ORIGINAL ARTICLE

Type 2 diabetes and treatment intensification in primary care in Finland

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Abstract

Aim To identify how the electronic health record (EHR) systems and national registers can be used for research purposes. We focused on how the primary care physicians adhere to clinical guidelines.

Methods Study population included incident type 2 diabetes patients from four selected regions. Data were collected in two phases. At the first phase study cohort was identified using the prescription registers of the Social Insurance Institution (SII) and EHR systems used within the study regions. At second phase, data were collected from SII's registers, local EHR systems, the hospital discharge and the primary care registers of National Institute for Health and Welfare.

Results Metformin was the most common choice as first drug. Among all study patients, 8375 (76.0%) started metformin monotherapy or combinations. The treatment was intensified at variable levels of HbA1c depending on the area. DPP4-inhibitors were by far the most common agent for treatment intensification. Sulphonylureas were used less often than basal insulin as the second-line agent. The use of DPP4-inhibitors increased between years 2009–2010, when first DPP4-inhibitor received reimbursement and this class became dominant drug for treatment intensification increasingly thereafter.

Conclusions The EHR systems and national registers can be used for research purposes in Finland. The realization of diabetes treatment national guidelines are followed in primary care to a large extent. However, the subsequent intensification of therapy was delayed and occurred at elevated Hba1c levels.

Keywords Diabetes · Electronic health records · Drug treatment · Current care guidelines · Type 2 diabetes

Introduction

Diabetes and associated micro- and macrovascular complications are an important cause of morbidity and mortality and a major economic burden. Intensive drug treatment of hyperglycemia at the onset of the disease decreases these complications [1], whereas in those with longstanding disease and multiple complications the impact of intensified therapy is less clear [2, 3]. The Steno-2 study demonstrated that intensified multifactorial treatment for 7.8 years in patients with

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type 2 diabetes (T2D) and microalbuminuria was associated with a 7.9 years longer median lifespan over a period of 21.2 years follow-up [4]. Swedish national diabetes registries have shown that the prognosis of patients with T2D has improved markedly on national level, but there remains a gap in cardiovascular morbidity and mortality as compared to the general population [5]. Lifestyle interventions are the treatment choice in patients with newly diagnosed type 2 diabetes. However, as lifestyle interventions may delay the start of drug treatment, the Finnish Current Care guideline (original version published in 2007 and updated several times) recommended that metformin should be initiated (if not contraindicated) concomitantly with lifestyle interventions [6]. The guideline also includes a clear algorithm of treatment choices after initiation of metformin as well as detailed guidance for the holistic treatment of type 2 diabetes. In particular, when metformin alone is ineffective, Current Care guidelines recommended multiple choices as a second-line drug. Although all the antihyperglycemic agents

including basal insulin were acceptable, guideline recommended individualized therapy. For example, in those with driving occupation drugs with little danger of hypoglycemia should be preferred. Less stringent glycemic targets may be appropriate for older patients, particularly for those with multiple chronic conditions and established vascular complications [2, 7, 8]. Patient information systems and nationwide health care registers contain information on diagnoses, prescriptions, medical treatments and procedures, home care, first aid care, and laboratory measurements. This information is recorded on patient level during normal daily routines when treating patients in hospitals and primary care units or from prescriptions from pharmacies. The nationwide health care registers are used in pharmacoepidemiologic research. The use of electronic health records (EHR) in Finland has been limited due to difficult and lengthy research permission processes. Combination of these two sources for research purposes would serve as a valuable resource for evaluation of risks, benefits and costs of various treatments and assessing how clinical practice guidelines are realized in large populations. Such research would support evidence-based decision making in healthcare and potentially guide better allocation of resources. The primary aim of this study was to identify how the EHR systems and national registers are feasible for research purposes in Finland. The target group was T2D herein. In this report, we analyzed to what extent and by which means the primary care physicians adhere to clinical practice guidelines and intensify drug treatment when metformin or other first-line agent are insufficient to control hyperglycemia.

Study design

This was a retrospective database linkage study using EHR system data from selected primary and specialty health care organizations in Finland as well as the nationwide registers.

