Antidiabetic and cardiovascular drug utilisation in patients diagnosed with type 2 diabetes mellitus over the age of 80 years: a population-based cohort study

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Abstract

Background: there is a lack of evidence to inform treatment recommendations for very old people with type 2 diabetes mellitus (T2DM).
Objective: to evaluate trends in antidiabetic and cardiovascular drug utilisation for patients developing T2DM over 80 years of age.
Methods: a population-based cohort was sampled from the UK Clinical Practice Research Datalink between 1990 and 2013. Eligible patients were those with T2DM diagnosed after the age of 80 years and prescribed antidiabetic drugs.
Results: twelve thousand eight hundred and eighty-one patients, with 61% of females, were included. From 1990 to 2013, use of sulphonylureas declined from 94 to 29%, while metformin use increased from 22 to 86%. Prescribing of antihypertensive drugs increased substantially from 46 to 77%, lipid-lowering drugs from 1 to 64%, antiplatelets from 34 to 47% and oral anticoagulants from 5 to 19%. Women were more frequently prescribed antihypertensive drugs (odds ratio 1.26, 95% confidence interval 1.17 to 1.37) but less prescribed antiplatelets (0.83, 0.78 to 0.89). Compared with those diagnosed with T2DM from 80 to 89 years (*n* = 11,467, 89%), patients diagnosed after the age of 90 years (*n* = 1,414, 11%) were less likely to be prescribed insulin (0.37, 0.24 to 0.58), metformin (0.67, 0.60 to 0.75), antihypertensive drugs (0.42, 0.38 to 0.48), lipid-lowering drugs (0.26, 0.23 to 0.30) and anticoagulants (0.55, 0.44 to 0.68).
Conclusions: there have been major increases in the intensity of pharmacological management of patients diagnosed with T2DM over 80 years of age, but the effectiveness and safety of these interventions in very old people require further evaluation.

Keywords: *aged, 80 and over, cardiovascular diseases, drug utilisation, older people, type 2 diabetes mellitus*

Introduction

Type 2 diabetes mellitus (T2DM) is a growing concern at all ages, and the condition accounts for considerable healthcare costs with antidiabetic drugs now being the single most costly element of drug expenditure [1]. Cardiovascular diseases (CVD) are the leading causes of mortality in patients with T2DM [2, 3], and CVD prevention is a major focus of diabetes care. Multifactorial interventions to control hyperglycaemia and to reduce cardiovascular risks are now a key element in the management of patients with T2DM [4]. In the UK,

NICE guidelines for T2DM recommend antihypertensive, lipid-lowering and antithrombotic therapies in addition to antidiabetic therapy [5].

Very old people represent an increasingly important group of health services users. In the UK, there are 3 million very old people, aged >80 years, and this figure is projected to almost double by 2030 [6]. However, despite a high prevalence of T2DM in old people [7], there is limited evidence to inform diabetes care for old people, because they have either not been included in clinical trials or only included in small numbers [8]. In particular, there is lack of evidence from randomised

controlled trials for very old patients with T2DM [9]. The UK Prospective Diabetes Study (UKPDS) included participants aged 25–65 years at diagnosis of T2DM [10]. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, participants aged 80 years or over were excluded because of higher rates of hypoglycaemia in the pilot phase [11]. Treatment recommendations for very old people with T2DM are largely based on professional opinion informed by evidence generated from younger patient samples.

Previous studies on utilisation of antidiabetic [12, 13] and cardiovascular drugs [14, 15] have evaluated all ages, and information on drug utilisation by very old people with T2DM is limited. Treatment decisions in very old people will usually be informed by a range of concerns, such as co-morbidities, declining physical and cognitive functioning, and perceptions of life expectancy, that may not be relevant in younger people [16]. As an initial step in evaluating drug therapy in older adults with diabetes, the present study aimed to evaluate trends in antidiabetic and cardiovascular drug utilisation for patients with T2DM diagnosed over 80 years.

Methods

Data source

A population-based cohort study was conducted using the UK Clinical Practice Research Datalink (CPRD). The CPRD is a database containing anonymised longitudinal electronic health records collected from primary care across the UK [17]. The database currently collects data from 680 general practices and includes 13.2 million patients, of which 5.7 million individuals are active [17]. CPRD data for prescriptions and diagnoses have been shown to be valid [18]. This study was approved by the CPRD Independent Scientific Advisory Committee (ISAC Protocol 14_053).

