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Health-related quality of life in subjects with and without Type 2 diabetes: pooled analysis of five population-based surveys in Germany

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Abstract

Aims To estimate population values of health-related quality of life (HRQL) in subjects with and without Type 2 diabetes mellitus across several large population-based survey studies in Germany. Systematic differences in relation to age and sex were of particular interest.

Methods Individual data from four population-based studies from different regions throughout Germany and the nationwide German National Health Interview and Examination Survey (GNHIES98) were included in a pooled analysis of primary data (N = 9579). HRQL was assessed using the generic index instrument SF-36 (36-item Short Form Health Survey) or its shorter version, the SF-12 (12 items). Regression analysis was carried out to examine the association between Type 2 diabetes and the two component scores derived from the SF-36/SF-12, the physical component summary score (PCS-12) and the mental component summary score (MCS-12), as well as interaction effects with age and sex.

Results The PCS-12 differed significantly by −4.1 points in subjects with Type 2 diabetes in comparison with subjects without Type 2 diabetes. Type 2 diabetes was associated with significantly lower MCS-12 in women only. Higher age was associated with lower PCS-12, but with an increase in MCS-12, for subjects with and without Type 2 diabetes.

Conclusions Pooled analysis of population-based primary data offers HRQL values for subjects with Type 2 diabetes in Germany, stratified by age and sex. Type 2 diabetes has negative consequences for HRQL, particularly for women. This underlines the burden of disease and the importance of diabetes prevention. Factors that disadvantage women with Type 2 diabetes need to be researched more thoroughly.

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Keywords age, health-related quality of life, pooled analysis, sex, Type 2 diabetes mellitus

Introduction

The high and increasing prevalence of Type 2 diabetes mellitus and the high incidence of associated complications and co-morbid conditions make the disease a prime case to assess health-related quality of life (HRQL), which is a central domain of patient-based outcomes and essential for health decision-making and planning processes [1,2]. Comparing a number of chronic diseases, Type 2 diabetes poses a particular risk of decline in physical health, with its relative position similar to that of congestive heart failure or chronic respiratory disease [3]. Summarizing the evidence for the magnitude of the adverse HRQL effects in women and men with Type 2 diabetes has important implications for public health efforts to lower the risk of developing the disease.

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Many studies and clinical trials of Type 2 diabetes include generic HRQL instruments, such as the EuroQol 5D and the SF-36 (36-item Short Form Health Survey) or its shorter version, the SF-12 (12 items) [4]. Most studies use practice-based samples and differ considerably in instruments used, designs and statistical models [1,2,5,6]. However, investigating general populations is important to provide estimates of the burden of Type 2 diabetes with regard to HRQL for the whole spectrum of the disease, including lifestyle-treated forms of type 2 diabetes [7]. Moreover, sample sizes need to be sufficiently large to allow for subgroup analyses of the effects of demographic and clinical characteristics on HRQL. However, there is a lack of such data in Germany and elsewhere.

The purpose of this study was to compare population values of HRQL measured with the SF-36/SF-12 in subjects with and without Type 2 diabetes, across several large population-based survey studies from different regions in Germany and a nationwide survey. The approach used here is that of a pooled analysis of individual data. With this, standardized criteria for modelling of exposure, confounding and outcome variables can be applied to the large data pool and estimates can be more precise [8]. Using a model of analysis that is restricted to age and sex as covariates, this paper aims to offer baseline data that can be easily compared across countries.

Subjects and methods

This study is part of the DIAB-CORE (Diabetes Collaborative Research of Epidemiologic Studies) research consortium, which investigates the prevalence and incidence of Type 2 diabetes as well as socio-economic covariates, medication, costs and HRQL of subjects with Type 2 diabetes in Germany in comparison with the population without Type 2 diabetes. Six population-based cohort studies were identified that had collected such data at baseline. Five of these studies (four regional and one national) are comparable in their assessment of HRQL and are included in the subsequent analysis (see Table 1 for acronyms and study region).