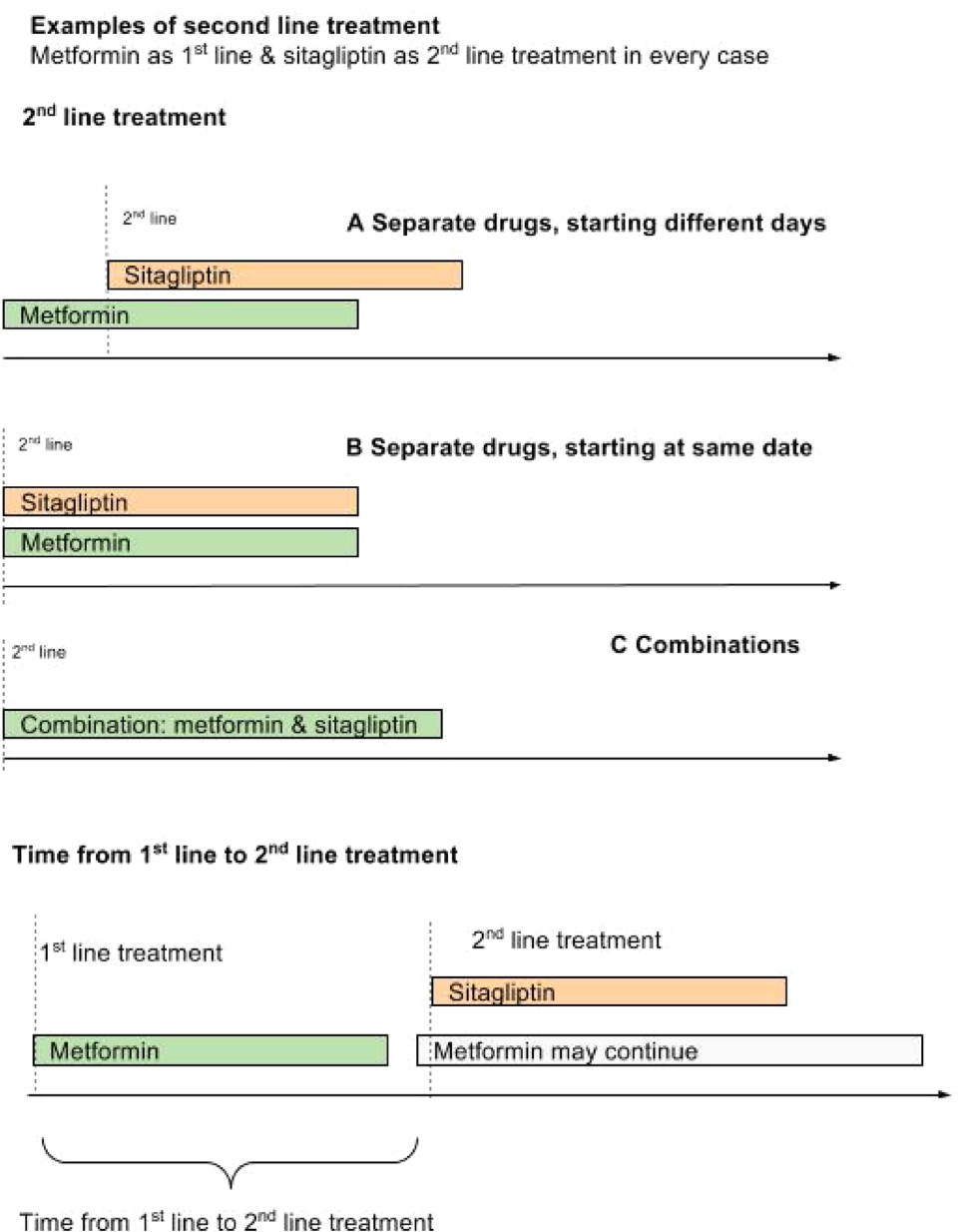## Population and data collection

Study population included incident (first time) type 2 diabetes patients from four selected regions, Kainuu, Kanta-Häme, Oulu and Pohjois-Karjala, in Finland corresponding to regions 1–4 for readability, respectively. Data were collected in two phases. At the first phase study cohort was identified using the prescription and reimbursement registers of the Social Insurance Institution (SII) and information contained in two different EHR systems used within the study regions. At second phase, data were collected from SII's registers, local EHR systems, the hospital discharge and the primary care registers of National Institute for Health and Welfare (THL) and the cause of death register of Statistics Finland (SF). The broad study population comprised all the patients of the catchment area with diagnosis