Study population

A population-based cohort of patients aged 80 years or older with diabetes diagnosed between January 1990 and December 2013 was identified from the CPRD. The diagnosis date of diabetes was defined as earlier of the first diagnosis of diabetes or the first prescription for antidiabetic drugs. Patients with potential type 1 diabetes mellitus were excluded. Patients first diagnosed over the age of 80 years, with at least 12-month record before the diagnosis date, were identified as incident cases. An incident cohort was selected, and only patients with T2DM who were ever prescribed antidiabetic drugs were selected. All patients were followed up until the earliest of death, transferred out from the database or last data collection for the practice.

Analysis

We evaluated the utilisation of antidiabetic drugs (British National Formulary sections 6.1.1 and 6.1.2), antihypertensive drugs (2.2.1, 2.4, 2.5.5 and 2.6.2), lipid-lowering drugs (2.12), antiplatelets (2.9, oral drugs only) and oral anticoagulants (2.8.2). All prescriptions after the diagnosis date of T2DM were counted by drug class.

Baseline characteristics of the study cohort were described. Logistic regression was used to evaluate the trend of drug utilisation. Effects of gender and age group on prescriptions of drugs were assessed by estimating odds ratio (OR) and 95% confidence interval (95% CI). Analyses were adjusted for gender, age group, diagnosis year (3-year interval) and clustering by general practice. All analyses were performed with STATA version 13 (StataCorp., TX, USA).

Results

Characteristics of the study cohort

There were 128,081 participants aged 80 years or older with diabetes from 1990 to 2013. Potential cases of type 1 diabetes mellitus were excluded ($n = 9,860$, 8%). There remained 118,221 patients with T2DM including 26,230 incident cases newly diagnosed at the age of 80 years or older (22%). Of these, 13,349 patients (51%) who did not receive prescription of antidiabetic drugs were not included in the present analyses of drug utilisation, leaving 12,881 patients (49%) for further analysis. The proportions of all patients with T2DM who received antidiabetic drugs by diagnosis year were 1990–93, 52%; 1994–96, 57%; 1997–99, 60%; 2000–03, 57%; 2004–06, 50%; 2007–09, 48%; and 2010–13, 39%. Patients without antidiabetic drugs included slightly older people (median age at diagnosis, 84 years; inter-quartile range, 81–86 years) compared with those treated with drugs ($P < 0.001$). Females accounted for 61% in both groups ($P = 0.337$). The proportions of patients with histories of atrial fibrillation and stroke were 18% ($P = 0.533$) and 9% ($P = 0.554$) in both groups, but more patients with coronary heart diseases were included in the group of patients without antidiabetic drugs (32%, $P < 0.001$). Notably, the median HbA1c level was 7.5% or 59 mmol/mol (inter-quartile range 6.7–9.0 or 50–75 mmol/mol) in patients who received antidiabetic medications which was significantly higher than those without antidiabetic drugs (6.5% or 48 mmol/mol, inter-quartile range 6.0–6.9 or 42–52 mmol/mol, $P < 0.001$).

Baseline characteristics of the study cohort are shown by gender in Table 1 and by age group (see Supplementary data, Table S1, available in *Age and Ageing* online). Female patients accounted for 61%, and the proportion was higher in 90+ group (71%, $P < 0.001$). The median age at diagnosis of T2DM was 83 years, and median duration of follow-up after diagnosis of T2DM was 3.4 years, with shorter duration of follow-up for 90+ group (1.9 years, $P < 0.001$). Two-thirds of patients with recorded values had high blood pressure (62% with diastolic ≥90 and/or systolic ≥140 mmHg) and a half of patients had high total cholesterol (50% with ≥5 mmol/l). Antihypertensive or lipid-lowering drugs were prescribed to 66 or 27% of overall patients within 12 months before the diagnosis. Among selected co-morbidities, atrial fibrillation, coronary heart diseases and stroke were recorded in 18, 28 and 9% of overall patients.

