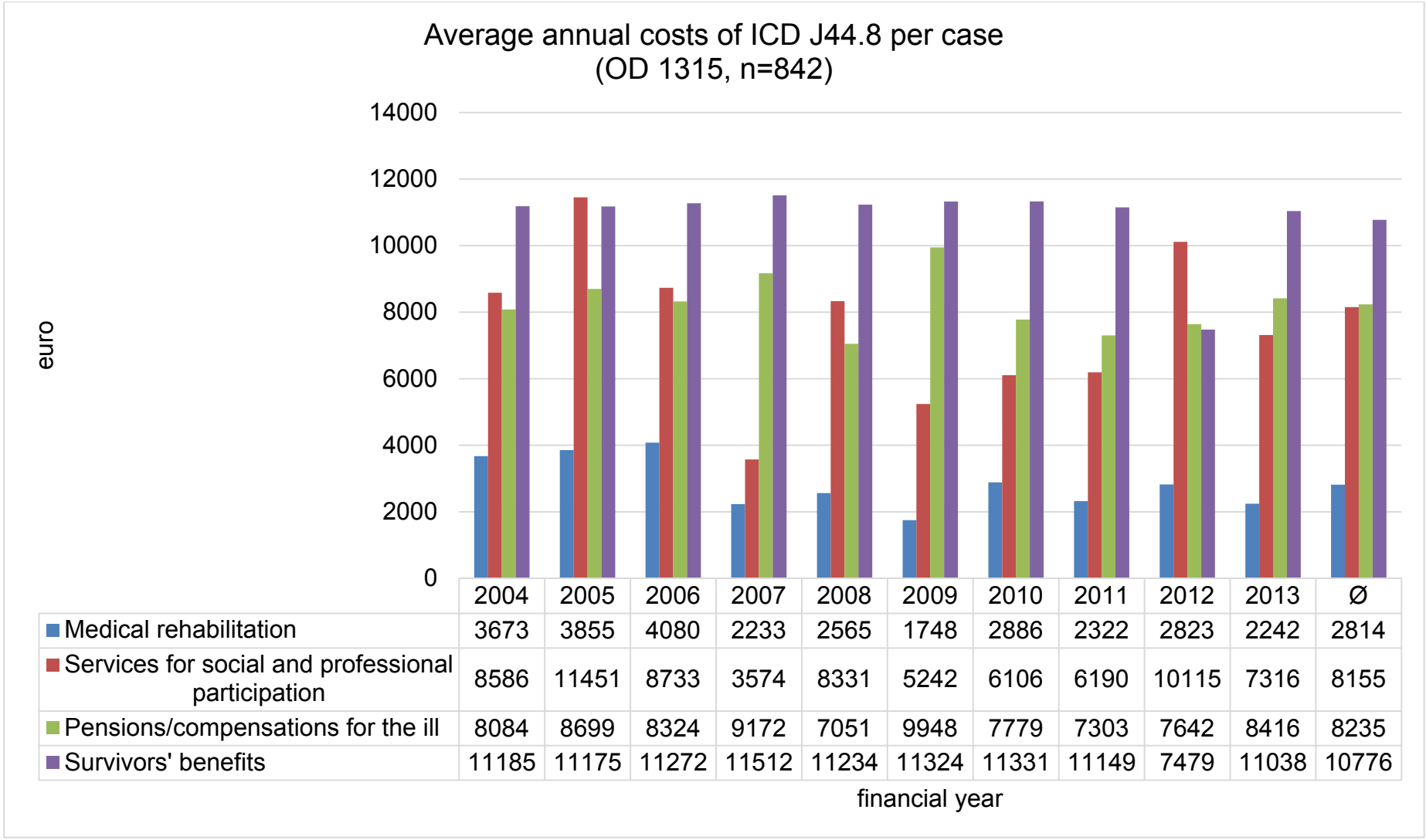


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Summe	11255	12527	11329	9694	8817	10273	9489	8552	9911	10046	10180
Survivors' benefits	425	399	393	606	406	419	405	380	325	248	397
Pensions/compensations for the ill	6038	6421	5807	6879	5097	8106	6205	5560	5732	6808	6249
Services for social and professional participation	2282	2999	2234	564	1305	388	509	844	1429	1151	1375
Medical rehabilitation	2511	2708	2894	1645	2008	1360	2370	1768	2425	1839	2159



