# Relationship between sleep disturbances and multimorbidity among community-dwelling men and women aged 65–93 years: results from the KORA Age Study

**A. Katharina Helbig, Doris Stöckl, Margit Heier, Barbara Thorand, Holger Schulz, Annette Peters, Karl-Heinz Ladwig, Christa Meisinger**

**Angaben zur Veröffentlichung / Publication details:**

Helbig, A. Katharina, Doris Stöckl, Margit Heier, Barbara Thorand, Holger Schulz, Annette Peters, Karl-Heinz Ladwig, and Christa Meisinger. 2017. "Relationship between sleep disturbances and multimorbidity among community-dwelling men and women aged 65–93 years: results from the KORA Age Study." *Sleep Medicine* 33: 151–59. https://doi.org/10.1016/j.sleep.2017.01.016.

# Relationship between sleep disturbances and multimorbidity among community-dwelling men and women aged 65–93 years: results from the KORA Age Study

A. Katharina Helbig [a, *], Doris Stöckl [a], Margit Heier [a], Barbara Thorand [a], Holger Schulz [b, c], Annette Peters [a], Karl-Heinz Ladwig [a, d], Christa Meisinger [a]

[a] *Institute of Epidemiology II, Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Neuherberg, Germany*
[b] *Institute of Epidemiology I, Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Neuherberg, Germany*
[c] *Comprehensive Pneumology Center Munich (CPC-M), Member of the German Center for Lung Research, Munich, Germany*
[d] *Department for Psychosomatic Medicine and Psychotherapy, Klinikum Rechts der Isar, Technische Universität München, Munich, Germany*

## 1. Introduction

Restorative sleep is an important factor for subjective well-being, daily performance and overall health for individuals at any age [1]. Physiologic changes in sleep architecture occur across the human lifespan [2–4]. Nevertheless, numerous studies have demonstrated a high prevalence of sleep disturbances among older adults [5–8]. In a German study of about 8000 participants, approximately every second person aged 60–79 years reported at least one symptom of insomnia per week, such as having trouble falling asleep or the difficulty of staying asleep [8]. Sleep difficulties, however, are not an inherent part of the normal aging process [2,5]. Even though sleep disturbances are known to be associated with various individual diseases including heart disease, diabetes and depression [9–11], the majority of older individuals suffered from more than one chronic disease simultaneously (this is labeled as multimorbidity) [12,13]. Multimorbidity is linked to more than

* Corresponding author. Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Institute of Epidemiology II, Ingolstädter Landstraße 1, 85764 Neuherberg, Germany. Fax: +49 89 3187 3364.
*E-mail address:* Katharina.Helbig@helmholtz-muenchen.de (A.K. Helbig).

twice as many physician contacts per year compared to individuals without multiple diseases, whereby the number of different physicians contacted increased continuously with each additional chronic condition [14–16]. For geriatric patients, multimorbidity is connected to the consumption of a variety of drugs, health service misuse, and frailty [17]; potential impacts of these aspects may include frequent adverse events, increased mortality and high healthcare costs [15,17]. As studies indicate that certain chronic diseases systematically co-occur [17–21], it is likely that beyond the number of diseases, the composition within frequently co-occurring pairs of diseases might determine individual and societal implications.

Currently, relatively little is known regarding the concept of multimorbidity [12,14]. One assumption is that common mechanisms of accelerated aging are shared between many chronic conditions [22]. As the predominant approach in medical training, care, and research remains focused on single diseases [17,20,23], studies investigating sleep disturbances – in particular, exceptional sleep duration – as contributing factors or consequences of multimorbidity among older individuals are scarce [12,24–27]. Furthermore, none of these studies investigated disturbed sleep in regards to its relationship with commonly occurring pairs of diseases.

Therefore, the objective of the present study was to examine the association between insomnia, unique symptoms of insomnia (trouble falling asleep, difficulty staying asleep, daytime tiredness) and exceptional sleep duration with multimorbidity, taking into account several potential confounding variables. An additional purpose was to investigate the relationship of these sleep disturbances with commonly co-occurring pairs of chronic conditions among a large sample of community-dwelling older men and women in Southern Germany.

Against the background of demographic changes [28,29], the results of the present study are of relevance for an increasing proportion of the general population in Germany. Besides the great importance at the public health level, an enhanced understanding of the relationship between sleep disturbances and multiple diseases might contribute to the awareness of potential target groups for sleep-related prevention and treatment.

## 2. Methods

### 2.1. Data source

For the present analyses, data were derived from the cross-sectional Cooperative Health Research in the Region of Augsburg (KORA) Age Study conducted in the years 2008 and 2009. The objectives of this study were to examine determinants and consequences of multimorbidity among older adults and to investigate factors of "successful aging" [30].

Four separate population-based studies were carried out in the city of Augsburg and the two adjacent counties in southern Germany, and the KORA Age Study is to be seen as a follow-up of individuals aged ≥65 years who have participated in at least one of these former studies [30,31]. The first three surveys were conducted in the framework of the World Health Organization MONItoring trends and determinants in CArdiovascular diseases (MONICA) project in the years 1984–1995. On completion of the MONICA project, the fourth survey was conducted under the name of KORA in the years 1999/2001. In all previous surveys, the participants were randomly selected from population registries, stratified by age and sex. Overall, 17,604 individuals aged 25–74 years participated in at least one of the four surveys (response between 68% and 79%) [32–35].

For the KORA Age Study, all 9197 prior MONICA/KORA participants, who were 65 years and older on the effective date December 31st in 2008, formed the basis. Of these 9197 individuals, 2734 persons had died, 45 had moved abroad or could not be located, and 427 refused to take part in future follow-up studies. The remaining 5991 individuals were contacted by post between November 2008 and September 2009 and asked to fill in a self-administered questionnaire regarding health issues and chronic conditions. If the individuals did not send back the postal questionnaire within three to four weeks, a postcard reminder was sent. After another three to four weeks, non-responders were contacted by telephone and if the person agreed, the questionnaire was completed by telephone. Questionnaire data were available for 4565 individuals (3833 by mail and 732 by telephone) [18,30,36]. Those who were interviewed by telephone were more often female, they were on average older and suffered from more chronic conditions compared to participants who returned the questionnaire by mail [36].

In addition to the mailed survey, approximately two weeks after this survey all 5991 eligible individuals were invited to participate in extended standardized 30-minute telephone interviews performed by trained medical staff and designed to gather more specific information on various aspects of health, including the duration of daily sleep and sleep disturbances. 4127 telephone interviews (response 68.9%) could be performed, the non-respondents could not be contacted or refused to participate [18,30]. In the case that a telephone interview was not possible, the people were offered the opportunity to either be interviewed at home (n = 60) or that proxies (e.g., relatives, friends or caregivers) can answer selected questions on their behalf (n = 185) [18,30,37].

For the present analyses, data from the 4127 telephone interviews, completed with additional information about these individuals regarding chronic conditions, smoking status and medication use from the postal survey formed the basis. Because the "proxy-version" of the telephone interview was focused on objectively ascertainable issues (e.g., utilization of medical services), the proxies were not asked to provide information about participants' sleep [30]. Therefore, the "proxy-interviews" were excluded from the analyses. After further exclusion of data from participants with missing values in at least one of the crucial variables for the statistical analyses (sleep variables: 24 missing values; other variables: 85 missing values), the study sample consisted of 3833 participants (1868 men and 1965 women) in the age span of 65–93 years.

The KORA Age Study received approval from the Ethics Committee of the Bavarian Medical Association ("Bayerische Landesärztekammer") and written informed consent was obtained from all study participants.

