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Trends in recording of diagnosis and prescribing in type 2 diabetes mellitus between 2000-2013 in primary care: a retrospective cohort study

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Abstract

Objective: To investigate trends in new and prevalent diagnoses of Type 2 Diabetes Mellitus (T2DM) and its pharmacological treatment between 2000-2013.

Design: Analysis of longitudinal electronic health records in The Health Improvement Network (THIN) primary care database.

Setting: UK primary care.

Participants: In total, we examined 8,838,031 individuals aged 0-99 years.

Outcome Measures: The rate of first recording and prevalence of T2DM between 2000-2013 and the effect of age, sex and social deprivation on these rates were examined. Changes in prescribing patterns of anti-diabetic therapy between 2000-2013 were also investigated.

Results: Overall, 406,344 individuals had a diagnosis of T2DM of which 203,639 were newly diagnosed between 2000-2013. The rate of first recording of T2DM rose from 3.69 per 1000 PYAR (95% CI 3.58-3.81) in 2000 to 3.99 per 1000 PYAR (95% CI 3.90-4.08) in 2013 among men; and from 3.06 per 1000 PYAR (95% CI 2.95-3.17) to 3.73 per 1000 PYAR (95% CI 3.65-3.82) among women . Prevalence of T2DM doubled from 2.39% (95% CI 2.37-2.41) in 2000 to 5.32% (95% CI 5.30-5.34) in 2013. Being male, older and from a more socially deprived area was strongly associated with having T2DM, ($p<0.001$). Prescribing changes over time reflected emerging clinical guidance and novel treatments. Metformin prescribing peaked in 2013; 83.6% (95% CI 83.4-83.8) while sulphonylureas reached a low 41.4% (95% CI 41.1-41.7). Both remained, however, the most commonly used pharmacological treatments as first line agents and add-on therapy. Thiazolidinediones and

incretin based therapies (gliptins and GLP-1 analogues) were also prescribed as alternate add-on therapy options, although rarely used first-line.

Conclusion: Prevalent cases of T2DM increased steadily between 2000-2013 while the rate of newly recorded cases initially increased but then plateaued after 2005. Changes in prescribing patterns observed may reflect the impact of national policies and prescribing guidelines on UK primary care.

Strengths and Limitations

- This is, to our knowledge, the first study to examine changes in rates of new and prevalent diagnosis of type 2 diabetes mellitus and anti-diabetic prescribing patterns using "real world" primary care data between 2000-2013.
- This study does not contain data from secondary care however type 2 diabetes mellitus is largely managed in the primary care setting.
- Although, several explanations for the factors that might have triggered changes in prescribing patterns of anti-diabetic medications over time are provided, there is no means of determining the exact rationale behind prescribing decisions without gathering more detailed information on prescribing for each therapeutic category.

Introduction

Type 2 diabetes mellitus (T2DM) is a growing health burden and managing the disease and its complications accounts for close to 10% of the entire NHS budget in the United Kingdom.[1] T2DM was historically managed in hospitals but there has been a gradual shift towards primary care. The NHS quality and outcomes framework (QOF), introduced as part of the GP contract in 2004 offers several financial incentives to encourage better recording and effective management of several diseases in primary care including diabetes.[2] Hence, primary care data from the United Kingdom is increasingly used to study the disease and its management.[3,4]

Significant developments over the last decade have influenced both the diagnosis and pharmacological treatment of T2DM in the United Kingdom. In 2000, for example, implementation of the revised World Health Organisation diabetes diagnostic criteria led to a lower fasting plasma glucose threshold of 7.0mmol/l being used for diagnosis rather than 7.8 mmol/l.[5] There has also been a greater awareness of the need for aggressive treatment of T2DM to reduce and delay long-term complications such as cardiovascular and renal disease.[6]

Several new therapies have emerged in the past decade such as incretin based therapies and SGLT-2 inhibitors, making the choice of suitable anti-diabetic regimens challenging.[7] This may partly explain the inertia in intensifying treatment for T2DM.[8] Periodic guidance from national and international bodies such as National Institute of Health and Care Excellence (NICE), American Diabetes Association (ADA) and European Association of Diabetics (EASD) in particular, have offered more objective advice to prescribers.[9,10]

Our aim was to investigate how the rate of recording of new and prevalent T2DM diagnoses as well as prescribing patterns have changed between 2000 and 2013 using data from The Health Improvement Network (THIN) primary care database.

Methods

Data Source

The Health Improvement Network (THIN) is one of the largest databases to collect information on patient demographic, disease diagnosis, management and prescribing from UK primary care. THIN contains anonymised medical records from over 550 general practices throughout the UK with around 12 million patients contributing data. It is reasonably representative of the UK population.[11,12] Information is collected during routine patient consultations with General Practitioners from when a patient registers at a THIN affiliated general practice. Symptoms and diagnosis of disease are recorded using the Read code, hierarchical coding system.[13,14] THIN also provides information on referrals made to secondary care, anonymised free text information as well as a measure of social deprivation as quintiles of Townsend scores.[15]

Study Population and Period

All data included in this study was from practices which met the acceptable mortality reporting (AMR) and acceptable computer usage (ACU) standards. These are measures of quality assurance for THIN data.[16,17] The AMR date is the date after which the practice is confirmed to have a rate of mortality sufficiently similar to that expected for a practice with its demographic characteristics, based on data from the Office for National Statistics.[16] The ACU date is the date after which the practice is confirmed to on average have at least one medical record, one additional health record and two prescriptions per patient per year.[17] We included all individuals aged 0-99 years who were registered with a general practice contributing data between 2000-2013.

The recording of diabetes diagnoses and management in THIN is comprehensive and hence, there are several ways an individual may be identified as diabetic. We developed an algorithm to identify individuals with diabetes based on whether they had at least two of the following records; (1) a diagnostic code for diabetes (2) supporting evidence of diabetes e.g. screening for diabetic retinopathy or (3) treatment for diabetes. The first record of any of these three was considered as the date of diagnosis. As some Read codes are non-specific we sought to distinguish diabetics as Type 2 based on age at diagnosis, types of treatment and timing of the diabetes diagnosis. A sample of 500 complete medical records were reviewed manually to confirm the validity of our algorithm.

Definition of Main Outcomes

Rate of first recording of T2DM (Incident recording)

The date at which the first recording of T2DM was made was classified as the index date for diagnosis. We excluded those who had their first recording of T2DM made within the first nine months of practice registration as these were more likely to be prevalent cases.[18]

Prevalence of T2DM

For our analysis on prevalence of T2DM, we included as our numerator all individuals who were first recorded as having T2DM in that particular calendar year and those recorded as having T2DM from previous years. All individuals registered with a general practice in that particular year were included as the denominator. As previously, we accounted for deaths and patients who had left the practices.

Prescription patterns Analysis

The prevalence of use of different anti-diabetic medicines for T2DM was also compared in the time period 2000-2013. We grouped anti-diabetic medications by therapeutic class into

nine categories; metformin, sulphonylureas, insulins, thiazolidinediones, gliptins, GLP-1 analogues, SGLT-2 inhibitors, meglitinides and acarbose. Prevalence of prescribed medications was calculated by dividing the total number of individuals issued a prescription for a particular anti-diabetic medication class by the total number of individuals issued any anti-diabetic medication in that calendar year.

Patients with a first recording of T2DM between 2000-2013 were analysed to examine how prescribing habits may have changed over time for newly diagnosed T2DM specifically. We determined what anti-diabetic drug was prescribed for initiating treatment in T2DM and then examined what anti-diabetic agents were typically added on by prescribers at a later stage (when the disease had progressed further).

Statistical Analyses

The rate of first recording of T2DM was estimated per 1000 person years at risk (PYAR) between 2000 and 2013. This was determined by totalling the number of patients with T2DM with a first recording of T2DM during this time and dividing by the total number of person years of follow up for all patient records. Person time was measured from the latest of: the date of registration plus nine months or 1st January 2000 to the earliest of: date of first recording of T2DM, date of death, date patient left the practice or last date of data collection from that practice or 31st Dec 2013. Multivariable Poisson regression analysis with (log) person time as an offset was used to analyse changes in recording of T2DM by age, sex and social deprivation (Townsend score).

The prevalence of T2DM was calculated by dividing the total number of patients with T2DM in a calendar year by the total number of GP registered patients for that calendar year accounting for deaths and patients who had left the practices. Multivariable Poisson

regression analysis was used to analyse changes in recording of T2DM and also the effect of age, sex and social deprivation.

To investigate the impact of clustering by practice, multilevel random intercept models were compared to all our standard Poisson models. Likelihood ratio tests were used to explore the significance of interaction between variables.

Prescription records were also analysed to describe changes over time in prescribing habits in primary care. The percentage of T2DM patients prescribed different anti-diabetic therapies for ever-use (prevalence), first-line use and as add-on therapy was determined for each calendar year and confidence intervals were calculated.

Stata 13.1 was used to conduct all analyses.

Ethics

THIN has been used for scientific research since approval from the National Health Service South-East Multi-Centre Research Ethics Committee in 2003. Scientific approval to undertake this study was obtained from CMD Medical Research's Scientific Review Committee in February 2015. (SRC Reference Number:15-011).

Results

In total, 406,344 individuals with T2DM were identified and among these 203,639 had their first recording of T2DM (newly diagnosed) between 2000-2013.

Rate of first recording of T2DM

The rate of first recording of T2DM increased from 3.69 per 1000 PYAR (95% CI 3.58 to 3.81) in 2000 to 3.99 per 1000 PYAR (95% CI 3.90 to 4.08) in 2013 for men; and from 3.06 per 1000 PYAR (95% CI 2.95 to 3.17) to 3.73 per 1000 PYAR (95% CI 3.65 to 3.82) in 2013 for women (Table 1). Rate of first recording peaked in 2004 for both men; 4.80 per 1000 PYAR (95% CI 4.70 to 4.90) and women; 4.28 per 1000 PYAR (95% CI 4.19 to 4.38). There was a significant interaction between age and gender ($p<0.001$), hence all results are presented separately for men and women in Table 1. Women were less likely to have new record of T2DM than men (Incidence rate ratios (adj) 0.81 (95% CI 0.80 to 0.82) and individuals from the most socially deprived areas were significantly more likely to have a new record of T2DM than individuals from the least deprived areas (Townsend Quintile 5 vs Townsend Quintile 1; (IRR 1.57 95% CI 1.54 to 1.60) for men and (IRR 1.92 95% CI 1.88 to 1.97) for women). In general, new recording of cases of T2DM increased with age peaking between 70-79 years. Between ages 10– 40 years, the rate of first recording of T2DM was higher among women. However, after the age of 40 years, the crude rate became higher among men though adjusted incidence rates were similar.

Prevalence of T2DM

The prevalence of T2DM more than doubled from 2.39% (95% CI 2.37 to 2.41) in 2000 to 5.32% (95% CI 5.30 to 5.34) in 2013 (Table 2). Prevalence was lower among women (IRR 0.77 95% CI 0.77 to 0.77) and highest among individuals in the most deprived areas

(Townsend quintile 5 vs Townsend quintile 1; (IRR 1.75 95% CI 1.74 to 1.75)). The prevalence increased with age; with the highest crude percentage of patients with T2DM being seen in the 60-69 ageband; 37.65% (95% CI 37.50 to 37.79) and the highest adjusted rate among the 70-79 ageband (70-79 ageband vs 40-49 ageband (IRR 5.95 95% CI 5.92 to 5.97)) (Table 2).

Prescribing in T2DM

Prevalence of anti-diabetic medicine prescribed in patients with T2DM

A total of 305,765 (75.2%) patients out of 406,344 with T2DM were prescribed anti-diabetic medication. The prescribing of metformin rose from 55.4% (95% CI 55.0 to 55.8) in 2000 to 83.6% (95% CI 83.4 to 83.8) in 2013 whilst the prescribing of sulphonylureas decreased from 64.8% (95% CI 64.3 to 65.2) in 2000 to 41.4% (95% CI 41.1 to 41.7) of treated patients with T2DM by 2013 (Figure 1).

Prescribing of thiazolidinediones peaked in 2007 at 16.0% (95% CI 15.8 to 16.3) while that of gliptins peaked in 2013 at 15.4% (95% CI 15.2 to 15.7) of all treated patients (Figure 1). Prescribing of acarbose and meglitinides declined with them prescribed in <0.5% of T2DM patients on anti-diabetic medications by 2013. Insulin prescribing however remained stable with 20-24% of treated patients annually prescribed insulin between 2000-2013.

Medicines used to initiate treatment in newly diagnosed patients with T2DM

A total of 127,523 (62.6%) of 203,639 newly diagnosed patients with T2DM identified were initiated on treatment between 2000-2013. In 2000, 51.1% (95% CI 49.2 to 53.0) were initiated on sulphonylureas and 45.1% (95% CI 43.2 to 47.1) on metformin (Figure 2). Use of metformin as first-line therapy increased annually and by 2013, 91.0% (95% CI 90.5 to 91.5) of newly diagnosed diabetics requiring treatment were being initiated on this therapy.

However, sulphonylureas usage as first line therapy declined by 2013; to 6.3% (95% CI 5.9 to 6.8). Few patients with newly diagnosed T2DM were prescribed insulin first-line in 2013; 1.7% (95% CI 1.4 to 1.9).

Use of thiazolidinediones as first-line therapy remained low and peaked in 2004 (1.1% (95% CI 0.9 to 1.3)). Other anti-diabetic therapies such as gliptins, GLP-1 analogues, acarbose or meglitinides were used very rarely as first line treatments (<1%) in any calendar year.

Medicines prescribed as add-on agents after initiation with metformin in patients with newly diagnosed T2DM

Sulphonylureas were annually the most common add-on therapy used in newly diagnosed patients with T2DM between 2000-2013 already on metformin (Figure 3). However, sulphonylurea use as an add-on declined from 75.9% (95% CI 72.6 to 79.3) in 2000 to 61.7% (95% CI 59.2 to 64.2) in 2013. The use of thiazolidinedione as add-on therapy to metformin peaked in 2002 at 26.9% (95% CI 25.0 to 28.8); after which prescribing declined to 1.9% (95% CI 1.2 to 2.7) in 2013.

Gliptins have become the second most common class of anti-diabetic added to metformin therapy with 26.9% (95% CI 24.7 to 29.2) in 2013. Other anti-diabetic therapies were less commonly added on (Figure 3).

Medicines prescribed as add-on agents after initiation with sulphonylureas in patients with newly diagnosed T2DM

Metformin was the most common treatment added on to newly diagnosed patients with T2DM between 2000-2013 who were already on sulphonylureas (Figure 4). 89.8% (95% CI

87.7 to 92.0) of patients diagnosed in 2000 went on to have metformin add-on therapy after a sulphonylurea while 79.9% (95% CI 74.8 to 85.0) were prescribed metformin in 2013.

Insulins was the second most common add-on therapy to sulphonylureas, accounting for 13.4% (95% CI 9.1 to 17.7) in 2013 (Figure 4). Thiazolidinediones and gliptins were the second and third most common add on therapies respectively. Prescribing of meglitinides remained <1% throughout, while GLP-1 analogues and acarbose were used in <0.3% of patients as add-on in any given year.

Discussion

The rate of first recording of T2DM in UK primary care rose significantly between 2000 and 2005 after which it stabilised around 3.99 per 1000 PYAR in men and 3.73 per 1000 PYAR in women. Prevalence more than doubled over the duration of the study to 5.3% in 2013. Men were 23% more likely to have T2DM and those who were most socially deprived were 75% more likely to have T2DM compared to those least deprived. Individuals aged 70-79 years had the highest adjusted prevalence of T2DM which was nearly six times higher than the reference ageband (40-49 years). Prescribing for T2DM also changed considerably over the study with metformin rising to account for 91.0% of first line therapy among newly diagnosed patients with T2DM and 79.9% of add on therapy for patients on sulphonylureas by 2013. Use of gliptin therapy also increased and was used as an add-on in 26.9% of metformin treated patients; while insulin rose to be used as an add-on in 13.4% of patients after a sulphonylurea by 2013.