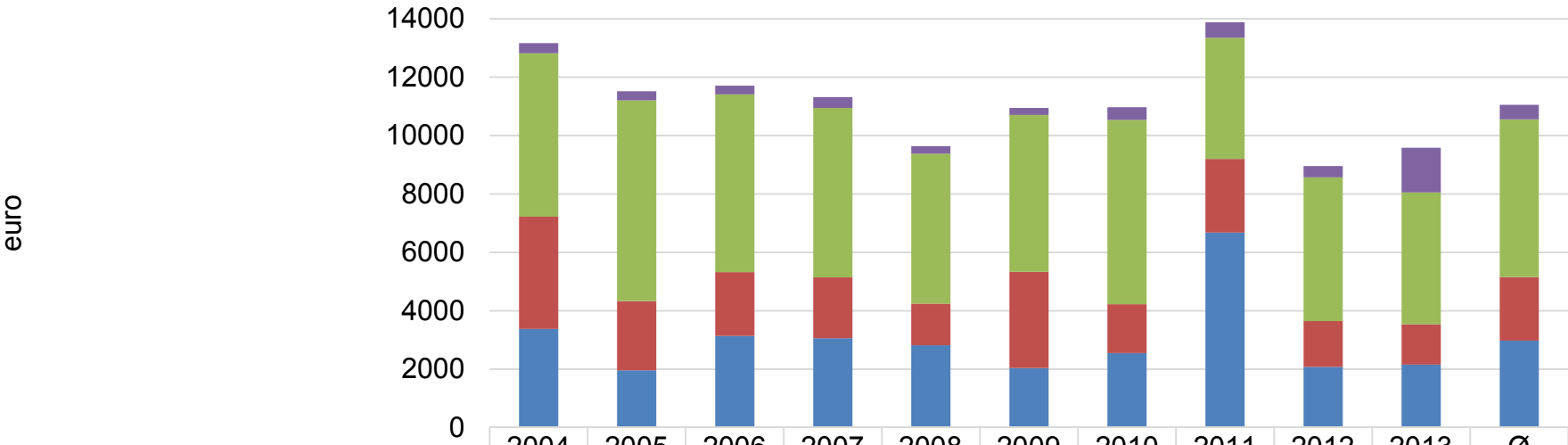
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	2511	2708	2894	1645	2008	1360	2370	1768	2425	1839	2159
Rest	1833	1730	1641	852	974	268	1490	901	986	691	1134
Inpatient treatment	471	747	965	538	775	635	362	377	825	741	647
Outpatient treatment (rest)	170	175	257	221	198	228	260	238	362	233	236
Medical aids	37	56	31	34	60	229	259	251	252	174	141

Please note that according to services of the DGUV sector (appendix 5) costs of medical aids are part of the outpatient treatment. In this figure medical aids are shown separately and subtracted from overall outpatient treatment costs.