### 2.2. Measures

#### 2.2.1. Chronic conditions

As a basis for the assessment of chronic conditions, the self-report-generated Charlson Comorbidity Index from Chaudhry et al. [38] was used. This instrument gathered the presence of the following ten chronic conditions/groups of chronic conditions: 1) asthma, emphysema, or chronic bronchitis, 2) arthritis or rheumatism, 3) cancer, 4) diabetes, 5) digestive problems, 6) heart trouble, 7) kidney disease, 8) liver problems, 9) stroke, and 10) HIV illness or AIDS (because there was no indication for HIV illness/AIDS, this condition was not considered any further) [38].

Due to the high relevance of depression/anxiety, neurological diseases, eye diseases and hypertension for investigating multimorbidity among older adults, these conditions were added to the above listed conditions [18]. Depressed mood was measured by

means of the 15-item short form of the Geriatric Depression Scale. The values ranged from 0 to 15, whereby participants with a score >10 were considered as having depressed mood [39]. Anxiety was measured by means of the Generalized Anxiety Disorder Scale-7. Possible values ranged from 0 to 21, and having an anxiety disorder was defined by a score ≥10 [40]. The presence of neurological diseases, eye diseases and hypertension was established by self-report. In addition, the participants were asked to provide information about any diseases that were not yet mentioned. If diseases were named, they were checked for inclusion regarding the defined chronic conditions/groups of chronic conditions.

Multimorbidity was defined as the simultaneous presence of ≥2 of the above listed conditions/groups of chronic conditions in one individual [13,18]. Most commonly co-occurring pairs of chronic conditions were identified by Kirchberger et al. [18] in previous analyses of the KORA Age Study.

#### 2.2.2. Sleep disturbances

In accordance with former MONICA/KORA studies [30], unique symptoms of insomnia were obtained by asking “Did you have trouble falling asleep?”, “Did you have problems with sleeping through the night?”, and “Do you feel tired or absolutely whacked during the day because of your sleep problems at night?” in the standardized telephone interview. Possible answers were “often”, “sometimes”, or “almost never”, with each sleep item being dichotomized for the analyses (yes as “often” and no as “sometimes/almost never”). To identify more severe cases, participants were rated as having insomnia, if they reported having trouble falling asleep and/or difficulty staying asleep and, additionally, having daytime tiredness. The amount of sleep was documented by responding to the open question: “How many hours a day do you usually sleep? Please also think of nap habits.” The participants' answers were required to be given in integer numbers. Analogous to previous studies [41,42], sleep duration was categorized in ≤5 hours (h) (short sleep duration), 6 h, 7–8 h (reference), 9 h and ≥10 h (long sleep duration).

#### 2.2.3. Socio-demographic characteristics and health-related issues

According to the World Health Organization, body mass index (BMI) was calculated by dividing the weight (in kilograms) by the square of height (in meters) [43]. For this, the height of the participants was measured by trained medical staff in the respective baseline examinations during former MONICA/KORA studies. The current weight in kilograms was reported by the participants in the mailed survey. Educational attainment was approximated through years of schooling, whereby ≤11 years were rated as low educational level and >11 years as high educational level [44]. Risk of malnutrition was measured by means of the SCREEN II (Seniors in the Community: Risk evaluation for eating and nutrition, Version II, short version). The range of score is between 0 and 48, and lower values indicated a higher risk [45]. Leisure time physical activity (e.g., cycling) in winter and in summer was obtained using one question apiece. Answer categories were Likert-scaled and ranged from “no sport activity” (four points) to “more than two hours per week regularly” (one point) [46]. A participant was classified as “active”, if the sum of these two responses was less than five. The consumption of alcoholic beverages “several times per week” up to a “daily consumption” during the last 12 months was rated as frequent alcohol consumption. Participants were categorized as a “smoker” if they indicated that they smoked regularly, or irregularly but currently, and as “non-smoker” if they reported to have smoked in the past or not at all. Finally, data about medication use seven days prior to the postal survey were collected and the substances were assigned following the anatomic–therapeutic–chemical classification system [47]. Psychotropic medication included all anxiolytics, hypnotics, sedatives, antidepressants and benzodiazepines. Polypharmacy was defined as the simultaneous consumption of ≥5 medications of any kind [48].

### 2.3. Statistical analyses

Depending on the distribution of data, means with standard deviations and medians with interquartile ranges were provided for describing the basic characteristics of the entire study population and stratified for individuals with and without insomnia. Relative frequencies were calculated for categorical variables. Using Student's t tests and nonparametric Mann—Whitney U tests, differences in continuous variables were tested. Chi-square tests were performed to compare prevalences.

To estimate the independent association between sleep disturbances and multimorbidity, three sequential logistic regression models were computed for each sleep variable [49,50]. Based on a prior literature search, factors presumed to be associated with sleep issues and multimorbidity were preselected. Afterwards, variables were considered for inclusion in the regression models as independent variables if they were bivariately associated with at least one sleep variable and the multimorbidity variable. All remaining variables with significant relationships were examined with regard to interrelationships and for multicollinearity. The variable psychotropic medication use overlaps strongly with the variables polypharmacy and anxiety/depressed mood. Therefore, only the variables polypharmacy (as independent variable) and anxiety/depressed mood (as part of the multimorbidity variable) were included. According to the literature [51], interactions were tested for all sleep variables with sex.

For the regression analysis, model 1 (“crude model”) comprised only the variable insomnia. Model 2 (“basic model”) extended model 1 with the variables of age (continuous), BMI (continuous) and educational status (low, high). Finally, model 3 (“health issues model”) was additionally adjusted for risk of malnutrition (continuous), physical activity (active, inactive), frequent alcohol consumption (yes, no), currently smoking (yes, no), and polypharmacy (yes, no). This structured modeling approach was similarly applied to the other sleep variables (trouble falling asleep, difficulty staying asleep, daytime tiredness, and sleep duration). To investigate the relationship between the sleep variables and commonly co-occurring pairs of chronic conditions, the model building strategy was identical.

In order to examine if the association between insomnia and multimorbidity was different among individuals with short, reference or long sleep duration, additional multivariable models were calculated. For these analyses, the sleep duration variable was reclassified in broader categories namely ≤6 h, 7–8 h, and ≥9 h of daily sleep. Furthermore, the multivariable relationships between sleep disturbances and the specific chronic conditions were examined.

Results were given as odds ratios (OR) and 95% confidence intervals (CI). For covariable selection and interaction tests, p-values of ≤0.2 were considered as statistically significant; for all other analyses p-values of ≤0.05. Significance tests were calculated two-tailed and the analyses were realized using SAS (Statistical Analysis System, version 9.2, SAS Institute Inc., Cary, NC).

## 3. Results

### 3.1. Population description

A total of 315 individuals (8.2%) were classified as having insomnia. Of all unique symptoms of insomnia, the prevalence of difficulty staying asleep was the highest in the whole sample

(40.7%), followed by trouble falling asleep (16.6%). Whereas 58.7% of the participants reported sleeping 7–8 h daily, 6.2% were categorized as regular short sleepers (≤5 h) and 7.8% as long sleepers (≥10 h). Of individuals with insomnia, 42.0% reported sleep duration of 6 h per day or less.

Table 1 describes the basic characteristics of the total sample and stratified by insomnia. In comparison to respondents without insomnia, there was a higher proportion of women among those suffering from insomnia, and participants with insomnia were, on average, significantly older than those without insomnia. Many of the participants with insomnia reported chronic conditions including hypertension (71.4%), eye diseases (53.7%) and heart diseases (43.2%). The frequency of any individual chronic condition was higher in participants with insomnia compared to those without insomnia.