The studies were conducted between 1997 and 2006. Detailed descriptions of study designs, samples and procedures are available elsewhere [9–13]. Ethical approval from designated Research Ethics Committees was obtained individually for each study.

The pooled data can be considered as representative of the German population. The studies included cover the major regions of Germany. Sampling methods were two-stage cluster sampling or stratified random sampling. Three of the studies included only respondents of German nationality (KORA, SHIP, CARLA). In the nationwide survey (GNHIES98), 3% of the respondents were non-German citizens; the other two studies collected information on birthplace only. Overall response rates ranged between 61% and 69%.

The primary data from the studies were added to a joint database and pooled at the individual level. Only the age groups covering 45–74 years, which was the common intersection of all studies, were included. Type 2 diabetes was defined based on self-report of physician-diagnosed diabetes mellitus or self-reported intake of oral anti-diabetic agents or insulin. Self-reported age at onset of diabetes was ascertained in all studies. Owing to a lack of information about the diabetes type in some of the studies, only subjects with an age at onset of diabetes of > 30 years were included. However, it can be estimated from the studies with diabetes type information (KORA, DHS) that approximately 5% of the subjects classified as subjects with type 2 diabetes in our sample were subjects with Type 1 diabetes.

To ensure a high degree of comparability, all variables were recoded in the pooled data following DIAB-CORE standard procedures, established for the homogenization of basic variables.

Assessment of HRQL

The outcome variable for this analysis is HRQL, which was assessed in three of the studies by the German version of the 12-item Short Form Health Survey (SF-12 version 1), a generic index instrument for HRQL derived from the SF-36 [4]. Two of the studies (GNHIES98, DHS) administered the SF-36 (version 1). The SF-36/SF-12 measures health status over the past 4 weeks. This instrument was applied as a self-administered questionnaire during a visit to the study centre in four studies and as part of a face-to-face interview in one study (KORA).

Table 1 Characteristics of the pooled sample (45–74 years) with complete SF-12 (12-item Short Form Health Survey)

Study	Region	Study period	*N* (%)	Age (years), mean (SD)	Women, *N* (%)	Type 2 diabetes, *N* (%)
KORA	South Germany (Augsburg region)	10/1999–4/2001	2340 (24.4)	58.8 (8.4)	1173 (50.1)	136 (5.8)
CARLA	East Germany (Halle)	12/2002–1/2006	1300 (13.6)	60.1 (7.9)	610 (46.9)	159 (12.2)
DHS	West Germany (Dortmund)	10/2003–3/2004	765 (8.0)	60.0 (8.5)	381 (49.8)	73 (9.5)
SHIP	North-east Germany (West Pomerania)	10/1997–5/2001	2045 (21.3)	58.8 (8.3)	1031 (50.4)	224 (11.0)
GNHIES98	Nationwide	10/1997–3/1999	3129 (32.7)	57.9 (8.0)	1593 (50.9)	254 (8.1)
Total		10/1997–1/2006	9579	58.8 (8.2)	4788 (50.0)	846 (8.8)

KORA (S4), Cooperative Research in the Region of Augsburg; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; SHIP (S0), Study of Health in Pomerania; GNHIES 98, German National Health Interview and Examination Survey 1998; SD, standard deviation.

The SF-12 yields summary scores for physical and mental health, the physical component summary (PCS-12) and the mental component summary (MCS-12). The SF-36 can be used to calculate these scores by drawing on a subset of respective items. Both scores range from 0 to 100, with higher values indicating better HRQL. Scores were calculated using standard algorithms, as published by Bullinger and Kirchberger [14]. These algorithms only allow complete cases to be included in the analysis.

Statistical analysis

Descriptive statistics included means and standard deviations (SD) for the PCS-12 and MCS-12 scores of subjects with and without type 2 diabetes, analysed separately for each study and in pooled analysis. The mean level of both summary scores and their 95% confidence intervals (95% CI) were calculated by adjusting for age (in years) and sex differences. Linear regression models were used for the PCS-12 and the MCS-12 scores to assess the effect of Type 2 diabetes, controlling for age, sex and study. All two-way interactions (age × diabetes, sex × diabetes, study × diabetes) were assessed. Interaction terms were only attained in the model when they reach statistical significance, which was assumed at P-values of < 0.05 in this study. Analysis was performed using SAS statistical software, version 9.1 (SAS Institute Inc., Cary, NC, USA).