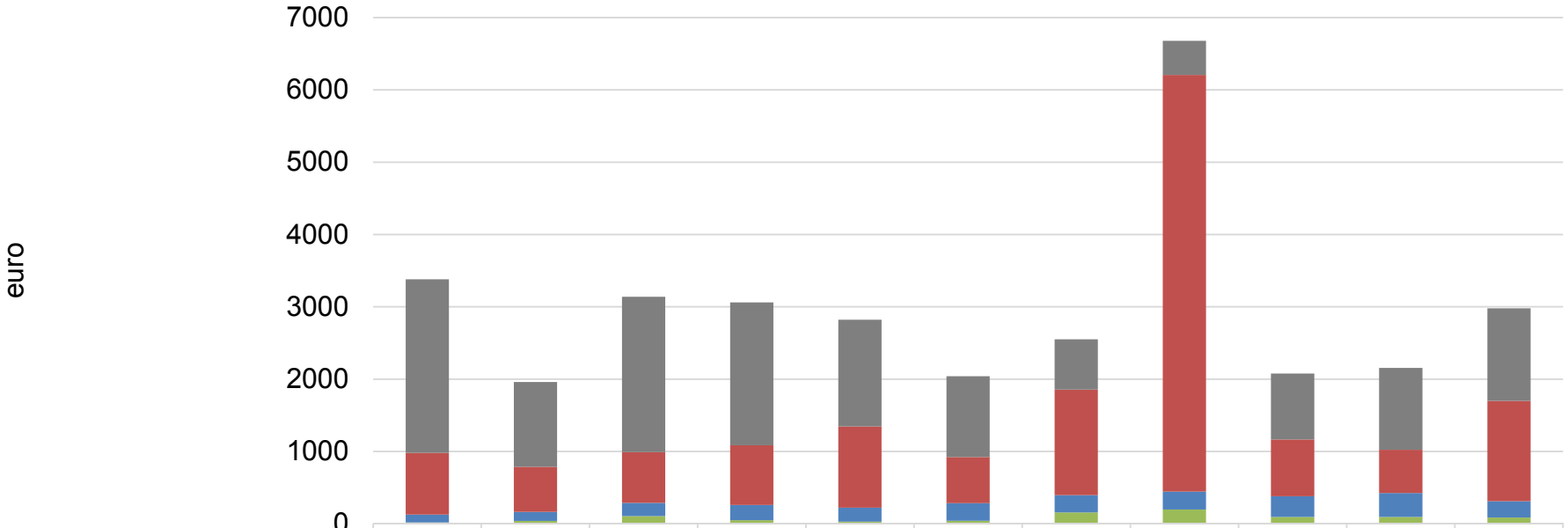


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	3673	3855	4080	2233	2565	1748	2886	2322	2823	2242	2814
Services for social and professional participation	8586	11451	8733	3574	8331	5242	6106	6190	10115	7316	8155
Pensions/compensations for the ill	8084	8699	8324	9172	7051	9948	7779	7303	7642	8416	8235
Survivors' benefits	11185	11175	11272	11512	11234	11324	11331	11149	7479	11038	10776

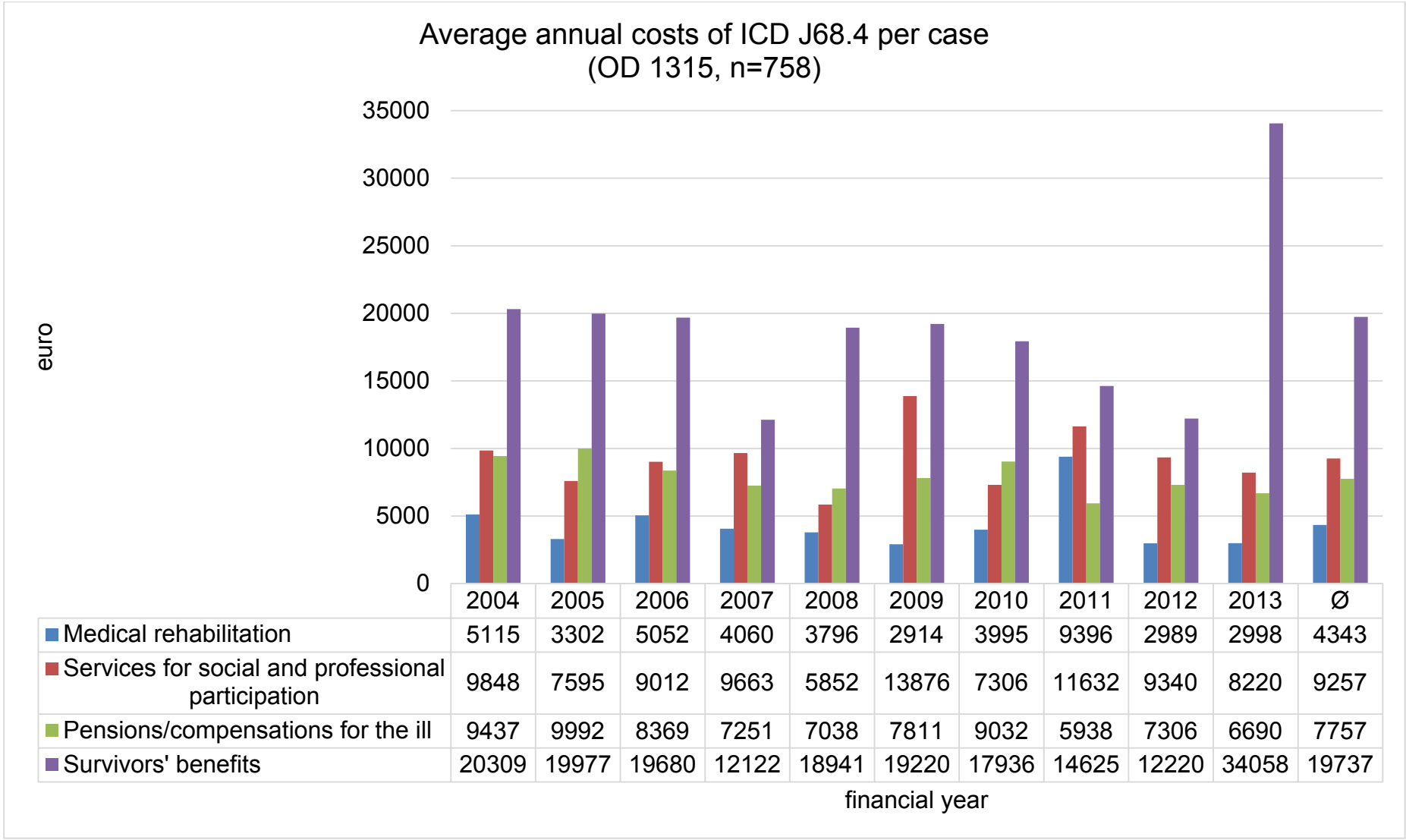
Appendix 9 Further DGUV results with regard to alveolitis