The rate of new diagnosis of T2DM observed in this study is comparable to data that has been published previously.[19,20] Previous studies were restricted to the period prior to 2010, our study includes data up to 2013. The initial rise in diagnoses between 2000 and 2005 and plateau thereafter may be explained by the lowering of plasma glucose threshold for diagnosis of diabetes in 2000.[5] Women were at greater risk of developing T2DM relative to men between the ages of 10-40 years, in keeping with other published work;[20] after this age, rates increased more significantly in men. Individuals from the most socially deprived areas in our study were at greatest risk of developing the disease. This is of concern as a study in the US has shown a strong association between socioeconomic status and diabetes related mortality.[21]

The rise in prevalence of T2DM described in this study was similar to that reported by Diabetes UK and the International Diabetes Federation in 2013.[22-24] This rise is also reflected in increasing NHS expenditure on diabetes care.[1]

Similar studies on prescribing conducted with smaller cohorts in the US have shown medication choices to be quite different. For example in a US cohort study on data between 2009-2013 (n=15,516), 57.7% of patients with T2DM initiated therapy with metformin, 23% with sulphonylurea, 6.1% with gliptins and 2.8% with thiazolidinediones,[25] while the corresponding percentages in our study (n=57,518) for same period 2009-2013 were; 90.0%, 7.6%, 0.4% and 0.1% respectively. This significant selection of metformin over other therapies in the United Kingdom suggests an adherence, particularly for treatment initiation, to cost-effective care as published via periodic updates by NICE.

Metformin use increased steadily from 2000 and was prescribed to 91% of newly diagnosed patients with T2DM requiring treatment in 2013. In 2000, metformin was recommended by NICE for use first-line in obese patients with T2DM only, while non-obese patients were still being recommended sulphonylureas and insulins.[26] However, by 2005, metformin was the recommended first-line treatment choice by all bodies[9,10] as it is well tolerated, does not induce weight gain or hypoglycaemia and was the only diabetic treatment found to have a long term benefit in reducing cardiovascular risks and organ damage.[6,10] Previous concerns regarding risks of metabolic acidosis have also been allayed.[27]

We found that the use of sulphonylureas as a first line agent declined among newly diagnosed patients with T2DM in keeping with published clinical guidance.[9,10] This decline may also be explained by the availability of more treatment options, the risk of weight gain and hypoglycaemia attributed to this class of drugs; and as a result of findings from the landmark

UKPDS study that sulphonylureas did not aid in reducing long-term complications of diabetes.[28,29] Nevertheless, 61.7% of patients with T2DM diagnosed in 2013 still had sulphonylureas added to their metformin treatment.

We observed a decline in thiazolidinedione prescribing after 2003 in response to an increasing awareness of adverse effects of these drugs following withdrawal of troglitazone in 1997. Risk of cardiotoxicity particularly heart failure was highlighted in safety alerts for rosiglitazone by regulatory agencies in 2007.[30] Additionally, risks of weight gain, fractures, bladder cancer and hypoglycaemias still exists among the currently licensed thiazolidinediones which may explain their limited use despite evident efficacy.[31]

Since their emergence in 2006, gliptins have rarely been used as first-line therapy in newly diagnosed patients with T2DM. However, their usage as add-on therapy has risen rapidly. Further increase in gliptin use may depend on data emerging on their long term benefits for microvascular and macrovascular complications.[32] Though these drugs are reported to cause pancreatitis, recent reports published by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) suggest that the absolute risk of occurrence is small.[33] Gliptins do not induce weight gain or hypoglycaemia.[34]

GLP-1 analogues were the first anti-diabetic treatments to become available that could induce weight loss, however we have shown that prescribing in primary care has remained low (5.3% in 2013). The may be explained by the publication of the NICE appraisal of the GLP-1 analogue, liraglutide in 2010 that advocated use of these drugs only in those patients who were already on two other therapies, had high BMIs or were contraindicated to at least three of metformin, sulphonylureas, gliptins or thiazolidinediones.[35] Recent NICE updates as of 2015, are less restrictive, which may increase prescribing.[9]

Meglitinides were used in less than <2% of patients annually between 2000-2013. These drugs require multiple daily dosing, carry a risk of inducing hypoglycaemias and are more costly than sulphonylureas.[9] Use of acarbose has also continued to fall perhaps as NICE restrict their recommendation to use in patients who cannot tolerate other oral agents.[36] SGLT-2 inhibitors have been the latest class of anti-diabetic therapy to emerge, hence, overall prescribing was low (0.5% in 2013). They have been recommended by NICE as add-on treatment and can aid with weight loss and blood pressure control without risk of hypoglycaemia. They do, however carry an increased risk of genito-urinary tract infections and long term benefits are unknown.[37,38]

A small percentage of newly diagnosed patients with T2DM (1.7%) are still being initiated on insulin and a growing number are having insulin prescribed as add-on therapy. Though current guidance does not support early introduction of insulin, some studies have demonstrated a benefit.[39] The UKPDS study did not show any benefit of introducing insulin over sulphonylureas, however insulin regimens used in the study are now outdated. They did not explore use of meal-based regimens or insulin in combination with metformin.[40]

Strengths and Limitations of this study

This is the first study to our knowledge to detail changes in recording of diagnoses and prescribing in primary care for T2DM between 2000-2013 and provided insight into factors that may have driven these changes. It has been shown that THIN is broadly representative of the UK population and a particularly suitable database for drug utilization work.[11] This study did not measure prescribing of anti-diabetic medicines in secondary care. However, it is well established that the majority of prescribing for T2DM is in primary care.[41] We did not examine changes in third line therapy as at this stage prescribing becomes too complex to be

of value in informing on population trends. Prescribing of a medication does not necessarily equate to adherence to therapy. However the purpose of this study was to examine recording of diagnosis and physician prescribing choices only. Variation in dosages or between drugs within the same therapeutic class were not considered. Some of this has been explored previously.[8]

Conclusion

There has been a significant increase in the number of new and prevalent cases of T2DM between 2000-2013. Though the rate of recording of new diagnosis has somewhat plateaued since 2005, the prevalence has continued to rise suggesting that patients with T2DM are being diagnosed younger and living longer. Being male, older and from a more socially deprived area were factors all strongly associated with having T2DM.

Prescribing patterns reflected clinical guidance from NICE in particular. Metformin emerged as the most widely prescribed agent though sulphonylureas, despite their limitations, remained the second most common therapy prescribed. Latest international guidelines which may be reflected in future NICE updates, encourages greater use of the broader armamentarium now available for T2DM. We may therefore begin to see more varied patient-specific prescribing. With these and further developments in practice anticipated, it will be important to review how prescribing patterns in primary care for T2DM have further changed in the next few years.

Table 1 Rate of first recording of Type 2 Diabetes Mellitus by socio-demographic factors and year

	Recording of Type 2 Diabetes			
	Rate per 1000 PYAR (95% CI)		Adjusted IRR (95% CI)*	
	Men	Women	Men	Women
Overall	4.19 (4.17 to 4.21)	3.72 (3.7 to 3.74)	1	0.81 (0.80 to 0.82)
Age, years				
0-9	0.04 (0.03 to 0.05)	0.04 (0.04 to 0.05)	0.01 (0.01 to 0.01)	0.01 (0.01 to 0.02)
10-19	0.11 (0.10 to 0.13)	0.28 (0.26 to 0.30)	0.03 (0.03 to 0.03)	0.09 (0.09 to 0.10)
20-29	0.36 (0.34 to 0.38)	1.15 (1.11 to 1.19)	0.09 (0.08 to 0.09)	0.37 (0.35 to 0.38)
30-39	1.36 (1.32 to 1.39)	1.91 (1.86 to 1.95)	0.33 (0.32 to 0.34)	0.63 (0.61 to 0.65)
40-49	4.02 (3.97 to 4.08)	3.00 (2.95 to 3.05)	1	1
50-59	7.86 (7.78 to 7.95)	5.43 (5.36 to 5.50)	1.98 (1.94 to 2.01)	1.83 (1.79 to 1.87)
60-69	11.87 (11.74 to 12.00)	8.48 (8.38 to 8.59)	2.98 (2.92 to 3.03)	2.84 (2.78 to 2.90)
70-79	12.68 (12.51 to 12.85)	10.32 (10.19 to 10.46)	3.18 (3.12 to 3.25)	3.43 (3.35 to 3.50)
80-89	9.08 (8.87 to 9.30)	8.00 (7.84 to 8.15)	2.26 (2.19 to 2.32)	2.57 (2.50 to 2.64)
90-99	5.96 (5.49 to 6.46)	4.55 (4.31 to 4.81)	1.48 (1.36 to 1.61)	1.45 (1.37 to 1.54)
Townsend Quintile				
1	3.86 (3.82 to 3.91)	2.99 (2.95 to 3.03)	1	1
2	4.19 (4.14 to 4.25)	3.50 (3.46 to 3.55)	1.09 (1.07 to 1.11)	1.15 (1.13 to 1.17)
3	4.29 (4.24 to 4.34)	3.86 (3.81 to 3.91)	1.25 (1.23 to 1.27)	1.37 (1.35 to 1.40)
4	4.47 (4.41 to 4.53)	4.32 (4.26 to 4.38)	1.42 (1.40 to 1.45)	1.63 (1.60 to 1.66)
5	4.62 (4.55 to 4.70)	4.75 (4.68 to 4.83)	1.57 (1.54 to 1.60)	1.92 (1.88 to 1.97)
Year				
2000	3.69 (3.58 to 3.81)	3.06 (2.95 to 3.17)	1	1
2001	4.20 (4.08 to 4.31)	3.52 (3.42 to 3.63)	1.14 (1.09 to 1.19)	1.16 (1.1 to 1.21)
2002	4.48 (4.37 to 4.59)	3.73 (3.63 to 3.83)	1.22 (1.17 to 1.27)	1.24 (1.18 to 1.29)
2003	4.52 (4.41 to 4.62)	3.96 (3.87 to 4.06)	1.24 (1.19 to 1.29)	1.32 (1.27 to 1.38)
2004	4.80 (4.70 to 4.90)	4.28 (4.19 to 4.38)	1.32 (1.27 to 1.37)	1.44 (1.38 to 1.50)
2005	4.56 (4.46 to 4.66)	4.04 (3.95 to 4.13)	1.25 (1.20 to 1.30)	1.36 (1.30 to 1.42)
2006	4.52 (4.42 to 4.61)	3.93 (3.84 to 4.02)	1.24 (1.19 to 1.29)	1.33 (1.27 to 1.39)
2007	4.62 (4.52 to 4.72)	4.07 (3.98 to 4.16)	1.26 (1.22 to 1.31)	1.37 (1.32 to 1.43)
2008	4.62 (4.52 to 4.71)	4.06 (3.97 to 4.15)	1.26 (1.21 to 1.31)	1.37 (1.32 to 1.43)
2009	4.71 (4.61 to 4.80)	4.26 (4.18 to 4.36)	1.29 (1.24 to 1.34)	1.45 (1.39 to 1.51)
2010	4.48 (4.39 to 4.58)	4.10 (4.01 to 4.19)	1.23 (1.18 to 1.28)	1.40 (1.34 to 1.46)
2011	4.26 (4.17 to 4.35)	3.97 (3.88 to 4.05)	1.16 (1.12 to 1.21)	1.35 (1.30 to 1.41)
2012	4.40 (4.31 to 4.49)	4.00 (3.91 to 4.09)	1.20 (1.16 to 1.25)	1.37 (1.31 to 1.43)
2013	3.99 (3.90 to 4.08)	3.73 (3.65 to 3.82)	1.09 (1.05 to 1.13)	1.28 (1.22 to 1.33)

* adjusted for other variables considered

**presented by gender due to significant age-gender interaction (p<0.001)

Table 2 Prevalence of Type 2 Diabetes Mellitus by socio-demographic factors and year

	Prevalence of Type 2 Diabetes	
	Percentage Prevalence (95% CI)	Adjusted IRR (95% CI)*
Overall	4.62 (4.60 to 4.64)	
Gender		
Men	52.90 (52.75 to 53.05)	1
Woman	47.10 (46.95 to 47.25)	0.77 (0.77 to 0.77)
Age, years		
0-9	0.09 (0.08 to 0.09)	0.01 (0.01 to 0.01)
10-19	0.41 (0.39 to 0.43)	0.03 (0.03 to 0.03)
20-29	2.19 (2.15 to 2.23)	0.12 (0.12 to 0.13)
30-39	6.54 (6.47 to 6.61)	0.38 (0.38 to 0.39)
40-49	15.18 (15.07 to 15.28)	1
50-59	27.30 (27.16 to 27.43)	2.28 (2.27 to 2.29)
60-69	37.65 (37.50 to 37.79)	4.13 (4.11 to 4.15)
70-79	36.75 (36.60 to 36.89)	5.95 (5.92 to 5.97)
80-89	22.18 (22.05 to 22.30)	5.59 (5.56 to 5.62)
90-99	4.85 (4.78 to 4.91)	4.00 (3.97 to 4.04)
Townsend Quintile		
1	20.23 (20.10 to 20.35)	1
2	19.80 (19.68 to 19.92)	1.12 (1.12 to 1.12)
3	20.74 (20.62 to 20.87)	1.32 (1.32 to 1.33)
4	19.90 (19.78 to 20.02)	1.53 (1.52 to 1.54)
5	14.95 (14.85 to 15.06)	1.75 (1.74 to 1.75)
Year		
2000	2.39 (2.37 to 2.41)	1
2001	2.60 (2.58 to 2.62)	1.10 (1.08 to 1.11)
2002	2.84 (2.83 to 2.86)	1.20 (1.19 to 1.21)
2003	3.11 (3.09 to 3.13)	1.32 (1.30 to 1.33)
2004	3.40 (3.38 to 3.42)	1.44 (1.43 to 1.45)
2005	3.66 (3.64 to 3.67)	1.55 (1.53 to 1.56)
2006	3.88 (3.86 to 3.90)	1.64 (1.63 to 1.65)
2007	4.10 (4.08 to 4.12)	1.73 (1.71 to 1.74)
2008	4.33 (4.32 to 4.35)	1.82 (1.81 to 1.84)
2009	4.56 (4.54 to 4.58)	1.91 (1.90 to 1.93)
2010	4.78 (4.76 to 4.80)	2.01 (1.99 to 2.02)
2011	4.98 (4.96 to 5.00)	2.08 (2.07 to 2.10)
2012	5.17 (5.15 to 5.19)	2.16 (2.14 to 2.18)
2013	5.32 (5.30 to 5.34)	2.21 (2.19 to 2.23)

*adjusted for other variables considered

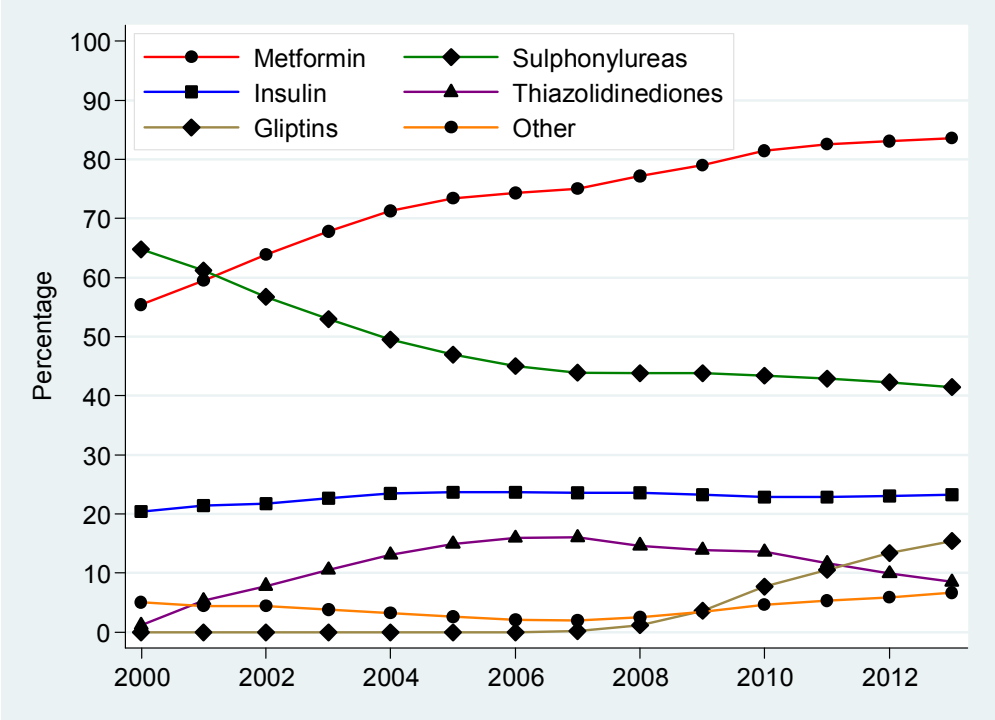

Figure 1 Percentage prevalence of prescribing of different anti-diabetic classes among all Type 2 diabetics on medication

*Other=Sum of prevalence of Acarbose, GLP-1 analogues, Meglitinides and SGLT-2 inhibitors.