Table 1. Baseline characteristics of the study cohort by gender

	All ($n = 12,881$)	Males ($n = 5,039$)	Females ($n = 7,842$)	P value (males versus females)
Gender—female	7,842 (61)	NA	NA	NA
Age at diagnosis of diabetes (years)[a]	83 (81–86)	83 (81–86)	84 (81–87)	<0.001
Duration of follow-up after diagnosis of diabetes (years)[a]	3.4 (1.5–6.0)	3.4 (1.5–5.9)	3.5 (1.5–6.1)	0.308
Year of diagnosis of diabetes				<0.001
1990–94	590 (5)	184 (4)	406 (5)	
1995–99	1,371 (11)	459 (9)	912 (12)	
2000–04	3,922 (30)	1,537 (31)	2,385 (30)	
2005–09	4,354 (34)	1,713 (34)	2,641 (34)	
2010–13	2,644 (21)	1,146 (23)	1,498 (19)	
Smoking status[b]				<0.001
Non-smoker	4,813 (37)	1,458 (29)	3,355 (43)	
Previous smoker	3,152 (24)	1,771 (35)	1,381 (18)	
Current smoker	1,617 (13)	732 (15)	885 (11)	
Missing	3,299 (26)	1,078 (21)	2,221 (28)	
BMI category (kg/m^2)[b]				<0.001
<18.5	151 (1)	37 (1)	114 (1)	
18.5–24.9	2,535 (20)	1,018 (20)	1,517 (19)	
25.0–29.9	3,841 (30)	1,807 (36)	2,034 (26)	
30.0–34.9	2,016 (16)	814 (16)	1,202 (15)	
≥35.0	714 (6)	216 (4)	498 (6)	
Missing	3,624 (28)	1,147 (23)	2,477 (32)	
HbA1c (%/mmol/mol)[b]				0.027
<6.5 (48)	1,579 (12)	595 (12)	984 (13)	
6.5 (48)–6.9 (52)	1,376 (11)	592 (12)	784 (10)	
7.0 (53)–7.4 (57)	1,356 (11)	548 (11)	808 (10)	
7.5 (58)–7.9 (63)	1,080 (8)	466 (9)	614 (8)	
8.0 (64)–8.4 (68)	790 (6)	326 (6)	464 (6)	
≥8.5 (69)	2,940 (23)	1,173 (23)	1,767 (23)	
Missing	3,760 (29)	1,339 (27)	2,421 (31)	
Diastolic/systolic blood pressure (mmHg)[b]				<0.001
<90 and <140	4,428 (34)	1,979 (39)	2,449 (31)	
90–94 | 140–149	2,721 (21)	1,059 (21)	1,662 (21)	
90–94 | 150–159	1,847 (14)	703 (14)	1,144 (15)	
≥95 | ≥160	2,808 (22)	942 (19)	1,866 (24)	
Missing	1,077 (8)	356 (7)	721 (9)	
Total cholesterol (mmol/l)[b]				<0.001
<4.0	1,805 (14)	1,039 (21)	766 (10)	
4.0–4.9	2,998 (23)	1,397 (28)	1,601 (20)	
5.0–5.9	2,614 (20)	1,001 (20)	1,613 (21)	
≥6.0	2,115 (16)	516 (10)	1,599 (20)	
Missing	3,349 (26)	1,086 (22)	2,263 (29)	
Atrial fibrillation[c]	2,323 (18)	901 (18)	1,422 (18)	0.716
Coronary heart diseases[c]	3,631 (28)	1,694 (34)	1,937 (25)	<0.001
Stroke[c]	1,155 (9)	499 (10)	656 (8)	0.003
Cognitive impairment/dementia[c]	591 (5)	163 (3)	428 (5)	<0.001
Depression[d]	1,204 (9)	308 (6)	896 (11)	<0.001

Frequencies (percentages) are shown otherwise specified.

[a]Median (inter-quartile range).

[b]When data were available during 12 months before the diagnosis of diabetes, the latest data were used. If not, data were compensated with the first data during 12 months after the diagnosis.

[c]Ever diagnosed before the diagnosis of diabetes.

[d]Diagnosed during 12 months before the diagnosis of diabetes, or ever diagnosed before the diagnosis of diabetes with prescriptions of antidepressants during 12 months before the diagnosis.

