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RESEARCH ARTICLE

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Regional differences in type 2 diabetes treatment and outcomes in Germany—An analysis of the German DPV and DIVE registries

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Abstract

Aims: On the basis of the Diabetes Versorgungs-Evaluation (DIVE) and Diabetes-Patienten-Verlaufsdokumentation (DPV) datasets, we aimed to explore the impact of differences in treatment modalities on outcomes in Germany and put these into a global context.

Methods: The 2014 to 2016 DIVE and DPV databases were combined, and a total of 127 838 patients 18 years and older was analysed with respect to demographics, cardiovascular risk factors, comorbidities, treatments, and outcomes, separately for each German state. Estimates were expressed as adjusted least squares means together with 95% confidence intervals.

Results: Saarland dataset recorded the lowest mean HbA_{1c} (6.7%; 6.6%-6.8%; 50 mmol/mol, 49-51 mmol/mol), Saxony-Anhalt showed the highest (8.3%; 8.2%-8.3%; 67 mmol/mol, 66-67 mmol/mol). The highest percentage of hypoglycaemic events was reported in Mecklenburg-West Pomerania (MWP) (4.7%; 3.9%-5.7%), the lowest in Thuringia (0.9%; 0.2%-3.4%). Metformin and sulfonylurea accounted for 36.4% to 53.3% of anti-diabetic treatments across states; other antihyperglycaemic drugs such as DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 analogues were used most often in MWP (40.0%; 37.8%-42.1%) and least in Rhineland-Palatinate (13.6%; 13.0%-14.2%). Treatment with insulin (alone or in combination) was reported most often in MWP (78.2%; 76.4%-80.0%) and least in Thuringia (26.0%; 20.1%-32.9%).

Conclusions: Federal states in Germany are heterogeneous concerning diabetes treatment and associated outcomes. These data should stimulate further discussion about how optimal diabetes care can be implemented in all areas of Germany, to achieve good treatment outcomes in all federal states.

KEYWORDS

diabetes outcome, diabetes treatment, German diabetes atlas, regional differences

1 | INTRODUCTION

The number of people with diabetes in Europe was estimated to be 56 million, with an overall estimated prevalence of 8.5%, in 2013. Diabetes prevalence varied widely across the 56 countries, ranging from 2.4% in Moldova to 14.9% in Turkey.[1] In Germany, the standardized prevalence of diabetes[2,3] increased from 8.9% in 2009 to 9.8% in 2015. This was primarily due to a rise in the prevalence of type 2 diabetes (T2DM).

In addition to national differences, within-country regional differences are important. For example, people in eastern regions of Germany consistently have an age standardized prevalence of known T2DM that is up to twofold higher (12.0%) than among people in the south (5.8%),[4] as well as a higher prevalence of hypertension[5] and increased waist circumference.[6] Regional differences in T2DM within countries have also been described for Finland[7] and the United Kingdom.[8] They are relevant for planning national and regional approaches to prevention and health care provision.

The socio-economic status (SES) of both individuals and municipalities determine individual health outcomes.[9] Results from six population-based studies in Germany conducted between 1997 and 2006 showed that, among persons with T2DM, treatment with oral anti-diabetic agents was reported more frequently in the south (56.9%) and less in the north-east (46.0%), whereas treatment with insulin alone was reported more frequently in the north-east (21.6%) than in the south (16.4%).[4]

Despite its importance, epidemiological data on diabetes treatment and outcomes comparing German regions or comparing Germany with other countries are scarce. Using the German diabetes registries Diabetes Versorgungs-Evaluation (DIVE) and Diabetes-Patienten-Verlaufsdokumentation (DPV), we aimed to analyse treatment modalities among patients with established T2DM and the potential impact on regional variations in outcomes and to compare the results to other countries.