** For detailed values of point estimates and confidence intervals, please consult Appendix 1.

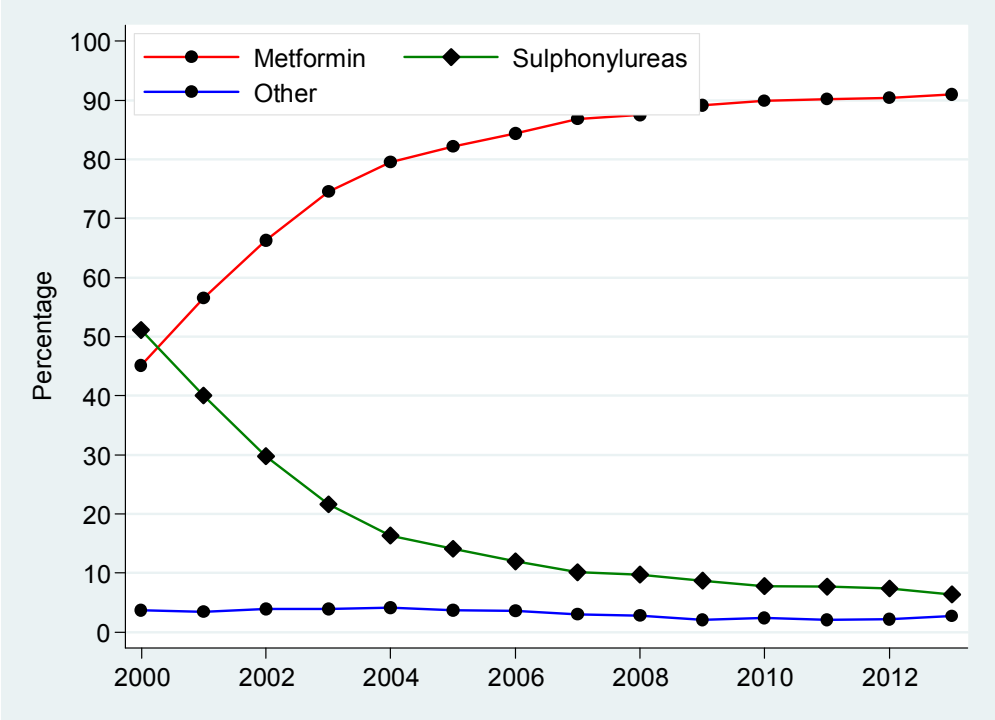

Figure 2 Percentage prevalence of prescribing of different anti-diabetic classes used to initiate treatment in newly diagnosed Type 2 Diabetics.
*Other=Sum of prevalence of Insulins, Thiazolidinediones, Gliptins, Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors.
** For detailed values of point estimates and confidence intervals, please consult Appendix 2.

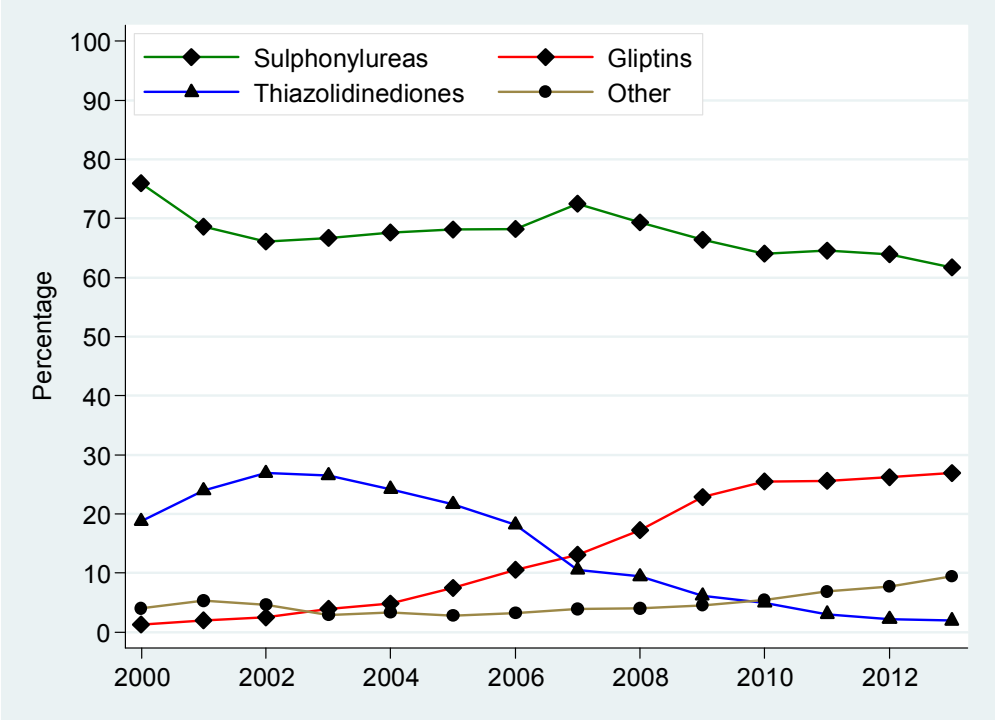

Figure 3 Percentage prevalence of prescribing of different anti-diabetic classes as add-on agents in Type 2 Diabetics after metformin.

*Other=Sum of prevalence of Insulins, Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors detailed individually in smaller graph.

** For detailed figures on point estimates and confidence intervals, please consult Appendix 3.

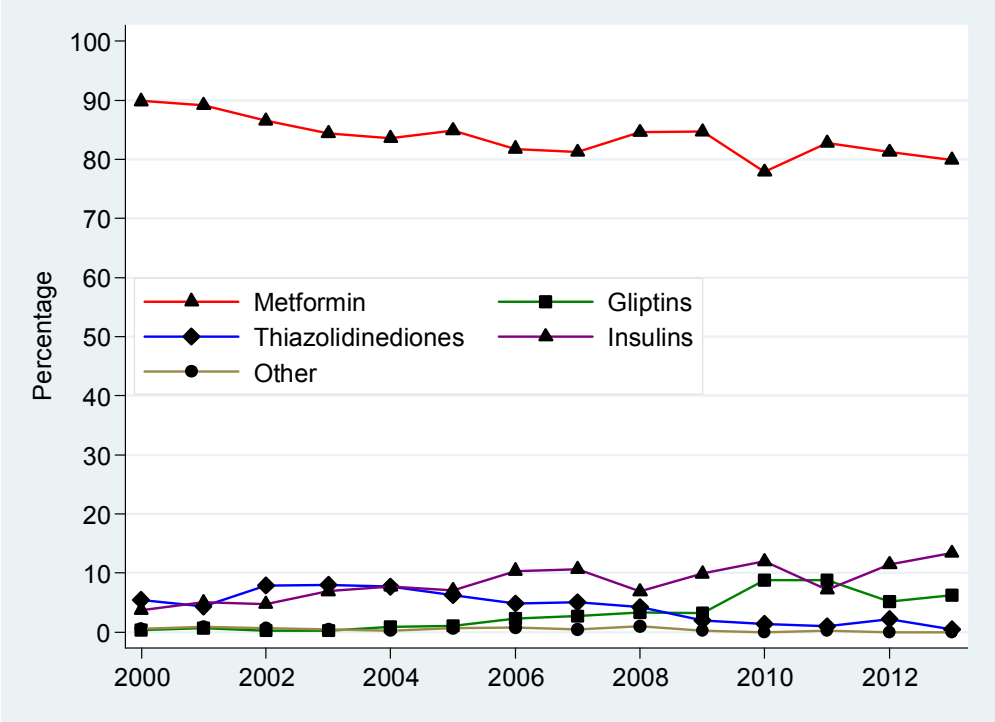

Figure 4 Percentage prevalence of prescribing of different anti-diabetic classes as add-on agents in Type 2 Diabetics after sulphonylureas.
*Other=Sum of prevalence of Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors.
** For detailed figures on point estimates and confidence intervals, please consult Appendix 4.

Contributorship Statement

MS, IN and IP were all involved in the conception and design of the study. MS performed the analysis while IN and IP helped with interpretation. MS prepared the manuscript and IN and IP helped revise it as needed. All authors have read and approved the final manuscript.

Disclosure of Competing Interests

IP, IN and MS report grants from Novo Nordisk A/S during the conduct of this study. They have nothing else to disclose.

Data Sharing Statement

No additional data are available.

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Supplementary Appendices

Appendix 1 - Table S1 Prevalence of prescribing of different anti-diabetic classes among all Type 2 diabetics on medication

N=Total number of Type 2 diabetics in a calendar year prescribed any anti-diabetic medicines; Metf=metformin; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

Year	N	Metf%(95%CI)	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	48,501	55.4 (55.0 to 55.8)	64.8 (64.3 to 65.2)	20.4 (20.0 to 20.7)	-	1.2 (1.1 to 1.3)	-	0.9 (0.8 to 1.0)	4.2 (4.0 to 4.4)	-
2001	54,339	59.5 (59.1 to 59.9)	61.2 (60.8 to 61.6)	21.4 (21.0 to 21.7)	-	5.4 (5.2 to 5.6)	-	1.2 (1.1 to 1.3)	3.3 (3.1 to 3.4)	-
2002	60,454	63.9 (63.5 to 64.2)	56.7 (56.3 to 57.1)	21.7 (21.4 to 22.1)	-	7.8 (7.6 to 8.0)	-	1.7 (1.6 to 1.8)	2.7 (2.5 to 2.8)	-
2003	65,828	67.8 (67.4 to 68.1)	53.0 (52.6 to 53.4)	22.6 (22.3 to 22.9)	-	10.6 (10.3 to 10.8)	-	1.6 (1.5 to 1.7)	2.2 (2.1 to 2.3)	-
2004	72,054	71.3 (71.0 to 71.6)	49.5 (49.2 to 49.9)	23.4 (23.1 to 23.7)	-	13.1 (12.8 to 13.3)	-	1.4 (1.3 to 1.5)	1.8 (1.7 to 1.9)	-
2005	77,384	73.4 (73.1 to 73.7)	47.0 (46.6 to 47.3)	23.7 (23.4 to 24.0)	-	14.9 (14.6 to 15.1)	-	1.1 (1.1 to 1.2)	1.5 (1.4 to 1.5)	-
2006	82,186	74.3 (74.0 to 74.6)	45.1 (44.7 to 45.4)	23.7 (23.4 to 23.9)	-	15.9 (15.7 to 16.2)	-	0.9 (0.8 to 1.0)	1.2 (1.1 to 1.3)	-
2007	86,871	75.0 (74.8 to 75.3)	43.9 (43.6 to 44.2)	23.5 (23.2 to 23.8)	0.2 (0.2 to 0.2)	16.0 (15.8 to 16.3)	0.1 (0.1 to 0.2)	0.9 (0.8 to 0.9)	1.0 (0.9 to 1.0)	-
2008	89,903	77.1 (76.9 to 77.4)	43.8 (43.5 to 44.1)	23.5 (23.3 to 23.8)	1.2 (1.1 to 1.2)	14.7 (14.4 to 14.9)	0.8 (0.8 to 0.9)	0.9 (0.8 to 0.9)	0.8 (0.7 to 0.9)	-
2009	93,041	79.0 (78.8 to 79.3)	43.7 (43.4 to 44.1)	23.3 (23.0 to 23.6)	3.6 (3.5 to 3.7)	13.9 (13.7 to 14.1)	2.0 (1.9 to 2.1)	0.8 (0.7 to 0.8)	0.7 (0.6 to 0.7)	-
2010	93,408	81.5 (81.2 to 81.7)	43.4 (43.1 to 43.7)	22.8 (22.6 to 23.1)	7.6 (7.5 to 7.8)	13.6 (13.4 to 13.8)	3.4 (3.3 to 3.5)	0.7 (0.6 to 0.7)	0.6 (0.5 to 0.6)	-
2011	94,025	82.6 (82.3 to 82.8)	42.8 (42.5 to 43.1)	22.8 (22.5 to 23.1)	10.5 (10.3 to 10.7)	11.7 (11.5 to 11.9)	4.3 (4.2 to 4.4)	0.6 (0.5 to 0.6)	0.5 (0.4 to 0.5)	-
2012	93,888	83.1 (82.8 to 83.3)	42.3 (41.9 to 42.6)	23.1 (22.8 to 23.3)	13.4 (13.2 to 13.6)	9.9 (9.7 to 10.1)	5.0 (4.8 to 5.1)	0.5 (0.5 to 0.5)	0.4 (0.4 to 0.5)	-
2013	91,619	83.6 (83.4 to 83.8)	41.4 (41.1 to 41.7)	23.3 (23.0 to 23.6)	15.4 (15.2 to 15.7)	8.5 (8.3 to 8.7)	5.3 (5.2 to 5.5)	0.5 (0.4 to 0.5)	0.4 (0.3 to 0.4)	0.5 (0.5 to 0.6)

Appendix 2 - Table S2 Prevalence of prescribing of different anti-diabetic classes used to initiate treatment in newly diagnosed Type 2 diabetics.

N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on anti-diabetic medicines; Metf=metformin; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

Year	N	Metf%(95%CI)	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	2,574	45.1 (43.2 to 47.1)	51.1 (49.2 to 53.0)	3.1 (2.4 to 3.7)	-	-	-	0.5 (0.3 to 0.8)	0.2 (0 to 0.3)	-
2001	4,385	56.6 (55.1 to 58.0)	40.0 (38.6 to 41.5)	2.8 (2.3 to 3.3)	-	0.1 (0 to 0.2)	-	0.3 (0.1 to 0.4)	0.2 (0.1 to 0.3)	-
2002	5,859	66.3 (65.1 to 67.5)	29.8 (28.6 to 31.0)	2.9 (2.5 to 3.4)	-	0.4 (0.3 to 0.6)	-	0.4 (0.2 to 0.6)	0.1 (0 to 0.2)	-
2003	7,192	74.5 (73.5 to 75.5)	21.6 (20.7 to 22.6)	2.9 (2.5 to 3.3)	-	0.6 (0.4 to 0.8)	-	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	-
2004	8,885	79.5 (78.6 to 80.3)	16.4 (15.6 to 17.1)	2.7 (2.3 to 3.0)	-	1.1 (0.9 to 1.3)	-	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	-
2005	9,416	82.1 (81.3 to 82.9)	14.1 (13.4 to 14.8)	2.4 (2.1 to 2.7)	-	1.1 (0.9 to 1.3)	-	0.1 (0 to 0.2)	0.1 (0.1 to 0.2)	-
2006	9,841	84.4 (83.7 to 85.1)	12.0 (11.4 to 12.7)	2.5 (2.2 to 2.9)	-	0.9 (0.7 to 1.1)	-	0.1 (0 to 0.1)	0.2 (0.1 to 0.2)	-
2007	10,763	86.9 (86.2 to 87.5)	10.2 (9.6 to 10.7)	2.3 (2.0 to 2.6)	-	0.5 (0.4 to 0.6)	-	0.1 (0 to 0.2)	0.1 (0 to 0.1)	-
2008	11,090	87.5 (86.9 to 88.1)	9.7 (9.2 to 10.3)	2.4 (2.1 to 2.6)	-	0.2 (0.1 to 0.3)	-	0.1 (0 to 0.1)	0.1 (0 to 0.1)	-
2009	12,311	89.1 (88.6 to 89.7)	8.7 (8.2 to 9.2)	1.8 (1.5 to 2.0)	0.1 (0.1 to 0.2)	0.1 (0.1 to 0.2)	0.1 (0 to 0.1)	0.1 (0 to 0.1)	-	-
2010	11,938	89.8 (89.3 to 90.4)	7.8 (7.3 to 8.2)	1.9 (1.6 to 2.1)	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.2)	0.1 (0 to 0.1)	-	-	-
2011	11,168	90.2 (89.6 to 90.7)	7.7 (7.2 to 8.2)	1.7 (1.5 to 1.9)	0.3 (0.2 to 0.4)	0.1 (0.0 to 0.1)	0.1 (0 to 0.1)	-	-	-
2012	11,271	90.4 (89.9 to 90.9)	7.4 (6.9 to 7.9)	1.5 (1.2 to 1.7)	0.5 (0.4 to 0.7)	-	0.1 (0 to 0.1)	-	0.1 (0 to 0.1)	-
2013	10,830	91.0 (90.5 to 91.5)	6.3 (5.9 to 6.8)	1.7 (1.4 to 1.9)	0.8 (0.7 to 1.0)	0.1 (0. to 0.1)	-	-	-	-

Appendix 3 - Table S3 Prevalence of prescribing of different anti-diabetic classes used as add-on agents in Type 2 Diabetics on metformin.