Results

Subjects

After exclusions resulting from case ascertainment and incomplete SF-12 data, 9579 respondents remained for analysis (see Figure 1). A total of 846 (8.8%) respondents were classified as subjects with Type 2 diabetes according to the standardized definition of diabetes in DIAB-CORE. The proportion of women ranged from 47% to 51% across the five studies; the proportion of subjects with Type 2 diabetes ranged from 6% to 12% across the regional studies and was 8.1% in the national survey study (GNHIES98). Respondents were characterized by a mean age of 58.8 years (SD 8.2 years). Respondents that were excluded from analysis because of missing values in the SF-12 (n = 758) had a mean age of 60.6 years (SD 8.2 years); 54.6% were women and 12% were subjects with Type 2 diabetes (data not shown).

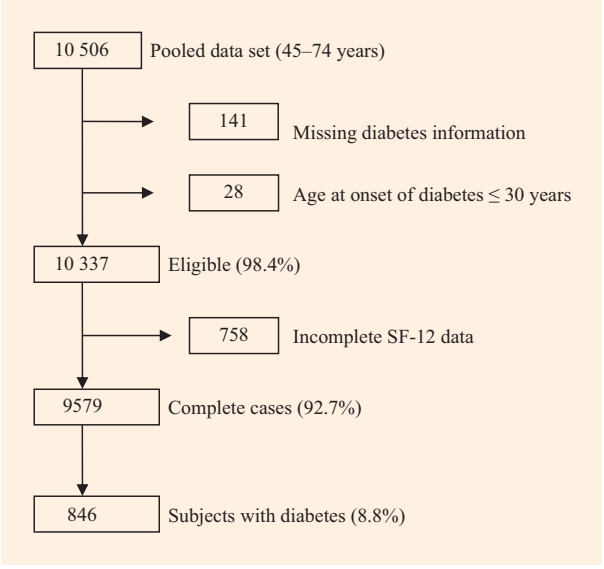

FIGURE 1 Study flow chart.

PCS-12 and MCS-12 scores

Table 2 shows the summary scores unadjusted for baseline differences in covariates between studies. The pooled summary scores are shown for women and men separately; scores for women are consistently lower than those for men.

Figure 2a and b show the age- and sex-adjusted mean differences in PCS-12 and MCS-12 scores, respectively, between subjects with and without type 2 diabetes by study and in pooled analysis. The PCS-12 score differences varied between 3.2 and 4.8 points across the five studies, with higher scores indicating a greater difference between subjects with and without diabetes. Thus, subjects with type 2 diabetes had significantly lower PCS-12 scores in each study as well as in the pooled analysis (Figure 2a). With regard to the MCS-12, the observed adjusted differences were smaller and not statistically significant in two of the studies. In the pooled analysis, the adjusted mean difference of −1.5 in MCS-12 scores was statistically significantly different from zero (Figure 2b). The pooled analysis shown here does not adjust for study effects, initially assuming full comparability of the single studies.

Table 3 shows the results of the multivariate regression analysis adjusting for age and sex as well as for study effects. The introduction of study effects into the statistical model for pooled analysis was necessary to allow for potential heterogeneity across studies resulting from variation in study designs, respondent characteristics and regional influences.

