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Regional disparities in the prevalence and incidence of type 2 diabetes mellitus and associated risk factors in Germany: Results from DIAB-CORE

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‘It needs to be better understood by the public, by policy makers,

and by medical scientists alike

that we can never be certain of anything.

Certainty is not a prerequisite for action.’

Geoffry Rose, Kay-Tee Khaw, Michael Marmot,
Rose’s Strategy of Preventive Medicine
Oxford University Press, USA; 1992.

Summary

Type 2 diabetes mellitus is one of the most challenging health problems for the next decades. The impact of type 2 diabetes mellitus on health care systems is largely driven by the increasing prevalence, the management of the disease and subsequent comorbidities, even in people with prediabetes or undiagnosed type 2 diabetes mellitus. An early detection of high risk groups is necessary to identify and modify risk factors such as obesity, physical inactivity or cigarette smoking which showed regional disparities in their distribution within a country. This leads to the assumption that there might be regional disparities regarding the prevalence and incidence of type 2 diabetes mellitus as well. For Germany as for other countries, comparable data on possible regional disparities in the prevalence and incidence of type 2 diabetes mellitus are missing.

The aim of the present dissertation is to estimate the prevalence and incidence of type 2 diabetes mellitus on regional level within Germany, and to estimate the smoking prevalence as a modifiable risk factor in individuals with type 2 diabetes mellitus using data from the Diabetes Collaborative Research of Epidemiologic Studies consortium (DIAB-CORE) within the Competence Net Diabetes in Germany. Well comparable data of five regional studies and one nationwide reference study are included: the Study of Health in Pomerania (SHIP); the Cardiovascular Disease, Living and Ageing in Halle Study (CARLA); the Dortmund Health Study (DHS); the Heinz Nixdorf Recall Study (HNR); the Cooperative Health Research in the Region of Augsburg Study (KORA); and the German National Health Interview and Examination Survey 1998 (GNHIES 98).

First, the prevalence of type 2 diabetes mellitus was estimated. Data from five regional population-based studies and one nationwide study conducted between 1997 and 2006 with participants aged 45 to 74 years were analyzed. Type 2 diabetes mellitus prevalence estimates based on self-reports (standardized to the German population for the regional studies, reference date 2007/12/31) were compared. Of 11,688 participants of the regional studies, 1,008 had a known type 2 diabetes mellitus, corresponding to a prevalence of 8.6% (95% confidence interval [CI] 8.1%-9.1%). The standardized prevalence was highest in the East with 12.0% (95% CI 10.3%-13.7%) and lowest in the South of Germany with 5.8% (95% CI 4.9%-6.7%).

Second, the incidence of type 2 diabetes mellitus was estimated. Data from participants (baseline age 45 to 74 years) from five regional population-based studies were included. The incidence rates per 1,000 person-years (95% CI) and the cumulative incidence (95% CI) from regional studies were directly standardized to the German population (reference date 2007/12/31) and weighted by inverse probability weights for losses to follow-up. Of 8,787 participants, 521 (5.9%) developed type 2 diabetes mellitus corresponding to an incidence rate of 11.8 per 1,000 person-years (95% CI 10.8-12.9). The incidence of known type 2 diabetes mellitus showed regional disparities within Germany. The incidence was highest in the East and lowest in the South of Germany with 16.9 (95% CI 13.3-21.8) vs. 9.0 (95% CI 7.4-11.1) per 1,000 person-years, respectively.

Third, the smoking prevalence in participants aged 20 to 79 years with type 2 diabetes mellitus in the regional SHIP and the nationwide GNHIES 98 was estimated. Prevalence estimates of cigarette smoking were calculated using weights reflecting the European adult population (reference date 2005/12/31). The overall prevalence of current smoking was lower among participants with type 2 diabetes mellitus than among participants without type 2 diabetes mellitus (17.3% vs. 38.0% in SHIP and 24.7% vs. 32.1% in GNHIES 98). In both studies, the prevalence of current smoking was highest in men aged 20 to 39 years, in particular among men with type 2 diabetes mellitus.

To conclude, considerable disparities in prevalence and incidence of type 2 diabetes mellitus indicate the need for interventions on the regional level within Germany. Former smoking was more prevalent among both men and women with type 2 diabetes mellitus in comparison to current and non-smoking. This finding probably reflects behavioural changes secondary to the disease onset and medical counselling. The finding that men aged 20 to 39 years with type 2 diabetes mellitus were more often current smokers than men without type 2 diabetes mellitus underpins the importance of smoking as one of the main modifiable risk factors for type 2 diabetes mellitus.

Zusammenfassung

Typ 2 Diabetes mellitus stellt eines der größten Gesundheitsprobleme für die nächsten Jahrzehnte dar. Die hohe Prävalenz des Typ 2 Diabetes mellitus sowie das erforderliche Management der Erkrankung, ihrer Vorstadien und Komorbiditäten bedingen eine immens große Belastung des Gesundheitssystems. Ein frühzeitiges Erkennen von Hochrisikogruppen ist wichtig, um bei modifizierbaren Risikofaktoren wie Übergewicht, Bewegungsmangel und Tabakkonsum intervenieren zu können. Diese Risikofaktoren weisen in ihrer Verteilung regionale Unterschiede innerhalb eines Landes auf. Dieses führt zu der Annahme, dass regionale Unterschiede hinsichtlich der Prävalenz und Inzidenz von Typ 2 Diabetes mellitus bestehen. Für Deutschland und für andere Länder fehlen weitestgehend Daten zu möglichen regionalen Unterschieden in der Prävalenz und Inzidenz von Typ 2 Diabetes mellitus.

Das Ziel dieser vorliegenden Dissertation besteht darin, die Prävalenz und Inzidenz von Typ 2 Diabetes mellitus auf regionaler Ebene innerhalb Deuschlands und die Prävalenz des Zigarettenrauchens als modifizierbaren Risikofaktor bei Personen mit Typ 2 Diabetes mellitus zu schätzen. Dazu wurden Daten des DIAB-CORE Verbundes (Diabetes Collaborative Research of Epidemiologic Studies) innerhalb des Kompetenznetz Diabetes in Deutschland analysiert. Es wurden vergleichbare Daten von fünf regionalen Studien und einer bundesweiten Referenzstudie eingeschlossen: die Study of Health in Pomerania (SHIP); die Cardiovascular Disease, Living and Ageing in Halle Studie (CARLA); die Dortmund Health Study (DHS); die Heinz Nixdorf Recall Studie (HNR); die Cooperative Health Research in the Region of Augsburg Studie (KORA); und der German National Health Interview and Examination Survey 98 (GNHIES 98).

Zunächst wurde die Prävalenz des Typ 2 Diabetes mellitus basierend auf der Selbstauskunft der Teilnehmer geschätzt. Die Prävalenzschätzungen des Typ 2 Diabetes mellitus im Altersbereich von 45 bis 74 Jahren wurden auf die deutsche Bevölkerung standardisiert (Referenzdatum 31.12.2007). Von allen 11.688 Teilnehmern der regionalen Studien hatten 1.008 Teilnehmer einen prävalenten Typ 2 Diabetes mellitus. Dies entspricht einer standardisierten Prävalenz von 8,6% (95% Konfidenzintervall [KI] 8,1%-9,1%). Die standardisierte Prävalenz war im Osten Deutschlands mit 12,0% (95% KI 10,3%-13,7%) am höchsten und im Süden Deutschlands mit 5,8% (95% KI 4,9%-6,7%) am niedrigsten.

Des Weiteren wurde die Inzidenz des Typ 2 Diabetes mellitus basierend auf der Selbstauskunft der Teilnehmer geschätzt. Die Inzidenzraten pro 1000 Personenjahre (95% KI) und die kumulative Inzidenz (95% KI) im Altersbereich von 45 bis 74 Jahren wurden auf die deutsche Bevölkerung standardisiert (Referenzdatum 31.12.2007) und mittels inverser Wahrscheinlichkeiten für Lost to follow up gewichtet. Von 8.787 Teilnehmern entwickelten 521 (5,9%) einen Typ 2 Diabetes mellitus. Dies entspricht einer Inzidenzrate von 11,8 pro 1000 Personenjahre (95% KI 10,8-12,9). Die Inzidenz des Typ 2 Diabetes mellitus zeigte regionale Unterschiede innerhalb Deutschlands. Die Inzidenz war im Osten Deutschlands am höchsten (16,9 pro 1000 Personenjahre; 95% KI 13,3-21,8) und im Süden am niedrigsten (9,0 pro 1000 Personenjahre; 95% KI 7,4-11,1).

Weiterhin wurde die Raucherprävalenz von Teilnehmern im Alter von 20 bis 79 Jahren mit Typ 2 Diabetes mellitus in der regionalen Studie SHIP und dem bundesweiten GNHIES 98 geschätzt. Die Schätzungen der Raucherprävalenz wurden entsprechend der Europäischen Standardbevölkerung (Referenzdatum 31.12.2005) ermittelt. Die Gesamtprävalenz aktueller Raucher war bei Teilnehmern mit Typ 2 Diabetes mellitus geringer im Vergleich zu Teilnehmern ohne Typ 2 Diabetes mellitus (17,3% vs. 38,0% in SHIP und 24,7% vs. 32,1% in GNHIES 98). In beiden Studien war die Prävalenz des aktuellen Rauchens bei Männern im Alter von 20 bis 39 Jahren am höchsten, insbesondere bei Teilnehmern mit Typ 2 Diabetes mellitus.

Zusammenfassend bestehen in Deutschland erhebliche regionale Unterschiede in der Prävalenz und Inzidenz von Typ 2 Diabetes mellitus. Hieraus ergibt sich die Notwendigkeit regionalspezifischer Interventionen. Früheres Rauchen war bei Männern und Frauen mit Typ 2 Diabtes melliuts häufiger prävalent als aktuelles Rauchen und Nichtrauchen. Das Resultat spiegelt Verhaltensänderungen als Effekt der Erkrankung oder einer medizinischen Beratung wider. Jüngere Männer im Alter von 20 bis 39 Jahren mit Typ 2 Diabetes mellitus waren allerdings häufiger aktuelle Raucher als männliche Nicht-Diabetiker. Dieses Ergebnis unterstreicht die Bedeutung des Tabakkonsums als einen wichtigen modifizierbaren Risikofaktor für Typ 2 Diabetes mellitus.

Content

List of Abbreviations

CARLA	Cardiovascular Disease Living and Aging in Halle
CI	Confidence intervall
DEGS1	German Health Interview and Examination Survey for Adults
DHS	Dortmund Health Study
GNHIES 98	German National Health Interview and Examination Survey 1998
HNR	Heinz Nixdorf Recall Study
KORA	Cooperative Health Research in the Region of Augsburg
SHIP	Study of Health in Pomerania

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1. Introduction

Over the past century, non-communicable diseases have replaced infectious diseases as the leading contributor to morbidity and mortality in the developed countries (1). As a result of this epidemiological transition, type 2 diabetes mellitus that historically used to be a rare condition shifted to one of the most common non-communicable diseases worldwide. Consequently, type 2 diabetes mellitus will be one of the most challenging health problems for the next decades (2).

In 2012, the International Diabetes Federation estimated that more than 371 million people worldwide had diabetes mellitus (2) corresponding to a global prevalence estimate of 8.3% in the general population (aged 20 to 79 years). The global regional prevalence ranged from 4.3% in Africa, 6.7% in Europe, 10.5% in North America and Carribbean to 10.9% in the Middle East and North Africa (3).

The impact of type 2 diabetes mellitus on health care systems is largely driven by the management of the disease and subsequent comorbidities including micro- and macrovascular complications (4). Even prediabetes carries a substantial risk for type 2 diabetes mellitus and associated comorbidities. Hence, the increase of the risk for morbidity and mortality starts many years before type 2 diabetes mellitus is diagnosed (5).

Given the large number of people with prediabetes or undiagnosed type 2 diabetes mellitus, the latter was estimated with about 50% of the prevalent cases (3, 6), an early detection of high risk groups is necessary to face the task of changing modifiable risk factors such as obesity, physical inactivity or cigarette smoking.

It has been reported that risk factors for type 2 diabetes mellitus such as obesity, the metabolic syndrome or smoking show regional disparities in their distribution within a country (7-11). This leads to the assumption that there might be regional disparities regarding the prevalence and incidence of type 2 diabetes mellitus as well. For Germany as for other countries, comparable data on possible regional disparities in the prevalence and incidence of type 2 diabetes mellitus are missing.

The present dissertation provides insight into regional disparities in the prevalence and incidence of type 2 diabetes mellitus in Germany including data from the Diabetes Collaborative Research of Epidemiologic Studies consortium (DIAB-CORE) which is part of the German Diabetes Competence Net. Further, the present work provides estimates on the prevalence of cigarette smoking as a risk factor for the development of type 2 diabetes mellitus.

1.1 Regional prevalence of type 2 diabetes mellitus in Germany

The International Diabetes Federation provides annually information regarding the worldwide prevalence of type 2 diabetes mellitus including both known and unknown cases (12). In 2009, the reported prevalence estimate for Germany was 12.0%. This prevalence comprised estimates from three different sources such as health insurance data (age <39 to 90 years), population-based data (age 55 to 74 years), and patient data (age 18 to 99 years) (13). The standardized prevalence estimates were 7.9%, 8.1%, and 11.8%, respectively. To report one estimate for the whole country, the International Diabetes Federation uses different correction factors, depending on the applied criteria for defining type 2 diabetes mellitus varying from self-report to oral glucose tolerance test (13). In 2012, the reported prevalence estimate for Germany was only 8.4% (12) in comparison to 12.0% in 2009. This lower prevalence may be a result of a real decrease in incidence or may be caused by methodological issues such as the consideration of different correction factors referring to the underlying data sources.

In Germany, several studies were performed to provide prevalence estimates for type 2 diabetes mellitus. Data sources include nationwide surveys, regional data, registry data, health insurance data and patient data (14). In 2012, the German Health Interview and Examination Survey in Adults (DEGS1; 2008 to 2011) reported that 7.2% (4.6 million) adults in the age of 18 to 79 years had type 2 diabetes mellitus based on self reports. In contrast, the German National Health Interview and Examination Survey 1998 (GNHIES 98; 1997 to 1998) reported a prevalence of 5.2%. Regarding regional prevalence estimates for type 2 diabetes mellitus, the DEGS1 reported prevalence estimates of 6.7% for the Northern, 7.6% for the Central, 6.3% for the Southern, and 8.1% for the Eastern part of Germany (14). The definition of the regions in these three surveys (15), however, was only rough and arbitrary and, consequently, only provides a crude overview of regional disparities in the diabetes prevalence.

Reliable and comparable data with respect to study design and methodological issues are required to explore the disparities in prevalence estimates between different regions of Germany. Due to the lack of comparability between the available studies, the DIAB-CORE consortium has been established within Germany including population-based studies of similar design and methods.

1.2 Regional incidence of type 2 diabetes mellitus in Germany

As for other countries, data on regional incidence estimates in Germany are scarce encompassing registry data and data from one population-based study, the Cooperative Health Research in the Region of Augsburg (KORA) (6).

The Karlsburg registry, a worldwide unique data collection on the prevalence and incidence of diabetes mellitus, was established in the former German Democratic Republic (East Germany). This registry covered the period from 1960 to 1989 and represented approximately 98% of all cases in the German Democratic Republic (16). After the German re-unification, the data collection had not been continued. Data from the Karlsburg registry demonstrated an increase in type 2 diabetes mellitus incidence from 1.0% to 3.6% in the time period from 1960 to 1984 (17). At the end of the 1980s, the incidence of type 2 diabetes mellitus was 12.0 per 1,000 person-years showing an age-dependent incidence with the highest rates in individuals aged 60 years and older (18). Regarding population-based data, only the KORA study provided regional data on the incidence of type 2 diabetes mellitus for the South of Germany in 2009. The incidence of type 2 diabetes mellitus was estimated in participants aged 55 to 74 years and was based on validated physicians' diagnosis or an oral glucose tolerance test (19). This study demonstrated a standardized incidence rate of 15.5 per 1,000 person-years, which was among the highest in Europe (19).

Current data on the incidence of type 2 diabetes mellitus on a regional level are entirely not available so far. To estimate regional incidence, it is essential to compare data from longitudinal population-based studies using similar study design and methods as provided by data from the DIAB-CORE consortium.

1.3 Risk factors for type 2 diabetes mellitus

Remarkable progress has been made in identifying risk factors to prevent or delay type 2 diabetes mellitus. Because type 2 diabetes mellitus is multifactorial, the risk is probably caused by both non-modifiable and modifiable factors. The most notable risk factors that might influence the development of type 2 diabetes mellitus are illustrated in Table 1 (20, 21). This present dissertation is focussing on modifiable risk factors.

Table 1: Risk factors for type 2 diabetes mellitus (20, 21)

Non-modifiable risk factors	Modifiable risk factors
Age	Overweight / Obesity
Race & Ethnicity	High blood glucose
Sex	Hypertension
Family history	Abnormal lipid metabolism
	Inflammation & Hyper-coagulation
	Physical inactivity
	Smoking

Smoking habits belong to the most cited modifiable risk factors for type 2 diabetes mellitus. There is evidence from observational studies that cigarette smoking is associated with the development of type 2 diabetes mellitus (22-25) which is addressed in the subsequent section.

1.3.1 Smoking prevalence in type 2 diabetes mellitus

A meta-analysis showed that there is a dose-response relationship between the frequency of cigarette smoking and incidence of type 2 diabetes mellitus (26). While the relative risk for heavy smokers (≥20 cigarettes/day) was 1.6 (95% confidence interval [CI] 1.4-1.8), it was 1.3 (95% CI 1.1-1.5) for lighter smokers (<20 cigarettes/day), and 1.2 (95% CI 1.1-1.3) for former smokers compared to never smokers. It has been demonstrated that smoking cessation increases insulin sensitivity and improves lipoprotein profiles (23, 27-29) suggesting that the smoking-related risk of type 2 diabetes mellitus is reversible in individuals who quit smoking (30). Data from a large prospective cohort study in the United States demonstrated that quitting smoking reduced the risk of developing type 2 diabetes mellitus to that of non-smokers after five years in women and after ten years in men (31).

In Germany, urban and rural disparities in cigarette smoking have been found (9). Even though cigarette smoking is already known as a risk factor for type 2 diabetes mellitus, epidemiological data on smoking prevalence in individuals with type 2 diabetes mellitus in Germany are missing.

In order to improve the basis for prevention and control programs it is important to gain insight into the smoking prevalence in individuals with type 2 diabetes mellitus and without type 2 diabetes mellitus.

1.4 Aims of the Studies

The following three aims of the present dissertation have been derived from the background information presented above. Data from the DIAB-CORE consortium were analysed resulting in three scientific publications as basis for the present dissertation.