of diabetes mellitus (International Classification of Disease 10th revision, ICD-10, code E10*, E11*, E13* or E14*, or International Classification of Primary Care 2nd revision, ICPC-2, code T89 or T90), a written prescription for diabetic medication (Anatomical Therapeutic Chemical, ATC, code A10A* or A10B*), HbA1c value $\geq 6.5\%$, glucose tolerance test 2-h glucose level ≥ 11 mmol/L or nutrition counselling related to diabetes in EHRs, or patients who had purchased prescriptions for diabetic medication (ATC code A10A* or A10B*) or who had special reimbursement for diabetes (refund code 103) in the SIIs registers during 2009–2012. For each patient, the first date of such event mentioned above was called index date which identified the start of follow-up. To identify incident type 2 diabetes patients, following exclusions were made: patients with diagnosis for diabetes in EHRs within 2 years prior to index date, patients with records of diabetic medication within 2 years prior to index date in EHRs or SII registers, patients with special reimbursement decisions for diabetes (refund code 103) in the SII reimbursement register within 2 years prior to index date. Furthermore, patients with diagnoses only for type 1 diabetes (ICD-10 code E10* or ICPC-2 code T89 in EHRs or refund code 103 attached with ICD-10 code E10* in the SII reimbursement register) were excluded. Data for study cohort identification was collected from 2007 to ensure that each patient had at least 2 years of record history available before index date. The patients were identified from SII registers and EHRs with the national identification numbers (IDs). Artificial study identifiers (SIDs) were formed from IDs by MD5 one-way hashing algorithm. The patient identification list was kept separately from the rest of the data and the personnel analysing the data was working with the data including SIDs only. In this way, the patient level data could be linked while transferring the IDs as little as possible. At the second phase, a patient identification list containing both the selected IDs and the artificial SIDs was sent to EHRs, SII, THL and SF. These data holders identified the protocol-specific data required for the study from their data sources and delivered these study data back with the SIDs. Data was collected from 2007, when available. From the hospital discharge register and SII registers' records were available since 2007, and from the primary care register since 2011. From EHRs diagnoses were available from 2007, otherwise availability of data was depending on region. When all study data were received from the data holders, further data consistency checks and data derivation steps were performed. As the first possible index date was 1.1.2009, each patient had at least a 2-year baseline period. The index date was replaced if the study data provided an earlier index date event compared to the first phase of data collection and the history for diagnoses, drugs and reimbursements were subsequently updated. Based on the place of domicile patients living abroad within 2 years prior to index date and those

who were not living in study region during the follow-up were excluded. As the study outcomes required records from the local EHRs (e.g., laboratory measurements), patients with a unique study region were included. Records of age and gender were collected from all the databases. HbA1c records for baseline and follow-up were collected from EHRs. For baseline HbA1c, last record before index date within 1 year was used. If such measurement was not available, the first record within 1 month after index date was used. BMI records were collected from EHRs and from the primary care register, either as BMI or as a calculated value. BMI records were available from three of the four sites. For baseline BMI, the last record before the index date was used, and if records before the index date were not available, the

first record within 1 month after index date was used. Diagnoses for concomitant diseases during the baseline period were identified based on the hospital discharge register, the primary care register and EHRs and the refund categories of the SII register. Records of diabetes medication were collected from SII and EHRs. Variables used to evaluate the realization of the Current Care guideline included the start of metformin as 1st line treatment, treatment intensification during follow-up by adding second-line treatment (e.g., sulphonylureas, glinides, gliptines, glitazones or insulin) after any first-line treatment and the follow-up HbA1c measurements. Treatment intensification from first to second line was defined as a prescription or a purchase of an antidiabetic drug with a new substance after first-line treatment (Fig. 1).