As shown in Table 2, the prevalence of multimorbidity was 58.7%, with more participants with insomnia suffering from two or more chronic conditions (83.5%) compared to those without insomnia (56.5%). The most frequent co-occurring pairs of chronic conditions among individuals with insomnia were hypertension/eye diseases (37.5%) and hypertension/heart diseases (33.3%).

### 3.2. Association between sleep disturbances and multimorbidity

Table 3 provides sex-specific information about the association between sleep issues and multimorbidity.

**Table 2**
Multiple chronic conditions in the total sample and stratified by insomnia; N = 3833 men and women aged 65–93 years.

| Multiple chronic conditions | Total | Insomnia | | p-value |
|---|---|---|---|---|
| | | Yes (n = 315) | No (n = 3518) | |
| **Multimorbidity** | | | | |
| ≥2 Chronic conditions (%) | 58.7 | 83.5 | 56.5 | <0.0001 |
| **Commonly co-occurring pairs of chronic conditions**[a] | | | | |
| Hypertension/eye diseases (%) | 23.4 | 37.5 | 22.2 | <0.0001 |
| Hypertension/heart diseases (%) | 17.9 | 33.3 | 16.5 | <0.0001 |
| Hypertension/diabetes mellitus (%) | 13.2 | 19.7 | 12.6 | 0.0004 |
| Joint diseases/hypertension (%) | 10.0 | 20.6 | 9.10 | <0.0001 |
| Eye diseases/diabetes mellitus (%) | 7.7 | 14.6 | 7.1 | <0.0001 |
| Joint diseases/eye diseases (%) | 7.7 | 16.2 | 6.9 | <0.0001 |
| Hypertension/lung diseases (%) | 6.6 | 13.3 | 5.9 | <0.0001 |
| Heart diseases/diabetes mellitus (%) | 6.0 | 13.7 | 5.3 | <0.0001 |
| Eye diseases/lung diseases (%) | 5.2 | 12.1 | 4.6 | <0.0001 |
| Joint diseases/heart diseases (%) | 5.1 | 13.7 | 4.3 | <0.0001 |
| Hypertension/gastrointestinal diseases (%) | 5.0 | 12.4 | 4.4 | <0.0001 |
| Hypertension/stroke (%) | 4.6 | 8.3 | 4.2 | 0.0011 |

Abbreviation: N: size of study population, n: number of individuals with or without insomnia.
[a] The most commonly co-occurring pairs of chronic conditions were identified in previous analyses of the KORA Age Study by Kirchberger et al. [18].

**Table 1**
Basic characteristics in the total sample and stratified by insomnia; N = 3833 men and women aged 65–93 years.

| Characteristics | Total | Insomnia | | p-value |
|---|---|---|---|---|
| | | Yes (n = 315) | No (n = 3518) | |
| **Socio-demographic and health issues** | | | | |
| Women (%) | 51.3 | 60.3 | 50.5 | 0.0008 |
| Age[a] (years) | 73.0 (5.8) | 74.1 (6.1) | 72.9 (5.8) | 0.0006 |
| Body mass index[a] (kg/m$^2$) | 27.5 (4.1) | 27.8 (4.7) | 27.4 (4.1) | 0.1569 |
| Low educational level (%) | 72.8 | 75.9 | 72.5 | 0.1956 |
| Physically inactive (%) | 42.3 | 57.5 | 40.9 | <0.0001 |
| Risk of malnutrition[b] (Score 0–48) | 39.0 (36.0–42.0) | 37.0 (32.0–41.0) | 39.0 (36.0–42.0) | <0.0001 |
| Frequent alcohol consumption (%) | 47.0 | 38.1 | 47.8 | 0.0009 |
| Current smoker (%) | 6.5 | 5.1 | 6.6 | 0.2869 |
| Psychotropic medication (%) | 8.3 | 20.0 | 7.2 | <0.0001 |
| Polypharmacy (%) | 26.3 | 42.9 | 24.8 | <0.0001 |
| **Chronic conditions** | | | | |
| Hypertension (%) | 58.7 | 71.4 | 57.5 | <0.0001 |
| Heart diseases (%) | 25.6 | 43.2 | 24.0 | <0.0001 |
| Stroke (%) | 6.0 | 9.5 | 5.7 | 0.0060 |
| Diabetes mellitus (%) | 16.7 | 22.9 | 16.2 | 0.0023 |
| Eye diseases (%) | 38.0 | 53.7 | 36.6 | <0.0001 |
| Joint diseases (%) | 16.5 | 28.6 | 15.4 | <0.0001 |
| Lung diseases (%) | 10.2 | 19.4 | 9.4 | <0.0001 |
| Gastrointestinal diseases (%) | 8.6 | 16.5 | 7.9 | <0.0001 |
| Anxiety/depressed mood (%) | 8.3 | 31.4 | 6.2 | <0.0001 |
| Cancer (%) | 4.3 | 6.4 | 4.1 | 0.0580 |
| Kidney diseases (%) | 3.8 | 8.6 | 3.4 | <0.0001 |
| Neurological diseases (%) | 2.8 | 7.0 | 2.4 | <0.0001 |
| Liver diseases (%) | 2.3 | 5.1 | 2.1 | 0.0006 |
| **Sleep issues** | | | | |
| Trouble falling asleep (%) | 16.6 | 58.1 | 12.9 | <0.0001 |
| Difficulty staying asleep (%) | 40.7 | 91.8 | 36.1 | <0.0001 |
| Daytime tiredness (%) | 9.6 | 100.0 | 1.5 | <0.0001 |
| Hours of daily sleep[c] (%) | | | | <0.0001 |
| ≤5 | 6.2 | 22.9 | 4.8 | |
| 6 | 12.3 | 19.1 | 11.7 | |
| 7–8 | 58.7 | 41.3 | 60.3 | |
| 9 | 14.9 | 10.5 | 15.3 | |
| ≥10 | 7.8 | 6.4 | 8.0 | |

Abbreviation: N: size of study population, n: number of individuals with and without insomnia.
[a] Mean ± standard deviation.
[b] Median with interquartile range.
[c] Specified as hours per 24 h.

**Table 3**
Sequentially-adjusted associations between sleep issues and multimorbidity (≥2 chronic diseases), unstratified results and results stratified by sex; N = 3833.

| Sleep issues | Model 1[a] | Model 2[a] | Model 3[a] |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Insomnia | | | |
| Unstratified | **3.89 (2.87–5.28)** | **3.65 (2.67–4.98)** | **2.92 (2.11–4.05)** |
| Men | **3.73 (2.33–5.97)** | **3.28 (2.03–5.28)** | **2.53 (1.53–4.20)** |
| Women | **3.97 (2.66–5.92)** | **3.93 (2.61–5.93)** | **3.22 (2.10–4.95)** |
| Trouble falling asleep | | | |
| Unstratified | **1.75 (1.46–2.10)** | **1.67 (1.38–2.03)** | **1.45 (1.18–1.77)** |
| Men | **1.67 (1.21–2.31)** | **1.57 (1.13–2.18)** | 1.24 (0.87–1.77) |
| Women | **1.76 (1.41–2.21)** | **1.72 (1.36–2.18)** | **1.55 (1.21–1.99)** |
| Difficulty staying asleep | | | |
| Unstratified | **1.76 (1.54–2.02)** | **1.59 (1.39–1.83)** | **1.54 (1.33–1.79)** |
| Men | **1.66 (1.37–2.02)** | **1.47 (1.20–1.79)** | **1.46 (1.18–1.80)** |
| Women | **1.85 (1.54–2.23)** | **1.74 (1.43–2.11)** | **1.65 (1.34–2.02)** |
| Daytime tiredness | | | |
| Unstratified | **3.94 (2.97–5.22)** | **3.64 (2.73–4.86)** | **2.90 (2.14–3.92)** |
| Men | **3.62 (2.36–5.55)** | **3.17 (2.05–4.89)** | **2.35 (1.48–3.74)** |
| Women | **4.15 (2.85–6.06)** | **4.02 (2.73–5.91)** | **3.34 (2.24–4.99)** |

Abbreviations: N: size of study population, OR: odds ratio, CI: confidence interval, BMI: Body mass index.
Significant results are highlighted in bold type.
Model 1: "Crude" model (unadjusted model).
Model 2: "Basic model" was adjusted for age, BMI and educational status.
Model 3: The full model ("health issues model") was, in addition to model 2, adjusted for risk of malnutrition, physical activity, frequent alcohol consumption, currently smoking and polypharmacy.
[a] Sex-stratified models were not adjusted for sex.