N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on metformin who were subsequently prescribed add-on therapy; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

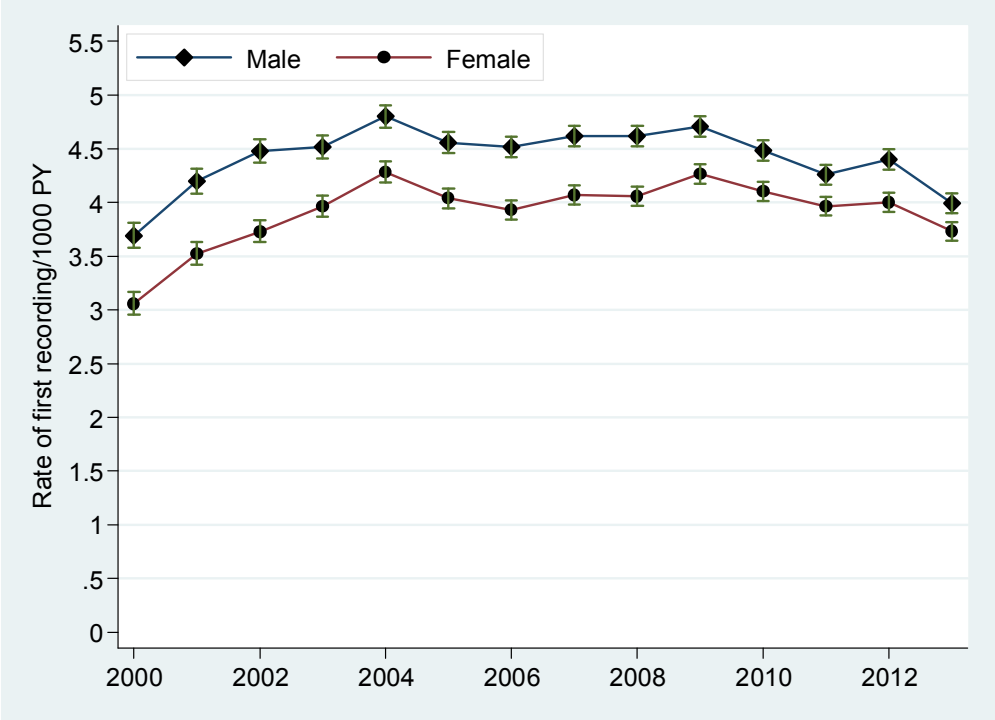
Year	N	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	640	75.9 (72.6 to 79.3)	0.8 (0.1 to 1.5)	1.3 (0.4 to 2.1)	18.8 (15.7 to 21.8)	-	2.2 (1.1 to 3.3)	1.1 (0.3 to 1.9)	-
2001	1,355	68.6 (66.2 to 71.1)	1.4 (0.8 to 2.0)	2.0 (1.2 to 2.7)	24.0 (21.7 to 26.3)	0.2 (0 to 0.5)	3.2 (2.2 to 4.1)	0.6 (0.2 to 1)	-
2002	2,067	66.0 (64.0 to 68.1)	1.3 (0.8 to 1.8)	2.5 (1.8 to 3.1)	26.9 (25.0 to 28.8)	0.3 (0.1 to 0.6)	2.4 (1.8 to 3.1)	0.5 (0.2 to 0.8)	-
2003	2,670	66.7 (64.9 to 68.5)	1.7 (1.2 to 2.2)	3.9 (3.2 to 4.7)	26.5 (24.8 to 28.2)	0.3 (0.1 to 0.6)	0.8 (0.5 to 1.1)	0.1 (0 to 0.2)	-
2004	3,330	67.6 (66.0 to 69.2)	1.9 (1.5 to 2.4)	4.9 (4.1 to 5.6)	24.2 (22.7 to 25.7)	0.5 (0.2 to 0.7)	0.6 (0.3 to 0.8)	0.1 (0 to 0.2)	0.2 (0.1 to 0.4)
2005	3,478	68.1 (66.6 to 69.7)	1.7 (1.3 to 2.2)	7.4 (6.6 to 8.3)	21.6 (20.2 to 23.0)	0.5 (0.3 to 0.8)	0.5 (0.3 to 0.7)	-	0.1 (0 to 0.1)
2006	3,646	68.2 (66.6 to 69.7)	1.8 (1.4 to 2.3)	10.5 (9.5 to 11.5)	18.1 (16.9 to 19.4)	0.8 (0.5 to 1.1)	0.4 (0.2 to 0.6)	0.1 (0 to 0.2)	0 (0 to 0.1)
2007	3,976	72.5 (71.1 to 73.9)	2.3 (1.8 to 2.8)	13.0 (12.0 to 14.1)	10.5 (9.6 to 11.5)	1.0 (0.7 to 1.3)	0.5 (0.2 to 0.7)	0.1 (0 to 0.2)	0.1 (0 to 0.2)
2008	3,955	69.3 (67.8 to 70.7)	2.0 (1.6 to 2.5)	17.2 (16.1 to 18.4)	9.4 (8.5 to 10.3)	1.4 (1.0 to 1.7)	0.4 (0.2 to 0.6)	-	0.2 (0.1 to 0.3)
2009	3,952	66.4 (64.9 to 67.9)	2.4 (1.9 to 2.9)	22.8 (21.5 to 24.2)	6.1 (5.4 to 6.9)	1.5 (1.1 to 1.9)	0.3 (0.1 to 0.4)	0.1 (0 to 0.2)	0.3 (0.2 to 0.5)
2010	3,273	64.1 (62.4 to 65.7)	2.3 (1.8 to 2.8)	25.5 (24.0 to 27.0)	4.9 (4.2 to 5.7)	2.1 (1.6 to 2.6)	0.3 (0.1 to 0.5)	-	0.8 (0.5 to 1.1)
2011	2,652	64.6 (62.7 to 66.4)	3.7 (3.0 to 4.5)	25.6 (23.9 to 27.2)	3.1 (2.4 to 3.7)	1.8 (1.3 to 2.4)	0.2 (0 to 0.4)	-	1.0(0.6 to 1.4)
2012	2,119	63.9 (61.9 to 65.9)	4.1 (3.2 to 4.9)	26.2 (24.3 to 28.1)	2.2 (1.6 to 2.8)	1.8 (1.3 to 2.4)	0.2 (0 to 0.4)	0.1 (0 to 0.2)	1.5 (1.0 to 2.0)
2013	1,440	61.7 (59.2 to 64.2)	3.8 (2.8 to 4.8)	26.9 (24.7 to 29.2)	1.9 (1.2 to 2.7)	1.3 (0.7 to 1.9)	0.1 (0 to 0.3)	0.1 (0 to 0.2)	4.0 (3.0 to 5.0)

Appendix 4 - Table S4 Prevalence of prescribing of different anti-diabetic classes used as add-on agents in Type 2 Diabetics on sulphonylureas.

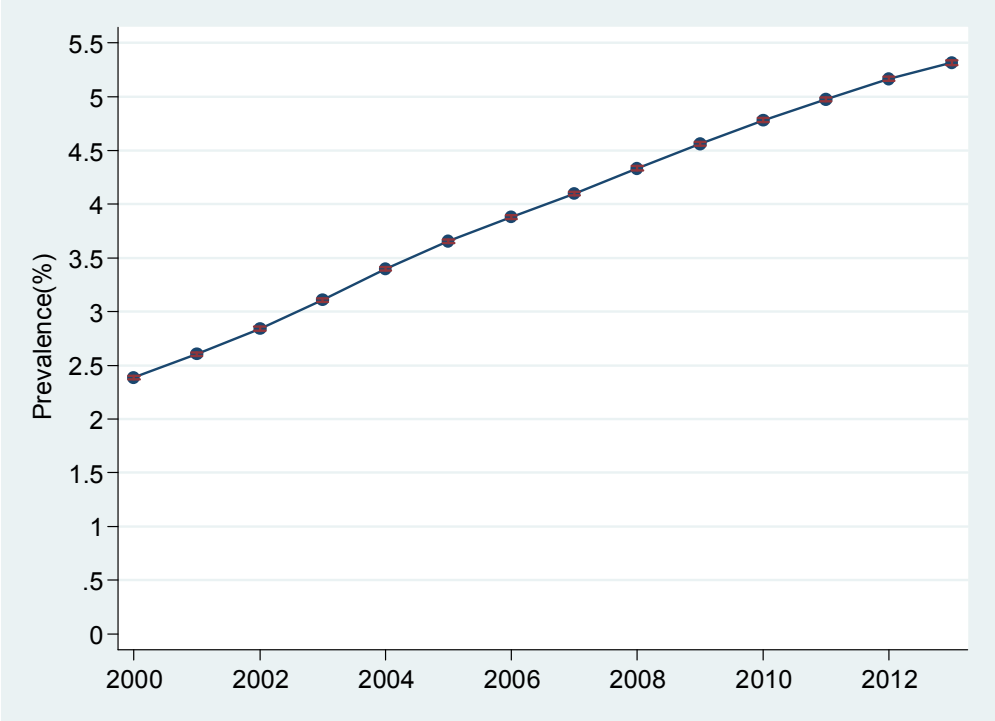
N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on sulphonylureas who were subsequently prescribed add-on therapy; Metf=metformin; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors.

Year	N	Metf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	747	89.8 (87.7 to 92.0)	3.7 (2.4 to 5.1)	0.4 (0 to 0.9)	5.5 (3.9 to 7.1)	-	0.3 (0 to 0.6)	0.3 (0 to 0.6)	-
2001	940	89.1 (87.2 to 91.1)	5.0 (3.6 to 6.4)	0.6 (0.1 to 1.1)	4.4 (3.1 to 5.7)	-	0.5 (0.1 to 1)	0.3 (0 to 0.7)	-
2002	904	86.5 (84.3 to 88.7)	4.8 (3.4 to 6.1)	0.2 (0 to 0.5)	7.9 (6.1 to 9.6)	-	0.4 (0 to 0.9)	0.2 (0 to 0.5)	-
2003	793	84.4 (81.8 to 86.9)	6.9 (5.2 to 8.7)	0.3 (0 to 0.6)	7.9 (6.1 to 9.8)	-	0.4 (0 to 0.8)	0.1 (0 to 0.4)	-
2004	705	83.5 (80.8 to 86.3)	7.7 (5.7 to 9.6)	0.9 (0.2 to 1.5)	7.7 (5.7 to 9.6)	-	0.1 (0 to 0.4)	0.1 (0 to 0.4)	-
2005	622	84.9 (82.1 to 87.7)	7.1 (5.1 to 9.1)	1.1 (0.3 to 2.0)	6.3 (4.4 to 8.2)	-	0.6 (0 to 1.3)	-	-
2006	521	81.8 (78.4 to 85.1)	10.4 (7.7 to 13.0)	2.3 (1.0 to 3.6)	4.8 (3.0 to 6.6)	-	0.6 (0 to 1.2)	0.2 (0 to 0.6)	-
2007	479	81.2 (77.7 to 84.7)	10.6 (7.9 to 13.4)	2.7 (1.3 to 4.2)	5.0 (3.1 to 7.0)	-	0.4 (0 to 1.0)	-	-
2008	421	84.6 (81.1 to 88.0)	6.9 (4.5 to 9.3)	3.3 (1.6 to 5.0)	4.3 (2.3 to 6.2)	-	0.7 (0 to 1.5)	0.2 (0 to 0.7)	-
2009	405	84.7 (81.2 to 88.2)	9.9 (7.0 to 12.8)	3.2 (1.5 to 4.9)	2.0 (0.6 to 3.3)	-	0.2 (0 to 0.7)	-	-
2010	352	77.8 (73.5 to 82.2)	11.9 (8.5 to 15.3)	8.8 (5.8 to 11.8)	1.4 (0.2 to 2.7)	-	-	-	-
2011	319	82.8 (78.6 to 86.9)	7.2 (4.4 to 10.1)	8.8 (5.7 to 11.9)	0.9 (0 to 2.0)	0.3 (0 to 0.9)	-	-	-
2012	314	81.2 (76.9 to 85.5)	11.5 (7.9 to 15.0)	5.1 (2.7 to 7.5)	2.2 (0.6 to 3.9)	-	-	-	-
2013	239	79.9 (74.8 to 85.0)	13.4 (9.1 to 17.7)	6.3 (3.2 to 9.4)	0.4 (0 to 1.2)	-	-	-	-

Appendix 5 – Figure S1 Rate of first recording of Type 2 Diabetes Mellitus



Appendix 6 – Figure S1 Percentage prevalence of Type 2 Diabetes Mellitus



STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **P1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **P2/3**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **P5**
Objectives	3	State specific objectives, including any prespecified hypotheses **P6**
Methods		
Study design	4	Present key elements of study design early in the paper **P7/8**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **P7/8**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up – **P7/8**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed – **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – **P8/9**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. **P8/9**
Bias	9	Describe any efforts to address potential sources of bias. **P10**
Study size	10	Explain how the study size was arrived at. **P11**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. **P9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding. **P9/10**
		(*b*) Describe any methods used to examine subgroups and interactions **P9/10**
		(*c*) Explain how missing data were addressed – **N/A**
		(*d*) If applicable, explain how loss to follow-up was addressed. **N/A**
		(*e*) Describe any sensitivity analyses. **P9/10**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. **P11-14**
		(b) Give reasons for non-participation at each stage. **P11-14**
		(c) Consider use of a flow diagram. **N/A**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders**. P11-14**

		(b) Indicate number of participants with missing data for each variable of interest. **N/A**
		(c) Summarise follow-up time (eg, average and total amount). **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures over time. **N/A**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. **P20/21**
		(*b*) Report category boundaries when continuous variables were categorized. P20/21
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. **P11-14**
Discussion		
Key results	18	Summarise key results with reference to study objectives. **P15**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. **P4/18/19**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. **P15-18**
Generalisability	21	Discuss the generalisability (external validity) of the study results **P15-18**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. – **P28**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Trends in recording of diagnosis and prescribing in type 2 diabetes mellitus between 2000-2013 in primary care: a retrospective cohort study.

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Trends in recording of diagnosis and prescribing in type 2 diabetes mellitus between 2000-2013 in primary care: a retrospective cohort study

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Abstract

Objective: To investigate trends in incident and prevalent diagnoses of Type 2 Diabetes Mellitus (T2DM) and its pharmacological treatment between 2000-2013.

Design: Analysis of longitudinal electronic health records in The Health Improvement Network (THIN) primary care database.

Setting: UK primary care.

Participants: In total, we examined 8,838,031 individuals aged 0-99 years.

Outcome Measures: The incidence and prevalence of T2DM between 2000-2013 and the effect of age, sex and social deprivation on these measures were examined. Changes in prescribing patterns of anti-diabetic therapy between 2000-2013 were also investigated.