Fig. 1 Treatment lines

Examples of second line treatment
Metformin as 1st line & sitagliptin as 2nd line treatment in every case

2nd line treatment

A Separate drugs, starting different days

B Separate drugs, starting at same date

C Combinations

Time from 1st line to 2nd line treatment

Drug combinations were treated as separate substances. In case there were multiple substances prescribed or purchased at the same date, the order of the treatment lines was evaluated in the following order: metformin, DDP4, sulphonylureas, GLP1 analogs, SGLT2 inhibitor, glitazone, insulin and other ATC A10. For example, if metformin combinations, or separate purchases of metformin and other antidiabetic drug occurred at the same date, metformin was assumed to be the first-line treatment. Treatment patterns were followed until the end of 2013, except in region 4 (Pohjois-Karjala), where records until the end of 2016 were available.

Statistical methods

Diabetes diagnoses for study population definition were collected from EHRs as either ICD-10 or ICPC-2 diagnoses. All EHRs had ICD-10 diagnoses, three regions had also ICPC-2 diagnoses. Diabetes drugs were searched by ATC codes A10A* and A10B* from EHR's written prescriptions and SII's purchased prescriptions. Patients with reimbursement code 103 were collected from SII's reimbursement register. Patients with fasting blood sugar level ≥ 11 mmol/L, or with high glycohemoglobin level (HbA1c $\geq 6.5\%$ or ≥ 47 mmol/mol) were collected from EHRs by laboratory test name or number. The Finnish classification of functions in outpatient primary healthcare (SPAT) is used to describe functions and procedures in outpatient primary health care. Nutrition counselling was identified from EHRs using codes for Nutrition survey (SPAT1139) or Nutrition and weight-control counselling (SPAT1306).

For study data laboratory test HbA$_{1c}$ was collected from EHRs based on test number of by test name. Measurement of HbA$_{1c}$ was provided as mmol/L (ICFF) or by % (NGSP). ICFF values were converted to NGSP using formula provided by National Glycohemoglobin Standardization Program [9]. ICD-10 diagnoses for concomitant diseases were identified using ICD-10 codes from the hospital discharge register, primary care register or local EHRs, ICPC-2 codes from primary care register and refund categories of the SII register. The further details regarding the selected diseases and operational codes are provided in the study protocol in the ENCePP register of studies [10].

BMI was collected as BMI record when available, otherwise it was calculated from height and weight, if possible. Records of patients with unrealistically high or low values, or more than 10 unit changes in BMI, were examined, and if were considered erroneous, were excluded.

Patients were followed from the index date until date of death or 31.12.2013 whichever happened first. Baseline information about age, gender, BMI, HbA1c level and number of comorbidities at index date and at treatment intensification were tabulated for each region separately and for all the patients in cohort. Choice of second-line agent was tabulated per first treatment, per region and per year. Differences between regions were not statistically tested, because the results would have been strongly affected by variability in the quality of data.

Results

At the first data collection phase, 66,937 patients with diabetes records during 2007–2012 were retrieved. After the exclusions of patients, who did not have records during 2009–2012 or who had history of diabetes records within 2 years before index date or who only had records referring to type 1 diabetes, a cohort of 15,771 type 2 diabetic patients were identified. After receiving the follow-up data of these patients, further 4740 patients were excluded due to rechecking of index dates, place of domiciles and history of diabetes records, and the resulting total cohort size was 11,022 patients. The different cohorts identified were as follows: all study patients ($n = 11,022$), patients who had either metformin or a metformin combination as their first antidiabetic drug ($n = 8375$) and patients whose antidiabetic treatment was further intensified from any A10* medication to the second-line treatment ($n = 3593$) during the follow-up. The total cohort consisted of 3666 patients with treatment intensification. However, patients with a third-line treatment at time of the first line ($n = 27$) or at time of the second line ($n = 46$) were excluded from treatment intensification analysis.

Patient characteristics

In general, the age and gender distributions were roughly similar between the regions. Mean age at index date was 63.3 years (SD 12.8), 52.3% of patients were male. BMI was also very similar at 31.2 kg/m^2. Mean HbA1c level was 6.8% (SD 1.65) and 36.7% of patients had HbA1c < 6.5% at index date. Over half of the patients (58.4%) had at least one comorbidity at index date. The number of comorbidities was highest in Region 4, where 66.3% had at least one comorbidity (Tables 1, 2). When analyzing the patient characteristics at the start of metformin, the results were fairly similar (Table 1 appendix).

