

# **Spatial patterns of dementia prevalence and its vascular risk factors in Germany**

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## **Abstract**

This is the first study that explored spatial patterns in the prevalence of dementia in Germany. Results about sub-national differences in other countries have been inconclusive. We used health claims data from the largest public health insurer in Germany for ages 65 and above in the year 2007 consisting of 1,312,594 persons. Dementia diagnosis was defined according to ICD-10 codes G30, G31.0, G31.82, G23.1, F00, F01, F02, F03, and F05.1. We distinguished 95 regions according to the 2-digit postal code of the place of residence.

Using meta-regression models we found significant geographical differences in the age standardized prevalence of dementia. Dementia prevalence was higher in East than in West Germany. In East Germany the prevalence declined from the north to the south, in West Germany the prevalence was low in the north and particularly high in the north and eastern regions of Bavaria. The regional prevalences of dementia were significantly correlated with the regional prevalences of the three major vascular risk factors hypertension, hypercholesterolemia, and diabetes. Together the regional variation in the three risk factors explained about 50% of the regional variation in dementia prevalence.

The relationship between vascular risk factors and dementia has been repeatedly demonstrated on the individual level. Our results confirm that this relationship also exists on a regional level. We conclude by discussing possible limitations of the data and how they might bias the results.

## **Introduction**

Dementia is one of the most common, yet incurable, diseases at old age. In Germany, dementia prevalence doubles about every 5 to 6 years from about 2% at age 65 to 30% - 40% at ages 90 to 100 (Doblhammer et al 2013). After cardiovascular disease, cancer and cerebrovascular disease it is the fourth most common cause of death (Bickel 2003) and it is a major predictor of death (Baldereschi et al. 1999). Dementia is one of the most costly diseases at old age, primarily due to the high demand for care (Leicht et al. 2011). Information about prevalence and incidence of dementia in Germany at the population level has only recently become available (Doblhammer et al. 2012). However, no information exists about spatial patterns in the prevalence, with the exception of a study that showed higher prevalence in East than in West Germany (Ziegler and Doblhammer 2009), as well as a study that reported prevalence at the level of states (Doblhammer et al. 2012).

The knowledge about spatial variation in dementia prevalence can help to identify socioeconomic determinants of dementia risks, it may support etiological investigations (Steele und McGeer 2008) and it is important for policy makers when dealing with the consequences of the disease for the health care system in general and the long-term care system in particular. Thus a series of studies have tried to establish the existence of sub-national variation in dementia prevalence.

A recent meta-study suggests a geographical clustering of dementia rates in terms of rural and urban living-circumstances in developed countries (Russ et al. 2012). Rural living at old age increased the risk of dementia, particularly Alzheimer's disease. Early-life rural living seemed to exacerbate this risk. Most evidence, however, is based on the comparison of dementia across studies that contrast geographical locations such as urban and rural areas, or different countries (Jorm et al. 1987; Ineichen 2000; Fratiglioni et al. 1999). As Russ et al. (2012) pointed out in their comprehensive review of geographical differences in dementia, these studies are difficult to compare since different diagnostic criteria or differences in their operationalization may bias the results. Single studies exploring the geographical distribution of dementia prevalence are, however, still rare and results are inconsistent (Russ et al 2012). Two Canadian studies did not find differences in dementia prevalence across Canada (Canadian Study of Health and Aging Working Group 1994; Hébert et al. 2000; Manfreda 1995) but suggested the existence of regional differences in dementia subtypes. US-studies found regional differences in Alzheimer's disease prevalence (Steenland et al. 2009; Laditka et al. 2006a; Laditka et al. 2008; Laditka et al. 2006b), in Puerto Rico dementia prevalence varied between the eight regions (Figueroa et al. 2008), in China a north-south gradient as well as a weaker east-west gradient existed (Zhang et al. 2005; Zhang et al. 2006). Differences in dementia prevalence were also found in Spain and Finland (Russ et al 2012), as well as in the eastern and western part of Germany (Ziegler und Doblhammer 2009). On the contrary, a study that used identical methodology in five different sites across the United Kingdom did not find evidence of geographical variation in dementia incidence (Matthews et al. 2005). Studies comparing geographical variation in dementia deaths found marked regional differences in dementia and AD mortality in the US (Gillum et al. 2011), in Australia (Jorm et al. 1989), and in AD mortality in Japan (Imaizumi 1992).

Vascular risk factors have been identified as major risk factors of dementia (Breteler, Monique M. B. 2000; Forette et al. 1998). Thus, regional variation in dementia should reflect regional variation in these risk factors which vary across Europe and within European sites

(Day et al. 1999). Matthews et al. 2005, however, did not find evidence that regional variation in vascular risk factors was correlated with dementia incidence. Also regional variation in Alzheimer's disease mortality in the US (Gillum et al. 2011) appeared not to be correlated with mortality from cardio-vascular disease.

Our study aimed to explore spatial differences in the prevalence of dementia in Germany and to analyze regional correlations with the three major vascular risk factors of dementia, namely hypertension, hypercholesterolemia and diabetes.

Hypertension is one of the most important risk factors of stroke and coronary heart disease and of vascular dementia (Breteler 2000); the link with Alzheimer's disease is less clear. Longitudinal studies showed that Alzheimer's disease was correlated with increased systolic and diastolic blood pressure ten to 15 years before the onset of the disease (Slooter and van Duijn 1997). On the contrary, cross-sectional studies reported that lower blood pressure was associated with lower cognitive performance or dementia (Kontula et al. 1995; Lee 1994; Skoog et al. 1996). Breteler and others pointed out that over a long time period hypertension might indeed increase the risk of Alzheimer's disease, but prior to the clinical onset of the disease blood pressure level start to decline, and decline even further with further progression of the disease (Qiu et al. 2005; Skoog und Gustafson 2006). There is even evidence for an association of midlife hypertension with pathological hallmarks of Alzheimer's disease upon brain autopsy (Petrovitch et al. 2000). Gorelick (2004) assumed that treating hypertension might be the most promising long-term intervention to reduce the risk of vascular dementia and possibly of Alzheimer's disease. Both longitudinal and cross-sectional studies showed that diabetes increased the risk of Alzheimer's disease while the mechanisms are not entirely clear, yet (for an overview see Breteler 2000; Gorelick 2004). Plasma cholesterol levels may influence the risk of Alzheimer's disease in relation to the APOE4 gene, which is a major risk factor of both, Alzheimer's disease and of increased plasma cholesterol, low-density lipoprotein levels, atherosclerosis, and cardiovascular disease (for an overview see Breteler 2000; Gorelick 2004).

Based on above findings we hypothesized that dementia prevalence in Germany differs between geographical regions. Following the distribution of vascular risk factors, the prevalence of dementia should be higher in East than in West Germany and should differ within these two regions. We used health claims data from the largest public health insurer in Germany. Given the large number of observations we were able to explore variation in dementia prevalence across 95 regions across the whole of Germany defined by the two-digit

postal code (PC). To our knowledge this is the first study that explored spatial variation in dementia prevalence in Germany.