Results: Overall, 406,344 individuals had a diagnosis of T2DM of which 203,639 were newly diagnosed between 2000-2013. The incidence of T2DM rose from 3.69 per 1000 person-years at risk (PYAR) (95% CI 3.58-3.81) in 2000 to 3.99 per 1000 PYAR (95% CI 3.90-4.08) in 2013 among men; and from 3.06 per 1000 PYAR (95% CI 2.95-3.17) to 3.73 per 1000 PYAR (95% CI 3.65-3.82) among women . Prevalence of T2DM more than doubled from 2.39% (95% CI 2.37-2.41) in 2000 to 5.32% (95% CI 5.30-5.34) in 2013. Being male, older and from a more socially deprived area was strongly associated with having T2DM, ($p<0.001$). Prescribing changes over time reflected emerging clinical guidance and novel treatments. In 2013, metformin prescribing peaked; 83.6% (95% CI 83.4-83.8) while sulphonylureas prescribing reached a low; 41.4% (95% CI 41.1-41.7). Both remained, however, the most commonly used pharmacological treatments as first line agents and add-on

therapy. Thiazolidinediones and incretin based therapies (gliptins and GLP-1 analogues) were also prescribed as alternate add-on therapy options, although rarely used first-line.

Conclusion: Prevalent cases of T2DM more than doubled between 2000-2013 while the number of incident cases increased more steadily. Changes in prescribing patterns observed may reflect the impact of national policies and prescribing guidelines on UK primary care.

Strengths and Limitations

- This is, to our knowledge, the first study to examine both changes in rates of incident and prevalent diagnosis of type 2 diabetes mellitus and anti-diabetic prescribing patterns using "real world" UK primary care data between 2000-2013.
- This study does not contain data from secondary care however type 2 diabetes mellitus is largely managed in the primary care setting.
- Although, several explanations for the factors that might have triggered changes in prescribing patterns of anti-diabetic medications over time are provided, there is no means of determining the exact rationale behind prescribing decisions without gathering more detailed information on prescribing for each therapeutic category.

Introduction

Type 2 diabetes mellitus (T2DM) is a growing health burden and managing the disease and its complications accounts for close to 10% of the entire NHS budget in the United Kingdom.[1] T2DM was historically managed in hospitals but there has been a gradual shift towards primary care. The NHS quality and outcomes framework (QOF), introduced as part of the GP contract in 2004 offers several financial incentives to encourage better monitoring and management of several diseases in primary care including diabetes.[2] Hence, primary care data from the United Kingdom is increasingly used to study the disease and its management.[3,4]

Significant developments over the last decade have influenced both the diagnosis and pharmacological treatment of T2DM in the United Kingdom. In 2000, for example, implementation of the revised World Health Organisation diabetes diagnostic criteria led to a lower fasting plasma glucose threshold of 7.0mmol/l being used for diagnosis rather than 7.8 mmol/l.[5] There has also been a greater awareness of the need for aggressive treatment of T2DM to reduce and delay long-term complications such as cardiovascular and renal disease.[6]

Several new therapies have emerged in the past decade such as incretin based therapies and SGLT-2 inhibitors, making the choice of suitable anti-diabetic regimens challenging.[7] This may partly explain the inertia in intensifying treatment for T2DM.[8] Periodic guidance from national and international bodies such as National Institute of Health and Care Excellence (NICE), American Diabetes Association (ADA) and European Association of Diabetics (EASD) in particular, have offered more objective advice to prescribers.[9,10]

Our aim was to investigate how the incidence and prevalence ofT2DM diagnoses as well as prescribing patterns have changed between 2000 and 2013 using data from The Health Improvement Network (THIN) primary care database.

Methods

Data Source

The Health Improvement Network (THIN) is one of the largest databases to collect information on patient demographic, disease diagnosis, management and prescribing from UK primary care. THIN contains anonymised medical records from over 550 general practices throughout the UK with around 12 million patients contributing data. It is reasonably representative of the UK population.[11,12] Information is collected during routine patient consultations with General Practitioners from when a patient registers at a THIN affiliated general practice. Symptoms and diagnosis of disease are recorded using the Read code, hierarchical coding system.[13,14] THIN also provides information on referrals made to secondary care, anonymised free text information as well as a measure of social deprivation as quintiles of Townsend scores.[15]

Study Population and Period

All data included in this study was from practices which met the acceptable mortality reporting (AMR) and acceptable computer usage (ACU) standards. These are measures of quality assurance for THIN data.[16,17] The AMR date is the date after which the practice is confirmed to have a rate of mortality sufficiently similar to that expected for a practice with its demographic characteristics, based on data from the Office for National Statistics.[16] The ACU date is the date after which the practice is confirmed to on average have at least one medical record, one additional health record and two prescriptions per patient per year.[17] We included all individuals aged 0-99 years who were registered with a general practice contributing data between 2000-2013.

The recording of diabetes diagnoses and management in THIN is comprehensive and hence, there are several ways an individual may be identified as diabetic. We developed an algorithm to identify individuals with diabetes based on whether they had at least two of the following records; (1) a diagnostic code for diabetes (2) supporting evidence of diabetes e.g. screening for diabetic retinopathy or (3) treatment for diabetes. The first record of any of these three was considered as the date of diagnosis. As some Read codes are non-specific we sought to distinguish diabetics as Type 2 based on age at diagnosis, types of treatment and timing of the diabetes diagnosis.[18] For example, diabetics aged ≥35 at time of diagnosis, on non-insulin anti-diabetic treatment or being managed without treatment were classified as Type 2. Diabetics diagnosed <35 years of age and on insulin were classified as Type 1. A sample of 500 complete electronic healthcare records for individuals with diabetes were reviewed manually in THIN to assess if our clinical classification algorithm for diabetes type based on parameters above had identified diabetes type correctly. In all 500 cases, manual assignment of diabetes type based on clinical assessment of the entire record and algothmic assignment led to equivalent classification.

Definition of Main Outcomes

Incidence of T2DM

The date at which the first recording of T2DM was made was classified as the index date for diagnosis. Therefore, our use of the term incidence with respect to T2DM in this study refers to the first record of T2DM to appear in a patient's electronic primary care record in the THIN database. We excluded those who had their first recording of T2DM made within the first nine months of practice registration as these were more likely to be prevalent cases.[19] We

accounted for deaths and patients who had left the practices in our denominator (follow-up time)

Prevalence of T2DM

For our analysis on prevalence of T2DM, we included as our numerator all individuals who were first recorded as having T2DM within our study period and those recorded as having T2DM from previous years. All individuals registered with a general practice between 2000-2013 having accounted for deaths and patients who had left the practices were included in our denominator.

Prescription patterns Analysis

The prevalence of use of different anti-diabetic medicines for T2DM was also compared across the time period 2000-2013. We grouped anti-diabetic medications by therapeutic class into nine categories; metformin, sulphonylureas, insulins, thiazolidinediones, gliptins, GLP-1 analogues, SGLT-2 inhibitors, meglitinides and acarbose. Prevalence of prescribed medications was calculated by dividing the total number of individuals issued a prescription for a particular anti-diabetic medication class by the total number of individuals issued any anti-diabetic medication in that calendar year.

Patients with an incident recording of T2DM between 2000-2013 were analysed to examine how prescribing habits may have changed over time for newly diagnosed T2DM specifically. We determined what anti-diabetic drug was prescribed for initiating treatment in T2DM and then examined what anti-diabetic agents were typically added on by prescribers at a later stage (when the disease had progressed further).

Statistical Analyses

The overall crude incidence of T2DM was estimated per 1000 person years at risk (PYAR). This was determined by totalling the number of patients with a first recording of T2DM between 2000-2013 and dividing by the total person years of follow up for all patient records for this period. We also determined crude incidence rates by age, gender, social deprivation (Townsend Score) and calendar year by restricting the person years of follow up to the respective category in question. Person time was measured from the latest of: the date of registration plus nine months or 1st January 2000 to the earliest of: date of first recording of T2DM, date of death, date patient left the practice, last date of data collection from that practice or 31st Dec 2013. Multivariable Poisson regression analysis with (log) person time as an offset was used to analyse changes in incidence by age, gender, social deprivation and calendar year whilst controlling for the other respective variables.

The overall crude prevalence of T2DM was calculated by dividing the total number of patients with T2DM by the total number of GP registered patients between 2000-2013 accounting for deaths and patients who had left the practices. Crude prevalence by age, gender, social deprivation and calendar year was also determined. Multivariable Poisson regression analysis was used to analyse changes in prevalence of T2DM and also the effect of age, gender, social deprivation and calendar year whilst controlling for the other respective variables.

To investigate the impact of clustering by practice, multilevel random intercept models were compared to all our standard Poisson models. Likelihood ratio tests were used to explore the significance of interaction between variables.

Prescription records were also analysed to describe changes over time in prescribing habits in primary care. The percentage of T2DM patients prescribed different anti-diabetic therapies for ever-use (prevalence), first-line use and as add-on therapy was determined for each calendar year and confidence intervals were calculated.

Stata 13.1 was used to conduct all analyses.

Ethics

THIN has been used for scientific research since approval from the National Health Service South-East Multi-Centre Research Ethics Committee in 2003. Scientific approval to undertake this study was obtained from CMD Medical Research's Scientific Review Committee in February 2015. (SRC Reference Number:15-011).

Results

In total, 406,344 individuals with T2DM were identified and among these 203,639 were newly diagnosed between 2000-2013.

Incidence of T2DM

The incidence of T2DM increased from 3.69 per 1000 person-years at risk (PYAR) (95% CI 3.58 to 3.81) in 2000 to 3.99 per 1000 PYAR (95% CI 3.90 to 4.08) in 2013 for men; and from 3.06 per 1000 PYAR (95% CI 2.95 to 3.17) to 3.73 per 1000 PYAR (95% CI 3.65 to 3.82) in 2013 for women (Table 1 & Appendix 1). Incidence peaked in 2004 for both men; 4.80 per 1000 PYAR (95% CI 4.70 to 4.90) and women; 4.28 per 1000 PYAR (95% CI 4.19 to 4.38). There was a significant interaction between age and gender ($p<0.001$), hence all results are presented separately for men and women in Table 1. Women had a lower incidence of T2DM than men (Incidence rate ratios (adj) 0.81 (95% CI 0.80 to 0.82) and individuals from the most socially deprived areas had a significantly higher incidence than individuals from the least deprived areas (Townsend Quintile 5 vs Townsend Quintile 1; (IRR 1.57 95% CI 1.54 to 1.60) for men and (IRR 1.92 95% CI 1.88 to 1.97) for women). In general, incidence of T2DM increased with age peaking between 70-79 years. Between ages 10– 40 years, the incidence of T2DM was higher among women. However, after the age of 40 years, the crude incident rate became higher among men though adjusted incidence rates were similar.

Prevalence of T2DM

The prevalence of T2DM more than doubled from 2.39% (95% CI 2.37 to 2.41) in 2000 to 5.32% (95% CI 5.30 to 5.34) in 2013 (Table 2 & Appendix 2). Prevalence was lower among women (IRR 0.77 95% CI 0.77 to 0.77) and highest among individuals in the most deprived

areas (Townsend quintile 5 vs Townsend quintile 1; (IRR 1.75 95% CI 1.74 to 1.75)). The prevalence increased with age; with the highest crude percentage of patients with T2DM being seen in the 60-69 ageband; 37.65% (95% CI 37.50 to 37.79) and the highest adjusted prevalence among the 70-79 ageband (70-79 ageband vs 40-49 ageband (IRR 5.95 95% CI 5.92 to 5.97)) (Table 2).

Prescribing in T2DM

Prevalence of anti-diabetic medicine prescribed in patients with T2DM

A total of 305,765 (75.2%) patients out of 406,344 with T2DM were prescribed anti-diabetic medication. The prescribing of metformin rose from 55.4% (95% CI 55.0 to 55.8) in 2000 to 83.6% (95% CI 83.4 to 83.8) in 2013 whilst the prescribing of sulphonylureas decreased from 64.8% (95% CI 64.3 to 65.2) in 2000 to 41.4% (95% CI 41.1 to 41.7) of treated patients with T2DM by 2013 (Figure 1 & Appendix 3).

Prescribing of thiazolidinediones peaked in 2007 at 16.0% (95% CI 15.8 to 16.3) while that of gliptins peaked in 2013 at 15.4% (95% CI 15.2 to 15.7) of all treated patients (Figure 1). Prescribing of acarbose and meglitinides declined and were prescribed in <0.5% of T2DM patients on anti-diabetic medications by 2013. Insulin prescribing however remained stable with 20-24% of treated patients annually prescribed insulin between 2000-2013.

Medicines used to initiate treatment in newly diagnosed patients with T2DM

A total of 127,523 (62.6%) of 203,639 newly diagnosed patients with T2DM identified were initiated on treatment between 2000-2013. In 2000, 51.1% (95% CI 49.2 to 53.0) were initiated on sulphonylureas and 45.1% (95% CI 43.2 to 47.1) on metformin (Figure 2 & Appendix 4). Use of metformin as first-line therapy increased annually and by 2013, 91.0% (95% CI 90.5 to 91.5) of newly diagnosed diabetics requiring treatment were being initiated

on this therapy. However, sulphonylureas usage as first line therapy declined by 2013; to 6.3% (95% CI 5.9 to 6.8). Few patients with newly diagnosed T2DM were prescribed insulin first-line in 2013; 1.7% (95% CI 1.4 to 1.9).

Use of thiazolidinediones as first-line therapy remained low and peaked in 2004 (1.1% (95% CI 0.9 to 1.3)). Other anti-diabetic therapies such as gliptins, GLP-1 analogues, acarbose or meglitinides were used very rarely as first line treatments (<1%) in any calendar year.

Medicines prescribed as add-on agents after initiation with metformin in patients with newly diagnosed T2DM

Sulphonylureas were annually the most common add-on therapy used in newly diagnosed patients with T2DM between 2000-2013 already on metformin (Figure 3 & Appendix 5). However, sulphonylurea use as an add-on declined from 75.9% (95% CI 72.6 to 79.3) in 2000 to 61.7% (95% CI 59.2 to 64.2) in 2013. The use of thiazolidinedione as add-on therapy to metformin peaked in 2002 at 26.9% (95% CI 25.0 to 28.8); after which prescribing declined to 1.9% (95% CI 1.2 to 2.7) in 2013.

Gliptins have become the second most common class of anti-diabetic added to metformin therapy with 26.9% (95% CI 24.7 to 29.2) in 2013. Other anti-diabetic therapies were less commonly added on (Figure 3).

Medicines prescribed as add-on agents after initiation with sulphonylureas in patients with newly diagnosed T2DM

Metformin was the most common treatment added on to newly diagnosed patients with T2DM between 2000-2013 who were already on sulphonylureas (Figure 4 & Appendix 6). 89.8% (95% CI 87.7 to 92.0) of patients diagnosed in 2000 went on to have metformin add-

on therapy after a sulphonylurea while 79.9% (95% CI 74.8 to 85.0) were prescribed metformin in 2013.

Insulins was the second most common add-on therapy to sulphonylureas, accounting for 13.4% (95% CI 9.1 to 17.7) in 2013 (Figure 4). Thiazolidinediones and gliptins were the second and third most common add on therapies respectively. Prescribing of meglitinides remained <1% throughout, while GLP-1 analogues and acarbose were used in <0.3% of patients as add-on in any given year.

Discussion

The incidence of T2DM in UK primary care rose significantly between 2000 and 2005 after which it stabilised around 3.99 per 1000 PYAR in men and 3.73 per 1000 PYAR in women by 2013. Prevalence more than doubled over the duration of the study to 5.3%. Men were 23% more likely to have T2DM and those who were most socially deprived were 75% more likely to have T2DM compared to those least deprived. Individuals aged 70-79 years had the highest adjusted prevalence of T2DM which was nearly six times higher than the reference ageband (40-49 years). Prescribing for T2DM also changed considerably over the study with metformin rising to account for 91.0% of first line therapy among newly diagnosed patients with T2DM and 79.9% of add on therapy for patients on sulphonylureas by 2013. Use of gliptin therapy also increased and was used as an add-on in 26.9% of metformin treated patients; while insulin rose to be used as an add-on in 13.4% of patients after a sulphonylurea by 2013.