Initiation of drug treatment

Metformin was the most common choice as first diabetes drug. Among all study patients, 9382 (85.1%) had prescription of A10A* or A10B* during follow-up, 8375 (76.0%) started metformin monotherapy or metformin combinations as first diabetes treatment and 7979 (72.4%) had metformin monotherapy as first diabetes drug. In Region 2, the initiation of metformin or metformin

Table 1 Patient characteristics at index date

	Region 1		Region 2		Region 3		Region 4		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex										
Female	1087	46.28	1064	46.77	1109	50.34	2000	47.68	5260	47.72
Male	1262	53.72	1211	53.23	1094	49.66	2195	52.32	5762	52.28
Total	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11,022	100.00
Age										
< 50	297	12.64	378	16.62	377	17.11	526	12.54	1578	14.32
50–59	556	23.67	594	26.11	512	23.24	1004	23.93	2666	24.19
60–69	699	29.76	692	30.42	639	29.01	1259	30.01	3289	29.84
70–79	566	24.10	453	19.91	459	20.84	940	22.41	2418	21.94
≥ 80	231	9.83	158	6.95	216	9.80	466	11.11	1071	9.72
Total	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11,022	100.00
BMI										
< 25	52	2.21	0	0.00	106	4.81	256	6.10	414	3.76
25–29	188	8.00	0	0.00	307	13.94	682	16.26	1177	10.68
30–34	189	8.05	0	0.00	294	13.35	674	16.07	1157	10.50
35–39	82	3.49	0	0.00	145	6.58	279	6.65	506	4.59
≥ 40	51	2.17	0	0.00	75	3.40	180	4.29	306	2.78
Unknown	1787	76.07	2275	100.00	1276	57.92	2124	50.63	7462	67.70
Total	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11,022	100.00
HbA1c										
< 6.5	1123	47.81	658	28.92	767	34.82	1501	35.78	4049	36.74
6.5–6.9	475	20.22	188	8.26	311	14.12	445	10.61	1419	12.87
7–7.9	195	8.30	92	4.04	137	6.22	193	4.60	617	5.60
≥ 8	242	10.30	206	9.05	133	6.04	287	6.84	868	7.88
Unknown	314	13.37	1131	49.71	855	38.81	1769	42.17	4069	36.92
Total	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11,022	100.00
Comorbidities										
0	1059	45.08	1196	52.57	918	41.67	1415	33.73	588	41.63
1	765	32.57	601	26.42	700	31.77	1225	29.20	3291	29.86
2	323	13.75	269	11.82	323	14.66	757	18.05	1672	15.17
≥ 3	202	8.60	209	9.19	262	11.89	798	19.02	1471	13.35
Total	2349	100.00	2275	100.00	2203	100.00	4195	100.00	11,022	100.00

Total cohort (*n* = 11,022)

Table 2 Index date

	Region 1		Region 2		Region 3		Region 4		Total	
	Mean	Std	Mean	Std	Mean	Std	Mean	Std	Mean	Std
Comorbidities	0.89	1.058	0.82	1.122	1.04	1.213	1.35	1.377	1.08	1.250
Age	63.96	12.476	61.87	12.649	62.67	13.361	64.14	12.593	63.34	12.769
BMI	31.14	5.906	–	–	30.94	6.033	31.37	6.084	31.22	6.044
HbA1c	6.89	1.667	7.11	1.937	6.68	1.360	6.74	1.615	6.83	1.649

Total cohort (*n* = 11,022)

Mean and standard deviation of number of comorbidities, age, BMI and HbA1c values

combinations occurred at higher HbA1c-levels (mean 7.1%) than in other sites. However, this region had also the highest frequency of unknown HbA1c-values (Table 2).