## **Data and Methods**

We used claims data of the AOK (Allgemeine Ortskrankenkasse), the largest public health insurance company in Germany which covers about one-third of the total population aged 50+, and more than 50% among the oldest-old. The claims data include complete records of the inpatient (§ 301 (2), SGB V) and outpatient treatment (§ 295 (2), SGB V) received by each insured person with at least one day of insurance coverage by the AOK. The data are compiled on a quarterly basis, and include all plan members, regardless whether they sought medical treatment or not. Diagnoses may stem from both outpatient and inpatient treatment and are coded according to the 10<sup>th</sup> Revision of the International Classification of Diseases and Related Health Problems (ICD-10). A detailed description of the data, its advantages and disadvantages, can be found in the chapter of Fink in this issue.

An age-stratified sample of all insured persons aged 65 and above in the first quarter of 2007 was drawn which consisted of 1,312,594 persons. These individuals were followed over the four quarters of the year 2007. Dementia was defined by the ICD numbers G30, G31.0, G31.82, G23.1, F00, F01, F02, F03, and F05.1. We did not further distinguish dementia according to aetiology. All plan members of the sample with at least one insured day in 2007 and with a dementia diagnosis were defined as prevalent dementia cases measured in person-days. The nominator of the prevalence was thus defined as the number of days with a valid dementia diagnosis. Since data were on a quarterly basis, each quarter with a valid dementia diagnosis contributed 91,25 days. In case of the event of mortality or of the exit from the AOK the number of days of the quarter until the event was taken. The population at risk, the denominator of the prevalence, was also based on the stratified sample and contained the number of AOK-insured person-days. Both prevalent dementia cases and the population at risk were aggregated by sex, age, and the place of residence. All calculations were based on insured person-years derived from the person-days. Over all insured individuals aged 65 and above the 467,834,506 insured person-days at risk amounted to 1,281,738 insured person-years at risk (Table 1).

The place of residence was defined by the two-digit level postal code. These are 95 regions with a minimum of 1902, and a maximum of 38440 insured person-years. The age-specific prevalence of dementia at age  $x$  in region  $i$  were calculated by

$$\text{Prevalence}_{x,i} = \frac{\text{insured person - years with dementia diagnosis}_{x,i}}{\text{total insured person - years}_{x,i}}$$

The estimation of the prevalences of the vascular risk factors diabetes, hypertension and hypercholesterolemia followed the same procedure. Diabetes mellitus diagnoses were based on ICD-10 numbers E10 to E14, hypercholesterolemia on E78.0, and hypertension was identified based on ICD-10 numbers I10 to I13, and I15.

For the sake of brevity Table 1 gives an overview of the risk population and the cases on a one-digit postal code level albeit all calculations are performed on the two-digit level. For each region we calculated age-standardized prevalence by applying direct age standardization. We defined seven five-year age-groups for the ages 64-69, 70-74, 75-79, 80-84, 85-89, 90-94, 95+. The minimum number of valid dementia cases was 44 at age 95+ in postal code region 44 (Dortmund, Hüne, Lerne, Bochum), the maximum was 314747 dementia cases at age 80-84 in postal code region 6 (Halle(Saale), Dessau-Roßau, Quedlingburg, Zeitz). German population data from 2007 for five-year age groups and both sexes combined from the Human Mortality Database (2013) served as the reference population.

We conducted spatial analyses by using maps to illustrate regional differences in the prevalence. In addition we calculated regional correlations between dementia and the three vascular risk factors by using random-effects meta-regression models. We assumed that the age-standardized prevalence of region  $i$ ,  $y_i$ , can be modelled as a normally distributed linear prediction from the risk factors  $x_i$  and their unknown parameters  $\beta$  (Harbord und Higgins 2008)

$$y_i \sim N(x_i \beta, \sigma_i^2 + r^2)$$

For the estimation of the parameters each region was weighted by its precision,  $1/\sigma_i^2$ , where  $\sigma_i^2$  is the within-region variance of the age-standardized prevalences  $y_i$ ;  $r^2$  is the between-region variance allowing for between-region heterogeneity not explained by the covariates

and is estimated from the data by applying the REML algorithm (Thompson und Sharp 1999). All calculations were performed in Stata 12.1 using the “metareg” command.

For better comparison of the effect sizes prevalence of the three explanatory diseases were standardized by their mean and standard deviation, and multiplied by a factor of 100. Thus, the resulting coefficients can be interpreted as the percentage increase in regional dementia prevalence when the respective risk factor increases by one standard deviation.

In the claims data for each diagnosis, an indicator reflects the validity of the diagnosis as assigned by the medical doctor. In the outpatient sector, the indicator distinguishes between diagnoses which were “verified”, and those which were assigned in cases of “suspicion of”, “condition after”, or “exclusion of”. In the inpatient sector, distinctions were made between admission, referral, discharge, and secondary diagnosis. In this study only diagnoses indicated as “verified” in the outpatient sector, and only the discharge and secondary diagnoses from the inpatient sector were considered.

## Results

All prevalences presented here were age standardized for ages 65 and above and refer to 100 person-years of risk. For the sake of brevity we refer to prevalence only.

In Germany considerable spatial differences existed in the prevalence of dementia. In West Germany they ranged between 0.06 (PC 20: Hamburg Mitte) and 0.11 (PC 20: Passau, Landau an der Isar, Regen, Straubing), in East Germany they extended from 0.07 (PC 8: Plauen, Zwickau, Aue, Klingenthal) to 0.10 (PC 16: Oranienburg, Eberswalde, Pritzwalk, Schwedt/Oder) as depicted in Figure 1. Over all regions, the weighted prevalence was 0.081. Prevalence clustered in regions, first of all they differed between East and West Germany but also within these two regions. In East Germany 16 out of the 19 regions were above the German average, in West Germany 22 out of 54. In East Germany we found a distinct north-south gradient with prevalence declining from the north to the south (Figure 2). In West Germany prevalence was low in the southern regions around Stuttgart, Frankfurt, Mainz, in central Germany around Köln-Bonn, in the northern state of Schleswig-Holstein and Niedersachsen. Regional prevalence was particularly high in north and eastern Bavaria, the Ruhr-area as well as in Saarland.

Similar patterns existed for the three vascular risk factors. Hypertension (Figure 3) and diabetes mellitus (Figure 4) revealed a strong east-west gradient with higher prevalence in East

Germany. In East Germany prevalence declined from the north to the south, in West Germany the north and the south stood out with low prevalence. North and eastern Bavaria, Saarland and the Ruhr-area had comparatively high rates.

The pattern is different for hypercholesterolemia (Figure 5). Here, East Germany was characterized by low prevalence with no particular north-south gradient. In West Germany, the north again revealed low levels whereas the south, particularly Bavaria, was characterized by high levels.