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	13163	11516	11707	11316	9636	10946	10967	13880	8957	9582	11051
Survivors' benefits	344	312	298	373	256	240	432	529	386	1531	495
Pensions/compensations for the ill	5598	6870	6086	5801	5136	5370	6311	4150	4922	4510	5403
Services for social and professional participation	3839	2373	2185	2081	1423	3296	1673	2523	1573	1385	2174
Medical rehabilitation	3381	1961	3138	3060	2821	2040	2551	6679	2077	2156	2979

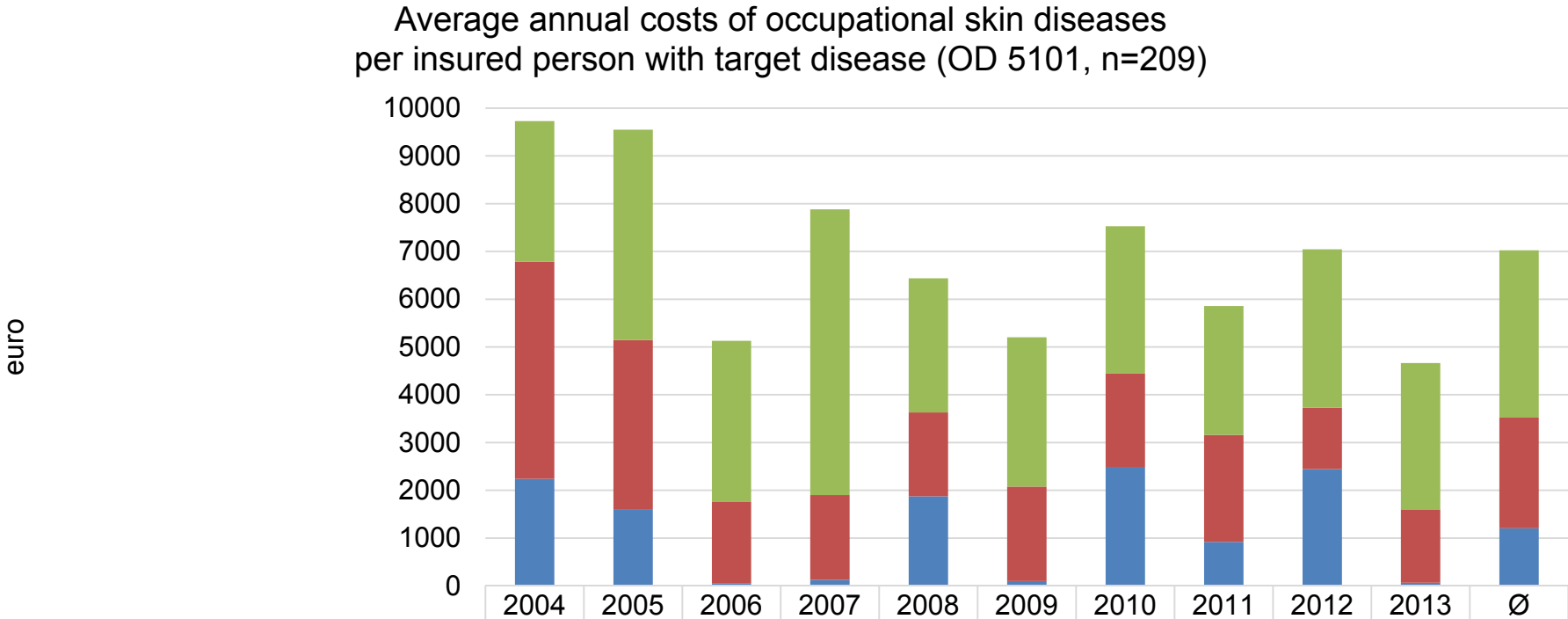


	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	3381	1961	3138	3060	2821	2040	2551	6679	2077	2156	2979
Rest	2400	1172	2148	1974	1475	1118	696	471	911	1132	1279
Inpatient treatment	853	624	701	826	1123	636	1458	5763	785	599	1387
Outpatient treatment (rest)	109	124	183	210	194	243	241	247	286	331	226
Medical aids	19	41	106	50	29	43	157	198	95	94	88



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Medical rehabilitation	5115	3302	5052	4060	3796	2914	3995	9396	2989	2998	4343
Services for social and professional participation	9848	7595	9012	9663	5852	13876	7306	11632	9340	8220	9257
Pensions/compensations for the ill	9437	9992	8369	7251	7038	7811	9032	5938	7306	6690	7757
Survivors' benefits	20309	19977	19680	12122	18941	19220	17936	14625	12220	34058	19737

Appendix 10 Further DGUV results with regard to occupational skin diseases



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Ø
Sum	9729	9548	5128	7880	6438	5204	7527	5857	7044	4665	6447
Pensions / compensations for the ill	2947	4404	3363	5979	2808	3128	3085	2699	3315	3066	3501
Services for social and professional participation	4544	3553	1716	1775	1755	1976	1953	2238	1286	1534	2318
Medical rehabilitation	2238	1591	49	127	1875	100	2490	920	2443	65	1204

Appendix 11 Further results for cost transfer to the EU-28 on case level

Average direct costs (medical rehabilitation, including "rest") of recognised occupational lung and skin diseases per case (DGUV) after adjustment to GDP PPP (non-modelling approach, in €, year 2013)

		Occupational lung diseases[2]				Lung diseases (OD 1315)[2]	Skin diseases (OD 5101)[1,2]