Type 2 diabetes is associated with lowering of PCS-12 scores by 4.1 points. Age is statistically significantly associated with both PCS-12 and MCS-12 scores, for subjects with and without type 2 diabetes. As shown in Figure 3a, greater age is associated with lower PCS-12 scores, but with increased MCS-12 scores. Differences between subjects with and without type 2 diabetes decreased slightly with age, but there was no statistically significant interaction between age and diabetes. Women had lower PCS-12 and MCS-12 scores than men, with the sex difference being more pronounced in MCS-12 scores. The only interaction effect that reached statistical significance was sex × diabetes for the MCS-12 score. Our data show a significant impact of type 2 diabetes on the MCS-12 scores for women only. The sex-specific MCS-12 scores are shown in Figure 4. Derived from the estimates from the regression model,

Table 2 Physical component summary (PCS-12) and mental component summary (MCS-12) unadjusted mean scores by study and diabetes status

	PCS-12 mean score (SD)			MCS-12 mean score (SD)		
Study	Total (SD)	Diabetes	No diabetes	Total (SD)	Diabetes	No diabetes
KORA	45.8 (9.6)	41.5 (10.1)	46.0 (9.5)	51.7 (9.5)	50.4 (10.7)	51.8 (9.4)
CARLA	45.7 (9.7)	42.3 (10.5)	46.1 (9.5)	53.5 (8.9)	52.6 (10.9)	53.7 (8.6)
DHS	44.5 (9.8)	39.6 (10.1)	45.0 (9.6)	52.2 (9.1)	52.0 (10.1)	52.2 (8.9)
SHIP	46.2 (9.5)	41.8 (10.4)	46.8 (9.2)	52.6 (8.5)	52.2 (9.7)	52.6 (8.3)
GNHIES98	45.7 (9.5)	40.4 (10.3)	46.2 (9.2)	51.9 (8.9)	50.2 (9.6)	52.1 (8.8)
POOL*	45.7 (9.5)	41.2 (10.3)	46.2 (9.4)	52.2 (9.0)	51.4 (10.2)	52.3 (8.8)
Women	44.9 (9.8)	40.1 (10.4)	45.4 (9.6)	51.0 (9.5)	49.3 (10.7)	51.2 (9.3)
Men	46.6 (9.2)	42.2 (10.1)	47.0 (9.0)	53.5 (8.3)	53.3 (9.3)	53.5 (8.1)

KORA (S4), Cooperative Research in the Region of Augsburg; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; SHIP (S0), Study of Health in Pomerania; GNHIES 98, German National Health Interview and Examination Survey 1998; SD, standard deviation. *Study data pooled at individual level.

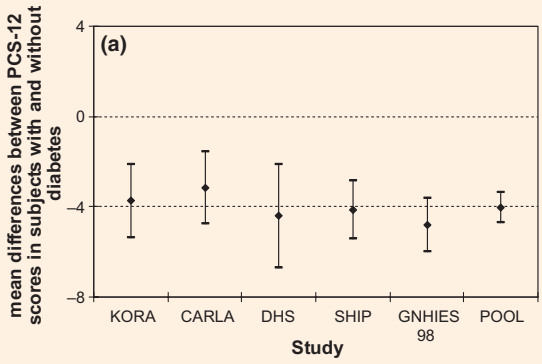

FIGURE 2 Mean differences in (a) physical component summary (PCS-12) and (b) mental component summary (MCS-12) scores and 95% CI between subjects with and without Type 2 diabetes per study and pooled, adjusted for age and sex. KORA (S4), Cooperative Research in the Region of Augsburg; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; SHIP (S0), Study of Health in Pomerania; GNHIES 98: German National Health Interview and Examination Survey 1998.

a mean difference of −4.1 (95% CI 2.9; 5.3) for women with Type 2 diabetes in comparison with men with type 2 diabetes was found for the MCS-12 score.

Looking at the heterogeneity between the studies, we used GNHIES98 as reference, because it was the only national survey study in the data pool. Study effects had a significant impact on both PCS-12 and MCS-12 results, with regional variation of up to 1.6 points in PCS-12 scores and 1.7 points in MCS-12 scores. Estimates ranged from −0.8 to 0.8 for the PCS-12 scores and from −0.4 to 1.4 for the MCS-12 score. The DHS study had lower than average scores for the PCS-12 and the CARLA study higher than average scores for the MCS-12. However, there was no significant study × diabetes interaction, indicating that the effect of Type 2 diabetes on HRQL was similar across all five studies.