Antidiabetic drugs

From 1990 to 2013, the mainstay of antidiabetic therapy changed from sulphonylureas (94% in the early 1990s to 29% in 2010s; Figure 1a) to metformin (22 to 86%). Insulin was the most frequently prescribed around 2000 (5%) but subsequently decreased (1% in 2010; Figure 1b). Prescriptions of thiazolidinediones increased from 3% in the late 1990s and peaked at 8% in 2003, but declined to 1% after 2010. Prescriptions of DPP-4 inhibitors started to rise in recent years (5% in 2010s). Sulphonylureas were more likely to be prescribed to 90+
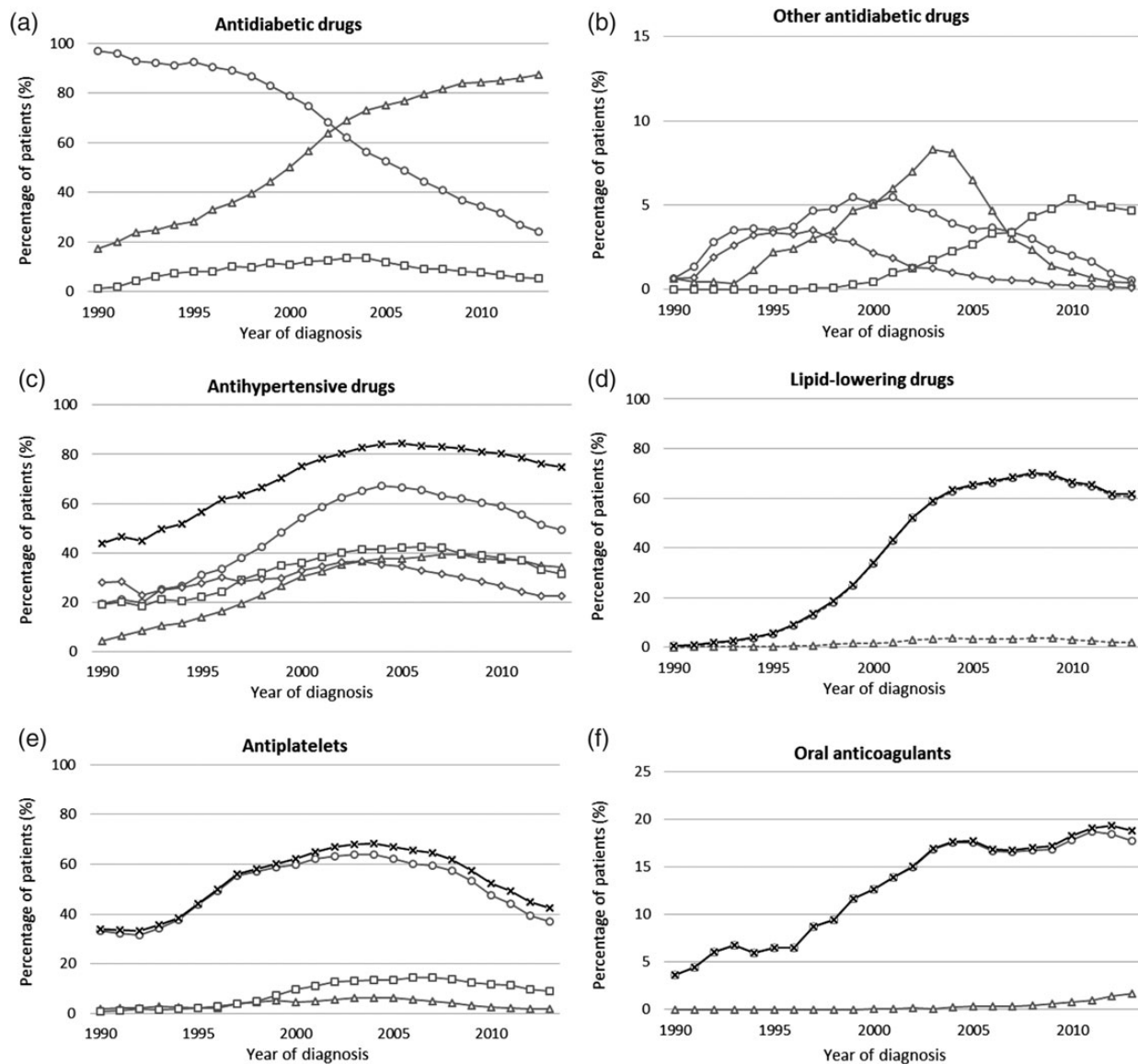
Figure 1. Utilisation of antidiabetic and cardiovascular drugs after the diagnosis date of diabetes by diagnosis year: (a) sulphonylureas (○), metformin (Δ) and others (□). (b) Insulin (○), thiazolidinediones (Δ), DPP4 inhibitors (□) and others (□). (c) Any antihypertensive drugs (×), renin–angiotensin system blockers (○), β-blockers (Δ), calcium channel blockers (□) and thiazide diuretics (□). (d) Any lipid-lowering drugs (×), statins (○) and non-statins (Δ). (e) Any antiplatelets (×), low-dose aspirin (○), dipyridamole (Δ) and thienopyridines (□). (f) Any oral anticoagulants (×), coumarins (○) and new oral anticoagulants (Δ).

group (OR 1.32, 95% CI 1.18 to 1.49), whereas insulin (0.37, 0.24 to 0.58) and metformin (0.67, 0.60 to 0.75) were less likely to be prescribed (Table 2).