Based on meta-regression we found a strong positive bivariate correlation of  $b=0.55$  ( $p<=0.001$ ) between the regional prevalences of dementia and of hypertension. This correlation implies that the prevalence of dementia increase by about half a percentage point, when the prevalence of hypertension increase by one standard deviation (Figure 6). Measured by the adjusted  $R^2$  the regional variation in hypertension explained 39.5% of the regional variation in dementia. We found an equally strong bivariate correlation between diabetes mellitus and dementia. Here the bivariate correlation was  $b=0.59$  ( $p<=0.001$ ) and the explanatory power of the model was 47.1%. Contrary to these findings, the bivariate correlation between hypercholesterolemia and dementia was statistically not significant (Figure 7). Only when we controlled for the overall level of hypercholesterolemia in East and West Germany by introducing an East/West indicator variable we found a positive correlation of  $b= 0.34$  ( $p=0.003$ ). The model explained 25.6% of the regional variation in dementia prevalence. A meta-regression model that included all three risk factors was able to explain 53.9% of the regional variation in dementia prevalence (Table 2). The regional prevalence of hypertension and diabetes were highly correlated, thus combining them into one model reduced their effect sizes to  $b=0.38$  ( $p=0.017$ ) for hypertension, and  $b=0.379$  ( $p=0.008$ ) for diabetes. They were then comparable to the effect size of hypercholesterolemia  $b=0.302$  ( $p=0.000$ ).

In sensitivity analyses we performed separate calculations for men and women. While the prevalence of dementia was significantly higher for women than for men (not shown), the spatial pattern as well as the correlation between dementia and the three cardiovascular risk factors remained unchanged.

## Discussion

This is the first study to explore spatial differences in dementia prevalence in Germany. We found distinct geographical patterns in dementia prevalence which were significantly correlated with the regional distribution of the three major vascular risk factors hypertension, hypercholesterolemia and diabetes mellitus. A series of studies (for an overview see Breteler, 2000) has previously linked these risk factors with the incidence and prevalence of dementia on an individual level; here we show that this link also exists on a regional level.

Given the lack of regional studies about dementia prevalence in Germany it was not possible to validate our finding with earlier studies. However, results from regional population-based cohort studies support the geographic patterns we found for the three risk factors hypertension, hypercholesterolemia, and diabetes.

Blood pressure has been continuously found higher in the East than in the West (Marti et al. 1990; Heinemann and Greiser 1993; Thamm 1999; Fischer et al. 2000) with signs of convergence during the 1990s (Thamm 1999). The comparison of the prevalence of hypertension in the Study of Health in Pomerania (SHIP) in the north-eastern region of Pomerania with the level in the MONICA/KORA study in the south-western city of Augsburg, based on nearly identical study designs and similar definitions of hypertension, showed considerable differences at ages 25 to 64. Hypertension among men in the SHIP study was 60%, in the MONICA/KORA study 41%. Among women the respective values were 39% and 29% (Meisinger et al. 2006).

Schipf et al. 2012 compared the age-standardized prevalence of diabetes mellitus at age 45 to 74 in the SHIP-study in the northeast, the CARLA-study in the east, the HNR-study and the DHS-study in the west, and the KORA S4-study in the south of Germany. Additionally, data from the nationwide German National Health Interview and Examination Survey 1998 were included. All of the studies used similar methods regarding the study design, selection of the study population, and the definition of type 2 diabetes resulting in similar response rates. The results showed a southwest-to-northeast gradient with the highest prevalence in the east (12.0%) and the lowest in the South (5.8%).

Little information about the regional distribution of hypercholesterolemia is available. Supporting our results, a study based on the analysis of serum-lipid levels of outpatient patients found that the prevalence of increased high-density lipoprotein cholesterol (HDL-C)

levels was lower among East than West German men; levels were only slightly higher among East than West German women (Moebus et al. 2008). We will discuss this study below in more detail.

Finally, we turn to the regional pattern of the metabolic syndrome which is a generic term for the co-occurrence of different diseases (Rosak 2003) including central obesity, impaired glucose tolerance, essential arterial hypertension and dyslipoproteinemia (Haak and Palitzsch 2012). The metabolic syndrome results in high morbidity and mortality by coronary, cerebral, and vascular diseases (Rosak 2003), as well as an increased risk of diabetes mellitus (Laaksonen et al. 2002; Lorenzo et al. 2003). In 2005, a study of more than 30.000 outpatient patients in 397 of 438 German counties found significant regional differences in the age-standardized prevalence of the metabolic syndrome (Moebus et al. 2008). Prevalence was highest in the East German states of Mecklenburg-Vorpommern, Brandenburg, and Saxony-Anhalt. In East Germany only Saxony reached West German levels. Among women the prevalence was lowest in Hamburg, Schleswig-Holstein and Hessen, and highest in the three East German states mentioned above. Among men a similar pattern emerged albeit at a generally higher level than among women. Prevalence was lowest in Saarland, Schleswig-Holstein, Hamburg and Bremen, and highest in Brandenburg, Thuringia, and Saxony-Anhalt.

We used health claims data for the study of spatial patterns in dementia and its vascular risk factors. The primary aim of medical claims is cost calculation which leads to limitations in the data that might result in a biased geographical pattern.

First, in the German medical system, only diagnoses leading to treatment are relevant for the purposes of cost calculation. Thus, a patient's cognitive impairment may not be documented if no further treatment is given. This might be particularly true for mild cases of dementia and cognitive impairment. There might be regional differences in the diagnosis and the treatment of dementia, as well as of the vascular risk factors. Note however, the geographical pattern of the vascular risk factors found in this study was supported by results from population-based cohort studies, which also lends credibility to the regional dementia pattern.

Second, regional differences in the proportion of individuals covered by the AOK insurance might bias the geographical pattern. This, however, would not bias the regional correlation between the dementia prevalence and the vascular risk factors. We estimated the AOK-insured population in each postal code region and included this information in our analysis. We found that regional dementia prevalence was weakly and statistically not significantly

correlated with the proportion of the AOK-insured population in the West, and not correlated at all in the East. The regional correlation between the dementia prevalence and the vascular risk factors remained unchanged.

Third, geographical patterns at the highest ages might be affected by the proportion of people living in nursing homes (Doblhammer et al. 2012). In these facilities, medical doctors might refrain from diagnosing dementia and prescribing treatment due to health rationing at old ages (Brockmann 2002), or because they realise that, at present, little can be done to halt the further development of the disease (Wagner and Abholz 2002). Regional differences in the proportion of elderly living in nursing homes might therefore bias the results.

Fourth, regional patterns in the distribution of the software used for cost-calculation might bias our results.