2 | MATERIALS AND METHODS

2.1 | Data source and subjects

Data were obtained from the DIVE registry and the DPV database. The DIVE registry was established in Germany[10-16] in 2011. Patients with diabetes mellitus, regardless of their disease stage and treatment strategy, were enrolled consecutively at 159 outpatient clinics across the country. Data were entered into local databases using DPV (Ulm University) or DIAMAX (Axaris software & systeme GmbH) software. All patients included in the DIVE registry provided written informed consent. The study protocol was approved by the ethics committee of the Medical School of Hannover (process number 6003). The DPV database was established in Germany in 1995 at Ulm University.[17-19] Approximately 450 centres in Germany currently use the DPV software. Every 6 months, locally documented data are anonymized and sent to the University of Ulm. The DPV initiative was approved by the ethics committee of the University of Ulm (process number 202/09), and data collection was approved by local review boards.

Individuals with a clinical diagnosis of T2DM and aged over 18 years who were documented in DPV (up to September 2016) and in DIVE (up to December 2016) and were attributed to a defined federal state were included in the present analysis. Participants who tested positive for beta-cell autoantibodies (GAD antibodies, ICA, IA-2 antibodies, and ZnT8 antibodies) were excluded.

A total of 549 881 patients were registered in the databases. Seventy percent of these were documented to have T2DM (N = 381 745). According to the inclusion criteria (T2DM, age over 18 years, negative autoantibodies, complete data since 2014), 127 838 patients were considered for the analyses. Numbers of inhabitants per federal state were shown according to the statistic portal of the Statistische Ämter des Bundes und der Länder[20] of 31.12.2015, census of 2011.

2.2 | Definitions

Hypertension was defined as blood pressure level >140 mm Hg systolic or 90 mm Hg diastolic and/or receiving antihypertensive drugs. Dyslipidaemia was defined as total cholesterol ≥200 mg/dL, LDL-cholesterol (LDL-C) ≥160 mg/dL, HDL-cholesterol <40 mg/dL, triglycerides ≥150 mg/dL, or treatment with lipid lowering drugs. The definition of "overweight" was a body mass index (BMI) ≥25 kg/m^2. Hypoglycaemia was defined as an event requiring assistance by another person to actively administer carbohydrates, glucagon, or other resuscitative actions[21]; hypoglycaemia with coma was defined when loss of consciousness or seizures occurred. HbA_{1c} measurements were standardized according to guidelines of the German Medical Association following the position of the IFCC working group on global standardization of glycated haemoglobin measurement in the laboratories of the participating centres.

2.3 | Statistics

Regional differences were estimated with adjustment for demographic differences based on linear regression models (HbA_{1c}), Poisson regression (rate of hypoglycaemia), and logistic regression models (rate of being overweight, treatment modalities), with federal state as a confounder. Adjustment was made for sex, age (in categories: ≤40 y, 41-50 y, 51-60 y, 61-70 y, 71-80 y, >80 y), migration background (yes/no), and duration of diabetes (in categories: <10 y, ≥10 y). Estimates were expressed as adjusted means (least squares means) or shown as colour-coded tertiles for each federal state in the German diabetes atlas. Because of low patient numbers in some states, the datasets of participants from Berlin and Brandenburg, Hamburg and Schleswig-Holstein, and Bremen and Lower Saxony were combined. Statistical analysis was performed using SAS version 9.4.

3 | RESULTS

3.1 | Patient characteristics

A total of 127 838 participants with T2DM who were aged >18 years, negative for beta-cell autoantibodies and documented in the databases as of 2014, were included in the present analysis (Figure 1). Numbers of participants per federal state are shown in Table 1.

