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Association of musculoskeletal pain with the achievement of treatment targets for type 2 diabetes among primary care patients

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ABSTRACT

Aims: To assess the association of diagnosed musculoskeletal (MS) pain (low back, neck, shoulder, and knee pain; and the number of pain sites) with the achievement of targets for glycosylated haemoglobin A1c (HbA1c), low-density-lipoprotein cholesterol (LDL), and systolic blood pressure (SBP) among primary care patients with type 2 diabetes (T2D).

Methods: The cross-sectional study population consisted of 3478 patients with a registry-based T2D diagnosis and available registry-based data on MS pain diagnoses, covariates, and outcomes between 2016 and 2019. Logistic regression analysis was used to evaluate the study aims.

Results: Overall, 22% had at least one of the four types of MS pain, and 73%, 57%, and 51% achieved the treatment targets of HbA1c, LDL, and SBP, respectively. T2D patients with or without MS pain did not differ in their achievement of T2D treatment goals. Of pain locations, low back pain was associated with higher rates of achievement of the LDL target (OR 1.29, 95% CI 1.01–1.65), but the association was attenuated in the adjusted model.

Conclusions: MS pain was relatively prevalent among primary care patients with T2D, but did not influence the achievement of T2D treatment goals.

1. Introduction

Type 2 diabetes (T2D) is a prevalent condition causing a significant cost and disability burden for those affected, and for societies worldwide [1,2]. It appears to co-exist with other long-term diseases [3–6] and show high prevalence, especially among those of working age and older adults [7]. T2D is known to be driven by both genetic and environmental/behavioural factors including unhealthy behaviours, such as physical inactivity and obesity [8,9].

Achieving treatment goals for glycosylated haemoglobin A1c (HbA1c), low-density-lipoprotein cholesterol (LDL), and systolic blood pressure (SBP) is considered an important dimension in the T2D care in order to decrease T2D-related complications and mortality [10–14]. Worryingly, only under half of the T2D patients record sufficient levels

of these outcomes globally [15]. Even though earlier studies have recognised a pattern of factors affecting the T2D treatment goal achievement (e.g. sex [16], age [16], duration of T2D [17] and patient-related factors such as self-care behaviours [17]), it seems that we are still lacking adequate knowledge on the field to understand this complex phenomenon comprehensively and to treat patients sufficiently enough. More productive prevention of undesirable complications would potentially be achieved by identifying the determinants accounting for insufficient treatment of T2D.

Musculoskeletal (MS) pain is among the most common co-existing diseases among patients with T2D [3–6] and significantly associated with T2D [18–21]. MS pain has been shown to have a negative influence on activity limitations and on the odds of disability [22,23], and be negatively associated with self-care behaviours, such as physical activity

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levels [24] and medication adherence [25]. Moreover, people with MS pain often report psychological problems [26], which are also suggested to be associated with T2D treatment [27]. On a speculative view, it could be hypothesised that MS pain would influence people's ability to meet the T2D treatment goals. To the best of our knowledge, however, no study has specifically investigated this.

The aim of this registry-based cross-sectional real-world study was to explore the potential associations between MS pain (low back, neck, shoulder, and knee pain; and the number of pain sites) and achievement of treatment goals for HbA1c, LDL, and SBP among a sample of primary care patients with registry-based T2D diagnosis between 2016 and 2019.

2. Methods

2.1. Study population and design

This study was part of the Rovaniemi T2D Study, which is a registry-based, real-world study conducted among primary care patients with T2D in the Rovaniemi Health Centre (the largest health centre in Lapland, Finland). During the data collection period (between 21st Feb 2016 and 20th Feb 2019), 3478 patients with T2D diagnosis were included (codes E11.1–11.9 according to the 10th revision of the World Health Organization's International Classification of Disease [ICD-10]). Data on ICD-10-based MS pain diagnoses, prescription of pain medications, potential confounders (except multimorbidity), and outcome variables were also gathered over the three-year interval from patient records of Rovaniemi's health centre. All 3478 patients had information on MS pain; HbA1c, LDL, and SBP data were available for 3408, 3346, and 1953 participants, respectively.