**Table 4**
Sequentially-adjusted associations between sleep duration and multimorbidity (≥2 chronic diseases), unstratified results and results stratified by sex; N = 3833.

| Daily sleep duration (h/24 h) | Model 1[a] | Model 2[a] | Model 3[a] |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Unstratified | | | |
| ≤5 | **2.04 (1.52–2.74)** | **1.90 (1.40–2.58)** | **1.64 (1.19–2.27)** |
| 6 | **1.25 (1.02–1.54)** | 1.15 (0.93–1.42) | 1.07 (0.85–1.33) |
| 7–8 | 1.00 | 1.00 | 1.00 |
| 9 | 1.03 (0.86–1.25) | 0.92 (0.76–1.12) | 0.89 (0.72–1.09) |
| ≥10 | **1.42 (1.11–1.83)** | 1.12 (0.87–1.46) | 0.98 (0.74–1.30) |
| Men | | | |
| ≤5 | 1.30 (0.82–2.07) | 1.23 (0.76–1.98) | 0.97 (0.57–1.64) |
| 6 | **1.53 (1.10–2.12)** | **1.42 (1.01–1.98)** | 1.31 (0.92–1.88) |
| 7–8 | 1.00 | 1.00 | 1.00 |
| 9 | 1.18 (0.92–1.51) | 1.06 (0.82–1.37) | 1.12 (0.85–1.48) |
| ≥10 | 1.31 (0.94–1.81) | 1.04 (0.74–1.45) | 0.91 (0.63–1.32) |
| Women | | | |
| ≤5 | **2.61 (1.76–3.86)** | **2.43 (1.62–3.66)** | **2.16 (1.42–3.30)** |
| 6 | 1.09 (0.84–1.42) | 0.99 (0.75–1.30) | 0.92 (0.69–1.23) |
| 7–8 | 1.00 | 1.00 | 1.00 |
| 9 | 0.88 (0.67–1.17) | 0.76 (0.57–1.02) | **0.65 (0.48–0.89)** |
| ≥10 | **1.67 (1.12–2.48)** | 1.28 (0.85–1.95) | 1.10 (0.71–1.71) |

Abbreviations: N: size of study population, OR: odds ratio, CI: confidence interval, BMI: Body mass index, h: hours.
Significant results are highlighted in bold type.
Model 1: "Crude" model (unadjusted model).
Model 2: "Basic model" was adjusted for age, BMI and educational status.
Model 3: The full model ("health issues model") was, in addition to model 2, adjusted for risk of malnutrition, physical activity, frequent alcohol consumption, currently smoking and polypharmacy.
[a] Sex-stratified models were not adjusted for sex.

In the multivariable models, insomnia was significantly related to multimorbidity in both sexes (men: OR 2.53, 95% CI: 1.53–4.20; women: OR 3.22, 95% CI: 2.10–4.95). Regarding the unique symptoms of insomnia, trouble falling asleep was associated with multimorbidity among women in all models (models 1–3). While this sleep disturbance was significantly related to multimorbidity in the unadjusted model (model 1) and in the basic model (model 2) among men, the association no longer remained significant after an additional adjustment for risk of malnutrition, physical activity, frequent alcohol consumption, currently smoking and polypharmacy (model 3). Nevertheless, the interaction term for trouble falling asleep*sex was not significant (p-value = 0.30). Difficulty staying asleep and daytime tiredness were significantly associated with multimorbidity in both sexes in all three models.

As shown in Table 4, the multivariable OR for the association between short and long daily sleep duration with multimorbidity were 2.16 (95% CI: 1.42–3.30) and 1.10 (95% CI: 0.71–1.71) for women respectively (model 3). However, neither short nor long sleep duration was significantly related to multimorbidity among men in all models (p-value for interaction sleep duration*sex = 0.17).

### 3.3. Association between sleep disturbances and commonly co-occurring pairs of chronic conditions

Table 5 shows the results of the fully-adjusted relationship between insomnia and unique symptoms of insomnia with commonly co-occurring pairs of chronic conditions among men and women. After adjusting for all covariables (models 3), insomnia and especially daytime tiredness were most strongly related to joint diseases/eye diseases among men (insomnia: OR 2.56, 95% CI: 1.47–4.46, daytime tiredness: OR 2.60, 95% CI: 1.53–4.40) and joint diseases/heart diseases among women (insomnia: OR 2.59, 95% CI: 1.57–4.27, daytime tiredness: OR 3.09, 95% CI: 1.94–4.91). Regarding sleep duration, the strongest positive associations occurred between short (OR 2.50, 95% CI: 1.41–4.43) and long (OR 2.33, 95% CI: 1.25–4.35) sleep duration with joint diseases/heart diseases among women (data not shown).

### 3.4. Additional analyses

The results for the association between insomnia and multimorbidity stratified by sleep duration were presented in the Supplementary Table S1 (p-value for the interaction between insomnia and sleep duration was 0.07). It can be seen that from a sleep duration of ≤6 h onwards, the OR for the association between insomnia and multimorbidity continuously decrease to the lowest values in the ≥9 h of daily sleep category.

Supplementary Tables S2 and S3 presented information about the relationships between sleep disturbances and specific chronic conditions. The highest values were identified for the association between sleep disturbances and anxiety/depression.

## 4. Discussion

### 4.1. General discussion

To a varying extent, insomnia and its unique symptoms were closely related to multimorbidity and commonly co-occurring pairs of chronic conditions among older adults, especially among older women. While exceptional sleep duration was not related to multimorbidity among men, short sleep duration was significant and positively associated among women. Regarding commonly co-occurring pairs of conditions, the clearest associations were observed between insomnia and daytime tiredness with joint diseases/eye diseases in men and joint diseases/heart diseases in women. These findings from a large sample of older individuals from the general population in Germany were independent of socio-demographic aspects and important risk factors, including reduced physical activity, impaired nutritional status and taking multiple medication.