		Allergic bronchial asthma (ICD J45.0)	Non-allergic bronchial asthma (ICD J45.1)	Chronic obstructive bronchitis (ICD J44.8)	Extrinsic allergic alveolitis (ICD J68.4)		
Group 1	Belgium	1601.98	2812.14	2101.61	2810.27	2050.05	2986.49
	France	1457.96	2559.32	1912.67	2557.61	1865.74	2718.00
	Italy	1358.18	2384.17	1781.77	2382.58	1738.06	2531.99
	Greece	984.28	1727.81	1291.25	1726.66	1259.58	1834.94
	Spain	1261.55	2214.54	1655.00	2213.06	1614.40	2351.84
	Czech Republic	1122.91	1971.17	1473.12	1969.86	1436.98	2093.38
	Lithuania	997.51	1751.04	1308.61	1749.88	1276.51	1859.61
	Estonia	1016.29	1784.01	1333.25	1782.82	1300.54	1894.62
	Latvia	855.08	1501.02	1121.77	1500.02	1094.25	1594.09
	Cyprus	1209.99	2124.03	1587.36	2122.62	1548.42	2255.72
	Portugal	1072.43	1882.55	1406.90	1881.30	1372.38	1999.27
	Slovenia	1111.93	1951.90	1458.72	1950.60	1422.93	2072.92
Group 2	Bulgaria	622.98	1093.59	817.27	1092.86	797.22	1161.39
	Hungary	911.71	1600.42	1196.05	1599.36	1166.71	1699.65
	Croatia	826.65	1451.11	1084.46	1450.14	1057.86	1541.08
	Poland	927.05	1627.36	1216.18	1626.27	1186.34	1728.25
	Romania	743.38	1304.93	975.22	1304.06	951.30	1385.84
	Slovakia	1031.03	1809.87	1352.58	1808.67	1319.40	1922.09
	Malta	1129.66	1983.01	1481.97	1981.69	1445.62	2105.96
Group 3	Denmark	1698.05	2980.78	2227.64	2978.79	2172.99	3165.59
	Austria	1749.98	3071.94	2295.76	3069.89	2239.44	3262.40
	UK	1502.59	2637.67	1971.22	2635.92	1922.86	2801.21
	Netherlands	1812.65	3181.95	2377.98	3179.83	2319.64	3379.23
	Sweden	1729.23	3035.51	2268.53	3033.48	2212.88	3223.71
	Ireland	1818.74	3192.64	2385.97	3190.51	2327.43	3390.58
	Finland	1552.02	2724.44	2036.06	2722.62	1986.11	2893.35
	Luxembourg	3628.90	6370.21	4760.67	6365.96	4643.88	6765.16
	Germany	1709	3000	2242	2998	2187	3186
Mean (weighted)[3]		1373.25	2410.61	1801.53	2409.01	1757.34	2560.07
Median		1169.82	2053.52	1534.67	2052.15	1497.02	2180.84
Min		622.98	1093.59	817.27	1092.86	797.22	1161.39
Max		3628.90	6370.21	4760.67	6365.96	4643.88	6765.16
Standard deviation		314.88	552.75	413.09	552.38	402.95	587.02