The study protocol was approved by the Ethics Committee of Lapland Central Hospital (05/2018). As all patient information analysed was assessed from patient records, no consent to use the participants' data was necessary according to contemporary Finnish legislation. Confidential data were stored at the Rovaniemi Health Centre and handled by replacing personal information with ID codes.

2.2. Musculoskeletal pain

Diseases considered to cause local pain in the low back, neck, shoulder, and knee anatomical areas were selected using ICD-10 classification. The codes used to identify each type of MS pain are presented in Table 1. Selection of ICD-10 codes for low back and neck pain was based on the potential non-specific characteristics of pain, while knee and shoulder pain groups included codes for pain originating from specific and non-specific reasons (for example, unspecified internal derangement of knee [M23.9] and osteoarthritis [M17]). All pain locations were analysed both separately and as dichotomised variables (any pain vs. no pain). Additionally, the number of MS pain locations (1, 2, 3, 4) was compared to those participants who were not diagnosed with any MS pain.

2.3. Clinical and biochemical outcomes

Achievement of the HbA1c, SBP, and LDL treatment targets were considered the outcomes of the current study. The latest values of each measurement at the time of recruitment were collected from the patient

Table 110th revision of the International Classification of Diseases (ICD-10) codes used to identify musculoskeletal (MS) pains.

| MS pain | ICD-10 |
|---------------|----------------------------------|
| Low back pain | M47.82; M51; M53.3; M54.4; M54.5 |
| Neck pain | M47.8; M50; M53.0; M53.1; M54.2 |
| Shoulder pain | M75 |
| Knee pain | M17; M22; M23 |

records within the three-year interval and the targets for these variables, and were defined according to national guidelines as follows: HbA1c $<53~\rm mmol/mol,\,SBP<135~\rm mmHg,\,and\,LDL<2.5~\rm mmol/L\,[28].$ Participants had their BP measured twice a day, twice in each session, for four consecutive days [29], and then the means of all measurements were calculated. If home-monitored values were not available, measurements performed during T2D consultations were used. Because of home-monitored values, the SBP goal was determined as $<135~\rm mmHg$ [30]. All outcome variables were handled as dichotomous variables, and those who did not achieve the treatment target were considered the reference group.

2.4. Confounding and demographic factors

The variables used as potential confounders included age, sex, body mass index (BMI), haemoglobin (Hb), prescription of medications (antihyperglycemic, antihypertensive, lipid lowering medication, and oral glucocorticoids), multimorbidity, defined as the presence of one or more diseases in addition to T2D (except MS pain), and health care utilisation. We collected data from patients' records on the prescribed pain medications to study their prescription rate and on the estimated glomerular filtration rate (eGFR) to characterise patients' renal function in the study sample.

Age and the latest Hb values were treated as continuous variables. Data on other chronic diseases were collected between 2011 and 2019. Of ICD-10-based chronic diseases, diseases of which pathophysiology are related to T2D (hypertension, hyperlipidemia, atrial fibrillation, heart failure, obesity, chronic kidney disease, and cardiovascular diseases) and those non-T2D-related diseases whose prevalence rate was 5% or over in the present study population (cancer, asthma/chronic obstructive pulmonary disease, hyperplasia of prostate, hypothyroidism, dementia/Alzheimer's disease, depression, and sleep disorders), were selected, as presented in our previous study [6]. In this study, we also included alcohol-related disorders in the latter category to evaluate alcohol as a potential covariate. Then, multimorbidity was grouped as: concordant (T2D-related), discordant (non-T2D-related), concordant and discordant, and no multimorbidity, as T2D-related and non-T2D-related diseases are differently associated with meeting the T2D treatment targets [6]. Weight and height were either based on self-reports or measured performed during T2D consultation visits and were converted into BMI (kg/m²). The following BMI categories were then created: underweight/normal weight (< 25.0), overweight (25.0-29.9), obese (30.0 or over), and unknown. Medications were grouped according to a generally accepted classification system: the anatomical therapeutic chemical (ATC) classification.