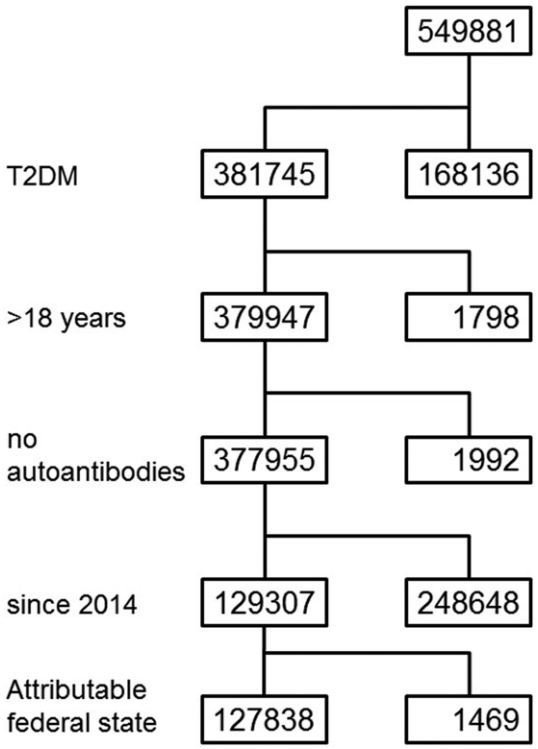

FIGURE 1 Patient flow. T2DM, diabetes mellitus type 2; >18 years, participants over 18 years of age; Ab, beta-cell autoantibodies; since 2014, complete data since 2014; attributable federal state, participants with attributable federal state

Participants had a long duration of diabetes (average, 11.3 ± 9.3 y). The mean HbA_{1c} of participants (7.5 ± 1.7% [58 mmol/mol, 40-77 mmol/mol]) reached targets recommended by national and international guidelines (Table 1). The mean BMI of 31.5 ± 6.7 kg/m^2 pointed towards a relevant prevalence of obesity.

The principal anti-diabetic drugs used were metformin (40.0% of participants), insulin alone (20.6% of participants), and DPP-4 inhibitors (19.0% of participants). Sulfonylureas (SU) were used in only 7.7% of participants, GLP-1 analogues in 3.9%, and glinides in 3.2%. Antihypertensive medication was prescribed in about half of the participants. (Table 1).

3.2 | Metabolic control quality parameters

Where available, we analysed parameters reflecting metabolic control, such as HbA_{1c}, being overweight (BMI ≥25 kg/m^2), and the rate of severe hypoglycaemia, and classified each federal state in the German diabetes atlas (Figure 2) into upper, middle, or lower tertiles for each parameter. Participants from Saarland and Rhineland-Palatinate had the lowest mean HbA_{1c} (6.7% ± 0.01 [50 mmol/mol] and 7.2% ± 0.02 [55 mmol/mol]), while Saxony-Anhalt and Mecklenburg-West Pomerania had the highest mean HbA_{1c} (8.3% ± 0.03 [67 mmol/mol] and 8.5% ± 0.04 [69 mmol/mol]) (Table 2). Participants of almost all eastern federal states (except Thuringia) and western federal states such as Baden-Wuerttemberg, Lower Saxony/Bremen, and Hesse missed an HbA_{1c} target of ≤7.5% (58 mmol/mol), which should be appropriate for most participants. Looking at hypoglycaemic events in the different federal states, the highest percentages were reported in Mecklenburg-West Pomerania and Hesse (4.7% ± 0.4 and 4.4% ± 0.1), while the lowest percentages were reported in Thuringia and Schleswig-Holstein/Hamburg (0.9% ± 0.6 and 1.0% ± 0.1). In all federal states, more than 80% of participants were overweight, with the highest percentages seen in Thuringia and Saxony-Anhalt (91.3% ± 2.2 and 90.4% ± 0.6) and the lowest percentages in Baden-Wuerttemberg and Hesse (85.2% ± 0.3 and 85.4% ± 0.4).

TABLE 1 Number of participants with type 2 diabetes per federal state, inhabitants per federal state[20] (31.12.2015, census of population 2011), number of participating centres, and overall patient characteristics[a]