Note: Base countries are marked in grey; Source: Own calculation based on DGUV-data for Germany

[1] Mean costs over the years 2004-2013 were used as basis for calculation

[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category

[3] Mean weighted according to population structure

Average direct costs (medical rehabilitation, including "rest") of recognised occupational lung and skin diseases per case (DGUV) after adjustment to Health PPP (non-modelling approach, in €, year 2013)

		Occupational lung diseases[2]				**Lung diseases (OD 1315)[2]**	**Skin diseases (OD 5101)[1,2]**
		Allergic bronchial asthma (ICD J45.0)	Non-allergic bronchial asthma (ICD J45.1)	Chronic obstructive bronchitis (ICD J44.8)	Extrinsic allergic alveolitis (ICD J68.4)		
Group 1	Belgium	1509.33	2649.51	1980.06	2647.74	1931.49	2813.77
	France	1462.49	2567.27	1918.60	2565.55	1871.54	2726.44
	Italy	1091.10	1915.33	1431.39	1914.06	1396.28	2034.08
	Greece	839.23	1473.20	1100.97	1472.22	1073.96	1564.54
	Spain	1027.90	1804.40	1348.48	1803.19	1315.40	1916.27
	Czech Republic	723.33	1269.75	948.93	1268.90	925.65	1348.47
	Lithuania	557.72	979.02	731.65	978.37	713.71	1039.72
	Estonia	546.90	960.03	717.46	959.39	699.86	1019.55
	Latvia	431.43	757.33	565.98	756.83	552.09	804.29
	Portugal	891.72	1565.34	1169.83	1564.29	1141.13	1662.39
	Slovenia	890.59	1563.34	1168.34	1562.30	1139.68	1660.27
Group2	Hungary	609.81	1070.47	800.00	1069.76	780.37	1136.84
	Poland	542.68	952.62	711.93	951.99	694.46	1011.69
	Slovakia	712.91	1251.45	935.25	1250.61	912.31	1329.04
Group 3	Denmark	1614.84	2834.71	2118.48	2832.82	2066.51	3010.47
	Austria	1614.74	2834.53	2118.34	2832.64	2066.37	3010.27
	UK	1147.21	2013.82	1505.00	2012.48	1468.08	2138.68
	Netherlands	1819.65	3194.24	2387.16	3192.11	2328.60	3392.28
	Sweden	1739.22	3053.04	2281.64	3051.01	2225.67	3242.33
	Finland	1220.65	2142.75	1601.35	2141.32	1562.07	2275.60
	Germany	1709	3000	2242	2998	2187	3186
Mean (weighted)[3]		1231.15	2161.18	1615.12	2159.74	1575.50	2295.17
Median		1027.90	1804.40	1348.48	1803.19	1315.40	1916.27
Min		431.43	757.33	565.98	756.83	552.09	804.29
Max		1819.65	3194.24	2387.16	3192.11	2328.60	3392.28
Standard deviation		384.56	675.05	504.49	674.60	492.11	716.91

Note: Base countries are marked in grey
[1] Mean costs over the years 2004-2013 were used as basis for calculation
[2] Basis for the calculation of direct costs: costs of medical rehabilitation including the residual category
[3] Mean weighted according to population structure
Source: Own calculation on the basis of data from the DGUV for Germany