Aim 1: To provide population-based estimates on the prevalence of self-reported type 2 diabetes mellitus on the regional level in Germany. The research question of the study conducted for that purpose (study 1) was: Are there regional disparities in the prevalence of type 2 diabetes mellitus within Germany?

This question was answered within this scientific paper:

> Schipf S, Werner A, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Berger K, Mueller G, Moebus S, Bokhof B, Kluttig A, Greiser KH, Neuhauser H, Ellert U, Icks A, Rathmann W, Volzke H. Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium). Diabet Med. 2012; 29(7):e88-95.

Aim 2: To provide population-based estimates on the incidence of self-reported type 2 diabetes mellitus on the regional level in Germany. The research question of the study conducted for that purpose (study 2) was: Are there regional disparities in the incidence of type 2 diabetes mellitus within Germany?

This question was answered within this scientific paper:

> Schipf S, Ittermann T, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Berger K, Mueller G, Moebus S, Slomiany U, Kluttig A, Greiser KH, Icks A, Rathmann W, Völzke H. Regional differences in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium). Epidemiol Community Health. Under review.

Aim 3: To provide population-based data on the prevalence of cigarette smoking in individuals with type 2 diabetes mellitus compared to individuals without type 2 diabetes mellitus in Germany. The research question of the study conducted for that purpose (study 3) was: Are there disparities in the smoking prevalence between individuals with type 2 diabetes mellitus compared to individuals without type 2 diabetes mellitus?

This question was answered within this scientific paper:

> Schipf S, Schmidt CO, Alte D, Werner A, Scheidt-Nave C, John U, Steveling A, Wallaschofski H, Völzke H. Smoking prevalence in type 2 diabetes: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES). Diabet Med. 2009; 26(8):791-7.

2. Material and Methods

All data for the present dissertation were derived from studies within the DIAB-CORE consortium (Table 2).

2.1 Diabetes Collaborative Research in Epidemiologic Studies (DIAB-CORE)

The DIAB-CORE consortium is a subproject of the Competence Net Diabetes in Germany (32). The main focus of the Competence network is to improve translation of research results into medical practice. The DIAB-CORE consortium established a central structure for pooling and analysing epidemiological data to investigate current research questions related to type 2 diabetes mellitus. DIAB-CORE is unique within Europe because it combines data of relevant population-based prospective studies throughout Germany using comparable standardized assessments of diabetes and other characteristics (32).

Data from five regional studies and one nationwide reference study are included in the present dissertation (Figure 1) (30, 33, 34):

- Northeast: the Study of Health in Pomerania (SHIP), Mecklenburg West Pomerania
- East: the Cardiovascular Disease, Living and Ageing in Halle Study (CARLA) in the city of Halle, Saxony-Anhalt
- West: the Dortmund Health Study (DHS) in the city of Dortmund, North Rhine-Westphalia; and the Heinz Nixdorf Recall Study (HNR) in the cities of Essen, Bochum and Mülheim of the Ruhr-Area, North Rhine-Westphalia
- South: the Cooperative Health Research in the Region of Augsburg Study (KORA) in the city of Augsburg and surrounding rural districts, Bavaria
- Nationwide: the German National Health Interview and Examination Survey 1998 (GNHIES 98)

Detailed information on these studies regarding baseline and follow-up characteristics are displayed in Table 2. In this context, the terms East and West are rather not used in the sense of mere cardinal directions but to refer to the northeastern territory of the former German Democratic Republic (East Germany) and to the southwestern states of the Federal Republic of Germany (West Germany) (33, 34).

Data collection was performed between 1997 and 2006. All studies were approved by local ethics committees and public data protection agencies. Informed written consent was obtained from all participants. All studies were monitored by review boards of independent scientists (30, 33, 34).

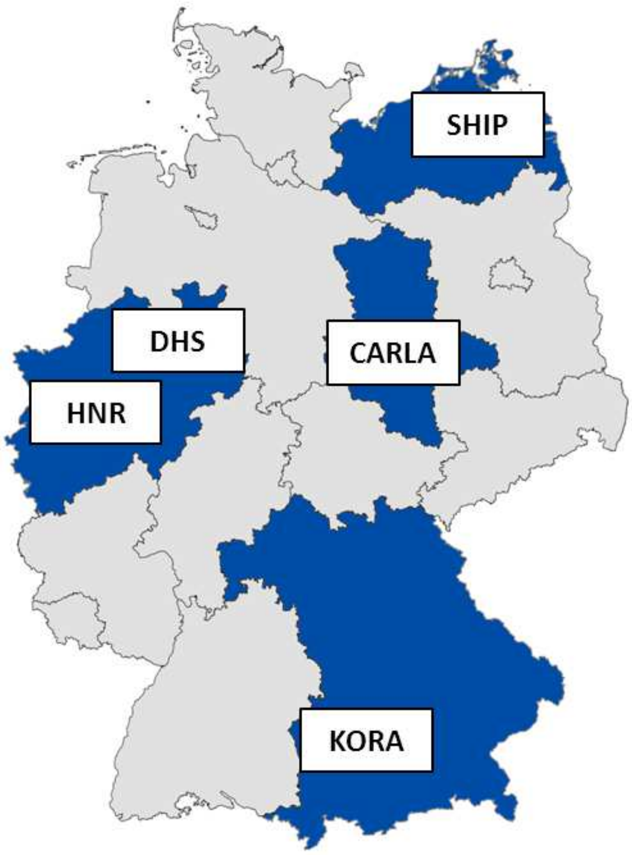

Figure 1: Five regional studies within the DIAB-CORE consortium, Geodata used for figures were provided by the German Federal Agency for Cartography and Geodesy, scale of 1:3,500,000

Table 2: Baseline and follow-up characteristics by studies in the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE)* (33, 34)

			Baseline		1. Follow-up			
Study	**Region**	**Sampling**	**Study-Period**	**N (response in %)**	**Study-Period**	**N (response in %)**	**Mean follow-up**	**Age range**
SHIP	Northeast	Two-stage Cluster-Sample	1997-2001	4,308 (69)†	2002-2006	3,300 (84)	5.0	20-79
CARLA	East	Stratified Random Sample	2002-2006	1,779 (64)	2007-2010	1,436 (86)	4.0	45-83
DHS	West	Stratified Random Sample	2003-2004	1,312 (67)	2006-2008	1,122 (86)	2.2	45-74
HNR	West	Stratified by City, Random Sample	2000-2003	4,814 (56)	2006-2008	4,157 (90)	5.1	25-74
KORA	South	Two-stage Cluster-Sample	1999-2001	4,261 (67)	2006-2008	3,080 (80)	7.1	25-74
GNHIES 98	Nationwide	Stratified Random Sample	1997-1999	7,124 (61)	n. a.	n. a.	n. a.	18-79

SHIP = Study of Health in Pomerania (35), CARLA = Cardiovascular Disease, Living and Ageing in Halle (36), DHS = Dortmund Health Study (37), HNR = Heinz Nixdorf Recall Study (38), KORA = Cooperative Health Research in the Region of Augsburg (6),
GNHIES 98 = German National Health Interview and Examination Survey 1998 (39)
n.a. = not available
*only participants aged 45 to 74 years at baseline were included to enhance comparability
†the baseline population for study 3 refered to 4,310 participants

2.2 Study population

The study population included in the present dissertation consisted of five regional population-based studies and one nationwide study within DIAB-CORE in Germany is illustrated in Table 3.

Table 3: Overview of the study population within DIAB-CORE included in each analysis of the present dissertation

	Study 1	Study 2	Study 3
Regional Studies			
SHIP	x	x	x
CARLA	x	x	
DHS	x	x	
HNR	x	x	
KORA	x	x	
Nationwide Study			
GNHIES 98	x		x

2.2.1 Study 1: Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium)

Altogether, this pooled analysis comprised 23,598 participants of five regional studies and one nationwide reference study. To enhance comparability, only the group of participants aged 45 to 74 years old was included. Participants with unclear diabetes status (n=1) and possible cases of type 1 diabetes mellitus (n=28) were excluded. Thus, the final study population consisted of 15,071 participants (7,581 women) (33).

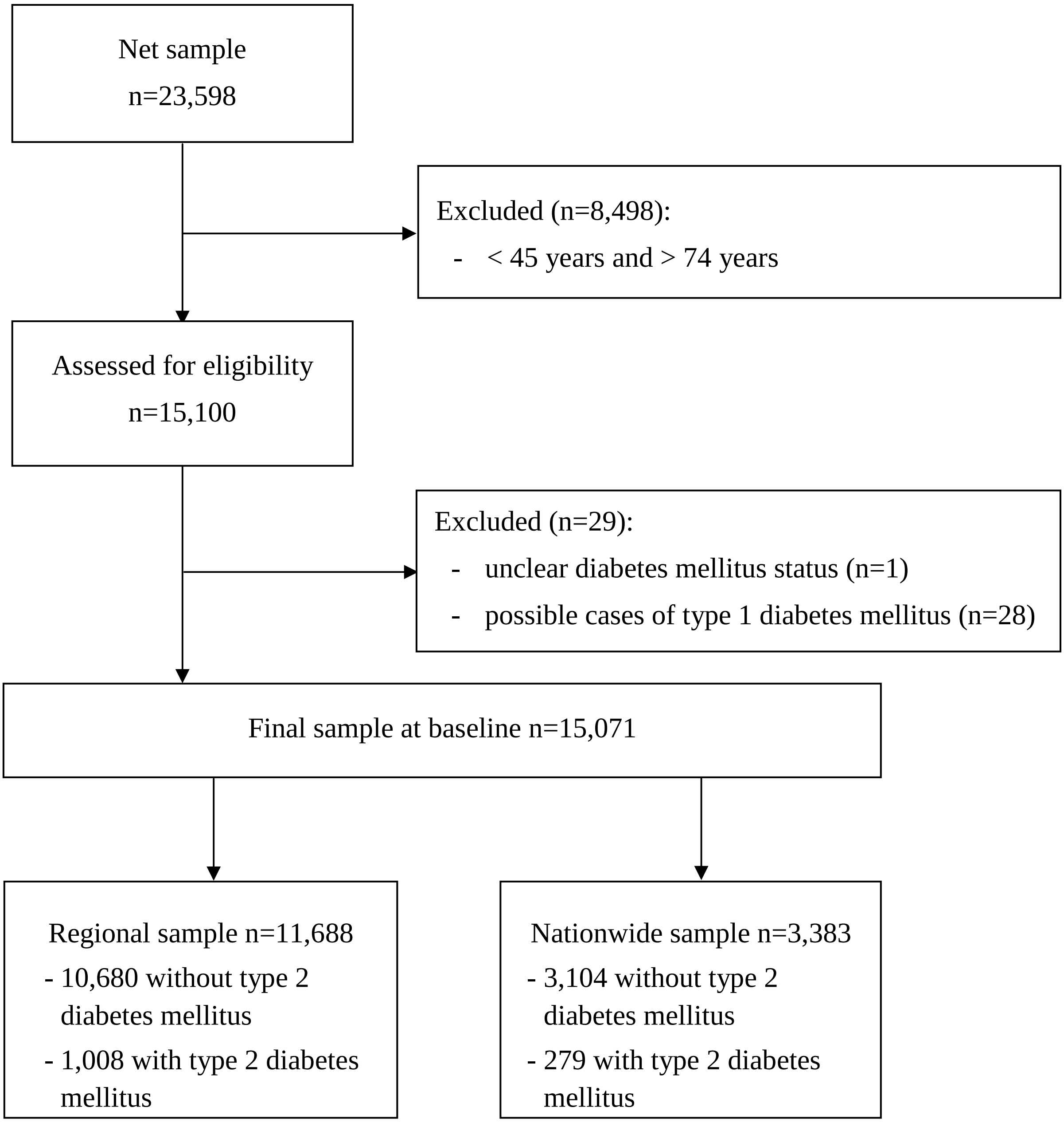

Figure 2: Flow chart of the sample recruitment in study 1

2.2.2 Study 2: Regional differences in the incidence of known type 2 diabetes mellitus in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

To enhance comparability, this pooled analysis comprised 11,688 participants aged 45 to 74 years at baseline from the five regional studies. From 11,688 participants (5,832 women), individuals who did not participate in the follow-up studies (n=2,015), with known type 2 diabetes mellitus at baseline (n=731), missing data on drop out weights (n=53) or missing data on diabetes status at follow-up (n=101) were excluded. Thus, the final study population consisted of 8,788 participants (4,475 women) (34).

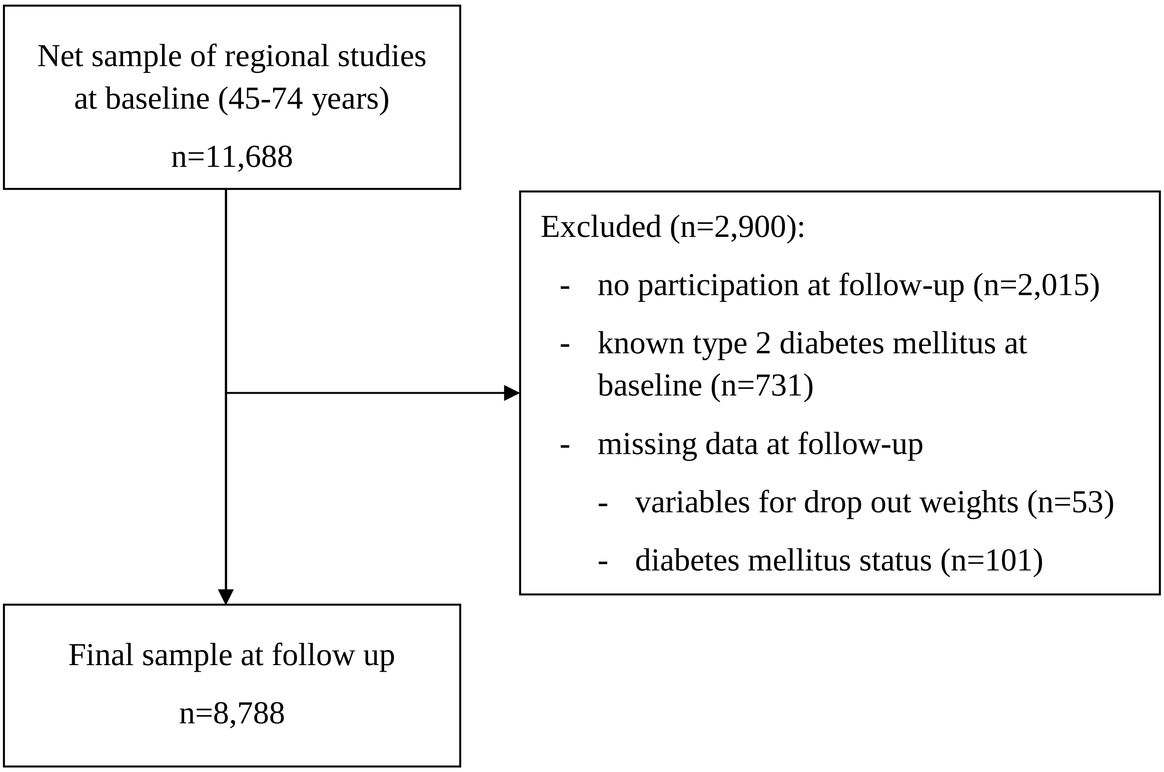

Figure 3: Flow chart of the sample recruitment in study 2

2.2.3 Study 3: Smoking prevalence in type 2 diabetes mellitus: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

The SHIP population comprised of 4,310 participants. Participants with type 1 diabetes mellitus (n=8) and without information on smoking status (n=19) were excluded. Thus, the final study population consisted of 4,283 participants (2,181 women), of which 339 participants with type 2 diabetes mellitus and 3,944 participants without type 2 diabetes mellitus (30).

The GNHIES 98 population comprised of 7,124 participants. Participants <20 years of age (n=266), those with type 1 diabetes mellitus (n=10), and those without information on diabetes status (n=25) or smoking status (n=160) were excluded. Thus, the final study population consisted of 6,663 (3,437 women) participants, of which 342 participants with type 2 diabetes mellitus and 6,321 participants without type 2 diabetes mellitus (30).

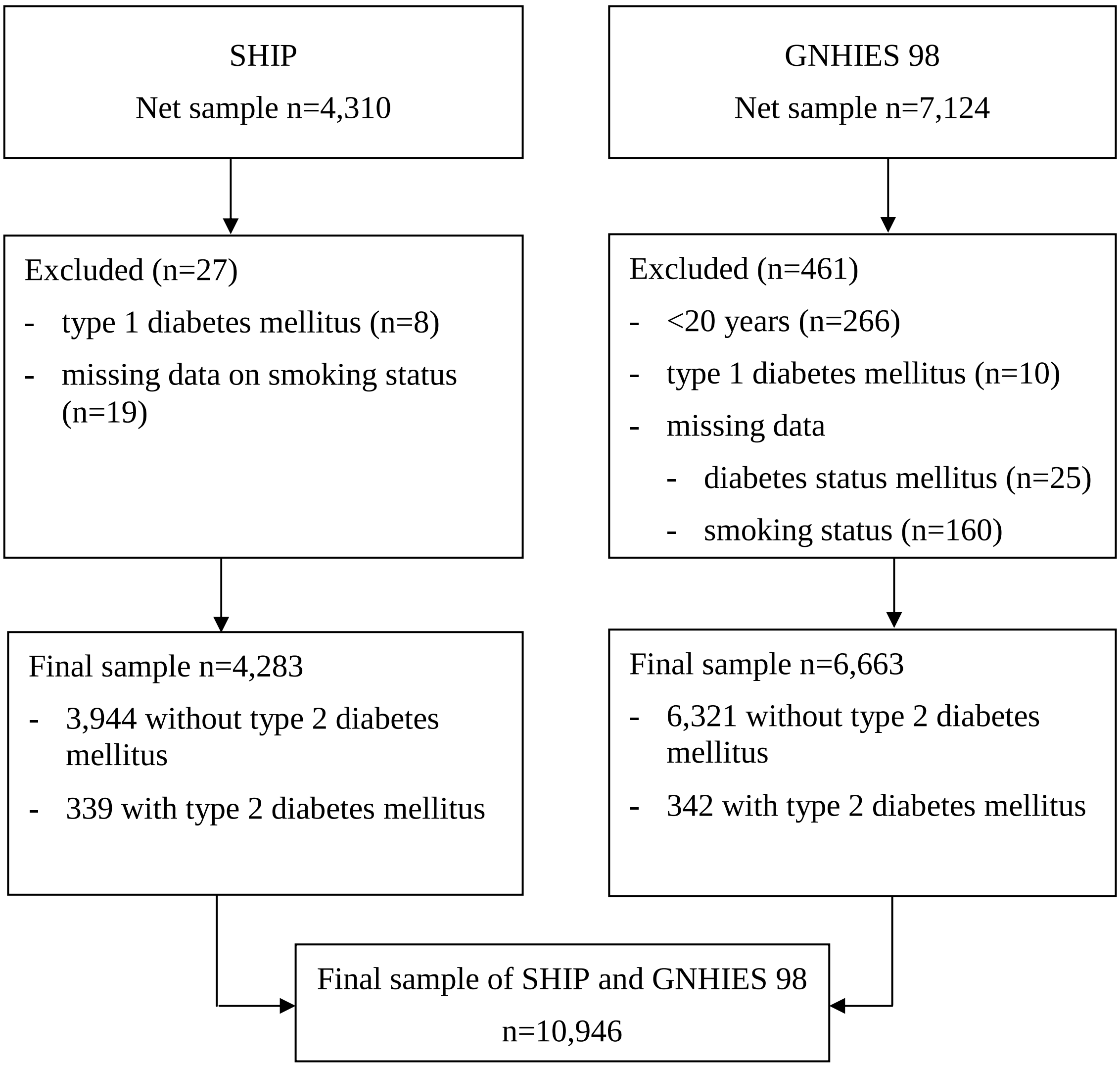

Figure 4: Flow chart of the sample recruitment in study 3

2.3 Measurements

In the following section the main measurements conducted in the studies 1 to 3 are described. More detailed descriptions of the measurements are given in the respective papers (30, 33, 34).