A registry-based evaluation of medication use has been shown to be a good tool compared to a survey-based approach [31]. Antihyperglycemic medication included oral diabetes medications (ATC code A10B) and insulins (A10A), and antihypertensive medication included angiotensin-converting enzyme inhibitors (ATC code C09A), angiotensin receptor blockers (C09C), beta blockers (C07AB), calcium blockers (C08CA), and diuretics (C03). Statins (ATC code C10AA) and ezetimibe (C10AX) comprised lipid lowering medication. Oral glucocorticoid medication was based on ATC codes (H02AB and H02B). The latest national guideline of pain [32] guided the inclusion of the following pain medicines: non-steroidal anti-inflammatory medicines (NSAIDs; M01A), paracetamol (N02BE01, N02BE51), neuropathic pain medicines (gabapentin N03AX12, pregabalin N03AX16, amitriptyline N06AA09, nortriptyline N06AA10, venlafaxine N06AX16, duloxetine N06AX21), and opioids (N02A). Medication groups were analysed as dichotomised variables, yes vs. no, and all but pain medications were used as covariates in the analysis of a corresponding T2D treatment goal. Health care utilisation covered all contacts, except emergency department contacts, to the primary health centre during the three-year interval.

In Rovaniemi, all patients with T2D who are treated at the health

centre are regularly called for planned T2D consultations at maximum intervals of one and a half years; therefore, the contacts were divided into 'planned T2D consultations', 'not planned primary care physician visits', and 'other contacts'. 'Not planned primary care physician visits' consisted of all but planned T2D consultations and 'other contacts' of physician services other than visits, i.e., consultations with a nurse, or a letter or telephone call to the patient. eGFR was reported as ml/min/ 1.73 m², and regarded as a continuous variable.

2.5. Statistical analyses

Means and standard deviations (SD) or proportions were calculated and presented for each variable. The statistical significance of the mean differences and proportions of categorical variables between MS pain groups were estimated by a Mann-Whitney U test and a chi square test, respectively. A p value < 0.05 was regarded as statistically significant. Logistic regression analyses, unadjusted and adjusted for age, sex, BMI, Hb, prescription of medications, multimorbidity, and healthcare utilisation, were used to explore cross-sectional associations between MS pain and achievement of treatment goals of T2D. Odds ratios (ORs) and 95% confidence intervals (CIs) characterise the statistical significances and strengths of these potential associations. As attaining T2D treatment targets relates to age, sex, and obesity [16,33], we also studied the potential modifying role of these factors in the association between MS pain and achievement of T2D treatment goals by adding corresponding interaction terms (e.g. MS pain*sex) to the unadjusted logistic models. For the moderating analysis, BMI was dichotomised as non-obesity and obesity, and patients without data on BMI were excluded. Statistical analyses were performed using IBM SPSS Statistics for Macintosh, Version 24.0. Armonk, NY: IBM Corp. IBM Corp. Released, 2016.

3. Results

3.1. Sample demographics

In the present primary care sample of 3478 patients with T2D, the mean age was 70.0 years (SD: 11.7), 55% of the participants were men (Table 2), and 22% of the participants were diagnosed with MS pain. These participants were slightly older (mean 70.9 [SD: 11.5] vs. mean 69.8 [SD: 11.8], p=0.032, respectively) and their mean BMI was significantly higher than those without MS pain (31.2 [5.94] vs. 29.5 [5.62], p<0.001, respectively). Knee and low back pain were the most frequently diagnosed MS pains (9% for all patients and 44% and 39% among patients with MS pain, respectively). Patients with MS pain were prescribed slightly more pravastatin, atorvastatin, and rosuvastatin than patients without MS pain (Supplement 1; p<0.05) but did not differ from patients without MS pain in regard to the prevalence of T2D-related complications (E11.1-E11.8 ICD-10 codes; p>0.05; data not shown).