Participants (T2DM) per Federal State, /Inhabitants/Number of Participating Centres, Total (n)	127 838	82 175 684	252
Baden-Wuerttemberg	13 629	10 879 618	33
Bavaria	24 168	12 843 514	39
Hesse	9622	6 176 172	20
Lower Saxony + Bremen	8893	8 598 088	21
North Rhine-Westphalia	38 490	17 865 516	67
Rhineland-Palatinate	12 766	4 052 803	21
Saarland	1822	995 597	3
Schleswig-Holstein + Hamburg	3108	4 646 122	11
Brandenburg + Berlin	9001	6 004 857	18
Mecklenburg-West Pomerania	2024	1 612 362	6
Saxony	2123	4 084 851	6
Saxony-Anhalt	2031	2 245 470	5
Thuringia	161	2 170 714	2
Age, y	68 ± 12.8		
Men, %	54.2		
Body mass index, kg/m^2	31.5 ± 6.7		
Diabetes duration, y	11.3 ± 9.3		
HbA_{1c} [% (mmol/mol)]	7.5 ± 1.7 (58, 40-77)		
Lipids			
Triglycerides, mg/dl	183.9 ± 115.1		
Total cholesterol, mg/dl	186.8 ± 48.98		
LDL-cholesterol, mg/dl	113 ± 39.8		
HDL-cholesterol, mg/dl	47.4 ± 17.3		
Anti-diabetic medication, %			
Biguanides	40.0		
Sulfonylurea	7.7		
Glinides	3.2		
Acarbose	0.4		
Glitazone	0.3		
GLP-1 analogues	3.9		
DPP-4 inhibitors	19.0		
SGLT2 inhibitors	4.3		
Insulin (total)	43.3		
Insulin (without OAD)	20.6		
Antihypertensive medication, %	51.3		
Lipid-lowering medication, %	29.3		

Abbreviations: OAD, oral anti-diabetic drug; T2DM, diabetes mellitus type 2.

[a]Data presented as total number (n), mean ± SD, or percentage (n/N).

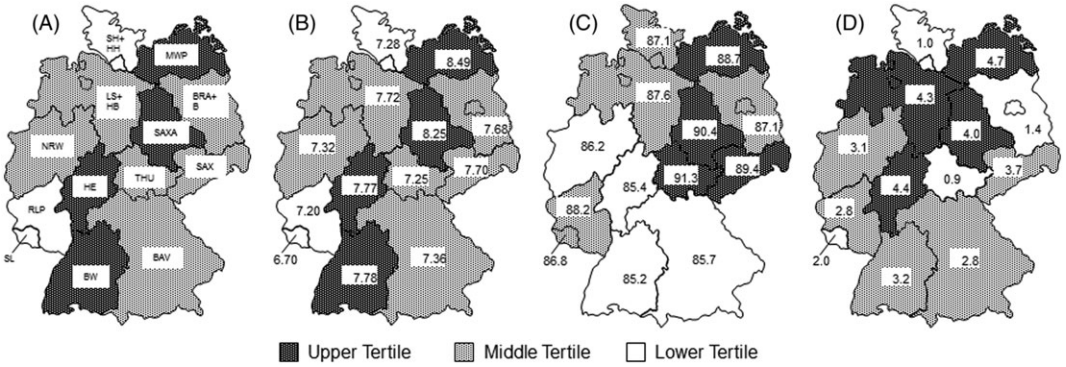

FIGURE 2 German diabetes atlas: Metabolic control quality parameters. Federal states of Germany A,: BAV, Bavaria; BRA + B, Brandenburg + Berlin; BW, Baden-Wuerttemberg; HE, Hesse; LS + HB, Lower Saxony + Bremen; MPW, Mecklenburg-West Pomerania; NRW, North Rhine-Westphalia; RLP, Rhineland-Palatinate; SAX, Saxony; SAXA, Saxony-Anhalt; SL, Saarland; SH + HH, Schleswig-Holstein + Hamburg; THU, Thuringia, HbA_{1c} B, BMI ≥25 kg/m^2 C, and hypoglycaemic events D, per federal state after adjustment for age, sex, migration background, and diabetes duration. Data are presented as adjusted means (least squares means) and shown as pattern coded tertiles for each federal state in the German diabetes atlas

TABLE 2 Metabolic control quality parameters[a]