Antihypertensive drugs

Prescriptions of antihypertensive drugs increased from 46% in the early 1990s to 77% after 2010 (Figure 1c). More than a half of the patients were prescribed drugs acting on the renin–angiotensin system (RAS) (54% in 2010s). Calcium channel blockers (OR 1.16, 95% CI 1.08 to 1.26) and thiazide diuretics (1.50, 1.37 to 1.63) were more likely to be prescribed to women (Table 2). All classes of antihypertensive

drugs were less likely to be prescribed to 90+ group (0.42, 0.38 to 0.48). Multiple classes of antihypertensive drugs were prescribed to 64% of the patients receiving antihypertensive drugs in 2010s. Of these, 85% included RAS blockers.

Lipid-lowering drugs

Prescriptions of lipid-lowering drugs increased from 1% in the early 1990s to 64% after 2010 (Figure 1d). Almost all the lipid-lowering drugs were statins; non-statins, such as fibrates and ezetimibe, were not prescribed frequently (<4%). Lipid-lowering drugs were less likely to be prescribed to 90+ group (OR 0.26, 95% CI 0.23 to 0.30; Table 2).

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Table 2. Effects of gender and age group on prescriptions

Drug class	Female		90+ groups	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Antidiabetic drugs				
Insulin	0.95 (0.75 to 1.19)	0.645	0.37 (0.24 to 0.58)	<0.001
Sulphonylureas	1.05 (0.98 to 1.13)	0.158	1.32 (1.18 to 1.49)	<0.001
Metformin	1.00 (0.94 to 1.07)	0.953	0.67 (0.60 to 0.75)	<0.001
Thiazolidinediones	1.07 (0.86 to 1.32)	0.555	0.71 (0.47 to 1.05)	0.089
DPP4 inhibitors	1.10 (0.83 to 1.46)	0.511	0.54 (0.32 to 0.89)	0.016
Others	1.12 (0.73 to 1.71)	0.596	0.47 (0.20 to 1.10)	0.080
Antihypertensive drugs				
Any class	1.26 (1.17 to 1.37)	<0.001	0.42 (0.38 to 0.48)	<0.001
Renin–angiotensin system blockers	1.04 (0.97 to 1.12)	0.308	0.46 (0.41 to 0.51)	<0.001
β-blockers	1.04 (0.96 to 1.13)	0.365	0.58 (0.50 to 0.67)	<0.001
Calcium channel blockers	1.16 (1.08 to 1.26)	<0.001	0.56 (0.48 to 0.65)	<0.001
Thiazide diuretics	1.50 (1.37 to 1.63)	<0.001	0.62 (0.54 to 0.72)	<0.001
Lipid-lowering drugs				
Any class	0.97 (0.89 to 1.05)	0.397	0.26 (0.23 to 0.30)	<0.001
Statins	0.96 (0.88 to 1.04)	0.284	0.27 (0.23 to 0.31)	<0.001
Non-statins	1.16 (0.88 to 1.53)	0.304	0.35 (0.19 to 0.63)	0.001
Antiplatelets				
Any class	0.83 (0.78 to 0.89)	<0.001	0.94 (0.84 to 1.06)	0.314
Low-dose aspirin	0.87 (0.81 to 0.93)	<0.001	0.97 (0.86 to 1.09)	0.624
Dipyridamole	0.79 (0.65 to 0.97)	0.026	0.88 (0.62 to 1.26)	0.481
Thienopyridines	0.69 (0.61 to 0.78)	<0.001	0.79 (0.62 to 1.01)	0.060
Anticoagulants				
Any class	0.99 (0.88 to 1.10)	0.802	0.55 (0.44 to 0.68)	<0.001
Coumarins	0.99 (0.89 to 1.11)	0.895	0.55 (0.44 to 0.68)	<0.001
New oral anticoagulants	0.51 (0.29 to 0.91)	0.022	0.50 (0.16 to 1.60)	0.244

References were male or 80s group. Odds ratios were adjusted for gender, age group, diagnosis year (3-year interval) and clustering by general practice.