2.3.1 Study 1: Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium)

In all six studies, data on demographics including age and sex as well as data on diabetes status and age at diagnosis were obtained by a self-administered questionnaire.

Type 2 diabetes mellitus was defined based on self-reports and age at diagnosis. Because information about the type of diabetes was not available for all studies, a restriction was imposed for the age at diagnosis of disease. To avoid inclusion of possible cases of type 1 diabetes mellitus, participants with an age of ≤30 years at diagnosis were excluded (30).

2.3.2 Study 2: Regional differences in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

In all five regional studies, type 2 diabetes mellitus at baseline and follow-up was defined based on self-reported diabetes. The KORA study was the only study where – in a subsample of participants aged 55 to 74 years without known type 2 diabetes mellitus – an oral glucose tolerance test was performed at baseline (19). Data on socio-demographics and on health-related behaviour were assessed by standardized face to face computer-assisted personal interviews. Body mass index was calculated as body weight divided by body height squared (kg/m^2). Smoking status was assessed (never/former/current smoker). The consumption of different types of alcohol (g/day) including wine, beer and liquor and their amount was assessed for an average week. Education was categorized into three sections according to the German school system (low, <10 years/intermediate, 10 years/ high, >10 years). Information on the monthly household per capita net income was collected (<600 / 600-900/ >900-1200/ >1200 €) (34). A commonly adopted procedure was applied to divide the household income by the square root of the number of household members, thus assuming an equivalence parameter of 0.5 (40).

2.3.3 Study 3: Smoking prevalence in type 2 diabetes: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

Data on demographics including age and sex as well as smoking status and number of cigarettes per day, diabetes status, age at diagnosis of diabetes, and diabetes medication were obtained bya self-administered questionnaire (30).

In both studies, the smoking status was classified as current smoking, former smoking and never smoking. Given their small amount (<1.5%), participants who smoked cigars or pipes were not considered. The number of pack years was calculated to further quantify cigarette smoking. One pack year was defined as smoking 20 cigarettes a day for one year (30).

In both studies, type 1 diabetes mellitus was defined as the onset of disease occurred <30 years of age and the use of insulin only. In SHIP, this condition was specified with insulin administration less than one year after disease onset. All other individuals with diabetes were defined as having type 2 diabetes mellitus.

2.4 Statistical analysis

Data analyses were performed using SAS release 9.1 (SAS Institute, Cary, NC, USA) and STATA 12.0 (Stata Corporation, College Station, TX, USA).

2.4.1 Study 1: Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium)

Prevalence estimates refering to age and sex were calculated and results for each age stratum (45-54 years, 55-64 years, and 65-74 years) were expressed as percentages with a 95% confidence interval (95% CI). Prevalence estimates from the five regional studies were directly standardized to the German adult population (reference date 2007/12/31) (41). Regional disparities were estimated carrying out a logistic regression including region as independent variable and adjusting for age and sex with type 2 diabetes mellitus (yes/no) as dependent variable. The nationwide GNHIES 98 was used as a reference study. The odds ratio (OR) was calculated with 95% CI (33).

2.4.2 Study 2: Regional differences in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

The cumulative incidence (%) was calculated for the follow-up period of each study as well as the incidence rate per 1,000 person-years and the average incidence per year with 95% CI for each of the sex and age strata (45 to 54 years, 55 to 64 years, and 65 to 74 years) (34). All incidence calculations were directly standardized to the German adult population (reference date 2007/12/31) (41) and weighted for losses to follow-up in each study (42).

Statistical weights were applied because participants commonly differ in their propensity to drop-out of surveys. This propensity depends on the participants' characteristics and can be expressed as a probability. By taking the inverse of this probability, it can be assumed how many participants at baseline are represented by each participating individual at follow-up (43). For this purpose, logistic regression models were rerunned using statistical weights that accounted for drop out from baseline to follow-up including sex, age, education, equivalent income, body mass index, smoking, and alcohol consumption to derive inverse probability weights that account for selective non-response.

The calculation of the incidence rate implies the assumption that the incidence is constant over different time periods. Because the exact onset of type 2 diabetes mellitus is unknown in the present analyses, the follow-up period in each study for participants without type 2 diabetes mellitus was defined as the interval between baseline and follow-up examinations, for participants with type 2 diabetes mellitus as the mean of this interval.

2.4.3 Study 3: Smoking prevalence in type 2 diabetes mellitus: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

Descriptive statistics were performed according to diabetes status, age (20-39 years, 40-59 years, 60-79 years) and sex. Continuous variables were expressed as median (with 25th and 75th percentiles), categorical data were expressed as percentages. For comparisons of smoking prevalence, results for each age stratum were expressed as percentages with a 95% CI (44). For all age groups, the age disparities in both populations were accounted for by direct standardization to the European adult standard population (reference date 2005/12/31) and by using statistical weights (45).

3. Results

3.1 Study 1: Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium)

Regarding baseline characteristics, men reported more often than women to have type 2 diabetes mellitus with the highest proportion in CARLA, followed by SHIP and HNR (Table 4). Participants with type 2 diabetes mellitus had a higher body mass index with the highest one measured in SHIP and DHS, followed by CARLA in comparison to participants without type 2 diabetes mellitus. Current and former smoking were more frequent in participants with type 2 diabetes mellitus compared to participants without type 2 diabetes mellitus, except for DHS with the highest proportion reported in CARLA, followed by SHIP (Table 4).

Of 11,688 participants of the regional studies, 1,008 had known type 2 diabetes mellitus corresponding to a prevalence of 8.6% (95% CI 8.1%-9.1%) (data not shown). For the nationwide study (GNHIES 98), a prevalence of 8.2% (95% CI 7.3%-9.2%) was estimated (Figure 5).

The regional standardized prevalence was highest in the East (CARLA), followed by the Northeast (SHIP), and lowest in the South (KORA) of Germany (Figure 5). The nationwide data revealed a higher prevalence for the East compared to the West of Germany (data not shown).

Using data from GNHIES 98 as reference, a logistic regression revealed that the prevalence of type 2 diabetes mellitus was lower in KORA (OR 0.6; 95% CI 0.5-0.8) and RECALL (OR 0.8; 95% CI 0.7-0.9), while the prevalence was higher in CARLA (OR 1.4; 95% CI 1.1-1.7) and SHIP (OR 1.3; 95% CI 1.1-1.6). No difference was found for the DHS (OR 1.0; 95% CI 0.8-1.3) in comparison to GNHIES 98.

Overall, the prevalence of type 2 diabetes mellitus was higher in men than in women (data not shown). Regarding age-specific prevalence estimates of type 2 diabetes mellitus, the studies from the North-East (SHIP) and East (CARLA) of Germany and the nationwide study (GNIHES 98) revealed an age-dependent pattern with higher estimates in older age.

Table 4: Baseline characteristics of participants aged 45 to 74 years at baseline by study and diabetes status – to be continued (34)

	SHIP N=1,615	**CARLA** N=1,048	**DHS** N=695	**HNR** N=3,738	**KORA** N=1,718
Sex (%, male)					
Type 2 diabetes mellitus	64 (61.5)	46 (68.7)	13 (50.0)	137 (62.0)	60 (58.3)
No diabetes mellitus	721 (47.7)	508 (51.8)	322 (48.1)	1679 (47.7)	762 (48.0)
Age (years)					
Type 2 diabetes mellitus	59 (55; 67)	61 (56;66)	64 (61; 68)	62 (56; 66)	61 (54; 67)
No diabetes mellitus	57 (51; 64)	60 (53; 66)	59 (53; 67)	59 (52; 65)	57 (50; 64)
Body Mass Index (kg/m^2)					
Type 2 diabetes mellitus	31.2 (27.8; 34.1)	30.9 (28.1; 35.3)	31.2 (27.0; 32.7)	30.5 (27.8; 33.3)	30.4 (28.1; 33.7)
No diabetes mellitus	27.4 (24.8; 30.3)	27.2 (24.6; 30.0)	27.6 (24.7; 30.4)	26.9 (24.5; 29.7)	27.4 (25.0; 30.0)
Smoking					
Type 2 diabetes mellitus					
Never	31.7	32.8	61.5	35.8	38.8
Former	46.2	40.3	30.8	42.1	37.9
Current	22.1	26.9	7.7	22.1	23.3
No diabetes mellitus					
Never	43.0	46.7	45.0	43.2	47.2
Former	35.7	32.5	34.8	34.2	36.0
Current	21.3	20.8	20.2	22.6	16.8
Alcohol consumption (g/day)					
Type 2 diabetes mellitus	5.5 (0.0; 21.8)	5.0 (0.0; 21.4)	0.0 (0.0; 5.7)	2.0 (0.0; 7.9)	6.6 (0.0; 22.0)
No diabetes mellitus	5.0 (0.0; 18.0)	6.4 (0.0; 18.5)	2.9 (0.0; 20.0)	2.0 (0.0; 9.4)	8.2 (0.9; 24.1)

Table 4: Baseline characteristics of participants aged 45 to 74 years at baseline by study and diabetes status – continued

	SHIP N=1,615	**CARLA** N=1,048	**DHS** N=695	**HNR** N=3,738	**KORA** N=1,718
Education (years)					
Type 2 diabetes mellitus					
< 10	67.3	29.9	68.0	68.8	73.8
10	25.0	49.3	12.0	15.4	12.6
>10	7.7	20.9	20.0	15.9	13.6
No diabetes mellitus					
< 10	50.5	19.7	62.0	57.9	60.4
10	33.5	54.2	18.2	19.0	21.3
>10	16.0	26.1	19.8	23.1	18.3
Per Capita Income (Euro)					
Type 2 diabetes mellitus	947 (676; 1,127)	1,237 (795; 1,591)	1,500 (1,061; 1,768)	1,403 (935; 1,870)	1,944 (1,389; 2,500)
No diabetes mellitus	1,037 (701; 1,352)	1,237 (1125; 1,591)	1,750 (1,061; 2,021)	1,445 (1105; 1,913)	1,944 (1,389; 2,786)

SHIP = Study of Health in Pomerania, CARLA = Cardiovascular Disease, Living and Ageing in Halle, DHS = Dortmund Health Study, HNR = Heinz Nixdorf Recall Study, KORA = Cooperative Health Research in the Region of Augsburg,
Data are expressed as median and interquartile range for continuous data and as total numbers and percentages for categorical data

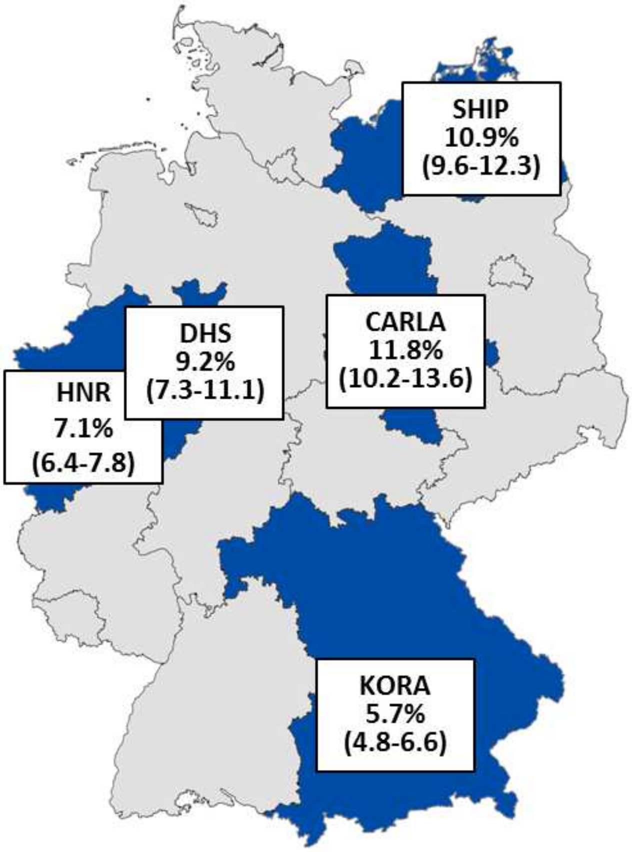

Figure 5: Regional prevalence estimates of type 2 diabetes mellitus of participants aged 45 to 74 years standardized to the German population (reference date 2007/12/31), Geodata used for figures were provided by the German Federal Agency for Cartography and Geodesy, scale of 1:3,500,000

3.2 Study 2: Regional differences in the incidence of known type 2 diabetes mellitus in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

Among the 8,787 participants, 521 (5.9%) reported an incident type 2 diabetes mellitus corresponding to a standardized overall incidence rate of 11.8 (95% CI 10.8-12.9) per 1,000 person-years and an average incidence per year of 1.2% (95% CI 1.1%-1.3%) (data not shown).

The regional incidence of type 2 diabetes mellitus across Germany was highest in the East (CARLA) and lowest in the South of Germany (KORA) with 16.9 (95% CI 13.3-21.8) vs. 9.0 (95% CI 7.4-11.1) per 1,000 person-years, respectively (Figure 6).

The incidence of type 2 diabetes mellitus increased with age and men were nearly twice as commonly affected as women (data not shown). The highest incidence in men was generally found in those aged 55 to 64 years, whereas in women the incidence was highest in those aged 65 to 74 years.

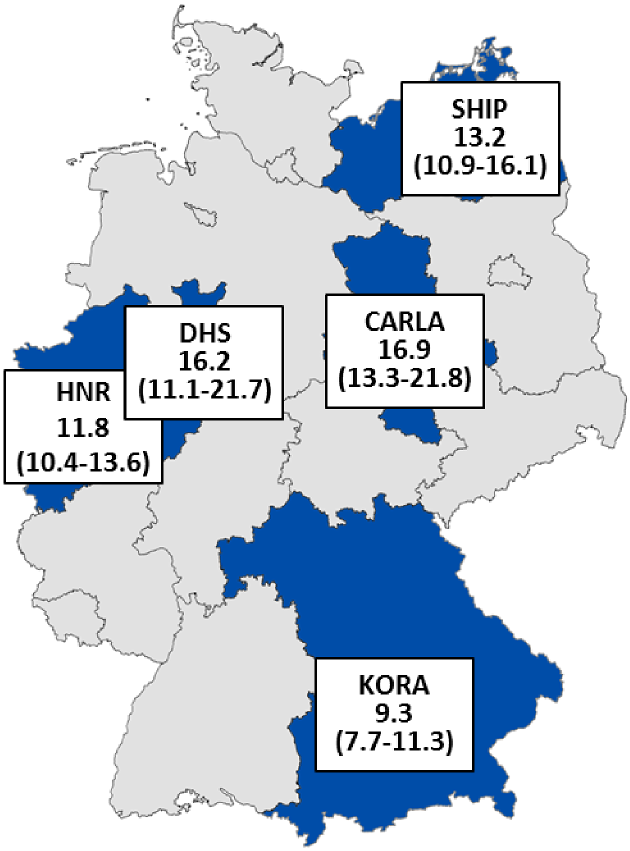

Figure 6: Regional incidence rates (per 1,000 person-years) of type 2 diabetes mellitus of participants aged 45 to 74 years standardized to the German population (reference date 2007/12/31), Geodata used for figures were provided by the German Federal Agency for Cartography and Geodesy, scale of 1:3,500,000

3.3 Study 3: Smoking prevalence in type 2 diabetes mellitus: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

The SHIP and the GNHIES 98 population comprised of 339 and 342 participants with type 2 diabetes mellitus and of 3,944 and 6,321 participants without type 2 diabetes mellitus, respectively. In both studies, participants with type 2 diabetes mellitus were older, more commonly overweight, less educated, and had a lower income compared to participants without type 2 diabetes mellitus (data not shown).

The overall prevalence of current smoking was lower among participants with type 2 diabetes mellitus than among participants without type 2 diabetes mellitus (17.3% vs. 38.0% in SHIP and 24.7% vs. 32.1% in GNHIES 98).

Regarding smoking status in men, data from both SHIP and GHNIES 98 showed that men with type 2 diabetes mellitus reported more often to be former smokers in comparison to current and non-smokers (Table 7). This pattern was more pronounced in SHIP. Men without type 2 diabetes mellitus reported more often to be current smokers. Regarding smoking status in women, data from SHIP and GHNIES 98 demonstrated that women with type 2 diabetes mellitus and without type 2 diabetes mellitus reported most frequently to be non-smoker than current and former smoker. This pattern was more pronounced in women with type 2 diabetes mellitus (Table 7).

In both studies, men and women with type 2 diabetes mellitus reported to smoke more cigarettes measured in pack-years than men and women without type 2 diabetes mellitus (Table 6).

Regarding different age groups, in both studies, the prevalence of current smoking was highest in men aged 20 to 39 years, in particular among men with type 2 diabetes mellitus (Table 6).