The incidence of T2DM observed in this study is comparable to data that has been published previously.[20,21] Previous studies were restricted to the period prior to 2010, our study includes data up to 2013. The initial rise in diagnoses between 2000 and 2005 and plateau thereafter may be explained by the lowering of plasma glucose threshold for diagnosis of diabetes in 2000.[5] The increase in incidence observed in 2004 in this study could also relate to the introduction of incentivised payments in the UK as part of the quality and outcomes framework for better monitoring of patients with T2DM. Women were at greater risk of developing T2DM relative to men between the ages of 10-40 years, in keeping with other published work;[21] after this age, rates increased more significantly in men. Individuals from the most socially deprived areas in our study were at greatest risk of developing the disease.

This is of concern as a study in the US has shown a strong association between socioeconomic status and diabetes related mortality.[22]

The rise in prevalence of T2DM described in this study was similar to that reported by Diabetes UK and the International Diabetes Federation in 2013.[23-25] Prevalence rates of T2DM observed in this study in the UK are similar to what has been observed in other European countries such as Denmark and Sweden but lower than that observed in Germany and the US, particularly for recent years.[26,27]

Similar studies on prescribing conducted with smaller cohorts in the US have shown medication choices to be quite different. For example in a US cohort study on data between 2009-2013 (n=15,516), 57.8% of patients with T2DM initiated therapy with metformin, 23.0% with sulphonylurea, 13.1% with gliptins and 6.1% with thiazolidinediones,[28] while the corresponding percentages in our study (n=57,518) for same period 2009-2013 were; 90.0%, 7.6%, 0.4% and 0.1% respectively. This significant selection of metformin over other therapies in the United Kingdom suggests an adherence, particularly for treatment initiation, to cost-effective care as published via periodic updates by NICE. This reliance on metformin for first line therapy has also been evident in other studies conducted in Germany and Denmark in particular.[29,30]

Metformin use increased steadily from 2000 and was prescribed to 91% of newly diagnosed patients with T2DM requiring treatment in 2013. In 2000, metformin was recommended by NICE for use first-line in obese patients with T2DM only, while non-obese patients were still being recommended sulphonylureas and insulins.[31] However, by 2005, metformin was the recommended first-line treatment choice by all bodies as it is well tolerated, [9,10] does not

induce weight gain or hypoglycaemia and was the only diabetic treatment found to have a long term benefit in reducing cardiovascular risks and organ damage.[6,10]

We found that the use of sulphonylureas as a first line agent declined among newly diagnosed patients with T2DM in keeping with published clinical guidance.[9,10] This decline may also be explained by the availability of more treatment options, the risk of weight gain and hypoglycaemia attributed to this class of drugs; and because they were shown not to reduce long-term complications of diabetes.[32,33] Nevertheless, 61.7% of patients with T2DM diagnosed in 2013 still had sulphonylureas added to their metformin treatment.

We observed a decline in thiazolidinedione prescribing after 2003 in response to an increasing awareness of adverse effects of these drugs such as cardiotoxicity, highlighted in safety alerts for rosiglitazone by regulatory agencies in 2007.[34] Additionally, risks of weight gain, fractures, bladder cancer and hypoglycaemias still exist among currently licensed thiazolidinediones which may explain their limited use despite evident efficacy.[35]

Since their emergence in 2006, gliptins have rarely been used as first-line therapy in newly diagnosed patients with T2DM. However, their usage as add-on therapy has risen rapidly, perhaps, as they do not induce weight gain or hypoglycaemia.[36] Further increase in gliptin use may depend on data emerging on their long term benefits for microvascular and macrovascular complications.[37]

GLP-1 analogues were the first anti-diabetic treatments to become available that could induce weight loss, however we have shown that prescribing in UK primary care particularly as add-on therapy after metformin remains low (1.1%). This is in considerable contrast to prescribing in Denmark where a study examining data for a similar period (2000-2012)

provided evidence that nearly 7% of patients with T2DM on metformin had GLP-1 therapy added on.[29] Lower use in the UK may be explained by the publication of the NICE appraisal of the GLP-1 analogue, liraglutide in 2010 that recommended use of these drugs only in those patients who were already on two other therapies, had high BMIs or were contraindicated to at least three other anti-diabetics.[38]

A small percentage of newly diagnosed patients with T2DM (1.7%) are still being initiated on insulin and a growing number are having insulin prescribed as add-on therapy. Though current guidance does not support early introduction of insulin, some studies have demonstrated a benefit.[39]

Meglitinides were used in less than <2% of patients annually between 2000-2013. These drugs require multiple daily dosing, carry a risk of inducing hypoglycaemias and are more costly than sulphonylureas.[9] Use of acarbose has also continued to fall perhaps as NICE restrict their recommendation to use in patients who cannot tolerate other oral agents.[40] SGLT-2 inhibitors have been the latest class of anti-diabetic therapy to emerge, hence, overall prescribing was low (0.5% in 2013). They have been recommended by NICE as add-on treatment and can aid with weight loss and blood pressure control without risk of hypoglycaemia. They do, however carry an increased risk of genito-urinary tract infections and long term benefits are unknown.[41,42]

Strengths and Limitations of this study

This is the first study, to our knowledge, to detail changes in recording of diagnoses as well as prescribing for T2DM using UK primary care data between 2000-2013. We have also provided insight into factors that may have driven these changes. Furthermore, THIN has been shown to be broadly representative of the UK population and a particularly suitable

database for drug utilization work.[11] There are however certain limitations to highlight. Though our algorithm for identification of patients with T2DM utilized several variables in addition to diagnostic codes such as treatment and time of diagnosis, there still remains a risk of some misclassification of T2DM. Also, this study did not measure prescribing of anti-diabetic medicines in secondary care. However, it is well established that the majority of prescribing for T2DM is in primary care.[43] We did not examine prescribing patterns in important clinical subgroups such as patients with chronic kidney disease which should be addressed in future work. Prescribing of a medication does not of course equate to adherence to therapy. However the purpose of this study was to examine recording of diagnosis and physician prescribing choices only. Variation in dosages or between drugs within the same therapeutic class were not considered. Some of this has been explored previously.[8]

Conclusion

There has been a significant increase in the number of incident and prevalent cases of T2DM between 2000-2013. Though the incidence of T2DM has somewhat plateaued since 2005, the prevalence has continued to rise suggesting that patients with T2DM are being diagnosed younger and living longer. Being male, older and from a more socially deprived area were factors all strongly associated with having T2DM.

Prescribing patterns reflected clinical guidance from NICE in particular. Metformin emerged as the most widely prescribed agent though sulphonylureas, despite their limitations, remained the second most common therapy prescribed. Latest international guidelines which may be reflected in future NICE updates, encourages greater use of the broader armamentarium now available for T2DM. We may therefore begin to see more varied, patient-specific prescribing. With these and further developments in practice anticipated, it

will be important to review how prescribing patterns in primary care for T2DM have further changed in the next few years.

Table 1 Incidence of Type 2 Diabetes Mellitus by socio-demographic factors and year

	Incidence of Type 2 Diabetes			
	Rate per 1000 PYAR (95% CI)		Adjusted IRR (95% CI)*	
	Men	Women	Men	Women
Overall	4.19 (4.17 to 4.21)	3.72 (3.70 to 3.74)	1	0.81 (0.80 to 0.82)
Age, years				
0-9	0.04 (0.03 to 0.05)	0.04 (0.04 to 0.05)	0.01 (0.01 to 0.01)	0.01 (0.01 to 0.02)
10-19	0.11 (0.10 to 0.13)	0.28 (0.26 to 0.30)	0.03 (0.03 to 0.03)	0.09 (0.09 to 0.10)
20-29	0.36 (0.34 to 0.38)	1.15 (1.11 to 1.19)	0.09 (0.08 to 0.09)	0.37 (0.35 to 0.38)
30-39	1.36 (1.32 to 1.39)	1.91 (1.86 to 1.95)	0.33 (0.32 to 0.34)	0.63 (0.61 to 0.65)
40-49	4.02 (3.97 to 4.08)	3.00 (2.95 to 3.05)	1	1
50-59	7.86 (7.78 to 7.95)	5.43 (5.36 to 5.50)	1.98 (1.94 to 2.01)	1.83 (1.79 to 1.87)
60-69	11.87 (11.74 to 12.00)	8.48 (8.38 to 8.59)	2.98 (2.92 to 3.03)	2.84 (2.78 to 2.90)
70-79	12.68 (12.51 to 12.85)	10.32 (10.19 to 10.46)	3.18 (3.12 to 3.25)	3.43 (3.35 to 3.50)
80-89	9.08 (8.87 to 9.30)	8.00 (7.84 to 8.15)	2.26 (2.19 to 2.32)	2.57 (2.50 to 2.64)
90-99	5.96 (5.49 to 6.46)	4.55 (4.31 to 4.81)	1.48 (1.36 to 1.61)	1.45 (1.37 to 1.54)
Townsend Quintile				
1	3.86 (3.82 to 3.91)	2.99 (2.95 to 3.03)	1	1
2	4.19 (4.14 to 4.25)	3.50 (3.46 to 3.55)	1.09 (1.07 to 1.11)	1.15 (1.13 to 1.17)
3	4.29 (4.24 to 4.34)	3.86 (3.81 to 3.91)	1.25 (1.23 to 1.27)	1.37 (1.35 to 1.40)
4	4.47 (4.41 to 4.53)	4.32 (4.26 to 4.38)	1.42 (1.40 to 1.45)	1.63 (1.60 to 1.66)
5	4.62 (4.55 to 4.70)	4.75 (4.68 to 4.83)	1.57 (1.54 to 1.60)	1.92 (1.88 to 1.97)
Year				
2000	3.69 (3.58 to 3.81)	3.06 (2.95 to 3.17)	1	1
2001	4.20 (4.08 to 4.31)	3.52 (3.42 to 3.63)	1.14 (1.09 to 1.19)	1.16 (1.1 to 1.21)
2002	4.48 (4.37 to 4.59)	3.73 (3.63 to 3.83)	1.22 (1.17 to 1.27)	1.24 (1.18 to 1.29)
2003	4.52 (4.41 to 4.62)	3.96 (3.87 to 4.06)	1.24 (1.19 to 1.29)	1.32 (1.27 to 1.38)
2004	4.80 (4.70 to 4.90)	4.28 (4.19 to 4.38)	1.32 (1.27 to 1.37)	1.44 (1.38 to 1.50)
2005	4.56 (4.46 to 4.66)	4.04 (3.95 to 4.13)	1.25 (1.20 to 1.30)	1.36 (1.30 to 1.42)
2006	4.52 (4.42 to 4.61)	3.93 (3.84 to 4.02)	1.24 (1.19 to 1.29)	1.33 (1.27 to 1.39)
2007	4.62 (4.52 to 4.72)	4.07 (3.98 to 4.16)	1.26 (1.22 to 1.31)	1.37 (1.32 to 1.43)
2008	4.62 (4.52 to 4.71)	4.06 (3.97 to 4.15)	1.26 (1.21 to 1.31)	1.37 (1.32 to 1.43)
2009	4.71 (4.61 to 4.80)	4.26 (4.18 to 4.36)	1.29 (1.24 to 1.34)	1.45 (1.39 to 1.51)
2010	4.48 (4.39 to 4.58)	4.10 (4.01 to 4.19)	1.23 (1.18 to 1.28)	1.40 (1.34 to 1.46)
2011	4.26 (4.17 to 4.35)	3.97 (3.88 to 4.05)	1.16 (1.12 to 1.21)	1.35 (1.30 to 1.41)
2012	4.40 (4.31 to 4.49)	4.00 (3.91 to 4.09)	1.20 (1.16 to 1.25)	1.37 (1.31 to 1.43)
2013	3.99 (3.90 to 4.08)	3.73 (3.65 to 3.82)	1.09 (1.05 to 1.13)	1.28 (1.22 to 1.33)

* adjusted for other variables considered; ageband, townsend quintile, calendar year respectively
**presented by gender due to significant age-gender interaction (p<0.001)
*** for figure displaying data above consult Appendix 1

Table 2 Prevalence of Type 2 Diabetes Mellitus by socio-demographic factors and year

	Prevalence of Type 2 Diabetes	
	Percentage Prevalence (95% CI)	Adjusted IRR (95% CI)*
Overall	4.62 (4.60 to 4.64)	
Gender		
Men	52.90 (52.75 to 53.05)	1
Woman	47.10 (46.95 to 47.25)	0.77 (0.77 to 0.77)
Age, years		
0-9	0.09 (0.08 to 0.09)	0.01 (0.01 to 0.01)
10-19	0.41 (0.39 to 0.43)	0.03 (0.03 to 0.03)
20-29	2.19 (2.15 to 2.23)	0.12 (0.12 to 0.13)
30-39	6.54 (6.47 to 6.61)	0.38 (0.38 to 0.39)
40-49	15.18 (15.07 to 15.28)	1
50-59	27.30 (27.16 to 27.43)	2.28 (2.27 to 2.29)
60-69	37.65 (37.50 to 37.79)	4.13 (4.11 to 4.15)
70-79	36.75 (36.60 to 36.89)	5.95 (5.92 to 5.97)
80-89	22.18 (22.05 to 22.30)	5.59 (5.56 to 5.62)
90-99	4.85 (4.78 to 4.91)	4.00 (3.97 to 4.04)
Townsend Quintile		
1	20.23 (20.10 to 20.35)	1
2	19.80 (19.68 to 19.92)	1.12 (1.12 to 1.12)
3	20.74 (20.62 to 20.87)	1.32 (1.32 to 1.33)
4	19.90 (19.78 to 20.02)	1.53 (1.52 to 1.54)
5	14.95 (14.85 to 15.06)	1.75 (1.74 to 1.75)
Year		
2000	2.39 (2.37 to 2.41)	1
2001	2.60 (2.58 to 2.62)	1.10 (1.08 to 1.11)
2002	2.84 (2.83 to 2.86)	1.20 (1.19 to 1.21)
2003	3.11 (3.09 to 3.13)	1.32 (1.30 to 1.33)
2004	3.40 (3.38 to 3.42)	1.44 (1.43 to 1.45)
2005	3.66 (3.64 to 3.67)	1.55 (1.53 to 1.56)
2006	3.88 (3.86 to 3.90)	1.64 (1.63 to 1.65)
2007	4.10 (4.08 to 4.12)	1.73 (1.71 to 1.74)
2008	4.33 (4.32 to 4.35)	1.82 (1.81 to 1.84)
2009	4.56 (4.54 to 4.58)	1.91 (1.90 to 1.93)
2010	4.78 (4.76 to 4.80)	2.01 (1.99 to 2.02)
2011	4.98 (4.96 to 5.00)	2.08 (2.07 to 2.10)
2012	5.17 (5.15 to 5.19)	2.16 (2.14 to 2.18)
2013	5.32 (5.30 to 5.34)	2.21 (2.19 to 2.23)

*adjusted for other variables considered; gender, ageband, townsend quintile, calendar year respectively
** for figure displaying data above consult Appendix 2.

Contributorship Statement

MS, IN and IP were all involved in the conception and design of the study. MS performed the analysis while IN and IP helped with interpretation. MS prepared the manuscript and IN and IP helped revise it as needed. All authors have read and approved the final manuscript.

Disclosure of Competing Interests

IP, IN and MS report grants from Novo Nordisk A/S during the conduct of this study. They have nothing else to disclose.

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Data sharing

No additional data are available.