Discussion

In this study, we sought to augment the sparse data on HRQL in Germany with pooled data from several large population-based studies, addressing the age- and sex-specific difference in HRQL between subjects with Type 2 diabetes compared with subjects without Type 2 diabetes. A pooled analysis of primary data has advantages in comparison with meta-analysis with published data as variables can be recoded to make them as compatible as possible and adjustments can be made to deal with heterogeneity between studies. Our population-based estimates can be compared with results from other countries.

The SF-12 mean scores in our data corresponded well with published mean scores in the German population from the 1994 normative sample [14]. Comparing across age groups, PCS-12 scores were lower in older age groups, whereas MCS-12 scores were relatively stable. This finding is consistent with previous research and has been shown for respondents with and without Type 2 diabetes [15,16].

Our results show that type 2 diabetes was associated with a decrease in HRQL by 4.1 points on the PCS-12 score. This is approximately half the SD for the PCS-12 and can be regarded as a difference of moderate to large magnitude [3,17]. The 4-point difference equals the decline in PCS-12 scores between subjects aged 45 years and 65 years, which can be regarded as an

Table 3 Physical component summary (PCS-12) and mental component summary (MCS-12) scores for subjects with and without Type 2 diabetes (multivariate regression analysis)

		PCS-12			MCS-12		
Effect		Estimate	SE	*P*	Estimate	SE	*P*
Intercept		58.76	0.70		47.52	0.67	
Diabetes	Yes	−4.11	0.34	< 0.0001	−0.73	0.44	0.0978
Age	Year	−0.20	0.012	< 0.0001	0.10	0.011	< 0.0001
Sex	Female	−1.80	0.19	< 0.0001	−2.25	0.19	< 0.0001
Sex × diabetes	Female × diabetes	–	–	–	−1.84	0.64	0.0039
Study*				0.0007			< 0.0001
	KORA	0.10	0.25		−0.36	0.24	
	CARLA	0.47	0.31		1.38	0.29	
	DHS	−0.77	0.37		0.05	0.36	
	SHIP	0.78	0.26		0.60	0.25	
	GNHIES98	Ref.	–		Ref.	–	

KORA (S4), Cooperative Research in the Region of Augsburg; CARLA, Cardiovascular Disease, Living and Ageing in Halle; DHS, Dortmund Health Study; SHIP (S0), Study of Health in Pomerania; GNHIES 98: German National Health Interview and Examination Survey 1998; SE, standard error.
**P*-value for overall study effect