Table 5: Smoking prevalence in participants aged 20 to79 years with and without type 2 diabetes mellitus in SHIP and GNHIES 98 (30)

	SHIP				GNHIES 98			
	Current smoker		**Former smoker**		**Current smoker**		**Former smoker**	
	Type 2 diabetes mellitus	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**
Men								
20-39 years*	66.7 (7.8-100.0)†	46.6 (42.2-51.0)	33.3 (0.0-92.2)†	22.6 (19.0-26.3)	60.0 (5.8-100.0)†	41.0 (37.6-44.5)	20.0 (0.0-64.3)†	14.0 (11.5-16.4)
40-59 years*	25.5 (8.7-42.4)	35.4 (30.5-40,8)	59.6 (40.6-78.5)	40.8 (35.8-45.8)	34.5 (16.9-52.1)	29.2 (25.5-32.9)	31.0 (13.9-48.2)	31.6 (27.8-35.3)
60-79 years*	8.3 (0.5-16.1)	15.1 (10.5-19.7)	73.5 (61.0-86.0)	64.8 (58.6-71.0)	17.8 (8.3-27.4)	13.7 (10.2-17.1)	51.5 (39.0-64.0)	51.7 (46.6-56.7)
Women								
20-39 years*	-**	35.4 (31.0-39.8)	-**	24.1 (20.1-28.0)	45.5 (6.2-84.8)	31.7 (28.3-35.1)	-**	14.9 (12.3-17.5)
40-59 years*	10.8 (0.0-25.4)	24.4 (20.0-28.8)	27.0 (6.1-48.0)	24.1 (19.7-28.5)	30.8 (8.9-52.6)	20.4 (17.1-23.7)	10.3 (0.0-24.6)	19.0 (15.8-22.2)
60-79 years*	1.7 (0.0-5.0)	8.4 (5.1-11.8)	23.5 (12.6-34.4)	19.6 (14.8-24.4)	5.5 (0.4-10.5)	8.8 (6.1-11.4)	11.7 (4.6-18.9)	10.5 (7.6-13.4)

*Percent values (95% CI) weighted according to the European standard population (reference date 2005/12/31)

†n<10

**No cases

Table 6: Smoking behaviour in participants aged 20 to79 years with and without type 2 diabetes mellitus in SHIP and GNHIES 98 (30)

	SHIP				GNHIES 98			
	Men		**Women**		**Men**		**Women**	
	Type 2 diabetes mellitus	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**	**Type 2 diabetes mellitus**	**Non-diabetes**
Smoking status (%)*								
Current smoker	17.3	38.0	3.9	25.4	24.7	32.1	12.9	22.7
Former smoker	66.1	35.6	24.4	23.2	43.7	26.1	10.6	14.7
Non-smoker	16.6	26.4	71.7	51.4	31.5	41.9	76.5	62.6
Starting age (years)	18 (16; 20)	17 (15; 19)	23 (19; 30)	18 (16; 20)	18 (17; 20)	17 (16; 19)	20 (17; 25)	18 (16; 20)
Pack-years								
Current smoker	26 (16; 36)	20 (10; 30)	10 (7; 28)	11 (7; 18)	26 (17; 44)	19 (11; 30)	16 (12; 31)	14 (8; 23)
Former smoker	22 (11; 36)	17 (7; 29)	11 (5; 21)	7 (3; 12)	18 (8; 35)	15 (7; 29)	17 (4; 33)	7 (3; 15)

*Data are expressed as percentages or median (25th; 75th) where appropriate. Percent values weighted according to the European standard population (reference date 2005/12/31)

4. Discussion

The present dissertation revealed that the prevalence and incidence of type 2 diabetes mellitus show regional disparities within Germany which was almost twice as high in the East and Northeast in comparison to the South using data from the DIAB-CORE consortium.

Regarding regional disparities in the prevalence of type 2 diabetes mellitus, the present findings are in line with results from a nationwide telephone survey from the Robert Koch Institute in Germany in 2009 (46). This survey reported considerable regional disparities with the lowest prevalence in the South based on self-reported type 2 diabetes mellitus. This pattern was in agreement, except for the Northern part, with the nationwide DEGS1 study (2008-2011) with prevalence estimates of type 2 diabetes mellitus of 6.7% for the Northern, 7.6% for the Central, 6.3% for the Southern, and 8.1% for the Eastern part of Germany (14). Comparisons with estimates from other studies in Germany including health insurance data, patient data, or registry data are limited because of methodological differences.

Regarding regional disparities in the incidence of type 2 diabetes mellitus which parallels the regional disparities for the prevalence of type 2 diabetes mellitus, the regional distribution is tightly associated with regional disparities in risk factor profiles including overweight, obesity and the metabolic syndrome (7, 8, 47). According to patient data, the prevalence of obesity was higher in the Northeast of Germany than in the Southwest which might partly explain the variation in type 2 diabetes mellitus prevalence and incidence across study regions (48). Similar to Germany, in the United States the regional disparities in the prevalence of type 2 diabetes mellitus are mainly linked to the regional obesity prevalence (49).

Besides regional disparities in modifiable risk factors which may be linked to the regional disparities in the prevalence and incidence of type 2 diabetes mellitus, social and environmental factors have been identified within the DIAB-CORE consortium (50, 51). The socio-economic status of municipalities plays a role in explaining the regional disparities in the prevalence and incidence of type 2 diabetes mellitus (50). It has been demonstrated that the prevalence of type 2 diabetes mellitus increases with increasing area deprivation with the highest deprived regions in the Northeast and lowest in the South of Germany (50).

The present data revealed sex-specific disparities in the prevalence and incidence of type 2 diabetes mellitus. Regarding the prevalence, men aged 45 to 54 years had higher estimates compared to women in this age group. In contrast, the prevalence of type 2 diabetes mellitus was higher in women aged 65 to 74 years compared to men in this age group. Regarding incidence, men had an almost twofold higher incidence than women except for DHS, for which the estimates are based on a short follow-up time and a smaller number of cases limiting the precision of the estimation. The finding of the present dissertation is in line with results from previous population-based studies reporting a higher incidence of type 2 diabetes mellitus in men than in women (52-54). Probably, potential explanatory factors for such sex-specific disparities focussing on sex hormones in the metabolic syndrome as a main risk factor for the development of type 2 diabetes mellitus (55, 56).

Further, there is evidence that cigarette smoking is a modifiable risk factor for type 2 diabetes mellitus (25, 26). The results from the present dissertation showed that men with type 2 diabetes mellitus reported more often to be former smokers, whereas men without type 2 diabetes mellitus reported to be more often current smokers. This result likely reflects behavioural changes secondary to the disease onset or medical counselling. However, men with type 2 diabetes mellitus reported to smoke more cigarettes per day than men without type 2 diabetes mellitus, in particular men aged 20 to 39 years. Findings from population-based data from the South of Germany emphasize the impact of cigarette smoking for the development of type 2 diabetes mellitus (22). In that study, a dose-response relationship between number of cigarettes per day and the risk of incidenct type 2 diabetes mellitus in men was evident (22). This result underpins the importance of cigarette smoking as a modifiable risk factor for type 2 diabetes mellitus, in particular in young men.

According to the nationwide DEGS1 study, in 2012, smoking was reported by 29.7% of the adults (men 32.6%, women 26.9%) (57). Even though in the past years tobacco control programmes were initiated in Germany, smoking is in particular distributed among young adults and individuals with low social status (57).It has been demonstrated that individuals with low social status stop smoking more seldom and begin earlier in comparison to people in a higher social status group (57, 58). Moreover, participants in the lower social status group are overrepresented among heavy smokers. Further, the smoking prevalence is highest among participants aged 18 to 29 years (57, 58). Several studies revealed that smoking cessation improves insulin sensitivity (23, 27-29) indicating that the smoking-related risk of type 2 diabetes mellitus is reversible (59, 60).

Results from population-based studies in Germany revealed urban and rural disparities in smoking behaviour (9). The regional variations show a different pattern than the distribution of the regional prevalence and incidence estimates of type 2 diabetes mellitus in Germany. Therefore, it can be hypothesized that the smoking behaviour plays only a minor role in the distribution of type 2 diabetes mellitus in Germany. This finding leads to the assumption that other risk factors are more important to explain the disparities in the regional distribution of type 2 diabetes mellitus.

According to current nationwide data for Germany, among adults aged 18 to 79 years, 67.1% of men and 53.0% of women were overweight and 23.3% of men and 23.9% of women were obese (61). Within the past decade, even though the prevalence of overweight has been stable over time, the prevalence of obesity considerably increased between the nationwide surveys GNHIES 98 and DEGS1, in particular among younger adults (61). Obesity comes along with physical inactivity (62). Hypothetically, this behaviour is due to a transition in working as well as in living conditions with a shift to automation and an increasingly sedentary lifestyle leading to less energy consumption. It is of importance to note that people with a physically active lifestyle seem to be less likely to develop insulin resistance (63-65). Further, randomized controlled trials confirmed that lifestyle changes are the most effective tool for preventing or delaying type 2 diabetes mellitus or even for reducing the risk of comorbidities in those already diagnosed with type 2 diabetes mellitus (66-68). Motivating people to decrease sedentary lifestyle while increasing overall physical activity may have beneficial effects on disease prevention and progression as well as reduction of cardiovascular risk (69).

Limitations and Strenghts

Some limitations of the present dissertation have to be noted. First, possible misclassification may has occurred. Since type 2 diabetes mellitus was defined by self-reports, the prevalence and incidence of type 2 diabetes mellitus may be underestimated because of undetected cases. Due to this fact, there may be an underestimation of the smoking prevalence in participants with type 2 diabetes mellitus. Second, nonresponse may also has influenced the results of the present dissertation. However, the potential bias was partly controlled by applying statistical weights that accounted for drop out from baseline to follow-up. Third, differences in response proportions between the studies could have biased the present results. Nonetheless, the overall response rates (56% to 69%) achieved in the present studies can be regarded as satisfactory for population-based studies. Fourth, data collection has been conducted in different time periods. It cannot be assessed to what extent the prevalence and incidence estimates of type 2 diabetes mellitus may be biased in the present dissertation. Fifth, the mean follow-up time varied between the studies such as between the DHS and KORA (2.2 vs. 7.1 years). Because the incidence of type 2 diabetes mellitus is age-dependent, a difference of five years of follow-up time is considerable and probably led to an underestimation of the incidence rate in the DHS. Sixth, it needs to be considered that due to methodological issues an overestimation of the incidence rates reported for the South of Germany may has occurred. A subsample of participants aged 55 to 74 years in KORA received an oral glucose tolerance test at baseline. It is likely that participants were subsequently diagnosed as having type 2 diabetes mellitus by their treating physicians in case of abnormal results of this examination. A particularly high incidence of type 2 diabetes mellitus would have been expected in the South of Germany; nevertheless the incidence in KORA was still the lowest among all five studies.

Some strenghts of the present dissertation should be emphasized. First, DIAB-CORE combines data from five regional population-based studies and one nationwide study carried out in Germany including a large sample size of pooled data. Second, all studies are very similar regarding study design (population-based sampling), selection of study population (two-stage cluster sampling, stratified random sampling), and regarding measurement methods. Third, the data are characterized by a high level of quality assurance and data management as well as the population representativeness.

5. Conclusion

In conclusion, the results of the present dissertation revealed regional disparities in the prevalence and incidence of type 2 diabetes mellitus in Germany which might be linked to regional dispartities in the distribution of risk factors for type 2 diabetes mellitus. Obesity is as a modifiable risk factor for type 2 diabetes mellitus and seems to be associated with the prevalence of type 2 diabetes mellitus. It should be considered that the time trend of the past decade in Germany showed an increasing prevalence of obesity. Moreover, regional deprivation might be an explanation for the reported regional disparities in type 2 diabetes mellitus. The present findings indicate that the consideration of nationwide estimates of type 2 diabetes mellitus prevalence and incidence is insufficient for planning prevention programs as considerable regional disparities have been observed throughout Germany. The present results further highlight the importance of improving prevention efforts for type 2 diabetes mellitus on the regional level but also in subgroups, especially young adults.

Regarding cigarette smoking, the findings of the present dissertation revealed that smoking prevalence was highest among men aged 20 to 39 years with type 2 diabetes mellitus. Smoking cessation for people with type 2 diabetes mellitus but also for people without type 2 diabetes mellitus, in particular at young age, should be emphasized in health promotion and disease prevention for guiding people in changing their behaviour.

An exemplary approach for planning prevention programs to improve the health of both the individual and the public was described by Geoffrey Rose as the ‘prevention paradox’ (70). According to Rose, the ‘corresponding strategies referred to the 'high-risk' approach, which seeks to protect susceptible individuals, and the population approach, which seeks to control the causes of incidence. The two approaches are not usually in competition, but the prior concern should always be to discover and control the causes of incidence’ (page 1; 70). It will be a challenge to translate the scientific discoveries into prevention programs that are broadly available for the public. Probably, it will be a greater challenge to motivate the people to change their behavior adapting to working and life conditions in the future.

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7. Scientific Papers

The present dissertation is based on the following three scientific papers of which two are are reprinted in this section. The third paper is under review. In addition, an overview of the first author's contribution to these publications is given.

1. Schipf S, Werner A, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Berger K, Mueller G, Moebus S, Bokhof B, Kluttig A, Greiser KH, Neuhauser H, Ellert U, Icks A, Rathmann W, Volzke H. (2012). Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium). *Diabetic Medicine. 29(7):*e88-95.
2. Schipf S, Ittermann T, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Kluttig A, Greiser KH, Berger K, Mueller G, Moebus S, Slomiany, U, Icks A, Rathmann W, Völzke H. (2013). Regional disparities in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium) *Journal of Epidemiology & Community Health. Under Review.*
3. Schipf S, Schmidt CO, Alte D, Werner A, Scheidt-Nave C, John U, Steveling A, Wallaschofski H, Völzke H. (2009). Smoking prevalence in type 2 diabetes: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES). *Diabetic Medicine. 26(8):*791-7.

Table 7: Overview of the first author's contribution to the scientific papers

Scientific paper	Conception and design	Data acquisition	Data analysis	Data inter-pretation	a) Writing draft b) Revision	Approval of final manuscript
(1) Schipf, Werner, Tamayo et al. (2012)	xx	n.a.	xxx	xxx	a) xxx b) xxx	yes
(2) Schipf, Ittermann, Tamayo et al. (2013)	xx	n.a.	xxx	xxx	a) xxx b) *	yes*
(3) Schipf, Schmidt, Alte et al. (2009)	xx	n.a.	xxx	xxx	a) xxx b) xxx	yes

Notes: xxx=own responsibility, xx=conducted together with co-authors, x=collaboration,
*manuscript is under review
n.a.=not applicable

7.1 Schipf S, Werner A, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Berger K, Mueller G, Moebus S, Bokhof B, Kluttig A, Greiser KH, Neuhauser H, Ellert U, Icks A, Rathmann W, Völzke H (2012)

Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium).

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Article: Epidemiology

Regional differences in the prevalence of known Type 2 diabetes mellitus in 45–74 years old individuals: Results from six population-based studies in Germany (DIAB-CORE Consortium)

S. Schipf[1], A. Werner[1], T. Tamayo[2], R. Holle[3], M. Schunk[3], W. Maier[3], C. Meisinger[4], B. Thorand[4], K. Berger[5], G. Mueller[5], S. Moebus[6], B. Bokhof[6], A. Kluttig[7], K. H. Greiser[7,8], H. Neuhauser[9], U. Ellert[9], A. Icks[2,10], W. Rathmann[2] and H. Völzke[1]

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Abstract

Aim In Germany, regional data on the prevalence of Type 2 diabetes mellitus are lacking for health-care planning and detection of risk factors associated with this disease. We analysed regional variations in the prevalence of Type 2 diabetes and treatment with antidiabetic agents.

Methods Data of subjects aged 45–74 years from five regional population-based studies and one nationwide study conducted between 1997 and 2006 were analysed. Information on self-reported diabetes, treatment, and diagnosis of diabetes were compared. Type 2 diabetes prevalence estimates (95% confidence interval) from regional studies were directly standardized to the German population (31 December 2007).

Results Of the 11 688 participants of the regional studies, 1008 had known Type 2 diabetes, corresponding to a prevalence of 8.6% (8.1–9.1%). For the nationwide study, a prevalence of 8.2% (7.3–9.2%) was estimated. Prevalence was higher in men (9.7%; 8.9–10.4%) than in women (7.6%; 6.9–8.3%). The regional standardized prevalence was highest in the east with 12.0% (10.3–13.7%) and lowest in the south with 5.8% (4.9–6.7%). Among persons with Type 2 diabetes, treatment with oral antidiabetic agents was more frequently reported in the south (56.9%) and less in the northeast (46.0%), whereas treatment with insulin alone was more frequently reported in the northeast (21.6%) than in the south (16.4%).

Conclusion The prevalence of known Type 2 diabetes showed a southwest-to-northeast gradient within Germany, which is in accord with regional differences in the distribution of risk factors for Type 2 diabetes. Furthermore, the treatment with antidiabetic agents showed regional differences.

Diabet. Med. 29, e88–e95 (2012)

Keywords DIAB-CORE, population-based studies, prevalence, regional differences, Type 2 diabetes

Introduction

Epidemiological data on the prevalence of Type 2 diabetes mellitus on a regional level are scarce in Germany as well as in other countries [1–6]. In Europe, the prevalence of known Type 2 diabetes showed regional differences without a clear pattern [7,8]. In Germany, previous data suggest geographical variations in known prevalence of Type 2 diabetes, with differences between northeast and southwest. However, the estimates are based on different data sources and related to different age groups. For example, health insurance data (age < 39–90 years) provided prevalence estimates for the German

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Federal State of Hesse, a region in central Germany, of 5.9% in 1998 and 7.9% in 2004 [9], whereas in 2005 nationwide practice-based data (age 18–99 years) yielded prevalence estimates for East and West Germany of 17.0% vs. 13.0% for men, and of 12.0% vs. 9.0% for women [10]. In addition to differences between east and west, these data also demonstrated sex-specific differences with higher prevalence estimates for men than for women [10]. For example, population-based data (age 55–74 years) from the south [Cooperative Health Research in the Region of Augsburg Survey 4 (KORA S4)] revealed prevalence estimates of known Type 2 diabetes of 9.3% for men and of 8.0% for women in 2000 [11].

Regional differences in the distribution of risk factors for Type 2 diabetes have also been reported previously. The prevalence of the metabolic syndrome varies between 16.0% and 24.0% across the German Federal States with the highest prevalence found in the northeast [10,12]. These data correspond to regional differences in the prevalence of obesity and hypertension, which are considerably higher in the northeast than in the southwest of Germany [13,14].

Therefore, the aim of the present study was to compare data from five regional studies and one nationwide study within the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE) to provide, for the first time, population-based information on regional variation of known Type 2 diabetes prevalence in Germany.