**Table 5**
Fully-adjusted associations between sleep issues and commonly co-occurring pairs of chronic conditions stratified by sex; N = 3833.

| | Insomnia | Trouble falling asleep | Difficulty staying asleep | Daytime tiredness |
|---|---|---|---|---|
| | OR[a] (95% CI) | OR[a] (95% CI) | OR[a] (95% CI) | OR[a] (95% CI) |
| Joint diseases/eye diseases | | | | |
| Men | **2.56 (1.47–4.46)** | **1.74 (1.03–2.94)** | **1.58 (1.06–2.34)** | **2.60 (1.53–4.40)** |
| Women | **1.77 (1.14–2.75)** | **1.45 (1.02–2.05)** | 1.28 (0.93–1.75) | **1.86 (1.23–2.81)** |
| Joint diseases/heart diseases | | | | |
| Men | **2.22 (1.21–4.07)** | **1.84 (1.05–3.25)** | 1.51 (0.97–2.38) | **2.19 (1.23–3.88)** |
| Women | **2.59 (1.57–4.27)** | **1.57 (1.03–2.41)** | 1.20 (0.81–1.79) | **3.09 (1.94–4.91)** |
| Joint diseases/hypertension | | | | |
| Men | **2.14 (1.31–3.50)** | **2.19 (1.43–3.36)** | 1.37 (0.99–1.91) | **1.97 (1.23–3.15)** |
| Women | **1.83 (1.23–2.73)** | **1.48 (1.08–2.03)** | 1.10 (0.83–1.47) | **2.12 (1.47–3.07)** |
| Hypertension/heart diseases | | | | |
| Men | **1.97 (1.28–3.02)** | **1.64 (1.13–2.37)** | 1.28 (0.99–1.64) | **1.92 (1.29–2.86)** |
| Women | **2.05 (1.40–3.00)** | **1.43 (1.06–1.93)** | **1.57 (1.20–2.04)** | **2.17 (1.52–3.10)** |
| Hypertension/eye diseases | | | | |
| Men | 1.36 (0.89–2.08) | 1.13 (0.78–1.64) | **1.39 (1.09–1.77)** | **1.56 (1.05–2.30)** |
| Women | **1.79 (1.28–2.52)** | **1.29 (1.00–1.65)** | 1.14 (0.92–1.41) | **1.89 (1.38–2.59)** |
| Hypertension/diabetes mellitus | | | | |
| Men | 1.31 (0.81–2.13) | 1.24 (0.81–1.89) | 0.94 (0.70–1.26) | 1.20 (0.76–1.89) |
| Women | 1.09 (0.69–1.73) | 1.09 (0.77–1.54) | 1.02 (0.76–1.38) | 1.00 (0.65–1.53) |
| Hypertension/lung diseases | | | | |
| Men | **2.10 (1.22–3.62)** | **1.95 (1.20–3.17)** | **1.78 (1.22–2.60)** | **1.87 (1.11–3.16)** |
| Women | 1.49 (0.89–2.49) | 0.90 (0.58–1.39) | 1.10 (0.76–1.59) | **1.77 (1.11–2.84)** |
| Hypertension/stroke | | | | |
| Men | **1.64 (0.87–3.08)** | 1.23 (0.68–2.24) | 0.85 (0.56–1.31) | **1.99 (1.13–3.50)** |
| Women | 1.23 (0.63–2.40) | 1.04 (0.61–1.77) | 1.43 (0.89–2.30) | 1.64 (0.91–2.97) |
| Hypertension/gastrointestinal diseases | | | | |
| Men | **2.48 (1.31–4.70)** | 1.19 (0.61–2.33) | 1.20 (0.75–1.91) | **2.40 (1.30–4.43)** |
| Women | **2.18 (1.32–3.59)** | 0.96 (0.61–1.51) | 1.41 (0.96–2.07) | **2.56 (1.56–4.07)** |
| Heart diseases/diabetes mellitus | | | | |
| Men | **2.27 (1.30–3.94)** | 1.57 (0.93–2.65) | 1.17 (0.80–1.73) | **2.13 (1.27–3.57)** |
| Women | 1.67 (0.93–2.98) | 1.48 (0.92–2.38) | 1.51 (0.97–2.34) | 1.26 (0.71–2.22) |
| Eye diseases/diabetes mellitus | | | | |
| Men | **1.79 (1.04–3.07)** | 1.29 (0.77–2.15) | 1.23 (0.86–1.76) | **1.94 (1.18–3.21)** |
| Women | 1.53 (0.93–2.52) | 0.88 (0.58–1.33) | 1.03 (0.72–1.46) | 1.46 (0.92–2.34) |
| Eye diseases/lung diseases | | | | |
| Men | **2.18 (1.20–3.96)** | 1.59 (0.90–2.79) | **1.54 (1.01–2.35)** | **2.08 (1.17–3.68)** |
| Women | **2.00 (1.18–3.38)** | 1.34 (0.86–2.10) | 1.43 (0.95–2.15) | **2.25 (1.38–3.68)** |

Abbreviations: N: size of study population, OR: odds ratio, CI: confidence interval, BMI: Body mass index.
Significant results are highlighted in bold type.
[a] OR were adjusted for the variables of model 3 (age, BMI, educational status, risk of malnutrition, physical activity, frequent alcohol consumption, currently smoking and polypharmacy).

Although growing evidence indicates the importance of sleep as a public health issue [52–54], relatively few large-scale studies examined the independent association of various sleep disturbances with multimorbidity among individuals from the general population. As in the present study, no significant association was observed between long sleep duration and multimorbidity among individuals of a Brazilian study [24]. Furthermore, in this cross-sectional study comprising of 2637 individuals aged at least 18 years, the authors reported a significant relationship of short sleep duration with three or more health conditions. While in the Brazilian study, results of sex-specific analysis were not reported; the findings of the present study suggest that short sleep duration was significantly related to multimorbidity only among women. However, the results are hardly comparable due to different definitions of sleep duration and multiple conditions, varying age distribution and other geographical contexts. Future studies are therefore desirable in order to help clarify the interplay between sleep duration and multimorbidity. In addition, these studies should be more extensive than the present one, as the number of cases in the exceptional sleep duration categories was somewhat low.

Regarding sleep disturbances, in a cross-sectional study including 378 individuals aged 75 years and above, with at least three medical diagnoses, 42% reported “feeling drowsy” and 40% had “difficulty sleeping” [25]. In a further cross-sectional study from Koyanagai et al. [26], conducted in nine countries comprising 42,116 participants at the age of at least 50 years, sleep disturbances were assessed with the single question: “Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?”. As a result, the authors found a notably dose-dependent relationship between the number of chronic conditions and the sleep disturbances-index variable. A study carried out by Kim et al. [27], comprising about 1200 individuals aged at least 65 years in South Korea, also considered the number of chronic conditions. They found out that the number of physical disorders at baseline was significantly associated with incident and prevalent insomnia. However, none of the above studies examined the association between sleep disturbances and the specific nature of commonly co-occurring pairs of chronic conditions. Although in the KORA Age Study pairs of chronic conditions including hypertension occur most often [18], condition-pairs containing joint diseases were primarily related to sleep disturbances. Joint diseases including arthrosis and arthritis are strongly associated with pain [55]. Therefore, it may be that the high frequency of pain among participants with joint diseases (in conjunction with another disease) provides a preponderant explanation for these associations [55,56]. This is confirmed in a study by Foley et al. [55], in which, after controlling for the presence of daily pain, arthritis as such was no longer significantly associated with insomnia or other sleep problems. In more detail, in the present study the strongest associations were identified between insomnia and daytime tiredness with joint diseases/eye diseases in men and joint diseases/heart

diseases among women. Eye diseases could be one of the extra-articular manifestations commonly occurring among individuals with severe rheumatoid arthritis [57]. The underlying mechanisms for the association between eye diseases and rheumatoid arthritis are unclear [58], but it has been assumed that an increase in inflammatory modulators in rheumatic diseases and adverse effects of the treatment of these diseases could be responsible for the onset of eye diseases (e.g., cataracts or glaucoma) [58–61]. Glucocorticoids are widely used for the treatment of rheumatic diseases [62,63], and possible side effects of these pharmaceuticals can include sleep disturbances [64,65]. An increased risk for individuals with rheumatoid arthritis for developing heart failure [66–68] or ischemic heart diseases [66,69] was reported by the literature, whereby rheumatic diseases and heart diseases also share common basements including inflammation [70].