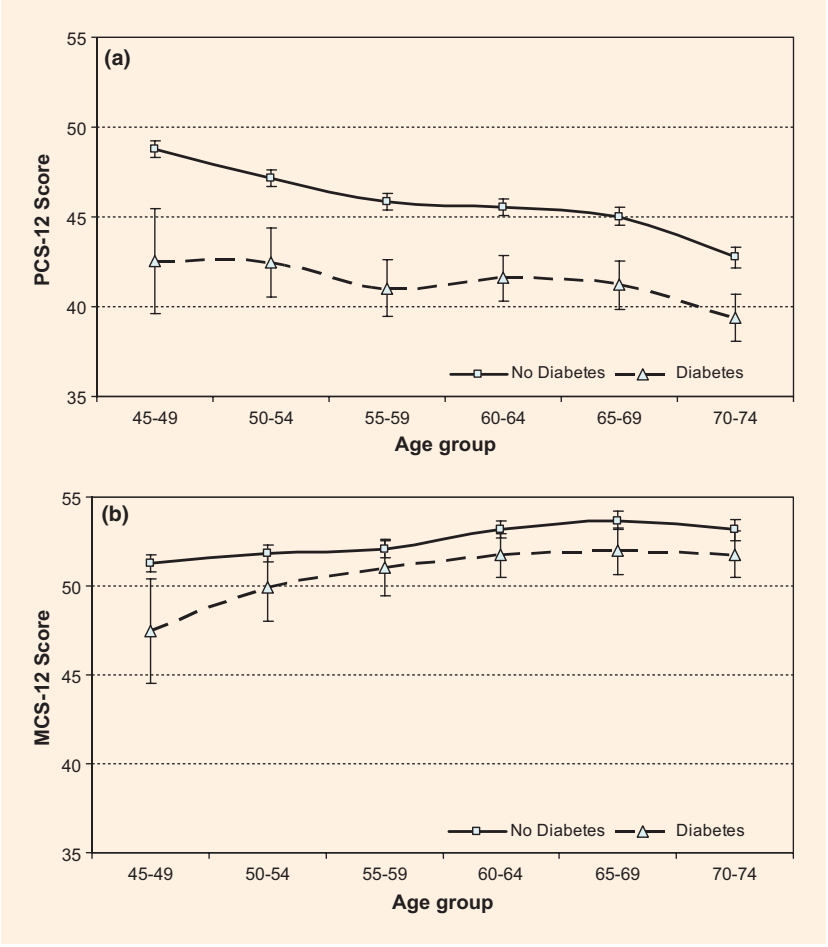

FIGURE 3 Pooled (a) physical component summary (PCS-12) and (b) mental component summary (MCS-12) mean scores and 95% CI per age group between subjects with and without Type 2 diabetes, adjusted for sex and study.

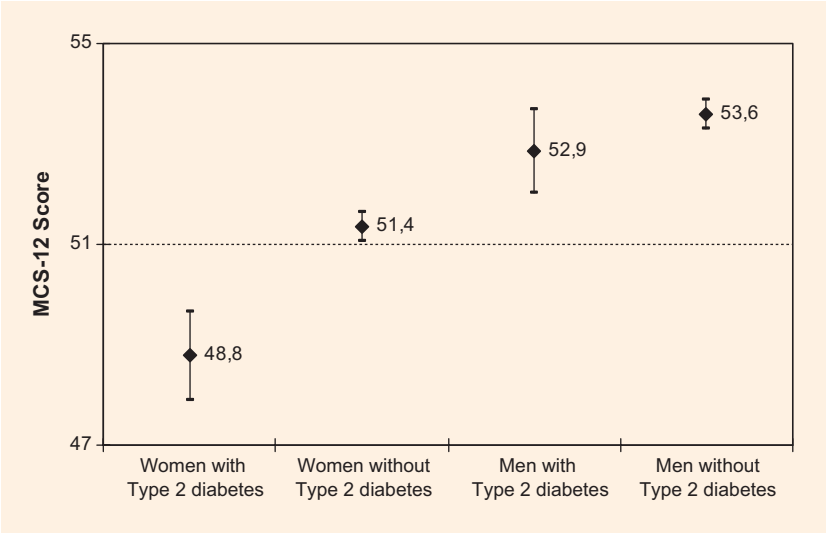

FIGURE 4 Pooled sex and Type 2 diabetes specific mental component summary (MCS-12) mean scores and 95% CI, adjusted for age and study.

indicator of how such differences are perceived. The difference on the MCS-12 score was smaller (−2.5 points) and only significant in women. This differential impact has been described previously [2,18]. Alonso *et al.* [17] examined a large pooled sample (N = 24 936) across eight countries and found a highly significant difference of −3.5 points ($P < 0.001$) on the PCS-36 for subjects with Type 2 diabetes compared with subjects with no chronic condition; the difference of −1.0 points ($P < 0.05$) for the MCS-36 was still significant, but to a lesser degree. In our study, the control group included patients with other chronic conditions. With regard to the difference between PCS-12 and MCS-12, it has been argued that the summary scores do not adequately reflect the interdependence of physical and mental health. In the case of diabetes, effects on mental health may be underestimated as a result of the coefficients used in the computation of the summary scores [19].