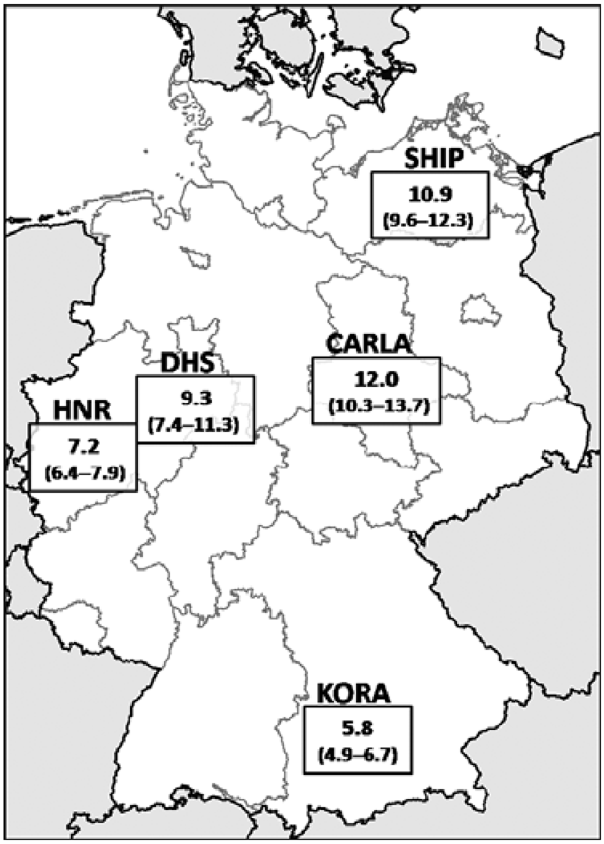

FIGURE 1 Regional prevalence estimates of Type 2 diabetes (age 45–74 years) standardized to the German population (31 December 2007). Map Scale 1:3 500 000; Based on VG250 (GK3), German Federal Agency for Cartography and Geodesy and NUTS 0, Eurostat, ©EuroGeographics for the administrative boundaries. By Werner Maier, Helmholtz Zentrum München, 2011. SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4.

Methods

Study population

For this meta-analysis based on individual data, we included data from five regional population-based studies and one nationwide study carried out in Germany (Fig. 1): northeast: the Study of Health in Pomerania (SHIP), Mecklenburg West Pomerania; east: the Cardiovascular Disease, Living and Ageing in Halle Study (CARLA) in the city of Halle, Saxony-Anhalt; west: the Dortmund Health Survey (DHS) in the city of Dortmund, North Rhine–Westphalia; west: the Heinz Nixdorf Recall Study (HNR) in the cities of Essen, Bochum and Mülheim of the Ruhr-Area; north Rhine-Westphalia, south: the Cooperative Health Research in the Region of Augsburg Survey 4 (KORA S4) study, Augsburg and surrounding rural districts, Bavaria; and nationwide: the German National Health Interview and Examination Survey 1998 (GNHIES 98). The terms east and west, in this context, refer to the northeastern territory of the former German Democratic Republic (East Germany) and to the southwestern states of the Federal Republic of Germany (West Germany). Data collection was performed between 1997 and 2006. We included all relevant population-based studies that used comparable methods of data collection and for which the same definition of Type 2 diabetes could be applied. The DIAB-CORE studies are very similar regarding study design (population-based sampling), selection of study population (two-stage cluster sampling, stratified random sampling) response rates (between 56% and 69%), and measurement methods, mainly derived from the MONICA project (CARLA, KORA S4, SHIP) and from the German National Health Interview and Examination Survey 1998 (DHS, HNR) (Table 1). Specific study details and methods have been described elsewhere [11,15–20]. All studies were approved by local ethics committees and public data protection agencies. Informed written consent was obtained from all participants. All studies were monitored by review boards of independent scientists.

Ascertainment of diabetes

In all studies, Type 2 diabetes was defined based on self-reported diabetes or self-reported diabetes treatment with oral antidiabetic agents, insulin, a combination of both, or exclusively dietary treatment and age at diagnosis. Owing to a lack of information about the diabetes type across all studies, a restriction was imposed for the age at diagnosis of disease. To

Table 1 Studies in the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE)

Study	Region	N	Response (%)	Sampling	Study period	Age range
SHIP	Northeast	4.308	69	Two-stage cluster-sample	1997–2001	20–79
CARLA	East	1.779	64	Stratified random sample	2002–2006	45–83
HNR	West	4.814	56	Stratified by city, random sample	2000–2003	45–74
DHS	West	1.312	67	Stratified random sample	2003–2004	25–74
KORA S4	South	4.261	67	Two-stage cluster-sample	1999–2001	25–74
GNHIES 98	Nationwide	7.124	61	Stratified random sample	1997–1999	18–79

SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4; GNHIES 98, German National Health Interview and Examination Survey 1998.

avoid inclusion of possible cases of Type 1 diabetes, individuals with an age at diagnosis of diabetes ≤ 30 years were excluded. Internal plausibility checks of the pooled data were performed and variables were recoded according to DIAB-CORE standard to ensure a high degree of comparability. Out of a total of 23 598 non-diabetic and diabetic participants (Table 1), 15 071 were eligible for the present analyses.

Statistical analysis

Data were reported as the median (25th, 75th) for continuous variables and as percentages for categorical variables. Age- and sex-specific prevalence estimates were calculated and results for each age stratum were expressed as percentages with a 95% confidence interval (95% CI). Prevalence estimates of the five regional studies have been directly standardized to the German adult population (reference date 31 December 2007) [21]. Regional differences were estimated carrying out a logistic regression including region as independent variable and adjusting for age and sex with Type 2 diabetes (yes/no) as dependent variable and using the GNHIES 98 as reference study. The odds ratio (OR) was calculated with 95% confidence interval (95% CI). Statistical analyses were performed with the SAS 9.1 software (SAS Institute Inc., Cary, NC, USA). Geodata used for Fig. 1 were provided by the German Federal Agency for Cartography and Geodesy and ©EuroGeographics for the administrative boundaries.

Results

After exclusion of participants with unclear diabetes status (n = 1) and possible cases of Type 1 diabetes (n = 28), the study population of the five regional and the nationwide studies comprised 15 071 subjects (7490 men, 7581 women) aged 45–74 years (Table 2). Among these, 1287 (706 men, 581 women) have prevalent Type 2 diabetes. Regarding the regional studies, out of 11 688 participants, 1008 have prevalent Type 2 diabetes, corresponding to a prevalence of 8.6% (8.1–9.1%) (Table 2). Nationwide data (GNHIES 98) (Table 2) reveal a higher prevalence for the east, with 10.7% (8.9–12.5%), compared with the west, with 6.9% (5.9–8.0%).

We estimated the highest regional standardized prevalence (Figs 1 and 2) in the east (CARLA) with 12.0% (10.3%–13.7%), followed by the northeast (SHIP) with 10.9% (9.6–12.3%). We estimated the lowest prevalence in the south (KORA S4) with 5.8% (4.9–6.7%).

We carried out a logistic regression adjusting for sex and age to estimate regional differences in Type 2 diabetes prevalence. In comparison with the GNHIES 98, the prevalence is lower in KORA (OR 0.6; 95% CI 0.5–0.8) and HNR (OR 0.8; 95% CI 0.7–0.9), while the prevalence was higher in CARLA (OR 1.4; 95% CI 1.1–1.7) and SHIP (OR 1.3; 95% CI 1.1–1.6). No difference is found for the DHS (OR 1.0; 95% CI 0.8–1.3) in comparison with GNHIES 98.

Overall, the prevalence of Type 2 diabetes is higher in men than in women (Table 3). An age-dependent pattern was found for age-specific prevalence estimates in the eastern studies (SHIP, CARLA) and in the nationwide study (GNIHES 98).

The age at diagnosis of Type 2 diabetes is lower in men than in women (Table 4). We observed the earliest age at diagnosis of Type 2 diabetes in the northeast (SHIP) at 54 years compared with 59 years in the west (DHS), although the results of the DHS are based on a smaller number of cases.

Regarding regional patterns in antidiabetic treatment (Table 5), the medication with oral antidiabetic agents is more

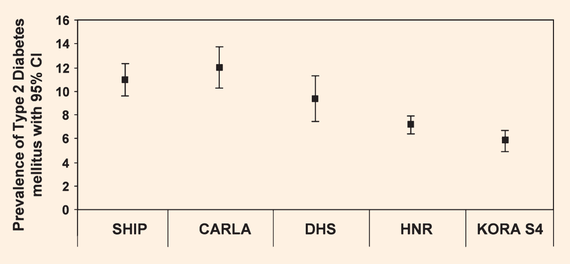

FIGURE 2 Regional prevalence estimates of Type 2 diabetes (age 45–74 years) standardized to the German population (31 December 2007). SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4.

Table 2 Characteristics of the total study populations and of participants with Type 2 diabetes by study

Total population (age 45–74 years)				Type 2 diabetes (age 45–74 years)			
Study	*N*	Men (%)	Age, median (25th, 75th)	*N*	Men (%)	Crude prevalence, % (95%CI)	Standardized prevalence*, % (95%CI)
SHIP	2.247	49.8	59 (52; 66)	251	51.0	11.2 (9.9–12.5†)	10.9 (9.6–12.3)
CARLA	1.382	52.9	61 (53; 67)	174	55.2	12.6 (10.8–14.3)†	12.0 (10.3–13.7)
DHS	883	49.4	61 (53; 68)	87	59.8	9.9 (7.9–11.8)	9.3 (7.4–11.3)
HNR	4.734	49.8	60 (53; 66)	350	60.0	7.4 (6.5–8.1)†	7.2 (6.4–7.9)
KORA S4	2.442	49.8	59 (52; 66)	146	54.8	6.0 (5.0–6.9)†	5.8 (4.9–6.7)
Total (regional studies)	11.688	50.1	60 (53; 66)	1.008	56.2	8.6 (8.1–9.1)	–
GNHIES 98	3.383	48.3	58 (51; 64)	279	50.2	8.2 (7.3–9.2)	–
East	1.188	46.3	58 (52; 64)	127	48.0	10.7 (8.9–12.5)	–
West	2.195	49.4	58 (51; 64)	152	52.0	6.9 (5.9–8.0)	–
Total	15.071	49.7	59 (52; 66)	1.287	54.9	8.5 (8.1–9.0)	–

SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4; GNHIES 98, German National Health Interview and Examination Survey 1998; GNHIES 98 East, East Germany; GNHIES 98 West, West Germany.
*Regional prevalence estimates standardized to the German population (31 December 2007).
†Differences in prevalence of Type 2 diabetes between study regions were estimated using a binary logistic regression model including region as independent variable and adjusting for age and sex with GNHIES 98 as the reference group.

frequently reported in the south (KORA S4) and less frequently in the northeast (SHIP), whereas treatment with insulin alone is more often reported in the northeast (SHIP) than in the south (KORA S4). We found the lowest proportion of treatment with insulin alone in the nationwide study (GNHIES 98).

Data of the regional studies demonstrate that treatment with both oral antidiabetic agents and insulin is more frequent in the east (CARLA) than in the west (HNR) (Table 5). This is in line with data from the nationwide study (GNHIES 98), where treatment with a combination is also more often reported in the eastern than in the western part of Germany.

We compared the frequency of insulin monotherapy with combination therapy and found different patterns between the regional studies in the west. Insulin monotherapy is more frequently reported in the DHS than the HNR but the combination therapy is similar in both studies, whereas more exclusively dietary treatment is reported in the HNR.

Discussion

Within the studies of DIAB-CORE the regional prevalence estimates of known Type 2 diabetes show a southwest-to-northeast gradient in Germany resulting in the lowest standardized prevalence in the south and the highest prevalence in the east, followed by the northeast. The overall regional estimates with a higher prevalence in the east than in the west are in line with the estimates in the nationwide study.

In agreement with our results from south Germany, similar low prevalence estimates for Type 2 diabetes from health insurance data are reported for the Federal State of Hesse in central Germany [9]. However, comparisons of practice-based or health insurance data with population-based data on the prevalence of Type 2 diabetes are limited because of methodological differences.

For Germany, results for self-reported known diabetes were similar in the German Health Update (GEDA), a nationwide telephone survey 2009/2010 [22]. This study also reported considerable regional differences with a lower prevalence in the south. However, in contrast to our study, the proportion of self-reported diabetes was higher in women than in men. For Europe, the overall prevalence of self-reported diabetes in Greece is higher in urban areas (8.2%) [4] than in rural areas (5.3%) [3]. For the USA, the prevalence of Type 2 diabetes by county level was assessed by the Behavioural Risk Factor Surveillance System 2007–2008 [23]. In line with our findings, the geographic differences in the USA are characterized as a diabetes belt following an inverse pattern with a north-to-south gradient with the highest prevalence of self-reported diabetes in the south with 11.7% compared with the rest of the USA with 8.5%. In the USA, the regional differences are associated with sedentary lifestyle and obesity [23]. These international data addressing regional prevalence of Type 2 diabetes so far differ in methods, such as age range, assessment of diabetes or time-periods, which should be taken into account when comparing these data.

The regional differences in the prevalence of Type 2 diabetes in Germany found in the present analyses are in agreement with recently reported regional differences in cardio-metabolic risk factors such as obesity and lifestyle habits, which might explain the variation in diabetes prevalence across study regions. For example, the prevalence of obesity is higher in the northeast than in the southwest of Germany [24]. Also, there are regional differences in fat distribution with the highest waist circumference in East Germany (13). Further, the prevalence of

Table 3 Regional prevalence estimates of Type 2 diabetes by sex and age

	Age (years)	SHIP, % (95% CI)	CARLA, % (95% CI)	DHS, % (95% CI)	HNR, % (95% CI)	KORA S4, % (95% CI)	GNHIES 98, % (95% CI)	GNHIES 98 East, % (95% CI)	GNHIES 98 West, % (95% CI)
Men	45–54	6.5 (3.9–9.2)	9.5 (5.5–13.5)	5.0 (1.0–8.9)	5.0 (3.4–6.6)	2.2 (0.8–3.6)	3.2 (1.8–4.6)	3.1 (0.6–5.6)	3.2 (1.5–5.0)
	55–64	12.5 (9.3–15.7)	11.8 (7.9–15.7)	13.9 (8.5–19.2)	9.2 (7.3–11.0)	7.3 (4.8–9.8)	12.0 (9.5–14.4)	15.6 (11.0–20.3)	10.0 (7.2–12.8)
	65–74	14.8 (11.2–18.4)	17.5 (12.8–22.2)	15.4 (9.6–21.3)	12.7 (10.2–15.2)	10.7 (7.6–13.9)	11.1 (7.8–14.3)	15.0 (8.5–21.5)	9.1 (5.4–12.7)
	45–74	11.4 (9.6–13.3)	13.1 (10.7–15.6)	11.9 (8.9–15.0)	8.9 (7.8–10.1)	6.6 (5.2–8.0)	8.6 (7.2–9.9)	11.1 (8.5–13.7)	7.3 (5.7–8.8)
Women	45–54	4.5 (2.5–6.5)	5.0 (1.9–8.0)	3.9 (0.8–6.9)	2.4 (1.3–3.5)	2.0 (0.7–3.3)	2.5 (1.2–3.7)	3.3 (0.9–5.8)	2.0 (0.6–3.4)
	55–64	11.2 (8.2–14.2)	11.5 (7.5–15.5)	5.6 (2.0–9.1)	5.0 (3.7–6.5)	5.5 (3.3–7.6)	7.2 (5.3–9.1)	8.4 (5.0–11.8)	6.6 (4.3–8.8)
	65–74	19.1 (14.6–23.6)	19.4 (14.0–24.9)	15.4 (9.1–21.7)	10.8 (8.4–13.1)	9.5 (6.5–12.5)	16.9 (13.3–20.5)	22.3 (15.9–28.7)	13.5 (9.3–17.6)
	45–74	10.9 (9.1–12.7)	12.0 (9.5–14.5)	7.8 (5.3–10.3)	5.9 (4.9–6.8)	5.4 (4.1–6.6)	7.9 (6.7–9.2)	10.3 (8.0–12.7)	6.6 (5.1–8.0)
Total	45–54	5.4 (3.8–7.0)	7.2 (4.8–9.8)	4.4 (1.9–6.8)	3.7 (2.8–4.7)	2.1 (1.1–3.0)	2.8 (1.9–3.8)	3.2 (1.5–5.0)	2.6 (1.5–3.8)
	55–64	11.8 (9.6–14.0)	11.6 (8.8–14.4)	9.8 (6.5–13.0)	7.1 (5.9–8.3)	6.3 (4.7–8.0)	9.5 (8.0–11.1)	11.8 (8.9–14.7)	8.2 (6.4–10.0)
	65–74	16.7 (13.9–19.5)	18.4 (14.8–21.9)	15.4 (11.2–19.7)	11.8 (10.1–13.5)	10.1 (7.9–12.3)	14.2 (11.8–16.7)	19.2 (14.6–23.8)	11.4 (8.6–14.1)
	45–74	11.2 (9.9–12.5)	12.6 (10.8–14.3)	9.9 (7.9–11.8)	7.4 (6.5–8.1)	6.0 (5.0–6.9)	8.2 (7.3–9.2)	10.7 (8.9–12.5)	6.9 (5.9–8.0)

SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4; GNHIES 98, German National Health Interview and Examination Survey 1998; GNHIES 98 East, East Germany; GNHIES 98 West, West Germany.

hypertension is higher in the northeast, with 60.1% for men and 38.5% for women, than in the south of Germany, with 41.4% for men and 28.6% for women [14]. In addition, there is a higher smoking prevalence in the northeast than in the south and west of Germany, especially in younger individuals [25] and in younger men with Type 2 diabetes [26]. Additional analyses of potential explanatory factors for such differences will be addressed in future analyses in DIAB-CORE, focusing on individual social factors and on regional indicators of deprivation.

The present analyses reveal regional sex-specific differences in the prevalence of Type 2 diabetes. For the East German studies, the prevalence of Type 2 diabetes for men in the youngest age group is higher than in women, whereas in the oldest age-group the prevalence is higher in women. Similar sex-specific differences are found in the nationwide practice-based German Metabolic and Cardiovascular Risk Project [24]. Possible explanations for these sex differences include the higher prevalence of the metabolic syndrome and its components in men compared with women [12].

Regarding treatment with antidiabetic agents, on the one hand, the regional patterns might be explained by differences in health care within the 16 Federal States of Germany. The structures in diabetes care have changed between 1998 and 2004 with a clear tendency towards the concentration of out-patient diabetes centres showing regional differences [27], which might have influenced the prescription patterns. In addition, in 2002, guidelines of the German Diabetic Association recommended the early combination of both insulin and oral antidiabetic agents [28]. Between 1998 and 2001 it has been observed that insulin monotherapy especially increased in patients with Type 2 diabetes, whereas the prescriptions for oral antidiabetic agents increased only marginally [29]. We found regional differences with the highest proportion of insulin monotherapy reported in the north and the lowest in the south whereas the highest proportion with oral antidiabetics was reported in the south and the lowest in the north. However, different times of data collection for the studies included may have influenced the results. The earliest studies include SHIP, KORA S4 and GNHIES 98, for which data collection was performed between 1997 and 2001.