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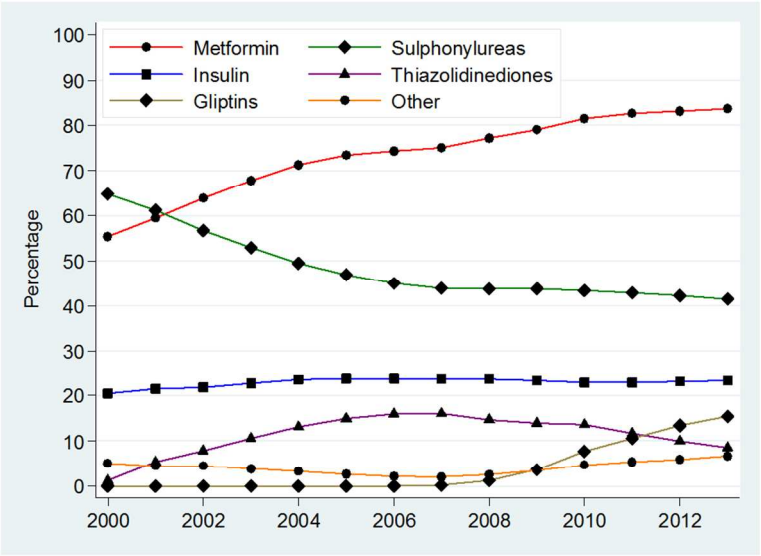


Figure 1 Percentage prevalence of prescribing of different anti-diabetic classes among all Type 2 diabetics on medication

*Other=Sum of prevalence of Acarbose, GLP-1 analogues, Meglitinides and SGLT-2 inhibitors.
** For detailed values of point estimates and confidence intervals, please consult Appendix 3.
338x190mm (96 x 96 DPI)

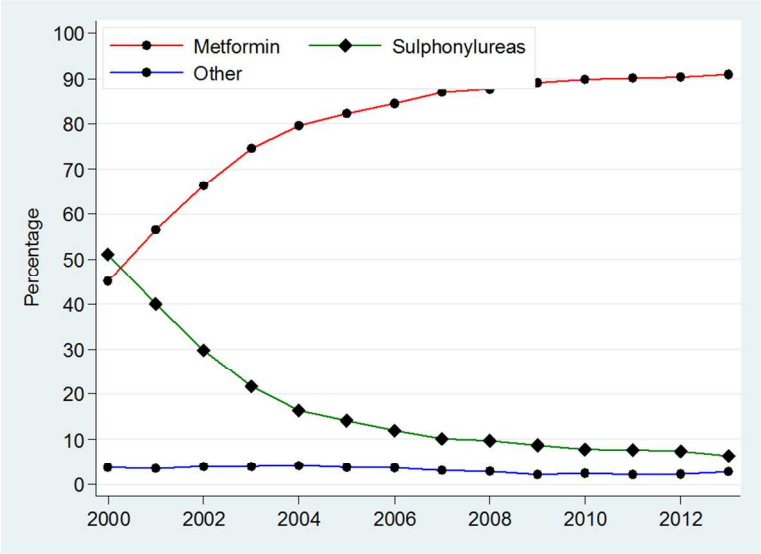


Figure 2 Percentage prevalence of prescribing of different anti-diabetic classes used to initiate treatment in newly diagnosed Type 2 Diabetics.

*Other=Sum of prevalence of Insulins, Thiazolidinediones, Gliptins, Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors.

** For detailed values of point estimates and confidence intervals, please consult Appendix 4.

338x190mm (96 x 96 DPI)

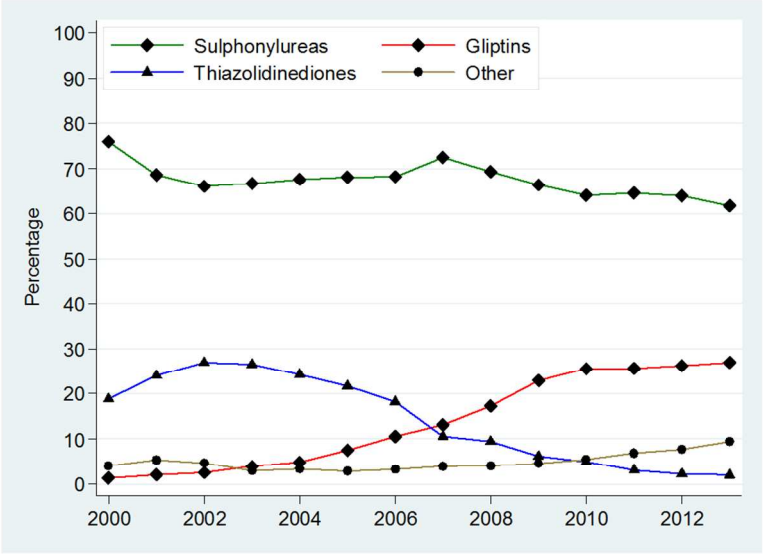


Figure 3 Percentage prevalence of prescribing of different anti-diabetic classes as add-on agents in Type 2 Diabetics after metformin.

*Other=Sum of prevalence of Insulins, Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors detailed individually in smaller graph.

** For detailed figures on point estimates and confidence intervals, please consult Appendix 5.

338x190mm (96 x 96 DPI)

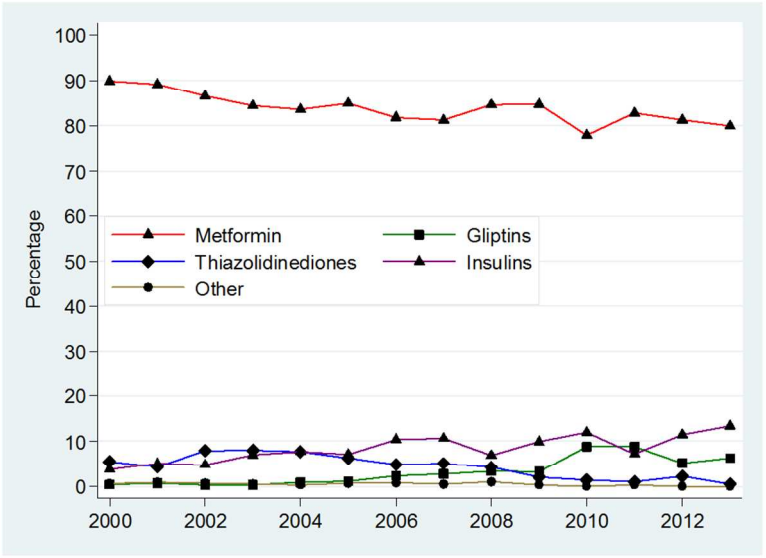


Figure 4 Percentage prevalence of prescribing of different anti-diabetic classes as add-on agents in Type 2 Diabetics after sulphonylureas.

*Other=Sum of prevalence of Acarbose, GLP-1, Meglitinides and SGLT-2 inhibitors.

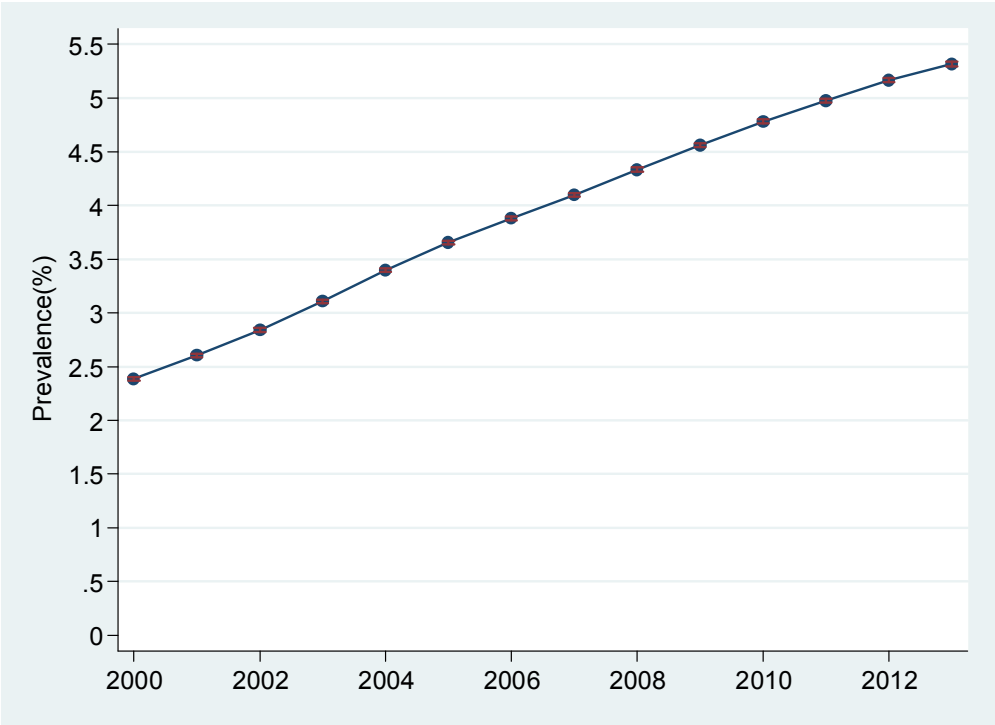
** For detailed figures on point estimates and confidence intervals, please consult Appendix 6.

338x190mm (96 x 96 DPI)

Supplementary Appendices

Appendix 1 – Figure S1 Incidence of Type 2 Diabetes Mellitus

Appendix 2 – Figure S2 Percentage prevalence of Type 2 Diabetes Mellitus



Appendix 3 - Table S1 Prevalence of prescribing of different anti-diabetic classes among all Type 2 diabetics on medication

N=Total number of Type 2 diabetics in a calendar year prescribed any anti-diabetic medicines; Metf=metformin; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

Year	N	Metf%(95%CI)	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	48,501	55.4 (55.0 to 55.8)	64.8 (64.3 to 65.2)	20.4 (20.0 to 20.7)	-	1.2 (1.1 to 1.3)	-	0.9 (0.8 to 1.0)	4.2 (4.0 to 4.4)	-
2001	54,339	59.5 (59.1 to 59.9)	61.2 (60.8 to 61.6)	21.4 (21.0 to 21.7)	-	5.4 (5.2 to 5.6)	-	1.2 (1.1 to 1.3)	3.3 (3.1 to 3.4)	-
2002	60,454	63.9 (63.5 to 64.2)	56.7 (56.3 to 57.1)	21.7 (21.4 to 22.1)	-	7.8 (7.6 to 8.0)	-	1.7 (1.6 to 1.8)	2.7 (2.5 to 2.8)	-
2003	65,828	67.8 (67.4 to 68.1)	53.0 (52.6 to 53.4)	22.6 (22.3 to 22.9)	-	10.6 (10.3 to 10.8)	-	1.6 (1.5 to 1.7)	2.2 (2.1 to 2.3)	-
2004	72,054	71.3 (71.0 to 71.6)	49.5 (49.2 to 49.9)	23.4 (23.1 to 23.7)	-	13.1 (12.8 to 13.3)	-	1.4 (1.3 to 1.5)	1.8 (1.7 to 1.9)	-
2005	77,384	73.4 (73.1 to 73.7)	47.0 (46.6 to 47.3)	23.7 (23.4 to 24.0)	-	14.9 (14.6 to 15.1)	-	1.1 (1.1 to 1.2)	1.5 (1.4 to 1.5)	-
2006	82,186	74.3 (74.0 to 74.6)	45.1 (44.7 to 45.4)	23.7 (23.4 to 23.9)	-	15.9 (15.7 to 16.2)	-	0.9 (0.8 to 1.0)	1.2 (1.1 to 1.3)	-
2007	86,871	75.0 (74.8 to 75.3)	43.9 (43.6 to 44.2)	23.5 (23.2 to 23.8)	0.2 (0.2 to 0.2)	16.0 (15.8 to 16.3)	0.1 (0.1 to 0.2)	0.9 (0.8 to 0.9)	1.0 (0.9 to 1.0)	-
2008	89,903	77.1 (76.9 to 77.4)	43.8 (43.5 to 44.1)	23.5 (23.3 to 23.8)	1.2 (1.1 to 1.2)	14.7 (14.4 to 14.9)	0.8 (0.8 to 0.9)	0.9 (0.8 to 0.9)	0.8 (0.7 to 0.9)	-
2009	93,041	79.0 (78.8 to 79.3)	43.7 (43.4 to 44.1)	23.3 (23.0 to 23.6)	3.6 (3.5 to 3.7)	13.9 (13.7 to 14.1)	2.0 (1.9 to 2.1)	0.8 (0.7 to 0.8)	0.7 (0.6 to 0.7)	-
2010	93,408	81.5 (81.2 to 81.7)	43.4 (43.1 to 43.7)	22.8 (22.6 to 23.1)	7.6 (7.5 to 7.8)	13.6 (13.4 to 13.8)	3.4 (3.3 to 3.5)	0.7 (0.6 to 0.7)	0.6 (0.5 to 0.6)	-
2011	94,025	82.6 (82.3 to 82.8)	42.8 (42.5 to 43.1)	22.8 (22.5 to 23.1)	10.5 (10.3 to 10.7)	11.7 (11.5 to 11.9)	4.3 (4.2 to 4.4)	0.6 (0.5 to 0.6)	0.5 (0.4 to 0.5)	-
2012	93,888	83.1 (82.8 to 83.3)	42.3 (41.9 to 42.6)	23.1 (22.8 to 23.3)	13.4 (13.2 to 13.6)	9.9 (9.7 to 10.1)	5.0 (4.8 to 5.1)	0.5 (0.5 to 0.5)	0.4 (0.4 to 0.5)	-
2013	91,619	83.6 (83.4 to 83.8)	41.4 (41.1 to 41.7)	23.3 (23.0 to 23.6)	15.4 (15.2 to 15.7)	8.5 (8.3 to 8.7)	5.3 (5.2 to 5.5)	0.5 (0.4 to 0.5)	0.4 (0.3 to 0.4)	0.5 (0.5 to 0.6)

Appendix 4 - Table S2 Prevalence of prescribing of different anti-diabetic classes used to initiate treatment in newly diagnosed Type 2 diabetics.

N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on anti-diabetic medicines; Metf=metformin; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

Year	N	Metf%(95%CI)	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	2,574	45.1 (43.2 to 47.1)	51.1 (49.2 to 53.0)	3.1 (2.4 to 3.7)	-	-	-	0.5 (0.3 to 0.8)	0.2 (0 to 0.3)	-
2001	4,385	56.6 (55.1 to 58.0)	40.0 (38.6 to 41.5)	2.8 (2.3 to 3.3)	-	0.1 (0 to 0.2)	-	0.3 (0.1 to 0.4)	0.2 (0.1 to 0.3)	-
2002	5,859	66.3 (65.1 to 67.5)	29.8 (28.6 to 31.0)	2.9 (2.5 to 3.4)	-	0.4 (0.3 to 0.6)	-	0.4 (0.2 to 0.6)	0.1 (0 to 0.2)	-
2003	7,192	74.5 (73.5 to 75.5)	21.6 (20.7 to 22.6)	2.9 (2.5 to 3.3)	-	0.6 (0.4 to 0.8)	-	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	-
2004	8,885	79.5 (78.6 to 80.3)	16.4 (15.6 to 17.1)	2.7 (2.3 to 3.0)	-	1.1 (0.9 to 1.3)	-	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	-
2005	9,416	82.1 (81.3 to 82.9)	14.1 (13.4 to 14.8)	2.4 (2.1 to 2.7)	-	1.1 (0.9 to 1.3)	-	0.1 (0 to 0.2)	0.1 (0.1 to 0.2)	-
2006	9,841	84.4 (83.7 to 85.1)	12.0 (11.4 to 12.7)	2.5 (2.2 to 2.9)	-	0.9 (0.7 to 1.1)	-	0.1 (0 to 0.1)	0.2 (0.1 to 0.2)	-
2007	10,763	86.9 (86.2 to 87.5)	10.2 (9.6 to 10.7)	2.3 (2.0 to 2.6)	-	0.5 (0.4 to 0.6)	-	0.1 (0 to 0.2)	0.1 (0 to 0.1)	-
2008	11,090	87.5 (86.9 to 88.1)	9.7 (9.2 to 10.3)	2.4 (2.1 to 2.6)	-	0.2 (0.1 to 0.3)	-	0.1 (0 to 0.1)	0.1 (0 to 0.1)	-
2009	12,311	89.1 (88.6 to 89.7)	8.7 (8.2 to 9.2)	1.8 (1.5 to 2.0)	0.1 (0.1 to 0.2)	0.1 (0.1 to 0.2)	0.1 (0 to 0.1)	0.1 (0 to 0.1)	-	-
2010	11,938	89.8 (89.3 to 90.4)	7.8 (7.3 to 8.2)	1.9 (1.6 to 2.1)	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.2)	0.1 (0 to 0.1)	-	-	-
2011	11,168	90.2 (89.6 to 90.7)	7.7 (7.2 to 8.2)	1.7 (1.5 to 1.9)	0.3 (0.2 to 0.4)	0.1 (0.0 to 0.1)	0.1 (0 to 0.1)	-	-	-
2012	11,271	90.4 (89.9 to 90.9)	7.4 (6.9 to 7.9)	1.5 (1.2 to 1.7)	0.5 (0.4 to 0.7)	-	0.1 (0 to 0.1)	-	0.1 (0 to 0.1)	-
2013	10,830	91.0 (90.5 to 91.5)	6.3 (5.9 to 6.8)	1.7 (1.4 to 1.9)	0.8 (0.7 to 1.0)	0.1 (0. to 0.1)	-	-	-	-

Appendix 5 - Table S3 Prevalence of prescribing of different anti-diabetic classes used as add-on agents in Type 2 Diabetics on metformin.