A total of 73% of the total study population had achieved the HbA1c target, 57% the LDL target, and 51% the SBP target. Similar prevalence rates were recorded among patients with and without MS pain, and these groups did not differ from each other according to the achievement of the treatment goals (p > 0.05 for all).

3.2. MS pain and meeting the guideline-recommended treatment targets

Table 3 presents the associations between MS pain and achievement of guideline-recommended treatment targets of T2D. Low back pain was significantly associated with higher rates of attainment of the LDL target (OR 1.29, CI 1.01–1.65), but in the fully adjusted model (age, sex, BMI, Hb, prescription of lipid lowering medication, multimorbidity, and healthcare utilisation), the association lost its significance (OR 1.22, CI 0.94–1.60). There were no significant associations between the presence of MS pain, neck, shoulder, or knee pain, or the number of MS pain sites and goal achievement in unadjusted analyses; therefore, further

Table 2
Characteristics and musculoskeletal (MS) pain prevalence

| Characteristics and musc | All (n = | Patients | Patients | P value |
|---|--------------------------|---------------------|-----------------------|-------------------------------|
| | 3478) | with MS pain (n = | without MS pain (n = | (patients with MS pain vs. |
| | | 753) | 2725) | patients without) |
| Sex, male, % (n) | 55 | 43 (326) | 58 (1573) | <0.001 |
| Age, mean (SD) | (1899) 70.0 (11.7) | 70.9 (11.5) | 69.8 (11.8) | 0.032 |
| HbA1c, mmol/mol, mean (SD)/N | 48.5 (12.4) / 3408 | 47.7 (10.9) /748 | 48.7 (12.8) / 2660 | 0.036 |
| LDL, mmol/l, mean (SD)/N | 2.52 (1.01) / 3346 | 2.51 (1.02) /742 | 2.52 (1.01) / 2604 | 0.686 |
| SBP, mmHg, mean (SD)/N | 136 (18.4) /1953 | 137 (18.0) /442 | 136 (18.6) / 1511 | 0.337 |
| BMI, mean (SD)/N | 29.9 (5.74) / 2205 | 31.2 (5.94) /518 | 29.5 (5.62) / 1687 | <0.001 |
| Underweight/normal weight, % (n) | 14 (486) | 10 (72) | 15 (414) | <0.001 |
| Overweight, % (n) | 24 (839) | 26 (192) | 24 (647) | <0.001 |
| Obese, % (n) | 25 (880) | 34 (254) | 23 (626) | <0.001 |
| Unknown, % (n) | 37 (1273) | 31 (235) | 38 (1038) | <0.001 |
| Hb, mean (SD)/N | 140 (16.8) / 3440 | 139 (15.7) /753 | 140 (17.1) / 2687 | 0.021 |
| eGFR, mean (SD)/N | 79.6 (19.3) / 3087 | 79.1 (19.4) /681 | 79.7 (19.3) / 2406 | 0.415 |
| Proportion of achieving target in | | | | |
| HbA1c, mmol/mol, % (n) | 73 (2495) | 76 (568) | 72 (1927) | 0.063 |
| LDL, mmol/l, % (n) | 57 (1911) | 59 (440) | 57 (1471) | 0.186 |
| SBP, mmHg, % (n) | 51 (992) | 48 (214) | 52 (778) | 0.279 |
| Prescription of Antihyperglycemic | 97 | 98 (737) | 97 (2630) | 0.078 |
| medication, % (n) Lipid lowering | (3367) 74 | 76 (572) | 73 (1994) | 0.135 |
| medication, % (n) Antihypertensive | (2566) 86 | 89 (672) | 86 (2331) | 0.011 |
| medication, % (n) Oral glucocorticoids, % | (3003) | 14 (107) | 11 (303) | 0.024 |
| (n) NSAIDs, % (n) | (410) 28 (972) | 50 (373) | 22 (599) | <0.001 |
| Paracetamol, % (n) | 50 (1749) | 74 (555) | 44 (1194) | <0.001 |
| Neuropathic, % (n) | 16 (548) | 30 (227) | 12 (321) | <0.001 |
| Opioids, % (n) | 28 (955) | 47 (352) | 22 (603) | <0.001 |
| Health care utilisation Planned T2D consultations, mean | 4.25 (3.28) / | 4.60 (3.40) /753 | 4.16 (3.24) / 2705 | 0.002 |
| (SD)/N Not planned primary care physician visits, | 3458 2.92 (3.30) / | 5.80 (4.42) /753 | 2.12 (2.35) / 2705 | <0.001 |
| mean (SD)/N Other contacts, mean (SD)/N | 3458 8.75 (8.51) / | 11.4 (8.80) /753 | 8.02 (8.29) / 2705 | <0.001 |
| Concordant disease(s), % (n) | 3458 29 (1023) | 1 (6) | 37 (1017) | <0.001 |
| Discordant disease(s), % (n) | 10 (338) | 17 (125) | 8 (213) | <0.001 |
| | Ç, | 82 (620) | 40 (1102) | <0.001 |