Federal State	HbA_{1c} (%;(mmol/mol))LSM (95%CI)	Participants with BMI ≥25 kg/m^2 (%)LSM (95% CI)	Severe Hypoglycaemia (%)LSM (95% CI)
Baden-Württemberg	7.78 (62) 7.75; 7.81	85.2 84.6; 85.9	3.2 3.0; 3.5
Bavaria	7.36 (57) 7.34; 7.38	85.7 85.3; 86.2	2.8 2.6; 2.9
Brandenburg + Berlin	7.68 (61) 7.65; 7.72	85.4 86.3; 87.8	1.4 1.2; 1.6
Hesse	7.77 (61) 7.74; 7.81	87.6 83.8; 85.3	4.4 4.1; 4.8
Mecklenburg-West Pomerania	8.49 (69) 8.42; 8.57	86.2 87.2; 90.1	4.7 3.9; 5.7
Lower Saxony + Bremen	7.72 (61) 7.68; 7.75	87.6 86.9; 88.3	4.3 4.0; 4.7
North Rhine-Westphalia	7.32 (57) 7.30; 7.34	86.1 85.8; 86.5	3.1 2.9; 3.2
Rhineland-Palatinate	7.20 (55) 7.17; 7.23	88.2 87.6; 88.7	2.8 2.6; 3.0
Saarland	6.70 (50) 6.63; 6.78	87.1 85.2; 88.2	2.1 1.7; 2.6
Saxony	7.70 (61) 7.62; 7.78	88.7 88.1; 90.6	3.7 3.1; 4.6
Saxony-Anhalt	8.25 (67) 8.17; 8.32	89.4 89.1; 91.6	4.0 3.3; 4.9
Schleswig-Holstein + Hamburg	7.28 (56) 7.22; 7.34	90.4 85.8; 88.3	1.0 0.8; 1.3
Thuringia	7.25 (56) 6.98; 7.52	91.3 85.9; 94.8	0.9 0.2; 3.4

Abbreviations: BMI, body mass index; LSM, least squares means.

[a]HbA_{1c}, BMI ≥25 kg/m^2, and rate of severe hypoglycaemic events per federal state after adjustment for age, sex, migration background, and diabetes duration. Data presented as LSM together with 95% confidence intervals (95% CI).

3.3 | Antihyperglycaemic therapy and lifestyle modification

Metformin and sulfonylurea accounted for 36.4% to 53.3% of anti-diabetic treatments across the different federal states (Table 3). This combination was reported most often in Thuringia and Brandenburg/Berlin (53.3% ± 4.0 and 51.5% ± 1.2) and least often in Saxony and Hesse (36.4% ± 1.1 and 37.7% ± 0.5). DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 analogues were most often used in Mecklenburg-West Pomerania and Baden-Wuerttemberg (39.9% ± 1.0 and 32.5% ± 0.4) and least in Rhineland-Palatinate and Saarland (13.6% ± 0.4 and 15.8% ± 0.2). Insulin alone or in combination with oral anti-diabetic drugs (OADs) was reported most often in Mecklenburg-West Pomerania and Saxony-Anhalt (78.2% ± 1.1 and 75.8% ± 0.9),

TABLE 3 Antihyperglycaemic therapy and lifestyle modification[a]

Federal State	Insulin Alone or in Combination(%)LSM (95% CI)	Metformin/sulfonylurea (%)LSM (95% CI)	DPP-4 and SGLT2 Inhibitors, GLP-1 Analogues(%)LSM (95% CI)	Lifestyle Intervention (%)LSM (95% CI)
Baden-Württemberg	45.5 44.6; 46.4	51.5 50.7; 52.4	32.5 31.7; 33.3	19.2 18.1; 19.8
Bavaria	41.9 41.3; 42.6	48.3 47.7; 49.0	29.7 29.1; 30.3	22.7 22.2; 23.2
Brandenburg+ berlin	55.6 54.6; 56.7	51.5 50.5; 52.6	25.9 25.0; 26.8	14.1 13.4; 14.8
Hesse	47.9 46.8; 48.9	37.7 36.8; 38.7	24.9 24.0; 25.8	20.8 0.20; 21.7
Mecklenburg-West Pomerania	78.2 76.4; 80.0	44.7 42.5; 46.9	40.0 37.8; 42.1	6.2 5.2; 7.3
Lower Saxony + Bremen	27.7 26.8; 28.7	39.4 38.4; 40.5	18.8 18.0; 19.6	36.1 35.1; 37.2
North Rhine-Westphalia	41.2 40.7; 41.8	37.8 37.3; 38.3	22.7 22.3; 23.2	28.7 28.2; 29.1
Rhineland-Palatinate	33.5 32.6; 34.3	38.2 37.4; 39.1	13.6 13.0; 14.2	33.7 32.9; 34.5
Saarland	33.6 31.4; 35.9	45.6 43.3; 48.0	15.8 14.2; 17.5	26.4 24.4; 28.4
Saxony	53.7 51.5; 55.9	36.3 34.3; 38.5	29.2 27.3; 31.2	21.5 19.8; 23.3
Saxony-Anhalt	75.8 73.9; 77.6	44.7 42.5; 46.9	31.5 29.6; 33.6	7.4 6.3; 8.6
Schleswig-Holstein + Hamburg	44.8 43.0; 46.7	50.7 48.9; 52.5	24.6 23.1; 26.1	23.5 22.0; 25.0
Thuringia	26.0 20.1; 32.9	53.3 45.5; 61.0	17.4 12.2; 24.1	24.0 17.8; 31.4