Second-line treatment intensification

The treatment was intensified with lower levels of HbA1c in regions 3 and 4 (Pohjois-Karjala), where second-line therapy was added to the treatment at mean HbA1c lower than 7.5% (7.42 and 7.45%, Table 3). Number of comorbidities reflecting the overall disease burden was higher at the treatment intensification compared to the baseline in all the regions, being always highest in region 4. DPP4-inhibitors were by far the most common agent for treatment intensification overall (Table 4) with highest frequency in Region 3 and lowest in Region 4 (Table 5). In Region 4, basal insulin was more commonly used second-line agent than in other regions, but sulphonylureas were used less than basal insulin as the second-line agent. Time-related changes in the choice of second-line agent are illustrated in Fig. 2 and Table 6. The use of DPP4-inhibitors increased between the years 2009–2010 (from 16 to 51%), when first DPP4-inhibitor received reimbursement and dominated in this respect thereafter (the highest percentage being at 2013, 80%). On the other hand, the use of sulphonylureas decreased markedly (from 26 to 1–3%) during the observation period (Table 6).

Table 3 At second-line treatment intensification (n = 3593)

	Region 1		Region 2		Region 3		Region 4		Total	
	Mean	Std	Mean	Std	Mean	Std	Mean	Std	Mean	Std
Comorbidities	1.31	1.305	1.30	1.424	1.41	1.495	2.03	1.624	1.62	1.541
Age	62.91	12.716	60.75	12.854	60.39	13.379	64.12	13.149	62.46	13.138
BMI	32.47	6.545	–	–	32.39	6.433	32.29	6.760	32.34	6.660
HbA1c	7.75	1.976	7.72	2.156	7.42	1.874	7.45	2.056	7.57	2.032

Mean and standard deviation of number of comorbidities, age, BMI and HbA1c values

Table 4 Choice of second-line agent

| First treatment	DDP4	Glitazones	GLP-1-analogs	Insulin	Metformin	Other A10	SGLT2-inhibitors	Sulfonylureas	Total
DDP4	0	3	1	35	37	2	0	9	87
Glitazones	4	0	0	4	5	0	0	0	13
GLP-1 analogs	0	0	0	0	1	0	0	0	1
Insulin	42	3	0	0	181	3	0	4	233
Metformin	2158	98	29	562	0	52	5	253	3157
Other .A10	1	0	0	1	19	0	0	2	23
Sulfphonylureas	20	5	0	19	35	0	0	0	79
Total	2225	109	30	621	278	57	5	268	3593

Patients with second-line treatment intensification (n = 3593)

Table 5 Choice of second-line agent per study site

	Region 1		Region 2		Region 3		Region 4		Total	
	N	%	N	%	N	%	N	%	N	%
DDP4	396	63.77	553	63.34	424	69.28	852	57.30	2225	61.93
Glitazones	28	4.51	36	4.12	24	3.92	21	1.41	109	3.03
GLP-1 analogs	11	1.77	1	0.11	3	0.49	15	1.01	30	0.83
Insulin	78	12.56	125	14.32	65	10.62	353	23.74	621	17.28
Metformin	42	6.76	46	5.27	45	7.35	145	9.75	278	7.74
OtherA10	25	4.03	11	1.26	5	0.82	16	1.08	57	1.59
SGLT2-inhibitors	1	0.16	0	0.00	0	0.00	4	0.27	5	0.14
Sulfphonylureas	40	6.44	101	11.57	46	7.52	81	5.45	268	7.46
Total	621	100.00	873	100.00	612	100.00	1487	100.00	3593	100.00

Patients with second-line treatment intensification (n = 3593)