Some limitations of the present study should be noted. First, we assessed the diabetes by self-report only, which demonstrates a relative low sensitivity. Therefore, the prevalence of Type 2 diabetes may be underestimated because of undetected cases [11]. Results of several studies indicate that for diabetes the accuracy of self-reports is generally high [30–32]. Confirmations of self-reported diabetes (sensitivity) have ranged from 66% to 99% (specificity 97% to 99%). Using self-reported Type 2 diabetes only vs. self report, clinical and laboratory evaluations in addition to self-reported Type 2 diabetes to define prevalent cases revealed similar results [33]. Adding information about diabetes treatment to the self-reported definition of Type 2 diabetes yields a satisfactory validity [34,35]. Our definition of Type 2 diabetes, based on self-

Table 4 Regional age at diagnosis for Type 2 diabetes by age and sex

	SHIP	CARLA	DHS	HNR	KORA S4	GNHIES 98	GNHIES 98 East	GNHIES 98 West
Men	51 (45; 59)	54 (49; 62)	58 (49; 64)	55 (46; 62)	55 (46; 62)	54 (49; 60)	55 (50; 59)	54 (46; 60)
Women	55 (50; 61)	56 (48; 63)	62 (50; 68)	57 (50; 63)	56 (50; 63)	55 (49; 62)	55 (49; 63)	55 (49; 60)
Total	54 (46; 60)	55 (48; 62)	59 (49; 65)	55 (48; 62)	55 (48; 62)	55 (49; 60)	55 (49; 61)	55 (48; 60)

SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4; GNHIES 98, German National Health Interview and Examination Survey 1998; GNHIES 98 East, East Germany; GNHIES 98 West, West Germany.
Data are median (25th; 75th).

Table 5 Antidiabetic treatment for type 2 diabetes (age 45–74 years) by study

	Antidiabetic treatment			
Study	No treatment or dietary treatment only, % (95% CI)	Insulin only, % (95% CI)	Oral antidiabetics and insulin (combination), % (95% CI)	Oral antidiabetics only, % (95% CI)
SHIP*	24.0 (18.7–29.3)	21.6 (16.5–26.7)	8.4 (5.0–11.9)	46.0 (39.8–52.2)
CARLA	18.4 (12.6–24.2)	16.1 (10.6–21.6)	16.1 (10.6–21.6)	49.4 (41.9–56.9)
DHS	17.2 (9.1–25.3)	24.1 (15.0–33.3)	9.2 (3.0–15.4)	49.4 (38.7–60.1)
HNR	24.6 (20.0–29.1)	16.9 (12.9–20.8)	7.4 (4.7–10.2)	51.1 (45.9–56.4)
KORA S4	13.7 (8.1–19.3)	16.4 (10.4–22.5)	13.0 (7.5–18.5)	56.9 (48.7–65.9)
Regional total	21.2 (18.6–23.7)	18.5 (16.1–20.9)	10.1 (8.3–12.0)	50.3 (47.2–53.3)
GNHIES 98	28.3 (23.0–33.6)	11.5 (7.7–15.2)	10.4 (6.8–14.0)	49.8 (43.9–55.7)
East	24.4 (16.8–32.0)	10.2 (4.9–15.6)	15.0 (8.7–21.5)	50.4 (41.6–59.2)
West	31.6 (24.1–39.1)	12.5 (7.1–17.8)	6.6 (2.6–10.6)	49.3 (41.3–57.4)
Total	22.7 (20.4–25.0)	17.0 (14.9–19.0)	10.2 (8.5–11.8)	50.2 (47.4–52.9)

SHIP, Study of Health in Pomerania; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; HNR, Heinz Nixdorf Recall Study; KORA S4, Cooperative Research in the Region of Augsburg S4; GNHIES 98, German National Health Interview and Examination Survey 1998; GNHIES 98 East, East Germany; GNHIES 98 West, West Germany.
*One Type 2 diabetes subject (SHIP) is missing because of unknown medication status

reported diabetes, is internally validated to determine cases with prevalent diabetes by adding information on self-reported treatment and self-reported age at diagnosis. However, prevalence of undiagnosed cases of Type 2 diabetes in the general population is considered to be high (30–50%) in most European countries and Germany [11]. Second, data collection for the studies included was done in different time-periods. It cannot be assessed to what extent the prevalence estimates may be biased in these analyses. Third, non-response is a common reason for bias in epidemiological studies. Even though the overall response rates between 56% and 69% achieved in the present studies can be regarded as satisfactory for population-based studies (Table 1) [36–38], differences in response proportions between studies could have biased the results.

The strengths of the present study include the large sample size of the pooled data and the high comparability of the studies in DIAB-CORE. Overall, all available population-based studies in Germany with comparable study design, response rates and similar assessment tools agreed to participate. Most studies (CARLA, KORA S4 and SHIP) used assessment methods derived from the World Health Organization MONICA project [39], and the remaining studies (DHS and HNR) used methods from the nationwide GNHIES 98. Further strengths are the population representativeness, and the high level of quality assurance and data management.

In conclusion, there are relevant regional differences in the prevalence and treatment of Type 2 diabetes within Germany. Our results give rise to the hypothesis that the differences observed may at least partly be caused by differences in common risk factors for Type 2 diabetes. The results are important for health-care planning, for the identification of high-risk groups and for the development of regionally tailored preventive measures.

Competing interests

Nothing to declare.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Appendix S1. Study Regions and Samples.

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7.2 Schipf S, Ittermann T, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Kluttig A, Greiser KH, Berger K, Mueller G, Moebus S, Slomiany, U, Icks A, Rathmann W, Völzke H (2014)

Regional differences in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

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Regional differences in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium)

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ABSTRACT

Background: Population-based data are paramount to investigate the long-term course of diabetes, for planning in health care and to evaluate the cost-effectiveness of primary prevention. We analysed regional differences in the incidence of known type 2 diabetes mellitus in Germany.

Methods: Data of participants (baseline age 45-74 years) from five regional population-based studies were included (mean follow-up 2.2-7.1 years). The incidence of self-reported type 2 diabetes mellitus at follow-up was compared. The incidence rates per 1000 person-years (95%CI) and the cumulative incidence (95%CI) from regional studies were directly standardized to the German population (12/31/2007) and weighted by inverse probability weights for losses to follow-up.

Results: Of 8,787 participants, 521 (5.9%) developed type 2 diabetes mellitus corresponding to an incidence rate of 11.8 per 1000 person-years (95%CI 10.8-12.9). The regional incidence was highest in the East and lowest in the South of Germany with 16.9 (95%CI 13.3-21.8) vs. 9.0 (95%CI 7.4-11.1) per 1000 person-years, respectively. The incidence increased with age and was higher in men than in women.

Conclusion: The incidence of known type 2 diabetes mellitus shows regional differences within Germany. Prevention measures need to consider sex-specific differences and probably can be more efficiently introduced toward those regions in need.

Key words: Incidence, Type 2 Diabetes, Regional Differences, Population-based Studies, DIAB-CORE

INTRODUCTION

Epidemiological data on the incidence of type 2 diabetes mellitus on a regional level are scarce. In Germany, only population-based data on the incidence of type 2 diabetes mellitus for the South in individuals aged 55-74 years are available based on validated physicians' diagnosis or an oral glucose tolerance test.[1] This study demonstrated a standardized incidence rate of 15.5 per 1000 person-years for this older age group, which was among the highest in Europe. Of note, for self-reported type 2 diabetes mellitus alone, in the South of Germany the lowest standardized prevalence (5.8%) has been observed compared to other regions in Germany.[2] The highest prevalence was observed in the East and Northeast which was almost twice as high as in the South. This pattern is in accordance with regional differences in risk factors for type 2 diabetes mellitus such as obesity in Germany.[3-5] Similarly to Germany, also in the United States the regional prevalence of type 2 diabetes mellitus is mainly linked to the regional obesity prevalence.[6]

Prevalence data are important to explore the current needs of regional health care. Incidence data are needed to assess the prognosis of newly diagnosed cases by practices of treating physicians, to identify high risk groups to face the challenge of changing modifiable risk factors, and to plan future health care allocations. Regional differences in type 2 diabetes mellitus incidence was examined in the United States in the youth (10-19 years) based on clinical information.[7] Further incidence differences for clinically diagnosed type 2 diabetes mellitus in rural and metropolitan areas were examined in China.[8] As for other European countries for Germany data on possible regional differences in the incidence of the type 2 diabetes mellitus is missing.

The aim of our study is to provide population-based estimates for the incidence of self-reported type 2 diabetes mellitus on a regional level within Germany. Data originate from five population-based cohort studies that used comparable methods in individuals aged 45-74 years at baseline within the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE) consortium in Germany.

MATERIALS AND METHODS

Study population

For this meta-analysis based on pooled individual data, we included follow-up data from five regional population-based cohort studies carried out in Germany (Table 1): Northeast: the Study of Health in Pomerania (SHIP), Mecklenburg West Pomerania; East: the Cardiovascular Disease, Living and Ageing in Halle Study (CARLA) in the city of Halle (Saale), Saxony-Anhalt; West: the Dortmund Health Survey (DHS) in the city of Dortmund, North Rhine-Westphalia, and the Heinz Nixdorf Recall Study (HNR) in the cities of Essen, Bochum and Mülheim of the Ruhr-Area, North Rhine-Westphalia; South: the Cooperative Health Research in the Region of Augsburg (KORA) study, city of Augsburg and municipalities in surrounding rural districts, Bavaria. Data collection for baseline studies was performed between 1997 and 2006 and for follow-up examinations between 2002 and 2010 (Table 1). The mean follow-up duration varied between 2.2 and 7.1 years (Table 1). Data of the DIAB-CORE studies used herein are similar regarding study design (population-based sampling), selection of study population (two-stage cluster sampling, stratified random sampling), response rates (61%-69%), and measurement methods, mainly derived from the MONICA project (CARLA, KORA S4, SHIP) and from the German National Health Interview and Examination Survey 1998 (DHS, HNR).[2] Specific study details have been described elsewhere.[9-13] All studies were approved by local ethics committees and public data protection agencies. Informed written consent was obtained from all participants. All studies were monitored by review boards of independent scientists.

Table 1: Baseline and follow-up characteristics by studies in the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE)

			Total N (response %)		Study-Period		Mean	Age range
Study	**Region**	**Sampling**	**baseline**	**follow-up**	**baseline**	**follow-up**	**follow-up**	**follow-up***
SHIP	Northeast	Two-stage Cluster-Sample	4,308 (69)	3,300 (84)	1997-2001	2002-2006	5.0	25-85
CARLA	East	Stratified Random Sample	1,779 (64)	1,436 (86)	2002-2006	2007-2010	4.0	49-87
DHS	West	Stratified Random Sample	1,312 (67)	1,122 (86)	2003-2004	2006-2008	2.2	27-76
HNR	West	Stratified by City Random Sample	4,814 (56)	4,157 (90)	2000-2003	2006-2008	5.1	50-80
KORA	South	Two-stage Cluster-Sample	4,261 (67)	3,080 (80)	1999-2001	2006-2008	7.1	31-82

SHIP= Study of Health in Pomerania, CARLA= Cardiovascular Disease, Living and Ageing in Halle, DHS= Dortmund Health Study, HNR= Heinz Nixdorf Recall Study, KORA= Cooperative Health Research in the Region of Augsburg
*only participants aged 45-74 years at baseline were included to enhance comparability

To enhance comparability of studies, only the age group 45-74 years at baseline was included. From 11,688 participants (5,832 women), individuals who did not participate in the follow-up studies (n= 2,015), with known type 2 diabetes mellitus at baseline (n= 731), missing data in drop out weights (n=52) or in diabetes status at follow-up (n= 101) were excluded. A total of 8,787 participants (4,484 women) were eligible for the present analyses.

Measurement

A history of self-reported diabetes mellitus, socio-demographic information, and data on health-related behaviour was assessed by standardized face to face computer-assisted personal interviews. Body mass index was calculated as body weight divided by body height squared (kg/m²). Smoking status was assessed (never/former/current smoker). Different types of alcohol (g/d) including wine, beer and liquor and their amount was assessed for an average week. Education was categorized into three sections according to the German school system (low, <10 years/intermediate, 10 years/high, >10 years). Information on the monthly household per capita net income was collected (<600/600-900/>900-1200/>1200€). We applied a commonly adopted procedure to divide the household income by the square root of the number of household members, thus assuming an equivalence parameter of 0.5.[14]

Ascertainment of incident type 2 diabetes mellitus

In all studies, incident type 2 diabetes mellitus was defined based on self-reported physicians' diagnosis within the follow-up period. The KORA study was the only study where – in a subsample of participants aged 55-74 years without known type 2 diabetes mellitus – an oral glucose tolerance test was performed at baseline.[1]

Statistical analyses

Characteristics of the study population are reported as the median (25^{th}, 75^{th} percentile) for continuous variables and as percentages for categorical variables. All incidence calculations were directly standardized to the German adult population (reference date 12/31//2007)[15] and weighted for losses to follow-up in each study.[16] We applied weights because individuals commonly differ in their propensity to drop-out of surveys. This propensity depends on the individuals' characteristics and can be expressed as a probability. By taking the inverse of this probability, we can assume how many persons at baseline sample are represented by each participating individual at follow-up. For this purpose, logistic regression models were rerunned using statistical weights that accounted for drop out from baseline to follow-up using sex, age, body mass index, smoking, alcohol consumption, education, and equivalent income to derive inverse probability that account for selective non-response. The follow-up period in each study for participants without type 2 diabetes mellitus was defined as the interval between baseline and follow-up examinations, for participants with type 2 diabetes mellitus as the mean of this interval. For each of the age and sex specific strata, the cumulative incidence (%) was calculated for the follow-up period of each study as well as the incidence rate per 1000 person-years and the average incidence per year with 95% confidence intervals (CI). Statistical analyses were performed with STATA 12.0 (Stata Corporation, College Station, TX, USA). Geodata used for figure 1 were provided by the German Federal Agency for Cartography and Geodesy and by ©EuroGeographics.

RESULTS

Among the 8,787 participants, 521 (5.9%) reported an incident type 2 diabetes mellitus corresponding to a standardized overall incidence rate of 11.8 (95%CI 10.8–12.9) per 1,000 person-years and an average incidence per year of 1.2% (95%CI 1.1%–1.3%) (Table 2).

Regarding baseline characteristics which were used as weighting variables for losses to follow-up, participants differed according to study with respect to a number of characteristics (Table 2). More men reported having type 2 diabetes mellitus with the highest proportion in CARLA, followed by SHIP and HNR. Participants with type 2 diabetes mellitus had a higher body mass index with the highest body mass index measured in SHIP and DHS, followed by CARLA. Current and former smokers were more frequent in type 2 diabetes mellitus, except for DHS with the highest proportion reported in CARLA, followed by SHIP.

Table 2: Baseline characteristics of participants as weighting factors (45-74 years at baseline) by study and diabetes status

	SHIP N= 1,615	CARLA N=1,048	DHS N=695	HNR N=3,738	KORA* 1,718
Sex (Men, %)					
Type 2 diabetes	64 (61.5)	46 (68.7)	13 (50.0)	137 (62.0)	60 (58.3)
No diabetes	721 (47.7)	508 (51.8)	322 (48.1)	1679 (47.7)	762 (48.0)
Age (years)					
Type 2 diabetes	59 (55; 67)	61 (56;66)	64 (61; 68)	62 (56; 66)	61 (54; 67)
No diabetes	57 (51; 64)	60 (53; 66)	59 (53; 67)	59 (52; 65)	57 (50; 64)
Body Mass Index (kg/m^2)					
Type 2 diabetes	31.2 (27.8; 34.1)	30.9 (28.1; 35.3)	31.2 (27.0; 32.7)	30.5 (27.8; 33.3)	30.4 (28.1; 33.7)
No diabetes	27.4 (24.8; 30.3)	27.2 (24.6; 30.0)	27.6 (24.7; 30.4)	26.9 (24.5; 29.7)	27.4 (25.0; 30.0)
Smoking					
Type 2 diabetes					
Never	31.7	32.8	61.5	35.8	38.8
Former	46.2	40.3	30.8	42.1	37.9
Current	22.1	26.9	7.7	22.1	23.3
No diabetes					
Never	43.0	46.7	45.0	43.2	47.2
Former	35.7	32.5	34.8	34.2	36.0
Current	21.3	20.8	20.2	22.6	16.8
Alcohol consumption (g/d)					
Type 2 diabetes	5.5 (0; 21.8)	5.0 (0; 21.4)	0 (0; 5.7)	2.0 (0; 7.9)	6.6 (0; 22.0)
No diabetes	5.0 (0; 18.0)	6.4 (0; 18.5)	2.9 (0; 20.0)	2.0 (0; 9.4)	8.2 (0.9; 24.1)

Education					
Type 2 diabetes					
< 10	67.3	29.9	68.0	68.8	73.8
10	25.0	49.3	12.0	15.4	12.6
>10	7.7	20.9	20.0	15.9	13.6
No diabetes					
< 10	50.5	19.7	62.0	57.9	60.4
10	33.5	54.2	18.2	19.0	21.3
>10	16.0	26.1	19.8	23.1	18.3
Per Capita Income (Euro)*					
Type 2 diabetes	947 (676; 1127)	1,237 (795; 1591)	1,500 (1061; 1768)	1,403 (935; 1870)	1,944 (1389; 2500)
No diabetes	1,037 (701; 1352)	1,237 (1125; 1591)	1,750 (1061; 2021)	1,445 (1105; 1913)	1,944 (1389; 2786)

SHIP = Study of Health in Pomerania, CARLA = Cardiovascular Disease, Living and Ageing in Halle, DHS = Dortmund Health Study, HNR = Heinz Nixdorf Recall Study, KORA = Cooperative Health Research in the Region of Augsburg,
*only participants aged 45-74 years at baseline were included to enhance comparability

Data are expressed as median and interquartile range for continuous data and as total numbers and percentages for categorical data

Regarding regional differences in the incidence of type 2 diabetes mellitus across Germany (Table 3, Figure 1), the incidence rate was highest in the East (CARLA) and West (DHS), followed by the Northeast (SHIP) and lowest in the South of Germany (KORA). Along these lines, the average incidence per year was highest in CARLA with 1.7% (95%CI 1.3-2.1), followed by DHS with 1.6 (95%CI 1.1-2.4), SHIP 1.3 (95%CI 1.1-1.6), HNR 1.2 (95%CI 1.0-1.3), and KORA with the lowest average incidence per year of 0.9 (95%CI 0.7-1.1) (data not shown).

The incidence of type 2 diabetes mellitus increased with age and men were nearly twice as commonly affected as women (Table 3). The highest incidence in men was generally found in those aged 55-64 years, whereas in women the incidence was highest in those aged 65-74 years.