(continued on next page)

Table 2 (continued)

| , , | | | | |
|------------------------------------|----------------|---------------------------------|--|--|
| | All (n = 3478) | Patients with MS pain (n = 753) | Patients without MS pain (n = 2725) | P value (patients with MS pain vs. patients without) |
| Concordant and discordant diseases | 50 (1722) | | | |
| No multimorbidity | 11 (395) | 0 (2) | 14 (393) | <0.001 |
| Low back pain, % (n) | 9 (297) | 39 (297) | | |
| Neck pain, % (n) | 1 (51) | 7 (51) | | |
| Shoulder pain, % (n) | 5 (185) | 25 (185) | | |
| Knee pain, % (n) | 9 (330) | 44 (330) | | |
| Number of MS pains, % (n) | | | | |
| 0 | 78 | 0 | | |
| | (2725) | | | |
| 1 | 19 | 86 (650) | | |
| | (650) | | | |
| 2 | 3 (96) | 13 (96) | | |
| 3 | 0 (7) | 1 (7) | | |
| 4 | 0 (0) | 0 (0) | | |

SD = standard deviation;HbA1c=glycosylated haemoglobin A1c; LDL = low-density-lipoprotein cholesterol; SBP = systolic blood pressure; BMI = body mass index; Hb = haemoglobin; eGFR = estimated glomerular filtration rate; NSAID = non-steroidal anti-inflammatory medicine; T2D = type 2 diabetes Statistically significant p values are bolded.

Table 3
Associations of MS pains with the achievement of treatment goals, odds ratios and their 95% confidence intervals.

| | Unadjusted | | | Adjusteda |
|-----------------|-------------|-------------|-------------|-------------|
| | HbA1c | LDL | SBP | LDL |
| MS pain | | | | |
| Yes | 1.20 | 1.12 | 0.88 | |
| | (1.00-1.45) | (0.95-1.32) | (0.72-1.09) | |
| No | 1 | 1 | 1 | |
| Low back pain | | | | |
| Yes | 1.02 | 1.29 | 1.03 | 1.22 |
| | (0.78-1.34) | (1.01-1.65) | (0.75-1.40) | (0.94-1.60) |
| No | 1 | 1 | 1 | 1 |
| Neck pain | | | | |
| Yes | 1.32 | 0.78 | 0.97 | |
| | (0.70-2.73) | (0.44-1.36) | (0.48-1.97) | |
| No | 1 | 1 | 1 | |
| Shoulder pain | | | | |
| Yes | 1.29 | 1.21 | 0.85 | |
| | (0.91-1.86) | (0.89-1.64) | (0.57-1.27) | |
| No | 1 | 1 | 1 | |
| Knee pain | | | | |
| Yes | 1.23 | 0.87 | 0.88 | |
| | (0.94-1.62) | (0.69-1.10) | (0.65-1.19) | |
| No | 1 | 1 | 1 | |
| Number of pains | | | | |
| One | 1.20 | 1.16 | 0.85 | |
| | (0.99-1.47) | (0.98-1.39) | (0.68-1.07) | |
| Two | 1.12 | 0.97 | 1.15 | |
| | (0.71-1.83) | (0.64-1.47) | (0.65-2.03) | |
| Three | 2.04 | 0.32 | 0.94 | |
| | (0.34-5.29) | (0.04-1.57) | (0.10-9.07) | |
| No MS pain | 1 | 1 | 1 | |