In the present study, variations in the association between sleep disturbances and multiple conditions were seen between men and women. While sex differences generally, refer to biological and physiological differences between both sexes, an interplay of environmental, social and cultural factors can contribute to gender differences [71]. Variations in (sleep-related) behavior, sleep disturbances, and chronic conditions may not only be influenced by biological aspects, but also by gender differences (e.g., with regard to the report of symptoms and diseases from men and women [71,72]). Although progress has been achieved in determined sex and gender differences in various areas of sleep, major research gaps – for instance, in the field of epidemiology – are still present [71] and existing results are inconsistent [73,74]. Typically, women report a poorer sleep quality and more interruptions of sleep during various stages of life [75]. Also in a study by van den Berg et al., the authors recognized that if sleep aspects were assessed by an interview, elderly women reported consistently shorter and poorer sleep compared to elderly men. Conversely, sleep measured by an actigraph revealed poorer sleep in men [73]. In a study by Voderholzer et al., however, the subjective estimates of sleep quality were comparable between both sexes and none of the continuity measures (e.g., sleep duration or sleep efficiency) showed significant differences for men and women in both groups of participants (individuals with insomnia and healthy controls) [74].

### 4.2. Strengths and limitations

While the KORA Age Study has various strengths, specific limitations should also be considered. Noteworthy strengths are the population-based design, high responses and a large number of participating individuals aged 65–93 years [30]. A standardized assessment of sleep issues, the use of proven multimorbidity measurements [76] and a careful collection of substantial influencing factors, including physical activity, nutritional status and medication intake, also enhance the results of the present study. Through experiences (e.g., implementing studies from the WHO MONICA project [32]), highest quality standards and controls for conducting the KORA Age Study can therefore be assumed [30,54].

One limitation is the cross-sectional study design; it is not permissible to anticipate conclusions about the causal direction of the association between sleep disturbances and multimorbidity. The present analyses shows, however, only whether and to what extent an association is present. Furthermore, in the present study a lot of logistic regression models were performed, thus the probability of finding associations by chance cannot be ruled out.

To calculate the BMI of the participants, current self-reported weight in kilograms was divided by the square of height in meters as measured at the respective baseline examinations. The literature indicates that self-reported weight may underestimate anthropometrically measured weight (among older individuals by about 0.9 kilograms (95% CI: −1.15; −0.48) [77,78]. Another aspect is the decrease in body height with age [43,79]. While a reduction in height generally will increase the BMI of an individual even if the weight is stable [79], in the present study baseline values of body height were used. Both factors may contribute to an underestimation of the BMI of the participants. Moreover, chronic conditions were assessed by self-report, so recall bias could potentially have occurred. The prevalence of multimorbidity (58.7%), lies in the range of the frequency of multimorbidity reported by the literature (55–98% among older adults) [12,17,58,80,81]. However, it is positioned at the lower end. Generally, the frequency of multimorbidity can be influenced by several factors including characteristics of the study population and the underlying list of diseases [17,82]. The KORA Age Study is a follow-up of all participants aged ≥65 years who took part in at least one of the former MONICA/KORA studies [30,31]. Therefore, it can be presumed that volunteer bias may have occurred. In addition, data from all proxy interviews were excluded, an issue which could also contribute to an underestimation of individuals with multiple conditions. In the present study, the list of chronic conditions/group of chronic conditions for the calculations was limited to 13. For example, it is possible that within the group of joint diseases, not only one condition was present, but several. Therefore, the results have to be interpreted as multimorbidity in terms of the simultaneous presence of ≥2 chronic conditions which fall into at least two groups of conditions (not as ≥2 chronic conditions of any kind). Nevertheless, the assessment of diseases is based on the standardized and widely-applied Charlson Comorbidity Index [38,83], supplemented by chronic conditions with a high epidemiological importance for individuals at advanced ages [18].

Finally, subjectively experienced sleep disturbances were obtained by self-report using standardized questions. These questions were implemented in the initial World Health Organization's MONICA Augsburg Study in the years 1984/85 and pursued for ensuring a comparability of the data [30]. However, in the future a psychometric verification of these questions would be desirable to provide solid assertions about validity and reliability. A further point concerns the overlapping of participants with insomnia with individuals classified as having anxiety and/or depression. In the present study, 31.4% of the 315 participants with insomnia were classified as having anxiety and/or depression (Table 1). In order to enhance the comparability with previous studies (e.g. Ref. [55] and [26]) the variable “anxiety/depression” was retained in the multimorbidity-variable. Additionally, to approximate insomnia participants were rated as having insomnia if they reported “often” having trouble falling asleep and/or difficulty staying asleep and, also, having daytime consequences “often” in terms of daytime tiredness. Unfortunately, other potential day-related impacts including impairments of social or occupational functioning [84,85] are not covered in the present study. Nevertheless, the prevalence of insomnia in the total sample was 8.2%, which corresponds to the results of previous studies [6–8,86].

## 5. Conclusion

Not surprisingly, the results of the present study suggest that sleep disturbances generally are widely associated with multiple diseases among older individuals. However, in more detail, sex-specific particularities were seen, especially regarding exceptional sleep duration. While short sleep duration seems to be associated with multimorbidity among women, neither short nor long sleep duration was related to multimorbidity among men. As the mechanisms of multimorbidity and their link to sleep disturbances are not yet fully understood, further prospective studies are needed to investigate the direction and reciprocal effect of sleep, aging and multiple chronic conditions in consideration of the aspects sex and gender.

## Funding sources

The Cooperative Health Research in the Region of Augsburg (KORA) Age Study was a part of the program "Health in old age", which was financed by the German Federal Ministry of Education and Research (BMBF FKZ 01ET0713). The KORA-Age project was conducted on the KORA platform, which was initiated and financed by the Helmholtz Zentrum München, German Research Center for Environmental Health (Neuherberg), and funded by the German Federal Ministry of Education, Science, Research and Technology and the State of Bavaria. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

## Acknowledgments

The authors would like to most warmly thank all of the study participants, the KORA Augsburg field staff, and all members of the Institute of Epidemiology II from the Helmholtz Zentrum München who were involved in planning or conducting the study.

## Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2017.01.016.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.sleep.2017.01.016.