Choice of second line agent per year
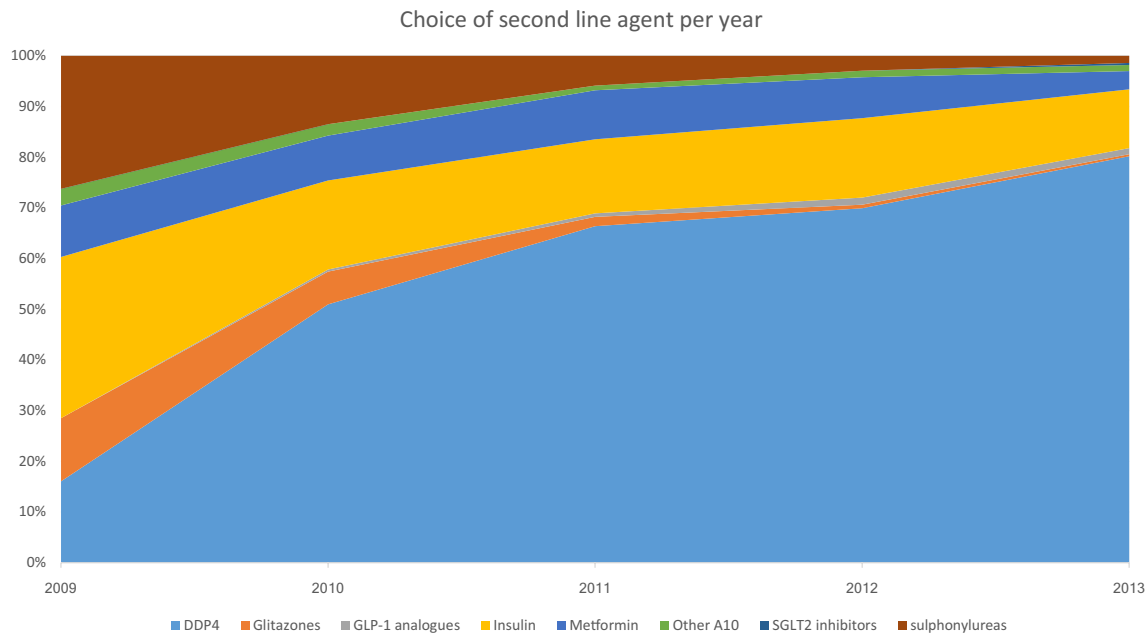
Fig. 2 Choice of second agent per year

Table 6 Choice of second-line agent per year

	2009		2010		2011		2012		2013		After 2013	
	N	%	N	%	N	%	N	%	N	%	N	%
DDP4	49	16.07	363	50.98	577	66.40	598	69.94	401	80.20	237	67.33
Glitazones	38	12.46	46	6.46	16	1.84	6	0.70	2	0.40	1	0.28
GLP-1 analogs	0	0.00	3	0.42	6	0.69	12	1.40	6	1.20	3	0.85
Insulin	97	31.80	125	17.56	127	14.61	134	15.67	58	11.60	80	22.73
Metformin	31	10.16	63	8.85	84	9.67	69	8.07	18	3.60	13	3.69
Other A10	10	3.28	16	2.25	8	0.92	11	1.29	6	1.20	6	1.70
SGLT2-inhibitors	0	0.00	0	0.00	0	0.00	0	0.00	2	0.40	3	0.85
Sulphonylureas	80	26.23	96	13.48	51	5.87	25	2.92	7	1.40	9	2.56
Total	305	100.00	712	100.00	869	100.00	855	100.00	500	100.00	352	100.00

Patients with second-line treatment intensification ($n = 3593$)

Discussion

Our aim was to assess the adherence to national Current Care guideline compared to the actual treatment patterns of type 2 diabetes in the primary care. Our focus was on the start of first drug (metformin) and treatment intensification when the first-line therapy alone is insufficient in controlling hyperglycemia. It seems that the initiation of metformin was quite successful as the vast majority of patients received metformin as first-line medication. Further, the initial drug treatment was started in the early phases of the disease at HbA1c levels below 7.0%. However, the inertia for treatment intensification was evident. Intensification occurred at much higher HbA1c-levels

(about 7.5%) than the first-line treatment and at higher HbA1c-levels than recommended (at 7.0%/53 mmol/mol) in national and international guidelines [6, 8]. This delay and subsequent hyperglycemic burden increases the risk of complications.