MS = musculoskeletal; HbA1c = glycosylated haemoglobin A1c; LDL = low-density-lipoprotein cholesterol; SBP = systolic blood pressure Statistically significant values are shown in bold.

Having not achieved the treatment target was used as a reference.

adjustments were not performed. To further investigate the role of MS pain in goal achievement, we conducted a subanalysis of patients with MS pain who had been prescribed opioids or neuropathic pain

medications and compared them to subjects without pain and prescriptions of these medications. The associations with meeting the T2D treatment targets were nonsignificant (data not shown).

The interaction terms including sex and age were nonsignificant (data not shown). Considering obesity, the interaction term MS pain*obesity was statistically significant only in the model using achievement of the LDL target as the outcome. However, after stratification by obesity status (obesity vs. no obesity) and after adjustments, the ORs attenuated to nonsignificant level (data not shown).

4. Discussion

4.1. Main findings

In the present study, we examined the association of MS pain with meeting the treatment goals of HbA1c, LDL, and SBP among 3478 primary care patients with T2D using registered data. A total of 22% of the participants (with a mean age of 70 years) with T2D were diagnosed with MS pain. Both patient groups—with and without MS pain—equally met the estimated treatment targets. Only achievement of the LDL goal was related to low back pain in the unadjusted but not in the adjusted model.

4.2. Prevalence of MS pain among patients with T2D

In a Spanish study [34], chronic neck pain and low back pain diagnosed by a medical doctor were found to occur among 32% and 38% of participants over 70 years of age with diabetes, respectively. A Canadian study evaluated knee osteoarthritis among diabetic patients with a median age of 68 years and reported that one-fifth of the subjects had osteoarthritis [35]. These reports are relatively in line with our observation that one-fifth of T2D patients had MS pain, although we found markedly lower rates of specific pain sites, e.g., low back pain, in the present study sample of primary care patients. Different settings and populations complicate straightforward prevalence comparisons, but our findings support the current knowledge suggesting that a significant part of T2D patients are affected by MS pain.

MS pain is known to be of a subsequent high level in the elderly general population, which may partly account for this finding. On the other hand, several studies comparing groups with and without diabetes have established that MS pains are more frequent among diabetic patients (e.g., [19,34]). One potential explanation for the co-existence may also be that congruent factors predispose for both diseases. For instance, being overweight is a well-known risk factor for T2D [36], and inflammatory processes occurring in diabetes may also contribute to MS pain [37]. Engagement in leisure-time physical activity, in turn, has been suggested to protect against lower back pain [38] and T2D [39]. Our results suggest that patients with T2D who also had MS pain were slightly more likely to receive a prescription for pravastatin, atorvastatin, and rosuvastatin. These drugs have been associated with MS pain adverse events and might partially explain our results. In this dataset, no differences were observed in the T2D-complication prevalence (data not shown), thus, T2D-related neuropathy is not likely to explain the presence of MS pain.