Table 3: Regional incidence rates per 1,000 person-years of known type 2 diabetes mellitus (45-74 years at baseline) by sex and age[#]

	Age	SHIP	CARLA	DHS	HNR	KORA*
Men	45-54	8.7 (5.0 – 16.4)	7.6 (3.2 – 22.7)	14.1 (4.4 – 70.1)	9.7 (6.8 – 14.2)	6.9 (4.2 – 12.0)
	55-64	20.6 (14.4 – 30.3)	33.0 (22.5 – 50.1)	26.1 (12.7 – 62.8)	19.4 (15.4 – 24.9)	11.2 (7.5 – 17.2)
	65-74	22.5 (15.0 – 35.0)	27.8 (17.3 – 47.8)	13.3 (4.1 – 65.8)	18.1 (13.4 – 25.2)	17.8 (11.7 – 28.3)
	45–74	16.3 (12.8 – 21.0)	21.9 (16.5 – 29.7)	17.8 (10.4 – 33.0)	15.3 (12.9 – 18.2)	11.1 (8.6 – 14.5)
Women	45-54	8.2 (4.8 – 15.0)	12.6 (6.0 – 31.1)	6.4 (1.4 – 63.9)	5.6 (3.6 – 9.3)	5.0 (2.9 – 9.4)
	55-64	9.2 (5.6 – 16.5)	10.3 (5.0 – 25.0)	10.5 (3.9 – 38.0)	9.0 (6.5 – 12.7)	8.9 (5.7 – 14.6)
	65-74	14.2 (8.4 – 26.2)	12.3 (5.9 – 29.6)	35.9 (17.2 – 86.8)	12.4 (8.8 – 18.2)	8.8 (5.1 – 16.6)
	45–74	10.0 (7.4 – 13.9)	11.7 (7.7 – 18.8)	15.0 (8.8 – 27.9)	8.6 (7.0 – 10.8)	7.2 (5.4 – 9.9)
Total	45-54	8.4 (5.8 – 12.8)	10.0 (5.7 – 19.0)	9.8 (4.1 – 29.4)	7.6 (5.8 – 10.3)	5.9 (4.1 – 8.8)
	55-64	14.7 (11.0 – 20.1)	21.9 (15.6 – 31.7)	17.5 (9.8 – 34.4)	14.0 (11.5 – 17.0)	10.0 (7.4 – 13.7)
	65-74	18.3 (13.3 – 26.0)	20.1 (13.5 – 31.3)	24.0 (13.1 – 49.0)	15.1 (11.9 – 19.3)	13.1 (9.4 – 18.9)
	45–74	13.0 (10.7 – 15.9)	16.9 (13.3 – 21.8)	16.3 (11.2 – 24.8)	11.8 (10.4 – 13.5)	9.0 (7.4 – 11.1)

SHIP = Study of Health in Pomerania, CARLA = Cardiovascular Disease, Living and Ageing in Halle, DHS = Dortmund Health Study, HNR = Heinz Nixdorf Recall Study, KORA = Cooperative Health Research in the Region of Augsburg

* results of KORA include some cases in a subsample which were diagnosed after an OGTT in the baseline study

[#] Regional incidence rates per 1,000 person-years standardized to the German population (12/31/2007) and weighted by inverse probability weights for loss to follow-up

DISCUSSION

In the present study we investigated regional differences in the incidence of known type 2 diabetes mellitus within Germany using data from five population-based cohort studies.

The observed regional differences in the incidence, which parallels the differences, recently reported for the prevalence of known type 2 diabetes mellitus.[2] The regional pattern is tightly associated with regional differences in risk factor profiles including overweight, obesity and the metabolic syndrome.[3-5] In the USA, about one third of the differences in the prevalence of type 2 diabetes mellitus is associated with sedentary lifestyle and obesity.[6] Additional analyses of potential explanatory factors for our findings will be addressed in future analyses in DIAB-CORE, focussing on individual risk factors.

The comparison of KORA, HNR, CARLA and SHIP data clearly demonstrates a regional gradient in the type 2 diabetes mellitus incidence. The DHS region was located only 50 km away from the HNR study region, but DHS demonstrated an incidence which was approximately 50% higher than the HNR incidence and similar to the incidence of the East German studies CARLA and SHIP. When interpreting these results the small number of participants in the DHS study which only counted for 26 incident cases of type 2 diabetes mellitus should be taken into account. This potentially resulted in a relative overestimation of the incidence. Nonetheless, public health initiatives are often carried out at a country level. With our results, scarce resources for prevention measures can probably be more efficiently implemented in regions in need.

Furthermore, the mean follow-up time varied between KORA and DHS (7.1 vs. 2.2 years). Because the incidence of type 2 diabetes mellitus is age-dependent, additional 5 years of follow-up time are considerable for the age-distributed estimates.

Another methodological issue need to be taken into account. A subsample of participants aged 55-74 years of the KORA study received an oral glucose tolerance test at baseline and was informed about the results. It is likely that participants were subsequently diagnosed for type 2 diabetes mellitus by the treating physicians. In addition, participants with disturbed glucose tolerance may have been followed-up closely by their treating physicians for identifying the diabetes onset at an early stage. In KORA, 8.2% of these participants had unknown type 2 diabetes mellitus at baseline, 7.2% impaired fasting glucose, and 16.4% impaired glucose tolerance.[12] Moreover, participants with prediabetes had a higher body mass index and waist circumference.[12] However, the KORA incidence was still the lowest among all five studies. Therefore, the 'real' differences of the type 2 diabetes mellitus incidence may even be more substantial than detected from our analyses.

As expected, we found a general age-dependency of the type 2 diabetes mellitus incidence. Regarding overall sex-specific differences, men had an almost twofold higher incidence than women except for DHS. In the DHS, the estimates are based on a short follow-up time and a smaller number of cases limiting the precision.

Men had not only a higher incidence estimate; they also reported an earlier diagnosis of type 2 diabetes mellitus than women. These results follow the pattern of the prevalence of known type 2 diabetes mellitus within DIAB-CORE. Men in the youngest age group (45-54 years) had higher prevalence estimates than women, whereas women had higher prevalence estimates in the oldest age group (65-74 years).[2] This sex specific pattern is mirrored by differences in risk profiles for developing type 2 diabetes mellitus such as the metabolic syndrome and its components,[17-19] the cardiovascular morbidity and mortality in men compared to women.[20, 21] Interventions should focus on sex-specific differences and have to consider particularly preventive measures tailored for men.

In addition to the aforementioned methodological considerations, two further limitations need to be considered when interpreting our results. First, possible misclassification of diabetes may have occurred by using self-reported type 2 diabetes mellitus only. The incidence of known type 2 diabetes mellitus may be underestimated due to undetected cases and false-negative self-reports of diabetes diagnoses. In general, the specificity of self-reported incident type 2 diabetes mellitus can be considered as high, whereas the sensitivity is relatively low.[22] Consequently, we may have underestimated the incidence for Germany. However, there is no reason to assume a differential information bias regarding self-reported information among the studies, which may have influenced our results on regional differences in incidence. Second, nonresponse is a common bias in cohort studies, which may have led to an underestimation of type 2 diabetes mellitus incidence. We partly controlled the bias by applying statistical weights that accounted for drop out from baseline to follow-up. Since responses were similar across the studies, selection may have played a minor role in biasing our results.

The strengths of the present study include the strict population-based design of all studies, similar response rates and the large sample size of the pooled data. Except for DHS and

KORA, data were collected during similar time periods which reduced bias by temporary public health initiatives.

In conclusion, our DIAB-CORE consortium demonstrates relevant regional differences in the incidence of known type 2 diabetes mellitus within Germany. The incidence pattern parallels the regional differences in the prevalence of type 2 diabetes mellitus. Our results strengthen the hypothesis that the observed differences may partly linked to prevalence differences in common risk factors for type 2 diabetes mellitus reflecting also sex-specific differences. Our findings are important for identifying groups at high risk to face the challenge of increasing prevalence of modifiable risk factors and for translating the results into municipality initiatives for preventing type 2 diabetes mellitus on a regional level.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest.

FUNDING

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What is already known on this subject?
In general, type 2 diabetes estimates are presented for the whole country why epidemiological data on prevalence and incidence on a regional level are scarce. Furthermore, estimates are often less comparable due to different methodological issues. Previously, regional differences in the distribution of risk factors for type 2 diabetes mellitus have been reported.

What this study adds?

The present study includes a large sample size with high comparable data of population based studies within the Diabetes Collaborative Research of Epidemiologic Studies (DIAB-CORE) consortium in Germany. Regional differences in the incidence of known type 2 diabetes mellitus where detected within Germany. Our results give rise to the hypothesis that the observed differences may at least partly be due to the differences in risk factors for type 2 diabetes.

LEGEND

Figure 1: Regional incidence rates (per 1000 person-years) of known type 2 diabetes mellitus (45-74 years at baseline) standardized to the German adult population (12/31/2007). Map Scale 1:3,500,000 for A4 prints. Data Sources: VG250 (GK3), German Federal Agency for Cartography and Geodesy and NUTS 0, Eurostat, © EuroGeographics for the administrative boundaries. Cartography: Werner Maier, Helmholtz Zentrum München, 2012

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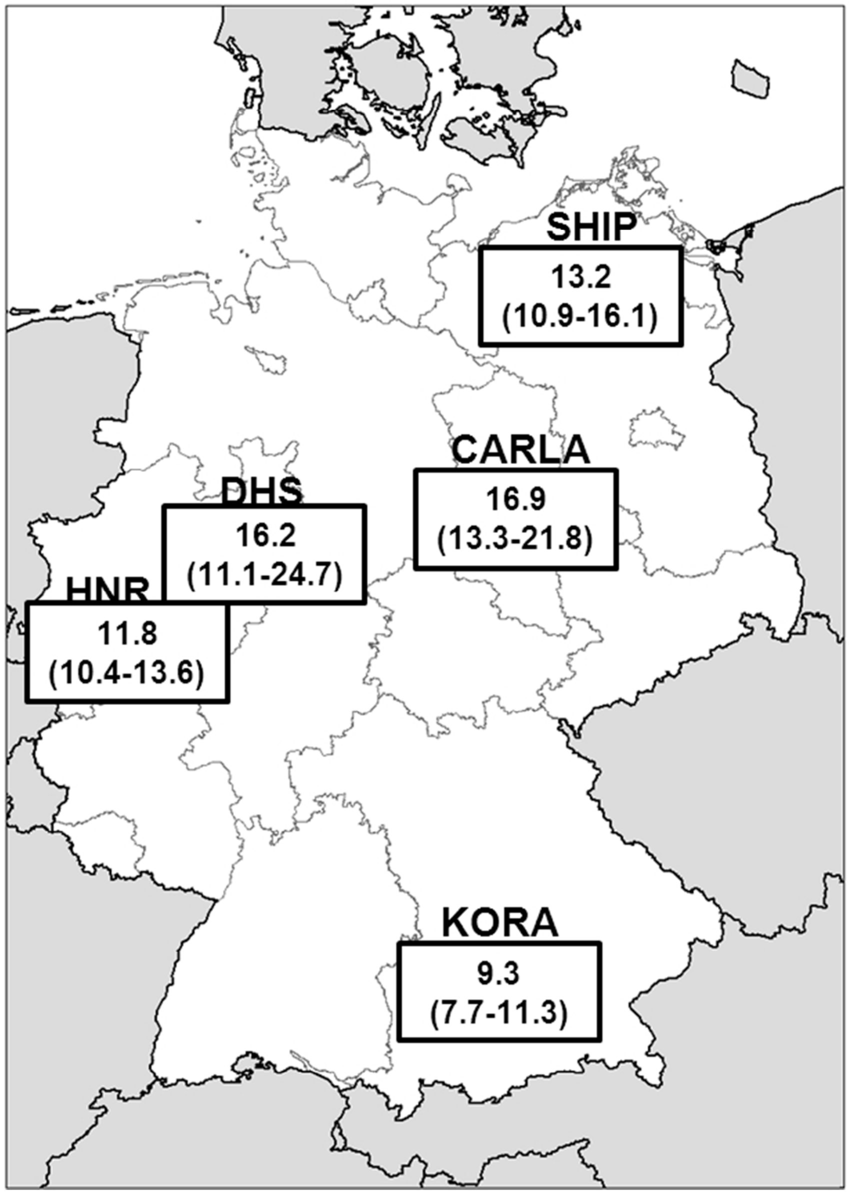

Regional differences in the incidence of type 2 diabetes mellitus in Germany

7.3 Schipf S, Schmidt CO, Alte D, Werner A, Scheidt-Nave C, John U, Steveling A, Wallaschofski H, Völzke H (2009)

Smoking prevalence in type 2 diabetes: Results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

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Original Article: Complications

Smoking prevalence in Type 2 diabetes: results of the Study of Health in Pomerania (SHIP) and the German National Health Interview and Examination Survey (GNHIES)

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Abstract

Aims Smoking contributes to the development of diabetes and diabetes-related complications. Currently, data on smoking prevalence in subjects with diabetes in Germany are lacking. The aim of our analysis was to determine smoking prevalence in adults with Type 2 diabetes mellitus using data from the two population-based studies in Germany.

Methods From the Study of Health in Pomerania (SHIP) (n = 4283) and the 1998 German National Health Interview and Examination Survey (GNHIES 98) (n = 6663) subjects aged 20–79 years were investigated. Descriptive statistics on smoking prevalence and behaviours were calculated for Type 2 diabetes mellitus and compared with the general population using weightings reflecting the European adult population.

Results Overall, the prevalence of current smokers was lower among persons with than without Type 2 diabetes mellitus in SHIP (17.3% vs. 38.0%) and in GNHIES 98 (24.7% vs. 32.1%). Only in men, there were more former smokers in Type 2 diabetic patients than in subjects without diabetes in both studies. Among current and former smokers, the number of cigarettes smoked was higher among persons with than without Type 2 diabetes mellitus. For men, this finding was consistent in SHIP and GNHIES 98, while in women, this difference was only observed in GNHIES 98.

Conclusions The associations between smoking and Type 2 diabetes mellitus are likely to reflect behavioural changes secondary to illness or medical counselling. The high proportion of current smokers among Type 2 diabetic patients, particularly men, should be monitored in repeated surveys following the introduction of disease management programmes.

Diabet. Med. 26, 791–797 (2009)

Keywords German National Health Interview and Examination Survey 98, public health, smoking prevalence, Study of Health in Pomerania, Type 2 diabetes mellitus

Abbreviations GNHIES 98, German National Health Interview and Examination Survey; HbA_{1c}, glycated haemoglobin; SHIP, Study of Health in Pomerania; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus; WHO, World Health Organization

Introduction

The World Health Organization (WHO) estimates that the global number of people affected by diabetes mellitus will be approximately 366 million by 2030 [1]. Diabetes mellitus is one of the most frequent chronic diseases in Germany, affecting approximately 6 million adults (7%) [2]. Diabetes mellitus leads to several micro- and macrovascular complications such as nephropathy, neuropathy, retinopathy and cardiovascular disease, all of which are lifestyle dependent and major causes of disability and mortality in Western countries [3–5].

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The evidence that cigarette smoking is an independent and modifiable risk factor for the development of Type 2 diabetes mellitus (T2DM) is still considered preliminary [6–8]. Although the biochemical mechanisms are in part hypothetical, smoking is involved in hormonal and metabolic changes that trigger the development of T2DM. Smoking appears to alter fat distribution, which is associated with insulin resistance, has direct toxic effects on pancreatic tissue and the progression of diabetes-related complications [9–14]. Meta-analyses have revealed that active smoking is associated with an increased risk of impaired glucose tolerance and T2DM [5,15].

Given these considerations, it is important to know the smoking prevalence in subjects with diabetes in order to improve prevention and control programmes. Little information on smoking prevalence in subjects with T2DM is available. In the USA and England, subjects with diabetes are about as likely to be smokers as the general population [16,17]. In Germany, thus far, there is a considerable lack of epidemiological data on smoking prevalence in diabetes. The aim of this investigation was to study the prevalence of cigarette smoking in subjects with T2DM compared with the general population from two large population-based studies in Germany; the Study of Health in Pomerania (SHIP) and the 1998 German National Health Interview and Examination Survey (GNHIES 98).

Methods

Study population

Two population-based studies, SHIP and GNHIES 98, were restricted to adult men and women between 20 and 79 years of age in defined regions. Both studies were approved by the local ethics committee and public data protection agencies. All subjects agreed to participate in the studies.

The Study of Health in Pomerania

SHIP is a cross-sectional, population-based survey from West Pomerania. This region is located in the north-eastern part of Germany, comprising of 212 157 inhabitants. A two-stage cluster sample adopted from the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project in Augsburg [18], Germany, yielded 12 5-year age strata (20–79 years) for both genders, each including 292 individuals. The sample was selected using German population registries. Only individuals with German citizenship and principal residency within the target regions were included in the study. The net sample comprised 6267 eligible subjects after excluding individuals who had migrated or died. The SHIP population had a total of 4310 participants, corresponding to a 68.8% final response proportion. In a non-responder analysis, only *ca*. 30% of the non-responders answered the questionnaire so that further analysis was impossible. Data were collected between 1997 and 2001 with further details described elsewhere [19,20].

A standardized computer-assisted personal interview was conducted face to face to assess medical history, lifestyle and socio-demographic variables. Subjects with Type 1 diabetes mellitus (T1DM) (n = 8) were excluded, as were subjects from whom information on smoking status was unavailable (n = 19). Altogether, 4283 (2181 women) subjects were included in this analysis, 339 subjects with T2DM and 3944 subjects without diabetes.

The 1998 German National Health Interview and Examination Survey

The GNHIES 98 is based on a stratified, multistage, cross-sectional, national representative sample of individuals aged 18–79 years from the non-institutionalized population of Germany. The 13 222 inhabitants were selected using German population registries. Subjects had their residency in East Germany if they lived in a region that belonged to the former German Democratic Republic including Berlin. The GNHIES 98 population had a total of 7124 participants corresponding to a 61.5% response proportion. Among non-responders, 16% answered a short standardized questionnaire on educational background, smoking habits, self-reported height and weight and subjective health. Previously conducted non-response analyses demonstrated that respondents were on average younger and better educated than non-respondents. No significant differences between respondents and non-respondents were observed regarding subjective health or the prevalence of daily smokers (26.6% vs. 28.0%) [21]. Subjects were eligible if they were familiar with the German language and were able to complete the questionnaires. Data were collected between 1997 and 1999 and with further details described elsewhere [21,22].

Participants were seen at local examination centres. A history of physician-diagnosed diabetes mellitus was assessed by standardized face-to-face computer-assisted personal interviews (CAPI) administered by specifically trained study physicians. Information on health-related behaviours (such as smoking habits) and socio-demographic variables were obtained by standardized self-administered questionnaires [23]. We excluded subjects under 20 years of age (n = 266), those with T1DM (n = 10) and individuals without available information on diabetic status (n = 25) or smoking habits (n = 160). Altogether, 6663 subjects (3437 women) were included in the analysis, 342 with T2DM and 6321 without diabetes.