Fifth, the diagnoses in medical claims data are neither specific nor standardised. Unlike the data used in community-based epidemiological studies, in which diagnoses are made during face-to-face examinations performed by specialists such as neurologists or psychiatrists who use defined protocols, health claims data contain diagnoses from all medical doctors, including from general practitioners. Thus, the different sub-types of dementia cannot not be meaningfully distinguished. In the AOK data, 45 per cent of the dementia diagnoses were of unspecified dementia. Only 27 per cent of these cases were diagnoses of Alzheimer's disease, a figure that appears to be much too low given the findings of other studies (Bickel 2000; Ott et al. 1995; Weyerer 2005;). Nevertheless, after comparing the prevalence of dementia based on medical claims data with national and international meta-studies of dementia prevalence, we found that our rates fit well in the overall picture. This implies that, while medical claims data are not useful in studies that seek to determine the etiology of dementia, they are useful for the surveillance of the functional status of dementia irrespective of its cause for public health purposes (Laurer 2011).

Finally, the regional correlation between dementia prevalence and the vascular risk factors might be an artefact caused by a correlation in the awareness of medical doctors for any of the four diseases. In other words, medical doctors that are more likely to diagnose the three vascular risk factors are also more likely to diagnose dementia. We tested this by exploring the regional correlation between dementia prevalence and the prevalence of smoking-related cancer on the one hand, and between dementia prevalence and non-smoking related cancer on the other hand. In the claims data the diagnosis of cancer should not be biased by differences

in regional awareness of cancer nor of dementia. Smoking has been linked to an increased risk of Alzheimer's disease (Peters et al. 2008), thus, the geographical pattern of smoking-related cancer should be correlated with dementia, which is indeed the case in our data. Furthermore, our data showed no correlation between non-smoking related cancer and dementia (results not shown).

Despite these shortcomings, health claims data carry also major advantages. The study of spatial patterns requires large numbers of observations, particularly at the highest ages. The AOK claims data cover the total population, including people who live in institutions, such as assisted living or nursing homes. In many community-based epidemiological studies, the institutionalised elderly are missing. This leads to a large bias, as the prevalence of dementia is four times higher among elderly people living in nursing homes than among older people who live in the community (Jakob et al. 2002). In the AOK population, 36 per cent of the women but only 24 per cent of the men with a dementia diagnosis at age 85 were living in a nursing home.

Since the AOK claims data contain the total insured population, there was no possibility that the study design or self-selection into the study could have introduced a bias in the results. While the socio-economic status of the AOK population is lower than that of the general population (Geyer und Peter 2000), the difference is larger among people at younger than at older ages, as up to 50 per cent of the elderly German population are insured under the AOK plan.

This study provides strong evidence for the existence of geographical patterns in dementia prevalence in Germany. A better understanding of these differences might be gained if not only the relationship with vascular risk factors were explored. Future studies should therefore aim at including regional context information. Information about geographical variation in the prevalence of dementia is important from a public health point of view. The identification of modifiable socio-economic and medical risk factors might help in delaying or even preventing dementia onset.

Table 1: Number of exposures (population at risk) and cases (in person-years) by 1-digit postal code in 2007, ages 65+

1-digit postal code	Exposures	Cases			
		Dementia	Hypertension	Hypercholesterolemia	Diabetes
0	179039	17609	124876	23639	57701
1	130111	14319	92411	19404	41357
2	116527	9689	71479	20094	26604
3	143865	12920	93754	25950	37727
4	106619	9100	65793	21899	26381
5	110219	9157	68519	21054	27119
6	99991	8765	63298	18953	26966
7	145265	11792	88266	30050	35732
8	111716	9751	67615	25077	28331
9	138386	13295	93214	30812	42793
total	1281738	116397	829225	236932	350710
Minimum	1902 <sup>(PC 20)</sup>	105 <sup>(PC 20)</sup>	1053 <sup>(PC 20)</sup>	318 <sup>(PC 20)</sup>	414 <sup>(PC 20)</sup>
Maximum	38440 <sup>(PC 1)</sup>	3441 <sup>(PC 6)</sup>	26334 <sup>(PC 6)</sup>	6060 <sup>(PC 1)</sup>	12377 <sup>(PC 6)</sup>

PC 20: Postal Code 20=Hamburg Mitte

PC 1: Postal Code 1=Dresden, Riesa, Meißen, Bischofswerda

PC 6: Postal Code 6= Halle(Saale), Dessau-Roßlau, Quedlinburg, Zeitz

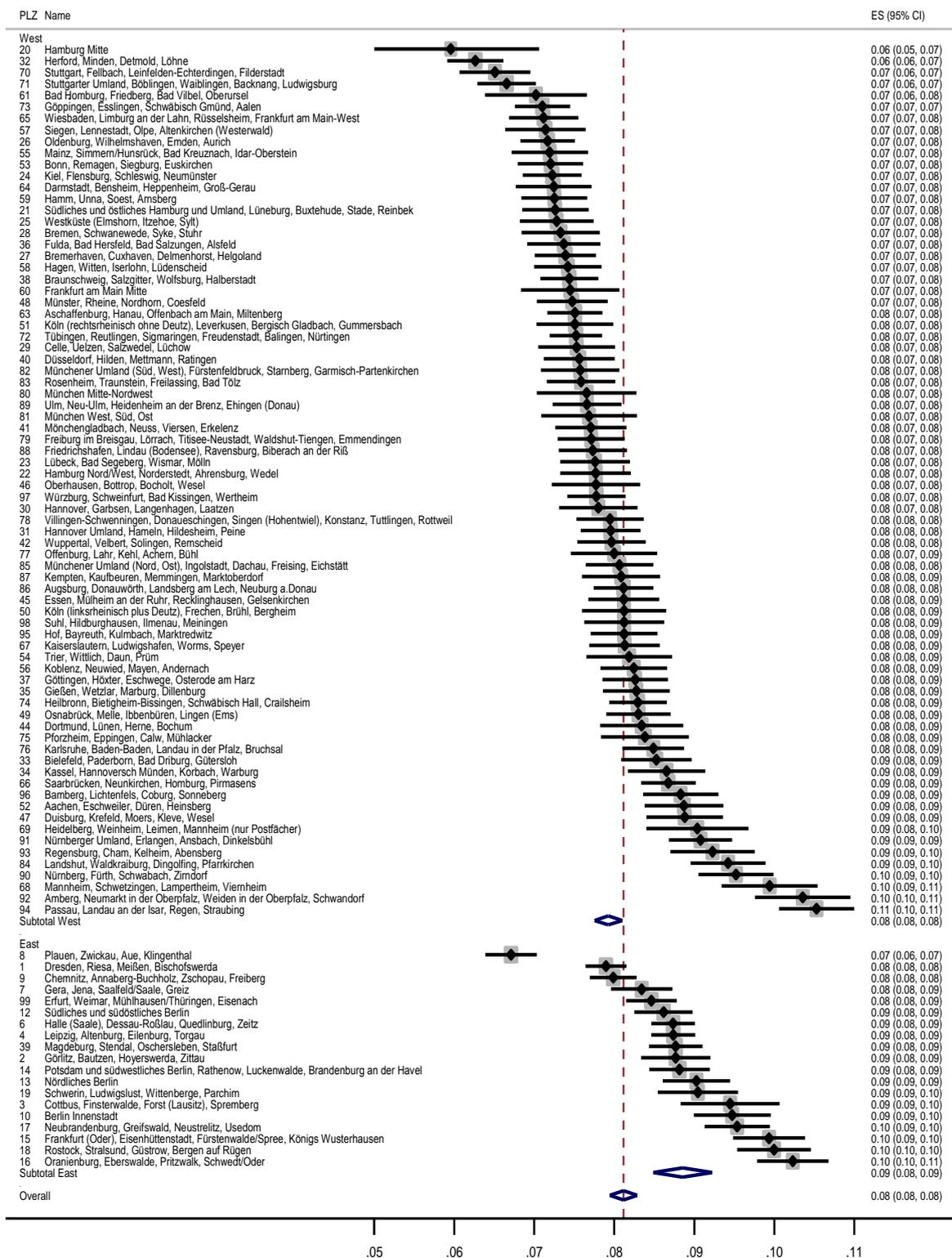
Source: AOK claims data 2007, own calculations