An important result of the present study is that the adverse impact of Type 2 diabetes on MCS-12 can be shown for women only. To our knowledge, there are no comparable studies providing such data for other countries. Women generally report lower levels of HRQL than men [20]. There is evidence that sex differences in HRQL are attributable to sex-specific differences in the impact of chronic diseases rather than a sex-specific reference bias [21]. Women with Type 2 diabetes are at greater risk of developing coronary artery disease, suffering from hypertension and experiencing symptoms of hyperglycaemia compared with men with type 2 diabetes [22]. Prevalence rates for illnesses relating to mental health, such as anxiety disorders and depression, are higher in women than in men [23]. Findings from Type 2 diabetes cost of illness studies confirm that women have higher average total costs than men, and these are associated with a greater utilization of medical services and drugs [24]. This needs to be researched more carefully to provide recommendations to clinical practice for additional support for women with Type 2 diabetes.

The strengths of this study are the large and unselected study sample, the use of standardized variable definitions and the uniform statistical models for analysis. However, a number of conceptual and methodological constraints need to be recognized. Although the standardized definition of variables enables the pooling of primary data, the range of variables is limited to those available across all studies. In the case of the definition of diabetes, this meant that it had to be based on self-report of physician diagnosis and treatment with insulin or anti-diabetic drugs rather than clinical measures. Studies that compared the validity of self-reported medication-treated diabetes with medical records indicated a generally high accuracy of self-reports, ranging from 59% to 99% in sensitivity and 97% to 99% in specificity [25]. However, this may be less accurate with regard to lifestyle-treated diabetes. Another limitation of this study is the age restriction to 45–74 years, especially as there is evidence that MCS-12 scores decline in age groups ≥ 75 years [26].

Studies are not totally comparable with regard to mode of assessment. One study used a face-to-face interview to assess the SF-12, which may have contributed to the heterogeneity between the studies captured in the study effect. Missing data in the SF-12 are of particular concern because there is no imputation rule defined and scores can only be computed for complete cases. All five studies had nearly complete data for the SF-12, which was above or close to 90% and was higher than in comparable studies [2,16]. Although HRQL assessment with the SF-12 questionnaire has proved to be of high validity and great practicability for epidemiological research and clinical studies, generic health status measurements such as the SF-12 may underestimate health loss associated with diabetes because they are not sensitive enough to capture domains that are of particular relevance to subjects with Type 2 diabetes [27,28]. Moreover, our results underestimate HRQL loss as it is experienced in the

population, because subjects with high medical needs are less likely to participate in survey studies.

Study effects are significant in our pooled analysis, with a smaller gap in HRQL between subjects with and without Type 2 diabetes in most of the regional studies compared with the national survey study. Notably, the observed association between Type 2 diabetes and HRQL was consistent across all studies. Differences between the regional studies can be caused by variation in study designs and methods or sample differences, for example with regard to disease severity and co-morbidities. A sensitivity analysis, controlling for disease severity expressed by insulin intake, shows that the HRQL of subjects with Type 2 diabetes is lower with increasing treatment intensity but age, sex and study effects are not altered. Co-morbid conditions, such as heart disease, stroke or arthritis, have been identified as frequently associated with Type 2 diabetes and lead to lower HRQL scores than for Type 2 diabetes alone [29,30]. Regional differences in the prevalence of chronic conditions are conceivable. However, further analysis of the impact of co-morbidities is hindered by the lack of comparable information in the pooled data set.

In conclusion, we offer a consistent and comparative description of HRQL in subjects with Type 2 diabetes in comparison with subjects without Type 2 diabetes, with pooled data from five population-based studies in Germany (one national survey and four from different regions in the country). We found that the physical health of subjects with Type 2 diabetes is significantly impaired. For mental health, only women with Type 2 diabetes report lower HRQL. These findings augment the call to increase efforts to identify men and women at high risk of developing Type 2 diabetes [31] and strengthen the need for gender-sensitive intervention programmes. Further cross-sectional and longitudinal studies are required to identify the impact of co-morbidities, socio-economic factors and other patient-level, regional-level or practice-level factors on the overall Type 2 diabetes health burden. The HRQL values for broad populations with Type 2 diabetes, such as those shown here, contribute a reference grid for future studies.

Competing interests

Nothing to declare.

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