N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on metformin who were subsequently prescribed add-on therapy; Sulf=sulphonylurea; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors

Year	N	Sulf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	640	75.9 (72.6 to 79.3)	0.8 (0.1 to 1.5)	1.3 (0.4 to 2.1)	18.8 (15.7 to 21.8)	-	2.2 (1.1 to 3.3)	1.1 (0.3 to 1.9)	-
2001	1,355	68.6 (66.2 to 71.1)	1.4 (0.8 to 2.0)	2.0 (1.2 to 2.7)	24.0 (21.7 to 26.3)	0.2 (0 to 0.5)	3.2 (2.2 to 4.1)	0.6 (0.2 to 1)	-
2002	2,067	66.0 (64.0 to 68.1)	1.3 (0.8 to 1.8)	2.5 (1.8 to 3.1)	26.9 (25.0 to 28.8)	0.3 (0.1 to 0.6)	2.4 (1.8 to 3.1)	0.5 (0.2 to 0.8)	-
2003	2,670	66.7 (64.9 to 68.5)	1.7 (1.2 to 2.2)	3.9 (3.2 to 4.7)	26.5 (24.8 to 28.2)	0.3 (0.1 to 0.6)	0.8 (0.5 to 1.1)	0.1 (0 to 0.2)	-
2004	3,330	67.6 (66.0 to 69.2)	1.9 (1.5 to 2.4)	4.9 (4.1 to 5.6)	24.2 (22.7 to 25.7)	0.5 (0.2 to 0.7)	0.6 (0.3 to 0.8)	0.1 (0 to 0.2)	0.2 (0.1 to 0.4)
2005	3,478	68.1 (66.6 to 69.7)	1.7 (1.3 to 2.2)	7.4 (6.6 to 8.3)	21.6 (20.2 to 23.0)	0.5 (0.3 to 0.8)	0.5 (0.3 to 0.7)	-	0.1 (0 to 0.1)
2006	3,646	68.2 (66.6 to 69.7)	1.8 (1.4 to 2.3)	10.5 (9.5 to 11.5)	18.1 (16.9 to 19.4)	0.8 (0.5 to 1.1)	0.4 (0.2 to 0.6)	0.1 (0 to 0.2)	0 (0 to 0.1)
2007	3,976	72.5 (71.1 to 73.9)	2.3 (1.8 to 2.8)	13.0 (12.0 to 14.1)	10.5 (9.6 to 11.5)	1.0 (0.7 to 1.3)	0.5 (0.2 to 0.7)	0.1 (0 to 0.2)	0.1 (0 to 0.2)
2008	3,955	69.3 (67.8 to 70.7)	2.0 (1.6 to 2.5)	17.2 (16.1 to 18.4)	9.4 (8.5 to 10.3)	1.4 (1.0 to 1.7)	0.4 (0.2 to 0.6)	-	0.2 (0.1 to 0.3)
2009	3,952	66.4 (64.9 to 67.9)	2.4 (1.9 to 2.9)	22.8 (21.5 to 24.2)	6.1 (5.4 to 6.9)	1.5 (1.1 to 1.9)	0.3 (0.1 to 0.4)	0.1 (0 to 0.2)	0.3 (0.2 to 0.5)
2010	3,273	64.1 (62.4 to 65.7)	2.3 (1.8 to 2.8)	25.5 (24.0 to 27.0)	4.9 (4.2 to 5.7)	2.1 (1.6 to 2.6)	0.3 (0.1 to 0.5)	-	0.8 (0.5 to 1.1)
2011	2,652	64.6 (62.7 to 66.4)	3.7 (3.0 to 4.5)	25.6 (23.9 to 27.2)	3.1 (2.4 to 3.7)	1.8 (1.3 to 2.4)	0.2 (0 to 0.4)	-	1.0(0.6 to 1.4)
2012	2,119	63.9 (61.9 to 65.9)	4.1 (3.2 to 4.9)	26.2 (24.3 to 28.1)	2.2 (1.6 to 2.8)	1.8 (1.3 to 2.4)	0.2 (0 to 0.4)	0.1 (0 to 0.2)	1.5 (1.0 to 2.0)
2013	1,440	61.7 (59.2 to 64.2)	3.8 (2.8 to 4.8)	26.9 (24.7 to 29.2)	1.9 (1.2 to 2.7)	1.3 (0.7 to 1.9)	0.1 (0 to 0.3)	0.1 (0 to 0.2)	4.0 (3.0 to 5.0)

Appendix 6 - Table S4 Prevalence of prescribing of different anti-diabetic classes used as add-on agents in Type 2 Diabetics on sulphonylureas.

N= Total number of newly diagnosed Type 2 diabetics in a calendar year initiated on sulphonylureas who were subsequently prescribed add-on therapy; Metf=metformin; Ins=Insulins; Glipt=gliptins; Thiazol=thiazolidinediones; GLP-1=glucagon-like-peptide-1 analogues; Megl-meglitinides; Acar=acarbose; SGLT=sodium-glucose co-transporter2 inhibitors.

Year	N	Metf%(95%CI)	Ins%(95%CI)	Glipt%(95%CI)	Thiazol%(95%CI)	GLP-1%(95%CI)	Megl%(95%CI)	Acar%(95%CI)	SGLT%(95%CI)
2000	747	89.8 (87.7 to 92.0)	3.7 (2.4 to 5.1)	0.4 (0 to 0.9)	5.5 (3.9 to 7.1)	-	0.3 (0 to 0.6)	0.3 (0 to 0.6)	-
2001	940	89.1 (87.2 to 91.1)	5.0 (3.6 to 6.4)	0.6 (0.1 to 1.1)	4.4 (3.1 to 5.7)	-	0.5 (0.1 to 1)	0.3 (0 to 0.7)	-
2002	904	86.5 (84.3 to 88.7)	4.8 (3.4 to 6.1)	0.2 (0 to 0.5)	7.9 (6.1 to 9.6)	-	0.4 (0 to 0.9)	0.2 (0 to 0.5)	-
2003	793	84.4 (81.8 to 86.9)	6.9 (5.2 to 8.7)	0.3 (0 to 0.6)	7.9 (6.1 to 9.8)	-	0.4 (0 to 0.8)	0.1 (0 to 0.4)	-
2004	705	83.5 (80.8 to 86.3)	7.7 (5.7 to 9.6)	0.9 (0.2 to 1.5)	7.7 (5.7 to 9.6)	-	0.1 (0 to 0.4)	0.1 (0 to 0.4)	-
2005	622	84.9 (82.1 to 87.7)	7.1 (5.1 to 9.1)	1.1 (0.3 to 2.0)	6.3 (4.4 to 8.2)	-	0.6 (0 to 1.3)	-	-
2006	521	81.8 (78.4 to 85.1)	10.4 (7.7 to 13.0)	2.3 (1.0 to 3.6)	4.8 (3.0 to 6.6)	-	0.6 (0 to 1.2)	0.2 (0 to 0.6)	-
2007	479	81.2 (77.7 to 84.7)	10.6 (7.9 to 13.4)	2.7 (1.3 to 4.2)	5.0 (3.1 to 7.0)	-	0.4 (0 to 1.0)	-	-
2008	421	84.6 (81.1 to 88.0)	6.9 (4.5 to 9.3)	3.3 (1.6 to 5.0)	4.3 (2.3 to 6.2)	-	0.7 (0 to 1.5)	0.2 (0 to 0.7)	-
2009	405	84.7 (81.2 to 88.2)	9.9 (7.0 to 12.8)	3.2 (1.5 to 4.9)	2.0 (0.6 to 3.3)	-	0.2 (0 to 0.7)	-	-
2010	352	77.8 (73.5 to 82.2)	11.9 (8.5 to 15.3)	8.8 (5.8 to 11.8)	1.4 (0.2 to 2.7)	-	-	-	-
2011	319	82.8 (78.6 to 86.9)	7.2 (4.4 to 10.1)	8.8 (5.7 to 11.9)	0.9 (0 to 2.0)	0.3 (0 to 0.9)	-	-	-
2012	314	81.2 (76.9 to 85.5)	11.5 (7.9 to 15.0)	5.1 (2.7 to 7.5)	2.2 (0.6 to 3.9)	-	-	-	-
2013	239	79.9 (74.8 to 85.0)	13.4 (9.1 to 17.7)	6.3 (3.2 to 9.4)	0.4 (0 to 1.2)	-	-	-	-

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **P1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **P2/3**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **P5**
Objectives	3	State specific objectives, including any prespecified hypotheses **P6**
Methods		
Study design	4	Present key elements of study design early in the paper **P7/8**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **P7/8**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up – **P7/8**
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed – **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – **P8/9**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. **P8/9**
Bias	9	Describe any efforts to address potential sources of bias. **P10**
Study size	10	Explain how the study size was arrived at. **P10**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. **P9**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding. **P10/11**
		(*b*) Describe any methods used to examine subgroups and interactions **P10/11**
		(*c*) Explain how missing data were addressed – **N/A**
		(*d*) If applicable, explain how loss to follow-up was addressed. **P10/11**
		(*e*) Describe any sensitivity analyses. **P10/11**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. **P12-15**
		(b) Give reasons for non-participation at each stage. **P12-15**
		(c) Consider use of a flow diagram. **N/A**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders**. P12-15**

		(b) Indicate number of participants with missing data for each variable of interest. **N/A**
		(c) Summarise follow-up time (eg, average and total amount). **N/A**
Outcome data	15*	Report numbers of outcome events or summary measures over time. **N/A**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. **P22/23**
		(*b*) Report category boundaries when continuous variables were categorized. **P22/23**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. **P12-15**
Discussion		
Key results	18	Summarise key results with reference to study objectives. **P16**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. **P4/19/20**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. **P16-19**
Generalisability	21	Discuss the generalisability (external validity) of the study results **P16-19**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. – **P30**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Correction

Sharma M, Nazareth I, Petersen I. Trends in incidence, prevalence and prescribing in type 2 diabetes mellitus between 2000 and 2013 in primary care: a retrospective cohort study. *BMJ Open* 2016;6:e010210.

The data in the original Table 2 showed proportional distribution by gender, social deprivation and age within the dataset rather that population prevalence. We have now replaced this information with estimates of prevalence and the updated Table 2 (see below). Table 2 now includes prevalence estimates by calendar year (as before) as well as prevalence estimates by gender, age and quintiles of Townsend deprivation

Table 2 Prevalence of type 2 diabetes mellitus per 100 individuals by calendar year and by socio-demographic factors for 2013 only

	Prevalence of Type 2 Diabetes in 2013 by socio-demographic factors Percentage Prevalence (95% CI)	Adjusted PR (95% CI)*
Gender		
Men	5.91 (5.88 to 5.94)	1
Woman	5.11 (5.08 to 5.14)	0.79 (0.79 to 0.80)
Age, years		
0–9	0.03 (0.02 to 0.03)	0.01 (0.01 to 0.01)
10–19	0.14 (0.13 to 0.15)	0.03 (0.03 to 0.04)
20–29	0.6 (0.58 to 0.62)	0.15 (0.15 to 0.16)
30–39	1.65 (1.62 to 1.68)	0.42 (0.41 to 0.43)
40–49	3.70 (3.66 to 3.75)	1
50–59	7.76 (7.69 to 7.82)	2.16 (2.13 to 2.20)
60–69	12.95 (12.85 to 13.04)	3.73 (3.67 to 3.79)
70–79	18.75 (18.61 to 18.88)	5.48 (5.40 to 5.56)
80–89	19.29 (19.11 to 19.46)	5.69 (5.60 to 5.78)
90–99	13.44 (13.14 to 13.75)	4.07 (3.96 to 4.19)
Townsend Quintile		
1	5.00 (4.95 to 5.04)	1
2	5.52 (5.47 to 5.56)	1.11 (1.10 to 1.13)
3	5.67 (5.63 to 5.72)	1.31 (1.30 to 1.33)
4	5.94 (5.89 to 5.99)	1.53 (1.51 to 1.54)
5	6.25 (6.19 to 6.31)	1.75 (1.73 to 1.78)
Annual Prevalence of Type 2 Diabetes between 2000–2013		
Year		
2000	2.39 (2.37 to 2.41)	1
2001	2.60 (2.58 to 2.62)	1.10 (1.08 to 1.11)
2002	2.84 (2.83 to 2.86)	1.20 (1.19 to 1.21)
2003	3.11 (3.09 to 3.13)	1.32 (1.30 to 1.33)
2004	3.40 (3.38 to 3.42)	1.44 (1.43 to 1.45)
2005	3.66 (3.64 to 3.67)	1.55 (1.53 to 1.56)
2006	3.88 (3.86 to 3.90)	1.64 (1.63 to 1.65)
2007	4.10 (4.08 to 4.12)	1.73 (1.71 to 1.74)
2008	4.33 (4.32 to 4.35)	1.82 (1.81 to 1.84)
2009	4.56 (4.54 to 4.58)	1.91 (1.90 to 1.93)
2010	4.78 (4.76 to 4.80)	2.01 (1.99 to 2.02)
2011	4.98 (4.96 to 5.00)	2.08 (2.07 to 2.10)
2012	5.17 (5.15 to 5.19)	2.16 (2.14 to 2.18)
2013	5.32 (5.30 to 5.34)	2.21 (2.19 to 2.23)

*PR (prevalence ratios) mutually adjusted for other variables considered; gender, age band, Townsend quintile respectively.
**For figure displaying data above consult online supplementary appendix 2.

for 2013 (the last year of our study period). Related changes have been made to the method, results and discussion section where relevant.

(1) **METHODS/Definition of main outcomes/Prevalence of T2DM** should read:
For our analysis on prevalence of T2DM by calendar year, we included as our numerator all individuals who had a record of T2DM on or before 1st January in the given year and as our denominator we included all patients registered to a general practice on or by 1st January in the given year.

To estimate prevalence by age, gender and social deprivation, we identified numerators and denominators as described above. Given age changed with time we focused on data from 2013 and calculated age at 1st January 2013. Gender and social deprivation were considered as fixed variables.

(2) **METHODS/Statistical Analysis paragraph 2** should read:
The crude prevalence of T2DM for each year was calculated by dividing the number of all individuals recorded as having T2DM on or before 1st January of that year by the total number of patients registered to a general practice on or by 1st January of that year. Multivariable Poisson regression analysis was used to estimate prevalence ratios of T2DM by year adjusted for age, gender and social deprivation as well as mutually adjusted ratios for age, gender and social deprivation for 2013.

(3) **RESULTS/Prevalence of T2DM** from second sentence should read:
Prevalence of T2DM in 2013 was 5.11 per 100 women and 5.91 per 100 men (Prevalence Ratio (PR) 0.79, 95% CI 0.79 to 0.80) (Table 2) and highest among individuals in the most deprived areas (Townsend quintile 5 vs Townsend quintile 1; (PR 1.75, 95% CI 1.73 to 1.78)). The prevalence increased with age. The highest prevalence for T2DM was seen in the 80–89 years age band: 19.29 per 100 individuals (95% CI 19.11 to 19.46). In comparison to individuals aged 40–49, the adjusted prevalence ratio for 80–89 years age band was 5.69, (95% CI 5.60 to 5.78) (Table 2).

(4) **DISCUSSION/Paragraph 1** from third sentence should read:
Data from 2013 showed women were 21% less likely to have T2DM than men and those who were most socially deprived were 75% more likely to have T2DM, as compared to those least deprived. Individuals aged 80–89 years had the highest adjusted prevalence of T2DM, which was nearly six times higher than individuals aged 40–49 years.

BMJ Open 2016;**6**:e010210corr1. doi:10.1136/bmjopen-2015-010210corr1