[a]Percentages of anti-diabetic medication and lifestyle intervention after adjustment for age, sex, migration background, and diabetes duration. Data are presented as least squares means (LSM) together with 95%-confidence intervals (95% CI).

while least insulin usage was seen in Thuringia and Lower Saxony/Bremen (26.0% ± 3.3 and 27.7% ± 0.5). Lifestyle modification only was recorded in just 6.2%-36.1% of participants, mostly in Lower Saxony/Bremen and Rhineland Palatinate (36.1% ± 0.4 and 33.7% ± 0.5) and least often in Mecklenburg-West Pomerania and Saxony-Anhalt (6.2% ± 0.9 and 7.4% ± 0.8).

4 | DISCUSSION

The aim of our study was to explore differences in treatment modalities and outcomes across Germany and put these into a global context. We found that federal states with mean HbA_{1c} values in the upper tertile also reported high rates of hypoglycaemic events. In these federal states, more than 75% of treatment regimens contained insulin. The percentages of overweight participants were highest in eastern federal states, but were also high in all other federal states.

4.1 | Metabolic control quality parameters

Differences in prevalence, treatment modalities, and outcomes are influenced by demographic trends, the socio-economic status of participants, and differences in health care modalities between German federal states. Our study contributes to the understanding of the regional effects influencing diabetes care. By combining data from the two German diabetes registries DIVE and DPV, we were able to analyse parameters of diabetes care for a very large number of participants with T2DM (127 838) from across all German federal states. Mean HbA_{1c} across all federal states was 7.5%, which is in accordance with data from a multinational observational study assessing insulin use in 4519 patients from primary care or specialty practice sites across 18 countries.[22] In this study, patients in Saudi Arabia had the highest HbA_{1c} values (9.0% ± 2.2 [75 mmol/mol]) followed closely by Turkey (8.9% ± 2.0 [74 mmol/mol]), while Germany and China had the lowest HbA_{1c} levels at 7.5% ± 1.4 (58 mmol/mol) and 7.6% ± 1.8 (60 mmol/mol), respectively.

Looking at mean HbA_{1c} on a regional basis in Germany, a mean treatment goal of HbA_{1c} <7.5% (58 mmol/mol) was reached in only six of 13 federal states. Federal states with mean HbA_{1c} in the upper tertile lie on a diagonal through Germany running from north-eastern Mecklenburg-West Pomerania to south-eastern Baden-Wuerttemberg. The highest percentages of hypoglycaemia were reported in federal states that also had the highest mean HbA_{1c}: Mecklenburg-West Pomerania, Saxony-Anhalt, and Hesse. In federal states with mean HbA_{1c} in the lower tertile (Saarland, Rhineland-Palatinate, Schleswig-Holstein, and Thuringia), percentages of hypoglycaemia were also low.

Excess bodyweight and obesity are determinants of diabetes development, but also influence treatment options and metabolic outcomes. Recent studies found a higher prevalence of obesity in

north-eastern Germany compared with south-western Germany but did not take address differences between federal states.[23] Our study confirms this finding, with the highest percentages of participants with obesity found in Mecklenburg-West Pomerania, Saxony-Anhalt, Saxony, and Thuringia and the lowest in North Rhine-Westphalia, Hesse, Baden-Wuerttemberg, and Bavaria.