Antithrombotic drugs

Prescriptions of antiplatelets, mainly low-dose aspirin, increased from 34% in the early 1990s and peaked at 68% in 2004, but declined to 47% after 2010 (Figure 1e). Prescriptions of thienopyridines, such as clopidogrel, increased from 5% in the late 1990s to 10% in 2010s. Antiplatelets were less likely to be prescribed to women (OR 0.83, 95% CI 0.78 to 0.89; Table 2). Prescriptions of oral anticoagulants increased from 5% in the early 1990s to 19% after 2010 (Figure 1f). Almost all the oral anticoagulants were warfarin, and new oral anticoagulants (NOACs), such as dabigatran and rivaroxaban, were not prescribed frequently (<2%). Oral anticoagulants were less likely to be prescribed to 90+ group (OR 0.55, 95% CI 0.44 to 0.68; Table 2).

Discussion

What this study shows

This study of patients with T2DM diagnosed over 80 years reveals a substantial increase in the level of exposure to pharmacotherapy over more than two decades. The proportion of all patients with T2DM who were treated with antidiabetic drugs tended to decrease in more recent years. This might have been accounted for by a trend towards earlier diagnosis at a time when dietary therapy may be sufficient for initial control of blood glucose and by a shorter follow-up duration. Another reason to explain the decline may be the emerging fact that it requires several years to obtain benefits from antidiabetic drugs [19]. We did not analyse the group of patients who did not receive antidiabetic drugs, but we recognise that this group may provide an important comparator in future studies of treatment outcomes.

Overall trends in utilisation of antidiabetic drugs in this study were generally similar to those observed in wider age groups in the UK, despite some differences in degrees and timing [12, 13, 20]. There have been shifts in the type of therapy prescribed with declining use of sulphonylureas, increasing use of metformin, and to a lesser extent insulin and newer antidiabetic drugs. Prescriptions of antihypertensive, lipid-lowering and antithrombotic medications generally increased over time, including the majority of the patients in recent years. Further research would be needed to explore which cardiovascular risk factors are managed as priority in very old patients, taking into account both how long is required to obtain the benefits from medications, and the risks of polypharmacy and adverse events. While it may be reasonable to extrapolate from available evidence to inform decisions for an older age group, the present data draw attention to the possibly limited generalisability, and perhaps excessively restrictive eligibility criteria, of some major trials.

The data presented raise questions concerning the reasons for these changes in treatment patterns. The UKPDS showed the efficacy of intensive control of blood glucose and promoted prescriptions of metformin in 1998 [21]. Conversely, the decline in use of sulphonylureas may be in recognition of their

propensity to cause hypoglycaemia, as well as concerns over possible cardiovascular risks [22]. Blood pressure management had been also emphasised to reduce the risk of diabetes complications from the same time [23]. In our study, about a half of patients were prescribed antihypertensive drug combinations including RAS blockers. The combination therapy is often needed to lower blood pressure by an appropriate goal, and RAS blockers are expected to play a role in preventing diabetic nephropathy [24]. Several studies demonstrated that control of cholesterol reduced mortality and new CVD events in people at high risk including those with diabetes [25, 26], leading to an increase in prescriptions of statins. It was already recognised, from the early 1990s, that antiplatelet therapy reduced both mortality and myocardial infarction and stroke events [27]. However, favourable results of antiplatelet therapy for primary prevention of CVD have not been shown [28], which might explain the recent decline in prescriptions of antiplatelets.

It may be debated whether or not this increase in use of antidiabetic and cardiovascular drugs has always been appropriate in terms of potentially increased harms. The recent decline of thiazolidinediones might result from increased risk of myocardial infarction and deaths from cardiovascular causes [13]. Low-dose aspirin is recommended in patients aged 50 years old or over if blood pressure is below 145/90 mmHg [5]. Given that our cohort included many patients with hypertension, proportions of patients treated with low-dose aspirin might have been too high, and thus, the risk of bleeding might exceed the possible benefits. It is clear that the balance of risks and benefits of pharmacological interventions for very old people with diabetes requires further careful evaluation. Further, in-depth analysis is also required to understand the evolution of prescribing in relation to, possibly multiple, co-morbidities.