4.3. Achievement of T2D treatment targets

In the current study, 73% of patients with T2D achieved the HbAc1 target, 57% achieved the LDL target, and 51% achieved the SBP target. A meta-analysis by Khunti et al. [15] evaluated 24 studies from 20 countries around the world and reported lower figures in each of the clinical and biochemical values (43%, 49%, and 29%, respectively). In turn, corresponding figures among primary care T2D patients were recorded in a large Scandinavian study, with approximately 34–53% achieving the HbA1c (< 53 mol/mmol) target, 46–70% the LDL target (< 2.5 mmol/L) and 29–40% the BP goal defined under 130/80 mmHg [40]. In

^a Adjustors: age, sex, body mass index, haemoglobin, prescription of lipid lowering medication, multimorbidity, and healthcare utilisation

Rovaniemi, all patients with T2D who are treated in primary health centres are followed up regularly by healthcare professionals, and therefore patients are likely to be exposed to regular assistance for self-care that may have favourable effects on T2D treatment balance [41], explaining at least a part of the outperforming.

MS pain in any of the studied forms was not relevant in meeting the T2D treatment targets of interest in a real-world setting after adjustments. Patients with low back pain were more likely to meet the LDL target before adjustments, but the relationship attenuated nonsignificant when a number of covariates were included in the model. This indicates that having achieved the LDL target is more influenced by other factors than low back pain itself. In their studies, Hoff et al., [19] and Molsted et al. [42] observed no relationship between MS pain and HbA1c levels, even when pain-related bothersomeness was evaluated [42]. Similarly, Real et al. [43] yielded corresponding results among Americans, yet in a subanalysis of normal-weight diabetic patients, the prevalence of low back pain was found to increase along with HbA1c levels. Although not exactly exploring meeting HbA1c targets as an outcome, being limited to estimates of HbA1c and not using primary care patients as a study population, the literature supports our findings. To our knowledge, there are no previous studies on low back pain and achievement of the LDL target.

In the present study, the levels of prescribed antihyperglycaemia, antihypertensive, and lipid lowering medication were similar among both patient groups, which may explain at least some of the results. Furthermore, a part of the nonsignificant associations may be related to the fact that patients with MS pain participated in T2D consultations more often than others (potentially due to higher level of other long-term diseases), and therefore might be given more assistance for self-care e.g. related to exercise and dietary behaviour and smoking. On the other hand, we found no statistically significant moderating effect of obesity on the adjusted association between MS pain and the achievement of T2D treatment targets. Clearly, further studies on the field are warranted.

4.4. Strength and limitations

A real-world setting with registry-based data on a large primary care study population of patients with T2D constitutes the main strength of the current study. Furthermore, to the best of our knowledge, the present study is the first to examine the associations between MS pain and a variety of clinical and biochemical markers describing the adequate T2D treatment balance among primary care patients. However, there are also some limitations to be noted. First, all patients' diagnoses may not be properly recorded in patient registers, which may have caused some underdiagnosis of MS pain. On the other hand, our results on MS pain prevalence are not overestimated. Second, since MS pain data relied on diagnoses collected across a three-year span, the duration of pain and the level of pain disability were not known. Moreover, we were not able to distinguish the exact aetiology of MS pain, which can be seen as a limitation. However, MS pain leading to healthcare centre visits is usually unpleasant and severe (e.g., [44]). Third, we had lifestyle data only on BMI and diagnosed alcohol disorders due to the registered data, and there were some missing data related to the real-world study setting. Fourth, the working age population may be underrepresented, as they may be treated at occupational healthcare services, for which we do not have information available. Fifth, we had no data on the duration of T2D. Finally, due to the cross-sectional design, some patients may have been recorded the outcome measure before the exposure (MS pain diagnosis) and cause-and-effect conclusions cannot be drawn.

5. Conclusions

MS pain is a typical co-existing symptom among patients with T2D, with most patients suffering from knee pain or lower back pain. Despite the major disability burden commonly related to MS pain, it appears that

MS pain has no relevant role in elderly primary care patients with T2D achieving their treatment targets. Consequently, focus should be targeted towards factors other than MS pain to maintain sufficient treatment levels among elderly T2D populations. Whether corresponding negative findings also exist among working-aged populations is an important issue to be addressed in the future.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pcd.2022.04.006.

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