4.2 | Antihyperglycaemic therapy and lifestyle modification

We analysed treatment modalities in different federal states. More intensive treatment modalities were not reflected by better outcome parameters. For example, Saarland and Mecklenburg-West Pomerania, which are the smallest federal states based on number of inhabitants (1.0 million and 1.6 million), show significant differences in treatment outcomes, with a mean HbA_{1c} of 6.7% (50 mmol/mol) in Saarland and 8.5% (69 mmol/mol) in Mecklenburg-West Pomerania and half the rate of hypoglycaemic events in Saarland compared with Mecklenburg-West Pomerania. However, when comparing treatment modalities, significant differences could be seen in the use of insulin, with 78.2% of participants from Mecklenburg-West Pomerania treated with insulin, which was more than double of the number of participants in Saarland (33.6%). Comparing these data with other European countries, a study from a primary care setting in the United Kingdom reported only 24% of participants were treated with insulin[24] in 2013. In addition, anti-diabetic medications such as DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 analogues were used far more often in Mecklenburg-West Pomerania.

Taking into account the higher prevalence of diabetes and higher HbA_{1c} levels, this greater use of all anti-diabetic medical treatment options might reflect a higher rate of more advanced diabetes, as diabetes is a progressive disease and more intensive treatment strategies, including insulin therapy, are needed over time. In contrast, lifestyle modification was reported quite rarely in Mecklenburg-West Pomerania compared with Saarland. The intensity and type of lifestyle modification was not reported in detail and might be difficult to compare. However, a recent German study by Bohn et al showed that lifestyle treatment became less frequent between the years 2002 and 2014 (36.0% vs 21.8%) while the use of anti-diabetic medication increased.[25]

These findings should therefore be the starting point for a more detailed evaluation, because clinical trials of the primary prevention of T2DM diabetes have demonstrated that diet and physical activity are important modifiable risk factors for diabetes.[26] In the InterAct study, a one-category difference in physical activity (equivalent to approximately 460 and 365 kJ/day in men and women, respectively) was independently associated with a 13% relative reduction in the risk of diabetes.[27,28] The Eurobarometer survey highlighted that although 41% of Europeans exercise or play sport at least once a week, a substantial proportion of EU citizens (59%) never or seldom do so. Since 2009, the proportion of EU citizens that never exercises or plays sport has even increased from 39% to 42%. It has been found that 48% do some form of other physical activity (such as cycling, dancing, or gardening) at least once a week, while 30% never do this kind of activity at all.[29] In a recent overview, Henson et al emphasize that simply regularly breaking sitting time with standing or light walking substantially reduces postprandial glucose levels, suggesting a new behavioural target for those with a high risk of, or diagnosed with, T2DM.[30] The low levels of physical activity in Europe provide an opportunity to intervene in order to prevent diabetes. Thus, efforts to understand the determinants of physical activity behaviour need to be intensified. With respect to nutrition, persisting differences between eastern and western federal states might also be relevant. For example, fruits were consumed more frequently in the territories of the former GDR, while leafy greens and other vegetables were predominantly consumed in the FRG.[31] Similar nutritional differences were found in a comparison of the EPIC-Potsdam (north-east) with the EPIC-Heidelberg (south-west) studies.[32] After reunification, many differences in life circumstances disappeared, which might have led to a gradual convergence of food consumption.

Looking at differences in treatment modalities between federal states, insulin was used less often as anti-diabetic medication in those states with lower HbA_{1c} than in federal states with higher HbA_{1c}, and this corresponded to differences in the percentages of hypoglycaemia (which were greater in federal states with high percentages of insulin use). Comparing the percentages of participants on insulin therapy (with or without other hypoglycaemic agents) with data from France (19.5% in France in 2013),[33] insulin was used much more often in all German federal states. Even though German national guidelines on the treatment of T2DM diabetes recommend lifestyle modification and metformin as first line therapy, metformin usage varied widely between different federal states, ranging from 33.0% in Saxony to 50.9% in Thuringia. Compared with other European countries, metformin is used less in Germany. For example, 67.8% of patients in Southern Italy were treated with metformin[34] in 2012, while 66% of patients were treated with metformin as monotherapy in France[33] in 2013, and 83.6% received metformin in a UK primary care setting[24] in 2013. In a Greek nationwide real-world data analysis, metformin was the most frequently prescribed medication (77.4%) for T2DM, followed by DPP-4 inhibitors (44.8%) and sulfonylureas (34.5%), while insulin was used by 19.4% of patients.[35] The national diabetes report of the United States showed that approximately 57% of all patients in 2014 were treated with OADs alone, while approximately 15% of patients were given a combination of insulin and OADs, and insulin monotherapy was established in 14% of patients. Compared with our data, OADs were prescribed more often, while the combination of OAD and insulin was less common.[36]