## References

[1] Frohnhofen H, Schlitzer J. Sleep and sleep disorders in the elderly: part 1: epidemiology and diagnostics. Z Gerontol Geriatr 2014;47:527–37.
[2] Rodriguez JC, Dzierzewski JM, Alessi CA. Sleep problems in the elderly. Med Clin North Am 2015;99:431–9.
[3] Ohayon MM, Carskadon MA, Guilleminault C, et al. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep 2004;27:1255–73.
[4] Ancoli-Israel S. Sleep and its disorders in aging populations. Sleep Med 2009;10(Suppl. 1):S7–11.
[5] Ancoli-Israel S, Ayalon L, Salzman C. Sleep in the elderly: normal variations and common sleep disorders. Harv Rev Psychiatry 2008;16:279–86.
[6] Morin CM, LeBlanc M, Daley M, et al. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Med 2006;7:123–30.
[7] Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97–111.
[8] Schlack R, Hapke U, Maske U, et al. Frequency and distribution of sleep problems and insomnia in the adult population in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1). Bundesgesundheitsblatt Gesundheitsforsch Gesundheitsschutz 2013;56:740–8.
[9] Michal M, Wiltink J, Kirschner Y, et al. Complaints of sleep disturbances are associated with cardiovascular disease: results from the Gutenberg Health Study. Plos One 2014;9:e104324.
[10] Najafian J, Mohamadifard N, Siadat ZD, et al. Association between sleep duration and diabetes mellitus: Isfahan healthy heart program. Niger J Clin Pract 2013;16:59–62.
[11] Lacruz ME, Schmidt-Pokrzywniak A, Dragano N, et al. Depressive symptoms, life satisfaction and prevalence of sleep disturbances in the general population of Germany: results from the Heinz Nixdorf Recall study. BMJ Open 2016;6:e007919.
[12] Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev 2011;10:430–9.
[13] van den Akker M, Buntinx F, Knottnerus J. Comorbidity or multimorbidity: what's in a name? A review of literature. Eur J Gen Pract 1996;2:65–70.
[14] Bahler C, Huber CA, Brungger B, et al. Multimorbidity, health care utilization and costs in an elderly community-dwelling population: a claims data based observational study. BMC Health Serv Res 2015;15:23.
[15] Scheidt-Nave C, Richter S, Fuchs J, et al. Challenges to health research for aging populations using the example of "multimorbidity". Bundesgesundheitsblatt Gesundheitsforsch Gesundheitsschutz 2010;53:441–50.
[16] van den Bussche H, Schon G, Kolonko T, et al. Patterns of ambulatory medical care utilization in elderly patients with special reference to chronic diseases and multimorbidity–results from a claims data based observational study in Germany. BMC Geriatr 2011;11:54.
[17] Abad-Diez JM, Calderon-Larranaga A, Poncel-Falco A, et al. Age and gender differences in the prevalence and patterns of multimorbidity in the older population. BMC Geriatr 2014;14:75.
[18] Kirchberger I, Meisinger C, Heier M, et al. Patterns of multimorbidity in the aged population. Results from the KORA-Age study. Plos One 2012;7:e30556.
[19] Prados-Torres A, Poblador-Plou B, Calderon-Larranaga A, et al. Multimorbidity patterns in primary care: interactions among chronic diseases using factor analysis. Plos One 2012;7:e32190.
[20] Marengoni A, Rizzuto D, Wang HX, et al. Patterns of chronic multimorbidity in the elderly population. J Am Geriatr Soc 2009;57:225–30.
[21] Schafer I, von Leitner EC, Schon G, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. Plos One 2010;5:e15941.
[22] Barnes PJ. Mechanisms of development of multimorbidity in the elderly. Eur Respir J 2015;45:790–806.
[23] Boyd C, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design? Public Health Rev 2010;32:451–74.
[24] Lima MG, Bergamo Francisco PM, de Azevedo Barros MB. Sleep duration pattern and chronic diseases in Brazilian adults (ISACAMP, 2008/09). Sleep Med 2012;13:139–44.
[25] Eckerblad J, Theander K, Ekdahl A, et al. Symptom burden in community-dwelling older people with multimorbidity: a cross-sectional study. BMC Geriatr 2015;15:1.
[26] Koyanagi A, Garin N, Olaya B, et al. Chronic conditions and sleep problems among adults aged 50 years or over in nine countries: a multi-country study. Plos One 2014;9:e114742.
[27] Kim JM, Stewart R, Kim SW, et al. Insomnia, depression, and physical disorders in late life: a 2-year longitudinal community study in Koreans. Sleep 2009;32:1221–8.
[28] He W, Goodkind D, Kowal P. An aging world: 2015-International population reports. Washington (DC): U.S. Government Publishing Office; 2016. https://www.census.gov/content/dam/Census/library/publications/2016/demo/p95-16-1.pdf [Accessed 13 March 2017].
[29] Federal Statistical Office of Germany. Germany's population by 2060 – results of the 13th coordinated population projection. Wiesbaden: Federal Statistical Office of Germany; 2015. https://www.destatis.de/EN/Publications/Specialized/Population/GermanyPopulation2060_5124206159004.pdf?__blob=publicationFile [Accessed 13 March 2017].
[30] Peters A, Doring A, Ladwig KH, et al. Multimorbidity and successful aging: the population-based KORA-Age study. Z Gerontol Geriatr 2011;44(Suppl. 2):41–54.
[31] Lacruz ME, Emeny RT, Bickel H, et al. Mental health in the aged: prevalence, covariates and related neuroendocrine, cardiovascular and inflammatory factors of successful aging. BMC Med Res Methodol 2010;10:36.
[32] Löwel H, Doring A, Schneider A, et al. The MONICA Augsburg surveys-basis for prospective cohort studies. Gesundheitswesen 2005;67(Suppl. 1):S13–8.
[33] Holle R, Happich M, Lowel H, et al. KORA-a research platform for population based health research. Gesundheitswesen 2005;67(Suppl. 1):S19–25.
[34] Icks A, Dickhaus T, Hormann A, et al. Differences in trends in estimated incidence of myocardial infarction in non-diabetic and diabetic people: monitoring trends and determinants on cardiovascular diseases (MONICA)/Cooperative health research in the region of Augsburg (KORA) registry. Diabetologia 2009;52:1836–41.
[35] Helbig AK, Stockl D, Heier M, et al. Symptoms of insomnia and sleep duration and their association with incident strokes: findings from the population-based MONICA/KORA Augsburg cohort study. Plos One 2015;10:e0134480.
[36] Hunger M, Thorand B, Schunk M, et al. Multimorbidity and health-related quality of life in the older population: results from the German KORA-age study. Health Qual Life Outcomes 2011;9:53.
[37] Hunger M, Schwarzkopf L, Heier M, et al. Official statistics and claims data records indicate non-response and recall bias within survey-based estimates of health care utilization in the older population. BMC Health Serv Res 2013;13:1.
[38] Chaudhry S, Jin L, Meltzer D. Use of a self-report-generated Charlson comorbidity index for predicting mortality. Med Care 2005;43:607–15.
[39] Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17:37–49.
[40] Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092–7.
[41] Patel SR, Malhotra A, Gottlieb DJ, et al. Correlates of long sleep duration. Sleep 2006;29:881–9.
[42] Kronholm E, Laatikainen T, Peltonen M, et al. Self-reported sleep duration, all-cause mortality, cardiovascular mortality and morbidity in Finland. Sleep Med 2011;12:215–21.
[43] World Health Organization. Physical Status: the use and interpretation of anthropometry: report of a WHO expert committee. Geneva: World Health