Table 2: Meta-regression of the regional correlation between dementia prevalence and the standardized prevalence of hypertension, hypercholesterolemia and diabetes

Risk factor	Univariate models			Multivariate model	
	Coefficient*100	p-value	adj. R <sup>2</sup>	Coefficient*100	p-value
Hypertension	0.547 0.400 - 0.693	0.000	39.54%	0.380 0.069 - 0.691	0.017
Hypercholesterolemia	-0.065 -0.249 - 0.120	0.489	-0.54%	0.302 0.141 - 0.101	0.000
Diabetes	0.591 0.453 - 0.728	0.000	47.05%	0.379 0.101 - 0.659	0.008
adj. R <sup>2</sup>	-			53.89%	
N	95				
Exposures	1,281,738				
Cases					
Dementia	116,397				
Hypertension	829,225				
Hypercholesterolemia	236,932				
Diabetes	350,710				

Source: AOK claims data 2007, own calculations

Figure 1: Age-standardized prevalence of dementia ages 65+ and confidence intervals by 2-digit postal code for both sexes combined; Weighted regional average for the AOK population in West Germany, East Germany and Total Germany



Source: AOK claims data 2007, own calculations

Figure 2: Age-standardized prevalence of dementia ages 65+ by 2-digit postal code for both sexes combined; AOK population in Germany 2007

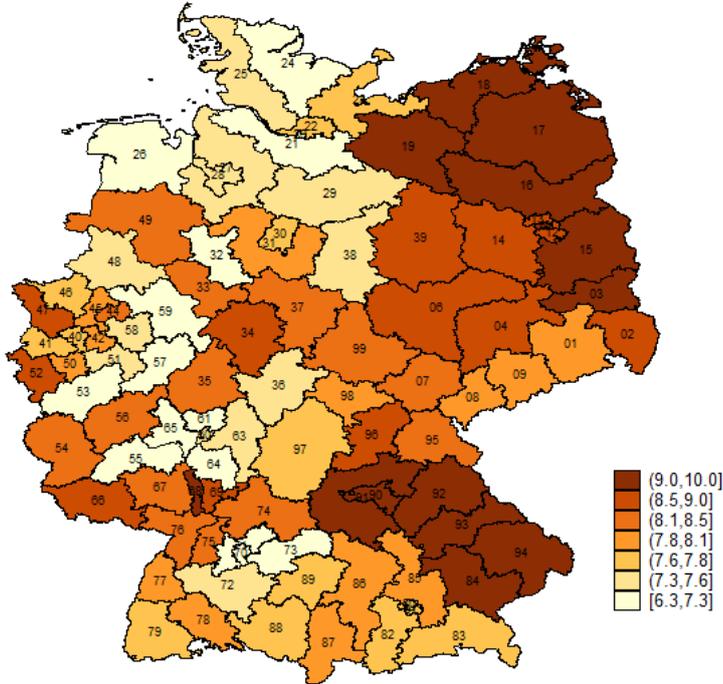


Figure 3: Age-standardized prevalence of hypertension ages 65+ by 2-digit postal code for both sexes combined; AOK population in Germany 2007

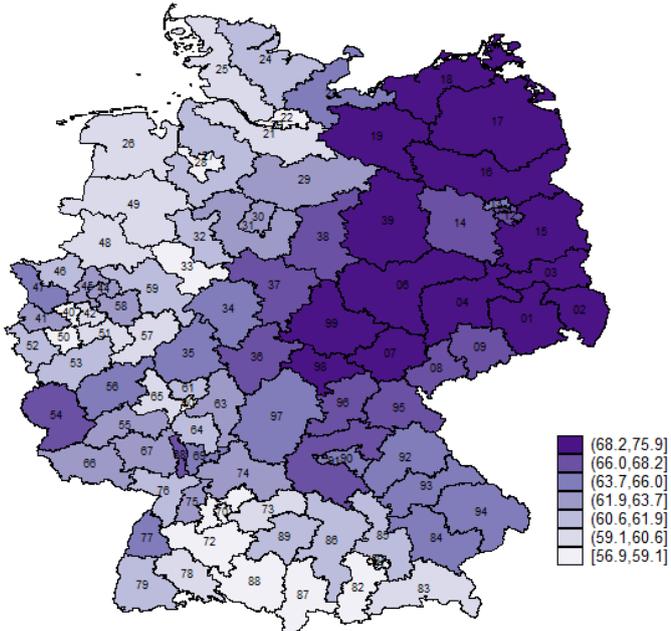


Figure 4: Age-standardized prevalence of diabetes mellitus ages 65+ by 2-digit postal code for both sexes combined; AOK population in Germany 2007

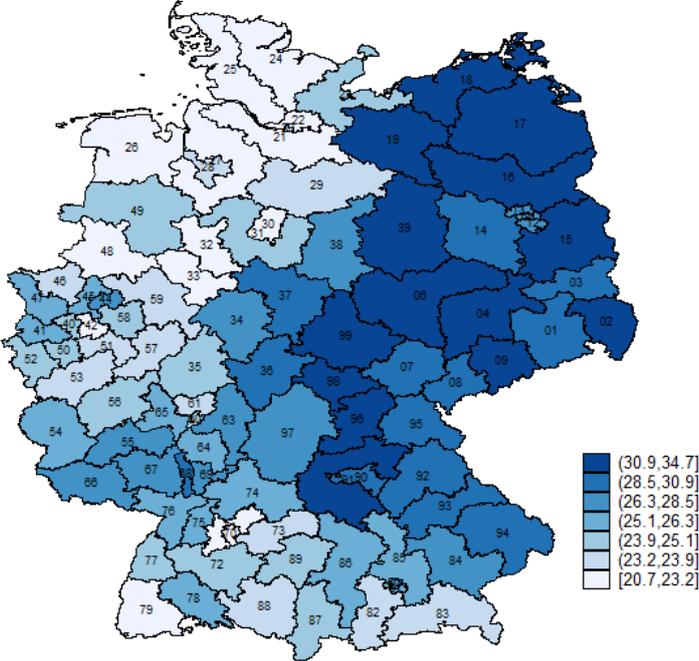


Figure 5: Age-standardized prevalence of hypercholesterolemia ages 65+ by 2-digit postal code for both sexes combined; AOK population in Germany 2007