Comparison with other studies

There have been limited data reported on trends in drug utilisation for very old patients with T2DM. In Canada, the trends of prescriptions of statins and antihypertensive drugs in patients aged 80 years or over seemed to be generally comparable with those of our study [29]. At the start of the study in 1996, statins were less frequently prescribed to patients aged over 80 years compared with younger patients, but a more rapid increase was observed over time. However, in contrast to our study where the prescriptions of RAS blockers showed a decrease in recent years, those have increased monotonically in the Canadian study.

The prescribing of sulphonylureas declined while that of metformin, RAS inhibitors, lipid-lowering drugs and antiplatelets increased between 2000 and 2010 in Italy [30]. The percentages of patients prescribed RAS inhibitors or antiplatelets seemed to be similar to our results, but prescriptions of lipid-lowering drugs were lower in Italy. They discussed less propensity to prescribe lipid-lowering drugs to patients aged ≥85 years possibly because there have been no large trials of lipid-lowering interventions specifically in older adults with diabetes.

Strength and limitations

The CPRD is generally representative of the UK population and provides an excellent data source for drug utilisation studies in primary care in the UK. There are several limitations in this study. Drug utilisation was summarised for all the prescriptions after the diagnosis of T2DM by diagnosis year, but the timing (when the drugs initiated), dosage and duration were not considered. Early diagnosis of T2DM and prolongation of survival could be influenced to drug utilisation, particularly in very old people.

Conclusions

There have been major changes in treatment of very old patients diagnosed with T2DM, with treatment decision also being gender and age dependent. A high proportion of people with T2DM are exposed to multiple drugs with the aim of reducing risk of adverse diabetes and cardiovascular outcomes. These analyses highlight an important gap in the evidence base concerning the long-term utility and safety of intensive risk reduction strategies for very old people with T2DM. The analyses indicate that there are significant opportunities for analytical studies to evaluate the effectiveness and safety outcomes of different approaches to treatment in this vulnerable group of patients.

Key points

- Treatment decisions for very old people are largely based on professional opinion drawing on evidence from younger patients.
- Utilisation of antidiabetic and cardiovascular drugs for patients with T2DM diagnosed over 80 years was evaluated.
- There have been major increases in the intensity of pharmacological management of very old diabetic patients.
- Further research is needed to examine clinical outcomes of these medications in patients with possibly limited life expectancy.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Acknowledgements

Conflicts of interest

None declared.

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References

1. Health and Social Care Information Centre. Prescribing for Diabetes. England 2005–06 to 2013–14. 2014. http://www.hscic.gov.uk/catalogue/PUB14681/pres-diab-eng-200506-201314-rep.pdf (20 May 2014, date last accessed).

2. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-Year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008; 359: 1577–89.

3. Preis SR, Hwang SJ, Coady S et al. Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. Circulation 2009; 119: 1728–35.

4. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med 2008; 358: 580–91.

5. National Institute for Health and Care Excellence. Type 2 Diabetes. 2014. http://www.nice.org.uk/guidance/cg66/resources/cg66-type-2-diabetes-full-guideline2 (20 May 2014, date last accessed).

6. Cracknell R. The Ageing Population. Key issues for the New Parliament 2010. http://www.parliament.uk/documents/commons/lib/research/key_issues/Full-doc.pdf (20 May 2014, date last accessed).

7. Health and Social Care Information Centre. National Diabetes Audit – 2011–12. 2013. http://www.hscic.gov.uk/catalogue/PUB12421 (20 May 2014, date last accessed).

8. Cruz-Jentoft AJ, Carpena-Ruiz M, Montero-Errasquín B, Sánchez-Castellano C, Sánchez-García E. Exclusion of older adults from ongoing clinical trials about type 2 diabetes mellitus. J Am Geriatr Soc 2013; 61: 734–8.

9. Moreno G, Mangione CM. Management of cardiovascular disease risk factors in older adults with type 2 diabetes mellitus: 2002–2012 literature review. J Am Geriatr Soc 2013; 61: 2027–37.

10. UK Prospective Diabetes Study (UKPDS). VIII. Study design, progress and performance. Diabetologia 1991; 34: 877–90.

11. ACCORD Study GroupBuse JB, Bigger JT et al. Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial: design and methods. Am J Cardiol 2007; 99: 21i–33i.