Organization; 1995. http://apps.who.int/iris/bitstream/10665/37003/1/WHO_TRS_854.pdf [Accessed 13 March 2017].
[44] Autenrieth CS, Baumert J, Baumeister SE, et al. Association between domains of physical activity and all-cause, cardiovascular and cancer mortality. Eur J Epidemiol 2011;26:91–9.
[45] Keller HH, Goy R, Kane SL. Validity and reliability of SCREEN II (Seniors in the community: risk evaluation for eating and nutrition, version II). Eur J Clin Nutr 2005;59:1149–57.
[46] Meisinger C, Lowel H, Thorand B, et al. Leisure time physical activity and the risk of type 2 diabetes in men and women from the general population. The MONICA/KORA Augsburg Cohort Study. Diabetologia 2005;48:27–34.
[47] German Institute of Medical Documentation and Information. Anatomic–therapeutic–chemical classification with daily doses. Cologne: German Institute of Medical Documentation and Information; 2009. http://www.dimdi.de/dynamic/de/klassi/downloadcenter/atcddd/vorgaenger/atc-ddd-amtlich-2009.pdf [Accessed 13 March 2017].
[48] Heppner HJ, Christ M, Gosch M, et al. Polypharmacy in the elderly from the clinical toxicologist perspective. Z Gerontol Geriatr 2012;45:473–8.
[49] Hosmer DW, Lemeshow S. Applied logistic regression. New York, Chichester, Weinheim, Brisbane, Singapore, Toronto: John Wiley & Sons, Inc.; 2000.
[50] Allison PD. Logistic regression using SAS®: theory and application. Cary, NC: SAS Institute Inc. and Wiley; 2001.
[51] Happe S, Paulus W. Sleep disturbances in old age. In: Deuschl G, Reichmann H, editors. Gerontoneurology. Stuttgart, New York: Georg Thieme Verlag; 2006. p. 85–96.
[52] Grandner MA, Petrov ME, Rattanaumpawan P, et al. Sleep symptoms, race/ethnicity, and socioeconomic position. J Clin Sleep Med 2013;9:897–905 [A-D].
[53] Institute of Medicine (US) Committee on Sleep Medicine and Research, Colten HR, Altevogt BM, editors. Sleep disorders and sleep deprivation: an unmet public health problem. Washington (DC): National Academies Press (US); 2006.
[54] Johar H, Kawan R, Emeny RT, et al. Impaired sleep predicts cognitive decline in old people: findings from the prospective KORA age study. Sleep 2016;39:217–26.
[55] Foley D, Ancoli-Israel S, Britz P, et al. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America survey. J Psychosom Res 2004;56:497–502.
[56] Jordan JM, Bernard SL, Callahan LF, et al. Self-reported arthritis-related disruptions in sleep and daily life and the use of medical, complementary, and self-care strategies for arthritis: the National Survey of Self-care and Aging. Arch Fam Med 2000;9:143–9.
[57] Turesson C, McClelland RL, Christianson T, et al. Clustering of extraarticular manifestations in patients with rheumatoid arthritis. J Rheumatol 2008;35:179–80.
[58] Garin N, Olaya B, Perales J, et al. Multimorbidity patterns in a national representative sample of the Spanish adult population. Plos One 2014;9:e84794.
[59] Falsarella GR, Coimbra IB, Barcelos CC, et al. Prevalence and factors associated with rheumatic diseases and chronic joint symptoms in the elderly. Geriatr Gerontol Int 2013;13:1043–50.
[60] Pincus T, Cutolo M. Clinical trials documenting the efficacy of low-dose glucocorticoids in rheumatoid arthritis. Neuroimmunomodulation 2015;22:46–50.
[61] Kaiser H. Glucocorticoids. In: Commission Quality Assurance of the German Society for Rheumatology, editor. Quality assurance in rheumatology. Darmstadt: Steinkopff; 2008. http://dgrh.de/fileadmin/media/Praxis___Klinik/Manual_QS_2007/kap5.pdf [Accessed 13 March 2017].
[62] Buttgereit F, Straub RH, Wehling M, et al. Glucocorticoids in the treatment of rheumatic diseases: an update on the mechanisms of action. Arthritis Rheum 2004;50:3408–17.
[63] Kirwan JR, Bijlsma JW, Boers M, et al. Effects of glucocorticoids on radiological progression in rheumatoid arthritis. Cochrane Database Syst Rev 2007:CD006356.
[64] Merck KGaA & Co. Decortin® H 50mg tablets. 2013. http://www.merckserono.de/cmg.merckserono_de_2011/de/images/PIL%20DECORTIN%20H%2050%20MG%20-%20DEU042013_tcm1635_102823.pdf?Version= [Accessed 13 March 2017].
[65] mibe GmbH. Methylprednisolon 4 mg JENAPHARM® tablets. 2015. http://www.mibe.de/tl_files/dp_de/content/produkte_mibe/gebrauchsinformationen/methylprednisolon_4mg/GI%20Methylprednisolon%204mg-12–2015.pdf [Accessed 13 March 2017].
[66] Wright K, Crowson CS, Gabriel SE. Cardiovascular comorbidity in rheumatic diseases: a focus on heart failure. Heart Fail Clin 2014;10:339–52.
[67] Nicola PJ, Maradit-Kremers H, Roger VL, et al. The risk of congestive heart failure in rheumatoid arthritis: a population-based study over 46 years. Arthritis Rheum 2005;52:412–20.
[68] Wolfe F, Michaud K. Heart failure in rheumatoid arthritis: rates, predictors, and the effect of anti-tumor necrosis factor therapy. Am J Med 2004;116:305–11.
[69] Corrao S, Messina S, Pistone G, et al. Heart involvement in rheumatoid arthritis: systematic review and meta-analysis. Int J Cardiol 2013;167:2031–8.
[70] Crowson CS, Liao KP, Davis 3rd JM, et al. Rheumatoid arthritis and cardiovascular disease. Am Heart J 2013;166. 622–8e1.
[71] Mallampalli MP, Carter CL. Exploring sex and gender differences in sleep health: a Society for Women's Health Research Report. J Womens Health (Larchmt) 2014;23:553–62.
[72] Eliassen BM, Melhus M, Tell GS, et al. Validity of self-reported myocardial infarction and stroke in regions with Sami and Norwegian populations: the SAMINOR 1 Survey and the CVDNOR project. BMJ Open 2016;6:e012717.
[73] van den Berg JF, Miedema HM, Tulen JH, et al. Sex differences in subjective and actigraphic sleep measures: a population-based study of elderly persons. Sleep 2009;32:1367–75.
[74] Voderholzer U, Al-Shajlawi A, Weske G, et al. Are there gender differences in objective and subjective sleep measures? A study of insomniacs and healthy controls. Depress Anxiety 2003;17:162–72.
[75] Mong JA, Cusmano DM. Sex differences in sleep: impact of biological sex and sex steroids. Philos Trans R Soc Lond B Biol Sci 2016;371:20150110.
[76] Autenrieth CS, Kirchberger I, Heier M, et al. Physical activity is inversely associated with multimorbidity in elderly men: results from the KORA-Age Augsburg Study. Prev Med 2013;57:17–9.
[77] Lopuszanska M, Lipowicz A, Kolodziej H, et al. Self-reported versus measured body height and weight in Polish adult men: the risk of underestimating obesity rates. Anthropol Anz 2015;72:263–77.
[78] May AM, Barnes DR, Forouhi NG, et al. Prediction of measured weight from self-reported weight was not improved after stratification by body mass index. Obesity Silver Spring 2013;21:E137–42.
[79] Droyvold WB, Nilsen TI, Kruger O, et al. Change in height, weight and body mass index: longitudinal data from the HUNT Study in Norway. Int J Obes Lond 2006;30:935–9.
[80] van den Bussche H, Koller D, Kolonko T, et al. Which chronic diseases and disease combinations are specific to multimorbidity in the elderly? Results of a claims data based cross-sectional study in Germany. BMC Public Health 2011;11:101.
[81] Nagel G, Peter R, Braig S, et al. The impact of education on risk factors and the occurrence of multimorbidity in the EPIC-Heidelberg cohort. BMC Public Health 2008;8:384.
[82] Hansen H. Patient-reported vs. from primary care physicians diagnosed moribidty. Results from the MulitCare Cohort Study (Dissertation). 2013. d-nb.info/1052332641/34 [Accessed 13 March 2017].
[83] Khan NF, Perera R, Harper S, et al. Adaptation and validation of the Charlson index for read/OXMIS coded databases. BMC Fam Pract 2010;11:1.
[84] Kryger M, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 6th ed. Philadelphia: Elsevier; 2017.
[85] Leger D, Partinen M, Hirshkowitz M, et al. Daytime consequences of insomnia symptoms among outpatients in primary care practice: EQUINOX international survey. Sleep Med 2010;11:999–1009.
[86] Buysse DJ. Insomnia. JAMA 2013;309:706–16.