In contrast, data on antihyperglycaemic medication from Germany are more similar to the prescription habits in Tyrol, based on an analysis of data from the Tyrol diabetes registry.[37] In this study, among all OADs prescribed, metformin was the most frequent (47.9%), followed by gliptins (27.2%), sulfonylurea (13.5%), glitazones (3.7%), SGLT2 inhibitors (3.7%), GLP-1 analogues (1.1%), and glucosidase inhibitors (0.4%). Metformin monotherapy was used in 16.6% of all patients. The authors of the study assumed as a possible explanation the frequent use of fixed dose combinations (including metformin and another OAD) in Tyrol and the fact that pharmacological second line treatments (eg, gliptins) are both less expensive and reimbursed to a considerable extent by the health care system. Dual therapy (metformin and another OAD) was prescribed in 17.2% of patients.

Oral anti-diabetic drugs alone were used in 43.4% of all patients, followed by OAD combined with insulin (21.2%), while use of insulin alone (human insulin and insulin analogues) was prescribed in 19.9% of patients.

4.3 | Strengths and limitations

Our study has several limitations. The study is not population based. Participants are recruited by specialized centres interested in participating in diabetes registries such as DIVE or DPV, which might lead to a bias towards more differentiated approaches to diabetes care. It also cannot be excluded that there is a recruitment bias between the different federal states that could take place at different levels of health care (ie, primary, secondary, or tertiary), which might vary between federal states. However, the strength of our analysis is that it reflects real world diabetes care in Germany in a large population of 127 838 participants from all federal states. In this real-world analysis of specialized centres, we found that treatment strategies and outcomes for T2DM vary regionally, even though a more homogenous treatment pattern should be found since disease management programmes with standardized quality-of-care targets and antihyperglycaemic treatment recommendations[3,38] were implemented in 2003. This is in concordance with a recent Finnish study involving data from 9606 participants of a regional primary health care patient database, which showed that even in an area with a relatively homogenous public primary health care system, area-level differences exist in the achievement of control and treatment targets of care of T2DM. The authors suggest that inequalities in health care by area may stem from differences in their socio-economic and demographic characteristics.[39] In a smaller, population-based, study of two German regions involving 622 participants, differences in diabetes therapy dependent on region and patients' socio-economic position were described, which are comparable with our results.[3]

5 | CONCLUSION

We conclude that treatment strategies and outcomes for T2DM vary worldwide, between different countries of Europe and even regionally in different federal states of Germany.[39] While patients' T2DM profile, genetic background, and adherence to therapeutic interventions on an individual level certainly play a role in treatment modality and outcome, differences at the population level concerning planning, resourcing, and targeting for health care services should also be taken into account.[3,38,40-43] It is difficult to obtain representative data on real-world diabetes care. The registries of DIVE and DPV contribute to this task, involving a large number of participants, despite limitations due to the recruitment process. Implementation of a German national diabetes registry would help to collect more valid information on diabetes treatment and outcome in Germany.

Our analysis aims to stimulate discussion on strategies to improve diabetes care and outcomes in Germany with an emphasis on regional characteristics and needs.

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CONFLICT OF INTEREST

B.H., S.L., M.H., M.K., D.R., W.R., H.R., J.S., and R.W.H. have no competing interests to disclose.

AUTHOR CONTRIBUTIONS

B.H. wrote/edited the manuscript and created figures. P.B., S.L., T.D., H.M., M.K., D.R., W.R., H.R., J.S., and R.W.H. contributed to the discussion and reviewed/edited the manuscript. R.W.H. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final manuscript to be submitted.

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