The Finnish practice on the use of drugs for treating hyperglycemia seem to differ markedly from the other Nordic countries [11]. The use by defined daily dose (DDD) per 1000 inhabitants is much higher in Finland and has increased much faster. In Finland in 2005 DDD/1000 inhabitants of ATC class 10A was 66.4 and in Sweden only 21.7. At 2012 the corresponding figures were 85.0 and 30.7. The use of insulins and analogs did not differ so markedly (in 2005 Finland 44.6 and Sweden 22.6 and in 2012 Finland 54.1 and Sweden 26.1), but the use of insulin analogs was more

frequent in Finland. The most striking difference was in the use of DPP4-inihitors: in Finland their use increased hugely after the introduction of reimbursement and was manifold as compared to Sweden during this period. This pattern was seen clearly in the second-line choice in our catchment area. Recent survey [12] assessed the similarities and differences of type 2 diabetes mellitus treatment patterns in daily practice in five European countries on patients initiating T2DM treatment. In total of 253,530 patients initiating T2DM treatment during the study period male prominence was observed (52–55%) and the mean age ranged from 62 to 67 years being in line with our cohort. Like in our study metformin was the most common initial treatment in all countries. After initial therapy, most patients in the Netherlands, Spain, and the United Kingdom switched to a combination of metformin and SU derivative. In Italy, the use of repaglinide (short-acting meal time insulin secretion enhancer) was prominent as a second-line use. In France, treatments including DPP4-inihitors were most frequent as second-line treatment. There were national differences regarding the use of newer incretin-based treatments, mainly prescribed for second and/or third treatments. Authors concluded that these variations reflected the differences between the national guidelines of these countries [12]. According to a database of 1.66 million privately insured and Medicare Advantage US patients with T2DM from 2006 to 2013 an increase in the use was observed for metformin (from 47.6 to 53.5%), DPP4-inhibitors (0.5–14.9%), and insulin (17.1–23.0%), but a decline for sulphonylureas (38.8–30.8%) and thiazolidinediones (28.5–5.6%) [13]. Thus, in US metformin was not as dominant as a first-line drug as in Europe. In Finland, it seems that the national guidelines are followed when considering the use of metformin as the first agent, but guideline recommendation does not explain the vast and rapid emergence of DPP4-inhibitors as the second-line agent. It is more likely that reimbursement policy along with the efficient marketing play dominant roles herein. The use of DPP4-inhibitors peaked sharply after the introduction of full reimbursement (year 2010) and resulted in markedly higher use of DPP4-inhibitors as compared to other Nordic Countries [9]. At the same time, the use of SUs fell rapidly. Another incretin-based drug class, GLP1-analogs are recommended in the national guideline. These drugs promote weight loss, whereas DPP4-inhibitors are neutral in this regard [8]. However, their use in the study cohort and in sale statistics have not increased so markedly. Major factor is that the use of GLP1-analogs requires injections and this class is partially reimbursed for restricted patient-group as compared to full reimbursement for other oral hypoglycemic drugs and insulin.

The choice of second- or third-line treatment is related to patient characteristics, as well. Regarding the treatment

intensification, the patients in the region 4 had higher number of comorbidities than others but treatment intensification occurred at the lowest Hba1c-levels. This may be explained by the long history of active diabetes treatment in the area and close collaboration within the public health system between the primary and specialized care allowing more complicated patients to be treated in the primary care. The more frequent use of insulin as means of treatment intensification in that area may also reflect more complicated patient characteristics. Likewise, in the recent survey from various European countries consisting of 485,120 patients (79% of the treated T2DM population) underwent treatment intensification. Changes in treatment choice were clearly visible over the 5-year study period, such as a decline in the use of thiazolidinediones in various countries and increases in the use of DPP-4 inhibitors and GLP-1 receptor agonists. With first-line treatment, advanced age and renal comorbidity were associated with the use of SUs in all countries, whereas high body mass index (BMI) was inversely associated with SU use in the United Kingdom and Spain [14]. The main factors driving treatment choice at any stage of intensification were age, hemoglobin A1c, BMI, renal and cardiac morbidity, and treatment history. These factors were consistent with guidelines and contraindications for specific medications. Differences in local guidelines and reimbursement policies explain the major part of these variations [14]. In summary, the electronic patient information systems and national registers are feasible for research purposes in Finland. National guidelines are followed as concerning the initiation of metformin as first-line agent. However, the intensification of therapy occurs still at quite high Hba1c-levels. Interestingly, the use of DPP4-inhibitors emerged rapidly as major second-line therapy at the time of reimbursement. Further, areal differences were seen in treatment intensification and this may be related to the organization of the primary care.

Compliance with ethical standards

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