Measurements

Current smokers were defined as those who presently smoked cigarettes, former smokers who had smoked in the past and non-smokers as those who had never smoked or smoked only occasionally (< 1 cigarette/day). Given the small number of subjects who smoked cigars or pipes (< 1.5%), they were not considered. One pack-year was defined as smoking 20 cigarettes a day for 1 year.

In SHIP, we defined T1DM if the onset of disease occurred before the age of 30 years and insulin was commenced less than

1 year after disease onset. Subjects in GNHIES 98 were defined as having T1DM if the onset of disease was < 30 years of age and subjects used only insulin. All other diabetic subjects were defined as having T2DM.

Education was categorized into three levels (< 10 years, 10 years and > 10 years) according to the German three-level schooling system. Current marital status comprised four categories (never married, married, divorced and widowed). The net income per capita was divided into four categories (< 1000 German marks, 1000 to < 2500 German marks, 2500 to < 4000 German marks and ≥ 4000 German marks; 100 German marks = 51.13 euros). Body mass index (BMI) was calculated as body weight divided by body height squared (weight in kg/height in m^2). The definitions of myocardial infarction and stroke were based on self-reported physician's diagnosis. Glycated haemoglobin (HbA_{1c}) was determined as per high-performance liquid chromatography (Bio-Rad Diamat, Munich, Germany).

Statistical analyses

Continuous variables were expressed as median (with 25th and 75th percentiles), categorical data were expressed as percentages. Descriptive statistics were performed with regard to diabetes status, age (20-year strata) and sex. For comparisons of smoking prevalence, results for each age stratum were expressed as percentages with a 95% confidence interval (95% CI). For all age groups, the age differences in both populations were accounted for by direct standardization to the European adult standard population by using statistical weighting [24]. Statistical analyses were performed with the SAS 9.1 software (SAS Institute Inc., Cary, NC, USA).

Results

SHIP and GNHIES 98 subjects with T2DM were older, less educated, more commonly overweight, more often widowed and less frequently single than subjects without diabetes (Table 1). In both studies, subjects with T2DM were more likely to have low income and higher HbA_{1c}. Almost half of the T2DM subjects were prescribed oral glucose-lowering medication. The proportion of those with myocardial infarction or stroke was threefold higher in SHIP and five- to sixfold higher in GNHIES 98 for T2DM subjects compared with subjects without diabetes. Regional analysis within GNHIES 98 demonstrated a higher proportion of T2DM subjects living in former East vs. West Germany (Table 1).

Among all participants of both populations, more men than women were current smokers (33.9% vs. 22.0%) and former smokers (35.5% vs. 18.3%). There was a lower proportion of current smokers in those with T2DM compared with subjects without diabetes in both study populations (Table 2). This difference was more pronounced in SHIP relative to GNHIES 98. However, among T2DM subjects, a higher proportion smoked more than 20 cigarettes a day compared with subjects without diabetes in both populations. This result was present in both populations and in current and former smokers (Table 2).

In both populations, the overall prevalence of current smokers was lower among T2DM compared with subjects without diabetes for both sexes, particularly in SHIP (Fig. 1). Among men, T2DM subjects were more likely to be former smokers than subjects without diabetes in both populations. This was also more prominent in SHIP (Fig. 1). Analyses for different age groups revealed that, among T2DM, the prevalence of current smokers was highest in men aged 20–39 years compared with their counterparts without diabetes and decreased with advanced age for both sexes (Table 3). Among men with T2DM, former smokers were more common relative to men without diabetes in both studies. In contrast, this difference was less prevailed in women. The prevalence of former male smokers increased with advancing age (Table 3).

Discussion

To investigate the smoking prevalence in relation to diabetes in Germany, we used two population-based studies, SHIP and GNHIES 98. Our investigation demonstrated a lower prevalence of current smoking among subjects with T2DM compared with the general population in both studies. This is in contrast to the prevalence of smoking among T2DM in the USA which continues to be very similar to that among the general population (1989: 27% vs. 26%; 1990–2001: 24% vs. 23%) [16,25] or is even higher according to another meta-analysis (33% vs. 27%) [26]. Even although in this analysis, the prevalence of current smoking among subjects with T2DM is lower in comparison with the general population, it is important to remember the elevated risk for subjects with T2DM for cardiovascular disease and other complications experienced by this group over their lifetimes.

One reason for the differences between our findings and the findings from other countries might be that at the time of data collection there have been almost no preventive efforts at the national or state level to decrease smoker rates. Survey data revealed that Germany had a particularly low 'anti-smoking climate' [27]. Hence, smoker rates in Germany may be estimated as uninfluenced by preventive measures. In the absence of any national measures to encourage stopping smoking, the individual's experience, including having an illness, remains the main motivation to stop smoking.

We found that subjects with T2DM aged 20–39 years were more likely to be current smokers than the general population. Other studies have confirmed the age-related prevalence of smoking and demonstrated it to be highest in young adults [16,28]. In England, the prevalence of smoking was highest for both sexes aged 35–54 years with diabetes in comparison with subjects without the disease; for men (33% vs. 30%) and women (36% vs. 28%) [17] and decreased with advancing age. In contrast, the smoking prevalence in the USA in individuals aged 18–44 years was similar for both sexes (28.0% vs. 27.4%) and highest in this age group. The high prevalence of smoking among

Table 1 Selected characteristics of subjects between the ages of 20–79 years by study population and diabetes status

	SHIP (n = 4283)				GNHIES 98 (n = 6663)			
	Men		Women		Men		Women	
	Type 2 diabetes n = 182	Non-diabetes n = 1920	Type 2 diabetes n = 157	Non-diabetes n = 2024	Type 2 diabetes n = 164	Non-diabetes n = 3062	Type 2 diabetes n = 178	Non-diabetes n = 3259
Age (years)	65 (57; 74)	50 (36; 64)	67 (60; 73)	47 (35; 61)	62 (57;68)	44 (33; 57)	65 (58;72)	45 (34; 58)
School education (years)								
< 10	67	40.3	78.8	34.4	65.6	42.2	75.9	43.1
10	19.8	42.1	18	49.1	17.5	31.8	17.7	36.1
> 10	13.2	17.6	3.2	16.6	16.9	26	6.5	20.8
Marital status (%)								
Single	3.8	21.8	7.6	18.4	6.7	23.7	4	16.7
Married	79.7	68.8	51.6	61.6	83	69.5	65.1	66.5
Divorced	4.4	5.9	9.6	9.2	3	4.8	3.4	7.5
Widowed	12.1	3.5	31.2	10.8	7.3	2	27.4	9.3
Monthly income (in German marks)* (%)								
< 1000	3.5	7.1	6.9	8.9	—	1.8	7.6	3.1
1000 to < 2500	34.9	34.4	60.7	37.8	20.2	10	26	16.1
2500 to < 4000	45.9	34.8	26.2	33.6	58.2	46.5	51.3	45.9
≥ 4000	15.7	23.7	6.2	19.7	21.6	41.7	15.1	34.9
BMI (kg/m^2)	29 (27; 32)	27 (25; 30)	30 (27; 34)	27 (23; 30)	28 (26; 31)	27 (24; 29)	30 (26; 34)	25 (23; 29)
HbA_{1c} (%)	7.0 (6.1; 8.2)	5.3 (5.0; 5.7)	7.0 (6.3; 8.0)	5.2 (4.8; 5.6)	7.6 (6.5; 8.9)	5.5 (5.2; 5.8)	7.2 (6.0; 8.7)	5.4 (5.1; 5.7)
Medication (%)								
Insulin	19.7	—	17.8	—	11	—	10.6	—
Oral medication	50.6	—	52.2	–	48.7	—	44.4	—
Both	8.8	—	10.2	–	9.2	—	7.9	—
Diet	20.9		19.8		31.1		37.1	
Co-morbidities (%)								
Myocardial infarction	12.1	5	7	0.9	11	3.1	9.2	1
Stroke	9.3	2.5	4.5	1.3	6.3	1.2	8.1	1
Residency in East Germany (%)	—	—	—	—	45.7	32.7	45	33.8

Data are presented as percentages or median (25th; 75th) where appropriate. *100 German marks = 51.13 euros .
BMI, body mass index; GNHIES 98, German National Health Interview and Examination Survey; HbA_{1c}, glycated haemoglobin; SHIP, Study of Health in Pomerania.

younger adults is particularly disconcerting given that cigarette smoking is a modifiable risk factor impacting on the development of T2DM and progression of diabetic complications, in both men and women [5].

Since the risk of cigarette smoking for T2DM has been identified, there has been increasing interest in its association. Population-based cohort studies provide a large body of evidence indicating smokers are at higher risk of developing glucose intolerance and T2DM compared with non-smokers during follow-up [10,15]. From a public health perspective, this is very important because the incidence of T2DM is increasing dramatically and imposes a growing public health burden with huge demands on scarce resources in healthcare systems. Smoking cessation for subjects with T2DM, but also for subjects without diabetes at a young age, should be emphasized in health promotion and disease prevention.

Cigarette consumption in former smokers was higher in T2DM compared with subjects without diabetes. Even although we are not able to draw causal conclusions from our cross-sectional study, this finding might indicate that the exposure has been a component in the development of T2DM. Hypothetically, individuals may have been more likely to stop smoking after being diagnosed with diabetes than the non-diabetic population.

The gender specific association between cigarette smoking and diabetes mellitus should also be considered [15,29]. Men with T2DM smoked considerably more cigarettes compared with subjects without diabetes in both populations. In previous studies, the amount of cigarettes smoked per day was associated with an increased risk of T2DM among men but not among women [6]. The difference between men and women might be explained by protective effects of oestradiol

Table 2 Smoking behaviour in subjects between the ages of 20–79 years with or without diabetes in SHIP and GNHIES 98

	SHIP				GNHIES 98			
	Men		Women		Men		Women	
	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes
Smoking status (%)*								
Current smoker	17.3	38	3.9	25.4	24.7	32.1	12.9	22.7
Former smoker	66.1	35.6	24.4	23.2	43.7	26.1	10.6	14.7
Non-smoker	16.6	26.4	71.7	51.4	31.5	41.9	76.5	62.6
Starting age (years)	18 (16; 20)	17 (15; 19)	23 (19; 30)	18 (16; 20)	18 (17; 20)	17 (16; 19)	20 (17; 25)	18 (16; 20)
Pack-years								
Current smoker	26 (16; 36)	20 (10; 30)	10 (7; 28)	11 (7; 18)	26 (17; 44)	19 (11; 30)	16 (12; 31)	14 (8; 23)
Former smoker	22 (11; 36)	17 (7; 29)	11 (5; 21)	7 (3; 12)	18 (8; 35)	15 (7; 29)	17 (4; 33)	7 (3; 15)

Data are expressed as percentages or median (25th; 75th) where appropriate. *Per cent values weighted according to the European standard population.
GNHIES 98, German National Health Interview and Examination Survey; SHIP, Study of Health in Pomerania.

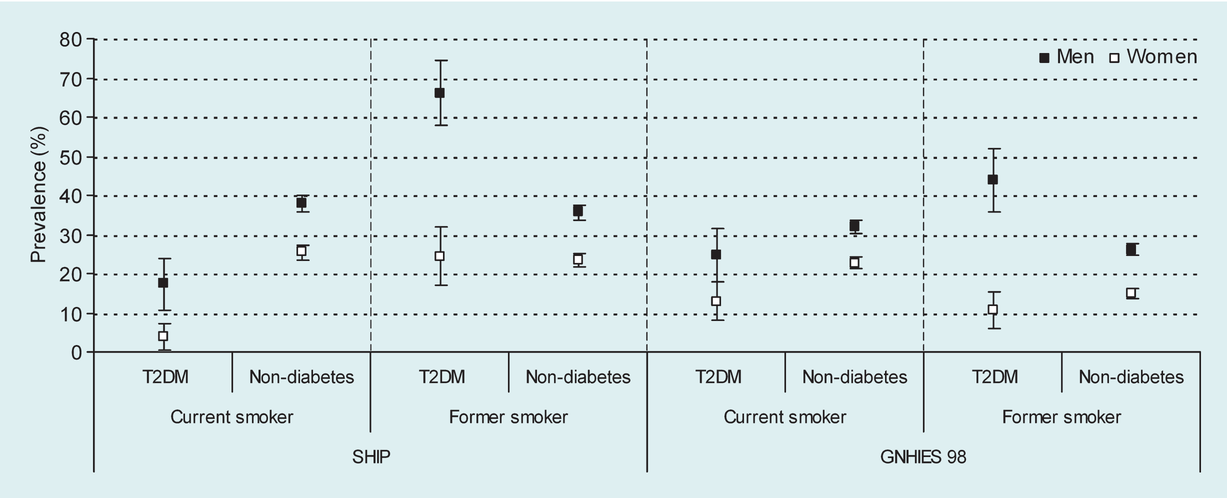

FIGURE 1 Overall smoking prevalence (95% CI) for both sexes weighted according to the European standard population. GNHIES 98, German National Health Interview and Examination Survey; SHIP, Study of Health in Pomerania.

on pancreatic B-cells [9]. A deterioration of B-cell function in men but not in women who smoked has been observed [29]. Furthermore, oestrogen replacement therapy improved insulin sensitivity in post-menopausal women with T2DM [30].

It is imperative to recognize the presence of potential risk factors and cofactors known to contribute to an increased risk of diabetes and late diabetes sequelae to improve the basis for prevention and control programmes. Since the late 1990s, disease management programmes have been introduced to enhance diabetic patient care. In the USA, a study including diabetic smokers confirmed that the majority did not consider stopping smoking on their own, but considered stopping when they had received recommendations from their doctors [31]. Advice from physicians and other health professionals was effective in reducing smoking, particularly when the advice was repeatedly given by different staff members [17]. It has also been demonstrated that smoking cessation increases insulin sensitivity and improves lipoprotein profiles [7,17,32,33], suggesting that the smoking-related risk of diabetes is reversible in individuals who stop smoking, despite a modest increase in weight. The beneficial long-term effects of smoking cessation seem to outweigh the short-term effects of weight gain [34,35]. Furthermore, former male smokers who did not restart for more than 20 years were no longer at increased risk of diabetes [7]. In Germany, disease management programmes were established in 2002. Approximately 2.5 million T2DM patients nationwide were registered in a health insurance programme by 2008 [36], demonstrating a potential for improving care for chronic diseases such as diabetes [37].

Table 3 Smoking prevalence in subjects between the ages of 20–79 years with or without diabetes in SHIP and GNHIES 98

	SHIP				GNHIES 98			
	Current smoker		Former smoker		Current smoker		Former smoker	
	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes	Type 2 diabetes	Non-diabetes
Men								
20–39 years*	66.7 (7.8-100.0)†	46.6 (42.2–51.0)	33.3 (0.0–92.2)†	22.6 (19.0–26.3)	60.0 (5.8–100.0)†	41.0 (37.6–44.5)	20.0 (0.0–64.3)†	14.0 (11.5–16.4)
40–59 years	25.5 (8.7–42.4)	35.4 (30.5–40,8)	59.6 (40.6–78.5)	40.8 (35.8–45.8)	34.5 (16.9–52.1)	29.2 (25.5–32.9)	31.0 (13.9–48.2)	31.6 (27.8–35.3)
60–79 years	8.3 (0.5–16.1)	15.1 (10.5–19.7)	73.5 (61.0–86.0)	64.8 (58.6–71.0)	17.8 (8.3–27.4)	13.7 (10.2–17.1)	51.5 (39.0–64.0)	51.7 (46.6–56.7)
Women								
20–39 years*	—	35.4 (31.0–39.8)	—	24.1 (20.1–28.0)	45.5 (6.2–84.8)	31.7 (28.3–35.1)	—	14.9 (12.3–17.5)
40–59 years	10.8 (0.0–25.4)	24.4 (20.0–28.8)	27.0 (6.1–48.0)	24.1 (19.7–28.5)	30.8 (8.9–52.6)	20.4 (17.1–23.7)	10.3 (0.0–24.6)	19.0 (15.8–22.2)
60–79 years	1.7 (0.0–5.0)	8.4 (5.1–11.8)	23.5 (12.6–34.4)	19.6 (14.8–24.4)	5.5 (0.4–10.5)	8.8 (6.1–11.4)	11.7 (4.6–18.9)	10.5 (7.6–13.4)

*Per cent values (95% confidence interval) weighted according to the European standard population. †$n < 10$.
GNHIES 98, German National Health Interview and Examination Survey; SHIP, Study of Health in Pomerania.

Our finding that young male smokers have a significant predisposition to diabetes raises an important issue for prevention in this target population.

We restricted our analyses to only complete records containing diabetes and smoking status. The number of incomplete records was low, indicating that missing data may not have considerably impacted our results. Participants may have under-reported their current smoking, creating misclassification bias and also leading to an underestimation of smoking prevalence. However, this would have affected the observed association between current smoking and diabetes only if under-reporting depended on diabetes status. While we cannot exclude such differential misclassification, it seems unlikely. Our case definition of diabetes mellitus was based on health interview data and is hence restricted to diagnosed diabetes. Thus, our findings regarding an overall lower prevalence of smokers among persons with than without T2DM is likely to reflect behavioural changes secondary to illness or medical counselling. Strengths of our investigation include the use of two population-based studies that may be generalized to other groups and, in contrast to other studies [16], the separation of subjects with T1DM from those with T2DM.

In summary, our population-based studies are one of the leading investigations to document smoking prevalence in participants with and without T2DM in Europe. The prevalence of current smokers among diabetic subjects, in particular among men, is troublesome and should be monitored in repeated surveys in the framework of disease management programmes.

Competing interests

Nothing to declare.

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Appendices

Appendix A – Eidesstattliche Erklärung

Appendix B – Wissenschaftliche Leistungen

Appendix C – Danksagung

Eidesstattliche Erklärung

Hiermit erkläre ich, dass ich die vorliegende Dissertation selbstständig verfasst und keine anderen als die angegebenen Hilfsmittel benutzt habe.

Die Dissertation ist bisher keiner anderen Fakultät und keiner anderen wissenschaftlichen Einrichtung vorgelegt worden.

Ich erkläre, dass ich bisher kein Promotionsverfahren erfolglos beendet habe und dass eine Aberkennung eines bereits erworbenen Doktorgrades nicht vorliegt.

Greifswald, den 03.03.2014 ____________________________________

Sabine Schipf

Wissenschaftliche Leistungen

Originalartikel

Schipf S, Ittermann T, Tamayo T, Holle R, Schunk M, Maier W, Meisinger C, Thorand B, Kluttig A, Greiser KH, Berger K, Mueller G, Moebus S, Slomiany, U, Icks A, Rathmann W, Völzke H. Regional disparities in the incidence of known type 2 diabetes in Germany: Results from five population-based studies in Germany (DIAB-CORE Consortium) *Under Review*

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