12. Filion KB, Joseph L, Boivin JF, Suissa S, Brophy JM. Trends in the prescription of antidiabetic medications in the United Kingdom: a population-based analysis. Pharmacoepidemiol Drug Saf 2009; 18: 973–6.

13. Leal I, Romio SA, Schuemie M, Oteri A, Sturkenboom M, Trifirò G. Prescribing pattern of glucose lowering drugs in the United Kingdom in the last decade: a focus on the effects of safety warnings about rosiglitazone. Br J Clin Pharmacol 2013; 75: 861–8.

14. Gulliford MC, Charlton J, Latinovic R. Trends in antihypertensive and lipid-lowering therapy in subjects with type II diabetes: clinical effectiveness or clinical discretion?. J Hum Hypertens 2005; 19: 111–7.

15. Petri A, de Lusignan S, Williams J, Chan T, Majeed A. Management of cardiovascular risk factors in people with diabetes in primary care: cross-sectional study. Public Health 2006; 120: 654–63.

16. Kirkman MS, Briscoe VJ, Clark N et al. Diabetes in older adults. Diabetes Care 2012; 35: 2650–64.

17. Independent Scientific Advisory Committee for MHRA database research (ISAC). Annual Report Jan 2013–Dec 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/388569/con448379.pdf (20 May 2014, date last accessed).

18. Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. Br J Clin Pharmacol 2010; 69: 4–14.

19. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837–53.

20. Holden SE, Gale EA, Jenkins-Jones S, Currie CJ. How many people inject insulin? UK estimates from 1991 to 2010. Diabetes Obes Metab 2014; 16: 553–9.

21. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998; 352: 854–65.

22. Li Y, Hu Y, Ley SH, Rajpathak S, Hu FB. Sulfonylurea use and incident cardiovascular disease among patients with type 2 diabetes: prospective cohort study among women. Diabetes Care 2014; 37: 3106–13.

23. UK Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ 1998; 317: 713–20.

24. Perk J, De Backer G, Gohlke H et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012; 33: 1635–701.

25. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383–9.

26. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002; 360: 7–22.

27. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ 1994; 308: 81–106.

28. Ikeda Y, Shimada K, Teramoto T et al. Low-dose aspirin for primary prevention of cardiovascular events in Japanese

patients 60 years or older with atherosclerotic risk factors: a randomized clinical trial. JAMA 2014; 312: 2510–20.

29. Shah BR, Booth GL, Lipscombe LL, Feig DS, Bhattacharyya OKBierman AS. Near equality in quality for medication utilization among older adults with diabetes with universal medication insurance in Ontario, Canada. J Eval Clin Pract 2014; 20: 176–83.

30. Baviera M, Cortesi L, Tettamanti M *et al.* Changes in prescribing patterns and clinical outcomes in elderly diabetic patients in 2000 and 2010: analysis of a large Italian population-based study. Eur J Clin Pharmacol 2014; 70: 965–74.

Randomised controlled trial of the effectiveness of community group and home-based falls prevention exercise programmes on bone health in older people: the ProAct65+ bone study

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Abstract

Background: exercise can reduce osteoporotic fracture risk by strengthening bone or reducing fall risk. Falls prevention exercise programmes can reduce fall incidence, and also include strengthening exercises suggested to load bone, but there is little information as to whether these programmes influence bone mineral density (BMD) and strength.
Objective: to evaluate the skeletal effects of home (Otago Exercise Programme, OEP) and group (Falls Exercise Management, FaME) falls prevention exercise programmes relative to usual care in older people.
Methods: men and women aged over 65 years were recruited through primary care. They were randomised by practice to OEP, FaME or usual care. BMD, bone mineral content (BMC) and structural properties were measured in Nottingham site participants before and after the 24-week intervention.
Results: participants were 319 men and women, aged mean(SD) 72(5) years. Ninety-two percentage of participants completed the trial. The OEP group completed 58(43) min/week of home exercise, while the FaME group completed 39(16) and 30(24) min/week of group and home exercise, respectively. Femoral neck BMD changes did not differ between treatment arms: mean (95% CI) effect sizes in OEP and FaME relative to usual care arm were $-0.003(-0.011,0.005)$ and $-0.002(-0.010,0.005)$ g cm^{-2}, respectively; $P = 0.44$ and 0.53. There were no significant changes in BMD or BMC at other skeletal sites, or in structural parameters.