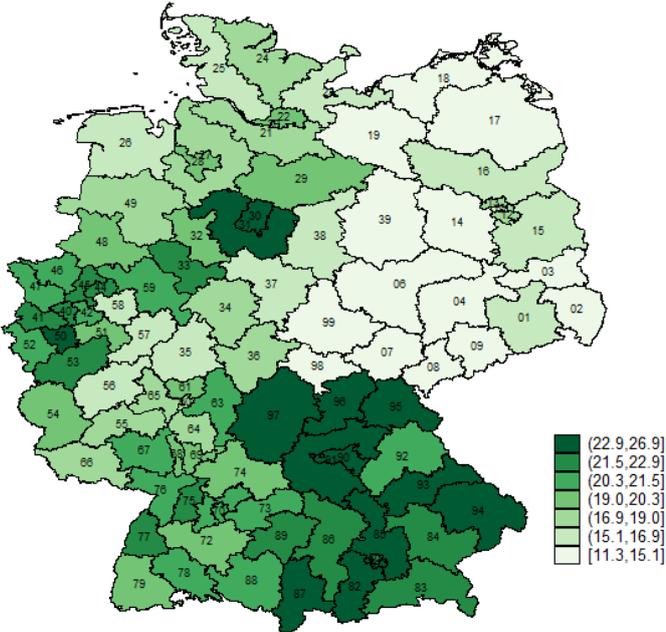
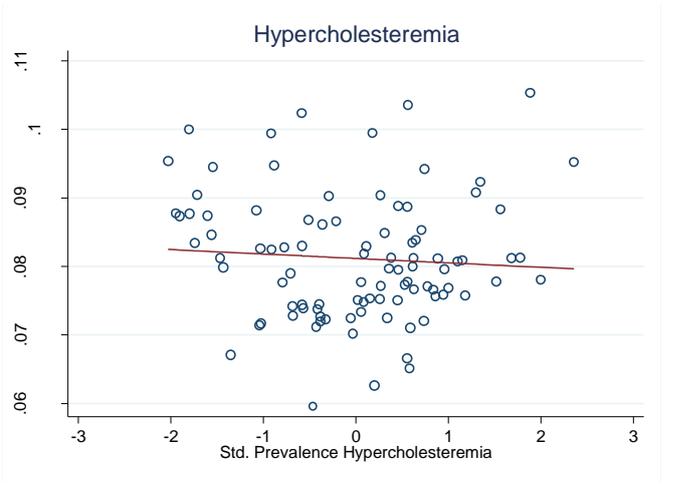
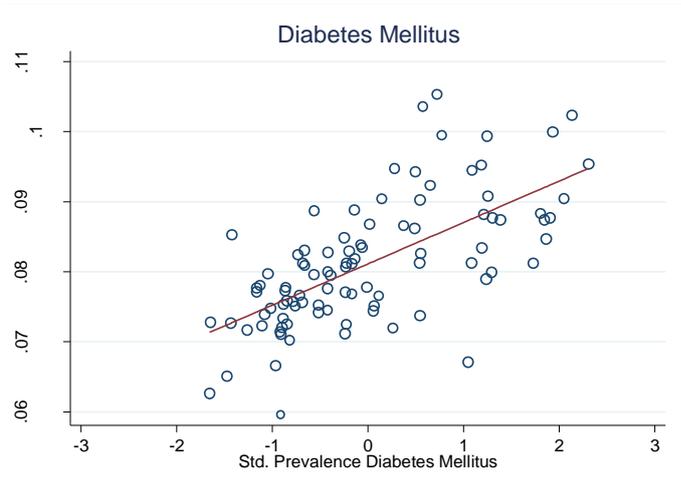
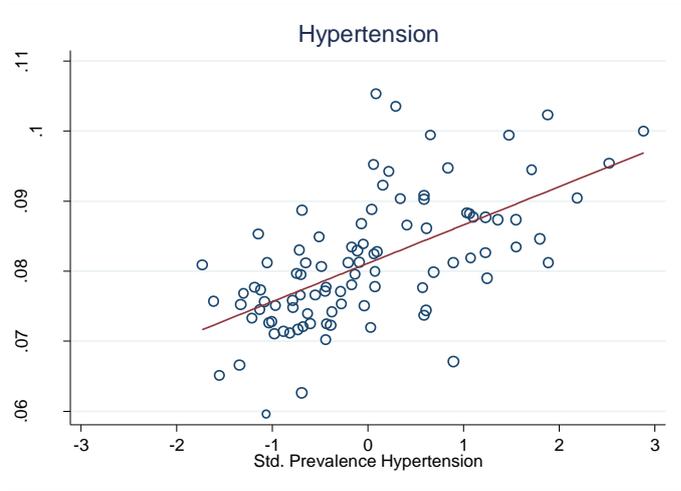


Figure 6: Regional correlation between dementia and hypertension, diabetes mellitus and hypercholesterolemia; age standardized prevalence for ages 65 +, AOK population 2007



## References

- Baldereschi, M.; Di Carlo, A.; Maggi, S.; Grigoletto, F.; Scarlato, G.; Amaducci, L.; Inzitari, D. (1999): Dementia is a major predictor of death among the Italian elderly. ILSA Working Group. Italian Longitudinal Study on Aging. In: *Neurology* 44: 52 (4), S. 709–713.
- Bickel, H.: Epidemiologie psychischer Erkrankungen im Alter. In: Förstl, G. (Hg.) Lehrbuch der Gerontopsychiatrie und -psychotherapie. Stuttgart: Thieme Verlag, 2003: 11-26.
- Bickel, H. (2000): Demenzsyndrom und Alzheimer Krankheit: Eine Schätzung des Krankenbestandes und der jährlichen Neuerkrankungen in Deutschland. In: *Das Gesundheitswesen* 62 (4), S. 211–218.
- Breteler, Monique M. B. (2000): Vascular risk factors for Alzheimer's disease: An epidemiologic perspective. In: *Neurobiology of aging* 21, S. 153–160.
- Brockmann, H. (2002): Why is less money spent on health care for the elderly than for the rest of the population? Health care rationing in German hospitals. In: *Social Science & Medicine* 55 (4), S. 593–608.
- Canadian Study of Health and Aging Working Group (1994): Canadian Study of Health and Aging: study methods and prevalence of dementia. In: *Can Med Assoc J* 150 (6), S. 899–913. Online verfügbar unter <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1486712/pdf/cmaj00286-0095.pdf>.
- Day, N.; Oakes, S.; Luben, R.; Khaw, K. T.; Bingham, S.; Welch, A.; Wareham, N. (1999): EPIC-Norfolk: study design and characteristics of the cohort. European Prospective Investigation of Cancer. In: *British Journal of Cancer* 80 (Suppl 1), S. 95–103. Online verfügbar unter [http://www.srl.cam.ac.uk/epic/publications/day\\_bjc\\_1999\\_clean.pdf](http://www.srl.cam.ac.uk/epic/publications/day_bjc_1999_clean.pdf).
- Doblhammer, G.; Schulz, A.; Steinberg, J.; Ziegler, U. (2012): Demografie der Demenz. Bern: Verlag Hans Huber, Hofgrete AG.
- Doblhammer, G., Fink, A., Fritze, T. (2013) The Demography and Epidemiology of Dementia, *Geriatric Mental Health Care* 1(2): 29-33; DOI: 10.1016/j.gmhc.2013.04.002
- Figuroa, Raul; Steenland, Kyle; MacNeil, Jessica; Levey, Allan I.; Vega, Irving E. (2008): Geographical Differences in the Occurrence of Alzheimer's Disease Mortality: United States

Versus Puerto Rico. In: *American Journal of Alzheimer's Disease & Other Dementias* 23 (5), S. 462–469. Online verfügbar unter <http://aja.sagepub.com/content/23/5/462.full.pdf>.

Fischer, F.; Schiele, R.; Zahn, R.; et al. (2000): Myocardial infarction in 1996–1998: a comparison between the "old" and "new" Lands of Germany. In: *Dtsch Med Wochenschr* 125 (1), S. 181–185.

Forette, F.; Seux, M. L.; Staessen, J. A.; Thijs, L.; Birkenhäger, W. H.; Babarskiene, M. R. et al. (1998): Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Sys-Eur) trial. In: *The Lancet* 24 (9137), S. 1347–1351.

Fratiglioni, L.; Ronchi, D. de; Aguero-Torres, H. (1999): Worldwide prevalence and incidence of dementia. In: *Drugs & Aging* 15 (5), S. 365–375. Online verfügbar unter <http://www.gwern.net/docs/1999-fratiglioni.pdf>.

Geyer, Siegfried; Peter, Richard (2000): Income, occupational position, qualification and health inequalities—competing risks? (Comparing indicators of social status). In: *Journal Epidemiol Community Health* 54, S. 299–305.

Gillum, Richard F.; Yorrick, Ralston; Obisesan, Thomas O. (2011): Population Surveillance of Dementia Mortality. In: *International Journal of Environmental Research and Public Health* 8 (4), S. 1244–1257. Online verfügbar unter <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3118887/?report=reader>.

Gorelick, Philip B. (2004): Risk Factors for Vascular Dementia and Alzheimer Disease. In: *Stroke* 35 (suppl 1), S. 2620–2622.

Haak, Thomas; Palitzsch, Klaus-Dieter (Hrsg.) (2012): Diabetologie für die Praxis. Fallorientierte Darstellung - Diagnostik und Therapie. Stuttgart, New York: Thieme Verlag. Online verfügbar unter 978-3-13-162191-7.

Harbord, R.M.; Higgins, J.P.T. (2008): Meta-regression in Stata. In: *The Stata Journal* 8 (4), S. 493–519.

Hébert, R.; Lindsay, J.; Verreault, R.; Rockwood, K.; Hill, G.; Dubois, M. F. (2000): Vascular dementia: incidence and risk factors in the Canadian study of health and aging. In: *Stroke* 31 (7), S. 1487–1493. Online verfügbar unter <http://www.ncbi.nlm.nih.gov/pubmed/10884442>.

Heinemann, L. A.; Greiser, E. M. (1993): Blood pressure, hypertension, and other risk factors in East and West Germany. In: *Ann Epidemiol* 3 (suppl), S. 90–95.

- Imaizumi, Y. (1992): Mortality rate of Alzheimer's disease in Japan: secular trends, marital status, and geographical variations. In: *Acta Psychiatrica Scandinavica* 86 (5), S. 501–505.
- Ineichen, B. (2000): The epidemiology of dementia in Africa: a review. In: *Social Science & Medicine* 50 (11), S. 1673–1677.
- Jakob, A.; Busse, A.; Riedel-Heller, S. G.; Pavlicek, M.; Angermeyer, M. C. (2002): Prävalenz und Inzidenz von Demenzerkrankungen in Alten- und Altenpflegeheimen im Vergleich mit Privathaushalten. In: *Zeitschrift für Gerontologie und Geriatrie* 35 (5), S. 474–481.
- Jorm, A. F.; Henderson, A. S.; Jacomb, P. A. (1989): Regional differences in mortality from dementia in Australia: an analysis of death certificate data. In: *Acta Psychiatrica Scandinavica* 79 (2), S. 179–185.
- Jorm, A. F.; Korten, A. E.; Henderson, A. S. (1987): The prevalence of dementia: a quantitative integration of the literature. In: *Acta Psychiatrica Scandinavica* 76 (5), S. 465–479.
- Kontula, Kimmo; Ylikorkala, Antti; Miettinen, Helena; Vuorio, Alpo; Kauppinen Makelin, Ritva; Hamalainen, Lisa et al. (1995): Arg506Gln factor V mutation in patients with ischaemic cerebrovascular disease and survivors of myocardial infarction. In: *Thrombosis & Haemostasis* 73 (4), S. 558–560.
- Laaksonen, D. E.; Lakka, H. M.; Niskanen, L. K.; Kaplan, G. A.; Salonen, J. T.; Lakka, T. A. (2002): Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. In: *American Journal of Epidemiology* 156 (11), S. 1070–1077.
- Laditka, James N.; Laditka, Sarah B.; Cornman, Carol B.; Porter, Candace N.; Davis, Dorothy R. (2006a): High variation in both Alzheimer's disease (AD) prevalence and factors associated with prevalence suggest a need for national AD surveillance in the United States. 10th International Conference on Alzheimer's Disease and Related Disorders (ICAD 2006). Madrid, Spain.
- Laditka, James N.; Laditka, Sarah B.; Eleazer, G. Paul; Cornman, Carol B.; Porter, Candace N.; Davis, Dorothy R. (2008): High variation in Alzheimer's disease prevalence among South Carolina counties. In: *Journal of South Carolina Medical Association* 104 (7), S. 215–218.
- Laditka, Sarah B.; Laditka, James N.; Cornman, Carol B.; Porter, Candace N.; Davis, Dorothy R. (2006b): Age-specific prevalence of Alzheimer's disease in a U.S. state with high

population risks: Is South Carolina a harbinger of future national prevalence? 10th International Conference on Alzheimer's Disease and Related Disorders (ICAD 2006). Madrid, Spain.

Launer, L. J. (2011): Counting dementia: There is no one "best" way. In: *Alzheimer's & Dementia* 7 (1), S. 10–14.

Lee, P.N. (1994): Smoking and Alzheimer's disease: a review of the epidemiological evidence. In: *Neuroepidemiology* 13 (4), S. 131–144.

Leicht, H.; Heinrich, S.; Heider, D.; Bachmann, C.; Bickel, H.; van den Bussche, H. et al. (2011): Net costs of dementia by disease stage. In: *Acta Psychiatrica Scandinavica* 124 (5), S. 384–395.

Lorenzo, C.; Okoloise, M.; Williams, K.; Stern, M. P.; Haffner, S. M. (2003): The metabolic syndrome as predictor of type 2 diabetes: the San Antonio heart study. In: *Diabetes Care* 26 (11), S. 3153–3159.

Manfreda, J.: The epidemiologic challenge: inter-regional and urban-rural differences. In: Wood, T. (ed.). *The Challenge of Dementia in Canada—From Research to Practice*. Aylmer, Québec: Health Canada, 1995.

Marti, B.; Rickenbach, M.; Keil, U.; Stieber, J.; Greiser, E.; Herman, B. et al. (1990): Variation in coronary risk factor levels of men and women between the German-speaking MONICA centres. In: *Rev Epidemiol Sante Publique* 38 (5-6), S. 479–486.

Matthews, Fiona; Brayne, Carol; Medical Research Council Cognitive Function and Ageing Study Investigators (2005): The Incidence of Dementia in England and Wales: Findings from the Five Identical Sites of the MRC CFA Study. In: *PLoS Medicine* 2 (8), S. 753–763.

Meisinger, Christa; Heier, Margit; Völzke, Henry; Löwel, Hannelore; Mitusch, Rolf; Hense, Hans-Werner; Lüdemann, Jan (2006): Regional disparities of hypertension prevalence and management within Germany. In: *Journal of Hypertension* 24 (2), S. 293–299.

Moebus, Susanne; Hanisch, Jens; Bramlage, Peter; Lösch, Christian; Hauner, Hans; Wasem, Jürgen; Jöckel, Karl-Heinz (2008): Regional unterschiedliche Prävalenz des metabolischen Syndroms. In: *Deutsches Ärzteblatt* 105 (12), S. 207–213.

Ott, A.; Breteler, M. M. B.; van Harskamp, F.; Claus, J. J.; Van der Cammen, T. J. M.; Grobbee, D. E.; Hofman, A. (1995): Prevalence of Alzheimer's disease and vascular

dementia: association with education. The Rotterdam study. In: *British Medical Journal* 310 (6985), S. 970–973.

Peters, Ruth; Poulter, Ruth; Warner, James; Beckett, Nigel; Burch, Lisa; Bulpitt, Chris (2008): Smoking, dementia and cognitive decline in the elderly, a systematic review. In: *BMC Geriatrics* 8 (1), S. 36.

Petrovitch, H.; White, L. R.; Izmirilian, G.; Ross, G. W.; Havlik, R. J.; Markesbery, W. et al. (2000): Midlife blood pressure and neuritic plaques, neurofibrillary tangles, and brain weight at death: the HAAS. Honolulu-Asia aging Study. In: *Neurobiology of aging* 21 (1), S. 57–62.

Qiu, C.; Winblad, B.; Fratiglioni, L. (2005): The age-dependent relation of blood pressure to cognitive function and dementia. In: *Lancet Neurology* 4 (8), S. 487–499.

Rosak, C. (2003): *Angewandte Diabetologie*. 3. Aufl. Bremen [u.a.]: Uni-Med-Verlag.

Russ, Tom C.; Batty, G. David; Hearnshaw, Gena F.; Fenton, Candida; Starr, John M. (2012): Geographical variation in dementia: systematic review with meta-analysis. In: *International Journal of Epidemiology* 41, S. 1012–1032.

Schipf, S.; Werner, A.; Tamayo, T.; Holle, R.; Schunk, M.; Maier, W. et al. (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). In: *Diabetic Medicine* 29 (7), S. e88-95.

Skoog, I.; Gustafson, D. (2006): Update on hypertension and Alzheimer's disease. In: *Neurol Res* 28 (6), S. 605–611.

Skoog, I.; Lernfelt, B.; Landahl, S.; Palmertz, I. B.; Andreasson, L. A.; Nilsson, L. et al. (1996): 15-year longitudinal study of blood pressure and dementia. In: *Lancet Neurology* 347 (9009), S. 1141–1145.

Slooter, A. J. C.; van Duijn, C. M. (1997): Genetic epidemiology of Alzheimer's disease. In: *Epidemiologic Reviews* 19 (1), S. 107–119. Online verfügbar unter <http://epirev.oxfordjournals.org/content/19/1/107.long>.

Steele, John C.; McGeer, Patrick L. (2008): The ALS/PDC syndrome of Guam and the cycad hypothesis. In: *Neurology* 44: 70 (21), S. 1984–1990.

Steenland, Kyle; MacNeil, Jessica; Vega, Irving; Levey, Allan (2009): Recent Trends in Alzheimer's Disease Mortality in the United States, 1999-2004. In: *Alzheimer Dis Assoc*

*Disord.* 23 (2), S. 165–170. Online verfügbar unter <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2719973/>.

Thamm, M. (1999): Blood pressure in Germany - update review of state and trends. In: *Gesundheitswesen* 61 (suppl), S. 90–93.

Thompson, Simon G.; Sharp, Stephen J. (1999): Explaining heterogeneity in meta-analysis: a comparison of methods. In: *Statistics in Medicine* 18 (20), S. 2693–2708.

Wagner, G.; Abholz, H-H. (2002): Diagnose und Therapiemanagement der Demenz in der Hausarztpraxis 78 (5), S. 239–244.

Weyerer, S. (2005): Altersdemenz. Gesundheitsberichterstattung des Bundes. Robert Koch-Institut. Berlin.

Zhang, Z. X.; Zahner, G. E.; Román, G. C.; Liu, J.; Hong, Z.; Qu, Q. M. et al. (2005): Dementia subtypes in China: prevalence in Beijing, Xian, Shanghai, and Chengdu. In: *Archives of Neurology* 62 (3), S. 447–453.

Zhang, Z. X.; Zahner, G. E.; Román, G. C.; Liu, X. H.; Wu, C. B.; Hong, Z. et al. (2006): Socio-demographic variation of dementia subtypes in china: Methodology and results of a prevalence study in Beijing, Chengdu, Shanghai, and Xian. In: *Neuroepidemiology* 27 (4), S. 177–187.

Ziegler, Uta; Doblhammer, Gabriele (2009): Prävalenz und Inzidenz von Demenz in Deutschland. Eine Studie auf Basis von Daten der gesetzlichen Krankenversicherungen von 2002. In: *Das Gesundheitswesen* 71, S. 281–290.